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Research Article

Evaluation of YouTube Videos for Learning Interfascial Plane Blocks

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Abstract

Aim: The internet and social media are becoming integral to our lives today. YouTube was founded in 2005 and can be helpful in health matters by providing quick and easy access to medical information. However, the reliability of medical videos on YouTube could be improved. Many videos on YouTube about interfascial plane blocks are widely used for analgesic purposes in anesthesia practice. In order to avoid causing incorrect and incomplete information and to prevent information pollution, interfascial plan block videos on YouTube should be examined. Therefore, this study evaluated the educational content and preparation quality of the interfascial plan block videos on YouTube.

Material and Method: Educational videos of eight different interfascial plane block types on YouTube were evaluated using two surveys. Each survey consists of 14 questions. Each question receives a score between 0 and 5. Each video receives a total score between 0 and 70 for each survey.

Results: A statistically significant positive correlation exists between video educational quality scores and video characteristics. A statistically significant positive correlation exists between the video preparation quality score and video characteristics. As the number of video views increases, the video quality score increases.

Conclusion: Although YouTube contains medical training videos, their reliability is questioned. Therefore, it is more accurate and reliable for researchers to obtain medical information from reliable sources, academic articles, or publications of official medical institutions.

Keywords: Analgesia, regional anesthesia, interfascial plane block, YouTube videos

INTRODUCTION

The Internet and social media are becoming integral to our lives today. People communicate, exchange information, have fun, and learn through these platforms. Platforms like YouTube offer a wide range of content, allowing users to gain knowledge in various fields. YouTube was founded in 2005, and over time, it has become one of the largest video platforms in the world with millions of video content. Users: They can obtain information from different perspectives on educational videos, entertainment content, news, works of art, and many more (1). Platforms such as YouTube provide a great environment that allows people to learn new skills in many subjects, discover content related to their interests, and get to know different cultures. With it, users find a space to share their experiences, ideas, and talents. Thus, YouTube users can influence each other by learning and sharing experiences, exchanging information, and making their voices heard on a global platform. YouTube can be helpful in health matters by providing quick and easy access to medical information. However, widespread use of these platforms may also lead to access to accurate and reliable information. This may make it difficult to access accurate information, especially on health issues, and lead to misdirection. It is essential to access accurate and reliable information on health-related issues. Medical content videos on YouTube are essential for healthcare professionals and medical students.

Moreover, these contents can make a significant contribution to learning. However, while watching these videos, there are points that viewers should pay attention to, such as 'checking the sources, taking into account reliable sources, paying attention to scientifically based content, seeking expert opinion' (2-8). Some health-related videos may have been created by people who need to gain experience in their expertise. In this case, there may be doubts about the content's accuracy, reliability and scientific basis. Additionally, some content may contain misleading or inaccurate information and mislead viewers (9,10). Although there are a limited number of studies evaluating regional anesthesia videos on YouTube, there

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are studies evaluating the reliability of the videos (11-13). Interfascial plane blocks, one of the regional anesthesia techniques, are now widely applied by anesthesiologists and assistants to reduce postoperative pain. There are various videos related to interfascial plan blocks on platforms where health videos are available, such as YouTube. Some of the studies evaluated the preparation quality of these videos (11,14). Studies have generally examined interfascial plane blocks specifically. Our study aimed to evaluate the educational content quality and video preparation quality of videos of eight different interfascial plan block types on YouTube.

MATERIAL AND METHOD

Since human and animal subjects were not used in this study, ethics committee approval is not required. Searching for videos on YouTube and recording URLs was completed in a single session on 29/10/2023. Searching videos can be found in the YouTube search engine using the terms 'Paravertebral block ultrasound, serratus plane block ultrasound, quadratus lumborum block ultrasound, transversus abdominis plane block, erector spinae plane block, pectoralis blocks 1 and 2, thoracolumbar interfascial plane block ultrasound, rectus sheath block ultrasound'. It was done by writing. Sorting was done according to the number of views in the filtering. For each block, the top 5 most watched videos were recorded according to the number of views. Because after the first five videos, the number of views decreased significantly. Five anesthesiologists with at least five years of clinical experience with interfascial plane blocks watched and evaluated the videos. Two different surveys were used to evaluate the videos on YouTube, evaluating the educational content of the videos (Survey 1) and the quality of the videos (Survey 2).

Inclusion criteria: Videos in English, videos with ultrasound guidance, and videos about interfascial plane blocks.

Exclusion criteria: Videos whose language is not English, videos that do not contain ultrasound images, irrelevant videos, videos less than 1 minute and longer than 20 minutes, videos without sound, and duplicate videos.

Survey 1 consists of 14 questions about the educational content quality of the videos. This survey form was created concerning previous studies (Table 1) (11,12,15).

Survey 2 consists of 14 questions and evaluates the quality of the videos' preparation (Table 2). It was created according to the guidelines prepared by the American National Career Development Association (NCDA) (16).

Table 1. Video educational content quality evaluation

Survey 1	
1.	Are the clinical indications for the block clearly explained?
2.	Are anatomical landmarks clearly explained or marked?
3.	Has the block anatomy been clearly explained?
4.	Has the suspected mechanism of action been clearly explained?
5.	Has technical information regarding probe selection and frequency of the ultrasound device been explained?
6.	Has ultrasound anatomy been clearly demonstrated and explained?
7.	Were the recorded sono-anatomical images and anatomical structures in the recording clear and easy to perceive?
8.	Was the ultrasound image of the needle visible and easy to follow?
9.	Are instructions for depth, alignment, and direction of needle movements clearly explained?
10.	Has information regarding the spread of local anesthetic been explained?
11.	Is information about in-plane or out-of-plane technique given in the video?
12.	Has sterile technique been clearly explained or emphasized?
13.	Has the information regarding the local anesthetic agent been explained clearly?
14.	Have the possible complications associated with this block technique been explained?

Table 2. Video preparation quality assessment

Survey 2	
1.	Is the purpose of the video clearly stated and explained in the first quarter of the video?
2.	Was the title or name of the video appropriate to the purpose of the video?
3.	Were the design and content of the video suitable for the intended educational purpose?
4.	Have the skills and technique of the procedure been explained using a standard, comparable, "step-by-step" method?
5.	Was the information provided in the video useful for viewers to develop/improve their skill base?
6.	Was the content of the video appropriate for the health and safety of both the patient and the practitioner?
7.	Was the quality of the picture acceptable in terms of colors and clarity?
8.	Was the quality of the video audio acceptable? (No sounds should be scored as zero)
9.	Was the length of the video balanced with the content of the video?
10.	Is information regarding production or release date, producers and references clearly explained?
11.	Are the objectives, learning tasks, and terminology clearly stated in the video to enable viewers to perform these tasks?
12.	Does the video contain additional aids such as stop-and-discuss points, scenarios, and/or summary of the procedure?
13.	Has information been provided about a way to evaluate the effectiveness and repeatability of the video?
14.	Did the content of the video encourage viewers to move from passive spectators to active practitioners in the implementation of the practice?

Anaesthesiologists who evaluated the videos scored each question between 0 and 5. (0- very bad, 1- bad, 2- fair, 3- good, 4- very good, 5- excellent). Each video was scored from 0 to 70 according to the questions shown in Survey 1 and Survey 2 (0-14: very bad, 15-28: bad, 29-42: fair, 43-56: good, 57-70: very good).

The following data was recorded for the videos: The relevant URLs of the videos, the duration of the videos, the number of days the videos were available, the number of viewers of the videos, the source of the videos (whether academic or not), the total number of likes of the videos, the survey one and survey two scores given to the videos by experts were recorded.

RESULTS

The words "Paravertebral block ultrasound, serratus plane block ultrasound, quadratus lumborum block ultrasound, transversus abdominis plane block, erector spinae plane block, pectoralis blocks 1 and 2 ultrasound, thoracolumbar interfascial plane block ultrasound, rectus sheath block ultrasound" were posted on YouTube. The first five most watched videos for each block (39 videos) were evaluated. Four videos were evaluated for the 'Thoracolumbar interfascial plane block'. A limited number of videos for 'Thoracolumbar interfascial plane block' and only four videos were evaluated according to the number of views (Table 3).

Table 3. Video characteristics and quality score values

Video characteristic feature		n (%) median (25-75th percentile)
Video views		68085 (30100-132694)
Number of video likes		444 (174-966)
Video duration (seconds)		629 (440-853)
Duration of presence on YouTube (months)		67 (38-107)
Video educational quality score		31 (21-39)
Video educational quality score classification	Very bad	4 (10.3%)
	Bad	11 (28.2%)
	It will do	16 (41%)
	Good	8 (20.5%)
Video preparation quality score		34 (30-42)
Video preparation quality score classification	Very bad	1 (2.6%)
	Bad	2 (17.9%)
	It will do	22 (56.4%)
	Good	9 (23.1%)
Group	PVTB	5 (12.8%)
	ESPB	5 (12.8%)
	TAPB	5 (12.8%)
	PECSB	5 (12.8%)
	SPB	5 (12.8%)
	TLIPB	4 (10.3%)
	QLB	5 (12.8%)
	RSB	5 (12.8%)

PVTB: paravertebral block, ESPB: erector spinae plane block, TAPB: transversus abdominis plane block, PECS: pectoralis blocks 1 and 2, SPB: serratus plane block, TLIPB: thoracolumbar interfascial plane block, QLB: quadratus lumborum block, RSB: rectus sheath block

When video characteristics are evaluated, "Number of video views" is 68085 (30100-132694), "Number of Video Likes" is 444 (174-966) (median (25-75 percentile), "Video duration (seconds)" is 629 (440-853) (The median (25-75 percentile) and the "Duration of presence on YouTube" of the Video were 67 (38-107) (median (25-75 percentile) months. The video educational quality score was 8 (20.5%), with "good" and "very bad", and the median (25-75 percentile) Video educational quality score was 31 (21-39). The video preparation quality score was 9 (23.1%) with "good" and 1 with "bad". (2.6%) video and median (25-75 percentile) Video preparation quality score was 34 (30-42) (Table 3). The 14 parameters and evaluation scores examined for the Video educational quality score were shown separately. The two parameters most marked for the Video, with "very poor" as the evaluation score, were "Was the sterile technique clearly explained or emphasized?" There were 25 videos (64.1%) for the option and 29 videos (87.9%) for the option "Is the suspected mechanism of action clearly explained?" The two parameters most marked for the Video with "excellent" as an evaluation score were "Was the block anatomy clearly explained?" 12 videos (30.8%) for the option and "Was the ultrasound anatomy clearly shown and explained?" For the option, there were ten videos (25.6%) (Table 4).

Table 4. Video educational quality questions					
Question	**Degree**	**n (%)**	**Question**	**Degree**	**n (%)**
Are the clinical indications for the block clearly explained?	**Very bad**	4 (10.3%)	**Was the ultrasound image of the needle visible and easy to follow?**	**Very bad**	8 (20.5%)
	Bad	11 (28.2%)		**Bad**	3 (7.7%)
	It will do	2 (5.1%)		**It will do**	4 (10.3%)
	Good	9 (23.1%)		**Good**	4 (10.3%)
	Very good	8 (20.5%)		**Very good**	14 (35.9%)
	Perfect	5 (12.8%)		**Perfect**	6 (15.4%)
Are anatomical landmarks clearly explained or marked?	**Very bad**	1 (2.6%)	**Are instructions for depth, alignment, and direction of needle movements clearly explained?**	**Very bad**	8 (20.5%)
	Bad	5 (12.8%)		**Bad**	13 (33.3%)
	It will do	9 (23.1%)		**It will do**	8 (20.5%)
	Good	11 (28.2%)		**Good**	8 (20.5%)
	Very good	7 (17.9%)		**Very good**	2 (5.1%)
	Perfect	6 (15.4%)		**Perfect**	0 (0%)
Was the block anatomy clearly explained?	**Very bad**	1 (2.6%)	**Has information regarding local anesthetic dissemination been explained?**	**Very bad**	9 (23.1%)
	Bad	1 (2.6%)		**Bad**	7 (17.9%)
	It will do	6 (15.4%)		**It will do**	15 (38.5%)
	Good	5 (12.8%)		**Good**	1 (2.6%)
	Very good	14 (35.9%)		**Very good**	7 (17.9%)
	Perfect	12 (30.8%)		**Perfect**	0 (0%)
Has the suspected mechanism of action been clearly explained?	**Very bad**	25 (64.1%)	**Was information given about the in-plane or out-of-plane technique in the video?**	**Very bad**	6 (15.4%)
	Bad	6 (15.4%)		**Bad**	7 (17.9%)
	It will do	2 (5.1%)		**It will do**	9 (23.1%)
	Good	3 (7.7%)		**Good**	9 (23.1%)
	Very good	2 (5.1%)		**Very good**	7 (17.9%)
	Perfect	1 (2.6%)		**Perfect**	1 (2.6%)
Has technical information regarding probe selection and frequency of the ultrasound device been explained?	**Very bad**	3 (7.7%)	**Has sterile technique been clearly explained or emphasized?**	**Very bad**	38 (97.4%)
	Bad	4 (10.3%)		**Bad**	0 (0%)
	It will do	9 (23.1%)		**It will do**	1 (2.6%)
	Good	14 (35.9%)		**Good**	0 (0%)
	Very good	9 (23.1%)		**Very good**	0 (0%)
	Perfect	0 (0%)		**Perfect**	0 (0%)
Has ultrasound anatomy been clearly demonstrated and explained?	**Very bad**	0 (0%)	**Was the information regarding the local anesthetic agent explained clearly?**	**Very bad**	19 (48.7%)
	Bad	2 (5.1%)		**Bad**	3 (7.7%)
	It will do	6 (15.4%)		**It will do**	5 (12.8%)
	Good	4 (10.3%)		**Good**	5 (12.8%)
	Very good	17 (43.6%)		**Very good**	7 (17.9%)
	Perfect	10 (25.6%)		**Perfect**	0 (0%)
Were the recorded sono-anatomical images and anatomical structures in the recording clear and easy to perceive?	**Very bad**	1 (2.6%)	**Have possible complications related to this block technique been explained?**	**Very bad**	16 (41%)
	Bad	2 (5.1%)		**Bad**	7 (17.9%)
	It will do	13 (33.3%)		**It will do**	4 (10.3%)
	Good	3 (7.7%)		**Good**	4 (10.3%)
	Very good	13 (33.3%)		**Very good**	6 (15.4%)
	Perfect	7 (17.9%)		**Perfect**	2 (5.1%)

The 14 parameters and evaluation scores examined for the video preparation quality score were shown separately. The two parameters most marked for the video were "very bad" as an evaluation score, 38 videos (97.4%) for the option "Was information given about a way to evaluate the effectiveness and repeatability of the video?" and "Stop and discuss points in the video, such as scenarios." There were 26 videos (66.7%) for the option "Are there additional aids and summary information about the procedure?" As an evaluation score, "excellent" is the parameter marked for the most videos and "Was the title or name of the video appropriate for the video?" For the option, there were 12 videos (30.8%) (Table 5).

Table 5. Video preparation quality questions

Question	Degree	n (%)	Question	Degree	n (%)
Is the purpose of the video clearly stated and explained in the first quarter of the video?	Very bad	1 (2.6%)	Was the quality of the video audio acceptable? (No sounds should be scored as zero	Very bad	1 (2.6%)
	Bad	6 (15.4%)		Bad	4 (10.3%)
	It will do	11 (28.2%)		It will do	3 (7.7%)
	Good	15 (38.5%)		Good	11 (28.2%)
	Very good	6 (15.4%)		Very good	18 (46.2%)
	Perfect	0 (0%)		Perfect	2 (5.1%)
Was the title or name of the video appropriate to the purpose of the video?	Very bad	0 (0%)	Was the length of the video balanced with the content of the video?	Very bad	1 (2.6%)
	Bad	0 (0%)		Bad	3 (7.7%)
	It will do	4 (10.3%)		It will do	4 (10.3%)
	Good	6 (15.4%)		Good	20 (51.3%)
	Very good	17 (43.6%)		Very good	11 (28.2%)
	Perfect	12 (30.8%)		Perfect	0 (0%)
Were the design and content of the video suitable for the intended educational purpose?	Very bad	0 (0%)	Is information about the production or release date, producers and references clearly explained?	Very bad	0 (0%)
	Bad	2 (5.1%)		Bad	25 (64.1%)
	It will do	4 (10.3%)		It will do	8 (20.5%)
	Good	10 (25.6%)		Good	4 (10.3%)
	Very good	19 (48.7%)		Very good	2 (5.1%)
	Perfect	4 (10.3%)		Perfect	0 (0%)
Have the skills and technique of the procedure been explained using a standard, comparable, "step-by-step" method?	Very bad	4 (10.3%)	Are the objectives, learning tasks, and terminology clearly stated in the video to enable viewers to accomplish these tasks?	Very bad	7 (17.9%)
	Bad	7 (17.9%)		Bad	16 (41%)
	It will do	15 (38.5%)		It will do	10 (25.6%)
	Good	10 (25.6%)		Good	3 (7.7%)
	Very good	3 (7.7%)		Very good	2 (5.1%)
	Perfect	0 (0%)		Perfect	1 (2.6%)
Was the information provided in the video useful for viewers to develop/ improve their skill base?	Very bad	1 (2.6%)	Does the video include additional aids such as stop-and-discuss points, scenarios, and/or summary of the procedure?	Very bad	26 (66.7%)
	Bad	3 (7.7%)		Bad	5 (12.8%)
	It will do	6 (15.4%)		It will do	5 (12.8%)
	Good	10 (25.6%)		Good	2 (5.1%)
	Very good	16 (41%)		Very good	1 (2.6%)
	Perfect	3 (7.7%)		Perfect	0 (0%)
Was the content of the video appropriate for the health and safety of both the patient and the practitioner?	Very bad	1 (2.6%)	Was information provided about a way to evaluate the effectiveness and repeatability of the video?	Very bad	38 (97.4%)
	Bad	2 (5.1%)		Bad	1 (2.6%)
	It will do	8 (20.5%)		It will do	0 (0%)
	Good	17 (43.6%)		Good	0 (0%)
	Very good	9 (23.1%)		Very good	0 (0%)
	Perfect	2 (5.1%)		Perfect	0 (0%)
Was the quality of the picture acceptable in terms of colors and clarity?	Very bad	0 (0%)	Did the content of the video encourage viewers to shift from passive spectator to active practitioner in the implementation of the practice? technical?	Very bad	2 (5.1%)
	Bad	4 (10.3%)		Bad	4 (10.3%)
	It will do	4 (10.3%)		It will do	2 (5.1%)
	Good	7 (17.9%)		Good	12 (30.8%)
	Very good	20 (51.3%)		Very good	13 (33.3%)
	Perfect	4 (10.3%)		Perfect	6 (15.4%)

When looking at the relationship between the video educational quality score and the video characteristics and video preparation quality score, there is a statistically significant positive correlation between the video educational quality score and all parameters. When looking at the relationship between video preparation quality score and video characteristics, there is a statistically significant positive correlation between the score and all parameters (Table 6). IBM-Statistical Pack Age for Social Sciences (IBM-SPSS Inc., Chicago, IL, USA) 22.0 program was used to analyze the data obtained in the study. The suitability of the data for normal distribution was examined

with the "Shapiro-Wilk test". Continuous variables were expressed as median (25-75 percentile) according to their distribution status, and categorical variables were expressed as numbers and percentages. A Spearman rho correlation test was applied to the correlation analyses for continuous variables. The statistical significance level was accepted as p<0.05.

Table 6. Relationship between video evaluation scores and video characteristics

Characteristic property	Video educational quality score		Video preparation quality score	
	R value	P value	R value	P value
Video views	0.561	**<0.001**	0.518	**<0.001**
Number of video likes	0.698	**<0.001**	0.664	**<0.001**
Video duration (seconds)	0.358	**0.025**	0.468	**0.003**
Video educational quality score			0.893	**<0.001**
Video preparation quality score	0.893	**<0.001**		

DISCUSSION

In our study, we evaluated the educational content quality and preparation quality of the videos on YouTube about interfascial plane blocks, which are widely applied in anesthesia clinics. In regional anesthesia applications, visual information is as important as theoretical knowledge. Therefore, evaluating the videos on platforms that publish educational videos, such as YouTube, is essential. Some studies have evaluated educational videos with different YouTube content (15,17,18). Two studies in the literature specifically evaluate interfascial plane blocks (11,14). Our study is the first to collectively evaluate videos of eight different interfascial plane block types on YouTube. Studies show that medical education videos on YouTube must include complete and correct information (19-21). Other studies have emphasized that the quality of videos on YouTube is low regarding medical content (12,15,22). In our study, while there were no videos with very good scores according to surveys 1 and 2, 8 videos received good scores in Survey 1, 9 videos received good scores in Survey 2, 15 videos received bad or very bad scores in Survey 1, and 15 videos received bad or very bad scores in survey 2. 3 videos received bad or very bad ratings. This shows us that, as in other studies, in our study, the videos on YouTube could be at a sufficient level. Therefore, such platforms should strive to ensure users have access to more reliable, informative and impressive content by improving their quality monitoring processes. Providing feedback to content providers and encouraging them to create better content can be an effective way for platforms to improve the quality of content. It is important to guide content creators in conveying accurate information, especially on health, education or other specialized topics. We generally did not find any incorrect information in the videos we evaluated in our study, but much information needed to be included. However, we evaluated the most viewed videos and the quality of the videos needed to be improved. Therefore, it may cause misunderstanding and misdirection by physicians who need more knowledge about regional anesthesia and who have just started to apply regional anesthesia techniques. We found a significant positive correlation between the videos' number of likes and duration and the quality of education and preparation. This shows us that video content information is more reliable and complete as the video duration increases. It shows that the number of likes of videos is important in accessing accurate and secure information. We found a significant positive correlation between surveys 1 and 2. Thus, it shows that as the preparation quality of the videos, such as sound and image, increases, the content quality of the videos also increases.

Contrary to some studies, we found a significant positive correlation between the number of views and the quality of the videos in our study (12,23). This shows that as the number of views of the videos increases, the medical content of that video is safer and more helpful in terms of education. It shows that more people watch quality videos, which helps us get accurate information.

CONCLUSION

As a result, the interfascial plan block videos on YouTube could be more adequate in terms of video quality. Therefore, although YouTube and similar platforms provide great convenience in accessing information, there are also aspects that users should be careful about. Using these platforms correctly is essential to discovering helpful content and interacting with other users. It is more accurate and reliable for students or those working in the medical field to obtain medical information from reliable sources, academic articles, or publications of official medical institutions.

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Research Article

Age-Related Variations in Treatment Patterns for Axial Spondyloarthritis

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Abstract

Aim: This study examines treatment patterns and preferences among patients diagnosed with Axial Spondyloarthritis (AxSpA) across different age groups.
Material and Method: Ankara Bilkent City Hospital registry enabled a comprehensive cross-sectional analysis of 2,811 patients stratified into three age groups: 18-40, 41-55, and over 55 years. These groups were compared in terms of their treatments.
Results: Our findings indicate an increasing prevalence of female patients and comorbidities with age. Medication usage patterns showed a trend towards increased use of Methotrexate and Colchicine with age, while Sulfasalazine and Leflunomide were more commonly prescribed in older age groups. Notably, the use of biologic Disease-Modifying Anti-Rheumatic Drugs (bDMARDs), including anti-Tumor Necrosis Factor (anti-TNF)", "anti-Interleukin (anti-IL) agents, demonstrated a declining trend with advancing age, though not reaching statistical significance. This trend was also reflected in gender-specific treatment distributions, where no significant difference was found in bDMARDs administration among patients over 55 years, contrasting with a higher usage rate in younger male patients.
Conclusion: Our study highlights a shift towards more conservative treatment approaches, such as increased conventional synthetic Disease-Modifying Anti-Rheumatic Drugs (csDMARDs) use in older patients, likely due to their safety profile and the specific challenges associated with treating older adults, including higher comorbidity rates and medication side effects. These findings emphasize the need for personalized treatment strategies and suggest potential adjustments in clinical practices to better accommodate the aging population, advocating for ongoing research to optimize treatment efficacy and safety for elderly patients with AxSpA.

Keywords: Axial spondyloarthritis, elderly, antiTNF, antirheumatic agents

INTRODUCTION

Axial spondyloarthropathy (AxSpA) is an inflammatory rheumatic disease that primarily affects the spine and peripheral joints. Characterized by chronic low back pain that typically begins before the age of 45, AxSpA may also manifest extra-articular symptoms such as uveitis, inflammatory bowel disease, and psoriasis (1). In 2009, AxSpA was categorized into ankylosing spondylitis (AS) and non-radiographic AxSpA (nr AxSpA). AS is identified through radiographic evidence of sacroiliitis, whereas nr AxSpA is diagnosed when such changes are not sufficiently apparent. Over time, the term AS has evolved into radiographic AxSpA in clinical parlance (2).

The disease's incidence ranges dramatically—from 0.4 per 100,000 in Iceland to 15 per 100,000 in Canada, as revealed by systematic reviews. In patients with nr-AxSpa, the data are incomplete because they are insufficient. In terms of prevalence, figures vary from 9 to 30 per 10,000, influenced by the demographic and ethnic makeup of the study population (3). A study in Türkiye reported an AS prevalence of 540 per 100,000 (4).

Gender disparities in AxSpA have traditionally posited a higher prevalence in males, especially within the AS cohort. However, no significant gender disparity is observed in nr-AxSpA patients. While axial symptoms predominate in males, peripheral joint and extra-articular manifestations appear equally across genders. The age of diagnosis is comparable between genders, albeit diagnostic delays are more prevalent among women (5,6).

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The management of AS focuses on alleviating symptoms, preserving functionality, preventing complications such as contractures from spinal involvement, addressing extra-articular manifestations, and supporting the patient's psychosocial well-being. A holistic approach that combines pharmacological and non-pharmacological treatments is essential. This regimen may include lifestyle changes, patient education, and regular physical or physiotherapy exercises. Treatment typically begins with non-steroidal anti-inflammatory drugs (NSAIDs), which are effective in 50-70% of cases (7,8). For patients who do not respond to NSAIDs, options like conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) or biological agents are considered, tailored to the patient's pattern of involvement, extraarticular findings and comorbidities. Although csDMARDs are crucial in managing rheumatoid arthritis, their efficacy in AxSpA, particularly for spinal symptoms, is not well-supported by evidence. However, they may be beneficial for peripheral symptoms, with studies indicating that sulfasalazine (SSZ) is more effective than methotrexate in treating peripheral arthritis (9,10). Meanwhile, biological agents are increasingly utilized based on current guidelines, with studies suggesting they maintain efficacy without significant serious side effects that would necessitate discontinuation of treatment (11).

The treatment efficacy and tolerability of NSAIDs in elderly AxSpA patients mirror those in younger cohorts, although there is a noted decrease in tolerability. The research on biological drugs in older patients is limited due to their frequent exclusion from randomized controlled trials. Nonetheless, preliminary studies suggest that these agents can be safely administered in elderly populations. The limited amount of research evaluating the impact of treatments on comorbidities and potential side effects in elderly patients highlights a substantial knowledge gap in the management of AxSpA among this demographic. Although the evidence remains sparse, recent studies support the safe administration of biological drugs in the treatment of elderly AxSpA patients, suggesting a cautious optimism for their use in this age group. This emerging data underscores the necessity for more comprehensive studies to better understand the efficacy and safety of these treatments in older populations, particularly in the context of their broader health challenges (11).

This study aims to analyze treatment preferences and patterns across different age groups, enhancing our understanding of AxSpA's clinical management across diverse patient demographics. This will provide insights into the clinical management of AxSpA in different patient populations.

MATERIAL AND METHOD

The Ankara Bilkent City Hospital registry, established in 2023, serves as a pivotal resource for the retrospective analysis and documentation of patients diagnosed with inflammatory rheumatological conditions. By June 2023, a longitudinal aspect was incorporated, transforming the registry into a single-center, observational, longitudinal cohort. This computerized system, characterized by its duplication-disabled feature, meticulously records data based on patients' medication reports, pertaining to various inflammatory rheumatological diseases monitored in our clinic.

The focus of the current study is on patients diagnosed with AxSpA was determined by rheumatologists' clinical evaluations. Eligibility for inclusion in the study was restricted to individuals aged 18 and above. Utilizing a cross-sectional approach, we analyzed retrospective cohort data from 2811 AxSpA patients who had complete and relevant records up between 2019 and 2023. Exclusion criteria for the study included individuals under the age of 18. Patients who did not have complete and relevant medical records for the period between 2019 and 2023 were also excluded.

Key variables examined in this study included demographic data, comorbidities, and treatment regimens. Patients were categorized into three age groups: Group 1: 18-40, Group 2: 41-55, and Group 3: over 55 years. Within these age strata, we assessed the choice of treatment modalities. The analysis focused on the usage of (ever/never) csDMARDs, Anti-TNF agents (such as etanercept,adalimumab, infliximab, certolizumab pegol and golimumab), and Anti interleukin treatments (including secukinumab, ustekinumab, ixekizumab and guselkumab). The Ethics Committee of Ankara Bilkent City Hospital approved the study protocol (Date=17.08.2022, Ethical approval number=E1-22-2826).

Statistical Analysis

Statistical analyses were conducted using Jamovi (v2.3.22, Sydney, Australia). Both visual methods (such as histograms and probability plots) and analytical methods (like the Kolmogorov-Smirnov test) were employed to assess the normality of the variables. Continuous variables that followed a normal distribution were presented as mean ± standard deviation (SD). Categorical variables were expressed as numbers and percentages. Comparisons between groups were performed using ANOVA for continuous variables and the chi-square test for categorical variables

RESULTS

2811 AxSpa patients were evaluated retrospectively. The mean age of patients in the first group was 32.8 (5.2), while 47.5 (4.2) in the second group, and 62.6 (6) at the third group. Percentage of female patients were found to be higher with increased age (39.1%, 45.8% vs 54.6%, $p<0.001$). As expected, having comorbidities increased with age (29%, 59% vs 81.6%, $p<0.001$, respectively).

Table 1 delineates the comparative usage of medications across the age-stratified groups (18-40 vs 41-55 vs over 55, until 2023). Significant differences are observed in the use of specific medications between the age groups. There were trends in methotrexate (5.2%, 6.5 %, and 7.9%,

p=0.115) and colchicine (7.8%, 9.3%, vs 11%, p=0.1) use being more frequent in patients over 55 years of age. Sulfasalazine (35.2% in Group 1, 40.1% in Group 2, and 42.1% in Group 3, p=0.01) and leflunomide (0.4%,0.6% vs 1.7%, p=0.008) were markedly more used in patients over 55 years of age. Corticosteroid use was comparable between the groups.

Tablo 1. Drug choices in axial spondyloarthritis patients according to age

	Age 18-40 (N=1030)	Age 41-55 (N=1263)	Age>55 (N=518)	Total (N=2811)	p value
Age, Mean (SD)	32.8 (5.2)	47.5 (4.2)	62.6 (6.0)	44.9 (11.8)	<0.001[1]
Sex, Female n(%)	403 (39.1%)	578 (45.8%)	283 (54.6%)	1264 (45.0%)	<0.001[2]
Comorbidity, n(%)	298 (29.0%)	744 (59.0%)	422 (81.6%)	1464 (52.2%)	<0.001[2]
Methotrexate, n (%)	54 (5.2%)	82 (6.5%)	41 (7.9%)	177 (6.3%)	0.115[2]
Leflunomide, n (%)	4 (0.4%)	7 (0.6%)	9 (1.7%)	20 (0.7%)	0.008[2]
Sulfasalazine, n (%)	363 (35.2%)	507 (40.1%)	218 (42.1%)	1088 (38.7%)	0.012[2]
Colchicine, n (%)	80 (7.8%)	117 (9.3%)	57 (11.0%)	254 (9.0%)	0.103[2]
Corticosteroids, n (%)	31 (3.0%)	34 (2.7%)	20 (3.9%)	85 (3.0%)	0.425[2]
AntiTNF, n (%)	469 (45.5%)	578 (45.8%)	207 (40.0%)	1254 (44.6%)	0.062[2]
AntiIL, n (%)	46 (4.5%)	50 (4.0%)	17 (3.3%)	113 (4.0%)	0.529[2]

1: Linear Model ANOVA, 2: Pearson's Chi-squared test

In terms of biologic drug usage, a trend towards decline with age in the use of anti-TNF agents (45.5% in Group 1, 45.8% in Group 2, and 40% in Group 3, p=0.06) and IL inhibitors were noted (4.5% in Group 1, 4.0% in Group 2, and 3.3% in Group 3, p=0.53). However, these are not statistically significant.

When patients over 55 years of age receiving antiTNF were compared in terms of gender, no statistically significant difference was found between both genders. 40.4% of male patients over 55 years of age were receiving antiTNF treatment, while 39.6% of female patients were receiving antiTNF treatment (p=0.844) . However, when the general group was analyzed, it was seen that 51.1% of male patients received antiTNF while 36.7% of female patients received antiTNF (p<0.001). In the light of this information, it can be said that antiTNF treatment is increased in elderly female patients.

DISCUSSION

The therapeutic landscape for patients diagnosed with AxSpA is witnessing an incremental expansion, broadening the scope of potential treatments available. Despite these advancements, managing older patient demographics, especially those with concurrent comorbidities, presents a significant challenge. This demographic is notably under-represented in randomized controlled trials (RCTs), a cornerstone for establishing evidence-based practices. Consequently, this under-representation precipitates a palpable dearth of high-level evidence, critical for guiding treatment selection in older patients. We aimed to investigate the impact of this lack of evidence on treatment selection with real-life data. Our observations revealed a trend towards increased use of methotrexate and colchicine with advancing age, whereas sulfasalazine and leflunomide were more commonly used at older ages. The administration of bDMARDs (anti-TNF and anti-IL) showed a declining trend with age, albeit not reaching statistical significance. However, while more male patients received biologic treatment in the general patient group, there was no significant difference between the genders in patients over 55 years of age receiving bDMARDs.

A pivotal finding of this study is the age-related increase in csDMARD usage and a corresponding decrease in bDMARD administration. Reviewing the literature reveals mixed evidence regarding the efficacy of conventional csDMARDs on axial symptoms in AS, with several studies indicating limited impact on disease activity indices such as BASDAI and BASMI. However, some research suggests benefits of csDMARDs on various assessment scales, though these findings are not universally significant (12,13). A Cochrane review on sulfasalazine found no significant impact on pain, disease activity, or radiographic progression, with only one study noting minor clinical improvements (14). Leflunomide was not found to be effective in patients with axial findings (15). However, there are also publications in the literature suggesting that csDMARDs are effective. In a double-blind randomised controlled trial involving 67 patients, significant changes in ASDAS, BASDAI and BASMI were seen in the sulfasalazine group compared with placebo (16). Similarly, in the study by Dougados et al, improvements in functional indexes were observed with sulfasalazine and it was shown to reduce the need for NSAID use (17).

For peripheral involvement, csDMARDs may be the first choice. There is a view that sulfasalazine in particular is effective in peripheral joint involvement. In the literature,

csDMARDs have been shown to be more effective in studies of ankylosing spondylitis, where the patient groups are predominantly composed of patients with peripheral arthritis. Nissila et al. showed that the use of sulfasalazine up to 3 g per day in a patient group dominated by peripheral arthritis led to improvements in acute phase reactants, morning stiffness and chest expansion (18). In another group of 99 patients with AS dominated by peripheral arthritis, improvement in clinical parameters (morning stiffness, ESR, number of painful and swollen joints) was observed (19).

Although the place of csDMARDs in the treatment of rheumatoid arthritis is well known, there are not enough studies to support the use of csDMARDs in AS. The increase in the rate of use with age can be interpreted as a preference for csDMARDs over bDMARDs due to safety concerns of physicians. The increased risk of developing potential drug-related side effects and the fact that patients have more comorbidities are behind these safety concerns. In addition to safety concerns, the fact that peripheral involvement is more common in older patients (late-onset AXSPA) may be another reason (20). There are studies in the literature on treatment management in elderly patients in RA, where there is a higher proportion of elderly patients, but there is also more limited data in AS patients. In a review evaluating treatment management in elderly AS patients, NSAIDs, which are known to have an effect on stiffness and pain in AS, may not be used in elderly patients due to an increased risk of side effects. Sulfasalazine has not been studied in elderly patients with AS, but may be preferred in RA patients, although GIS intolerance increases with experience. Close monitoring of liver enzymes, creatinine and haemogram is recommended with methotrexate (21).

There are studies in the literature on the use of biologics in older patients. Although no significant difference was found in terms of efficacy, there are different opinions that side effects are different in elderly patients. In patients with rheumatoid arthritis, which is known to have a higher proportion of elderly patients, no difference in biological treatment was found with advanced age (22). In another study, etanercept was found to be safer in older patients, but medically important infections were more common in patients aged >65 years (23). In a study of 83 RA and AS patients aged >70 years treated with infliximab, the risk of serious infection was found to be 6.5 times higher than in younger patients. It was observed that the risk of tuberculosis in RA patients receiving infliximab was not higher in the older group (24). This information may explain the hesitation to use biologic therapies in older patients in routine follow-up.

An intriguing aspect of our research highlights a disparity in the utilization of biological therapies between genders within the general patient cohort, with a higher usage rate observed in males. However, this trend equalizes within the elderly patient group, where the employment of biological therapies does not significantly differ between sexes. Traditionally, AxSpa has been more commonly associated with the male gender, yet no significant gender difference is noted in nr AxSpA patients. Despite a higher prevalence of axial manifestations in males, the occurrence of peripheral joint and extra-articular symptoms appears comparably across genders. Furthermore, the age at initial diagnosis remains consistent between sexes, although research indicates a more frequent occurrence of delayed diagnoses in females, a factor potentially contributing to increased disease activity in older female patients. (5,6,25). In our study, the proportion of female patients increased with increasing age. There are also publications in the literature supporting that BASDAI and quality of life scores are higher in female patients. This may explain why the need for biological treatment in women tends to increase with age, and why the rate of biological treatment in women in the older age group is similar to that of men, in contrast to the younger group.

Our investigation is subject to several noteworthy constraints. Firstly, the data utilized in this study were obtained through a retrospective review of patient records. Despite the implementation of an electronic patient record system that mandates all treatments to be logged, the risk of incomplete data capture persists. Additionally, the study's reliance on data sourced exclusively from one center constrains the applicability of its findings to broader populations. Furthermore, the lack of data on disease activity, axial or peripheral predominance means that cause and effect cannot be fully established in some conclusions, and such conclusions have been avoided.

CONCLUSION

In summary, our investigation illuminates the nuanced differences in treatment strategies for AxSpA across various age demographics. While csDMARDs are not typically endorsed by clinical guidelines for the treatment of NSAID-resistant patients, their inclusion in practical treatment plans suggests a deviation towards personalized care. This adjustment is particularly pronounced in the management of older patients, highlighting the complexities and necessitating bespoke treatment modifications. Our findings indicate an age-related increase in the preference for csDMARDs and a corresponding decline in the propensity towards biologics, suggesting that while guideline-based treatment algorithms provide a foundation, the ultimate therapeutic decision is influenced by the unique characteristics of each patient. Continued clinical research is essential to develop effective treatments to meet the health needs of the ageing population and improve the quality of life of older people.

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Research Article

Pediatric Head Injuries Occur During the Play Childhood Period of 3-6 Years: A Sample from the South of Türkiye

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Abstract

Aim: Pediatric head traumas (HT) are of significant concern due to their potential for high mortality rates, which are influenced by the clinical progression of traumatic brain injury (TBI). HT poses a substantial risk of morbidity and mortality across all pediatric age groups, underscoring the importance of effective clinical management and follow-up procedures. The current study aims to evaluate the epidemiology, causes, and clinical outcomes of head injuries during childhood play between the ages of 3 and 6.

Material and Method: Focused on pediatric patients aged 3-6 years who were admitted to the emergency department (ED) for HT, and required consultation from a neurosurgeon. Data collected included patients' demographics, trauma etiology, cranial examination findings, laboratory results upon admission, cranial computed tomography findings, classification of TBI, treatment administered, and clinical progression.

Results: The median Glasgow Coma Scale (GCS) scores were found to be significantly lower in the group with intraparenchymal injury compared to the group without intraparenchymal injury (p=0.008). The group with intraparenchymal injury exhibited a higher than expected occurrence of moderate TBI (p=0.012). Females exhibited significantly lower mean rank scores for age compared to males (p=0.032). Patients hospitalized for HT had significantly lower GCS scores than those discharged (p=0.001). There is a higher prevalence of moderate TBI than expected in the group of hospitalized patients (p=0.008). The mortality rate among hospitalized patients was 5.6%, with lower GCS scores and hyperglycemia upon admission significantly associated with fatalities (p=0.015, p=0.045).

Conclusion: Identification and management of moderate TBI are imperative in children presenting to the ED with HT during early childhood play. Children with intraparenchymal injury should be hospitalized. Additionally, hyperglycemia in pediatric HT patients may signify high-energy trauma.

Keywords: Pediatric, head trauma, emergency department, neurosurgery, hyperglycemia

INTRODUCTION

Pediatric head traumas (HT) are of critical importance due to their high mortality potential. Traumatic brain injury (TBI) is at the root of being a significant social problem and burden on the healthcare system. Surviving children have high risks such as lifelong neurological sequelae, living dependent on others, deteriorated quality of life, and loss of productivity (1,2).

Most cases of pediatric HT admitted to Emergency Department (ED) are mild and do not require further examination and treatment. A few children develop serious TBI. However, in this group, early diagnosis and rapid intervention are critical for preventing neurological sequelae that may develop in the future (3,4,5). TBI in pediatrics are classified into mild (14-15), moderate (9-13) and severe (3-8) categories based on the Glasgow Coma Scale (GCS) score (6).

Approximately 500,000 children are admitted to ED in the United States of America (USA) every year with complaints of HT, and approximately 12% of them are hospitalized (7).

Children's interest in the outside world increases during play childhood (ages 3-6). Children gain mobility and begin to walk and run without knowing what is or is not dangerous for them (8,9). Considering that this makes

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children aged between 3-6 more susceptible to HT, we focused on this group. Data on the epidemiology, etiology, and clinical course of clinically important HT during play childhood between the ages of 3-6 are limited. We think that our study will contribute to the literature at this point.

MATERIAL AND METHOD

Study Design and Ethical Considerations

The research was designed as a retrospective study. The study protocol was approved by Non-Interventional Ethics Committee of Niğde Ömer Halisdemir University, Faculty of Medicine (14.12.2023, No:2023/98). Written informed consent from the patients (or their parents or guardians) was not obtained as the study was designed as a retrospective study that does not publicize any personal medical data, and both the institutional/national code and World Medical Association Declaration of Helsinki do not require written informed consent in retrospective studies.

Population and Sample

The study includes pediatric patients aged 3-6 years who were admitted to Niğde Ömer Halisdemir University Training and Research Hospital ED between 15.01.2023 and 01.10.2023 and for whom a neurosurgeon's opinion due to HT was requested.

In the retrospective screening, patients whose data could not be accessed through our hospital's automation system, patients who had HT outside the 3-6 age range, cases with HT accompanied by abdomen, thorax, and large bone injuries, patients with active bleeding or known coagulopathy, patients who had had previous neurosurgery, and patients with neurological deficits or developmental delay, assessed as mild TBI in ED were evaluated by an emergency medicine specialist and discharged without the need for neurosurgery consultation were excluded from the study.

The patients' age, sex, trauma etiology, cranial examination findings, laboratory results at the time of admission, cranial computed tomography (CT) findings, classification of TBI, treatment applied, and clinical course were examined in the study. Data were obtained through the hospital automation system (Karmed). Microsoft Excel 2021 software was used to record the data.

Statistical Analysis

All statistical data were analyzed using SPSS version 22.0 for Windows (IBM Corp., Armonk, NY, USA). Sex, trauma etiology, cranial examination findings, CT results, classification of TBI and hospital discharge/hospitalization status data, which are categorical variables in statistics, were presented as numbers and percentages, while data on age, GCS score, length of hospital stay in inpatients, and blood glucose value at admission were given as mean±standard deviation for those with normal distribution and as median and interquartile range (IQR 25-75) for those with non-normal distribution. The Shapiro-Wilk test was applied to show whether the data were normally distributed. The Mann-Whitney U test was used to investigate the relationship between age, GCS score, and glucose values and sex, discharge/hospitalization status, and clinical outcome (survival/death). Fisher's exact test was used to research whether there was a significant relationship between the part of the head affected by impact and discharge/hospitalization status and clinical outcome. Fisher's exact test was conducted to examine the relationship between sex and discharge/hospitalization status and clinical outcome. A value of $p<0.05$ was considered statistically significant.

RESULTS

Thirty-six patients who met the study criteria were identified. The median age was 4 (IQR 4-6) years. Concerning age distribution, 7 patients were 3 years old (19.4%), 13 patients were 4 years old (36.1%), 4 patients were 5 years old (11.1%), and 12 patients were 6 years old (33.3%). Twenty cases were male (55.6%), and 16 were female (44.4%). The median GCS value of the patients was 13 (percentile 25-75%: 12-14), and the mean blood glucose value was 137±39 (min-max: 88-242) mg/dl. The median length of stay of the hospitalized patients was 3 days (min-max 1-15) (Table 1).

Table 1. Demographic and clinical data of patients

Parameters		Values
Age (year), (SD)		4.58±1.15
Sex	Male, n (%)	20 (55.6)
	Female, n (%)	16 (44.4)
GCS (25-75% percentile)		13 (12-14)
Glucose (mg/dl), (SD); min-max		137±39; 88-242
Hospital stay (day), min-max		3, 1-15

GCS: Glasgow Coma Score, %: percentage, min-max: minimum-maximum, mg/dl: milligram/deciliter, SD: standard deviation

The etiology of ED admissions included 11 falls from height (30.6%) (2 meters or higher), 10 falls from own height (27.8%), 7 in-vehicle traffic accidents (19.4%) and 7 out-vehicle traffic accidents (19.4%), and one natural disaster victim (2.8%) (earthquake). Seventeen children had isolated scalp hematoma (47.2%), 6 had local abrasion and laceration (16.7%), 3 had orbital edema and hyperemia (8.3%), 3 had scalp hematoma and convulsions due to generalized seizures (8.3%), 2 had scalp hematoma and laceration (5.6%), 1 had orbital laceration (2.8%), and 4 had normal physical examination findings (11.1%). In the computed imaging results, there were findings of multiple injuries (fracture and intraparenchymal hemorrhage) (33.3%) in 12 patients, contusion (25.0%) in 9 patients and isolated linear fracture (25.0%) in 9 patients, and isolated subdural (2.8%) and epidural hemorrhage (2.8%) in 1 patient each. There was no pathological CT finding in 4 patients (11.1%) (Table 2).

Table 2. ED admission etiologies of patients, cranial examination findings, cranial CT image results

Etiology	(n=36)	%
Falls from height	11	30.6
Falls from own height	10	27.8
In-vehicle traffic accidents	7	19.4
Out-vehicle traffic accidents	7	19.4
Natural disaster	1	2.8
Physical examination		
Isolated scalp hematoma	17	47.2
Local abrasion and laceration	6	16.7
Orbital edema and hyperemia	3	8.3
Scalp hematoma and convulsions	3	8.3
Scalp hematoma and laceration	2	5.6
Orbital laceration	1	2.8
Normal	4	11.1
Imaging		
Fracture and intraparenchymal hemorrhage	12	33.3
Contusion	9	25
Isolated linear fracture	9	25
Isolated subdural hemorrhage	1	2.8
Isolated epidural hemorrhage	1	2.8
Normal	4	11.1

After six hours of ED observation, 5 patients were discharged with recommendations regarding intracranial pressure (13.9%). Thirty-one patients were hospitalized and treated (86.1%). Surgical intervention was performed in only 2 of our cases (5.6%). The other 34 cases received symptomatic treatment (94.4%).

When patients were categorized into mild, moderate, and severe TBI groups using the GCS score, only 2 patients were classified in the severe TBI group. In order to perform appropriate statistical analysis, these 2 patients were added to the moderate TBI group. Thus, a total of 15 patients were classified as having mild TBI (41.7%), and 21 patients were classified as having moderate to severe TBI (58.3%).

Patients with intraparenchymal hemorrhage, subdural hematoma, epidural hematoma, and contusion on CT scans were categorized separately as "patients with intraparenchymal injury". A total of 23 patients (63.9%) were identified in this group.

There was no statistically significant difference between sex and the GCS score and blood glucose value mean rank scores (p=0.59, p=0.17). No significant relationship was identified between sex and discharge/hospitalization status and clinical outcome (p=0.35, p=0.69). There was no statistically significant difference between right, left, and bilateral head injuries, discharge/hospitalization status and clinical outcome (p=0.47, p=0.38).

The median GCS scores were found to be significantly lower in the group with intraparenchymal injury compared to the group without intraparenchymal injury (p=0.008) (Figure 1). The group with intraparenchymal injury exhibited a higher than expected occurrence of moderate TBI (p=0.012). There is a higher prevalence of moderate TBI than expected in the group of hospitalized patients (p=0.008) (Table 3).

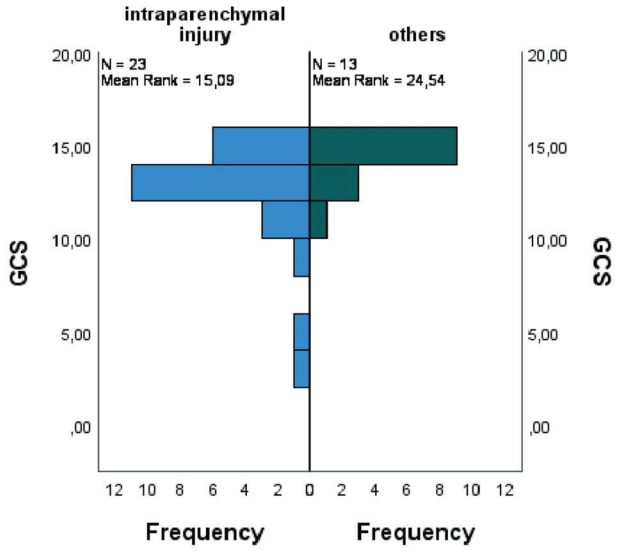

Figure 1. The median GCS value is lower in patients with intraparenchymal injury (p=0.008)* GCS: Glasgow Coma Scale, *: Mann-Whitney U test

Table 3. The association between TBI with the patients of hospitalization and intraparenchymal injury

		TBI		
		Mild	Moderate	p value*
Intraparenchymal injury	Count	6	17	0.012
	Expect	9.6	13.4	
Hospitalized patients	Count	10	21	0.008
	Expect	12.9	18.1	

* Chi-Square Tests, TBI: Traumatic Brain Injury

When comparing age and sex, lower age mean rank scores were revealed in females, which was found to be statistically significant (p=0.032). GCS score was found to be statistically significantly lower in hospitalized patients compared to discharged patients (p=0.001). Two of the hospitalized patients died in the intensive care unit (Mortality rate: 5.6%). A low GCS score and hyperglycemia at the time of admission in patients who died after trauma were found to be statistically significant compared to surviving patients (p=0.015, p=0.045) (Table 4).

Table 4. Analysis of statistically significant demographic and clinical data of patients

		n	Mean rank	Sum of ranks	U	p*
Age	**Male**	20	21.7	434	96	0.032
	Female	16	14.5	232		
GCS	**Discharge**	5	33	165	5	0.001
	Hospitalization	31	16.16	501		
GCS	**Survival**	34	19.5	663	0.0001	0.015
	Death	2	1.5	3		
Glucose	**Survival**	34	17.65	600	5	0.045
	Death	2	33	66		

GCS: Glasgow Coma Scale, *Mann-Whitney U

DISCUSSION

Children in the play childhood period (ages 3-6) have a higher affinity for the environment compared to the newborn and infancy periods. Furthermore, reality, danger perception, and person and place orientation are lower in comparison with the school childhood period (10,11).

In children between the ages of 0 and 4, the risk of brain damage due to HT is approximately twice as high compared to other age groups (6). In line with these data, more than half of the children in our study were 3 and 4 years old. The fact that children have not fully acquired the ability to walk in this period and the balance problem that occurs due to the change in the center of gravity due to the higher head-to-body ratio may explain the higher incidence of HT in this age group.

HT is more common in males than in females in all pediatric age groups (5). Our results are compatible with this situation, which can be called general acceptance. We think that this is caused by the fact that boys are more active and aggressive than girls, and family members such as fathers, uncles, and elder brothers play rougher games with boys.

The etiology of pediatric HT is multifactorial. However, the most common cause is falling during play childhood. Falls may occur from one's own height or a greater height (12). Falls were the cause of HT in approximately 60 percent of the children in our study. Cranial fracture or parenchymal hemorrhage occurred in all children who fell from a significant height. In some cases, both clinical pictures were observed together. Children who fell from their own height had a history of either hitting the hard floor or colliding with a sharp object at home. We think that this situation developed due to high trauma energy.

Another cause of HT in children is traffic accidents. Children may be exposed to HT inside or outside the vehicle (13). The cause of HT in 14 of the children in our study was a traffic accident. In addition to HT, traffic accident cases in our also had orbital injuries, facial abrasions and lacerations. Therefore, we believe that it would be more appropriate to take a multidisciplinary approach in children who develop TBI secondary to a traffic accident by consulting not only neurosurgery but also other surgical branches such as ophthalmology and plastic surgery.

Earthquake disasters can lead to clinical conditions such as TBI, spinal cord injury, peripheral nerve damage, and limb loss in children (14). In one of our cases, the HT was caused by an earthquake. A psychiatric opinion was also received after the HT follow-up. We think that providing psychosocial support after trauma follow-up in children in case of disasters such as earthquakes would be an appropriate clinical approach.

Lesions after HT in children usually occur in the area that receives the impact. Various physical examination findings such as erythema, hematoma, abrasion, and laceration can be detected (12). The most common examination finding in our study was scalp hematoma. There is no clear information about a linear relationship between the presence of scalp hematoma and TBI. However, scalp hematoma may be the only clue we have in predicting TBI. A large hematoma size and scalp hematomas outside the frontal region increase the risk of TBI (15). In three cases with generalized seizures in our study, there was a scalp hematoma in the temporoparietal region. We think that more care should be taken in terms of convulsion follow-up in children with scalp hematoma outside the frontal region.

Ophthalmological problems may accompany HT in children (16). Four of our cases had an orbital injury in addition to HT.

Cranial CT is the standard diagnostic test to diagnose TBI (17). CT imaging was performed in all of our cases. In line with the literature (18), our imaging results consisted of linear fracture, parenchymal hemorrhage, contusion, subdural and epidural hemorrhage.

The most common pathological CT imaging finding in HT cases causing TBI is cranial bone fractures (19,20). Our data are in line with this situation, and the most common finding we observed was parenchymal hemorrhage accompanied by cranial bone fracture, which we call the multiple injury finding. Moreover, nine of our cases had isolated cranial linear fractures.

While Tavor et al. (21) observed epidural hemorrhage most frequently in their study, contrary to these data, in our study, isolated epidural hemorrhage was observed in only one case after a traffic accident.

According to Hung (22), subdural hemorrhage is the most common pathological CT finding observed in abused children. There was no abused child among our cases, and isolated subdural hemorrhage due to a traffic accident was detected in only one case.

There is no clear information in the literature about the length of hospital stay after HT. However, if there is an intracranial injury finding, observation for at least 24 hours is recommended (23). In our study, cases that were hospitalized were predominantly those with intraparenchymal injuries and moderate TBI. Therefore, our current data suggest a possible proportional relationship between the presence of any brain parenchymal injury and hospitalization. The 31 cases in our study were followed up with hospitalization for an average of 3.5 days. GCS score was found to be statistically significantly lower in hospitalized patients compared to discharged patients.

It is known that the presence of hyperglycemia at the time of admission in pediatric HT cases increases the length of hospital stay and mortality (24). The mean blood glucose level of our cases measured at the ED admission was above the laboratory glucose upper limit. We predict that hyperglycemia occurs with the elevation of stress hormones due to trauma. However, no statistically significant relationship was found between the presence of hyperglycemia and sex, GCS score and clinical outcome. We think that if the number of cases in our study had been higher, we would have obtained a statistically significant result in the inpatient group.

TBI is considered an important cause of mortality in the pediatric group (25,26). Two of our cases died due to falling from height and out-vehicle traffic accidents. In patients who died, a low GCS score and high blood glucose level at the time of admission were found to be statistically significant. We think that these data are valuable in terms of contributing to the literature.

Limitations of the Study

The main limitations of the present study are that the retrospective case screening period was approximately 1 year, our hospital is located in a small province with a population of 237 thousand, and the number of cases in our study was low. Since the presence of moderate TBI was predominant in our cases, detailed comments regarding severe TBI could not be made.

CONCLUSION

During the period of 3-6 years when neuronal development is not yet completed, the progression of HT into the intraparenchymal region and the hospitalization status of patients are directly proportional to the severity of TBI. Identification and management of moderate TBI are imperative in children presenting to the ED with HT during early childhood play. Children with intraparenchymal injury such as GCS scores below 14 should be hospitalized for close monitoring and rapid access to treatment, as well as for the surveillance of potential complications. Additionally, hyperglycemia in pediatric HT patients may signify high-energy trauma. Clinical implications of study are recognizing demographic differences and prioritizing clinical indicators, such as GCS scores and blood glucose levels, can enhance patient outcomes and decrease mortality rates.

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Research Article

Mediating Role of Emotional Intelligence in the Relationship between Hospital Perception and Fear of Medical Procedures in Children

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Abstract

Aim: This study investigated the relationship between children's hospital perceptions, their fear of medical procedures, and the role of emotional intelligence as a potential mediator.

Material and Method: The population of the research consists of 4th grade students (10-year-old students) studying in primary schools in the 2023-2024 academic year. The study included 343 students and employed a relational-cross-sectional-descriptive design. Data were collected using the Personal Information Form, Medical Procedure Fear Scale, Hospital Perception Scale for Healthy Children, and Ten-Year-Old Emotional Intelligence Scale. Data were analyzed with IBM SPSS V23 and IBM AMOS V24. Compliance with normal distribution was examined with the assumption of skewness, kurtosis, and multiple normality. Path analysis was used to test the mediator model, and Maximum Likelihood (ML) was used as the calculation method. Analysis results were presented as frequency (percentage) for categorical variables, mean±standard deviation, and median (minimum–maximum) for quantitative variables. The significance level was taken as $p<0.05$.

Results: The study found that children's hospital perceptions predicted their fear of medical procedures. Specifically, there was a statistically significant positive relationship between hospital perception and fear of medical procedures ($\beta=0.565$; $p<0.05$). According to the mediated structural model analysis results, hospital perception had a statistically significant negative effect on the mediator variable emotional intelligence ($\beta=-0.327$; $p<0.05$). By including the mediator variable emotional intelligence in the model, the path coefficient between hospital perception and fear of medical procedures was statistically significant ($\beta=0.554$; $p<0.05$).

Conclusion: In the study, it was found that emotional intelligence, the mediator variable, played a role in the relationship between hospital perception and fear of medical procedures.

Keywords: Child, emotional intelligence, fear of medical procedures, hospital perception

INTRODUCTION

Children may need to go to hospital for diagnosis, treatment, and short or long-term hospitalizations. Children's perceptions of hospitals can vary widely depending on various factors such as their age, previous experiences, and understanding of illness and medical procedures (1). Children's perceptions can be affected by their developmental levels, personal experiences, indirectly acquired information, supportive environment, and parental attitudes. Younger children may have a limited understanding of medical concepts and may perceive hospitals as scary or intimidating due to unfamiliarity. As children age, their knowledge of illness and medical procedures becomes more sophisticated, which may help alleviate some fears. Positive experiences, such as receiving gentle care from hospital staff or successfully recovering from an illness, can shape a child's perception of hospitals in a positive way. Conversely, negative experiences, such as painful procedures or feeling frightened or lonely during a hospital stay, can lead to negative associations with hospitals (1,2). Children may form perceptions of hospitals based on what they see in media, books, or stories from friends and family. Depictions of hospitals in media can range from reassuring to frightening, and these portrayals can influence how children view hospitals. A supportive and child-friendly environment within the hospital can play a significant role in shaping children's perceptions. Child life specialists, playrooms, and other amenities designed to make the hospital experience more comfortable can help alleviate anxiety and foster positive associations with hospitals (2-4). The attitudes and behaviors of parents and caregivers can impact children's perceptions of hospitals. If parents convey fear or anxiety about hospitals, children may adopt similar feelings. On the other hand, parents who provide

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reassurance and support can help children feel more at ease. Healthcare providers must consider children's perceptions and emotional needs when providing care in hospital settings. Creating a supportive and child-friendly environment can help mitigate fears and promote positive experiences for pediatric patients (4,5). Suppose a child has been hospitalized before, involving an invasive procedure, pain, discomfort, discomfort, fear, or much crying. In that case, they will likely experience the same fears during another hospital experience. Some children may even experience fear of disability or death (2-4). Pediatric patients experience anxiety and stress at different levels due to fears such as being separated from family and loved ones, physical and emotional harm, medical procedures, and the unknown, starting from their hospitalization (4). These fears of children reduce their participation in health practices, may prevent them from receiving health care in case of illness, and may negatively affect the treatment process (5). Studies have shown that children often experience high levels of anxiety during hospital experiences (3,6). That negative childhood experiences are associated with harmful effects on children's well-being (7). Therefore, nurses are essential in protecting children from the negative emotions and effects caused by hospital experiences and stressful medical procedures (8).

Of course, children's perceptions of the hospital may differ depending on their developmental level and cognitive status. Developing logical thinking skills in children between 7 and 10 affects their perceptions. As rational thinking skills develop, children ages 7 to 10 begin to have a more complex understanding of disease and medical treatment. They may be able to grasp concepts such as cause and effect more efficiently, which can help them understand why they need to visit the hospital and what treatment involves. Children in this age group may fear the unknown less than younger children (9). They are more likely to ask questions and seek information to understand what to expect during hospital visits; This can help relieve anxiety. With the development of logical thinking skills, children in this age range can better follow instructions given by healthcare providers. This can make medical procedures and treatments less stressful for the child and the healthcare team. As children become more independent at this stage of development, they may also desire more autonomy and control over their healthcare experience (8). Healthcare providers can include them in decision-making whenever possible, empowering them and making them feel more comfortable in the hospital environment. Children in this age group may also be influenced by their peers' perceptions and experiences of hospitals. Positive experiences shared by friends or classmates can help reinforce a child's positive perception of hospitals. In general, children between the ages of 7 and 10 become more capable of understanding and coping with hospital visits. Healthcare providers can adapt their communication and care approaches to accommodate these developmental changes and promote positive experiences for pediatric patients (7-10).

Stressful medical procedures cause emotionally damaging behavioral changes in children (8). The ability of people to define their emotions correctly and cope with the problems they encounter is closely related to the concept of emotional intelligence (10). The most important innovation that the concept of emotional intelligence has brought to the literature is that it treats emotions as developable abilities rather than personal characteristics that are difficult to change (11). Definitions put forward by different researchers in the field of emotional intelligence generally refer to the ability of a person to make sense of the emotions they have, to understand the emotions of others, to develop appropriate reactions to them, to adapt to the environment, to cope with the difficulties they encounter, to take action to perform desired actions by taking advantage of the motivating power of emotions, and to They are united in being able to accurately control negative emotions that may hinder actions (12). In the literature research, no research was found examining the role of emotional intelligence in the relationship between children's hospital perceptions and their fear of medical procedures. The current study contributes to the literature in this sense. In this context, this study aimed to examine the role of emotional intelligence in the relationship between children's hospital perceptions and their fear of medical procedures.

MATERIAL AND METHOD

Universe and Sample

This study was conducted in a correlational-cross-sectional-descriptive model. The population of the research consists of 4th grade students (10-year-old students) studying in primary schools in the 2023-2024 academic year. There are 35 primary schools in the city center and 851 students studying in the 4th grade in these schools. These schools provide full-time education. The research sample must be at least 269 with a 95% confidence interval and a 5% margin of error (13). The study was conducted with 343 students who met the inclusion criteria.

Inclusion Criteria

- Parent and child volunteering to participate in the research.

Exclusion Criteria

- The child has a neurodevelopmental and psychiatric problem,
- The child has a chronic disease,
- The child has vision, hearing and speech problems that may prevent the child from communicating.

Data Collection Tools

In collecting data; Personal Information Form, Medical Procedure Fear Scale, Hospital Perception Scale for Healthy Children and Ten-Year-Old Emotional Intelligence Scale were used.

Personal Information Form

Form; it consists of 12 questions that question the sociodemographic characteristics of the mother/father

such as age, education, employment and income status and family type, and the child's information such as gender and hospital experience (14,15).

Medical Procedure Fear Scale (MPFS)

The validity and reliability study of the scale in Türkiye was conducted by Alak (14). The scale is a Likert type scale with 29 questions and 3 options. For each item in the scale, the child is asked to choose one of the following statements: "I am not afraid at all" (1 point), "I am a little afraid" (2 point), "I am very afraid" (3 point). The lowest score on the scale is 29 and the highest score is 87. Those who score 0-29 on the scale are considered less fearful; those who get between 29-58 points are a little afraid; a score between 58-87 is considered very fearful. The Cronbach alpha internal consistency coefficient for the total scale was found to be 0.93 (14). In this study, the scale's Cronbach alpha internal consistency coefficient is 0.91.

Hospital Perception Scale for Healthy Children (HPSHC)

The scale was developed by Ekici (15) to evaluate the hospital perception of children aged 8-10 years. The scale consists of 25 items designed to assess different aspects of children's perceptions of hospitals. These items are rated on a 3-point Likert scale, ranging from "I never think this way" (0 points) to "I sometimes think this way" (1 point) to "I always think this way" (2 points). Factor Structure: The scale has a six-factor structure, each representing a different aspect of hospital perception: Factor 1: Separation, Factor 2: Invasive and non-invasive interventions, Factor 3: Fear and loss of control, Factor 4: Body image, Factor, 5: Physiological needs and Factor 6: Hospital environment. The total score range of the scale is from 0 to 50 points. A score of 0-24 indicates a "less negative hospital impression," while a score of 25-50 indicates a "largely negative hospital perception." A higher score suggests a more negative opinion about hospitals. The Cronbach alpha internal consistency coefficient for the total scale was found to be 0.87 (15). In this study, the scale's Cronbach alpha internal consistency coefficient is 0.86.

Ten Years Emotional Intelligence Scale (TYEIS)

Coşkun et al. validity and reliability analyses of TYEIS developed by (2017) were conducted based on data obtained from 492 primary school students. TYEIS has a single-factor structure consisting of ten items. The scale is rated into three categories: "Not True" (1 point), "Somewhat True" (2 point), and "Very True" (3 point). In the TYEIS, negative items are reverse-scored. The highest score that can be obtained from the scale is 30, and the lowest score is 10. The Cronbach alpha internal consistency coefficient for the total scale was found to be 0.89 (16). In this study, the scale's Cronbach alpha internal consistency coefficient is 0.72.

Data Collection

The research data was collected between November 30, 2023, and February 15, 2024. Before the researcher collected the data, information about the study was given, and written consent of the parents and verbal consent of the children were obtained. Informed consent was obtained from all participants and their legal guardians. Children who volunteered and met the inclusion criteria were included in the study. Personal Information Form, Medical Procedure Fear Scale, Hospital Perception Scale for Healthy Children, and Ten-Year-Old Emotional Intelligence Scale were administered face to face to the children, and their data were collected. Before starting the research, ethics committee approval was obtained from the university, and institutional permission was obtained from the Provincial Directorate of National Education.

Data Analysis

Data were analyzed with IBM SPSS V23 and IBM AMOS V24. Compliance with normal distribution was examined with the assumption of skewness, kurtosis, and multiple normality. Before starting to work on structural equation modeling, all problems with the data (outlier values, flat and skewed values, missing data, etc.) must be resolved. In order to use maximum likelihood, the data must comply with normal distribution. In the Multivariate normality test, the critical value was determined to be 0.375 (Table 1). Byrne, considered values >5 as an indicator of non-normally distributed data (17). While this value is below 10 is an excellent result, studies have shown that it generally does not pose a problem up to 20. The assumption of multiple normality is satisfied. Path analysis was used to test the mediator model, and Maximum Likelihood (ML) was used as the calculation method. Analysis results were presented as frequency (percentage) for categorical variables, mean±standard deviation, and median (minimum–maximum) for quantitative variables. The significance level was taken as $p<0.05$.

Table 1. The result of the multivariate normality test should be reported

	Minimum	Maximum	Skewness	Critical rate of skew	Kurtosis	Critical rate of kurtos
Hospital perception total score	0	40	0.234	1.773	-0.465	-1.757
Emotional intelligence total score	16	30	-0.616	-4.654	0.226	0.854
Medical procedures fear total score	29	76	0.749	5.667	-0.196	-0.740
Multivariate					0.222	0.375

Ethical Approval

The Bayburt University Research Ethics Committee approved the research (2023/402-21). Before the researchers collected the data, the Declaration of Helsinki informed parents and children about the study, and their written/verbal consent was obtained. All methods

were conducted according to relevant guidelines and regulations.

RESULTS

47.8% of the participants are girls and 52.2% are boys. 74.1% have a nuclear family type. 47.2% have two siblings. 82.8% have a medium income. The mother's education level, 23.6%, is high school. The mothers of 71.4% are housewives. The father's education level, which is 34.1%, is high school. The father of 46.1% is a worker. 48.1% have never been hospitalized 70.8% of them have a family member who has been hospitalized before. The average age of the mother is 35.69, and the average age of the father is 41.32. All descriptive statistics are presented in detail in Table 2.

Table 2. Descriptive statistics

		Frequency	Percentage
Gender	Female	164	47.8
	Male	179	52.2
Family type	Nuclear family	254	74.1
	Extended family	89	25.9
Number of siblings	No siblings	28	8.2
	Two siblings	162	47.2
	Three siblings and above	153	44.6
Income status	Low	32	9.3
	Middle	284	82.8
	High	27	7.9
Mother's education level	Primary school	118	34.4
	Middle school	120	35
	High school	81	23.6
	University and above	24	7
Mother's occupation	Housewife	245	71.4
	Civil servant	51	14.9
	Worker	47	13.7
Father's education level	Primary school	79	23
	Middle school	93	27.2
	High school	117	34.1
	University and above	54	15.7
Father's profession	Tradesman	54	15.7
	Civil servant	95	27.7
	Worker	158	46.1
	Retired	36	10.5
Hospitalization experience	Never	165	48.1
	Once	96	28
	2 or more	82	23.9
Previous hospitalization of a family member	No	100	29.2
	Yes	243	70.8
		Mean±S.Deviation	Median (Min-Max)
Mother's age		35.69 ± 5.46	35 (25 - 49)
Father's age		41.32 ± 5.52	41 (31 - 56)

The mediating role of emotional intelligence in the effect of hospital perception on fear of medical procedures is given in Table 3. According to the analysis results, it was determined that hospital perception predicted the fear of medical procedures (β=0.565; p<0.05). The coefficient of determination (R^2) for fear of medical procedures is 31.9%.

A separate model was built in which emotional intelligence was the mediating variable. According to the mediated structural model analysis results, hospital perception had a statistically significant negative effect on the mediator variable emotional intelligence (β=-0.327; p<0.05). Emotional intelligence's coefficient of determination (R^2) is 10.7% (Table 3).

The effect of the mediator variable, emotional intelligence, on the dependent variable, fear of medical procedures, was not statistically significant (β=-0.035; p>0.05). However,

when the mediator variable, emotional intelligence, was included in the model, the path coefficient between hospital perception and fear of medical procedures was found to be statistically significant (β=0.554; p<0.05) (Table 3, Figure 1).

An analysis was conducted based on the Bootstrap method to test whether the emotional intelligence variable mediates the relationship between hospital perception and fear of medical procedures. 5000 resamples were preferred in bootstrap analysis. The 95% confidence interval (CI) obtained from the analysis performed with the Bootstrap technique should not include the zero value. As a result of the bootstrap analysis, the indirect effect of hospital perception on fear of medical procedures through emotional intelligence was not found to be statistically significant (β=0.011; 95% CI [-0.021-0.046]) (Table 3).

Table 3. The mediating role of emotional intelligence in the effect of hospital perception on fear of medical procedures

Prediction variables	Outcome variables			
	Emotional intelligence		Fear of medical procedures	
	β (95% CI)	SE	β (%95 CI)	SE
Hospital perception (Total impact)			0.565 (0.489;0.634)*	0.037
R^2			0.319	
Hospital perception	-0.327 (-0.426;-0.219)*	0.052		
R^2	0.107			
Hospital perception (Direct effect)			0.554 (0.476;0.636)*	0.041
Emotional intelligence			-0.035(-0.137;0.064)**	0.050
R^2			0.320	
Indirect effect			0.011(-0.021;0.046)***	0.017

*p<0.05; **p>0.05; ***Bootstrap indirect effect; SE: Standard error; β: Standardized coefficients; R^2: Coefficient of determination

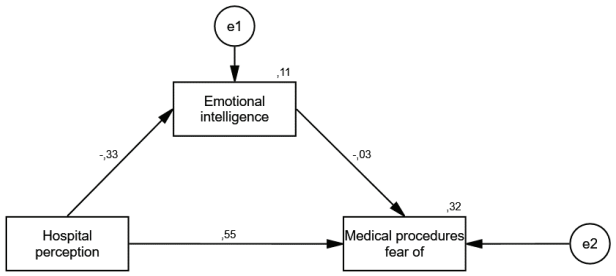

Figure 1. Standardized path coefficients

DISCUSSION

Although hospital perception varies depending on age group, it generally creates anxiety and fear in the child (18). Hospital perception and fear of medical procedures may reduce children's participation in health care practices, prevent them from receiving health care in case of illness, and negatively affect the treatment process (18,19). Physical diseases significantly affect children's psychological states and social lives and can even be traumatic (19). Emotional intelligence helps individuals cope with problems more efficiently by correctly recognizing their emotions and feelings (10).

The study examining the role of emotional intelligence in the relationship between children's hospital perceptions and their fear of medical procedures determined that hospital perception predicted the fear of medical procedures. Children's perceptions of hospitals vary depending on their developmental level, their own experiences, and the indirect knowledge they have previously acquired about hospitals (1,20). Children who have been hospitalized before, experienced an invasive procedure, and experienced pain, fear, and distress will probably experience fear in another hospital experience (2-4). Research has shown that children often experience high levels of anxiety about the hospital (4,6,21). Additionally, research has shown that adverse childhood experiences negatively affect physical and psychological health (7). In a study, the difference between children's fear of hospitalization, chronic disease, constant medication use, and invasive procedures and their fear of medical procedures was found to be statistically insignificant (22). Children's perceptions of hospitals vary according to their developmental levels and needs. For example, children between the ages of 7 and 10 have different ways of thinking because they begin to develop logical thinking skills at this age. They begin to isolate themselves from their environment. As the influence of the social environment on children increases, their need for autonomy and control over their bodies and lives increases (20-22).

According to the mediated structural model analysis results, hospital perception had a statistically significant adverse effect on the mediator variable emotional intelligence. The ability of a person to recognize their emotions correctly and to cope with the problems he encounters more easily is related to the concept of emotional intelligence (10). The most important innovation that the concept of emotional intelligence has brought to the literature is that it treats emotions not as personal characteristics that are difficult to change but as skills that can be developed (11).

The effect of the mediator variable, emotional intelligence, on the dependent variable, fear of medical procedures, was not statistically significant. However, when the mediator variable, emotional intelligence, was included in the

model, the path coefficient between hospital perception and fear of medical procedures was statistically significant. Children's perceptions of health care are critical. The positive/negative experiences experienced by hospitalized children will be recorded in their memories and affect their reactions to the disease (23). The child's developmental period, the type of disease, family support, and the attitudes of the healthcare team are the main factors affecting children's hospital experience. In this context, the attitude of pediatric nurses is critical (24). Diseases, hospitalization, and invasive/noninvasive interventions can leave significant scars, especially in the lives of children (5,25,26). Emotional intelligence is the individual's ability to perceive, define, and manage their emotions, distinguish differences between emotions, and reflect these situations in their behaviors (27). Baltaş (2015) defined emotional intelligence as the individual's ability to recognize, understand, and effectively use emotions that help him cope with himself and others (28). Emotional intelligence effectively copes with negative emotions such as unhappiness and stress (29). It is known that children experience fear and anxiety due to medical procedures. Children's hospital perceptions and fears of medical procedures are affected by many variables, such as the child's age, previous experiences, disease status, parents' education level, and approach (25,26,30,31).

In the study, the indirect effect of hospital perception on fear of medical procedures through emotional intelligence was not found to be statistically significant. Salmela et al., in 2011 (32), when the fear levels of school and hospitalized children were compared about the equipment used in the hospital, it was stated that the fear levels of both groups were the same. In line with these results, it can be seen that the child's fear of medical procedures does not change whether he has hospital and medical procedure experience or not. A similar study by Eren and Örsal (2023) stated that the fear of medical equipment in hospitalized children was higher than that of children at school (33). Additionally, another study examining hospital fear reported that hospital fear was higher in children who experienced injections (30). In a similar study, children with hospital experience feared medical procedures more than those without (22). Hospitals are foreign environments where children are far from home, full of unknowns and often painful procedures, and where they see their parents less (34-36). Children may experience more fear in such an environment due to their experiences (1).

Hospital perception, emotional intelligence, and fear of medical procedures have a complex structure as they can be affected by many factors in daily life and need to be tested with different models. Importantly, future research should further investigate the design, feasibility, and effectiveness evaluation of interventions focused on increasing children's levels of emotional intelligence.

Limitations and Strengths

The strength of this study is that it is the first time that the role of emotional intelligence in the relationship between children's hospital perception and their fear of medical procedures has been investigated. The study results show the importance of emotional intelligence for developing strategies to reduce children's hospital perceptions and fears of medical procedures. However, this research had some limitations. First, although the results suggest the importance of emotional intelligence in the relationship between children's perceptions of hospitals and their fear of medical procedures, the cross-sectional study design must accurately investigate the causal process. Therefore, more longitudinal studies are needed. Another limitation of the study is that the scales used are based on self-report.

CONCLUSION

Study results showed that children's perception of hospitals predicted their fear of medical procedures. According to the mediated structural model analysis results, hospital perception had a statistically significant negative effect on the mediator variable, emotional intelligence. The impact of the mediator variable, emotional intelligence, on the dependent variable, fear of medical procedures, was not statistically significant. However, when the mediator variable, emotional intelligence, was included in the model, the path coefficient between hospital perception and fear of medical procedures was statistically significant. In the study, the indirect effect of hospital perception on fear of medical procedures through emotional intelligence was not found to be statistically significant.

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Ethical approval: *The Bayburt University Research Ethics Committee approved the research (2023/402-21). Before the researchers collected the data, the Declaration of Helsinki informed parents and children about the study, and their written/verbal consent was obtained. All methods were conducted according to relevant guidelines and regulations.*

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MEDICAL RECORDS-International Medical Journal

Research Article

An Approach to Thorax Morphometry with New Reference Values: A Morphological Study

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Abstract

Aim: Radiological evaluation is frequently used in the evaluation of healthy individuals or patients. When performing radiological evaluations, certain anatomical reference regions and values must be known in order to discover anomalies or variations. In this study, it was aimed to bring new anatomical reference values, which have not been studied before, to the literature and clinical evaluation.
Material and Method: This is a retrospective study that examines the patient archives in the Department of Radiology of Adıyaman University Training and Research Hospital. 57 women, 55 men, a total of 112 cases (age range 0-50 years) were included in the study. By using radiological measurements with Computed Tomography (CT); Manubrio-Sternal Angle (MSA), Manubrio-Vertebral Distance (MVD), Xipho-Vertebral Distance (XVD), Manubrio-Xiphoid Distance (MXD) were measured.
Results: When the measurements were evaluated statistically, there was a significant gender difference in Louis angle (SA) and MVD values of the individuals participating in the study; There was a significant age-related difference in MXD and XVD values.
Conclusion: With this study, some morphometric measurements of the thorax cavity are presented. It will contribute to the literature in determining the normal reference values of the thorax and adjacent structures. Knowing the normal anatomical structure in the clinic will contribute to the physician in the differentiation of pathologies, diagnosis.

Keywords: Chest deformity, computed tomography, sternal reference values, thorax morphometry

INTRODUCTION

Sternum; It is a flat bone that consists of the manubrium, body and xiphoid process sections that form the front part of the rib cage (1). Louis angle (SA) is formed between the manubrium and body of the sternum at the level of this joint facing the back (2-4). Because it points to some anatomical regions, the SA is an important anatomical reference point. The pleura on both sides, just below the level of the SA, is in direct contact, and the brachiocephalic veins converge at this point and form the superior vena cava. Also at this level, the trachea is divided into bronchi and the thoracic duct crosses the vertebral column (5).

The normal shape of the breastbone can vary depending on the age and the structure of the individuals. In studies conducted, sternum measurements can also be used for gender determination (6). Normal reference values were determined by measurements made in various populations (7,8). Differences in the sternum and thorax cause various pathologies in the clinic (6-10).

Pectus excavatum (Shoemaker chest), Pectus carinatum (Pigeon chest), Poland syndrome and sternaldefects are some of these. Chest deformities are common pathologies in the clinic and are frequently the subject of research articles (8-11).

There are important anatomical structures in the area localized behind the thorax and the sternum (9). Therefore, it is important to know the sternum anatomy and its variations and to distinguish it from pathological conditions and for many surgical fields.

The aim of this study is to present the anatomical and radiological approaches to cases frequently encountered in the clinic by making morphological analysis of the sternum. We believe that the data obtained from this study will provide ease of diagnosis and diagnosis to our physicians.

CITATION
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MATERIAL AND METHOD

This study is a retrospective study that examines the patient archives in the Department of Radiology of Adıyaman University Training and Research Hospital. Ethical approval for the study was granted by the Adıyaman University Medical Faculty Ethics Commitee for Non-ınterventional Procedures (Ethics Number is 2019-5-10). In our study, 57 women, 55 men, a total of 112 cases (age range 0-50 years), who underwent Thorax Computed Tomography (CT) between January 1, 2017 and January 1, 2019, were included. Radiological images were evaluated by a radiologist with over 10 years of experience. Cases with poor CT image quality, history of previous chest or thoracic surgery, with thorax CT examination due to trauma and tumor, with congenital skeletal system deformation (such as marfan syndrom, ankylospospondylitis), and extensive bone degeneration or osteporosis were excluded.

CT Protocol and Visualization Analysis

Figure 1 shows anatomical illustration of chest bones and thorax cavity in a saggital plane. This figure also shows some anatomical reference points snd sternal angle. When deciding on our methodology, we decided on our new reference measurements based on these reference points (sternal joint, xiphoid process etc.). Because these anatomical points are also preferred in indexes used in chest diseases and deformities. However, they are not fully sufficient.

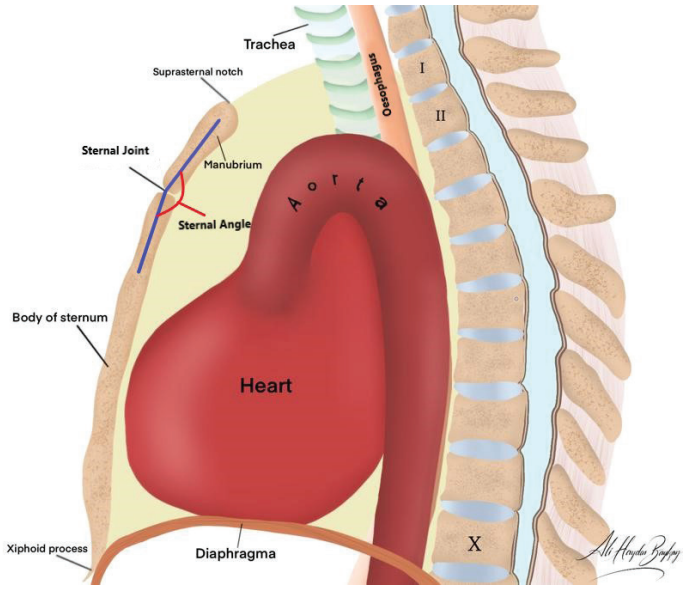

Figure 1. Illustration of the sternum and adjacent anatomical structures on sagittal plane

All cases were performed using a Toshiba Aquilion 64 (Toshiba Medical, Tochigi, Japan) computed tomography device. CT scanning; (FOV: 400mm, thickness: 3mm, kV: 120, mAs: effective mAs: 90). Radiological images were obtained in the supine position. Measurements were evaluated on sagittal reformat images (Figure 2). Measurements were calculated in millimeters and recorded.

Manubrio-Vertebral Distance (MVD): Measured in the midsagittal plane as the vertical distance that connects the upper edge of the sternum with the anterior edge of the vertebral column (Figure 2, a).

Xipho-Vertebral Distance (XVD): It was determined as a vertical distance that connects the lower edge of the xiphoid with the anterior edge of the vertebral column in the midsagittal plane (Figure 2, b).

Manubrio-Xiphoid Distance (MXD): The vertical line connecting the MVD and the XVD (Figure 2, c).

Manubrio-Sternal Angle (MSA): The angle between the horizontal line and the vertical axis parallel to the axis of the manubrio-sternal joint (Figure 2, d).

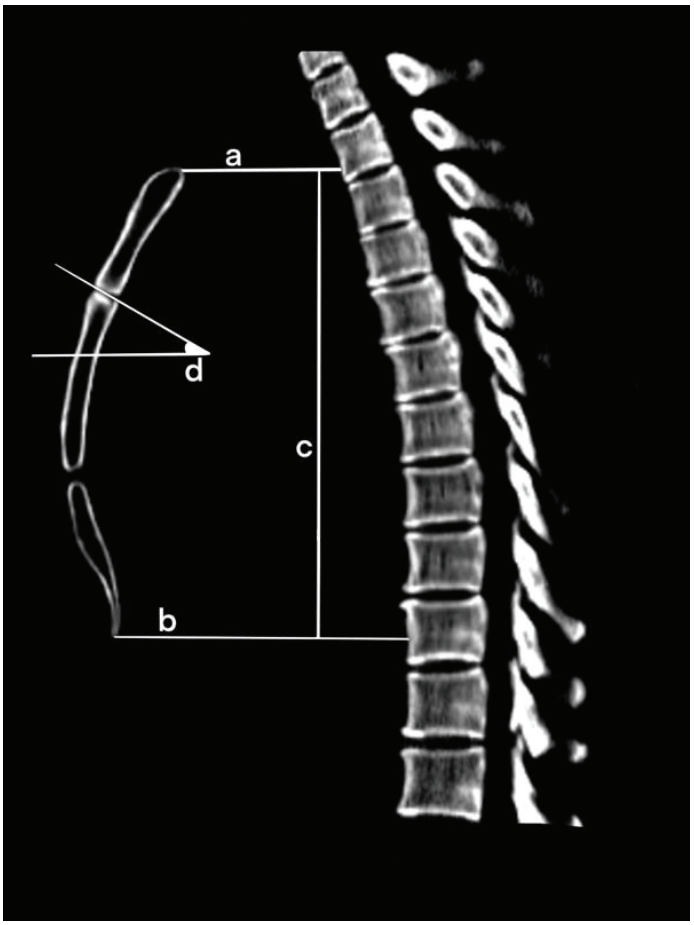

Figure 2. T1 weighted sagittal plane computed tomography image of thorax. Manubrio-vertebral distance (a), Xipho-vertebral distance (b), Manibrio-xiphoid distance (c), Manubrio-sternal angle (d).

Statistical Analysis

All the statistical analysis was performed with SPSS 15.0 for Windows (SPSS Inc.). The one sample Kolmogorov-Smirnov test was used to determine whether the data was distributed normally. Groups were compared using independent two samples t-test in terms of all the characteristics. The results were reported as mean±SD.

The standard normal distribution was used to determine the reference range. The reference interval is given as 95%. $p<0.05$ was considered statistically significant.

RESULTS

When the measurements were evaluated statistically, no significant difference was found in the gender-based measurements of the MSA in the individuals participating in the study (p=0.427), but when this angle was evaluated based on age, a statistically significant difference was found (p<0.001), (Table 1).

When the reference interval for age and gender is determined, the MSA in men is in the range of 25.74-29.84; in women, it was measured as 24.93-28.45. The reference values for the MSA between the ages of 0-30 were 22.07-26.27 degrees while the reference values for the age of 31 and above were 27.70-30.87. The XVD was shorter in males than females, and this difference was not significant (p=0.63). When the same measurement was evaluated as age-dependent, it was seen that the distance between 0-30 years was insignificantly shorter (p=0.347), (Table 1). Gender-based measurements of MVD were found to be statistically significant (p=0.032), (Table 1). The MXD was statistically significant (p=0.028). When age-dependent variables were analyzed, although there was a difference between men and women, this difference was not significant (Table 1).

Table 1. Age and gender based anthropometric measurement values of sternum

	MSA	MVD	XVD	MXD
Sex				
Male n=55	27.79±7.77	52.29±9.37	121.45±22.32	166.45±20.22
Female n=57	26.69±6.77	55.84±7.94	123.19±21.19	174.26±16.70
p value	0.427	0.032	0.673	0.028
Age				
0-30	24.17±7.19	55.42±10.47	119.98±20.01	166.62±22.22
31 and over	29.29±6.61	53.21±7.46	123.93±22.73	172.99±15.85
p value	<0.001	0.194	0.347	0.080

MSA: Manubrio-Sternal Angle, MVD: Manubrio-Vertebral Distance, XVD: Xipho-Vertebral Distance, MXD: Manubrio-Xiphoid Distance

The reference values of the MVD were determined as 49.81-54.77 in men and 53.78-57.90 in women. MVD in the 0-30 age range was 52.36-58.48, while it was between 31.42 and 54.99 at the age of 31 and above (Table 2). The reference values for the XVD are determined as 115.56-127.35 mm in men and 117.69-128.69 mm in woman. Reference values between the ages of 0-30 founded as 114.13-125.82 mm and over the age of 31 was 118.48-129.37 mm (Table 2).

The reference range for the MXD was 161.11-171.80 mm and 169.93-178.60 mm in males and women, respectively. The reference values between the ages of 0-30 founded as 160.13-173.11 mm and over the age of 31 was 169.19-176.78 mm.

Table 2. Reference interval values of the sternum based on age and gender

	MSA	MVD	XVD	MXD
Sex				
Male	(25.74-29.84)	(49.81-54.77)	(115.56-127.35)	(161.11-171.80)
Female	(24.93-28.45)	(53.78-57.90)	(117.69-128.69)	(169.93-178.60)
Age				
0-30	(22.07-26.27)	(52.36-58.48)	(114.13-125.82)	(160.13-173.11)
31 and over	(27.70-30.87)	(51.42-54.99)	(118.48-129.37)	(169.19-176.78)

MSA: Manubrio-Sternal Angle, MVD: Manubrio-Vertebral Distance, XVD: Xipho-Vertebral Distance, MXD: Manubrio-Xiphoid Distance

DISCUSSION

Sternum, which forms the front wall of the skeleton of thorax, is of a great importance in the clinic for surgical fields (12). Although various anatomical differences have been defined and standardized in morphometric studies conducted on many organs and systems, sufficient information about sternum morphology has not been found (13). Our study is radiology based and includes various morphological measurements of the sternum. We believe that these findings will be of great importance for anthropological and morphological researches.

Selthofer R. et al. reported that the general structure of the sternum has some basic differences although it is equal for both genders (13). In our study, when we examined the various measurements of the stenum, we found that some female morphometric measurements were different compared to men. We determined that the MVD was longer in women compared to the men and this measurement was statistically significant.

Measurements of the sternum are frequently used in gender determination (6,14,15). Despite this, the information that MVD is used for gender determination has not been found

in the literature. With this aspect, our study is a first in the literature in terms of MVD in the use of the sternum for gender determination and offers a different perspective. We think that this measurement will be useful in gender determination in forensic medicine.

Yet another data obtained from this study; MXD is longer in females than in males. In the study of Ateşoğlu et al., they stated that body length of sternum is a very useful parameter in determining gender, and the total sternum length is more reliable than the manubrium or the body of sterni length (16). Our data reveal that the MXD is between 161-171 in males and 169-178 in females. These statistically significant findings present a different approach to the data in the literature (16).

In our study; for MSA, age and sex-dependent reference value ranges that would contribute to the literature and to determine the surgical line were also determined. Hong-MingXu and his team emphasized that sternal angle values show a gender difference (17). In our measurements about MSA supports his study. We think that these important anatomically reference values will contribute to the physicians to determining the appropriate surgical intervention methods.

Measurements obtained directly from skeletal remains or radiological methods are very important in the formation of anthropological data in forensic medicine and to define surgical procedures. It has been reported in the literature that morphometric pelvic studies, morphometric parameters of the craniofacial region, morphometric analysis of the maxillary sinuses are the basic anatomical data for gender prediction (18). Also it's known that the sternum used as another anatomical structure to is gender determination, nowadays (6,16-18). Although the data of this study are compatible with the literature, the fact that it includes sternum measurements that have not been used in previous studies makes the study unique. At the same time, the new measurements mentioned in the study are also determinative in terms of gender determination.

Morphometric data belonging to the sternum have been fixed with the studies conducted to determine the differences between the populations (18). When the population-specific study datas are examined; average sternum measurements in South African, Indian, European, US and Canadian populations were determined (18-24). We believe that our study data will also be of great importance for the sternal measurements of the Turkish population.

CONCLUSION

In this study, anatomical and radiological approaches to pathologies frequently encountered in the clinic are presented by obtaining anatomical and morphometric measurements of the sternum. These data, which indicate that the MVD can be used for gender determination, may be useful in forensic medicine. In addition, the data obtained from our research will assist surgeons in determining the appropriate surgical intervention before surgery. Our study data will also contribute to the literature in determining the normal reference values of the sternal measurements.

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Research Article

Evaluation of Online Information on Bruxism in Children: A Study on YouTube™ Videos

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Abstract

Aim: Bruxism in children is a common health issue that causes discomfort in the jaw joint and surrounding muscles, negatively affecting daily activities and quality of life. As individuals increasingly turn to online platforms for health information, the accuracy and reliability of this information become crucial. This study aims to evaluate the content and quality of online information on bruxism in children, facilitating access to accurate and reliable patient information and aiding in more informed decision-making regarding treatment options.

Material and Method: This study searched the term 'Bruxism in Children' on YouTube™, evaluating the first 100 relevant videos and selecting 18 videos for further analysis. Data on view count, video length, time since upload, likes and dislikes, number of comments, uploader, interaction index, and views were recorded. The Quality Criteria for Consumer Health Information (DISCERN), the Journal of American Medical Association (JAMA), and Global Quality Scale (GQS) assessed patient viewers' medical accuracy, content quality, understandability, and suitability.

Results: Most videos were uploaded by health professionals and educators. However, videos uploaded by health professionals did not have significantly higher GQS scores than those uploaded by patients. When categorized by the source of upload, videos from health professionals did not score significantly higher in reliability than other groups.

Conclusion: There is a scarcity of videos on bruxism in children on the YouTube™ platform, providing limited benefits and insufficient information. Despite expectations for more accurate information from health professional-produced content, these professionals must upload more comprehensive and understandable videos.

Keywords: Bruxism in children, Global Quality Scale, video, Youtube

INTRODUCTION

Bruxism can be described as involuntary muscle activity of the chewing system (1). This muscle activity may manifest as teeth clenching or grinding (2). Although it can occur at any stage of life, it is known to be expected in childhood (3). The literature shows that bruxism is classified as diurnal bruxism, occurring during the day while awake, or nocturnal bruxism, occurring during sleep (4,5). Various studies on the causes of bruxism have been conducted, and researchers agree on the idea that it may emerge idiopathically, without any specific cause, or iatrogenically, due to neurological, psychiatric, or similar reasons (6,7). Bruxism is a problem affecting children and adults (8). The literature predominates with views that it may be more common in children compared to adults and tends to decrease with age (9). This problem damages the teeth and surrounding periodontal tissues and can cause discomfort in the chewing muscles and temporomandibular joint, leading to sleep disorders (10). While different treatment options are suggested for adults, choices for treatment in children are more limited and dependent on many factors (11). A study indicated that the prevalence of bruxism among children ranges from 3.5% to 40.6% (1). When examining its etiology, it is argued that emotional factors, high levels of stress and anxiety, occlusion disorders, and widespread cavities can also contribute to this issue, besides the potential relation to the central nervous system (8). Recent studies have focused on the existence of a relationship between bruxism and genetics (12). Diagnosis of bruxism in pediatric patients is often based on reports from families, highlighting the importance of family awareness regarding bruxism; however, lack of knowledge about bruxism

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usually complicates its detection (13).

In today's world, thanks to computers or smartphones that nearly everyone owns, obtaining information on any subject has become incredibly simple due to the increased internet use (14). The preference of individuals for online methods to access information has also directed health professionals to focus on this area, as evidenced by studies analyzing YouTube™ videos, especially on systemic diseases such as diabetes and hypertension (15,16). Since health professionals can reach individuals more easily and quickly through these online platforms, such studies have also become popular in dentistry (17,18).

YouTube™, one of the most popular video-sharing sites worldwide, including in our country, is increasingly used for acquiring information (19). Compared to other social media platforms, YouTube™ is visited multiple times daily by individuals seeking information on general health and dental and aesthetic practices due to its ability to provide visual and verbal information (20).

The Quality Criteria for Consumer Health Information (DISCERN), a 16-question instrument developed in 1999 by Charnock and colleagues at the University of Oxford, initially used for assessing the quality of written information sources, is now preferred for evaluating the quality of web-based information (21,22).

Silberg, Lundberg, and Musacchio recommend using the Journal of American Medical Association (JAMA) criteria for evaluating the standards of information obtained from health-related written information sources. These criteria assess four essential features that health-related website content should contain, including authorship, attribution, financial support, disclosures of conflicts of interest, and update dates in the content, making it more objective than other assessment tools. It's a measurement tool developed to measure the reliability of information based on precise data without considering the individual knowledge and competence of the evaluator (23,24).

The Global Quality Score (GQS) is an assessment tool consisting of a 5-point scale (25) that ranges from low quality (not beneficial for patients) to high quality and utility (very useful for patients).

This study aims to evaluate the reliability, quality, and content of the most-watched videos on YouTube™ (www.youtube.com) related to bruxism in children and determine whether they benefit patients.

MATERIAL AND METHOD

Our study did not require ethical committee approval as it was conducted using a publicly available internet site and did not involve humans or samples taken from humans.

Video Selection and Data Collection

In January 2024, when the phrase "bruxism in children" was searched on Google Trends™ (https://trends.google.com/trends/), no popular keyword related to the topic was found. The first 100 videos that appeared when "bruxism in children" was typed into YouTube™ (www.youtube.com) were reviewed. Studies related to YouTube™ have noted that up to 90% of users look at the first three pages of search results, and 79% of those who do not find what they are looking for check other pages (26). Another study suggested that 95% of YouTube™ searchers watch the first 60 videos and are unlikely to continue beyond the first five pages (27). Therefore, the first 100 videos were examined, and their URLs were archived since search results may vary on different days. The selection of videos for the study was completed on the same day by two experienced professionals, an oral and maxillofacial surgeon and a pediatric dentist, with the data from the first observer (E.E.Ö.) being the basis for evaluation and the data from the second observer (T.N.Ş.) used for comparison in terms of correlation (January 20, 2024).

The inclusion criteria determined that the videos must be in Turkish, longer than 30 seconds but shorter than 30 minutes, contain spoken narration without text on screen, be relevant to the topic, and not contain advertisements. Additionally, for each video, information such as the title and URL, video duration (minutes: seconds. milliseconds), time elapsed from the upload date to the date of the study (in days), who uploaded the video (healthcare professionals/laypeople), number of views, likes, and dislikes, number of comments were recorded, and the Interaction Index (%) and Viewing Rate (%) were calculated (20).

Interaction Index (%) = ((Number of Likes - Number of Dislikes) / (Number of Views)) × 100

Viewing Rate (%) = ((Number of Views) / (Time Since Upload in Days)) × 100

The DISCERN instrument was used to evaluate the reliability and quality of information in the videos (23). The DISCERN questionnaire consists of 16 questions and three sections. Each question is scored between “1” (no) and “5” (yes). The scores at the end of the evaluation range between “8 to 40” for the reliability section, “7 to 35” for the treatment options section, and “1 to 5” for the overall score section evaluating the website. The total DISCERN score obtained after all evaluations ranges between “16 to 80”. A score range of “16 to 26” is considered “very poor,” “27 to 38” as “poor,” “39 to 50” as “fair,” “51 to 62” as “good," and scores above “63” as “excellent” quality (22).

The study used the JAMA scoring to evaluate the quality and safety of medical information in the videos (23). JAMA evaluation criteria assess health-related information on the internet against basic quality standards. In the JAMA scale evaluation, four essential features were investigated for clear expression: authorship, attribution, disclosure, and currency. Authorship: Authors and contributors should share their affiliations and relevant credentials. Attribution: References and sources for all content should be clearly stated, along with copyright information. Disclosure: Potential conflicts of interest, website ownership, sponsorship, advertising, insurance

responsibility, commercial funding, or support should be clear and comprehensive. Currency: Dates of publication and updates should be stated. A score between 0 and 1 was given to evaluate each video against the JAMA criteria. A score of '1' was given if the criterion was met and '0' if not, with the total JAMA score derived from the sum of these points (24).

GQS was used to evaluate the overall quality of the videos. The scoring system is based on the quality and overall usefulness of the video to the patient (28). The scoring is as follows: 1 point for "Low quality, slow video flow, insufficient information, not useful for patients"; 2 points for "Generally low quality and slow flow, some information but missing key details, partially useful for patients"; 3 points for "Somewhat useful for patients, some important information available but insufficient, medium quality"; 4 points for "Useful for patients, generally well-listed information but with missing parts, good quality"; and 5 points for "High quality and flow, beneficial for patients" (25).

Statistical Analysis

Data analysis of the study was performed using the IBM SPSS Statistics Version 26 (SPSS Inc., Chicago, IL, USA) software package. The normal distribution of the data was calculated using the Shapiro-Wilk test. According to the results, most data did not follow a normal distribution; therefore, nonparametric tests were utilized for comparative analyses. Descriptive data are presented as frequency (percentage), count, and mean ± standard deviation. The Mann-Whitney U test was used to compare two groups, while the Kruskal-Wallis test was employed for comparisons among more than two groups. The Spearman correlation test was applied to analyze the relationship between scales. The Chi-Square test was used to compare categorical data. The interclass correlation coefficient (ICC) was calculated to determine the degree of agreement between two observers. This research accepted a statistical significance value of $p<0.05$.

RESULTS

As shown in Figure 1, 100 videos were initially reviewed as part of the research. Of the reviewed videos, 18 were deemed suitable and included in the study. A significant portion of the excluded sources was directed toward adults and hence could not be included in the study's scope.

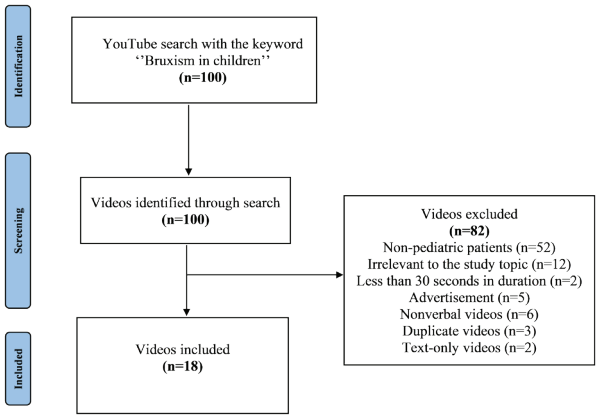

Figure 1. PRISMA Flowchart of the process of identification and screening of the included videos

As presented in Figure 2, of the 18 sources included in the study, 11.1% were prepared by pediatricians, 22.2% by dentists, and 38.9% by pediatric dentists.

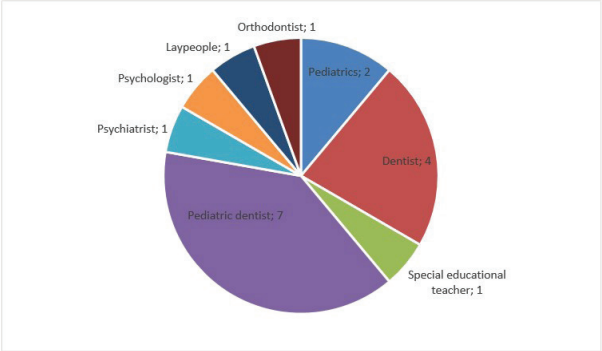

Figure 2. Distribution of videos by sources

In the scope of the study, the mean views of the analyzed videos are 7332.5±10648.7, the mean duration is 2 minutes and 26 seconds ±1 minute and 38 seconds, the mean number of days since upload is 1597.5±1228.6, and the mean likes are 36.6±57.0. The mean number of comments on the videos is 2.6±7.5, the mean interaction index is 2.6±4.5, and the mean viewing rate is 421.0±454.9 (Table 1).

Table 1. Basic descriptive information related to the videos

	n	Min	Max	Mean	SD
Number of views	18	28	34000	7332,5	10648,7
Duration (minutes:seconds.milliseconds)	18	00:57:00	06:23:00	02:26:10	01:38:34
Days since upload	18	240	4015	1597.5	1228.6
Number of likes	18	1	224	36.6	57.0
Number of dislikes	18	0	0	0.0	0.0
Number of comments	18	0	32	2.6	7.5
Interaction Index (%)	18	0	15	2.6	4.5
Viewing Rate (views per day)	18	3.83	1291.58	421.0	454.9

While there was a statistically significant difference among the sources of the videos in terms of their durations and the number of likes (p<0.05), no statistically significant difference was found among the sources in terms of the number of views, the number of days since upload, the number of comments, the interaction indices, and the viewing rates (p>0.05). The most extended video duration was observed in videos produced by pediatricians, and the highest mean number of likes was also attributed to videos created by pediatricians. The highest mean number of views was identified in videos from the laypeople group, whereas the lowest viewing rate belonged to the dentist group, despite these videos being the oldest. The highest mean number of comments was observed in videos produced by pediatricians, and the highest interaction index mean was found in videos from the pediatric dentist group (Table 2).

Table 2. Detailed information of videos by uploaders (mean ± standard deviation)

	Number of views	Duration (minutes:seconds. milliseconds)	Days since upload	Number of likes	Number of comments	Interaction Index (%)	Viewing rate (views per day)
Pediatric dentist (n=7)	6804.4±12240.8	01:44.29±00:20.80	1455.6±1637.0	22.6±36.4	1.3±2.2	4.8±6.9	424.7±471.1
Dentist (n=4)	2194.5±3809.0	01:25.25±00:26.96	1962.5±1294.9	6.3±6.0	0.3±0.5	1.3±1.2	78.5±86.4
Pediatrician (n=2)	4545.5±6016.8	04:13.00±03:03.85	730.0±516.2	114.0±155.6	16.0±22.6	2.0±0.8	616.0±833.6
Other (n=5)	13297.0±12727.7	03:30.80±01:58.07	1851.2±667.7	49.4±35.6	0.8±1.1	0.6±0.5	611.7±430.8
p	0.483	0.044*	0.686	0.030*	0.044*	0.437	0.340

In the study, the mean DISCERN value for the first observer (E.E.Ö.) was 47.3, while the second observer's (T.N.Ş.) mean DISCERN value was 47.05, with an ICC=0.98 calculated. This indicates a very good agreement between the two observers. For JAMA, the ICC was calculated as 1, showing perfect agreement between the observers. The first observer's mean GQS was 3.4, while the second observer's GQS was 3.39, with an ICC=0.77, indicating good agreement between the two observers.

Looking at the total JAMA score classification of the analyzed videos, 83.3% scored 1, 11.1% scored 0, and 5.6% scored 4. According to DISCERN, 66.7% of the videos were rated as moderate quality, and 33.3% were rated as good quality. When evaluating the GQS of the videos, 61.1% were considered "Somewhat useful for patients, some important information available but insufficient, medium quality," and 38.9% were "Useful for patients, generally well-listed information but with missing parts, good quality." (Table 3).

Table 3. Classification of videos by JAMA, DISCERN, and GQS

		f	%
JAMA	**0**	2	11.1
	1	15	83.3
	4	1	5.6
DISCERN	**Moderate**	12	66.7
	Good	6	33.3
GQS	**Somewhat helpful for patients, some critical information available but insufficient, medium quality**	11	61.1
	It is helpful for patients, generally well-listed information but with missing parts, good quality	7	38.9

The mean JAMA scores of the videos were determined to be 1.1±0.8, the mean DISCERN scores were 47.3±5.1, and the mean GQS scores were 3.4±0.5.

Basic information related to the videos was compared according to DISCERN scores. According to the results, there was no statistically significant difference between DISCERN scores and the number of views (p>0.05). Still, the mean number of views for videos classified as "Good" was higher. No statistically significant difference was found between DISCERN scores and duration (p>0.05), yet the mean duration of videos classified as "Good" was longer. There was no statistically significant difference between DISCERN scores and the number of days since upload (p>0.05), but the mean number of days since upload was higher for videos classified as "Moderate." There was no statistically significant difference between DISCERN scores and the number of likes (p>0.05), but the mean number of likes for videos classified as "Good" was higher. No statistically significant difference was found between DISCERN scores and the number of comments (p>0.05), yet the mean number of comments was higher for videos classified as "Moderate." There was no statistically significant difference between DISCERN scores and the interaction index (p>0.05), but the mean interaction index

for videos classified as "Good" was higher. No statistically significant difference was found between DISCERN scores and the viewing rate (p>0.05); however, the mean viewing rate for videos classified as "Good" was higher (Table 4).

Table 4. Examination of data according to DISCERN

	Moderate (n: 12)	Good (n: 6)	p
Number of views	7041.4±10164.1	7914.7±12555.9	0.964
Duration (minutes:seconds.milliseconds)	01:57.00±01:26.95	03:24.50±01:41.38	0.032
Days since upload	1840.4±1344.7	1111.7±853.8	0.291
Number of likes	34.4±65.6	40.8±39.4	0.291
Number of comments	3.3±9.1	1.0±1.7	0.964
Interaction index (%)	2.0±4.0	3.6±5.8	0.213
Viewing rate (views per day)	392.3±442.5	478.3±516.7	0.494

In the JAMA category of authorship, attribution, and disclosure, only 1 video evaluated in the "Other" section was accepted. Videos from other sources did not receive positive evaluations in this section. In the currency category, all videos from pediatric dentists and pediatricians were accepted, 75% of the videos from dentists were accepted, and 80% of the videos evaluated in the "Other" category were accepted. The highest mean JAMA score was found in videos categorized under "Other," while the lowest mean JAMA score was found in videos belonging to dentists (Table 5).

Table 5. Evaluation of video sources according to JAMA

	Authors	Attribution	Disclosure	Currency	Total JAMA score (mean ±SD)
Pediatric dentist (n=7)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (%100.0)	1.00±0.00
Dentist (n=4)	0 (0.0%)	0 (0.0%)	0 (0.0%)	3 (%75.0)	0.75±0.50
Pediatrician (n=2)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (100.0%)	1.00±0.00
Other (n=5)	1 (20.0%)	1 (20.0%)	1 (20.0%)	4 (80.0%)	1.40±1.15

A statistically significant positive correlation of moderate strength was identified between the DISCERN and JAMA scores of the videos (r: 0.552, p<0.05). A statistically significant positive and strong correlation was found between the DISCERN and GQS of the videos (r: 0.829, p<0.05). A statistically significant positive but weak correlation was detected between the DISCERN scores and GQS of the videos (r: 0.382, p<0.05) (Table 6).

Table 6. Examination of videos' relationship between JAMA, DISCERN, and GQS (1st observer)

	DISCERN	JAMA	GQS
DISCERN	1	0.552**	0.829**
JAMA		1	0.382*
GQS			1

DISCUSSION

Although numerous studies on health topics have been conducted on YouTube (14,17,19), the limited number of YouTube studies on "bruxism in children" in Turkish within the literature prompted our investigation into this subject.

During the study, 100 videos were initially reviewed by two observers, of which only 18 were deemed suitable for inclusion. The aim was to examine videos on bruxism in children; however, it was found that videos related to teeth grinding primarily explain the condition in adults, suggesting that while numerous videos on teeth grinding exist, only a few address the condition in children. For this, the videos were evaluated by experienced researchers from pediatric dentistry (T.N.Ş), and oral and maxillofacial surgery (E.E.Ö), two branches that often work cooperatively on bruxism in children, and their compatibility was found to be good and very good. We believe that working with researchers from different branches related to the subject in studies involving such subjective evaluations will benefit the study results.

When evaluating the sources of the included videos, 11.1% were from pediatricians, 22.2% from dentists, and 38.9% from pedodontists, which seems reasonable and aligns with the literature (18).

The shortest video examined during the study was 57 seconds, and the longest was 6 minutes and 23 seconds. This duration range aligns with video lengths used in other studies (29,30).

The analyzed videos had a mean view count of 7332, a mean duration of 02:26, a mean of 1597 days since upload,

and a mean of 36.6 likes. The mean number of comments was 2,6, the interaction index mean was 2,6, and the mean viewing rate was 421, with these figures varying depending on the topic according to the literature (18,29).

Statistically significant differences were found among the sources of the videos in terms of their durations ($p<0.05$), with the longest mean duration observed in videos produced by pediatricians, possibly due to more informative content. Similarly, a statistically significant difference was observed in the number of comments ($p<0.05$), with the highest mean number of comments found in videos by pediatricians, possibly due to the diversity of topics covered in longer videos encouraging more comments.

No statistically significant difference was observed in viewing rates among the video sources ($p>0.05$), but the lowest mean was found in dentist group videos. This may indicate an interest in videos produced by pediatric dentists or pediatricians regarding the issue of teeth grinding in children. The literature explains why health professionals' videos are viewed more frequently (18).

The quality of video content was evaluated using JAMA, DISCERN, and GQS. According to the total JAMA score, 83.3% scored 1, 11.1% scored 0, and 5.6% scored 4, suggesting low-quality videos. According to DISCERN, 66.7% of the videos were rated moderate and 33.3% good quality. According to GQS, 61.1% were deemed "somewhat useful but insufficient, medium quality," and 38.9% as "useful, good quality," indicating a medium quality overall.

The low JAMA scores suggest deficiencies in the videos regarding authorship, references, copyright information, and currency. Only one video categorized as "other" by health professionals addressed these aspects adequately, though currency scores were better among health professionals' videos.

A statistically significant moderate positive correlation was found between DISCERN and JAMA scores (r: 0.552, $p<0.05$), a strong positive correlation between DISCERN scores and GQS (r: 0.29, $p<0.05$), and a weak positive correlation between DISCERN scores and GQS (r: 0.382, $p<0.05$), suggesting a positive relationship between these scales and their reliability.

In a similar study conducted in English with keywords related to children's bruxism, 80 videos were analyzed, yielding mean JAMA, DISCERN, and GQS scores of 1,3, 2,4, and 2,8, respectively. Similar to our study, these low scores reflect the lack of accurate and reliable information on pediatric bruxism on YouTube™ in Turkish and English (30).

The study's limitations include using a single search term, being conducted solely in Turkish, and including a limited number of videos. YouTube is a constantly updated platform, making it challenging to comment on the future quality of videos. Variations might also be seen in videos across different geographies and languages.

CONCLUSION

The study found a limited number of videos on bruxism in children on the YouTube™ platform, indicating that the videos provided low benefits and lacked sufficient information. Health professionals should upload more and clearer videos, as their content is expected to contain more accurate information.

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Research Article

An Investigation of the Effect of Anemia on Prognosis in Chronic Obstructive Pulmonary Disease

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Abstract

Aim: The majority of healthcare facility admissions in individuals with chronic obstructive pulmonary disease (COPD) are attributable to exacerbations, known to negatively impact prognosis. This study aims to examine the relationship between anemia in COPD patients and the frequency of exacerbations, and consequently, its effect on prognosis.

Material and Method: Twenty-nine anemic, 30 normocytic, and 28 polycythemic patients diagnosed with COPD were enrolled and evaluated based on their Forced Expiratory Volume in One Second (FEV1) values, symptoms, exercise ability, and number of exacerbations. At one-year follow-up appointments, the history of emergency department visits, outpatient clinic visits, intensive care admissions, and hospitalizations requiring respiratory support during the year were recorded for patients.

Results: Similar to other research on anemia in COPD, the anemia seen in the current study was most typically consistent with chronic disease anemia. When the anemic group was compared with the normostemic and polycystic groups with regard to the frequency of exacerbations, both the count of emergency department visits and hospitalizations requiring intensive care were found to be statistically meaningfully higher in the anemic group compared to the non-anemics.

Conclusion: The results obtained in the present study show that anemia in COPD is associated with increased hospital admissions and exacerbations. Given that increased exacerbation frequency is a known poor prognostic factor, it can be inferred that anemia, by increasing exacerbation frequency, contributes to poor prognosis.

Keywords: Chronic obstructive pulmonary disease, anemia, exacerbation, prognosis

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is defined as persistent and often progressive airflow restriction accompanied by chronic respiratory symptoms (1). It ranks third among the leading causes of death worldwide (2). COPD develops as a result of a chronic inflammatory process triggered primarily by harmful gases and particles, notably cigarette smoke. Inflammation not only remains confined to the lungs but also exhibits systemic characteristics (3). In COPD, compensatory secondary erythrocytosis is expected to occur to correct tissue oxygen transport impaired by prolonged hypoxemia (4). However, contrary to popular belief, polycythemia is observed in approximately 6% of COPD patients, while anemia is a much more common finding, occurring in 13-33% of patients (5). Anemia develops in COPD patients due to a variety of factors, including nutritional deficiencies, stress ulcers particularly in the context of frequent systemic steroid use, continued smoking leading to carboxyhemoglobinemia and shortened mean erythrocyte lifespan due to chronic inflammation, erythropoietin resistance, and disruption of iron homeostasis (6). It is known that in COPD, chronic inflammation causes a decrease in the proliferative response to erythropoietin and a shortening of the lifespan of red blood cells. In addition, in COPD, anemia of chronic disease develops due to factors such as a decrease in erythropoietin production triggered by hypoxia, deterioration in iron metabolism, and iron deficiency due to malnutrition (7,8). Anemia in COPD

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is associated with impaired tissue oxygen transport, exercise intolerance, and increased mortality. Studies have shown that in COPD, characteristics of anemia are highly consistent with chronic disease anemia (CDA) (9,10). CDA is a form of anemia that can arise in various conditions, both immune and non-immune, such as infection, inflammation, neoplastic diseases, severe trauma, heart failure, and diabetes mellitus (11). In a two-year prospective study involving 130 patients aimed at determining the frequency of anemia in COPD, it was found to be 6.2%. Additionally, in the anemic group, statistically significantly lower body mass index (BMI), higher erythropoietin, and interleukin-6 (IL-6) assays were found compared to non-anemic individuals (12). Anemic COPD patients have a greater mortality rate and require longer hospitalizations than non-anemic individuals (13). It is known that increased hospital admissions due to acute exacerbations result in a worse patient prognosis (14). There are few studies about the effects the effects of anemia on exacerbation frequency and, consequently, prognosis. The purpose of this study was to examine the effect of anemia on exacerbation frequency and, consequently, the prognosis of COPD.

MATERIAL AND METHOD

Following local ethics committee approval on November 18. This study is a prospective observational study. Ethics permission was obtained before starting the study (project number: 2394). Twenty-nine anemic, 30 normocytic, and 28 polycythemic patients diagnosed with COPD were enrolled in the study. Patients with chronic kidney failure, chronic liver failure, acute and chronic infections, autoimmune diseases, malignancies, a history of heart failure, hematological diseases, and gastrointestinal bleeding, which can be causes of anemia, were excluded from the study. Three patients with malignancies detected during follow-up were excluded. As a total, 87 individuals included in the study were observed for one year. Tests for chronic disease anemia, iron deficiency anemia, vitamin B12, and folate deficiency were requested. The threshold value for anemia was accepted as a hemoglobin concentration of <13 g/dL for males and 12 g/dL for females (15).

The diagnostic criteria for chronic disease anemia include hemoglobin concentration under 13 g/dL in males and 12 g/dL in females, absence of another cause to explain anemia, normal or elevated serum ferritin levels, low total iron-binding capacity and transferrin saturation, and normal levels of vitamin B12 and folate (16).

All patients diagnosed with COPD were evaluated based on their Forced Expiratory Volume in One Second (FEV1) values, symptoms, exercise ability, and exacerbation frequency. The modified Medical Research Council (mMRC) dyspnea classification was administered for the evaluation of symptoms (17). The patients' physical activity ability was evaluated using the 6-minute walking distance (6MWD) test.

The BODE index (body mass index [BMI], airflow obstruction, dyspnea, and exercise capacity in COPD) was appraised (Table 1). This index is calculated based on four predictors. Body mass index (BMI), FEV1, mMRC dyspnea scale, and the 6MWD test. Scoring is done in four ways in the BODE index. The highest score is indicative of the worst disease.

At one-year follow-up appointments, the history of emergency department visits, outpatient clinic visits, intensive care admissions, and hospitalizations requiring respiratory support during the year were questioned through face-to-face interviews or telehealth consultations.

Table 1. BODE index calculation

Variables	0	1	2	3
FEV1 (% of predicted)	>65	50-65	35-49	<35
mMRC Dyspnea Scale	0-1	2	3	4
6MWD (meters)	>350	250-349	150-249	<149
BMI (kg/m²)	>21	<21	-	-

FEV1: forced expiratory volume in one second, mMRC: modified medical research council, 6MWD: 6-min walking distance, BMI: body mass index

Statistical Analysis

Statistical assessments were carried out using the SPSS (Statistical Package for Social Sciences) 15.0 software (Chicago, IL). Quantitative variables were pointed out as mean and standard deviation values, while qualitative variables were expressed as numbers and percentages. Parameters were compared for normal distributions using the Student's t-test and for non-normal distributions using the Mann-Whitney U test. Qualitative variables were assessed using the Chi-Square test. The mean values of quantitative variables before and after treatment in each group were assessed by the Paired-Samples T-test. A p value of <0.05 was defined as statistically significant in all analyses.

RESULTS

A total of 87 patients with COPD (29 anemic, 30 normocytic, 28 polycythemic) were included in this research.

The demographic features of the patients are shown in Table 2.

Table 2. Demographics and characteristics of the patients

	Anemic	Normocytic	Polycythemic
Male (n)	24	26	24
Female (n)	5	4	4
Smoking (pack-years)	43.5±4.8	36.9±4.8	46.9±6.7
Never smoked	5	2	4
Ex-smoker	23	21	21
Current smoker	1	7	3
LTOT +	10	24	12
LTOT -	19	6	14
No comorbidities	15	13	14
Exitus	1	0	2
6MWD	0 (0-420)	400 (0-550)	330 (0-580)
Annual number of emergency-outpatient clinic visits	5 (0-20)	0 (0-20)	1 (0-15)
Annual number of intensive care hospitalizations	1 (0-3)	0 (0-2)	0 (0-2)
Ferritin (14-30 ng/ml)	157.0±29.2		
Folic acid (4.6-18.7 ng/mL)	9.7±0.9		
Vitamin B12 (214-900 pg/mL)	530.8±69.8		

Parametric data is shown as mean±S.E.M or median (minimum-maximum); 6MWD: 6-min walking distance, LTOT: long-term oxygen therapy

When comparing anemic and normocytic patients (Table 3), the anemic group was older (p=0.03), had a lower FEV1 value (p=0.02), and had a statistically meaningful shorter 6MWD (p<0.05). BMI and smoking (pack-years) showed no significant differences.

When comparing anemic and polycythemic patients (Table 3), the two groups had no significant age differences, FEV1 value, and smoking history. However, when compared based on BMI, the anemic group had a lower BMI (p=0.02), and the 6MWD was meaningfully shorter in the anemic patients (p<0.001).

BMI was highest in the polystemic group and lowest in the anemic group. This result was statistically meaningful (p=0.03).

Table 3. Comparison of laboratory, demographic and respiratory parameters of the patients

	Anemic	Normocythemic	Polycythemic	P1	P2
Age (years)	67.1±1.6	60.5±2.5	63.0±1.8	0.03	0.10
BMI (kg/m²)	25.7±0.8	26.3±0.7	29.2±1.3	0.59	0.02
Hemoglobin (g/dl)	11.7±0.1	14.6±0.1	17.8±0.2	<0.001	<0.001
Hematocrit (%)	37.0±.5	44.1±0.5	55.3±0.7	<0.001	<0.001
FEV1 (%)	45.1±4.1	59.6±4.1	47.7±3.5	0.02	0.64
FEV1 (ml)	112.7±10.1	175.9±11.4	126.9±10.3	0.03	0.05
6MWD (m)	93.4±25.6	388.0±23.3	286.4±32.4	<0.001	<0.001

P1: anemic-normocytic P2: anemic-polycythemic comparison; parametric data is expressed as mean±S.E.M or median (minimum-maximum); BMI: body mass index, 6MWD: 6-min walking distance, FEV1: forced expiratory volume in one second

When mMRC dyspnea score and BODE score were compared between the anemic and non-anemic groups (Table 4), both scores were higher in the anemic group. This result was statistically significant (p<0.001).

When comparing the mean hemoglobin levels of 39 patients receiving Long-Term Oxygen Therapy (LTOT) and 48 patients not receiving LTOT, no significant difference was found (14.9±0.3 and 14.3±0.5, respectively, p=0.35).

Table 4. Comparison of mMRC and BODE scores between anemic and non-anemic subjects

	Anemic (n: 29)	Non-anemic (n: 58)	p
mMRC	3 (0-4)	2 (0-4)	<0.001
BODE	7 (0-10)	3 (0-10)	<0.001

Parametric data is shown as median (minimum-maximum); mMRC: modified medical research council, BODE: body mass index, airflow obstruction, dyspnea, and exercise capacity in COPD

When comparing exacerbation frequency among the anemic, normocytic, and polycythemic groups, it was found that both emergency department and outpatient clinic visits, as well as the number of hospitalizations requiring intensive care, were higher in the anemic group (Table 5). This difference was statistically significant (p<0.01).

Table 5. Comparison of patients in terms of exacerbation frequency

		Average number of visits	P
Annual emergency - outpatient clinic visits	**Anemic**	**6.6±0.9**	<0.001
	Normocytic	**1.8±0.7**	
Hospitalization requiring intensive care	**Anemic**	**0.8±0.1**	<0.001
	Normocytic	**0.1±0.0**	
Annual emergency - outpatient clinic visits	**Anemic**	**6.6±0.9**	0.01
	Polycythemic	**3.4±0.9**	
Hospitalization requiring intensive care	**Anemic**	**0.8±0.1**	< 0.001
	Polycythemic	**0.2±0.1**	

Parametric data is expressed as mean ±S.E.M

During the one-year follow-up, two polycythemic patients and one anemic patient died. In the normostemic group, all patients were alive after one year. Statistical evaluation of patient groups in terms of mortality could not be performed due to a total of 3 patient deaths.

When anemic COPD patients were evaluated for the etiology of anemia, 21 patients (72.5%) were consistent with chronic disease anemia.

DISCUSSION

An increasing body of evidence has shown that COPD is a more complex disease than a simple airway restriction. Factors associated with mortality in COPD include malnutrition, increased dyspnea, decreased exercise capacity, and the presence of comorbid conditions (18).

In assessing the severity of COPD and mortality risk, multidimensional indices like BODE are commonly used, but FEV1 alone can also be utilized (19). Higher BODE score were related with a higher mortality (20).

Although polycythemia is commonly assumed to be the most prevalent hematologic abnormality in COPD, studies have demonstrated that anemia is actually more commonly observed (9). In a prospective study by C. Cote et al. involving 683 stable COPD patients, the prevalence of anemia was found to be 17%, while the prevalence of polycythemia was 6%. In contrast, there are also publications stating that the percentage of anemia is lower in COPD (9,12). It is difficult to define the true percentage of anemia in COPD. Factors such as the omission of patients' comorbidities, inclusion of different patient groups, variations in the severity of lung disease, differences in age distribution, and socioeconomic disparities can affect the true prevalence of anemia etiologies. Previous studies revealed that the percentage of anemia in COPD ranges from 7.5% to 34% (21).

It was also shown that hematocrit value decreases with age and increasing severity of obstruction in COPD, while it increases with increasing BMI (22). In one study, it was reported that anemia can be observed in up to 10% of people over the age of 65. In the same study, nutritional factors -especially iron deficiency-, chronic inflammation, and unexplained causes were suggested to be the most common causes in the occurrence of senile anemia (23). In this study, when comparing the anemic and normocytic groups, it was observed that anemic patients were older and had lower FEV1 values, while their BMI values were similar. While anemia and polycythemia patients showed no difference in terms of age and FEV1, BMI was found to be lower in anemic patients. However, the mean BMI of the anemic group was still within the normal range. Considering that anemic patients included in the present study were older, Senility may be an influential factor in the developming of anemia in these patients.

One important factor associated with mortality in COPD is the post-bronchodilator FEV1 value. There are publications showing that the BODE index is superior to FEV1 alone in determining mortality in COPD (19). In the present study, mean BODE score was 10 in anemic patients and 6 in polycythemic patients. It was observed that as FEV1 values decreased, the frequency of anemia increased, hospital admissions were more frequent, and although statistical evaluation could not be performed, mortality appeared to be higher in anemic patients compared to non-anemic ones.

Boutou AK et al. investigated the prevalence of anemia in COPD and its impact on exercise and dyspnea. Anemic patients were found to be older, had lower FEV1 values, and had higher mMRC dyspnea scores, indicating more severe disease (24). In this investigation, there was no distinction between anemic and non-anemic patients in terms of BMI, smoking, and LTOT. When comparing the anemic and normocytic groups, similar results were found. However, when the anemic and polycythemic groups were compared, there were no notable differences in age, FEV1 values, or smoking history, but anemic patients had a significantly lower BMI. In Cote et al.'s study, the anemic group also had significantly higher mMRC dyspnea scores

and shorter 6MWD (9). A decrease in 6MWD was found to be associated with a decrease in survival. Anemia has been found to be a crucial factor in decreased exercise capacity and increased dyspnea. In the present study, between the anemic group and the non-anemic group, significantly higher mMRC and BODE scores, as well as shorter 6MWD results, were obtained. The mMRC dyspnea score has been shown to be a predictor of expected survival (25). The 6MWD is a test that has been recognized as a determinant for functional status and mortality (26). In the present study, it was shown that the 6MWD was lower in anemic patients compared to non-anemic ones. When looking at the three patients with mortality, consistent with the literature, all three patients had high mMRC dyspnea scores and the 6MWD was less than 250 meters.

In the study by Cote et al., the median survival of COPD patients was 49 months in the anemic group and 74 months in the non-anemic group. In another investigation by Halpern et al., it was observed that the mortality rate in the anemic COPD group was twice as high as in the non-anemic COPD group (27). The most extensive research of increased mortality related to low hemoglobin levels in COPD is the ANTADIR (Association Nationale pour le Traitement à Domicile de l'Insuffisance Respiratoire) study. In a 10-year retrospective analysis of 2524 patients with COPD, the percentage of anemia was discovered to be 12.6% in males and 8.2% in females. 3-year survival rate was 24% among those with a hematocrit value below 35% compared to 70% among those with a hematocrit value above 55% (28). In the present study, one anemic patient and two polycythemic patients died during one year of observation. In the normocytic group, all patients were alive at the end of the year. Statistical evaluation could not be made because of the low number of deaths, but these results suggested that the prognosis was better in the normocytic group. The impact of average hemoglobin levels on mortality could have been more clearly evaluated if the follow-up period of patients had been longer than one year. This was one of the limitations of the study.

In the current investigation, no difference was identified in hemoglobin levels with respect to LTOT use. The shorter 6MWD in patients using LTOT can be explained by the fact that these were more severe cases due to lower FEV1 values.

Exacerbations of COPD are defined as acute deteriorations characterized by changes in the patient's daily respiratory symptoms and necessitating alterations in current treatment (29). Exacerbations are responsible for a significant portion of health care and are known to negatively impact quality of life and prognosis (30). Low hematocrit levels are associated with increased hospital admission frequency and length of stay, leading to increased morbidity and mortality (28). Differently, in a recent study, patients who were hospitalized due to COPD exacerbations were followed for 3 months after discharge. There was no significant difference in attack frequency in anemic patients, but mortality was observed to be higher (31). In the present study, between the anemic group and the non-anemic group in terms of exacerbation frequency, significant differences were observed in both emergency and outpatient visits and the number of hospital admissions requiring intensive care. Consistent with the literature, these findings show that anemia is a poor prognostic factor for COPD.

The main limitations of the investigation are the small number of patients, the short observation period, and the inability to follow the variability in anemia parameters during the follow-up period.

CONCLUSION

In conclusion, anemia in COPD is a poor prognostic factor associated with increased hospital admissions and exacerbation frequency, reduced functional capacity, and worsened dyspnea. It should be considered that anemic patients with COPD are more severe cases. Although the impact on mortality was not directly evaluated in this study, the outcomes indirectly infer that an increased frequency of exacerbations may lead to an increase in mortality.

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MEDICAL RECORDS-International Medical Journal

Research Article

Evaluation of Patient Information Texts About Bruxism on the Internet in Terms of Readability and Content

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Abstract

Aim: Bruxism is a common health problem in our society. The treatment method to be preferred should be determined by the decision of the patient and the physician together. Individuals' knowledge of the course of the disease, symptoms, and treatment options will contribute to the treatment process. There are many websites on the Internet that can guide patients about health and illness. The aim of this study is to evaluate the patient information texts about bruxism on web sites in terms of content and readability.
Material and Method: Websites reached in a search using the keyword "bruxism" on Google were evaluated in terms of readability and content. The readability assessment was classified according to the level of education. Text content accuracy was also evaluated according to information level separately.
Results: Forty-four of the 100 websites examined were included in the study. The average grade level is 11.41±0.82. The readability level of 79% (n=35) of the 44 texts examined is at a difficult level. It is seen that the definition and etiology of the disease are mentioned in 68% (n=30) of the texts examined in the study.
Conclusion: Although the content of the English texts prepared to inform patients about bruxism on the Internet is sufficient, it has been found that the readability level is low.

Keywords: Bruxism, Access to information, Search engine

INTRODUCTION

Today, the internet has become a tool used by individuals to have detailed information about their diseases and to obtain information about treatment options and diagnostic methods (1). On the Internet, there are a lot of websites that can give patients information about their health and their illness. Regarding oral and dental health, it was found that 53.7% of patients use the internet to find out about their treatment options and how this is carried out (2). However, some patients feel safer in terms of their medical conditions through the information they obtain from the internet (3). In the systematic review study in which information on health issues on the Internet is evaluated, it is seen that 70% of the information is insufficient in terms of quality (4).

Bruxism is a frequent health problem in society. The reported incidence ranges from 8% to 31% in adults (5). The etiology of bruxism is multifactorial, so a multifactorial perspective is required in treatment. Preventing the harmful effects of bruxism is the main goal of treatment (6,7). In the treatment of bruxism, undesirable effects can be prevented by methods such as botulinum toxin applications, biofeedback, hypnotherapy, cognitive therapy, behavioral therapy, occlusal therapy, and the use of intraoral devices (8). It should be the decision of the patient and the doctor together as to which treatment method is preferred. For this reason, individuals' knowledge of the course of the disease, symptoms, and treatment options will contribute to the treatment process.

Patient information texts on the internet in the field of health have an important place in understanding the disease and accepting the treatment process by the patient (9,10). In addition to the sufficient information contained in these texts, it is also important that they be read by patients. Readability is a mathematical concept. For this

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reason, it has a measurable feature. It is recommended that the texts about health be written in accordance with the 6th grade and below in order to be understandable by the patients (11). The texts written above this level will be more difficult for the reader to understand. Studies have been conducted to evaluate the readability of texts written about health problems such as cataracts and voice disorders (12,13). In addition, both readability and content evaluations were made regarding common health problems such as osteoporosis and headache (14,15). However, the literature has not identified a study that examined patient information texts on bruxism. The purpose of this research is to analyze the content and readability of patient information about bruxism on websites.

MATERIAL AND METHOD

Search Strategy

The search using the keyword "bruxism" in November 2023 was carried out by a single researcher (DIK). The searches were made using the Google Search Engine. The first 100 websites that were found as a result of the search were examined. Considering the inclusion and exclusion criteria, the websites to be included in the study were determined.

Inclusion criteria

1. Websites containing patient information texts about bruxism,
2. Websites containing English content.

Exclusion criteria

1. Websites containing academic articles,
2. Websites containing less than 20 sentences of information,
3. Websites aiming to inform patients with video visuals,
4. Websites prepared for healthcare professionals.

The contents of the texts were evaluated in order to distinguish the web sites for healthcare professionals and patient education. Texts containing less than 20 sentences of information were excluded from the study because they were considered insufficient in terms of content.

Data Collection

Patient information texts about bruxism on 44 websites included in the study were transferred separately to Microsoft Word 2013 (Microsoft Corporation, Redmond, Washington, USA) applications. The title, author information, site address, additional links, and images were deleted, preventing the readability measurement from being negatively affected.

Readability Measurement

A free website called The Readability Calculator was used to make readability measurements.(http://www.online-utility.org) The text to be analyzed on this website is transferred to the specified box, and readability data can be accessed. This program has been used in some scientific studies before (16,17). The readability data obtained from the program is as follows:

I. Flesch Reading Ease score
II. Gunning Fog index
III. Coleman–Liau index
IV. Flesch–Kincaid Grade level
V. Automated Readability Index (ARI)
VI. Simple Measure of Gobbledygook (SMOG) index

The calculation formulas for these indices are shown in Table 1. Indices II and IV indicate the level of the text at the educational level in the United States. Most formulas take into account the average sentence length and the number of words with more than 3 syllables when determining the readability level. The Flesch Reading Ease scale gives a value between 0 and 100 for the entire text. The higher the value, the higher the readability. The Flesch Reading Ease score and Flesch-KKincaid Grade Level determine the readability value according to word length and sentence length. Gunning Fog index and SMOG index are evaluated by considering the number of polysyllabic words. On the other hand, the Automated Readability Index and the Coleman-Liau Index are based on the number of characters per word rather than the number of syllables per word.

Table 1. Method of calculating readability scores

Index	Formula
Flesch reading ease score	206.835 – (1.015 9 Average number of words per sentence) – (84.6 9 Average number of syllables per word)
Flesch–Kincaid grade level	(0.39 9 Average number of words per sentence) + (11.8 9 Average number of syllables per word) – 15.59
Gunning Fog index	0.4 9 (Average sentence length + Percentage of complex words*)
Coleman–Liau index	0.0588 9 (Average number of letters per 100 words) – 0.296 9 (average number of sentences per 100 words) – 15.8
Automated readability index	4.71 9 (Number of letters per word) + 0.5 9 (Number of words per sentence) – 21.43
SMOG index	3 + Square root of polysyllable* count per 30 sentences

*Words with three or more syllables

In order to determine the average education level, the averages of the II and IV indices were determined. In addition, the linguistic statistical data of the texts is also calculated in this readability analysis program. (Number of characters, number of words, number of sentences, average number of characters in a word, average number of syllables in a word, average number of words in a sentence.)

Evaluation of Text Contents

In order to evaluate the content of patient information texts, "Has the disease been defined?" "Has the etiology of the disease been explained?" "Has the preventive medicine practices been mentioned?" "Is the treatment method specified?" "Has alternative treatment options been mentioned?" and "Are the symptoms of the disease specified?" answers were sought. In determining the questions, meta-analysis by Melo et al. was used (18). The text content was evaluated by an oral and maxillofacial surgeon (D.I.K.) and a physical therapy and rehabilitation specialist (S.T.).

Statistical Analysis

Statistical analyses were performed using the Statistical Package of Social Sciences 23.0 (SPSS Chicago, IL, USA) program. The mean and standard deviation were calculated from normally distributed data according to the Kolmogorov-Smirnov test. The evaluation of the contents was calculated as a percentage according to whether they answered the specified questions or not.

RESULTS

Forty-four of the 100 websites examined were included in the study. The statistical data obtained from the readability analysis website are shown in Table 2.

Table 2. Readability indices

Index	Mean	SD	Median	Minimum	Maximum
Flesch Reading ease score	50.96	9.25	51.40	23.74	67.65
Gunning Fog index	11.99	2.41	11.63	7.61	21.05
Coleman-Liau index	11.15	1.40	11.03	8.45	14.72
Flesch-Kincaid grade level	10.83	2.23	10.48	7.07	20.44
Automated readability index	10.88	2.68	10.24	6.14	22.65
SMOG index	11.71	1.58	11.66	8.58	16.24
Average grade level	11.41	0.82	11.41	10.83	11.99

The average Flesch Reading Ease Score value was determined to be 50.96±9.25. While the lowest value is 23.74, the highest value is 67.65. The average grade level is 11.41±0.82. The readability level of 79% (n=35) of the 44 texts examined is at a difficult level. According to all indices, the average reading level is at the "difficult" level. When linguistic statistics are examined, it is seen that there is a wide variation in the number of characters (4586.5±5774.89), the number of words (935.38±1121.12), and the number of sentences (50.95±54.40) (Table 3).

The definition and etiology of the disease were included in 68% (n=30) of the texts examined in the study. While at least one treatment method is mentioned in 95% of the texts, alternative treatment options are described in only 34% (n=15). Symptoms of the disease were described in 86% (n=38) (Table 4).

Table 3. Linguistic statistics

	Mean	SD	Median	Minimum	Maximum
Number of characters (without spaces)	4586.5	5774.89	3336	1312	39985
Number of words	935.38	1121.12	685.5	265	7764
Number of sentences	50.95	54.40	39	20	369
Average number of characters per word	4.86	0.22	4.85	4.37	5.45
Average number of syllables per word	1.61	0.08	1.61	1.44	1.81
Average number of words per sentences	18.84	4.87	18.73	12.07	42.23

Table 4. Evaluation of the content of patient information texts		
Description of the disease	68%	n=30
Etiology of the disease	68%	n=30
Preventive medicine practices	34%	n=15
Treatment method	95%	n=42
Alternative treatment options	34%	n=15
Symptoms of the disease	86%	n=38

DISCUSSION

The Internet is the most frequently used source of information on health problems (1). Most patients use the internet as a guide when making health-related decisions and communicating with the doctor (3). At this stage, the information on the websites must be qualified so that patients do not make the wrong decisions. In this study, 44 websites related to bruxism that can be accessed via Google search engines were evaluated in terms of readability and content. In our literature review, no other study evaluating patient information forms on bruxism was found.

The readability levels of all the texts examined in the study are above the 10th grade level for each index. The average readability education level of the texts was determined to be 11.41. In a study evaluating the readability of texts related to headaches, it was understood that the average readability education level of texts on websites was above 10th grade (14), in the study where the texts about eye diseases were evaluated, the education level was above the 12th grade (19), and the readability level was found to be above the 11th grade in the study in which the texts about breast cancer were evaluated (20). In this respect, our study gave similar results to other studies. According to the criteria of the U.S. Department of Health and Human Services, the readability level of the texts prepared for the 10th grade and above education level is classified as "difficult," and those for the 6th grade and below education level are classified as "easy" (21). It is noteworthy that while the readability level is above 10 in a large part of 44 texts, such as 79%, no text with an education level of less than 6th grade is found. According to Weiss, health texts should be written for 6th grade and below in order to be understandable by patients (11). The fact that most of the texts are above 10th grade will make it difficult to convey information about bruxism. In the editorial process, care should be taken to make such texts suitable for readers in the readers in the 6th grade and below.

According to the recommendations of dental prosthesis specialists, various precautions should be taken to avoid the unwanted effects of bruxism (22). Mention of preventive medicine practices in patient information texts will increase this awareness. Bruxism does not have an established treatment; there are treatment options that vary according to patient complaints, symptoms, and social status (23). The contents of the examined patient information forms were varied. While the symptoms and treatment options of bruxism are generally mentioned, very few of them have mentioned alternative treatment options and preventive medicine practices. In the texts we examine in our study, a single treatment method is mostly mentioned (Table 4). It has been described by 34% of alternative treatment options. The treatment that is planned to be applied may not give satisfactory results because it is not specific to the person.

For a text in which medical terms are used frequently, sentences created with standard length sentences will be more difficult to understand. According to Flesch, the average number of words per sentence in an English text is 17 for a text of standard difficulty (24). However, this value was found as a result of an analysis made with adult reading materials written in English. In our study, when the linguistic statistics in Table 3 were examined, the average number of words in a sentence was determined to be 18.84, and the average number of syllables was determined to be 1.61. Similar results were obtained in Jayaratne's study on dental implants (25). According to Flesch, this value corresponds to the "difficult" and "rather difficult" ranges (24). This value proves that medical terms are used excessively in the texts examined in our study.

In this study, six different readability formulas were used to determine the level of readability. The formulas with numbers I, II, and IV indicated in Table 1 are the classical readability formulas, and the formulas with numbers III, V, and VI are included in the literature as new readability formulas (26). The fact that we obtained similar results in different formulas in classical and current formulas is one of the strengths of the study. Another strength of the research is that the top 100 websites in the Google search engine have been examined. The websites we have reviewed are inclusive of websites to be listed in a search to be made in another search engine.

This paper has some limitations. In our study, we only examined patient information texts on websites. However, as it becomes easier to access information, the alternatives to the information also increase. People are guided about health on other social platforms (Facebook, Twitter, and Instagram). It will be appropriate to compare patient information texts on different platforms in the future. Another limitation of our study is that only the contents written in English were evaluated. We recommend that studies be conducted to evaluate the readability and content of non-English websites.

If the texts written about bruxism are not understandable by the patients, the intended effect on the reader will not be seen. These should be rearranged by considering readability principles.

CONCLUSION

Although the content of the English texts prepared to inform patients about bruxism on the Internet is sufficient,

it has been found that the readability level is low. The excessive use of medical terms may have reduced the comprehension of the texts. It is very important to have sufficient knowledge about the disease in decisions made on health-related issues. Revision of these texts, which should be more understandable by patients, will increase the level of understandability.

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MEDICAL RECORDS-International Medical Journal

Research Article

Could There Be a Relationship Between Paranasal Sinus and Migraine Etiology?

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Abstract

Aim: Migraine is a complex neurological disease with a neurogenic inflammatory component in which nitric oxide (NO) levels increase. Studies have shown that the NO level produced in adults is closely related to the paranasal sinus volume. The aim of this study is to investigate the differences in paranasal sinus volumes responsible for NO synthesis in migraine patients.
Material and Method: The paranasal sinuses of migraine patients (n=50) and healthy subjects (n=50) were examined using cranial T1-weighted magnetic resonance images (MRI). Right and left maxillary, sphenoid and frontal-ethmoid sinus volumes of the groups were calculated in 3D Slicer program and recorded in mm^3. Statistical analysis of the study was performed with IBM SPSS 23.0 and $p<0.05$ values were considered significant.
Results: A statistically significant difference was observed between migraine patients and healthy subjects across all sinus volumes, with the sinus volumes of migraine patients being higher than those of healthy subjects ($p<0.05$).
Conclusion: We think that the fact that the paranasal sinus volume, which is primarily responsible for NO synthesis, was found to be high in migraine patients may be related to the high NO level in migraine patients.

Keywords: Paranasal sinus, nitric oxide, migraine, pain, maxillary sinus

INTRODUCTION

Migraine is a recurring, moderate or severe headache that can occur at any age and usually lasts between 4 hours and 3 days. In migraine, problems such as headache, sensitivity to sound and light, nausea and vomiting can be seen (1). While migraine headache is among the 10 most common diseases in men, it is among the five most common diseases in female (2). Although the pathophysiology of migraine is not yet clear, it has been reported in many studies that nitric oxide (NO) production and level may play a role in migraine pathophysiological mechanisms (3-6). NO, which has different roles in many systems, is accepted as a biological regulator. NO has a vasodilatation effect on vessels, a relaxant effect on smooth muscles, and a neurotransmitter effect on the peripheral and central nervous systems (7). Although NO is synthesized in more than one anatomical region in the human body, it is known to be produced mostly by epithelial cells in the paranasal sinuses (8,9). Paranasal sinuses are located within the bones of the same name and are called maxillary, frontal, ethmoid and sphenoid sinuses (10). Many studies have reported that NO is synthesised to a large extent in migraine patients (4-6.) Studies have shown that the NO level produced in adults is closely related to the paranasal sinus volume (9,11).

Considering the aforementioned explanations, determining whether the paranasal sinus volumes, which are responsible for NO synthesis, change in migraine patients may give an idea about the etiology of migraine. Therefore, the aim of this study was to compare the paranasal sinus volumes obtained using magnetic resonance images (MRI) in migraine patients with those of healthy individuals without migraine.

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MATERIAL AND METHOD

Study Design

The study received approval from the Kayseri City Training and Research Hospital Clinical Research Ethics Committee under decision number 1017, dated December 15, 2023. The cross-sectional cohort study was conducted in a single center in accordance with the Declaration of Helsinki. Participants who met the study criteria were informed about the study and their written informed consent was obtained.

Participants

In a pilot study with 7 individuals for each of the two groups, the sample size was determined to be at least 40 participants for each group, with an effect size of 0.636 using a power of 0.80 and α=0.05. The primary outcome measure for this calculation was right maxillary sinus volume.

Migraine Group (n=50): It consists of a total of 50 migraine patients, 30 female and 20 male, diagnosed with migraine.

Control group (n=50): Consists of a total of 50 healthy individuals, 26 female and 24 male.

Although there is no specific test for the diagnosis of migraine, the criteria set by the International Headache Society for migraine in 2018 are used. Patients with migraine were evaluated according to the criteria of the International Headache Society and patients who met the criteria were included in the study. The criteria set by the International Headache Society for migraine are given in the table below (12).

Participants with a history of trauma or surgery in the neurocranium and viscerocranium bones or problems affecting the paranasal sinus volume, such as loss of molar teeth, were excluded.

Data Acquisition

MRI procedures were performed with a 3T (Tesla) Siemens Magnetom Skyra, Netherlands brand device. T1-weighted MPRAGE sequence settings were used to evaluate paranasal sinus volumes in the study; sagitial was determined as Slice Thicknes=1mm, Repetition time (TR)=2300ms, FOV=250mm, Matrix: 256x256, Echo Time (TE)=3.4ms.

Data Processing

The volume calculation of the paranasal sinuses was done in the 3D Slicer program. 3D Slicer is a free and open source software application. It is used for volume, area calculation or visualization of any anatomical structure (13,14).

The MRI data of the participants was uploaded to the 3D Slicer tool set and the “Modules” tab was navigated to the “Segment Editor” tab. The first step of volume calculation was completed with the "Segmentation" tab opened as a result of these operations. In the second step, the image was "Thresholded" using the "Threshold Range" to cover the anatomical boundaries of the paranasal sinuses to be measured. The three-dimensional raw image of the paranasal sinus measured with these procedures was accessed using the "Apply" and "Show 3D" tabs. The raw image obtained was checked from the axial, sagittal and coronal planes, and if there were overflows or deficiencies in the anatomical border of the measured paranasal sinus, it was corrected using the "Erase", "Scissors" and "Paint" tabs (Figure 1). As a result of these procedures, the paranasal sinus volumes in mm^3 were calculated and compared between the groups.

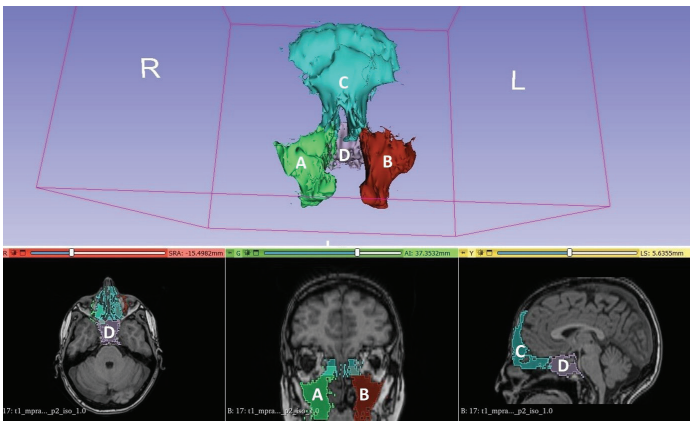

Figure 1. Three-dimensional representation of paranasal sinuses; A: The right maxillary sinus; B: The left maxillary sinus; C: The frontal-ethmoid sinuses; D: The sphenoid sinus

Statistical Analysis

Statistical analysis was performed using IBM® SPSS© 24 software (IBM SPSS Corp., Armonk, NY, USA). The normality of numerical variables was assessed using both visual methods, such as histograms and probability plots, and analytical methods, including the Kolmogorov-Smirnov test. Descriptive statistics, comprising means and standard deviations, were employed for normally distributed numerical variables, while frequencies and percentages were used for summarising categorical variables. The Independent Samples t-test was utilised to compare two independent groups with a normal distribution, and the chi-square test was employed for categorical data. A value of $p<0.05$ was considered statistically significant.

RESULTS

The demographic characteristics of individuals in the groups are presented in Table 1. No statistically significant differences were observed between the groups concerning these demographic characteristics ($p>0.05$). The volumes of the right maxillary sinus, left maxillary sinus, sphenoid sinus, and frontal-ethmoid sinus for both groups are detailed in Table 1. A statistically significant difference was observed between migraine patients and healthy subjects across all sinus volumes, with the sinus volumes of migraine patients being higher than those of healthy subjects ($p<0.05$).

Table 1. Analysis of data between control and migraine groups

		Control group (n=50)	Migraine group (n=50)	
		X±SD	X±SD	Sig. (p)
Age (years)		23.34±3.32	23.02±3.50	0.869
BMI (kg/m²)		23.88±2.87	24.11±2.49	0.414
		n (%)	n (%)	
Gender	M	24 (48.0)	20 (40.0)	0.567
	F	26 (52.0)	30 (60.0)	
Right maxillary sinus (mm³)		22541.66±3004.94	25617.34±3409.25	0.027*
Left maxillary sinus (mm³)		21830.03±3119.25	25254.53±3382.97	0.030*
Sphenoid sinus (mm³)		18154.20±2746.16	20794.68±3063.32	0.019*
Frontal-ethmoid sinuses (mm³)		38067.60±3004.92	41411.07±2958.96	0.022*

X: mean, SD: standard deviation, *p<0.05, BMI: body mass index, M: male, F: female

DISCUSSION

Although the etiopathogenesis of migraine remains unclear, it has been suggested that high levels of NO synthesis may play a role (15). In the present study, it was determined that the volume of the paranasal sinuses, which are responsible for synthesizing high amounts of NO, was significantly different in migraine patients compared to healthy individuals.

Migraine is a complex neurological disease with a neurogenic inflammatory component in which NO levels increase (16). It has been assumed that paranasal sinus-derived NO spread in the nasal mucosa is the primary molecule that initiates migraine, and this situation is called the sinus hypoxic nitric oxide theory. According to this theory, NO originating from the paranasal sinus spreads to the nasal mucosa, causing repetitive or intermittent stimulation of the trigeminal nerve. It has been suggested that this situation causes vasodilation in the blood vessels in the nasal mucosa and in the extracranial blood vessels that initiate the migraine attack, respectively (15).

In the presented study, all paranasal sinus volumes, especially the sinus maxillaris, were found to be higher in migraine patients than in healthy individuals. High paranasal sinus volume also affects NO synthesis. We believe that the high volume of the paranasal sinus, which is primarily responsible for NO synthesis in the body, in migraine patients may explain the high levels of NO observed in migraine patients. It has been reported that the NO content of air absorbed from the paranasal sinuses of migraine patients during an acute attack is 132.5 parts per billion (ppb) and 154 ppb on the left and right sides, respectively, while in controls it is 36 ppb and 34.5 ppb, respectively. This study further reports that NO levels are not only elevated in migraine patients compared to healthy individuals but also demonstrate asymmetry between the right and left side nasal air (17). In the present study, the volume of the right sinus maxillaris in migraine patients was found to be higher than the volume of the left sinus maxillaris, which may be an explanation for the high level of NO in the right side airway of the nose.

Mechanical suction of paranasal air is used to reduce NO production and NO stagnation in the nasal and paranasal cavities (18). In migraine patients, mechanical suction of paranasal air has been proven to neutralise nasal NO and reduce migraine attacks and severity (19). In the study, the fact that migraine patients have larger paranasal sinuses than healthy individuals may have increased the stored NO level and caused the formation of very high concentrations of NO. In humans, NO has been reported to be produced by epithelial cells in the paranasal sinuses (8). The number of epithelial cells in the paranasal sinuses is directly related to the surface area and, therefore, the volume of the paranasal sinuses. A larger volume means more epithelial cells and more NO.

Although it is known that NO synthesis is closely related to paranasal sinus volume, NO level could not be evaluated in migraine patients in this study. In addition, the study was conducted in a single center. In some individuals, it is very difficult to determine the exact boundary between the frontal sinus and ethmoid sinus. Therefore, frontal and ethmoid sinus volumes were measured together in this study. These processes related to the study can be seen as a limitation of the study.

CONCLUSION

The etiology and pathogenesis of migraine remain mysterious despite dozens of studies. Although certain topics are emphasized in the studies, it is seen that the increase in NO level is effective on the etiology of migraine. In the present study, we think that the fact that the paranasal sinus volume, which is primarily responsible for NO synthesis, was found to be high in migraine patients may be related to the high NO level in migraine patients. We believe that this study will contribute to the elucidation of the high NO level in migraine.

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Research Article

Turkish Validity and Reliability of Oral Health Impact on Daily Life Questionnaire in Endodontic Patients

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Abstract

Aim: Oral health has an important role in the general health. It was aimed to evaluate the validity and reliability of Turkish version of Oral Health Impact on Daily Life Questionnaire (OHIDL) in adult endodontic patients.
Material and Method: The OHIDL was translated and adapted into Turkish. The Turkish version of OHIDL (Turkish-OHIDL) and Turkish version of the Oral Health Impact Scale (OHIP-14-TR) were applied to 222 adult endodontic patients (18 years and older) with no systemic disease. The reliability of the questionnaire was examined by test-retest reliability and internal consistency. The validity was evaluated by the correlations between domains and global questions, and between Turkish-OHIDL and OHIP-14-TR. The structure of the hypothesized domains of the OHIDL was analyzed by confirmatory factor analysis (CFA).
Results: The Turkish-OHIDL exhibited high internal consistency (Cronbach's alpha=0.89) and test-retest reliability (Intraclass Correlation Coefficient=0.86). There was a significant correlation between Turkish-OHIDL and OHIP-14-TR among all domains. There was a very strong correlation in terms of total score as well (rs: 0.78, p<0.001). The total OHIDL score showed the highest correlation with the global question regarding the overall impact of oral health on daily life (G3/rs:0.54), indicating a moderate correlation. Five factors containing more than one item, were statistically verified as acceptable fit using CFA.
Conclusion: Turkish-OHIDL has been proven as a valid and reliable tool for the measurement of oral health-related quality of life.

Keywords: Oral Health Impact on Daily Life Questionnaire, Oral Health Impact Scale, Oral health, Quality of life

INTRODUCTION

Scientific research in medicine consistently shows that health begins in the mouth. Today, good oral health is not just about dental health, it is also of great importance for the overall health and well-being of our body (1). Improving oral health may have significant systemic effects on the human health, and effect the quality of life of society and individuals (2).

The Dental Patient-Reported Outcome (dPRO) is a report regarding the subjective experiences in oral health, obtained directly from the dental patients, and for which the clinician does not interpret responses (3). Oral Health-Related Quality of Life (OHRQoL) is the most essential dPRO. The concept of OHRQoL for consistent measurement of patient-perceived impact in different oral conditions is widely acknowledged (4).

Several OHRQoL scales have been developed for pediatric, adolescent, adult, and older dental populations (5,6). The effect of many factors, such as caries, socioeconomic status, malocclusion and periodontal diseases on OHRQoL have been investigated with these scales (7-9). Adapting these existing scales that have been proven to be effective in OHRQoL assessment to other cultures is common, because it is cheaper and less time consuming than creating a new tool. Additionally, validity and reliability studies of an effective tool in other languages allow the impact of the same factors on OHRQoL to be reliably assessed in different cultures (10).

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The Oral Health Impact on Daily Living Questionnaire (OHIDL) was developed to measure OHRQoL with severity measures, particularly among older Chinese adults (11). The validity and reliability of OHIDL have been proven (12). In a longitudinal validation study using OHIDL for measurement of the perceived change in OHRQoL after dental treatments, it was emphasized that endodontic treatment significantly improved the OHRQoL, which supports using the scale, especially in endodontics (13).

The aim of this study was to adapt the OHIDL into Turkish and test its validity and reliability in the study group that applied to our clinic for endodontic treatment.

MATERIAL AND METHOD

Ethical Considerations

Permission for the Turkish validity and reliability study of the questionnaire was received from the original developers of OHIDL via e-mail. The study was approved by the Ethics Committee of Recep Tayyip Erdoğan (RTE) University (Protocol no: 2023/118). Informed consent was obtained from all the participants, and the questionnaire was completed.

Study Population

This study was planned for the methodological design and carried out between May 2023 and June 2023 at RTE University Faculty of Dentistry, Department of Endodontics. Patients aged 18 years and older who applied to our clinic with endodontic complaints were included in the study. Patients who did not speak Turkish, had cognitive impairment, and had communication difficulties were excluded from the study. There is no widely accepted calculation formula or absolute rules for the sample size required for validity and reliability studies. However, using the participant-survey item ratio is generally recommended by the guidelines, and a ratio of 10:1 is generally accepted in the literature (14,15). The required number of participants was determined as ten times the number of items in the questionnaire. Since the questionnaire to be tested consisted of 16 items, it was aimed to include at least 160 participants. However, considering that there may be data loss, 222 patients were included in the study to apply the questionnaires.

Translation and Cultural Adaptation

The original OHIDL questionnaire was translated from English to Turkish by three academics who are experts in their fields and fluent in English, according to the guidelines suggested by Beaton et al. (16). A team of translators and researchers evaluated the Turkish-translated versions. Conflicting terms were reviewed, the most appropriate terms were selected by consensus, and the first Turkish version of the questionnaire was obtained. Two independent translators who were unaware of the original questionnaire back-translated the first Turkish version into English. Afterward, the backtranslated version was rechecked and compared with the original questionnaire, and after minor adjustments, the Turkish version to be used for the pilot study was created. After applying it to a pilot group of 10 patients, confusing questions and patterns were identified and re-examined. The confusing questions were edited, and the final Turkish version was created.

The Questionnaries

Sociodemographic data of each patient who filled out the questionnaires, such as age, gender, education level, who they lived with, and the reason for going to the dentist, were recorded.

OHIDL

In this section the Turkish version of OHIDL (Turkish-OHIDL) questionnaire was applied to participants. OHIDL consists of a total of 16 questions in 7 domains including eating, speaking, appearance, social, psychological, health, and finance (12). The questions were scored by perceived intensity. Intensity measurement was graded in the range of 0-4 as none, mild, moderate, severe, and very severe, respectively. The total score of the questions under each domain was determined as the domain score. The sum of the domain scores was recorded as the total OHIDL score.

Global Questions

Five global questions were asked and recorded in a 5-point Likert system.

- G1) self-rating of oral health (very unhealthy- very healthy),
- G2) satisfaction with oral health (very dissatisfied-very satisfied),
- G3) perceived impact of oral health on daily living (none- very severe),
- G4) bothered by the impacts of oral health (not at all-a great deal),
- G5) overall life satisfaction (very dissatisfied- very satisfied) (12).

Oral Health Impact Profile (OHIP-14)

Turkish version of OHIP-14 (OHIP14-TR) was also applied to participants. It includes 14 questions under 7 subgroups (functional limitation, physical pain, psychological discomfort, physical disability, psychological disability, social and handicap) (17). The answers were recorded in a 5-point Likert system, scoring 0-4 as never, rarely, sometimes, often, and always. Higher levels indicates more significant impact of dental health on quality of life.

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS), version 20 software package (IBM Corp, Armonk, NY, USA) was used for statistical analysis. A p-value of <0.05 was considered statistically significant.

Reliability

Internal Consistency

The internal consistency and homogeneity of the Turkish-OHIDL scale was determined by the Cronbach's alpha coefficient, with α value of 0.6-0.7 indicating acceptable internal consistency (18).

Test-retest

For test-retest, the Turkish-OHIDL was applied to 31 patients twice at a 2-week interval. Patients who received no dental treatment during the two weeks were selected. Test-retest reliability was evaluated with the intraclass correlation coefficient (ICC). The reliability levels expressed by ICC values are as follows: <0.5 poor, 0.5-0.75 moderate, 0.75-0.9 good, and >0.9 excellent reliability (19).

Validity

For construct validity, the correlation of the overall OHIDL score and domain scores with the global questions were evaluated using the Spearman's correlation coefficient (rs). Additionally, the relationship between Turkish-OHIDL and the OHIP-14-TR, was analyzed by the Spearman's correlation, for convergent validity. In the medical field, rs values of <0.1, 0.1-0.3, 0.3-0.5, 0.5-0.75, 0.75-0.9, and >0.9 indicate none, poor, fair, moderate, very strong, and perfect validity, respectively (20). To verify the factors, confirmatory factor analysis was performed using AMOS 24. Model fit was examined using the $\chi 2/df$, comparative fit index (CFI), normed fit index (NFI), root mean square error of approximation (RMSEA), the goodness of fit index (GFI), and the adjusted goodness of fit index (AGFI). RMSEA values should be ≤0.08 and CFI, NFI and GFI values should be ≥0.90 for acceptable fit. AGFI values of ≥0.85 indicate acceptable fit (21).

RESULTS

Of the 222 patients who participated in the study, 52.3% were female, and 47.7% were male. The mean age was 35.04 years, 0.9% of the respondents are illiterate, 17.1% are primary school graduates, 6.3% are secondary school graduates, 38.8% are high school graduates, and 38.8% are university graduates. While 12.2% of the participants live alone, 87.8% live with their families. 24.3% of the participants applied to our clinic for examination/follow-up and 75.7% for treatment.

The discriminant ability of the questions in the questionnaire was assessed using the ceiling and floor effects (22). If more than 90 percent of the respondents answered a question with the lowest or highest grade of "none" or "very severe", that question was considered low in discrimination. The distinguishing feature of all questions in the questionnaire was considered good, as more than 90% of the respondents did not answer "none" or "very severely" to any of the questions.

Test-retest and Internal Consistency

Regarding the internal consistency of the Turkish-OHIDL, Table 1 shows satisfactory internal consistency, with the Cronbach's alpha coefficient of 0.89 for the overall OHIDL and ranging from 0.84 to 0.71 for eating, appearance, health, psychological, and social domains.

Regarding the test-retest reliability, the ICC for overall OHIDL was 0.86, showing good reliability, and ranged between 0.82 and 0.53 for individual domains, showing moderate to good reliability (Table 1).

Table 1. Test-retest (ICC) and internal consistency (Cronbah's α) measures

		n=222	n=31
	Number of items	Cronbach α	ICC
OHIDL-total	16	0.89	0.86
Eating	6	0.84	0.82
Speaking	1	-	0.65
Appearance	2	0.83	0.81
Social	2	0.71	0.82
Psychological	2	0.77	0.53
Health	2	0.77	0.69
Finance	1	-	0.73

ICC: Intraclass Correlation Coefficient

Validity

The total OHIDL score was significantly correlated with the global scores ($p<0.05$) other than the self-rating of oral health (G1/rs: -0.09, $p=0.17$). The highest correlation was with the overall impact of oral health on daily life (G3/rs: 0.54, $p<0.001$), indicating a moderate correlation. It was fairly correlated with being bothered by oral health impacts (G4/rs: 0.50, $p<0.001$). Satisfaction with oral health status (G2/rs: -0.25, $p<0.001$) and overall life satisfaction (G5/rs: -0.18, $p=0.01$) were poorly correlated with total OHIDL score. Self-rating of oral health (G1) was poorly correlated only with the appearance domain (rs: -0.18, $p=0.01$) (Table 2).

Table 2. Spearman's rank correlation coefficient (rs) and p values among intensity measurement of domains and global questions

	G1) Self-rating of oral health	G2) Satisfaction on oral health status	G3) Overall oral health impact	G4) Bothered by oral health impact	G5) Overall life satisfaction
Eating	-0.01	-0.11	**0.44**	**0.35**	-0.08
	0.88	0.12	**0.00**	**0.00**	0.25
Speaking	-0.06	-0.07	**0.22**	**0.27**	-0.08
	0.36	0.32	**0.00**	**0.00**	0.24
Appearance	**-0.18**	**-0.30**	**0.26**	**0.36**	**-0.16**
	0.01	**0.00**	**0.00**	**0.00**	**0.02**
Social	-0.12	**-0.21**	**0.25**	**0.29**	**-0.23**
	0.07	**0.00**	**0.00**	**0.00**	**0.00**
Psychological	-0.12	**-0.24**	**0.55**	**0.53**	**-0.20**
	0.08	**0.00**	**0.00**	**0.00**	**0.00**
Health	-0.02	**-0.21**	**0.39**	**0.32**	-0.09
	0.89	**0.00**	**0.00**	**0.00**	0.16
Finance	-0.13	**-0.23**	**0.29**	**0.29**	-0.12
	0.06	**0.00**	**0.00**	**0.00**	0.09
OHIDL-total score	-0.09	**-0.25**	**0.54**	**0.50**	**-0.18**
	0.17	**0.00**	**0.00**	**0.00**	**0.01**

OHIDL: Oral Health Impact on Daily Life

The correlations between OHIP-14-TR and Turkish-OHIDL total scores and domain scores are shown in Table 3. A significant correlation was found between all subgroups, and a very strong correlation (rs: 0.78, p<0.001) was observed between two scales in terms of total score.

Table 3. Spearman's rank correlation coefficient (rs) and p values among Turkish-OHIDL and OHIP-14-TR

	OHIP 14-TR							
Turkish-OHIDL	**Functional limitation**	**Physical pain**	**Psychological discomfort**	**Physical disability**	**Psychological disability**	**Social**	**Handicap**	**Total score**
Eating	0.41	0.60	0.3	0.60	0.39	0.47	0.36	0.63
	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Speaking	0.52	0.28	0.16	0.32	0.27	0.24	0.25	0.40
	0.00	0.00	0.02	0.00	0.00	0.00	0.00	0.00
Appearance	0.40	0.30	0.27	0.31	0.58	0.37	0.32	0.50
	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Social	0.44	0.29	0.28	0.42	0.58	0.44	0.37	0.57
	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Psychological	0.39	0.48	0.40	0.43	0.45	0.46	0.50	0.62
	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Health	0.19	0.55	0.27	0.47	0.32	0.39	0.43	0.54
	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Finance	0.31	0.20	0.16	0.32	0.44	0.24	0.37	0.41
	0.00	0.00	0.02	0.00	0.00	0.00	0.00	0.00
OHIDL-total score	0.52	0.63	0.38	0.64	0.60	0.57	0.53	0.78
	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

OHIDL: Oral Health Impact on Daily Life, OHIP: Oral Health Impact Profile

To verify the construct validity of the questionnaire, CFA was conducted for five factors containing more than one item, based on the model put forward while developing the questionnaire. Although χ2/df, GFI, AGFI, CFI values showed acceptable, NFI and RMSEA values did not show acceptable fit. To improve the models, it is recommended to add the covariances between the items with the largest "modification indices" values (23). The covariance structure between item 5 and item 6, was added. The second model produced acceptable fit results except NFI value (0.894), which is very close to 0.90 (Figure 1 and Table 4).

Table 4. Confirmatory factor analysis

	X2/df	CFI	NFI	RMSEA	GFI	AGFI
Five factors	2.517	0.927	0.887	0.083	0.909	0.858
Five factor with one covariance	2.394	0.934	0.894	0.079	0.916	0.866

CFI: Comparative fit index, NFI: Normed fit index, RMSEA: Root mean square error of approximation, GFI: Goodness of fit index, AGFI: Adjusted goodness of fit index

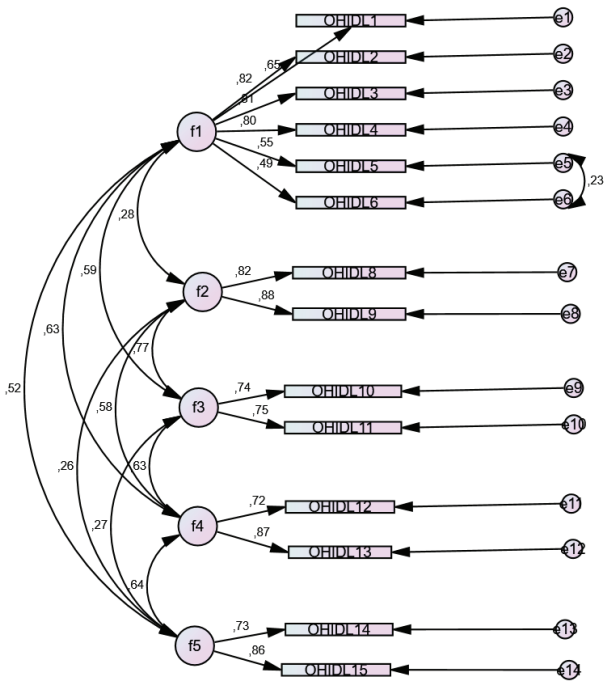

Figure 1. Path diagram of confirmatory factor analysis

DISCUSSION

OHIDL is a questionnaire developed on elderly patients (55 years and older) in Hong Kong, and its validity and reliability have been proven. The OHIDL scale developers recommended testing the scale's validity and reliability in other age groups and countries (12). This methodologically designed study aimed to adapt the OHIDL to Turkish and evaluate the Turkish version in terms of validity and reliability in Endodontic patients aged 18 and over.

The Turkish-OHIDL exhibited satisfactory internal consistency, with Cronbach's alpha values (0.71-0.84 for domains; 0.89 for the entire OHIDL) consistent with the original OHIDL (0.72-0.85 for domains; 0.88 for the entire OHIDL) (12).

According to test-retest results, the Turkish version of OHIDL showed good test-retest reliability with an ICC value of 0.86 for overall OHIDL. Eating (0.82), appearance (0.81), and social (0.82) domains showed good reliability, while finance (0.73), speaking (0.65), health (0.69), and psychological (0.53) domains showed moderate reliability. In another study, the developers of the original OHIDL evaluated the validity and reliability of the OHIDL transition scale, and they assessed test–retest reliability by re-administering randomly selected five items right after the follow-up interview (13). The authors reported ICC values ranging from 0.28 (eating time prolonged) to 1.00 (headache) and stated that the scale had satisfactory reliability. Additionally, they suggested future studies, evaluating test-retest reliability of OHIDL with a longer time interval. Considering this, in the present study, for test-retest reliability, all items were re-administered with a two-week interval, and high reproducibility of the Turkish-OHIDL was proven.

A systematic review stated that OHIP-14 is the most frequently used tool to measure the quality of life in adults (24). Additionally, it has been used several times in studies evaluating OHRQoL in endodontic patients (25,26). Thus, the Turkish version of the OHIP-14 scale, whose validity and reliability were proven in 2014 by Başol et al., was used for the convergent validity in the present study (17). Spearman's correlation analysis was performed between OHIP-14 and OHIDL, and a high correlation was found between the two scales in terms of total scores (rs: 0.78, $p<0.001$). At the same time, all of the domains were correlated with each other. As expected, the correlation between domains with similar questions was stronger, while the domains with different question contents showed a weaker correlation.

Exploratory Factor Analysis (EFA) is used to discover the factors between the items of the questionnaire, and the items determining the existing factors, and CFA can be used to investigate the existence of a previously proven structure with a new data set. Therefore, in questionnaire development studies, CFA should be used following EFA to test the validity while in adaptation studies CFA may be used solely or together with EFA (27). Since prior knowledge about the factors were reported, CFA was conducted on the factors determined in the original questionnaire and found that the model exhibited acceptable fit, supporting construct validity of Turkish-OHIDL.

The Turkish-OHIDL was correlated with all global ratings except the self-rating of oral health (G1). It was found that the overall OHIDL score exhibited a moderate correlation with item G3 (overall impact of oral health on daily life), which can be considered as indicator of OHRQoL. It was also found that the total Turkish-OHIDL score was correlated with overall life satisfaction (G5), albeit poorly. Considering these findings, it can be suggested that the Turkish-OHIDL is a powerful tool for measuring OHRQoL and can also contribute to assessing overall life satisfaction, although it has a poor correlation.

There is a direct relationship between oral-dental health and eating (28). A study conducted among patients living in a nursing home showed that chewing activity significantly affected OHRQoL (29). Speaking, as well as eating, is an essential determinant of quality of life related to oral health (30). In the Turkish version of OHIDL, eating and talking difficulties, both functional limitations, were correlated with the global questions that are indicators of OHRQoL (G3, G4).

Individuals unhappy with their appearance may exhibit behaviors such as avoiding smiling or smiling without showing their teeth, covering their mouth with their hands while speaking, or avoiding social interactions (31). Additionally, studies comparing life satisfaction before and after treatment show that aesthetics significantly affect life satisfaction (32,33). In support of these, in the Turkish-OHIDL appearance domain was correlated with all global questions and stood out as an essential determinant in assessing OHRQoL and overall life satisfaction. In addition, the patient's self-rating of oral health (G1) was not correlated with any domain other than appearance (rs: -0.18, p=0.01). This can be explained by the fact that individuals exhibit higher awareness of appearance/aesthetics rather than functional awareness, and aesthetics concerns affect people in many ways in daily life.

While all domains of the questionnaire showed a correlation with the the overall impact of oral health on daily life (G3) and being bothered by these effects (G4), only appearance, social, and psychological domains were correlated with the overall life satisfaction (G5). This can be interpreted as factors related to pain and functional limitations only affect OHRQoL, whereas appearance dissatisfaction, lack of self-confidence, and dental anxiety affect both OHRQoL and overall life satisfaction.

Dental pain is the most common acute pain in the orofacial region and is often associated with an endodontic problem (34). In endodontic patients, spontaneous widespread pain may be observed, as well as severe pain triggered by chewing, heat, or cold during eating (35). In addition, pain that disrupts sleep is expected in cases of irreversible pulpitis, especially at night (36). In a previous study, the anxiety level of patients with irreversible pulpitis was higher than that of patients undergoing other dental treatments. It is stated that the most significant cause of this anxiety is pain during treatment (37). Anxious people exaggerate the intensity of unpleasant events, such as fear and pain (38). So, in this Turkish-OHIDL questionnaire applied to endodontic patients, it was an expected finding that the psychological, eating, and health domains showed the highest correlation with the oral health impact on daily life.

A limitation of this study is that it was designed to investigate the internal consistency, test-retest reliability, and validity of the Turkish-OHIDL, however, responsiveness was not evaluated. Further studies are required to investigate responsiveness and sensitivity to changes in the treatment process.

CONCLUSION

Within the scope of the findings of this study, the validity and reliability of the Turkish-OHIDL have been proven and were found to be helpful as an alternative scale to OHIP-14 in the evaluation of OHRQoL. Cross-sectional and longitudinal study designs in larger sample groups may increase evidence-based results. Analyzing the OHIDL together with patients' clinical oral findings may serve to determine the impact of different oral conditions on quality of life measurement.

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MEDICAL RECORDS-International Medical Journal

Research Article

Does Fetal Renal Disease Have a Hemodynamic Effect in the Prenatal Period? A Detailed Analysis Method with Fetal Echocardiography

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Abstract

Aim: Is there a change in the circulatory system in fetuses with renal disease in the prenatal period to make hemodynamic assessments. In addition, fetal cardiac functions in the same patients will be studied in detail using fetal echocardiography.
Material and Method: Thirty-one fetuses with renal disease were included in the study; 4 with polycystic kidneys, 4 with bilateral hydronephrosis, 12 with unilateral hydronephrosis, and 28 with pelvicalyceal ectasia. In the control group, there were 30 fetuses of the same gestational week without renal disease. The circulatory system and hemodynamic status were examined in detail by fetal echocardiography in both groups.
Results: High umbilical artery pulsatility index (PI) values were observed in 2 fetuses with bilateral hydronephrosis and 2 fetuses with unilateral hydronephrosis. The PI values of the middle cerebral artery were high in 2 fetuses with bilateral hydronephrosis and 2 cases with isolated pelvicalyceal ectasia. When the right and left myocardial performance index values of fetuses with renal disease were compared with normal fetuses, no significant results were observed, but the tricuspid valve pulse Doppler was abnormal in fetuses with fetal kidney disease. In addition, the right spherical index was higher in fetuses with renal disease than in the control group.
Conclusion: Although there is no functional change, morphologic findings of right ventricular overload can be observed in fetuses with fetal renal disease.

Keywords: Fetal renal disease, hydronephrosis, polycystic kidney disease, fetal echocardiography, myocardial performance index

INTRODUCTION

If renal disease (such as polycystic kidney or hydronephrosis) develops in the fetus during the prenatal period, knowledge of the hemodynamic effects on the cardiovascular system will help the physician determine the appropriate time of delivery and plan postnatal treatment (1, 2). It provides information about the presence of hemodynamic effects in the prenatal period and also whether renal dysfunction is present in oligohydromnios. Previously, the Doppler findings of the renal arteries have been evaluated to assess renal function, but the parameters of the fetal heart and other flow indices of the fetal arteries have not been used together (3,4). The fetal heart and fetal arteries should be examined by fetal echocardiography and color Doppler. These are noninvasive methods that provide information about the hemodynamic status of the fetal circulatory system (5).

Myocardial performance index (MPI), systolic excursion of the mitral anular plane (MAPSE), systolic excursion of the tricuspid anular plane (TAPSE), and sphericity index (SI) for cardiac function and morphologic changes are different ultrasound indices that provide information about fetal hemodynamic changes. In addition, Doppler velocity parameters of the major arteries in the fetal circulation such as the renal artery, middle cerebral artery (MCA), and umbilical artery are commonly used for hemodynamic assessment of the fetal circulation (6-8).

MATERIAL AND METHOD

A prospective cohort study was conducted in pregnant women with polycystic kidney, hydronephrosis, and pelvicalyceal ectasia. Thirty-one pregnant women with polycystic kidney, hydronephrosis, and pelvic ectasia were enrolled between January 2021 and May 2022 at 2nd and

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3rd trimester. Informed consent was obtained from all pregnant women who participated in the study. The study protocol was approved by the hospital's Department of Medical Research Ethics. The authors have confirmed that they have complied with the World Medical Association Declaration of Helsinki regarding the ethical conduct of research involving human subjects.

In the perinatology clinic, 31 fetuses were diagnosed with renal disease by abdominal ultrasonography. Among the fetuses with renal disease included in this study, polycystic kidney disease was present in 4 fetuses, bilateral hydronephrosis in 4 fetuses, unilateral hydronephrosis in 12 fetuses, and pelvicalyceal ectasia in 28 fetuses. A polycystic kidney was defined as a kidney with cysts 7 mm or more in diameter in at least two locations. We defined a hydronephrotic kidney as one with an anteroposterior pelvic diameter of 7 mm or more (9-11). 30 fetuses without renal disease were also included in the study as a control group.

Twenty fetuses at the same week of gestation (2nd and 3rd trimesters) without abnormal kidneys and other congenital additional anomalies were studied. Informed consent was obtained. Exclusion criteria included multiple pregnancy, premature rupture of membranes, chorioamnionitis, placental abruption, severe fetal growth restriction, fetal congenital heart diseases, preeclampsia, oligohydramnios, and maternal diabetes.

During the evaluation of the study group and the control group: Voluson 730 Ultrasound (GE Healthcare, Zipf, Austria), the kidneys were examined by a specialist in perinatology. Vivid S6 fetal echocardiography device (GE Healthcare, Zipf, Austria) was used by a pediatric cardiologist for measurement of fetal cardiac structure, cardiac functions, and pulse Doppler, umbilical artery pulsatility index (PI), fetal renal artery PI, and MCA PI. To obtain an effective wave analysis during Doppler measurements, it was attempted to obtain them at the lowest point of uterine contractions and fetal activity and at an angle of less than 30°. Spectral recording was performed with at least six pulse streams. PI pulse Doppler measurements were used to evaluate the waveforms of the umbilical artery, fetal MCA, and renal artery (12-15).

We studied the functions and morphological changes of the fetal heart using the following methods (5,6,8,16-18).

1. Diastolic functions of the left and right ventricles: Early diastolic ventricular filling (E), active contractility of the atria (A), mitral and tricuspid valves E/A. Pulse Doppler spectra were obtained for E-, A-, and S-wave velocities and MPI measurements. In the apical four-chamber section, the cursor of the device was placed near the anterior leaflet of the mitral valve in the left ventricle and near the posterior leaflet of the tricuspid valve in the right ventricle. Velocities were recorded as metres per second (m/s) values. For the left and right ventricles, the time from artioventricular (AV) valve closure to semilunar valve opening was measured as isovolumic contraction time (IVCT) and the time from semilunar valve closure to AV valve opening was measured as isovolumic relaxation time (IVRT). Ejection time (ET) is the time from opening to closing of both semilunar valves. Times were expressed in millisecond (ms). MPI was calculated using the following equation: IVCT+IVRT/ ET (Figure 1).

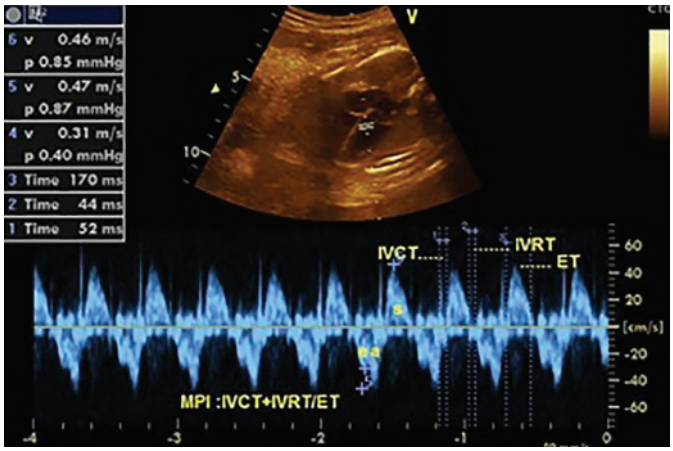

Figure 1. Illustration of myocardial performance index (MPI) assessment by spectral Doppler. Placing the Doppler sample volume on the medial wall of the ascending aorta in a four-chamber view, biphasic mitral inflow (e and a-waveforms) and aortic outflow (s-waveform) are displayed in the same spectral image. MPI is calculated by measuring the following time intervals: isovolumic contraction time (IVCT) from closure of the mitral valve to opening of the aortic valve; ejection time (ET) from opening to closure of the aorta; and isovolumic relaxation time (IVRT) from closure of the aortic valve to opening of the mitral valve

2. Systolic functions of the left and right ventricles were measured: Ventricular contractility per minute (Heart rate), mitral valve S velocity, tricuspid valve S velocity, TAPSE for the right ventricle, MAPSE for the left ventricle. It is the representation and measurement of the displacement of the mitral and tricuspid valves in the systolic phase in the M-mode spectra. It is referred to as MAPSE for the left ventricle and TAPSE for the right ventricle (Figure 2).

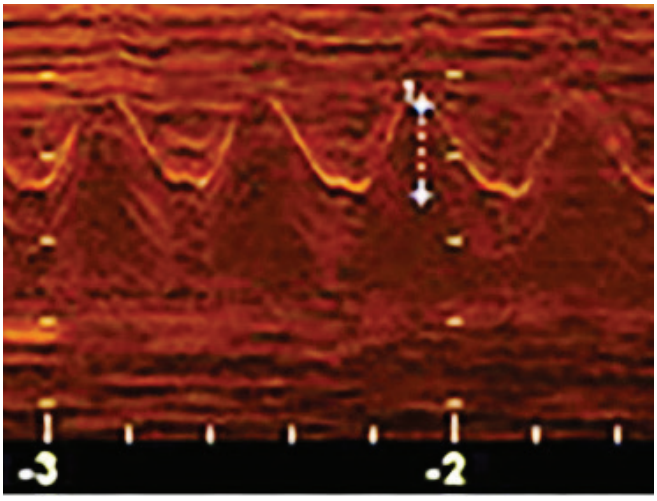

Figure 2. MAPSE M-mode spectra image

3. Morphologic features of the left ventricle and right ventricle: Cardio-thoracic ratio (CTR) was calculated, and left spherical index and right spherical index were evaluated. CTR is the ratio of the circumference of the

heart to the circumference of the chest. SI is the ratio of the apical length of the AV valve planes to the basal length of the valves in diastole.

SPSS was used for all statistical analyzes (23.0; SPSS Chicago, USA). Statistics were expressed as mean±standard deviation, and variables were expressed as percentages. Student's t test was used to evaluate normally distributed groups, and Mann Whitney U test was used to compare nonnormally distributed groups. The Kolmogorov-Smirnov test was used to show whether the groups had a normal distribution. Statistical Results: At 95% confidence interval, p values <0.05 were considered significant.

RESULTS

Thirty-one women were included in this study. The mean maternal age was 27.3 years (range, 21.4-42.5 years), and the mean gestational age of women with fetal kidney disease was 28±1.8 weeks. The mean estimated fetal weight was 1.81 g (range: 760-2,460 g). There were no fetal deaths or preterm births.

Renal diseases were unilateral hydronephrosis (n=12), bilateral hydronephrosis (n=4), polycystic kidney disease (n=4), and pelvicalyceal ectasia (n=28) (Table 1 and Figure 3). The mean PI values of the renal artery, umbilical artery, and middle cerebral artery are summarized in graphs 1, 2, 3. The umbilical artery PI values of all cases, high PI values were observed in 2 bilateral hydronephrosis cases and in 2 unilateral hydronephrosis cases. Values close to the 95% percentile limit were observed in 2 isolated cases of pelvicalyceal ectasia. For MCA pulsatility indices, PI values were high in 2 cases of bilateral hydronephrosis and 2 cases of isolated pelvicalyceal ectasia. MCA PI -values were in the 50-95th percentile range in most patients with renal disease. The PI graphics of umbilical artery, renal artery and MCA was shown in Figure 4.

Table 1. Distribution of renal diseases

Renal diseases	Unilateral hydronephrosis	Bilateral hydronephrosis	Polycystic kidney	Pelvicalyceal ectasia
Unilateral hydronephrosis	1	-	1	10
Bilateral hydronephrosis	-	-	-	4
Polycystic kidney	1	1	-	2
Pelvicalyceal ectasia	10	4	2	12

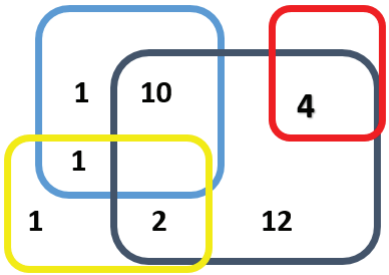

Figure 3. Blue color: unilateral hydronephrosis, Red color: bilateral hydronephrosis, Yellow color: polycystic kidney, Black color: pelvicalyceal ectasia

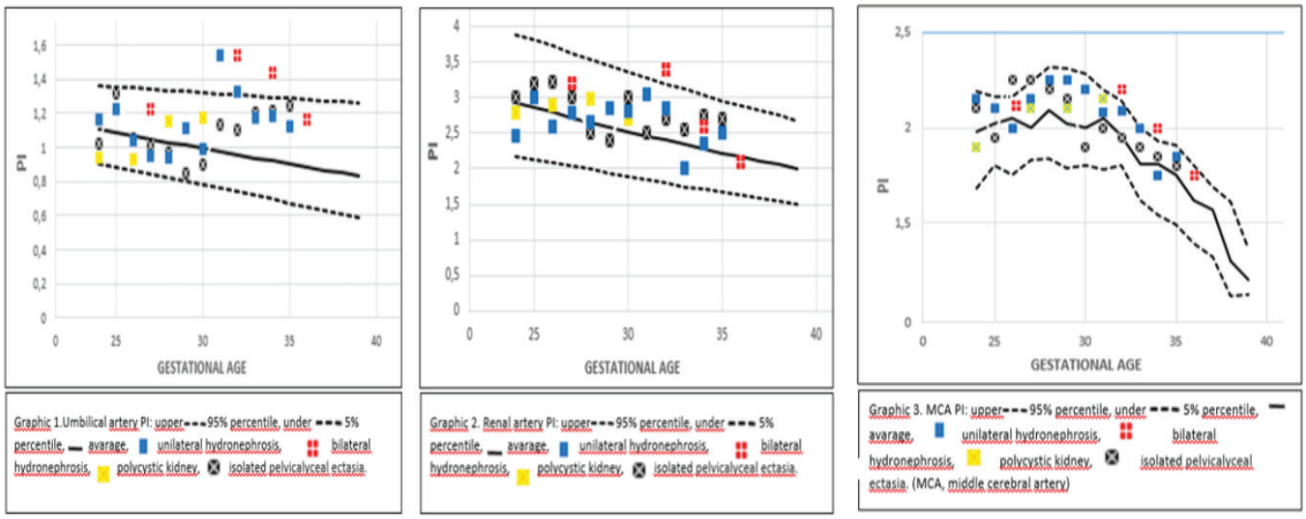

Figure 4. The PI graphics of umbilical artery, renal artery and MCA

Diastolic, systolic, and diastolic-systolic functional parameters and morphometric values of the fetal heart of the study group and the control group were compared in Table 2.

The right and left MPI values of the fetuses with renal disease were compared with those of normal fetuses. The E and A values of the tricuspid valve were higher than those of the normal fetuses (p<0.05). Right spherical index was found to be statistically significantly higher in renal disease (p=0.048).

The results of TAPSE, MAPSE, mitral S, and tricuspid S to evaluate systolic functions of fetuses with renal disease were compared with normal fetuses, and no significant difference was found between cytolic functions in both

groups. Similarly, the results of cardiothoracic ratio, left spherical index, and right spherical index were compared between the two groups to compare the morphological characteristics of the heart, and no significant difference was found (Table 2).

Table 2. Diastolic, systolic and diastolic-systolic function parameters and morphometric values of fetal heart in fetal kidney disease and control group

	Renal disease (n=31)	Control (n=30)	p
Diastolic function			
Left ventricle MPI[a]	0.51±0.01	0.54±0.01	0.09
Mitral maximum E wave velocity (m/s)	39±2.14	41±1.95	0.18
Mitral maximum A wave velocity (m/s)	61±3.22	62±2.65	0.64
Mitral E/A	0.64±1.16	0.66±0.21	0.09
Right ventricle MPI[a]	0.53±0.02	0.55±0.01	0.1
Tricuspid maximum E wave velocity (m/s)	48±2.14	44±1.95	**0.044**
Tricuspid maximum A wave velocity (m/s)	66±2.21	62±1.32	**0.046**
Tricuspid E/A	0.73±2.12	0.71±1.28	0.09
Systolic function			
Heart rate, bpm	142	140	0.14
MAPSE[b] (mm)	7.28±0.98	7.02±0.80	0.28
TAPSE[b] (mm)	7.68±0.98	7.22±0.80	0.26
Mitral S (cm/sn)	6.6±0.56	6.5±0.8	0.40
Tricuspid S (cm/sn)	7.9±0.56	7.2±0.8	0.22
Cardiac morphometry			
Cardiothoracic ratio	0.31±0.2	0.30±0.2	0.35
Left spherical index	1.95±0.04	1.85±0.06	0.09
Right spherical index	0.77±0.08	0.68±1.28	**0.048**

Mann Whitney U test was performed; a: myocardial performance index, b: mitral annular plane systolic excursion, c: tricuspid annular plane systolic excursion; results were accepted as 95% confidence interval and p value <0.05 significant

DISCUSSION

The most frequently detected renal diseases in the fetal period: fetal hydronephrosis, polycystic kidney disease, pelvicalyceal ectasia. Fetal hydronephrosis may be unilateral or bilateral. Fetal renal disease is easily detected here with fetal ultrasound. We included the cases of unilateral hydronephrosis, bilateral hydronephrosis, polycystic kidney and pelvicalyceal ectasia (2,19,20). The fact that the functional parameters were normal and the right spherical index was higher in the fetal renal disease than in the control group suggests that early-onset cardiac overload may be present morphologically, if not functionally.

Studies have shown that diagnosed fetal renal disease may have hemodynamic effects. The studies used hemodynamic effects in fetal renal artery and descending aorta Doppler parameters. However, the studies investigating the cardiac functions and renal hemodynamic effects in fetal renal disease in the fetal period are insufficient (3,21-23). In this study, we investigated the umbilical artery, MCA Doppler parameters of fetuses with renal disease in the fetal term, fetal renal arteries, and also showed the systolic and diastolic functional parameters of the heart and the results of the morphological structure of the heart. The cases with fetal renal disease included in the study were compared with normal fetuses at the same gestational week.

Wladimiroff et al. studied the PI of renal arteries in patients with bilateral hydronephrosis, unilateral hydronephrosis, and unilateral multicystic kidney. In this study, the majority values of the renal artery PI did not differ from normal values in both bilateral and unilateral obstructive uropathy (4). Gudmundsson et al. obtained similar results in their studies (24). In two studies by Lura, the use of PI in renal disease showed little change with gestational age and no statistically significant difference was found (2,3). However, Wladimiroff et al. showed a positive correlation between renal artery PI and severe hydronephrosis. In patients with multicystic kidneys, the renal artery PI was found to be above the normal range in two quarters (4). Among the fetuses in our study, only one case with bilateral hydronephrosis had a high renal artery value PI. When we consider the umbilical artery values PI of all cases, high PI values were observed in 2 bilateral hydronephrosis cases and in 2 unilateral hydronephrosis cases. Values close to the 95% percentile limit were observed in 2 isolated cases of pelvicalyceal ectasia. For MCA pulsatility indices, PI values were high in 2 cases of bilateral hydronephrosis and 2 cases of isolated pelvicalyceal ectasia. MCA PI -Values were in the 50-95th percentile range in most patients with renal disease. Apart from renal artery values PI, it should be noted that umbilical artery and MCA PI values can also

provide valuable results in renal disease.

In previous studies, fetal MPI has been increasingly used as an indicator of fetal cardiac function in various pathologies, including intrauterine growth retardation and twin-to-twin transfusion syndrome. as well as in diabetic pregnancies (16,17). In our study, when the right and left MPI values of fetuses with renal disease were compared with normal fetuses, there was no significant result, but the E and A values of the tricuspid valve were higher than normal values ($p<0.05$). The difference between E/A values of the tricuspid valve was insignificant. The E wave is caused by the pressure in the ventricles falling below the pressure in the atria during the cardiac cycle, and therefore atrial pressure is affected by ventricular compliance and the rate of relaxation of the ventricles. The A wave or wave of atrial contraction is located immediately after the E wave in Doppler flow analysis. It is influenced by ventricular compliance, atrial pressure, and atrial contraction rate. The E and A waves are influenced by preload and afterload. In the fetal period, the A velocity is greater than the E velocity. Flow, preload, and heart rate (including arrhythmias) change with age (25,26). The proportional increase in E and A velocities of tricuspid flow in the group with renal disease may actually be related to increased preload rather than diastolic dysfunction. The fact that the functional parameters were normal in the fetal renal disease detected in our study and the right spherical index was higher than in the control group supports this situation.

When TAPSE, MAPSE, mitral S, and tricuspid S results were compared to evaluate systolic functions of fetuses with renal disease with normal fetuses, no significant difference was found between cytolic functions in both groups. In fact, in fetuses with renal disease, except for the abnormally high values in bilateral hydrops fetalis, there were no major changes in umbilical artery, renal artery, and MCA Doppler data, and cardiac morphology and systolic and diastolic functions were hardly affected. There may be volume loading on the right side of the heart that does not affect cardiac functions. The fact that MCA PI values are above the mean in most patients with renal pathology may be explained by a volume load that is higher than expected hemodynamically (25).

Limitations

Our study has some limitations. First of all, our sample size is partially small. Although prenatal ultrasound has revolutionized the management of renal anomalies by providing definitive, early intervention, it also reveals the vast majority of clinically and literally "not sick" newborns.

CONCLUSION

In summary, we can use fetal echocardiography analysis methods to reveal the hemodynamic influence and cardiac function in the prenatal period with sensitive measurements. In contrast to previous studies, it may be useful to use other criteria that indicate hemodynamic changes. In particular, in fetuses with renal disease, the PI values of the renal artery, umbilical artery, and MCA, as well as the E and A velocity values of the tricuspid valve, may be evaluated differently than in normal fetuses. In addition, the high right spherical index indicates that there may be a morphological burden on the right heart in fetal kidney disease that does not affect the functional parameters. However, to make the results more meaningful and reliable, more comprehensive studies are needed that include cases with multiple fetal kidney diseases.

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Research Article

Investigation of the Relationship Between Kinesiophobia and Pain, Quality of Life and Physical Functions in Osteoarthritis Patients

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Abstract

Aim: Osteoarthritis (OA) is a chronic, degenerative joint disease that is characterised by joint pain and stiffness. The development of kinesiophobia is common in OA patients, especially related to pain and loss of function. The aim of our study was to determine the relationship between kinesiophobia and pain, quality of life and physical functions in patients with knee OA.
Material and Method: A total of 60 patients (30 females and 30 males, aged 40-65 years) diagnosed with Kellgren-Lawrence (KL) grade 2 and 3 OA participated in this cross-sectional study. Tampa Scale for Kinesiophobia (TSK), Short Form Health Survey (SF-12), Visual Analogue Scale (VAS), Knee Injury and Osteoarthritis Outcome Score Physical Function Short Form (KOOS-PS), Oxford Knee Score (OKS), Lower Extremity Functional Scale (LEFS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Berg Balance Scale (BBS) scales and Timed Up and Go (TUG), 6-Minute Walking Test (6MWT), The Five Repetition Sit to Stand Test (5STS) and Stair-Climbing Test (SCT) functional tests were performed.
Results: A statistically significant difference was observed between the male and female groups in all scales and functional test results, with the exception of TSK ($p<0.05$). A positive correlation was found between kinesiophobia and SCT in the female group, while a negative correlation was found between TUG and SF-12 PCS in the male group ($p<0.05$).
Conclusion: The findings indicated that, in general, kinesiophobia was not significantly correlated with pain, knee score, balance, quality of life and functional tests in male and female OA patients. However, some scales and tests showed positive and negative correlations with kinesiophobia in both groups, although limited.

Keywords: Osteoarthritis, kinesiophobia, pain, quality of life, physical function

INTRODUCTION

Osteoarthritis (OA) is a degenerative joint disease that is characterised by the deterioration of cartilage in joints, as well as the formation of new bone and sclerosis (1,2). Radiologically, it can be examined in five different grades according to the Kellgren-Lawrence (KL) classification, which indicates that radiologic findings progressively worsen from zero to grade four (3,4). It is estimated that approximately 250 million people worldwide are affected by OA, a degenerative joint disease (5). In the treatment of OA, pharmacologic methods are usually limited to the use of paracetamol or non-steroidal anti-inflammatory drugs (6). In addition to drug treatment, there are various conservative treatment options including patient education, weight control, activity modification, exercise therapy, appropriate footwear selection, supportive devices and various physical therapy methods (7-9).

OA is characterized by pain and stiffness in the joints and this may lead to loss of function in daily life activities (10). It has been observed that joint movements, especially flexion and rotation, increase the level of pain in OA patients (11). Increased pain during these movements may lead to a tendency to avoid movements and even fear of movement (12). In conditions such as chronic musculoskeletal pain, individuals generally tend to avoid activities due to fear of pain rather than actual pain (13). This may lead to a

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decrease in the ability to perform basic tasks in daily life such as sitting, walking, standing and climbing stairs (14). Lack of regular physical activity in OA patients is considered an important risk factor for functional decline (15). Conversely, elevated levels of physical activity are frequently linked to enhanced knee strength and improvements physical performance (16). Nevertheless, despite the established advantages of physical activity, a considerable number of individuals with knee OA continue to engage in minimal or no physical activity (17). Previous studies has identified several factors that influence participation in physical activity in OA patients. These factors include older age, non-white ethnicity, increasing OA symptoms and female gender (18). Moreover, psychological factors, such as anxiety and depression, are believed to be more prevalent in women with knee OA and are thought to be a significant contributing factor to the persistence of pain (19). Avoidance of activities and weight bearing on the knee joint for long periods of time due to fear of painful injury or re-injury, known as kinesiophobia, which is common in OA patients, may decrease knee muscle strength and endurance (8,20). It can be reasonably deduced that the presence of kinesiophobia may serve to exacerbate functional performance deficits in patients with OA and diminish quality of life by interfering with activities of daily living (21,22). A review of the literature reveals a correlation between kinesiophobia and several key factors in musculoskeletal disorders, including high pain intensity, poor functional status, and high psychological and physical disability (23,24). Furthermore, high levels of kinesiophobia in OA patients, especially in the elderly, can be associated with increased pain levels and decreased functional performance (25).

OA is a very important and influential factor for the patient in terms of both health and socioeconomic costs. For this reason, it is thought that determining the relationships between factors such as functional status, pain, quality of life and kinesiophobia in OA may contribute to the OA treatment process. The aim of our study was to investigate the relationship between kinesiophobia, pain, quality of life, and physical functions in patients with knee osteoarthritis. The main hypothesis of this study is that kinesiophobia may have positive correlations with pain parameters and negative correlations with knee scores, quality of life scales and functional performance in OA patients.

MATERIAL AND METHOD

Participants

A total of 60 patients, 30 females and 30 males, aged 40-65 years, diagnosed with KL grade 2 and 3 OA, who completed filled out informed consent forms were included in this study. The G*Power 3.1 software was employed to ascertain the requisite number of subjects for inclusion in the study. The results indicated that a total of 22 subjects in each group would be an appropriate sample size (effect size r: 0.85, lower and upper critical p: 0.55, true power: 0.93). Inclusion criteria for participants: (i) over 25 years of age, (ii) knee pain for more than three months, (iii) radiologic presence of bilateral OA changes in the tibiofemoral joint. Exclusion criteria for participants: (i) a history of injury or surgical intervention affecting the lower extremities, (ii) history of the development of systemic inflammatory arthritis, (iii) infiltration corticosteroids in the knees in the last six months, and (iv) history of meniscus or ligament injury in the knee.

Experimental Design

This observational study was a cross-sectional design. All measurements were completed on two consecutive days and during the same time period (13.00-15.00). On the first day, participants completed the Tampa Scale for Kinesiophobia (TSK), Visual Analogue Scale (VAS), Knee Injury and Osteoarthritis Outcome Score Physical Function Short Form (KOOS-PS), Lower Extremity Functional Scale (LEFS), Oxford Knee Score (OKS), Short Form Health Survey (SF-12), Western Ontario and McMaster Universities v Index (WOMAC) and Berg Balance Scale (BBS). In addition, the 6-Minute Walking Test (6MWT) and The Five Repetition Sit to Stand Test (5STS) were performed on the same day. On the second day, Timed Up and Go (TUG) and Stair-Climbing Test (SCT) tests were performed (Figure 1). The primary endpoint of the study was the successful completion of the tests and the secondary endpoint was the patient's unwillingness to continue the study for various reasons and the occurrence of any trauma to the index joint.

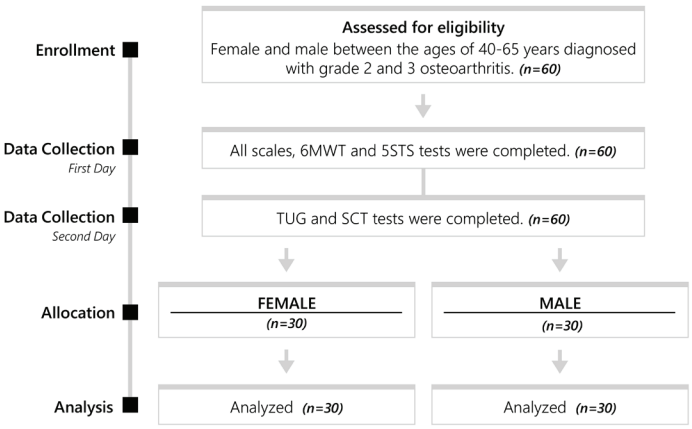

Figure 1. Flowchart

This study was conducted in accordance with the ethical guidelines stated in the Declaration of Helsinki and ICH Good Clinical Practice guidelines. Approval from the ethics committee of Gümüşhane University Scientific Research and Publication Ethics Committee was obtained (protocol no: E-95674917-108.99-222915).

Outcome Measures

Pain and Quality of Life Scales

VAS: This scale is used to assess knee pain and is self-assessed by patients. Patients mark a point on a 10 cm long line between "no pain" and "worst possible pain" according to their level of pain. Higher scores indicate more pain.

TSK: TSK is a scale that assesses fear of injury. It consists of 17 questions and is rated on a scale from 1 to 4. The total score ranges from 17 to 68, with higher scores indicating

an increased severity of pain-related fear. A score of 17 represents no kinesiophobia and a score of 68 represents severe kinesiophobia.

KOOS-PS: KOOS-PS is a seven-item scale used to assess the difficulties people experience in daily activities related to knee health. All items are evaluated on a five-point Likert scale, with scores ranging from 0 to 4 (none, mild, moderate, severe, extreme). The scale is scored from 0 (no problems) to 100 (extreme problems), assessing how smoothly people are able to perform these activities.

OKS: OKS assesses the patient's pain and functional status in the last 4 weeks and consists of 12 questions. It is assessed on a scale of 0 to 48, with lower scores indicating better pain and functional status.

SF-12: SF-12 is a shortened version of the SF-36 and is used to assess health-related quality of life. The scale consists of 12 items and physical and mental component summary scores (PCS and MCS) are calculated and evaluated with a specific scoring algorithm. The scores are expressed on a scale of 0 to 100, with higher scores indicating a superior quality of life.

LEFS: LEFS is a scale that assesses lower limb function and activity limitation. The questionnaire consists of 20 items in total and each item is scored from 0 to 4 on a scale from "extremely difficult" to "no difficulty". The highest total score is 80, with higher scores indicating a higher functional level.

WOMAC: The scale comprises 24 items and was developed for the purpose of assessing pain, joint stiffness and physical function in individuals with knee and hip OA. Higher scores indicate more severe pain, stiffness and functional limitations.

Functional Performance Tests

TUG: For TUG, a tape was placed on the floor 3 meters in front of a standard height chair. Patients were seated on the chair, asked to rest their backs on the chair backrest and arms on the armrests. They were instructed to walk 3 meters at a normal speed, turn around, return to the chair and sit down, and the elapsed time was recorded in seconds.

6MWT: 6MWT was conducted indoors in a long and straight corridor. The walking track was 30 meters long with markings every 2.5 meters. Before the test, patients rested seated for 10 minutes and then were asked to walk the course for 6 minutes. They could pause and rest if needed and were allowed to use assistive devices such as canes if necessary. The distance covered during walking was recorded in centimeters.

5STS: The 5STS involves patients getting up and sitting down from a chair five times as quickly as possible with their arms crossed at chest level. The timing started as soon as the patients lifted their hips off the chair and stopped on their fifth sit-up. The test was repeated twice for each patient and the best result was used for analysis. The elapsed time was measured with a stopwatch.

SCT: The staircase required for the test consisted of 6 steps, each step being 17,5 cm high. Patients completed the test by climbing up and down the 6 steps at their own pace and could use the handrail when necessary. The elapsed time was recorded in seconds.

BBS: BBS consists of 14 common tasks assessing static and dynamic balance. Each task is scored between 0 and 4, with 0 indicating that the task was not accomplished and 4 indicating that it was accomplished independently. The total score of the 14 tasks is summed to obtain a total score between 0 and 56. Higher scores may predict better balance performance, while scores ≤45 may predict fall risk.

Statistical Analysis

Statistical analyses were performed using the SPSS 24.0 (SPSS Inc., Chicago, IL, USA) package program. The normality of the data was tested using the Kolmogorov-Smirnov test and the data were found to exhibit a normal distribution. Descriptive statistics were presented as number (n), percentage (%), mean, standard deviation (SD), minimum (Min.) and maximum (Max.) values. Independent samples t test was used in the comparisons of scale and test results between female and male groups. Pearson correlation analysis was used to determine the correlations of the scale and test results with TSK in both groups. Statistical significance level was taken as $p<0.05$ in all analyses performed in the study.

RESULTS

In Table 1, the descriptive data of the groups are presented as mean±standard deviation.

Table 2 shows the comparison of pain, kinesiophobia and quality of life scale results between male and female groups. When the evaluations were examined, a statistically significant difference was found between the female and male groups in VAS, KOOS-PS, OKS, SF-12 PCS, SF-12 MCS, LEFS and WOMAC P., WOMAC S., WOMAC F. and WOMAC T. scores ($p<0.05$). In the TSK scale, there was no statistically significant difference between the female and male groups and the results were similar between the groups ($p>0.05$).

Table 3 includes the comparisons of the intergroup evaluations of functional test and scale results between male and female groups. Statistically significant differences were shown between male and female groups in TUG, 6MWT, 5STS, SCT and BBS ($p<0.05$).

Table 4 shows the relationship between kinesiophobia and pain, quality of life, functional test and scale results in the female group. There was a positive correlation between SCT and kinesiophobia ($p<0.05$). Although there was a positive correlation between kinesiophobia and OKS and SF-12 PCS scores, there was no statistical significance ($p>0.05$). Also, there was no statistical correlation between 6MWT, 5STS, BBS, VAS, KOOS-PS, SF-12 MCS, LEFS and WOMAC P., WOMAC S., WOMAC F. and WOMAC T. scores ($p>0.05$).

Table 5 shows the relationship between kinesiophobia and pain, quality of life, functional tests and scale results in the male group. There was a negative correlation between kinesiophobia and TUG and SF-12 PCS ($p<0.05$). There was no statistical correlation between kinesiophobia and 6MWT, 5STS, SCT, BBS, VAS, KOOS-PS, OKS, SF-12 MCS, LEFS and WOMAC P., WOMAC S., WOMAC F. and WOMAC T. scores ($p>0.05$).

Table 1. Descriptive data of female and male subject groups

	Mean	SD	Min.	Max.
Age (year)				
Female	53.90	6.81	42.00	65.00
Male	50.07	8.55	40.00	65.00
Height (cm)				
Female	162.23	5.35	150.00	175.00
Male	174.10	8.77	156.00	184.00
Weight (kg)				
Female	87.17	12.61	66.00	120.00
Male	92.07	12.41	75.00	118.00
BMI				
Female	33.14	4.61	24.24	41.52
Male	30.03	3.99	23.89	40.83
OA side	**Left**		**Right**	
Female	16 (53%)		14 (47%)	
Male	25 (83%)		5 (17%)	

BMI: body mass index, OA: osteoarthritis, SD: standard deviation, Min.: minimum, Max.: maximum

Table 2. Intergroup evaluation of pain, kinesiophobia and quality of life scale results

	Female		Male		t	ES	95% CI		p
	Mean	SD	Mean	SD			LB	UB	
TSK	42.23	8.52	38.90	8.43	1.52	0.39	-1.05	7.72	0.133
VAS	8.17	1.54	5.01	2.66	5.63	1.45	2.04	4.28	<0.001*
KOOS-PS	22.20	12.56	11.10	6.12	4.35	1.12	5.99	16.21	<0.001*
OKS	24.47	7.83	14.10	6.97	5.42	1.40	6.54	14.20	<0.001*
SF-12 PCS	29.57	7.60	40.29	9.85	-4.72	-1.22	-15.26	-6.17	<0.001*
SF-12 MCS	43.27	10.64	52.22	8.23	-3.64	-0.94	-13.87	-4.04	<0.001*
LEFS	30.03	13.80	46.63	15.58	-4.37	-1.13	-24.20	-9.00	<0.001*
WOMAC P.	9.27	3.98	5.50	4.00	3.66	0.94	1.70	5.83	<0.001*
WOMAC S.	3.43	2.30	1.77	1.92	3.04	0.79	0.57	2.76	0.004*
WOMAC F.	36.63	13.10	20.97	11.88	4.85	1.25	9.20	22.13	<0.001*
WOMAC T.	51.23	18.59	29.41	16.71	4.78	1.23	12.69	30.96	<0.001*

*p<0.05; SD: standard deviation, t: independent samples t tests results, ES: effect size, CI: confidence interval, LB: lower bound, UB: upper bound, TSK: tampa scale for kinesiophobia, VAS: visual analogue scale, KOOS-PS: knee injury and osteoarthritis outcome score physical function short form, OKS: Oxford knee score, SF-12 PCS: short form healthy survey physical, SF-12 MCS: short form healthy survey mental, LEFS: lower extremity functional scale, WOMAC P.: womac pain, WOMAC S.: womac stiffness, WOMAC F.: womac physical function, WOMAC T. womac total

Table 3. Intergroup evaluation of functional tests and BBS results

	Female		Male		t	ES	95% CI		p
	Mean	SD	Mean	SD			LB	UB	
TUG (s)	12.50	3.71	8.67	1.78	5.10	1.32	2.33	5.33	<0.001*
6MWT (m)	342.83	93.34	430.97	76.61	-4.00	-1.03	-132.27	-44.00	<0.001*
5STS (s)	23.03	8.91	14.04	2.90	5.25	1.36	5.56	12.41	<0.001*
SCT (s)	14.11	5.61	8.92	3.43	4.32	1.11	2.78	7.59	<0.001*
BBS	50.77	5.75	55.50	1.04	-4.44	-1.15	-6.87	-2.60	<0.001*

*p<0.05; SD: standard deviation, t: independent samples t tests results, ES: effect size, CI: confidence interval, LB: lower bound, UB: upper bound, TUG: timed up and go, 6MWT: 6-minute walking test, 5STS: the five repetition sit to stand test, SCT: stair-climbing test, BBS: berg balance scale

Table 4. Evaluation of the relationship between kinesiophobia and pain, quality of life, functional test and scale results in female

Correlation variable	r	p
TUG (s)	0.199	0.292
6MWT (m)	-0.012	0.950
5STS (s)	0.120	0.528
SCT (s)	0.377*	0.040*
BBS	-0.214	0.256
VAS	0.020	0.915
KOOS-PS	0.177	0.350
OKS	0.340	0.066
SF-12 PCS	-0.327	0.078
SF-12 MCS	-0.262	0.162
LEFS	-0.278	0.137
WOMAC P.	0.290	0.121
WOMAC S.	0.229	0.224
WOMAC F.	0.270	0.149
WOMAC T.	0.299	0.108

*p<0.05; TUG: timed up and go, 6MWT: 6-minute walking test, 5STS: the five repetition sit to stand test, SCT: stair-climbing test, BBS: berg balance scale, VAS: visual analogue scale, KOOS-PS: knee injury and osteoarthritis outcome score physical function short form, OKS: oxford knee score, SF-12 PCS: short form healthy survey physical, SF-12 MCS: short form healthy survey mental, LEFS: lower extremity functional scale, WOMAC P.: womac pain, WOMAC S.: womac stiffness, WOMAC F.: womac physical function, WOMAC T.: womac total

Table 5. Evaluation of the relationship between kinesiophobia and pain, quality of life, functional test and scale results in male

Correlation variable	r	p
TUG (s)	-0.368*	0.045*
6MWT (m)	-0.146	0.440
5STS (s)	-0.025	0.896
SCT (s)	0.107	0.574
BBS	0.143	0.450
VAS	0.011	0.954
KOOS-PS	0.036	0.849
OKS	0.020	0.916
SF-12 PCS	-0.535*	0.002*
SF-12 MCS	-0.205	0.277
LEFS	-0.241	0.199
WOMAC P.	0.310	0.095
WOMAC S.	-0.076	0.690
WOMAC F.	0.305	0.101
WOMAC T.	0.294	0.114

*p<0.05; TUG: timed up and go, 6MWT: 6-minute walking test, 5STS: the five repetition sit to stand test, SCT: stair-climbing test, BBS: berg balance scale, VAS: visual analogue scale, KOOS-PS: knee injury and osteoarthritis outcome score physical function short form, OKS: oxford knee score, SF-12 PCS: short form healthy survey physical, SF-12 MCS: short form healthy survey mental, LEFS: lower extremity functional scale, WOMAC P.: womac pain, WOMAC S.: womac stiffness, WOMAC F.: womac physical function, WOMAC T.: womac total

DISCUSSION

The aim of this study was to investigate the correlations between kinesiophobia levels and various pain, knee score, quality of life, balance and functional test results in male and female knee OA patients and to determine whether kinesiophobia level has a predictive effect on these parameters in OA patients.

The results showed that, in overall terms, kinesiophobia did not have a statistical correlation with pain, quality of life, knee score, balance and functional tests in OA patients. However, although limited, some scales and tests were positively or negatively correlated with kinesiophobia in both groups.

OA is primarily associated with pain, which in turn has a negative impact on flexibility, physical function and activities of daily living (26,27). In fact, several studies have reported significant correlations between the level of OA and pain (28,29). Depending on the level of pain after OA, patients may suffer from kinesiophobia. The results of our study indicate that there is no statistically significant correlation between the kinesiophobia scores obtained with the TSK and the pain scores obtained with VAS and WOMAC P. scales in both groups. Although various studies in the literature have reported significant correlations between kinesiophobia and pain level in OA patients, there are also studies in which this correlation was not found (13,21,25,26,30-32). The conflicting results in the literature regarding the correlation between kinesiophobia and pain in OA patients make it difficult to evaluate clearly between these two parameters. It is important to note, however, that the terms "presence of pain" and "severity of pain" are not synonymous (31). The absence of significant correlations in our study and in other similar studies may not be indicative of the absence of a causal relationship between pain and kinesiophobia. There are also studies emphasizing the importance of the changing nociceptive processing mechanism related to OA pain (33,34). Therefore, physical and psychosocial differences as well as nociceptive pain dominance may cause individuals to be more affected by structural and biomechanical factors (30,35).

The findings of this study indicated that OA -related kinesiophobia was not significantly correlated with various knee scores and quality of life scales as well as pain. KOOS-PS, OCS, SF-12 MCS, LEFS and WOMAC scores were not significantly correlated with kinesiophobia in both groups. However, SF-12 PCS scores were moderately negatively correlated with kinesiophobia, especially in male patients (r=-0.535, p=0.002). There was also a similar moderate correlation in female patients (r=-0.327, p=0.078). Selçuk and Karakoyun (2020) analyzed the correlations of kinesiophobia with SF-12 and WOMAC results in OA patients and found that both scales were moderate correlated with kinesiophobia (4). In a similar study, Alaca (2019) reported moderate correlations between kinesiophobia and WOMAC scores in OA patients (36). In another study, Padave et al. (2023) found a low

correlation between kinesiophobia and OKS scores in OA patients (30). Literature studies examining the correlations between the level of kinesiophobia related to OA and various scale results show variable results similar to the level of pain. This may be related to the fact that the scales included in the study consist of results based on direct self-assessment and therefore individual differences may affect the scale scores considerably.

It can be anticipated that in patients with OA, parameters related to balance, which is a fundamental prerequisite for functional movement, may be impaired (31). Therefore, it is important to examine the possible relationships between balance and kinesiophobia in OA patients. The results of our study indicated no statistically significant correlation between the BBS and TSK results. This outcome is in accordance with the findings of other studies in the existing literature (30,31). It may be thought that kinesiophobia may have an effect on balance performance, but the fact that other factors such as range of motion and muscle strength are also important factors on balance may prevent kinesiophobia from directly producing high-level effects (22).

Considering the loss of physical function and psychological effects in each joint affected by OA, differences in functional performance may be expected to occur with kinesiophobia in OA patients (37). Alshahrani et al. (2022) found a moderate significant correlation between kinesiophobia and 5STS test results in their study with OA patients (25). In another study in which the subject group consisted mostly of female OA patients, a low correlation was reported between kinesiophobia and SCT results (r=0.239, p=0.066) (30). In our study, a moderate significant correlation was found between kinesiophobia and SCT results in the female group (r=0.377, p=0.040). In a different study by Gür et al. (2021), there was no significant correlation between the same parameters (r=-0.230, p=0.341) (32). However, in the same study, moderate significant correlations were reported between kinesiophobia and both TUG and 5STS results (32). Ekediegwu et al. (2022) reported no significant correlation between kinesiophobia and TUG results in their study (38). In our study, TUG results showed a moderate negative correlation with kinesiophobia in the male group (r=-0.368, p=0.045). No significant correlations were found in other functional test results. When previous studies are examined, it is seen that the effects of kinesiophobia, especially on functional performance, reveal highly variable results. This may be related to the presence of many different important factors on functional performance and the fact that these factors may show wide differences in individuals with OA.

Although the study results showed conflicting findings regarding kinesiophobia, it is possible that this is due to various limitations of the study. These limitations include a relatively wide age range, not specifically targeting a particular level of OA, the number of subjects, and not comparing the results with age and BMI variables.

CONCLUSION

The results of the study showed that it may be conflicting to establish a direct statistical correlation between kinesiophobia and various scale and test results in OA patients. Nevertheless, the study makes an important contribution to the field in terms of revealing the variable effects of kinesiophobia. In future studies, in addition to the current parameters evaluated, direct comparison of kinesiophobia level with functional findings such as muscle strength and joint range will provide important contributions. In addition, considering that individual differences may be significant especially in studies to be conducted with OA patients, limiting the subject groups as much as possible in terms of parameters such as gender, age range and OA levels may contribute to the emergence of more clear results.

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Research Article

Are YouTube™ Videos Useful for Patients? An Evaluation of YouTube™ Videos on Zygomatic Implants

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Abstract

Aim: The aim of this study was to evaluate the quality of information provided by YouTube™ videos on zygomatic implants.
Material and Method: YouTube™ videos were searched using the keyword "Zygomatic implants". The first 200 videos were analyzed. After exclusion, the remaining 94 videos were independently analyzed by two investigators for demographic characteristics and content usefulness. All videos were rated as poor, fair, or excellent based on a usefulness score that assessed the quality and flow of the content. Overall video ratings included duration, views, likes, dislikes, and comments. Video content was analyzed using an 8-point scoring list. All videos were categorized according to their source. Categorical data were analyzed using Pearson's chi-squared test. For non-normally distributed data, the Kruskal-Wallis test was used for between-group comparisons, and post-hoc Dunn's test was used for multiple comparisons. The significance level was set at $p<0.050$.
Results: Analysis of the video upload locations showed that the highest rate was from the USA (51.1%), followed by India (21.3%) and Spain (5.3%). Regarding the source of the uploaded videos, 11.7% were educational videos produced by doctors, 54.2% were patient information videos, and 34% were promotional videos. There was a statistically significant difference in the median number of views, likes, and dislikes depending on the source of the video upload ($p<0.001$), but no statistically significant difference was found in other video parameters.
Conclusion: Healthcare professionals should evaluate YouTube™ videos on zygomatic implants for clinical accuracy and content quality, and recommend videos to patients that meet professional standards and achieve the intended educational goals.

Keywords: E-healthcare, social media, zygomatic implants

INTRODUCTION

Certain patients with significant upper jaw bone deterioration (advanced bone resorption and/or large maxillary sinuses) are not eligible for conventional dental implant treatment in the edentulous maxilla. This is due to a lack of sufficient bone density to support the implants. Bone grafting has become a standard practice in oral rehabilitation for the past three decades and can be performed either as a separate procedure or in conjunction with implant placement (1,3). While bone grafting may address the lack of suitable bone for implants, it introduces another challenge—the donor site. This results in more invasive surgery, a longer procedure, and a higher overall cost (4-6). In search of ways to bypass bone grafting, the dental field has embraced zygomatic implants. Over the last twenty years, this technology has emerged as a successful treatment for severely atrophied upper jaws and even for jawbone removal surgery. Additionally, various techniques and implant designs have been developed, such as curved and/or short implants, implants anchored through the pterygomaxillary suture, and transnasal implants in cases of advanced bone resorption (7,8).

Designed to restore full functionality in patients with significant upper jawbone loss, zygomatic implants offer a solution for those with large defects caused by tumor removal, injuries, or congenital abnormalities (9,10). The zygomatic arch is used to anchor a long implant that can be combined with conventional implants to support

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dentures, prostheses, and/or obturators. For patients with significant maxillary defects, zygomatic implants provide a pathway to complete oral rehabilitation. This technique restores lost function, enhances facial aesthetics, and allows many patients to resume a fulfilling social life.

The explosion of internet accessibility across the globe has fueled a surge in people turning to online resources for information on healthcare (11,12). The rise of social media has further accelerated the growth of user-generated content, transforming the way information spreads. People of all ages and backgrounds can now share information instantly across the globe, bypassing traditional barriers of time and location (13). One of these social media platforms, ranking as the second most visited website in the world, is YouTube™ (14). With over 2 billion daily views, YouTube™ boasts a vibrant community where new videos are uploaded every minute, and users remain engaged for an average of 15 minutes daily (15). Social media platforms also provide information that allows people to cross-reference information provided by clinicians, bringing together new, additional, or conflicting material (16). However, these sites have minimal guidelines for the content of uploaded material and operate on the principle of freedom of expression. The ability to create health information extends beyond medical professionals; anyone with internet access can contribute and share health-related content on these platforms, which may lead to the dissemination of false information (17). A review of the literature showed that videos uploaded to YouTube™ about maxillofacial surgery have been evaluated. However, although many videos about zygomatic implants exist from various sources, these videos have not been evaluated. This research investigated the quality, accuracy, and content of the most popular YouTube™ videos on zygomatic implants. The goal was to determine if these videos serve as a trustworthy and informative resource for viewers.

To the best of our knowledge, no study has analyzed the usefulness and effectiveness of YouTube™ videos on zygomatic implants. The aim of this study is to evaluate the information flow and quality of YouTube™ videos on zygomatic implants and to inform health professionals who may produce content on this topic in the future.

MATERIAL AND METHOD

Study Design and Sample

This study adopted a cross-sectional approach to address the research objective. The target population for this analysis comprised all YouTube™ videos that provided information on zygomatic implants between 9 AM and 6 PM on August 22, 2022. The following search term was used: "zygomatic implants." The "Sort by relevance" filter was used as the default for YouTube™ searches. A sample of the first 150 videos retrieved from YouTube™ using this search query was subsequently analyzed for content. The videos were initially screened to restrict the sample to English-language videos only, excluding duplicate videos, videos without audio or titles, and unrelated videos. Only videos in English, with acceptable sound and image quality, and with primary content about zygomatic implants were included in this study (Figure 1). When the inclusion and exclusion criteria were applied, 94 videos were deemed eligible for the study.

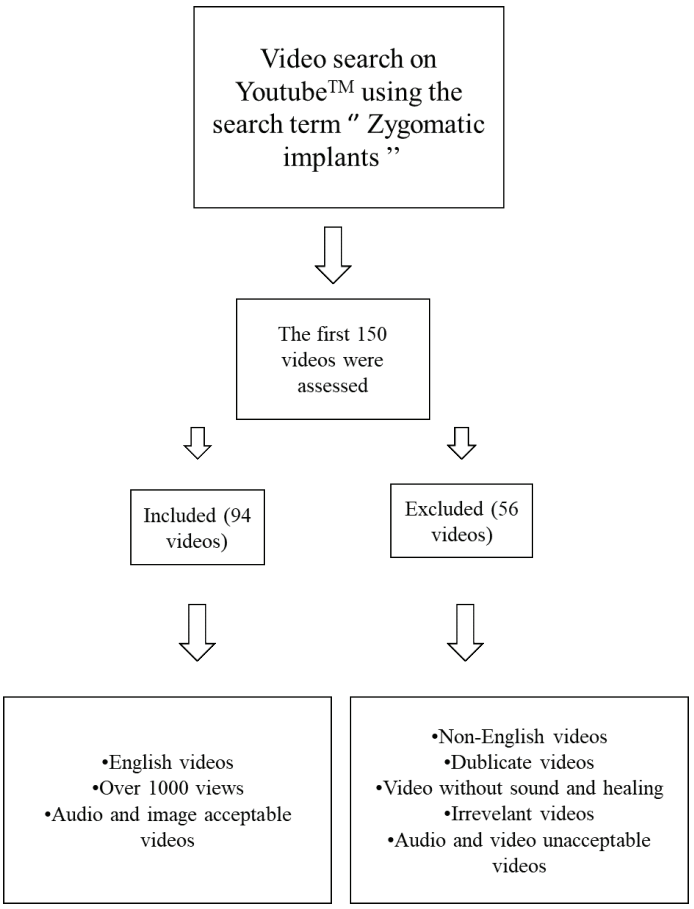

Figure 1. YouTube video selection for analysis

Variables

Each video was analyzed for various engagement metrics, including view count, total length, comments, likes, dislikes, upload date, and country of origin. Additionally, viewer interaction was assessed through two key metrics: interaction index (calculated as the percentage difference between likes and dislikes divided by total views) and view rate (calculated as the daily view count since upload).

All videos were grouped into three categories according to the type of person uploading the video. These categories were identified as educational videos made by healthcare professionals for doctors, informational videos for patients, and promotional videos.

The videos were assessed for their coverage of key topics related to zygomatic implants. This included definitions, candidate suitability (indications), reasons for unsuitability (contraindications), potential advantages (benefits), any additional procedures that might be involved (related procedures), possible risks and complications, associated costs, and long-term outcomes (prognosis and survival). A summary of these categories is shown in Table 1.

Table 1. Scored video content topics	
Scoring item	Score points
Definition	1
Indications	1
Contraindications	1
Advantages	1
Procedures involved	1
Complications	1
Cost	1
Prognosis and survival	1
Total score	8

Two investigators watched and analyzed the videos independently. Inter-rater blinding was used to ensure that the raters evaluated the videos independently. The two researchers, both oral and maxillofacial surgeons with up-to-date knowledge of zygomatic implants, rated the videos. To avoid potential bias, the raters evaluated the videos without prior knowledge of view counts, likes, dislikes, or comments.

Each video was evaluated across eight key content areas (Table 2) and assigned a score from 0 to 8 points. Videos receiving scores from 0 to 2 were categorized as having poor content quality and deemed unsuitable for patients. Scores of 3 to 5 indicated fair content that delivered a useful message but lacked in-depth coverage on certain aspects. Finally, videos scoring 6 to 8 points were deemed excellent, providing patients with comprehensive and accurate information (18).

Table 2. Video usefullness scoring	
Score	Definition
Poor (0-2 points)	Poor quality and poor flow of video, some information is listed but most is missing, not at all useful for patients
Moderate (3-5 points)	Moderate quality and suboptimal flow of video, some important topics are discussed but others are poorly mentioned, somewhat useful for patients
Excellent (6-8 points)	Excellent quality and flow of video, excellent and accurate information is mentioned, very useful for patients

Statistical Analysis

Statistical analysis was performed using IBM SPSS V23 software. Data normality was assessed using the Shapiro-Wilk test. Categorical data were analyzed using the Pearson chi-squared test. For non-normally distributed data, the Kruskal-Wallis test was employed for intergroup comparisons, with post-hoc Dunn's test for multiple comparisons. Spearman's rank correlation coefficient was utilized to evaluate relationships between non-normally distributed variables. Inter-rater reliability for video categorization and scoring was assessed using the intraclass correlation coefficient (ICC). Results are presented as frequencies (percentages) for categorical variables and mean±standard deviation (SD) and median (minimum-maximum) for quantitative variables. The significance level was set at $p<0.050$.

RESULTS

When analyzing the upload locations of the videos, the highest rate was in the USA at 51.1%, followed by India at 21.3%, and Spain at 5.3%. Regarding the source of the uploaded videos, 11.7% were educational videos made by doctors, 54.2% were informative videos for patients, and 34% were promotional videos (Table 3).

Table 3. Distribution of upload source of videos and countries where they were uploaded		
Countries where videos are uploaded	Frequency	Percentage
Usa	48	51.1
Australia	3	3.2
Brazil	1	1.1
Costa Rica	1	1.1
India	20	21.3
England	4	4.3
Spain	5	5.3
Switzerland	3	3.2
Italy	2	2.1
Canada	3	3.2
Mexico	3	3.2
Romania	1	1.1
Video source		
Educational videos made by doctors	11	11.7
Informative videos for patients	51	54.3
Promotional videos	32	34

Our analysis revealed a statistically significant difference in the median view count based on the video upload source ($p<0.001$). The median view count for educational videos uploaded by doctors was 13,957, for informative videos for patients was 2,412, and for promotional videos was 639. Additionally, there was a statistically significant difference in the median number of likes based on the video upload source, suggesting that the uploader's identity may influence viewer engagement, as evidenced by the variation in both views and likes across different uploaders ($p<0.001$). The median number of likes for educational videos uploaded by doctors was 143, for informational videos for patients was 23, and for promotional videos was 8. The number of likes for promotional videos differed significantly from the others.

The analysis also revealed a statistically significant variation in the median number of dislikes depending on the upload source ($p<0.001$). The median value for educational videos shot by doctors was 6, while it was 0 for both informational videos for patients and promotional videos. The number of dislikes for promotional videos differed from the others. A statistically significant

difference was found between the median values of the number of views per time elapsed since upload according to the video upload source (p<0.001). The median value for educational videos uploaded by doctors was 9.48, for informational videos for patients was 2.59, and for promotional videos was 0.99. The number of views per time elapsed since uploading differed for all uploaders. Other parameters did not show a statistically significant difference according to the source of the video upload (p>0.050) (Table 4).

Table 4. Comparison of video parameters according to video upload source

	Video source				
	Educational videos made by doctors (n=11)	Informative videos for patients (n=51)	Promotional videos (n=32)	Test statistic	p*
Number of views	17391.73±6366.54 13957 (10925-28339)[c]	3026±1950.78 2412 (955-8108)[b]	699.25±211.72 639 (499-1563)[a]	72.244	**<0.001**
Duration	437.36±425.31 361 (66-1386)	823.16±1315.15 299 (43-6168)	1592.97±2806.5 254.5 (36-13907)	0.539	0.764
Comment	7.45±12.34 2 (0-41)	5.78±12.36 1 (0-71)	2.09±3.5 1 (0-14)	2.669	0.263
Like	158.09±155.57 143 (0-492)[a]	38.37±58.7 23 (0-395)[a]	11±10.63 8 (0-56)[b]	19.962	**<0.001**
Dislike	5.09±4.99 6 (0-16)[a]	1.37±1.89 0 (0-7)[a]	0±0 0 (0-0)[b]	25.923	**<0.001**
Time elapsed	2270.64±1969.22 1534 (271-5352)	1223.76±1031.23 1001 (63-5284)	1122.75±1070.08 786.5 (99-4186)	3.316	0.191
Interaction index	0.85±0.86 0.81 (0-2.76)	1.19±1.08 1.04 (0-6.05)	1.6±1.55 1.29 (0-8.25)	3.861	0.145
Viewing rate	20.29±20.38 9.48 (2.16-51.6)[c]	4.91±8.43 2.59 (0.35-58.68)[b]	1.65±1.76 0.99 (0.16-6.48)[a]	27.807	**<0.001**

*Kruskal-Wallis test; mean±standard deviation; median (minimum - maximum); a-c No difference between groups with same letter

A statistically significant difference was found between the medians of the number of comments according to the countries where the videos were uploaded (p=0.021). The median number of comments for videos uploaded from the USA was 1, from India was 5, and from other countries was 1. The number of comments for videos uploaded from India differs from the number of comments in the USA and other countries. Additionally, a statistically significant difference was found between the median values of Like-Dislike/Total Views according to the countries where the videos were uploaded (p=0.033). The median for the USA was 1.21, for India was 1.24, and for other countries was 0.84. The Like-Dislike/Total Views ratio of videos uploaded from India and other countries differs. Other parameters did not show statistically significant differences according to the countries where the videos were uploaded (p>0.050) (Table 5).

Table 5. Comparison of video parameters by country of upload

	Video source				
	USA (n=48)	India (n=20)	Others (n=26)	Test statistic	p*
Number of views	3112.17±3563.91 1469 (511-13957)	1979.65±1820.57 1372 (499-6429)	6885.92±8878.69 2889 (513-28339)	2.786	**0.248**
Duration	998.73±1473.46 281.5 (39-5876)	1178.1±1885.05 355 (100-6168)	1010.23±2672.79 308.5 (36-13907)	1.52	0.468
Comment	2.63±4.06 1 (0-17)[a]	11.45±18.04 5 (0-71)[b]	3.42±8.44 1 (0-41)[a]	7.756	0.021
Like	28.92±37.97 16.5 (0-199)	49.6±87.75 24.5 (3-395)	64.15±120.22 12 (0-492)	0.637	**0.727**
Dislike	0.79±1.69 0 (0-8)	1.3±1.98 0 (0-6)	2.38±3.94 0 (0-16)	3.467	**0.177**
Time elapsed	1422.58±1433.05 990 (99-5352)	976.95±623.13 815 (63-2250)	1365.15±1136.56 1016.5 (140-4025)	0.524	0.770
Interaction index	1.23±0.93 1.21 (0-4.45)[ab]	1.98±1.99 1.24 (0.41-8.25)[b]	0.87±0.76 0.84 (0-2.76)[a]	6.839	0.033
Viewing rate	4.15±7.14 2.37 (0.17-47.56)	5.94±12.9 1.47 (0.24-58.68)	8.02±13.98 2.79 (0.16-51.6)	1.084	**0.582**

*Kruskal-Wallis test; mean ± standard deviation; median (minimum - maximum); a-b No difference between groups with same letter

A statistically excellent agreement was found between the usefulness scores of the observers (ICC=0.990; p<0.001). The median value of the usefulness score according to the source of the video upload did not show a statistically significant difference (p=0.851) (Figure 2).

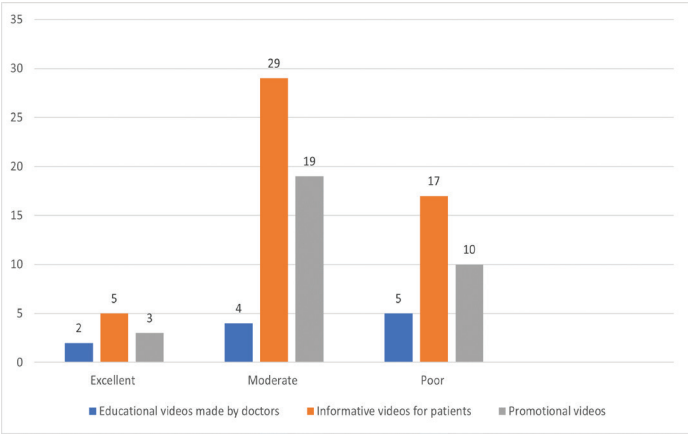

Figure 2. Source of upload of videos according to usefulness score

A statistically significant difference (p=0.007) was found between the median values of duration (seconds) according to the usability score categories. The median duration was 898 seconds in the excellent category, 333.5 seconds in the average category, and 204 seconds in the poor category, indicating that the durations of videos in the excellent category differed from those in the poor category. Additionally, a statistically significant difference was found between the median values of likes according to the usefulness score categories (p=0.039). The median number of likes was 33.5 in the excellent category, 12 in the average category, and 18 in the poor category, suggesting that the number of likes in the excellent category differed from those in the average category. A statistically significant difference was also found between the median values of dislikes according to the usefulness score categories (p=0.019). The median number of dislikes was 2 in the excellent category and 0 in both the average and poor categories, indicating that the number of dislikes in the excellent category differed from those in the average category (Table 6).

Table 6. Comparison of video parameters according to usefulness score categories

	Usefulness score categories				
	Excellent (n=10)	**Moderate (n=52)**	**Poor (n=32)**	**Test statistic**	**p***
Number of views	4620.5±5504.93 2242 (553-17582)	3353.06±5286.04 1245.5 (511-28339)	4607.72±6302.87 1701.5 (499-25857)	2.251	0.324
Duration	3286.7±4354.04 898 (114-13907)[b]	925.88±1370.76 333.5 (39-5876)[ab]	523.56±851.97 204 (36-3895)[a]	10.01	**0.007**
Comment	8.4±13.66 1(0-41)	4.77±10.67 1 (0-71)	3.5±8.48 1 (0-47)	0.335	0.846
Like	96.2±146.7 33.5 (2-492)[b]	31.65±64.27 12 (0-395)[a]	45±71.37 18 (0-327)[ab]	6.497	**0.039**
Dislike	2.9±3.25 2 (0-8)[b]	0.9±2.56 0 (0-16)[a]	1.56±2.37 0 (0-8)[ab]	7.975	**0.019**
Time elapsed	1149±879.88 811 (140-3291)	1363.81±1356.17 828.5 (99-5352)	1278.41±1105.58 1058 (63-4186)	0.054	0.973
Interaction index	1.77±0.92 1.72 (0.36-3.15)	1.33±1.49 1.02 (0-8.25)	1.07±0.81 0.96 (0-3.68)	4.338	0.114
Viewing rate	6.14±8.71 2.99 (0.17-29.9)	3.26±3.31 2.14 (0.16-13.6)	9.24±16.8 2.79 (0.23-58.68)	1.012	0.603

*Kruskal-Wallis test; mean ± standard deviation; median (minimum - maximum); a-b No difference between groups with same letter

A statistically significant positive but weak relationship was found between the usefulness score and the duration of the videos (r=0.337; p=0.001). There was no statistically significant relationship between any of the other parameters and the usefulness score.

The distributions of the usefulness score categories according to the source of the video upload did not show a statistically significant difference (p=0.735). Similarly, the distributions of the usefulness score categories according to the country where the video was uploaded did not show a statistically significant difference (p=0.618).

DISCUSSION

In the era of digital healthcare information seeking, patients increasingly utilize online resources to understand their medical conditions and explore treatment possibilities. This study aimed to evaluate the quality of information regarding zygomatic implants on YouTube™, a prominent open-access video-sharing platform with a continuously growing repository of healthcare-related content (19). Prior research within the domains of dentistry and oral and maxillofacial surgery has investigated the quality of information available online for various procedures, including wisdom tooth extraction, orthognathic surgery, dental implant placement, botox applications, and head and neck cancer treatment (20,21,23).

A consistent trend has emerged within the literature, with numerous studies evaluating the quality of online information for various healthcare procedures across dentistry (e.g., wisdom tooth extraction, orthognathic

surgery, dental implants), oral and maxillofacial surgery, orthopedics, neurology, and rheumatology. The overwhelming conclusion from this body of research suggests that these online resources are generally of low quality (22,24). Wong et al. proposed that YouTube™ videos on botulinum toxin injections for wrinkles may deviate from the norm, exhibiting high-quality content and potentially serving as a valuable resource for patients (25). Furthering the debate on the quality of online healthcare information, Gaş et al. suggested that YouTube™ videos on botulinum toxin applications for bruxism treatment can yield positive patient outcomes, arguing that such videos have the potential to provide scientifically accurate information on this specific use of Botox injections (18).

Although there are studies in the literature suggesting that YouTube™ videos can have positive informational outcomes, our study echoes the findings of many other studies and shows that the quality of videos commonly viewed on YouTube™ about zygomatic implants is generally questionable.

Highlighting the need for intervention, Hassona et al. emphasized the responsibility of healthcare professionals, academic institutions, and professional organizations to contribute to a more informative YouTube™ landscape. They advocate for the creation and upload of high-quality videos on oral cancer to address the current shortcomings in online resources (26). The escalating popularity of social media platforms like YouTube™ has paradoxically revealed a concerning deficit in the availability of trustworthy healthcare information. This coincides with a growing trend of patients seeking health knowledge through these platforms, placing a potential burden on professional organizations to enhance the quality and credibility of online health resources.

Some researchers have proposed the development of interfaces that can synergistically integrate YouTube™ content with evidence-based references, thereby promoting the dissemination of accurate health information (27). Further research suggests that video presentations may enhance patient information retention, potentially impacting future informed consent practices (28). Considering the existing body of literature alongside the findings of our study, it is evident that health-related YouTube™ videos warrant a degree of quality control.

Looking at the source of the videos, 11.7% were educational videos made by doctors, 54.3% were informational videos for patients made by doctors, and 34% were promotional videos. A few videos included patient comments, but these were classified as promotional videos because they were clearly clinic advertisements. The absence of independent videos from patients or their relatives suggests that the subject matter primarily concerns older patients, who are less likely to upload videos to YouTube™. The significantly different number of views, likes, and dislikes for educational videos filmed by doctors compared to other groups may be due to this topic being more interesting to medical professionals.

The average duration of doctors' educational videos was longer than that of other sources, but this difference was not statistically significant. Examining the usefulness scores, the average score for educational videos made by doctors was 3.09, for informational videos made by doctors was 3.14, and for promotional videos was 3.28. Based on these scores, it may not be accurate to compare the videos in terms of content, as the focus of each video type may differ. For example, educational videos made by doctors primarily focused on the procedure, whereas informational videos for patients focused more on indications, and promotional videos emphasized benefits.

It is important to acknowledge that this study has some limitations. Firstly, the results may be influenced by the specific keywords employed during the search process on YouTube™. Someone without sufficient knowledge of the subject may obtain different results by using different search terms. Secondly, videos on YouTube™ can be uploaded or deleted at any time, impacting the stability of the video dataset. Thirdly, the selection of videos presented in a YouTube™ search can be influenced by personalization algorithms that consider a user's search history and browsing habits, stored as cookies and cached data on their device. Due to the influence of these personalization algorithms, YouTube™ search queries can yield unique results for individual users. While the popularity of zygomatic implant procedures extends beyond English-speaking countries and into regions with non-English primary languages, this study was limited to evaluating English-language videos directly uploaded to YouTube™. This restriction limits the generalizability of our findings to a specific linguistic audience.

CONCLUSION

It is clear that social media platforms offer many conveniences, but care and caution should be exercised when sharing and receiving health-related information on these platforms. As demonstrated in our study, videos related to zygomatic implants on YouTube™ are not sufficiently reliable, high-quality, or comprehensive in content. Video producers should thoroughly define the topic, mention the indications and contraindications, describe the procedure, and objectively discuss the advantages and complications. Additionally, informing viewers about the cost and prognosis will increase the quality and reliability of the videos. Health-related topics should not be addressed without the assistance of health professionals, as incorrect procedures can lead to irreversible consequences.

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Research Article

The Role of Laboratory Parameters in the Differentiation of Stroke Cases

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Abstract

Aim: Globally, stroke is considered as one of the most important causes of mortality and morbidity. The most important steps for the diagnosis of stroke include rapid and focused physical examination followed by determination of the stroke's type. The study was conducted to determine the relationship between laboratory parameters frequently requested in the emergency department and stroke type.

Material and Method: The study is a retrospective cross-sectional study. Patients' age, gender, comorbidities, stroke type, hospitalization, in-hospital mortality and laboratory parameters were recorded and compared. p value of <0.05 was considered statistically significant.

Results: 251 patients were included in the study. The median age of the patients included in the study was 74 [64-81]. 137 (54.6%) of the patients were women. The most common comorbidity in the patients included in the study was hypertension. Ischemic stroke was seen in 236 (94%) patients and 236 (94%) were hospitalized. the platelet count in the hemorrhagic stroke and ischemic stroke group was 173 (153–204) 10^9/L and 218 (180–2262) 10^9/L, respectively. Platelet count in patients in the hemorrhagic stroke group was found to be significantly lower than in the ischemic stroke group (p=0.013). There was no significant difference in white blood cell, lymphocyte, sodium, potassium, C-reactive protein levels between both groups (p=0.318, 0.245, 0.461, 0.202, 0.322; respectively).

Conclusion: Platelet count may be used as a biomarker to differentiate between ischemic and hemorrhagic stroke in patients who are examined for stroke.

Keywords: Differentiation, hemorrhagic, ischemic, platelet, stroke

INTRODUCTION

Globally, stroke is considered as one of the most important causes of mortality and morbidity (1). Although the incidence and prevalence of hemorrhagic stroke has gradually decreased compared to ischemic stroke, both rank among the major causes of disability and long-term hospitalization (2). After 25 years of age, for all people, the lifetime risk of having a stroke is accepted as 25% (3).

The most important steps for the diagnosis of stroke include rapid and focused physical examination and exclusion of stroke mimics, followed by determination of the stroke's type (3). Neuroimaging is an important technique that determines stroke type; however, there are certain challenges in early diagnosis and treatment including the difficulty associated with detecting early and small infarct areas via computed tomography (CT) and the availability of neuroimaging means at healthcare facilities (4). Furthermore, it is well-established that non-contrast CT, as diagnostic tool, may have reduced accuracy in patients with subarachnoid hemorrhage more than 6 hours after symptom onset (5). Thus, the availability of objective, simple, and inexpensive blood parameters for the diagnosis and prognosis of this patient group may facilitate the management of patients.

Ionic imbalance, electrical disturbances, and thrombotic events caused by ischemia and associated damage begin within minutes following ischemic stroke. This pathophysiologic cascade results in necrosis or apoptosis after a certain time period (6). In hemorrhagic stroke,

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proinflammatory and anti-inflammatory pathways are simultaneously activated following the hemorrhage (3). These pathophysiologic changes may influence changes in biomarkers. The present study assesses the efficacy of low-cost and easy-to-access laboratory parameters, which are frequently used in emergency departments to determine stroke type.

MATERIAL AND METHOD

Study Design

The study is a retrospective cross-sectional study that includes patients >18 years of age who were presented to the emergency department between January 02, 2023–January 02,2024 and diagnosed with stroke. This study adhered to the principles of the Declaration of Helsinki. The study was conducted after the approval of the Institutional Ethics Committee (2024/1782). All data was carefully anonymized to ensure confidentiality, and thorough statistical analyses were conducted following this meticulous process.

Patient Selection

The study encompassed patients who had been diagnosed with stroke in the emergency department of our hospital. Exclusions comprised patients under 18 years of age, pregnant women, individuals diagnosed with transient ischemic attack, those with a history of head trauma, patients for whom complete data could not be retrieved from the hospital information system, and those who received a different diagnosis after being hospitalized following a stroke diagnosis in the emergency department.

Data Collection

Patients' age, gender, comorbidities (cardiac disease, diabetes mellitus, hypertension, previous cerebrovascular disease, chronic obstructive pulmonary disease, chronic renal failure, and malignancy), hospitalization, stroke type, and mortality were recorded. Laboratory parameters, including platelet, white blood count (WBC), hemoglobin, lymphocyte, C-reactive protein (CRP), albumin, urea, creatinine, AST, ALT,sodium, potassium, and international normalized ratio levels were recorded. The data were taken from the institutional automation system.

Outcome

To determine the relationship between laboratory parameters frequently requested in the emergency department and stroke type.

Statistical Analysis

For the purpose of conducting statistical analyses, we utilized IBM SPSS version 22.0. The normal distribution hypothesis for the continuous variables was tested using the Shapiro-Wilks and Kolmogorov-Smirnov tests. We presented data with normal distribution as mean ± standard deviation, and data without normal distribution as median (1st and 3rd quartile values). Group differences were assessed using Student's t-test or Mann-Whitney U-test as appropriate, while Pearson's chi-squared test was employed to compare categorical data. To illustrate the sensitivity and specificity of the platelet count, Receiver Operating Characteristic (ROC) analysis was conducted, and specific values were calculated to depict sensitivity and specificity. We considered a p-value of <0.05 to be indicative of statistical significance.

RESULTS

251 patients were included in the study. The median age of the patients included in the study was 74 [64-81]. 137 (54.6%) of the patients were women. The most common comorbidity in the patients included was hypertension. Of the 185 patients (73.7%), hypertension was an additional disease. Regarding other comorbidities, 121 (48.2%) of the patients had coronary artery disease, 89 (35.5%) had diabetes mellitus, and 66 (26.3) had a history of cerebrovascular disease. Ischemic stroke was seen in 236 (94%) patients and 236 (94%) were hospitalized. The number of mortalities was 13 (5.2%). The demographic data for the patients is conveniently available in Table 1.

Table 1 . Demographic data of the patients

Variable	Overall (n=251)
Age (year) median [Q1-Q3]	74 [64-81]
Gender n (%)	
Female	137 (54.6)
Male	114 (45.4)
Comorbidities n (%)	
Hypertension	185 (73.7)
Coronary artery disease	121 (48.2)
Diabetes mellitus	89 (35.5)
Past cerebrovascular event	66 (26.3)
Chronic obstructive pulmonary disease	25 (10.0)
Chronic renal failure	19 (7.6)
Malignancy	11 (4.4)
Stroke type n (%)	
Hemorrhagic	15 (6.0)
Ischemic	236 (94.0)
Hospital admission n (%)	
Yes	236 (94.0)
No	15 (6.0)
Mortality n (%)	
Yes	13 (5.2)
No	238 (94.8)

On examining the relationship between laboratory parameters and hemorrhagic and ischemic stroke subgroups, the platelet count in the hemorrhagic stroke and ischemic stroke group was 173 (153–204) 10^9/L and 218 (180–2262) 10^9/L, respectively. Platelet count in patients in the hemorrhagic stroke group was found to be significantly lower than in the ischemic stroke group (p=0.013). The median WBC count in the hemorrhagic stroke group was 9.4 [6.7–10.6] 10^9/L, while in the ischemic group it was 7.7 [6.2–9.7] 10^9/L. There was not any

significant difference in WBC count between both groups (p=0.318). Similarly, while the median CRP level in the hemorrhagic stroke group was 5.5 [3.8-9.8] mg/L, it was 8.8 [4.0-17.4] mg/L in the ischemic stroke group, and no significant difference was found between the two groups (p=0.322). While lymphocyte, sodium and potassium in the hemorrhagic stroke group were 1.30 [1.1–2.1], 139 [139-140] and 4.6 [4.2–5.1], significant difference was not detected between the hemorrhagic and ischemic stroke groups (p values=0.245, 0.461, 0.202; respectively). Data on the relationship between parameters and subgroups are given in Table 2.

Table 2. Relationship between laboratory parameters and hemorrhagic/ischemic subgroups

Variable	Hemorrhagic	Ischemic	p
Hgb (mg/dl) mean±SD	13.4±1.4	12.7±1.9	0.187
WBC (10^9/L) median [Q1-Q3]	9.4 [6.7-10.6]	7.7 [6.2-9.7]	0.318
Lymphocyte (10^9/L) median [Q1-Q3]	1.30 [1.1-2.1]	1.8 [1.3-2.3]	0.245
Platelet (10^9/L) median [Q1-Q3]	173 [153-204]	218 [180-262]	0.013*
Urea (mg/dl) median [Q1-Q3]	46 [36-51]	51.4 [34-57]	0.999
Creatinine (mg/dl) median [Q1-Q3]	0.8 [0.7-1.2]	0.9 [0.7-1.2]	0.484
AST (U/L) median [Q1-Q3]	27 [19-35]	23 [18-28]	0.229
ALT (U/L) median [Q1-Q3]	15 [11-23]	16 [11-23]	0.982
Albumin median [Q1-Q3]	4.3 [4.0-4.6]	4.1 [3.9-4.4]	0.413
Na mEq/L median [Q1-Q3]	139 [139-140]	139 [137-141]	0.461
K mEq/L median [Q1-Q3]	4.6 [4.2-5.1]	4.4 [4.0-4.8]	0.202
CRP mg/L median [Q1-Q3]	5.5 [3.8-9.8]	8.8 [4.0-17.4]	0.322
INR median [Q1-Q3]	1.0 [0.9-1.2]	1.0 [0.9-1.1]	0.905

Hgb: hemoglobin, WBC: white blood cell, AST: aspartate aminotransferase, ALT: alanine transaminase, Na: sodium, K: potassium, CRP: C-reactive protein, INR: international normalized ratio

Sensitivity, specificity, positive predictive value, and negative predictive values were 64.83%, 73.33%, 97.45%, and 11.7%, respectively, for the ROC analysis to test the effectiveness of platelet count for determining ischemic stroke, (area under the curve=0.692) (Figure 1) when the platelet count was set to 196×10^9/L.

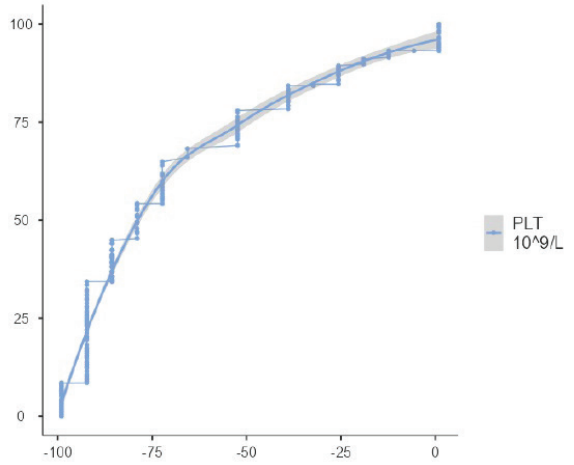

Figure 1. The ROC analysis to test the effectiveness of platelet count for determining ischemic stroke

DISCUSSION

Our study showed a significant difference in platelet count between hemorrhagic and ischemic stroke patients. Specifically, patients with hemorrhagic strokes exhibited a notably lower platelet count in comparison to those with ischemic strokes. Previous studies focusing on the role of platelets in atherosclerotic events (7) reported elevated platelet counts in isolated thrombotic events, including pulmonary embolism (8). Other studies suggested that mean platelet volume, i.e., a biomarker of platelet turnover, was increased in patients with deep vein thrombosis (8,9). Prodan et al. reported that coated platelets, a platelet subgroup, were lower in patients with spontaneous intracerebral hemorrhage than in the control group (10). In the same study, high levels of coated platelets were observed in patients with non-lacunar ischemic infarction with even lower levels of coated platelets in patients with non-lacunar ischemic stroke and early hemorrhagic transformation (10). A retrospective study of 455 cases reported that elevated platelet count and low platelet count were risk factors for ischemic and hemorrhagic stroke, respectively (11). This suggests that our study findings are consistent with some studies in the literature.

Kakhki et al., in a 2020 study, reported that the lymphocytes percentage and WBC were higher in patients with ischemic stroke than in patients with hemorrhagic stroke (12). In a particular study, no significant difference was found between the hemorrhagic and ischemic stroke subgroups based on lymphocyte values (13). In one study, there was no significant difference in leukocyte values between hemorrhagic and ischemic stroke groups (14), however, Kaya et al. reported a significant increase in WBC levels within the hemorrhagic stroke group (15). In the relevant literature, the use of these biomarkers, which contribute to inflammation, for the purposes of hemorrhagic–ischemic differentiation is under debate. In the study of ours, there was no significant difference between ischemic and

hemorrhagic stroke groups based on WBC and lymphocyte counts.

Certain studies in the literature report that CRP levels were significantly higher in patients with ischemic stroke than in patients with hemorrhagic stroke (12,16,17). In our study, CRP levels were slightly higher in patients with ischemic stroke, but there was no statistically significant difference. This can be explained by the differing number of cases included in the literature. Furthermore, the time of hemorrhage and ischemia onset was not recorded as a parameter in the present study, which may have an effect on the CRP levels, an inflammatory biomarker.

A 2018 study reported that there was no significant difference between patients with hemorrhagic and ischemic stroke based on sodium and potassium levels (18), while another reported that sodium levels were significantly lower in the hemorrhagic stroke group (12). The study by Mansoor et al. revealed that sodium levels were notably lower in the ischemic stroke group, while potassium levels were significantly higher in the hemorrhagic stroke group (19). Setyawati et al. found no significant difference in sodium levels, yet they reported that potassium levels were higher in patients with ischemic stroke (20). However, in the study of ours, there was no significant intergroup difference based on sodium and potassium levels consistent with some previous studies in the literature.

Limitation

Our study is a single-center study with a relatively smaller sample size. In addition, the time between the evaluated parameters and the onset of the patient's symptoms could not be determined exactly. It is not known whether the patients had inflammatory processes that were not present in their records before the application process.

CONCLUSION

Laboratory parameters are tests that might be important in distinguishing between ischemic and hemorrhagic stroke because they are easily accessible and cost-effective. Platelet count may be considered as a biomarker to differentiate between ischemic and hemorrhagic stroke in patients who are examined for stroke in the emergency department.

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MEDICAL RECORDS-International Medical Journal

Research Article

Determinants of Parental Satisfaction with Rehabilitation Service Delivery to Children with Childhood-Onset Physical Disabilities: A Turkish Sample

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Abstract

Aim: Studies have demonstrated that family centeredness, or family involvement in decision-making and care provision, is crucial for achieving the best results in pediatric rehabilitation and is also directly associated to parental/caregiver satisfaction with rehabilitation services. This study aimed to explore the potential determinants of parents'/caregivers' satisfaction with rehabilitation services based on the various elements of family centeredness.

Material and Method: Authors included the parents/caregivers of 120 children with physical disabilities aged 5-18 years (mean 10.14 years, SD 4.17). The Measure Process of Care-20 (MPOC-20) was used to assess parents'/caregivers' perceptions of the family centeredness in provision of rehabilitation services and therefore parental/caregiver satisfaction with rehabilitation service delivery to children.

Results: Service-related and child-related factors accounted for 78% and 67% of the variances in the parents'/caregivers' satisfaction with being provided opportunities for them to make decisions about rehabilitation services (MPOC-20-Enabling and Partnership subscale), respectively. Parental/caregiver satisfaction with service delivery in the context of sharing information about child's progress was correlated with service-related, child-related, and parent/caregiver-related factors (adjusted R^2=0.75, 0.71, and 0.68, respectively). Satisfaction with service delivery regarding coordinated and comprehensive care was significantly influenced by the service provider and the parent/caregiver-related variables (R^2=0.63 and R^2=0.59, respectively). Finally, in the event of satisfaction with services in terms of respectful and supportive care, each factor accounted for a small and approximately equal amount of variance in the mean score of relevant MPOC-20 subdomain (range of adjusted R^2=0.10–0.18).

Conclusion: Factors or determinants identified in the current study as having the potential to increase parents'/caregivers' satisfaction with rehabilitation services should be considered when providing rehabilitation services.

Keywords: Childhood disability, rehabilitation service, family-centered service, children, physiotherapy

INTRODUCTION

Childhood-onset physical disability is a complex medical condition that arises from the interaction between an underlying health condition (e.g., early brain insult) and contextual factors (1). On the other hand, children with physical disabilities have the same right as their typically developing peers to receive high-quality healthcare services that enable them to participate independently in community activities, make their own decisions, and even attend regular school (2). However, a significant proportion of children with physical disabilities lack access to adequate rehabilitation services, including institutionalized or specialized rehabilitation centers, experienced health professionals, modern assistive technologies, and evidence-based intervention approaches (3). Regrettably, it is widely acknowledged that numerous children with physical developmental impairments, especially in low- and middle-income countries, do not receive evidence-based rehabilitation services and are often subjected to unnecessary, ineffective, or harmful medical interventions (4).

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Family-centered services (FCS) are designed to facilitate collaboration between families and service providers to make informed decisions about the delivery of services and to support both children and their families/caregivers (5). FCS refers to a philosophy or strategy for providing rehabilitation services to individuals with physical disabilities through both family-centered and child-centered practices (6). Family-centered rehabilitation services typically follow a top-down model, where the primary goal is to engage in task-specific practice of whole tasks (7). Thus, in family-centered approaches, service providers and parents/caregivers collaborate to recognize the specific needs of the child (8). The elements underlying family-centeredness (including enabling and partnership, providing general information, providing specific information about the child, coordinated and comprehensive, respectful and supportive care) are also in line with the international "*Convention on the Rights of Persons with Disabilities*" (9). Previous research has demonstrated that family-centered rehabilitation strategies are crucial in pediatric physiotherapy to enhance parental and caregiver satisfaction with rehabilitation services and promote their psychological well-being (10). In conclusion, FCS acknowledges the vital role of families in providing rehabilitation services to their children and encourages their active involvement in the care process (11). That is, FCS encompasses developing partnerships with families or caregivers, viewing them as experts who can contribute to the clinical team (12). It also recognizes that families/caregivers are experts at figuring out what's best for themselves and their children. Within the context of the pediatric rehabilitation, the identification of potential factors influencing parents'/caregivers' satisfaction with service delivery may be useful to enhance the satisfaction of families/caregivers with rehabilitation services. It is essential to provide family-centered rehabilitation services to children with physical disabilities, especially those in low-income countries, as FCS have been proven to significantly reduce parental/caregiver stress and increase successful rehabilitation outcomes (11). In contrast, most of children with childhood-onset physical disability are unable to access such services due to various barriers. For this reason, understanding the factors that are likely to affect family centeredness in provision of rehabilitation services is very important in families/caregivers to decide where or how they can receive best practices for their children. Moreover, determining potential factors that may influence parents'/caregivers' satisfaction with service delivery will provide both health care managers and service providers with information about whatever should be done in terms of service delivery. Therefore, our aim was to identify determinants of parental satisfaction with rehabilitation services based on the concept of family centeredness.

MATERIAL AND METHOD

This was a cross-sectional study conducted between May 15, 2022, and December 15, 2022 in 15 special education and rehabilitation centers. The study was conducted after approval from the Human Research Ethics Committee at Muş Alparslan University (no: 03.04.2022-45864). For a regression model with five predictors, an estimated sample size of 120 participants was determined, assuming a population R-square of 0.30, alpha=0.05, and desired power=0.80, using G*Power 3.1.

Participants

The study included children aged between 5 and 18 years (mean age 10.14±4.17; 56 males and 46 females) receiving rehabilitation services from government-funded rehabilitation centers, their parents, rehabilitation service providers, and health care/rehabilitation center managers. Children in the study were those with physical disabilities of any severity of motor function, including cerebral palsy, spinal cord injury, muscular dystrophy, and juvenile rheumatoid arthritis. All service providers who provided rehabilitation services to the participating children were physiotherapists. Individual (child's age, prognosis, etc.) and contextual factors (primary caregiver's age, level of education, etc.) were noted through face-to-face interviews with parents/caregivers. Study data were collected from 15 rehabilitation centers operating in two different cities located in different regions (Karaman and Bingöl) where at least two physiotherapists are employed. Additionally, each rehabilitation center in which data was gathered was run by different company. Each rehabilitation center from which data collected served a wide range of disability types, including rachial plexus injury, down syndrome, spina bifida, hydrocephaly, muscular dystrophy, poliomyelitis, rheumatoid arthritis, developmental coordination disorder, fragile, x syndrome, acquired brain injury. All families/caregivers who wanted to participate in the measurement process as well as had ability to comprehend items in the MPOC-20 were randomly selected. In contrast, families whose children had started receiving rehabilitation services recently, i.e., who lacked adequate opinion with rehabilitation services delivered to their children were not enrolled in the study.

Identification and measurements of potential determinants of satisfaction with rehabilitation services

The possible determinants of parents'/caregivers' satisfaction with rehabilitation services were identified based on the previously published studies on family-centered services (13,14) as well as the authors' clinical experience in the field of pediatric rehabilitation. A comprehensive set of variables that would potentially predict family-centeredness of rehabilitation services were outlined in Table 1.

Table 1. Measurement of potential determinants of family-centered approach

Determinants	Scale of measurement
Child-related factors	
The type of disease or disorder	CP / other
Age	0-12 / 13-18
Gender	female / male
Comorbidity	yes / no
Severity of gross motor impairment	GMFCS I-III / GMFCS IV-V
Service provider-related factors	
Length of service (clinical experience)	<5 years / ≥5 years
Postgraduate education/master's degree	yes / no
Occupational course after graduation	yes / no
Parent/caregiver-related factors	
Age	<35 years / ≥35 years
Educational level	≤high school / university
Type of caregiver	parent / caregiver
Belief in rehabilitation services	yes / no
Expectation of rehabilitation services	yes / no
Satisfaction with the clinical environment	yes / no
Service/care-related factor	
The type of rehabilitation service	standardized care / functional or goal -directed
Facility/rehabilitation center-related factors	
Environmental modification	satisfied / dissatisfied
Experience of active work in the field of pediatric rehabilitation	<10 years / ≥10 years

CP: cerebral palsy, GMFCS: gross motor function classification system

Procedure

Parents/caregivers of the children in the study were provided with detailed information about the family-centered program before data collection. Before the beginning of the study, researchers held a series of workshops with parents/caregivers to explain concepts "family-centeredness" and "satisfaction with the rehabilitation services." Additionally, parents/caregivers were informed in detail about the following family-centeredness principles: 1) parents/caregivers are experts on their children's needs, 2) family-centeredness is a respectful, supportive, coordinated, and comprehensive service, 3) family-centered rehabilitation services enable partnerships between parents/caregivers and rehabilitation providers.

Instruments

Gross Motor Function Classification Systems–Expanded & Revised

The severity of the participants' gross motor function impairment was described using Turkish version of Gross Motor Function Classification System–Expanded and Revised (GMFCS–E&R) (15). The GMFCS was firstly released by Palisano et al. in 1997 to describe gross motor function of children with CP between 2 and 12 years of age (16). Then, the GMFCS–E&R was developed in 2007 as an expanded and revised version of the GMFCS by including an age band of 12–18 years to classify youth with CP (17). The GMFCS–E&R consists of five levels to classify the severity of involvement in the gross motor function of children with CP between of 2 and 18 years of age based on their self-initiated movement (18). The GMFCS has been widely for children with different health conditions other than CP (19). The GMFCS-E&R has been validated for Turkish CP population and shown to have an excellent test-retest reliability coefficient of 0.94 (15).

Measure of Processes of Care (MPOC-20)

The Measure of Processes of Care (MPOC-20) was used to evaluate parental/caregiver satisfaction with rehabilitation services since MPOC-20 was developed to evaluate family- centeredness in health care which has been reported to be closely related to increased parental satisfaction with services (20). MPOC-20 is a shorter and more updated version of the original 56-item MPOC that was established to assess parent/caregiver perceptions of the service delivery processes for their children with physical disabilities (20). In the context of our sample, it was used to assess parent/caregiver perceptions of the behavior exhibited by rehabilitation service providers to examine the extent to which specific rehabilitation services delivered to children with physical disabilities are family centered. The initial version of the MPOC was a 56-item survey based on the notion that parents/caregivers are experts on their children's needs, as their perspective mediates between the delivery of health services and the outcomes of those treatments (21). It evaluates five domains: "*enabling and partnership, providing general information, providing specific information about the child, coordinated, and comprehensive care, and respectful and supportive care*". The MPOC-20 is a self-administered questionnaire with 20 items that rate healthcare services or rehabilitation center staff's behavior on a 7-point scale (*1=not at all, 7=to a very great extent; 1=never, 4=sometimes, and 7=to a great extent*). The MPOC-20's average score is derived by summing all of the item scores and then dividing them by 20 (22). The Turkish version of the MPOC-20 has been found to be valid and reliable for use with Turkish parents/caregivers of children with disabilities (23).

Statistical Analysis

Statistical analyses included data from children with at least five potential determinants of parent satisfaction with rehabilitation services. SPSS software version 25 was used for the statistical analyses. Visual (histograms, probability plots) and analytical (Kolmogorov–Smirnov) methods were performed to test whether the continuous data were normally distributed. When possible, Pearson correlation and Student's t-test were used to establish the parameters (potential determinants) that determined parental satisfaction with rehabilitation services. The reference category was set to 0 since all probable predictors of parent satisfaction with rehabilitation services were

characterized as two-level variables (dichotomy). Five fitted multiple linear regression analyses with a backward model were performed separately for each subdomain of the MPOC to identify independent predictors of parental satisfaction with rehabilitation services. Through this, the predefined potential variables related to each factor were first included in the model, then the variables that were unable to contribute significantly to the model ($p<0.05$) were each excluded from the model. Therefore, the number of predefined variables was gradually reduced. The model fit was evaluated using appropriate residual and goodness-of-fit indices. A 5% types I error level was used to infer statistical significance.

RESULTS

Initially, a total of 141 children with various types of developmental disabilities were screened for eligibility, and 21 were removed from the statistical analysis because they reported more than one missing variable for any predetermined predictor factor. As a result, the study enrolled 120 children and their families or primary caregivers. Table 2 outlines the demographic characteristics of the study participants.

Determinants of parents'/caregivers' satisfaction with rehabilitation services in terms of enabling and partnership

The "*enabling and partnership*" model showed that service-related factors (standardized care or functional/goal-directed intervention) and child-related factors (type of disorder, age, and presence of comorbidity) were the most significant predictors (adjusted R^2=0.78 and 0.67, respectively) (Table 3). More specifically, it was found that parents/caregivers of children with CP were more satisfied with rehabilitation services than those of parents/caregivers of children with non- CP. Moreover, it was demonstrated that parents'/caregivers' satisfaction with rehabilitation services improved when the services was functional/goal directed intervention.

Determinants of parents'/caregivers' satisfaction with rehabilitation services in terms of providing specific information about the child

The model of the MPOC- "*specific information about the child*" revealed that service-related, child-related, and parent/caregiver-related factors were the strongest predictors and explained 75%, 71%, and 68%, respectively, of the variance in the subdomain score (Table 4). "In the event of child-related factors, it was revealed that service providers provided with parents/caregivers more information about the child if she/he had a diagnosis of CP".

Determinant of parents'/caregivers' satisfaction with rehabilitation services in terms of "coordinated and comprehensive care"

In terms of the "*coordinated and comprehensive care*" model, the service provider and parent/caregiver-related factors proved to be the best predictors, accounting for 63% and 59% of the variance in this subdomain mean score, respectively. More specifically, the physiotherapist's clinical experience, postgraduate occupational course, and master's degree status led to more coordinated and comprehensive physiotherapy (R^2=63) (Table 5).

Determinant of parents'/caregivers' satisfaction with rehabilitation services in terms of respectful and supportive care

In relation to MPOC- 20 "respectful and supportive care", each factor explained a small and approximately equal amount of variance in this subdomain mean score (range of adjusted R^2=0.10–0.18) (Table 6)

Determinant of parents'/caregivers' satisfaction with rehabilitation services in terms of providing general information

Concerning the subdomain of "*providing general information*", only the facility/rehabilitation center-related factors explained a considerable amount of variance in the mean score (R^2=37) (Table 7).

Table 2. Characteristics of study participants (n=120)

Characteristics	Summary data	
Age (mean±SD)	10.14 (4.17)	
Range (max-min)	2.5-15	
	n	%
Gender		
Male	56	46.7
Female	64	53.3
Type of disability		
Cerebral palsy	50	41.7
Unilateral (hemiplegic, monoplegia)	21	42
Bilateral (diplegic, quadriplegic)	25	50
Ataxy	4	8
Non-cerebral palsy	70	58.3
Brachial plexus injury	5	7.14
Down syndrome	8	11.42
Spina bifida	3	4.28
Hydrocephaly	3	4.28
Muscular dystrophy	7	10
Poliomyelitis	5	7.14
Rheumatoid arthritis	9	12.85
Developmental coordination disorder	13	18.57
Fragile X syndrome	10	14.28
Acquired brain injury	7	10
Mobility level		
GMFCS I-III	75	62.27
GMFCS IV-V	45	37.5
Type of caregiver		
Parent	77	64.2
Paid caregiver	43	35.8

SD: Standard deviation, n: Number of participants, GMFCS: Gross Motor Function Classification system; Summary data are presented as mean and SD for continuous variables, while categorical data are presented as %

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Table 3. Multiple regression models of the Measure of Processes of Care (MPOC-20)- 'Enabling and Partnership' subdomain

	MPOC-Enabling and Partnership					
Determinants	**Correlation (p)**	**Estimate (95% CI)**	**Standard error of coefficient**	**Adjuste R^2**	**Intercept**	**P*****
Child-related factors						
Type of disease or disorder	0.76 (0.000)	2.83 (2.25-3.42)	0.29			
Age	-0.32 (0.000)	0.69 (0.16-1.22)	0.26			
Gender*	0.00 (0.47)**	0.00 (-0.4 to 0.41)	0.2	0.67	3.09	0.000
Comorbidity	-0.51 (0.000)	-0.86 (-1.34 to -0.39)	0.24			
Severity of gross motor impairment	0.45 (0.000)	0.44 (-0.03 to 0.91)	0.24			
Service provider-related factors						
Length of service (clinical experience) *	0.28 (0.09)**	0.67 (-0.21 to 1.54)	0.44			
Postgraduate education/master's degree	0.49 (0.000)	1.6 (0.97-2.23)	0.32	0.23	3.5	0.000
Postgraduate occupational course*	0.23 (0.65) **	0.05 (-0.68 to0.77)	0.37			
Parent/caregiver-related factors						
Age*	0.00 (0.47)**	-0.27 (-0.84 to 0.31)	0.3			
Educational level	0.48 (0.000)	1.3 (0.7-1.9)	0.3			
Type of caregiver*	0.13 (0.87)**	0.27 (-0.43 to 0.97)	0.35	0.38	2.5	0.000
Belief in rehabilitation services	0.38 (0.000)	1.03 (0.45-1.62)	0.3			
Expectation to rehabilitation services	0.39 (0.000)	1.1 (0.521-68)	0.29			
Satisfaction with the clinical environment*	0.14 (0.34)**	0.37 (-0.35 to 1.09)	0.36			
Service/care-related factors						
Type of rehabilitation service	0.86 (0.000)	1.52 (0.88-2.17)	0.32	0.78	3.8	0.000
Facility/rehabilitation center-related factors						
Environmental modification	0.46 (0.000)	1.25 (0.59-1.91)	0.33	0.32	3.05	0.000
Experience of active work in the field of pediatric rehabilitation	0.48 (0.000)	1.26 (0.6-1.91	0.33			

*The variables that were removed from the proposed regression model due to an insignificant correlation coefficient with MPOC- 'Enabling and partnership' subdomain, CI: confidence interval, ***A P value of less than 0.001 was considered to show a statistically significant result

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Table 4. Multiple regression models of the Measure of Processes of Care (MPOC-20)- 'Providing Specific Information About the Child' subdomain

MPOC- Providing Specific Information About the Child						
Determinants	**Correlation (p)**	**Estimate (95% CI)**	**Standard error of coefficient**	**Adjuste R^2**	**Intercept**	**P*****
Child-related factors						
Type of disease or disorder	0.75 (0.000)	2.83 (2.26-3.39)	0.29			
Age	-0.32 (0.000)	0.72 (0.2-1.23)	0.26			
Gender*	0.00 (0.49**)	-0.02 (-0.42 to 0.38)	0.2	0.71	3.15	0.000
Comorbidity	-0.52 (0.000)	-0.87(-1.33 to-0.41)	0.23			
Severity of gross motor impairment	0.41 (0.000)	0.42 (-0.03 to 0.88)	0.23			
Service provider-related factors						
Length of service (clinical experience) *	0.13 (0.09**)	0.7 (-0.17 to 1.56)	0.44			
Postgraduate education/master's degree	0.42 (0.000)	1.6 (0.97-2.2)	0.31	0.44	3.56	0.000
Postgraduate occupational course*	0.21 (0.000)	0.00(-0.71 to 0.71)	0.36			
Parent/caregiver-related factors						
Age*	-0.00 (0.48)**	-0.32 (-0.88 to 0.25)	0.29			
Educational level	0.48 (0.000)	1.00 (0.3-1.7)	0.36			
Type of caregiver*	0.33 (0.000)	0.28 (-0.4 to 0.97)	0.35	0.68	2.57	0.000
Belief in rehabilitation services	0.37 (0.000)	0.98 (0.4-1.57)	0.3			
Expectation to rehabilitation services	0.39 (0.000)	1.03 (0.45-1.63)	0.29			
Satisfaction with the clinical environment*	0.7 (0.56)**	0.34 (-0.36 to 1.04)	0.36			
Service/care-related factors						
Type of rehabilitation service	0.4 (0.000)	1.5 (0.87-2.14)	0.32	0.75	3.71	0.000
Facility/rehabilitation center-related factors						
Environmental modification	0.46 (0.000)	1.22 (2.6-3.61)	0.33	0.29	3.1	0.000
Experience of active work in the field of pediatric rehabilitation	0.47 (0.000)	1.26 (0.61-1.9)	0.32			

*The variables that were removed from the proposed regression model due to an insignificant correlation coefficient with MPOC- 'Providing Specific Information About the Child' subdomain, CI: confidence interval, ***A P value of less than 0.001 was considered to show a statistically significant result

Table 5. Multiple regression models of the Measure of Processes of Care (MPOC-20)- 'Coordinated and Comprehensive Care' subdomain

MPOC- Coordinated and Comprehensive Care						
Determinants	**Correlation (p)**	**Estimate (95% CI)**	**Standard error of coefficient**	**Adjuste R^2**	**Intercept**	**P*****
Child-related factors						
Type of disease or disorder	0.74 (0.000)	2.8 (2.22-3.36)	0.29			
Age	-0.32 (0.000)	0.69 (0.17-1.21)	0.26			
Gender*	0.00 (0.48)	-0.04 (-0.44 to 0.37)	0.21	0.55	3.11	0.000
Comorbidity	-0.52 (0.000)	-0.88 (-1.35 to-0.41)	0.24			
Severity of gross motor impairment	0.41 (0.000)	0.43 (-0.03 to 0.89)	0.23			
Service provider-related factors						
Length of service (clinical experience) *	0.4 (0.000)	0.72 (-0.14 to 1.6)	0.44			
Postgraduate education/master's degree	0.42 (0.000)	1.12 (0.26-1.97)	0.43	0.63	3.5	0.000
Postgraduate occupational course*	0.21 (0.54) **	-0.02 (-0.74 to 0.7)	0.36			
Parent/caregiver-related factors						
Age*	0.00 (0.5) **	-0.31 (-0.88 to 0.26)	0.29			
Educational level	0.48 (0.000)	1.28 (0.68-1.87)	0.3			
Type of caregiver*	0.23 (0.67) **	0.29 (-0.4 to 1.00)	0.35	0.59	2.1	0.000
Belief in rehabilitation services	0.57 (0.000)	0.98 (0.4-1.56)	0.29			
Expectation to rehabilitation services	0.39 (0.000)	1.08 (0.51-1.66)	0.29			
Satisfaction with the clinical environment*	0.41 (0.000)	0.31 (-0.4-1.02)	0.36			
Service/care-related factors						
Type of rehabilitation service	0.89 (0.000)	1.49 (0.85-2.12)	0.32	0.46	3.64	0.000
Facility/rehabilitation center-related factors						
Environmental modification	0.46 (0.000)	1.22 (0.57-1.87)	0.33	0.29	3.01	0.000
Experience of active work in the field of pediatric rehabilitation	0.48 (0.000)	1.26 (0.62-1.91)	0.32			

*The variables that were removed from the proposed regression model due to an insignificant correlation coefficient with MPOC- 'Coordinated and Comprehensive Care' subdomain, CI: confidence interval, ***A P value of less than 0.001 was considered to show a statistically significant result

Table 6. Multiple regression models of the Measure of Processes of Care (MPOC-20)- 'Respectful and Supportive Care' subdomain

MPOC- Respectful and Supportive Care						
Determinants	**Correlation (p)**	**Estimate (95% CI)**	**Standard error of coefficient**	**Adjuste R^2**	**Intercept**	**P*****
Child-related factors						
Type of disease or disorder	0.35 (0.000)	3.93 (2.04-5.82)	0.96			
Age	-0.2 (0.081)***	0.22(-2.21 to 2.65)	1.23			
Gender*	-0.08 (0.207)**	-0.82 (-2.7-1.06)	0.95	0.12	3.9	0.000
Comorbidity	-0.25 (0.341)**	-1.31(-3.5 to 0.87)	1.1			
Severity of gross motor impairment	0.21 (0.213)**	0.81(-1.33 to 2.94)	1.08			
Service provider-related factors						
Length of service (clinical experience) *	0.22 (0.49)	1.13 (-1.55 to 3.8)	1.35			
Postgraduate education/master's degree	0.24 (0.005)	0.67-4.60)	1	0.10	3.13	0.009
Postgraduate occupational course*	0.15 (0.051)	0.48 (-1.8 to 2.76)	1.15			
Parent/caregiver-related factors						
Age*	-0.8 (0.2)**	-1.4 (-3.31 to 0.57)	0.98			
Educational level	0.24 (0.004)	2.3 (0.27-4.34)	1.03			
Type of caregiver*	0.087) **			0.18	2.61	0.007
Belief in rehabilitation services	0.2 (0.65)**	1.6 (-0.44 to 3.63)	1.03			
Expectation to rehabilitation services	0.21 (0.012)	1.75 (-0.3 to 3.8)	1.03			
Satisfaction with the clinical environment*	0.22 (0.097)**	0.29 (-2.22 to 2.8)	1.27			
Service/care-related factors						
Type of rehabilitation service	0.22 (0.009)	2.42 (0.42-4.41)	1.00	0.11	3.56	0.018
Facility/rehabilitation center-related factors						
Environmental modification	0.23 (0.005)	1.86 (-0.35 to 4.1)	1.12	0.11	2.78	0.010
Experience of active work in the field of pediatric rehabilitation	0.14 (0.46)**	2.65 (0.65-4.65)	1.01			

*The variables that were removed from the proposed regression model due to an insignificant correlation coefficient with MPOC- 'Respectful and Supportive Care' subdomain', CI: confidence interval, ***A P value of less than 0.001 was considered to show a statistically significant result

Table 7. Multiple regression models of the Measure of Processes of Care (MPOC-20)- 'Providing General information' subdomain

MPOC- Providing General information						
Determinants	**Correlation (p)**	**Estimate (95% CI)**	**Standard error of coefficient**	**Adjuste R^2**	**Intercept**	**P*****
Child-related factors						
Type of disease or disorder	0.75 (0.000)	2.93 (2.5-3.5)	0.29	0.15	2.96	0.81
Age	-0.32 (0.000)	0.73 (0.2-1.27)	0.73			
Gender*	0.01 (0.45**)	0.02 (-0.38-0.44)	0.20			
Comorbidity	-0.49 (0.000)	-0.79 (-1.27 to -0.32)	0.24			
Severity of gross motor impairment	0.40 (0.000)	0.44 (-0.02 to 0.90)	0.23			
Service provider-related factors						
Length of service (clinical experience)*	0.38 (0.000)	0.69 (-0.19 to1.57)	0.45	0.17	3.46	0.32
Postgraduate education/master's degree	0.41 (0.000)	1.11 (0.24-1.99)	0.44			
Postgraduate occupational course*	0.22 (0.008)	0.06 (-0.67 to 0.8)	0.36			
Parent/caregiver-related factors						
Age*	0.02 (0.4)	-0.19 (-0.78 to 0.38)	0.29	0.23	2.45	0.42
Educational level	0.48 (0.000)	1.09 (0.35-1.83)	0.37			
Type of caregiver*	0.31 (0.08)	0.16 (-0.54 to 0.87)	0.35			
Belief in rehabilitation services	0.37 (0.000)	0.98 (0.37-1.58)	0.30			
Expectation to rehabilitation services	0.38 (0.000)	1.04 (0.43-1.64)	0.30			
Satisfaction with the clinical environment*	0.40 (0.000)	0.36 (-0.36 to 1.08)	0.36			
Service/care-related factors						
Type of rehabilitation service	0.39 (0.000)	1.52 (0.87-2.17)	0.32	0.14	3.6	0.23
Facility/rehabilitation center-related factors						
Environmental modification	0.45 (0.000)	1.22 (0.55-1.89)	0.26	0.37	3.03	0.000
Experience of active work in the field of pediatric rehabilitation	0.46 (0.00)	1.24 (0.57-1.91)	0.33			

*The variables that were removed from the proposed regression model due to an insignificant correlation coefficient with MPOC- 'Providing General information' subdomain', CI: confidence interval, ***A P value of less than 0.05 was considered to show a statistically significant result

DISCUSSION

This study sought to investigate determinants that may influence parents'/caregivers' satisfaction with rehabilitation services in individuals with childhood-onset physical disabilities. The findings indicated that each satisfaction domain, as measured by the MPOC-20, was determined by different factors, with varying degree of variances in the relevant subdomains.

The primary predictors of parents'/caregivers' satisfaction with rehabilitation services in terms of "*enabling and partnership*" were found to be service-related and child-related variables. More specifically, the findings showed that the parents or caregivers were more actively involved in the service delivery when the rehabilitation service was functional, or goal directed. This is compatible with the fact that the caregivers/parents are involved more actively in finding solutions to their children's motor problems in functional or goal-directed rehabilitation services (24). As previously noted, in functional or goal-directed rehabilitation services, therapeutic goals are established in consultation with the parent/caregiver or child, with strong encouragement for the involvement of the parent/caregiver in the physiotherapy session (25). In summary, the results indicated that more interaction between the parent/caregiver and the physiotherapist may be possible when rehabilitation services are functional, or goal -directed. Moreover, child-related factors, including being younger than 13 years of age, having a diagnosis of CP, not having a comorbidity, and having a mobility level of GMFCS I–III were found to allow for a more interactive rehabilitation service. This is in line with studies of goal-directed or functional rehabilitation services where inclusion criteria are higher mobility level (GMFCS I–II or III), age less than 12 years, CP, and no severe comorbidity (26-28). This is also consistent with another previous study documenting that parents'/caregivers' satisfaction with rehabilitation services was associated with fewer health and development issues experienced by the patients. In Law et al.'s study, in which they examined factors improving parents'/caregivers' satisfaction with services delivery for children with disabilities, they concluded that parent satisfaction with services delivery was affected by perception whether the services were family-centered, fewer clinical settings in which services were carried out, and fewer developmental difficulties for their child (29). As a result, child- and service-related variables enhanced the partnership between parents/caregivers and service providers. The improved satisfaction observed among parents/caregivers of children with CP regarding rehabilitation services suggests that service providers should be strongly encouraged to deliver family-centered rehabilitation services not only to children with CP but also to children with non-CP conditions. In the current study, service-related, child-related, and parent/caregiver-related factors were found to be indicators of whether parents or caregivers were provided with information about their own child. As emphasized above, functional or goal-directed rehabilitation services include child or person-centered goals that are established in collaboration with the parents/caregivers based on the notion that parents/caregivers spend more time with their children in daily activities (30). In functional or goal-directed rehabilitation services, service providers are expected to meet children's specific needs by providing parents or caregivers with detailed information about their children. Additionally, child-related factors (i.e., <13 years of age, CP diagnosis, no comorbidity, higher mobility level) and parent/caregiver-related factors (i.e., higher education level, type of caregiver being the parents, belief in rehabilitation services, and expectations of rehabilitation services) were found to be appreciable determinants of family-centeredness in service delivery in respect to *sharing information about the child*. The finding that parents'/caregivers' beliefs in rehabilitation services (parent/caregiver-related factors) increased their satisfaction with rehabilitation services is supported by a previous study (29), suggesting that parents' beliefs about service delivery influence their perceptions of rehabilitation services. "*Coordinated and comprehensive care*" refers to whether service delivery is continuous and consistent over time. The model of "*coordinated and comprehensive care*" showed that service provider-related and parent/caregiver-related variables were considerable predictors of parents'/caregivers' satisfaction with rehabilitation services. In other words, service provider-related factors, including having a 5 or over years of clinical experience, postgraduate education, and postgraduate occupational course, were found to facilitate continuous and consistent rehabilitation service. This is consistent with a previous study, demonstrating that parental/caregiver satisfaction with pediatric rehabilitation is significantly influenced by both personal experience and professional competence (31). In conclusion, parental and caregiver satisfaction with pediatric rehabilitation is significantly influenced by the personal qualities and professional competence of healthcare providers. Similarly, parents'/caregivers' satisfaction with collaboration in rehabilitation services was significantly influenced by parent/caregiver-related factors, including a higher education level, type of caregivers being parents, belief in rehabilitation services, and expectations of rehabilitation services. As a result, both service provider-related and parent/caregiver-related factors might lead to (physio)therapist to plan rehabilitation services together with the parents or caregivers. These implications align with the study's results, which indicated that consistent service provision had a strong correlation with the satisfaction of parents or caregivers with healthcare services (32). Regarding parental satisfaction with "*respectful and supportive care*", all factors were associated with improved levels of satisfaction, with parent/caregiver-related variables having slightly stronger predictive factors. Finally, it has been demonstrated that facility/rehabilitation center-related variables influence whether parents/caregivers receive adequate information regarding their children's problems, advice on where to find information, and information about rehabilitation services.

Limitations

In the current study, the data were collected from a total of 15 rehabilitation centers located in two different cities, each employing an average of 2-3 physiotherapists. This may have led to limited diversity in the data related to both service providers and facility/rehabilitation centers. Second, study sample was only representative of urban centers rather than rural centers because all rehabilitation centers in which data were collected were selected from the centers of the cities. Therefore, future research, including a larger number of rehabilitation centers that are located both in urban and rural regions, as well as more service providers, needs to be carried out.

CONCLUSION

This study provided new insights into possible factors that improve parents'/caregivers' satisfaction with rehabilitation services. First, the findings indicated that both service-related and child-related factors are important variables in improving parents'/caregivers' satisfaction with rehabilitation services as to "*enabling and partnership*." Second, service-related, child-related, and parent/caregiver-related factors were associated with parental satisfaction with service delivery in relation to "*specific information about the child*". Later, when examining parental satisfaction with service delivery in respect to "*coordinated and comprehensive care*", it was found that the variables of the service provider and the parent/caregiver are the most important determinants. Finally, parental satisfaction with rehabilitation services with respect to "*providing general information*" was determined to be influenced by the facility/rehabilitation center-related variables. As a result, given that family-centeredness in service delivery is closely related to parents'/caregivers' satisfaction with rehabilitation services, the factors or variables identified in the current study as having the potential to increase parents'/caregivers' satisfaction with rehabilitation services should be considered when providing rehabilitation services.

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Informed consent: *Written informed consent was obtained from both families/guardians and children aged 12 years or older after the research objectives were explained in detail.*

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MEDICAL RECORDS-International Medical Journal

Research Article

Could ELABELA be a Protective Biomarker in Patients with Abnormal Uterine Bleeding?

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Abstract

Aim: Abnormal uterine bleeding (AUB) is a health problem characterized by various symptoms such as heavy and prolonged menstrual bleeding, affecting approximately 30% of female patients both physiologically and psychologically. The objective of this study was to assess serum Elabela (ELA) concentrations in women aged 18 and above diagnosed with functional AUB, and to compare these concentrations with those of healthy women.

Material and Method: This prospective case-control study was performed from August 18, 2022 to December 30, 2022. This was a cross-sectional study including 50 women who applied to the gynecology service of Malatya Turgut Özal Training and Research Hospital with complaints of AUB and 50 women without AUB who underwent gynecological examination. The presence of AUB in patients was determined based on clinical examination conducted by a gynecologist and medical records. Demographic and clinical characteristics were recorded. Serum ELA levels were determined by commercial ELISA kit.

Results: Serum ELA levels was significantly lower in patients with AUB (581.54±272.25 pg/mL) compared to the healthy group (744.55±300.31 pg/mL, p=0.005). In this study, ELA in patients with AUB showed 98% sensitivity and 80% specificity with a cut off value of 411.41 pg/mL (area under the curve [AUC], 68.1%; p=0.002).

Conclusion: Serum ELA levels in patients with AUB were significantly lower than in healthy women. These results show that ELA is a good predictor of the pathophysiological process of AUB.

Keywords: Elabela, abnormal uterine bleeding, PALM-COEIN

INTRODUCTION

The abnormal uterine bleeding (AUB), defined as bleeding exceeding 80 mL per menstrual cycle, affects approximately 3-30% of women worldwide, and up to 50% of women during the perimenopausal period (1,2). Functional AUB can profoundly affect a woman's quality of life, leading to physical, emotional, and social constraints, impaired sexual function, decreased productivity throughout the day, financial constraints, and negative effects on fertility and reproduction (3-5).

The patterns of AUB, which can be influenced by various factors such as hormonal imbalances, systemic conditions, uterine fibroids, polyps, endometrial hyperplasia, endometrial cancer, pelvic infections, certain medications, iatrogenic causes and bleeding disorders, are determined based on criteria including duration, intensity, regularity, and frequency of bleeding (3,6). The International Federation of Gynecology and Obstetrics (FIGO) has classified AUB as either structural causes (polyp, adenomyosis, leiomyoma, malignancy and hyperplasia [PALM]) or nonstructural causes (coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, not otherwise classified [COEIN]) (7). The treatment of AUB can vary depending on factors such as the causes of bleeding, severity of symptoms, the patient's medical history, and preferences. It may involve medical treatments such as hormonal therapy, nonsteroidal anti-inflammatory drugs, levonorgestrel intrauterine devices or surgical treatment options such as endometrial ablation, myomectomy, or hysterectomy, based on the diagnosis (8,9). In the patient population presenting with AUB complaints, endometrial sampling is the gold

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standard for the most accurate detection of premalignant and malignant lesions. However, it is known that other diagnostic methods such as blood tests and ultrasound are insufficient (10).

The endogenous hormonal peptide known as elabela (ELA), also referred to as the G protein-coupled Apelin receptor agonist peptide (APLNR), consists of 32 amino acids (11). The expression of apelin/ELA-APJ is limited to several tissues including lung, prostate, adipose tissue, placenta, nervous system gastrointestinal tract, and vascular endothelium (11,12). Despite the research in the literature regarding ELA's involvement in embryonic development, bone homeostasis, angiogenesis, regulation of vascular and cardiac functions, anti-hypertensive effects, anti-renal fibrosis, prevention of kidney remodeling, and regulation of water homeostasis, its specific function in diverse pathophysiological events remains unknown (13). In recent times, the role of ELA in thrombosis has begun to attract attention. Moreover ELA may promote platelet aggregation, which plays a role in the formation of blood clots (14). Based on this information, we aimed to compare the serum ELA concentrations of women with AUB evaluated in accordance with the PALM-COEIN diagnostic criteria with those of healthy women without complications.

MATERIAL AND METHOD

The Research Methodology and Characteristics of the Study Participants

This study is a prospective case-control study including patients who presented with complaints of AUB to the Department of Obstetrics and Gynecology at Malatya Turgut Özal University Training and Research Hospital between August-December 2022.

All patients were investigated for the cause of bleeding according to the International Federation of Gynecology and Obstetrics PALM-COEIN classification through history, systemic examination, gynecological examination, and laboratory findings. Fifty women aged 18-49, diagnosed with menorrhagia, were included in the study after excluding identifiable pelvic pathology, endocrine diseases, or pregnancy, and meeting all specified exclusion criteria. The control set consisted of fifty healthy female volunteers, age- and body mass index-matched, who had regular menstrual cycles transpiring every 27-32 days. Power analysis was performed to determine the sample number (G Power 3.1.9.4).

Pregnant or lactating mothers, individuals with a body mass index of <18 kg/m² or >30 kg/m², those with polycystic ovary syndrome (PCOS), endocrine disorders, chronic systemic conditions, ectopic pregnancy, gestational trophoblastic disease, coagulopathy, or hematologic diseases, as well as those with benign or malignant ovarian, uterine, or vulvovaginal lesions, postmenopausal or hysterectomized women, users of medication, tobacco, alcohol, or drugs, and patients with intrauterine devices (IUDs) were not included in the study.

Biochemical Analysis

On the second or third day of menstruation, following an overnight period of not eating, blood samples were obtained from the arm veins of individuals in both the patient and control groups, using gel separator and anticoagulant tubes, between 08:00 and 09:00 A.M. The tubes were left to clot for 20–30 minutes. Once clotting occurred, tubes for collecting serum samples were spun at 1800 revolutions per minute (RPM) for 10 minutes at room temperature using a centrifuge.

A part of blood samples was used biochemical analysis platelet, mean corpuscular volume (MCV), hematocrit (%), hemoglobin, albumin, total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), C-reactive protein (CRP), iron, iron binding capacity, activated partial thromboplastin time (APTT), international normalized ratio (INR), and hormone analysis follicle-stimulating hormone (FSH), luteinizing hormone (LH), thyroid-stimulating hormone (TSH). The analysis utilized a biochemistry device (Abbott Architect, USA) and a hormone device (Roche Diagnostics Cobas, Japan). ELA levels were determined by the commercial Enzyme-Linked Immunosorbent Assay (ELISA) kit (Bioassay Technology Corp., Cat. No: E7331Hu, China) following the guidelines provided by the manufacturer.

Statistical Analysis

The analyses of the data included in the study were conducted using SPSS (Statistical Program in Social Sciences) 25. The data's adherence to a normal distribution was evaluated through the Kolmogorov-Smirnov Test. Descriptive statistics such as mean, standard deviation, frequency, and percentage were employed. A significance level (p) of 0.05 was chosen for comparison tests. Since the variables followed a normal distribution ($p>0.05$), parametric test methods were employed for analysis. Comparisons in independent binary groups were conducted using the independent t-test. Receiver operating characteristic curve (ROC) analysis was applied to determine the cut-off point for a measurement value, and indices were calculated accordingly.

RESULTS

The study sample consisted of one hundred individuals in total, with fifty patients presenting AUB and fifty healthy controls. There were no statistically significant variations identified between the groups concerning demographic variables such as age and BMI ($p>0.05$) (Table 1).

According to the variables albumin, LDL, HDL, CRP, LH, APTT and INR, no statistically significant variations identified between the AUB and control groups ($p>0.05$). Significant statistical differences were noted between the AUB and healty control groups in terms of total cholesterol, iron, iron binding, hemoglobin, platelets, MCV, hematocrit, TSH, and FSH variables ($p<0.05$) (Table 2).

Table 1. Comparison of gender and BMI distributions between disease groups

Variable	Groups	Mean±SD	t	p values
Age (years)	AUB	38.09±5.79	0.840	0.404
	Control	31.59±6.43		
BMI (kg/m²)	AUB	26.37±2.8	0.836	0.406
	Control	24.16±2.92		

p value: statistical significance, sd: standart deviation, t: independent t test; *p<0.05: there is a statistical difference between the groups

Table 2. Comparison of laboratory biomarker values according to disease

Variables	Groups	Mean±SD	t	p values
Platelet (10³/µL)	AUB	330.79±77.84	**4.092**	**0.001***
	Control	270.43±65.26		
MCV (fL)	AUB	79.6±6.99	**-3.014**	**0.003***
	Control	83.3±5.2		
Hematocrit %	AUB	36.72±2.88	**-4.482**	**0.001***
	Control	39.3±3.03		
Total Cholesterol (mg/dL)	AUB	180.35±33.75	**2.357**	**0.020***
	Control	167.19±31.47		
LDL (mg/dL)	AUB	110.4±29.13	1.756	0.082
	Control	99.22±25.34		
HDL (mg/dL)	AUB	51.21±12.78	-0.105	0.917
	Control	51.23±10.98		
Iron (µg/dL)	AUB	48.6±28.97	**-4.412**	**0.001***
	Control	79.07±33.77		
Iron Binding Capacity (µg/dL)	AUB	341.83±71.31	**5.445**	**0.001***
	Control	262.08±58.93		
CRP (mg/dL)	AUB	0.42±0.79	1.742	0.085
	Control	0.17±0.27		
Albumin (g/dL)	AUB	4.28±0.37	-1.34	0.183
	Control	4.39±0.37		
Hemoglobin (g/dL)	AUB	11.92±1.28	**-5.139**	**0.001***
	Control	13.42±1.47		
FSH (mU/mL)	AUB	10.34±9.39	**3.863**	**0.001***
	Control	5.37±2.72		
TSH (mU/L)	AUB	2.16±0.91	**2.207**	**0.030***
	Control	1.8±0.75		
LH (mU/mL)	AUB	6.54±4.79	0.261	0.794
	Control	6.6±2.87		
APTT (s)	AUB	25.62±2.37	0.579	0.564
	Control	25.28±1.99		
INR	AUB	0.98±0.05	-0.615	0.54

p value: statistical significance, sd: standart deviation, t: independent t test, *p<0.05: there is a statistical difference between the groups; note: bold values are statistically significant values (p<0.05)

Evaluation of serum ELA levels

There was a statistically significant difference detected between the groups in serum ELA levels (p<0.05) (Figure 1, Table 3).

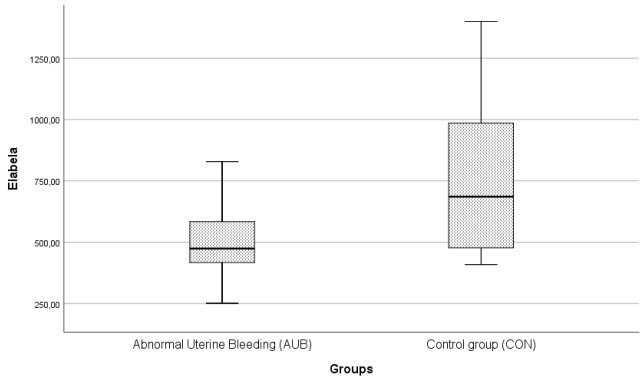

Figure 1. Box-plot of the distribution of elabela in groups

Table 3. The comparison of serum elabela levels in all study groups

Variables	Groups	Mean±SD	t	p value
ELA (pg/mL)	AUB	581.54±272.25	-2.844	0.005*
	Control	744.55±300.31		

p value: statistical significance, sd: standart deviation, t: independent t test, *p<0.05: there is a statistical difference between the groups; note: bold values are statistically significant values (p<0.05)

ROC curve analysis

ROC analysis was applied to determine the cut-off point for ELA measurement values. The analysis result is given in the table below. The areas under the curve calculated for ELA were found to be statistically significant (p<0.05, Figure 2). Serum ELA levels serve as a distinguishing factor in patients with AUB. When the ELA threshold was set at 411.41 pg/mL for AUB patients, the test showed 98% sensitivity, meaning it accurately identified 98% of those with AUB. Additionally, it displayed 80% specificity, indicating that it correctly ruled out AUB in 80% of cases where it wasn't present. (AUC=0.681, 95% CI=0.577–0.786, p=0.002) (Figure 2, Table 4).

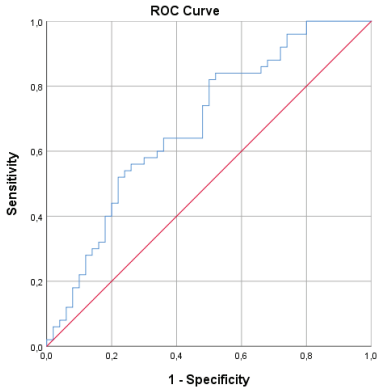

Figure 2. Receiver operating characteristic (ROC) curve analysis of the utility of ELA to predict AUB patients

Table 4. ROC analysis results of ELA levels

Test result variable(s)	Cut off	Sensitivity	Specificity	AUC	p value	95% C.I.for Exp (β)	
						Lower bound	Lower bound
ELA	411.41	0.980	0.800	0.681	**0.002***	0.577	0.786

AUC: area under the curve, C.I.: confidence interval

DISCUSSION

Abnormal uterine bleeding causes both physiological and psychological distress to female patients with various symptoms such as heavy and prolonged menstrual bleeding. This condition, affecting approximately ~30% of the female population worldwide, reduces the quality of life for women both physically and psychologically (1). In the patient population presenting with AUB complaints, endometrial sampling is the gold standard for the most accurate detection of premalignant and malignant lesions. However, it is known that other diagnostic methods such as blood tests and ultrasound are insufficient.

In this study, total cholesterol, iron binding, platelet, TSH, and FSH were found to be significantly high in AUB participants (p<0.05). However, iron, hemoglobin, MCV, and hematocrit levels were found to be significantly low in the AUB patient group compared to the healty group (p<0.05). Severe blood loss and menstrual periods lasting more than 7 days can lead to the depletion of iron stores in women, resulting in iron deficiency. Iron is crucial in numerous biological processes, encompassing DNA synthesis, cellular metabolism, and cell division. The decrease in iron levels affects hemoglobin levels. The reduction in hemoglobin levels disrupts and impairs RBC production, leading to the development of anemia (15,16). Karatoprak et al. reported an increased rate of iron loss and the development of anemia in women experiencing prolonged and heavy menstrual bleeding (17). FSH, produced by the anterior pituitary gland, plays a role in many physiological events such as gonadal sex hormone synthesis, menstruation, and follicular development. To compensate for the decrease in ovarian function before menopause, FSH increases before the decrease in estrogen (18). The enzyme 3-Hydroxy-3-methylglutaryl-coenzyme A reductase (HMGCR) serves as the key regulatory enzyme in the biosynthesis of cholesterol. Guo et al. demonstrated that, during the premenopausal and perimenopausal periods, FSH significantly increases cholesterol levels progressively by regulating HMGCR (19). Our study results are consistent with the literature.

Additionally, our findings revealed that ELA expression was significantly lower in patients with AUB compared to the control group (p<0.05). Based on the results obtained, ELA could be a novel diagnostic biomarker for AUB. AUB is associated with molecular and cellular processes

such as decreased endometrial vasoconstriction, impaired endometrial angiogenesis, apoptosis, increased unpredictable vascular fragility through loss of integrity of endothelial, epithelial and stromal support structures and increased vascular fragility, defective hemostatic processes, cell proliferation, inflammation and repair mechanisms (2,10,15). Active peptides in the human body are integral to the maintenance of health and proper functioning of various physiological systems. Their dysregulation or imbalance can contribute to the development of various diseases and disorders (20).

Elabela peptide expression was found in humans in the prostate, kidney, renal distal collecting tubes, lungs, and veins, cardiovascular system, retina, ovary, testis, skin, stomach, placenta and embryonic stem cells (21). In recent studies, the ELA-apelin/APJ system has been found to be associated with many thrombotic diseases such as atherosclerosis, myocardial infarction, cerebral infarction, acute coronary syndrome, stroke and cancer (14,22). All these studies show that ELA/APJ signaling and regulating actions play a role in many physiological processes such as blood pressure control, cardiac and vascular modulation, hypertrophy, inflammation, apoptosis, angiogenesis, cell motility, cell proliferation and migration (23). It has been reported that the expression of Apelin/APJ plays a significant role in angiogenesis, metastasis, and cell proliferation, showing a significant increase in ovarian cancer (24). In another study, it was determined that Apelin and APJ receptor were expressed in obese individuals and women with presenting only ≥12 follicles per ovary and polycystic ovary syndrome (PCOS) (25).

Chen et al. reported that ELA, a hormone peptide belonging to the adipokine group and a component of the apelinergic system, activates the pannexin1 (PANX1)-P2X7 signaling pathway, inducing platelet aggregation and thrombosis (14). In an interventional study conducted by Coquerel et al., to evaluate the effects of ELA and Apelin-13 on vascular and cardio-renal function in a rat model of septic shock, it was demonstrated that ELA had superior effects on fluid homeostasis and cardiovascular hemodynamic recovery (26).

According to the results obtained in this study, a decline in ELA peptide expression was detected among AUB patients as opposed to the control group. In addition when the cut-off value for ELA was determined as 411.41 pg/mL in AUB patients, the sensitivity was 98% and the specificity was 80% (AUC=0.681, 95% CI=0.577–0.786, p=0.002). In line with these results, serum ELA levels serve as a predictive factor in patients with AUB.

Control of menstrual blood loss in women is achieved by vasoconstriction, hemostasis and re-epithelialization mechanisms. Local vasoactive mediators, which play a role in regulating vascular tone and hemostasis also have an important role in determining the amount of menstrual bleeding. However, expression of local endometrial factors has been observed to be abnormal in patients with AUB (27). Kacar et al. showed that rat apelin levels increased at the end of pregnancy and that apelin may be an endogenous peptide that triggers uterine contractions at birth (28). Apelin has been found to exert an inhibitory effect on spontaneous and oxytocin-induced contractions in human myometrium obtained during cesarean section (29,30).

The low serum ELA concentration in AUB patients may be explained by inadequate/slow hemostatic thrombus formation or insufficient vasoconstriction, leading to inadequate hemostasis. The significant decrease in serum ELA levels in AUB patients, along with the detection of high sensitivity (98%) and specificity (80%) at a cutoff value of 411.41 pg/mL, indicates that the ELA/APJ system plays an active role in AUB.

CONCLUSION

There was a significant decrease in serum ELA levels among patients with AUB when compared to healthy women. These results show that ELA is a good predictor of the pathophysiological process of AUB.

Limitations of the Study

Among the limitations of our study are its design as a single-center study and the relatively small sample size of the research population. These limitations may lead to the oversight of different factors that could contribute to the occurrence of AUB. More comprehensive prospective studies (detection in cervicovaginal fluids) could be useful in determining the predictive and therapeutic value of the ELA/APJ system in women with AUB.

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Ethical approval: *The research was carried out in accordance with the Declaration of Helsinki (1989) of the World Medical Association. The study was approved by the Ethics Committee of Malatya Turgut Özal University, Türkiye (Date: 18 Aug 2022, Issue: 2022/37). Written informed consent was obtained from each patient.*

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MEDICAL RECORDS-International Medical Journal

Research Article

The Relationship between Perceived Social Support and Postoperative Comfort in Coronary Artery Bypass Graft: A Cross-Sectional Study in Türkiye

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Abstract

Aim: This study examined the relationship between perceived social support and comfort in coronary artery bypass graft patients.
Material and Method: This is a descriptive and cross-sectional study. The study was conducted with 250 patients hospitalized for CABG surgery in a public hospital in southern Türkiye between April 1, 2022 - April 1, 2023. Research data were collected using a personal information form, the Multidimensional Perceived Social Support Scale (MSPSS), and the General Comfort Questionnaire (GCQ). The principles of the Declaration of Helsinki were adopted at every stage.
Results: A statistically significant difference was found between the participants' MSPSS score averages according to having children, marital status, and income level ($p<0.05$). A significant difference was found between the participants' average GCQ scores according to marital status, having children, age, profession, and previous surgery history ($p<0.05$). The patients' mean MSPSS total score is 69.67±21.91 and their GCQ total mean score is 2.93±0.36. A moderate positive correlation was found between the MSPSS and the GCQ perceived by the patients ($r=0.495$, $p<0.001$).
Conclusion: It is understood that strengthening patients' social support systems are important in increasing comfort. For this reason, during surgical care, nurses should ensure that patients receive support from social resources in addition to professional nursing care to increase patient comfort.

Keywords: Care, coronary artery bypass surgery, education, nurse, social support, society

INTRODUCTION

It is reported that ischemic heart disease, defined as coronary artery disease (CAD), remains at the top of the list of deaths all over the world, as in our country (1-3). Coronary artery bypass graft (CABG) is the most used method in the surgical treatment process of CAD (4). The frequency of the disease also increases the frequency of surgical operations. Surgery aims to reduce the possibility of coronary ischemia and myocardial infarction (MI) and to increase exercise tolerance (5).

It has been stated that individuals need social connections and social support to manage their anxiety, fear, and depression after surgery. It is important to get support from children, friends, and relatives rather than a single source of support such as a partner (6,7). The fact that the sick individual distances himself from society and family, that is, experiences social isolation, causes him to stay in the hospital longer than necessary. Long-term hospitalization affects the individual's depression and recovery after discharge, causing the individual to return to the hospital (8-11). Patients who have strong ties with their family, relatives, friends, and other elements of society recover faster in the perioperative period and have a better quality of life. It has been reported that high perceived social support in patients is effective in coping with postoperative depression and increases the patient's comfort level (12).

Comfort, known as comfort in daily life, is one of the indispensable preferences of the individual's life and is a desired result of nursing care in the perioperative period. The goals of nursing care are to recognize the indication, course, or possible complications of any disease early and take precautions, or to provide treatment and care for the individual and social problems of this disease as early as possible (13,14). Surgical procedures can cause deterioration in comfort as it is a trauma that affects all aspects of patients undergoing surgical procedures

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(14). In a study, it was reported that the comfort level of unmarried patients was lower than married patients, and since divorced people lost the social support of the family, surgical intervention triggered problems that negatively affected comfort (15).

It has been reported that family support is effective in reducing symptoms in individuals who have open heart surgery. It has also been reported that there is a relationship between social support received after birth and postpartum comfort, and as the level of social support increases, postpartum comfort increases. Accordingly, we can think that the result obtained indicates that perceived comfort affects recovery in the postoperative periods of other diseases (16,17). One study reported that social isolation and lack of social support were determinants of CAD incidence and mortality, and social support increased survival in CABG (12).

In this context, social support is a two-way process; It is a source of interaction that provides comfort, help, and encouragement. According to the results we have obtained so far, no study has been found or reached examining the relationship between perceived social support and comfort level in individuals undergoing open heart surgery. This study is expected to contribute to the literature in this sense. This study was conducted to examine the relationship between perceived social support and postoperative comfort in CABG patients.

MATERIAL AND METHOD

Study Type

This study was conducted as descriptive and cross-sectional.

Study Group

The study population consisted of patients hospitalized for CABG surgery at Mersin City Training and Research Hospital between April 1, 2022 - April 1, 2023. The sample size in the study was "G. With the "Power 3.1.9.2" program, 237 patients were determined with the assumption of 1-β=0.99 power and α=0.01 error level and effect size f=0.3 (18). The study was conducted with 250 patients who met the inclusion criteria.

Research Inclusion Criteria

Patients who are hospitalized in the cardiovascular surgery clinic, are 18 years of age or older, are oriented to person, place, and time, do not have a condition that prevents them from communicating or have a psychiatric problem, and accept the research.

Study data were collected by assistant researchers using the face-to-face interview method at Mersin city hospital between April 1, 2022 - April 1, 2023. It took approximately 10-15 minutes to fill out the survey form.

Dependent and Independent Variables

The independent variables of this research are age, gender, department, income, and marital status. The dependent variables are the Multidimensional Perceived Social Support Scale (MSPSS) and General Comfort Questionnaire Scale (GCQ).

Procedures

Research data were collected with a personal information form, Multidimensional Perceived Social Support Scale, and General Comfort Questionnaire.

Personal Information Form: It consists of a total of 10 questions regarding the sociodemographic information of the patients, including age, gender, personal information form, marital status, having children, education, profession, income level, previous surgery history, and whether there is an accompanying person in the hospital (9,11,13,16,17).

Multidimensional Perceived Social Support Scale (MSPSS): The scale was developed by Zimmet et al. (1988) and its Turkish validity and reliability were determined by Eker and Arkar (1995). The scale consists of 12 items and is a 7-point Likert type. The scale includes Family (items 3, 4, 8, 11), Friend (item 6, 7, 9, 12) and A Special Person (item 1, 2, 5, 10). It has three sub-dimensions: The subscales are independent of each other and give the total score that includes all subgroups of the scale. The minimum score from the scale is 12 and the maximum score is 68. A high score indicates that the perceived social support is high. The Cronbach's alpha value of the scale varies between 0.77 and 0.92 (19,20). In this study, Cronbach's alpha value for the total scale was determined as 0.89, and Cronbach alpha values of the scale sub-items were found between 0.71 and 0.73.

General Comfort Questionnaire (GCQ): The scale was developed by Kolcaba (1992), and its Turkish validity and reliability study was conducted by Kuğuoğlu and Karabacak (2004). It was created by taking as a guide the taxonomic structure of three levels and four dimensions that constitute the theoretical elements of comfort. The scale is a four-point Likert type (1=strongly agree, 4=strongly disagree) and consists of 48 items. The negative items in the scale are reverse-coded and summed with the positive items. The lowest score that can be obtained from the scale is 48 and the highest is 192. The average value is determined by dividing the calculated total score by the number of scale items. A high score indicates a high level of comfort. The Cronbach alpha value of the scale was calculated as 0.88 (21,22). In this study, Cronbach's alpha value for the total scale was determined as 0.81. Cronbach alpha values of the scale sub-items were found between 0.71 and 0.78.

Statistical Analysis

In the research, data were evaluated using the SPSS 25.0 statistical program. The normality test was evaluated with Kolmogorov-Smirnov and it was determined that the data did not comply with normal distribution. For the data, descriptive statistics including percentage, frequency, mean, standard deviation, minimum and maximum values, as well as Kruskal-Wallis and Mann-Whitney U tests in independent groups were used. Spearman Correlation analysis was used to measure the relationship between the total and subscales of MSPSS and GCQ. Dunn's test, one of the post-hoc multiple comparison tests, was used

to determine which group the independent variables' significance came from. Internal consistency Cronbach's alpha coefficient was calculated, and the p significance level was p<0.05.

Ethical Considerations

Toros University Scientific Research and Publication Ethics Committee (No: 2022/94) and institutional permission were obtained to conduct the research. Before data was collected, the purpose of the study was explained to the patients, and their written consent was obtained. The research was planned and conducted following the Principles of the Declaration of Helsinki.

RESULTS

The average age of the patients is 66.33±9.70, 44.8% are between the ages of 65 - 74, 74.0% are male, 94.4% are married, 93.2% have children, 51.6% are primary school graduates, 32.0% are retired, % It was determined that 58.8% of the patients had a medium income level, 58.8% had a history of surgery, and 48.8% were accompanied by a child (ren) in the hospital. A statistically significant difference was determined between the patients' mean MSPSS total scores according to their marital status, having children, and income level (p<0.05). In the advanced analysis, a significant difference was found between those with good income and those with poor income (p<0.05) for MSPSS. A significant difference was found between the patients' average GCQ scores according to age, marital status, having children, profession, and previous surgery history (p<0.05). In the advanced analysis, for GCQ, 32 - 50 years of age and ≥ 75 years of age (p<0.05); Significance was determined between civil servants and those in other professional groups (p<0.05) (Table 1).

Table 1. Comparison of patients' sociodemographic characteristics and MSPSS and GCQ total score averages (n=250)

			MSPSS Total		GCQ Total	
		n (%)	Mean±SD	Statistic/p	Mean±SD	Statistic/p
Age 66.33±9.70, Min.=32, Maks.=90	**32—50 age (A1)**	17 (6.8)	75.76±17.73	*KW=6.473 p=0.091	2.99±0.27	KW=12.689 p=0.005 A1—A4/0.003
	51—64 age (A2)	74 (29.6)	70.40±22.39		2.95±0.38	
	65—74 age (A3)	112 (44.8)	69.94±21.83		2.83±0.32	
	≥75 age (A4)	47 (18.8)	65.68±22.67		2.78±0.41	
Gender	**Famale**	65 (26.0)	75.43±14.93	**Z=-1.826 p=0.068	3.00±0.23	Z=-1.181 p=0.238
	Male	185 (74.0)	67.65±23.59		2.91±0.39	
Mariatal status	**Married**	236 (94.4)	70.85±20.86	Z=-2.924 p=0.003	2.95±0.35	Z=-2.649 p=0.008
	Single	14 (5.6)	49.85±29.79		2.66±0.43	
Having children	**Yes**	233 (93.2)	70.84±20.89	Z=-2.580 p=0.010	2.95±0.34	Z=-2.645 p=0.008
	No	17 (6.8)	53.70±29.23		2.64±0.45	
Education level	**Illiterate**	68 (27.2)	64.13±24.33	KW=6.011 p=0.111	2.86±0.42	KW=1.726 p=0.631
	Primary education	129 (51.6)	72.02±20.16		2.96±0.32	
	High school	40 (16.0)	69.82±23.30		2.94±0.40	
	≥University	13 (5.2)	74.92±17.27		2.97±0.21	
Job	**Housewife (A1)**	53 (21.2)	75.67±15.28	KW=10.556 p=0.061	2.99±0.24	KW=11.849 p=0.037 A3—A6/0.025
	Worker (A2)	26 (10.4)	67.50±21.28		2.90±0.33	
	Officer (A3)	23 (9.2)	71.69±23.35		3.05±0.39	
	Self-employed (A4)	26 (10.4)	71.80±23.14		2.91±0.43	
	Retired (A5)	80 (32.0)	69.83±20.40		2.96±0.32	
	Other* (A6)	42 (16.8)	60.71±28.04		2.76±0.46	
Economic status	**Ggood (A1)**	54 (21.6)	72.88±21.34	KW=6.190 p=0.045 A1—A3/0.039	2.94±0.35	KW=0.086 p=0.958
	Moderate (A2)	147 (58.8)	70.18±22.19		2.93±0.35	
	Poor (A3)	49 (19.6)	64.61±21.31		2.91±0.40	
Previous surgical experience	**Yes**	147 (58.8)	70.89±20.60	Z=-0.658 p=0.510	2.89±0.35	Z=-2.810 p=0.005
	No	103 (41.2)	67.93±23.66		2.99±0.37	
Relationship	**Wife**	74 (29.6)	68.45±21.86	KW=8.870 p=0.114	3.00±0.29	KW=8.084 p=0.152
	Childs	122 (48.8)	70.85±21.30		2.91±0.38	
	Siblings	11 (4.4)	59.27±26.67		2.76±0.39	
	Friend	7 (2.8)	71.71±16.41		2.98±0.35	
	Relative	28 (11.2)	76.21±18.30		2.95±0.40	
	Paid employee	8 (3.2)	52.62±31.66		2.69±0.40	

SD: standard deviation, MSPSS: Multidimensional Perceived Social Support Scale, GCQ: General Comfort Questionnaire; *KW=Kruskal-Wallis test, **Z=Mann-Whitney U test

The mean MSPSS total score of the patients was 69.67±21.91, the mean scores of the Family, Friend, and Special Person subscales were 25.14±5.90, 22.02±9.17, and 22.50±8.96, respectively; the mean total score of the GCQ was 2.93±0.36, the mean scores of the Physical subscale were 31.26±5.95, the mean scores of the Psychospiritual subscale were 41. 48±5.44, Environmental sub-dimension mean score 37.15±5.10, Sociocultural sub-dimension mean score 31.10±5.04, and Relief level mean score 46.53±6.12, Relaxation level mean score 49.93±7.05, Superiority level mean score 44.63±6.83 (Table 2).

Table 2. Distribution of the mean scores and minimum-maximum values of the total and sub-dimensions of the MSPSS and the GCQ

	Mean	SD	Received (Min-Max)	Available (Min-Max)
MSPSS total	69.67	21.91	15-84	12-84
Family	25.14	5.90	4-28	4-28
Friends	22.02	9.17	4-28	4-28
A special person	22.50	8.96	4-28	4-28
GCQ total	2.93	0.36	1.58-3.54	1-4
Physically	31.26	5.95	15-45	12-48
Psychospiritual	41.48	5.44	23-52	13-52
Environmental	37.15	5.10	21-48	14-56
Socio-cultural	31.10	5.04	13-38	10-40
Refreshment	46.53	6.12	26-58	16-64
Relaxation	49.93	7.05	26-65	17-68
Superiority	44.63	6.83	23-59	15-60
GCQ total score	141.10	17.16	81-170	48-192

SD: standard deviation, MSPSS: Multidimensional Perceived Social Support Scale, GCQ: General Comfort Questionnaire

A moderate positive correlation was found between perceived MSPSS and GCQ (r=0.495, p<0.001). In other words, as social support increases in patients, the comfort level also increases. A correlation was found between MSPSS and GCQ sub-dimensions (Table 3).

Table 3. Correlational Distribution of MSPSS, GCQ total and subscales

		1	2	3	4	5	6	7	8	9	10	11
1. MSPSS total	**r***	1										
	p											
2. Family	**r**	0.750	1									
	p	**<0.001**										
3. Friends	**r**	0.981	0.689	1								
	p	**<0.001**	**<0.001**									
4. A special person	**r**	0.958	0.662	0.944	1							
	p	**<0.001**	**<0.001**	**<0.001**								
5. GCQ total	**r**	0.495	0.540	0.483	0.434	1						
	p	**<0.001**	**<0.001**	**<0.001**	**<0.001**							
6. Physically	**r**	0.363	0.394	0.350	0.328	0.858	1					
	p	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**						
7. Psychospiritua	**r**	0.459	0.466	0.444	0.419	0.792	0.609	1				
	p	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**					
8. Environmental	**r**	0.160	0.250	0.173	0.111	0.546	0.367	0.190	1			
	p	**0.011**	**<0.001**	**0.006**	**0.081**	**<0.001**	**<0.001**	**0.003**				
9. Socio-cultural	**r**	0.633	0.582	0.610	0.574	0.748	0.558	0.675	0.152	1		
	p	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**0.016**			
10. Refreshment	**r**	0.451	0.403	0.440	0.407	0.749	0.645	0.615	0.364	0.637	1	
	p	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**		
11. Relaxation	**r**	0.528	0.531	0.531	0.489	0.856	0.713	0.762	0.347	0.783	0.526	1
	p	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	
12. Superiority	**r**	0.258	0.399	0.256	0.206	0.777	0.720	0.548	0.666	0.432	0.361	0.555
	p	**<0.001**	**<0.001**	**<0.001**	**0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**

MSPSS: Multidimensional Perceived Social Support Scale, GCQ: General Comfort Questionnaire; *Spearman's correlation test

DISCUSSION

To examine the relationship between perceived social support and comfort in patients diagnosed with CAD and undergoing CABG surgery, this cross-sectional study was conducted. Ensuring patient comfort in the perioperative process is one of the main goals expected to be achieved in the nursing care process. By increasing the comfort of the individual, the individual is empowered and included in the treatment process (13,23,24). The surgical nurse utilizes the physical, psychospiritual, environmental, and sociocultural areas in the taxonomic structure of the comfort theory to increase the comfort of the individual in the perioperative process. The relationship between an individual's perceived social support and comfort level was examined in this study.

In this study, it was determined that the social support perceived by the patients was above the moderate level. It was determined that the mean score of the family subscale of the scale (25.14±5.90) was higher than the friend and special person subscales. According to this result, our study group receives support from more families. A meta-analysis similarly noted that patients generally reported moderate to strong social support (7). In studies conducted in our country with a similar sample group, patients' perceived social support was found to be high, similar to our findings (1,25). It is thought that the supportive traditional family structure of Turkish society is effective in this result (26,27). It was determined that the mean MSPSS total score of the patients included in the study who were married and had children was significantly higher. Having a partner, happier marriages, increased physical activity and more social interaction have been reported to be effective in increasing comfort. In our society, individuals want to receive support from their first-degree relatives. While caregivers are preferred in developed countries, traditional family care is preferred in Türkiye (26,27).

In this study, the patients' comfort levels were found to be above the moderate level. Similarly, studies conducted in Türkiye support our findings (13,28-31). CABG is considered a risky surgery due to the emotional, cognitive, and physiological reactions that can be seen after surgery (1,2,13). For this reason, during the postoperative period, patients are taken to single rooms and, whenever possible, they are provided with support from at least two relatives. This approach is thought to be effective in this result. It was determined that as the age of the patients increased, the average GCQ score decreased, and the comfort level of the younger age group was higher. There are results supporting the findings of this study (28). Contrary to our findings, there are studies reporting that there is no relationship between age and GCQ (26,31,32). It is thought that these contradictory results among the research findings should be examined by considering the effect of different demographic data.

Among the patients included in the study, it was found that the mean total score of the patients who were married and had children was higher. Although there is a study that supports our findings (15), there are also studies that state the opposite of our findings (28,31). It is thought that the fact that the majority of the study participants received support from their families and children was effective in this result. It was determined that the average GCQ scores of patients with no previous hospital history were significantly higher. A study similarly reported that the hospital experience negatively affects overall comfort (27). In one study, those with hospital experience found high GCQ scores (32). Since detailed information regarding previous hospital experience (such as the reason for admission, type of surgery, accompanying relative, and duration of hospital stay) was not investigated in this study, the results are difficult to interpret.

This study shows that as social support increases, the comfort level also increases. Kok et al. (2023) examined the correlation between social support and preoperative anxiety and reported that strong social support, although weak, was significantly associated with reduced anxiety (7). Although not similar to this study group, Yıldırım and Tanrıverdi (2021) reported that there was a significant relationship between social support and life satisfaction in their study with university students (33). A study reported that social support has a positive effect on improving the quality of life, which also significantly affects comfort, in individuals who have undergone CABG (34). Depending on the recovery process after CABG and the patient's condition, the type and level of support requests may vary. After CABG, patients experience psychological problems due to multiple post-operative health problems. In this process, individuals need to be supported for rapid recovery and adaptation to medication. Social support can improve psychological findings by alleviating emotional stressors and facilitate the postoperative psychological adjustment and recovery process (34). With various nursing interventions, patients' comfort level and even their independence after surgery can be increased (32). One of the aims of nursing care is to strengthen the individual. The individual who receives the support he needs in an acute process will be stronger. Nurses should consider all possibilities necessary to ensure this (15). One limitation of such correlational studies is their inability to demonstrate causality. Future research should be conducted with a larger sample of participants from different parts of the country and with a design that investigates cause-and-effect relationships.

CONCLUSION

The main conclusion that can be drawn from this study is that the patients' perceived social support and general comfort levels are above average. It was determined that the perceived social support and general comfort scores of patients who were married and had children were higher, and that comfort decreased as age increased. It was determined that as patients' social support increased, their comfort level also increased. In this context, it may be recommended to ensure that individuals, especially those who live alone and are of advanced age, benefit

from social support resources by providing appropriate conditions in hospitals during the perioperative period. Through counseling, nurses can provide information to patients and their relatives to increase the social support and comfort of patients and ensure the participation of families in patient care. In addition, by using social support networks, a positive contribution can be made to increasing the comfort of the individual in the adoption, care, and management of a healthy lifestyle in the perioperative period.

In future studies, the relationship between the level of volunteering of relatives accompanying the patient and the comfort perceived by the patients can be examined. In future experimental studies, the effect of artificial intelligence in supporting individuals without relatives can be investigated.

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Research Article

Effects of Modified Pilates Training on Hemodynamic Responses in Children with Cerebral Palsy: A Single-Blinded Randomised Controlled Study

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Abstract

Aim: This study aimed to ascertain the impact of Modified Pilates Exercises (MPE) and neurodevelopmental therapy (NDT) on hemodynamic response in children with Cerebral Palsy (CP).
Material and Method: We randomly assigned 18 CP children between expanded and revised gross motor function categorization system (GMFCS-E&R) I–III to study (MPE) and control (NDT) groups. Tests for core stability, the 6-minute walk test (6MWT), and the pressure biofeedback unit test (PBU) were conducted. Prior to and following the 6MWT and physiotherapy sessions, hemodynamic responses, including heart rate (HR), respiration rate (RR), and blood pressure (BP), were assessed before (BPT) and after physiotherapy (APT).
Results: There was a significant difference observed in the MPE group's BP (sistolic) of 6MWT (post) (p=0.006), the modified side bridge (MSBT) test (p<0.05), the sit-ups test (p=0.011), the pressure biofeedback unit test (p=0.024), and the abdominal fatigue test (AFT) (p=0.014) APT. The Modified Biering Sorensen Trunk Extensor Test (MBSTET) (p<0.001), MSBT (p=0.034), AFT (p=0.002), PBU (p=0.015), SUT (p<0.001), Modified Push Ups Test (MPUT) (p=0.018), BP (sistolic) of 6MWT (post) (p=0.007) following the walk, and RR (p=0.005) before and after 6MWT (p=0.006) in the MPE group were all significantly different APT, according to the initial measurements of the percentage changes.
Conclusion: When compared to NDT, MPEs have a favorable impact on core stability muscles, transversus abdominus (TrAb) activity, and hemodynamic and respiratory responses in children with CP.

Keywords: Cerebral palsy, core, hemodynamics, modified pilates, transversus abdominus

INTRODUCTION

The neurodevelopmental disease known as cerebral palsy (CP) is non-progressive, causes movement and postural abnormalities, and limits an individual's activities (1). Decreased postural and trunk control, muscle weakness, balance issues, stiffness, and other motor and sensory impairments cause children with CP to struggle with transfer, mobility, and social involvement (1).

Trunk control, formed by activating the core muscles, determines automatic postural reactions, postural control, balance, gait, and functional activities (2,3). Pilates exercises that target the Transversus Abdominus (TrAb) muscle can improve trunk muscle stabilization by fostering control as a result of core stabilization training. Additionally, the primary respiratory muscle, the diaphragm, collaborates with the TrAb muscle. Respiratory capacity can be increased by training the TrAb muscle, and thus, hemodynamic responses can be regulated.

Studies examining the effects of Pilates training in healthy adults, the elderly population, multiple sclerosis (MS), stroke, and musculoskeletal problems has shown that pilates increases trunk stabilization (4-6). Therefore, pilates training can be used to improve muscle strength and postural control in selected CP children who can walk and stand on their own but still need to establish a variety of skills for controlled movement (2).

There are deficiencies in their capacity to take part in play and sports activities in which they need to maintain their cardiorespiratory fitness in children with CP (7-9). Studies have reported that these children have

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significant differences in muscle strength, speed, agility, anaerobic endurance, and flexibility measurements in comparison with their peers (9). Children with CP have reduced cardiorespiratory responses, including anaerobic and aerobic exercise responses. However, compared to what motor impairment would have us believe, deficits in aerobic exercise responses and respiratory capacity are not as severe (9). Children with CP are treated using a variety of techniques to improve their cardiorespiratory fitness. To find out which exercise regimens are best for increasing aerobic exercise capacity, more research is necessary (10).

Research has revealed that the hemodynamic responses of children with CP during walking are also crucial in terms of risk factors for chronic diseases at an advanced age (9,11-13). There is a need for applicable and effective interventions to enhance the cardiorespiratory performance of children with CP by increasing their mobility (14). The literature has conflicting data regarding the benefits of exercise for cardiorespiratory and strength training. Therefore, it is thought that most physiotherapy interventions have limited efficacy on cardiorespiratory performance in children with CP (9,10). However, more investigation is required to determine the most effective strategies for improving functional outcomes in children with CP (15). Hence, it is remarkable that the impacts of Modified Pilates Exercises (MPE) training targeting the TrAb muscle, particularly in children with CP, on walking distance and hemodynamic responses have not been researched in the literature. The effects of MPE are not studied enough, and there is a lack of study on the effects of hemodynamic responses and core muscular endurance in children with different clinical forms of CP (16,17). The current research aimed to reveal the impacts of MPE and the traditional Neurodevelopmental Therapy (NDT) approach on hemodynamic responses in children with CP.

MATERIAL AND METHOD

Study Design

This research is randomized controlled (RC) and single-blinded. After being classified based on the Expanded and Revised Gross Motor Functional Classification System (GMFCS-E&R) to identify their degree of functional ability, children with CP (n=18) were randomly assigned using block randomization to either the study (MPE) (n=9) or the control group (NDT) (n=9). An overview of every stage of the research process is provided by the Consolidated Standards of Reporting Trials (CONSORT) flowchart in Figure 1.

The MPE group received care from a blinded physiotherapist who had completed training in MPE, was certified by the Australian Physiotherapy & Pilates Institute (APPI), had 5 years experience with pediatric rehabilitation, and was not involved in the assessments, while the control group received NDT-based physiotherapy for two days a week, one hour per day, for eight weeks. Neither the data collection nor the data analysis were done by the researcher who monitored the randomization procedure. All of the children were evaluated at baseline before physiotherapy (BPT) and eight weeks later after physiotherapy (APT) by a doctor physiotherapist who were experienced in pediatric rehabilitation for 5 years blinded throughout the randomization (Figure 1).

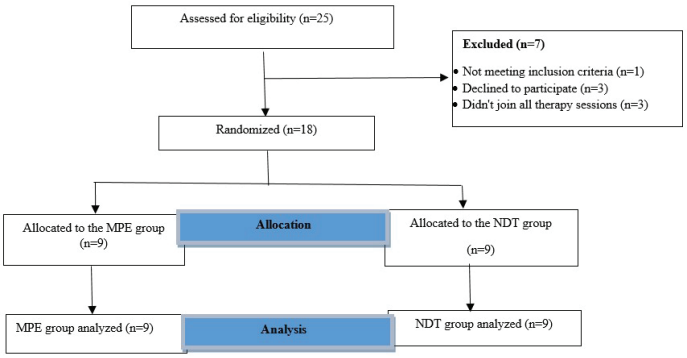

Figure 1. CONSORT flowchart of the study

Participants

Children who applied to the Developmental Physiotherapy and Pediatric Rehabilitation Unit of Gazi University, were diagnosed with CP according to the European CP Surveillance (SCPE) criteria were included. The following criteria had to be met in order to be included: being between the ages of 8 and 18; being able to perform a sit-to-stand activity; and being able to walk with or without the assistance of walking aids (18), having full range of motion with the lower extremity; Modified Ashworth (MAS) score for lower extremity spasticity between 1 and 1+; no recent lower extremities surgery or Botox; able to communicate and follow the verbal instructions. There were 25 children that qualified. Nine patients from each group made up the final total of 18 participants in the trial (10 Diparetic, 4 Hemiparetic, 4 Ataxic). Children with multiple disabilities, congenital or acquired cardiorespiratory diseases, those who had undergone surgery, received special MPE training within the last six months, or received botox injections to the lower extremities were not allowed. Parents gave their written, informed consent. The Ethics Commission at Gazi University gave its approval for this work (2022/09-The research number: 2022-634), and performed acoording to the principles of the Declaration of Helsinki. The clinical trial number is NCT05221307.

Measurements

Functional motor classification was determined by the GMFCS-E&R, lower extremity muscle tone was measured by MAS, TrAb muscle strength was measured by Sharman's core stability test (PBU=Pressure Biofeedback Unit Test), gait endurance and speed was measured by 6 Minutes Walking Test (6MWT). Also the 6MWT walking distance was measured in meters (m) and recorded.

Respiratory rate (RR), blood pressure (BP), and heart rate (HR) were measured and recorded for hemodynamic responses and cardiorespiratory endurance before and after 6MWT. Modified Beiring Sorensen test (MBSTET),

prone plank test (PBT), modified side plank test (MSBT), abdominal fatigue test (AFT) was used for core stability performance measurements, and core muscle strength were evaluated by sit ups (SUT) and modified push ups (MPUT) tests.

Modified Ashworth Scale (MAS): Ashworth is a five-point ordinal scale for rating the resistance experienced during against the passive range of motion (19). The hip adductors, flexors, ankle plantar flexors, and knee flexors's tone were measured.

Expanded and Revised Gross Motor Functional Classification System (GMFCS-E&R): Children with CP are categorized using a standart categorization system into levels I through V based on their gross motor skills (18).

6 Minute Walk Test (6MWT): A self-paced, submaximal test called the 6MWT assesses a person's functional ability to walk long distances. A 20 × 45 m calm corridor served as the walking route, and markers were posted to the walls every 30 m. Chronometer started when a participant started to take a step. The finish line for the participant was marked on the wall by the examiner at six minutes. The duration of the completition of 6MWT and the total distance was recorded. The test was conducted without the use of orthotics on a straight line at the subjects' typical gait speed. The test's psychometric properties have been investigated (20).

Core Stability Performance Measurements

Core Muscle Static Endurance Tests

Core stability was evaluated using McGill's core muscular endurance tests (21-23). A stopwatch was used to time each core muscle endurance test, and the results were recorded in seconds (sec). For each test position, subjects were urged to hold their isometric positions for as long as possible. Children's ability to hold the right position for a given amount of time was noted. Every measurement was made twice, and the best measurement was noted as sec. When the position couldn't keep, the tests were stopped and the duration was recorded as sec. These tests:

Modified Biering-Sorensen Trunk Extensor Test (MBSTET): The children stretched their upper bodies over a treatment table while seated with their anterior superior iliac spine aligned with the edge. The treatment table was attached to the participants' knees, hips, and pelvis by the assessor. A chair supported the upper extremities and the body. The chair was then taken away, and the contestants remained on the chessboard with their arms crossed for as long as they could (23). When the position couldn't keep, the test were stopped and the duration was recorded as sec.

Prone Bridge Test (PBT): The children straightened their knees and positioned their elbows and forearms underneath their shoulders. They elevated their hips while keeping their forearms and toes firmly planted on the ground (23). They did this for as long as they could. If necessary, they were supported. When the position couldn't keep, the test were stopped and the duration was recorded as sec.

Modified Side Bridge Test (MSBT): Lying on their left or right sides, the children used their forearms and elbows beneath their shoulders to support themselves as they flexed their legs and raised their hips off the ground (23). They got help if they needed it. When the position couldn't keep, the test were stopped and the duration was recorded as sec.

Abdominal Fatigue Test (AFT): The children were supported at a 60-degree angle from the floor with their trunks in a sit-up position. They crossed their arms over their chest while bending their knees and hips 90 degrees. From having their feet on the ground, they were balanced. Then the trunk support was taken away, and the children stayed in this posture for as long as they could keep this position (23). When the position couldn't keep, the test were stopped and the duration was recorded as sec.

Sharman's Core Stability Test (PBU=Pressure Biofeedback Unit Test): A stopwatch (Heuer Microsplit 1000) and a Chattanooga Stabilizer pressure biofeedback sensor were used to record pressure measurements. Any spesific strategies connected to this were noticed and categorized, such as holding one's breath and raising one's ribcage, using Richardson and Jull classifications. The inflatable device's lower border was positioned in the center of the abdomen, at the level of the anterior superior iliac spines (ASIS). The children were taught how to perform a 10-sec contraction of the abdominal drawing-in maneuver to selectively contract their TrAb. A baseline pressure of 70 mm Hg was used to calculate pressure changes. The calculated mean change in pressure (mmHg) at the end of the three contractions was recorded (24,25).

Core Muscle's Power Tests

Sit-Ups Test (SUT): The children were instructed to flex their trunks while their knees were bent and their feet were supported. The number of sit-ups the children performed from a supine position in 30 secs was counted (26).

Modified Push-Ups Test (MPUT): Children were instructed to elevate their head, shoulders, and trunk off the ground while lying on their backs with their arms, knees, and elbows flexed. They were timed to see how many push-ups they could complete in 30 secs (26). The total number of push-ups was recorded.

Intervention

Modified Pilates Exercises (MPE): The physical therapist presented the fundamentals of Pilates during the first session. All of the sessions began with supine centering and segmental extremity motions as a warm-up. Included were exercises from Matwork levels I–II as per the APPI. Every activity was altered to accommodate the limitations associated with CP as well as the age-specific physical and cognitive needs. For the first five sessions, each exercise was done five times; in subsequent courses, this was increased to ten to fifteen times. The exercises were offered in escalating difficulty order. Also:

1. If any pain strikes, the children stop or take a rest.
2. Without moving their spines or rib cages, the children slowly completed 5 to 10 repetitions of each activity.
3. All of the children underwent multiple training sessions in the five Pilates principles prior to starting the program: breathing, centering (neutral spine posture), positioning the ribs and shoulder blades, and positioning the head and neck. Consequently, the children learned how to regulate their segments, perform the abdominal drawing movement, imprint, contract the TrAb and multifidus muscles, and manage their lumbar region.
4. As a cool-down, posture, breathing, and stretching exercises were performed.

The controlled motions out of neutral position of the lumbar-pelvic region were gradually integrated. Furthermore, the movements were soft and painless. In order to adjust the workout or progression to the children's needs, maintain proper technique, control speed, assist with optimal muscle activation, etc., the physiotherapist provided customized facilitation approaches. Examples of facilitation strategies include the use of verbal or physical cues, mental and visual pictures, and demonstration.

Neurodevelopmental Therapy (NDT-Bobath): Every child received a personalized, traditional exercise program designed in the NDT-Bobath baseline, crafted by a qualified physiotherapist with five years of NDT experience. Therapy included weight-bearing exercises in various positions for equal weight transfer on both upper and lower extremities without interfering with the postural control, enhancing writhing and balance reactions in all positions, and supporting sense-perception-motor development. Proprioceptive and vestibular training, dynamic balance training, functional reaches in many directions, and walking drills in various directions can all be achieved with exercise balls and balancing boards.

Statistical Analysis

For continuous variables that were measured, descriptive statistics provided the mean, standard deviation, median, and minimum and maximum values; for qualitative variables, descriptive statistics provided the frequency and percentage values. Utilizing the Shapiro-Wilk W test, one might assess how well the data fit into the normal distribution. The Mann-Whitney U test was used in group comparisons because the measurement-specified continuous variables did not meet the requirements for parametric tests. When comparing qualitative variables between groups, the chi-square test was used. For normally distributed data, the Wilcoxon paired-sample test was employed in dependent measurement comparisons; for non-normally distributed data, the significance test of the difference between two pairs was utilized. At the $p<0.05$ level, the results were acknowledged to be significant. Based on post hoc power analysis, the sample size was calculated (power=0.80, p=0.05, n=9 for each group; G*power version 3.1.9.2, Axel Buchner, Universität Kiel). Since there isn't a comparable study in the literature to calculate the effect size, the post-hoc power analysis used the 6MWT score of nine participants from each group.

RESULTS

Concerning the mean age of the study groups, it was 9±1.58 (7-11) in the MPE group (n=9) and 10±2.73 in the NDT group (n=9) Table 1 contains the other sociodemographic characteristics of the children.

Table 1. Demographic information of the children in the study

	MPE group (n=9) Median (min-max)	NDT group (n=9) Median (min-max)	Total (n=18) Median (min-max)	p value
Age (years)	9 (7-11)	10 (7-15)	9 (7-15)	0.605
Height (cm)	130 (110-145)	130 (110-155)	130 (110-155)	0.489
Weight (kg)	25 (17-42)	30 (20-50)	28,5 (17-50)	0.136
PT duration (years)	8 (5-10)	7 (5-12)	7,5 (5-12)	1.000
PT frequency (day/week)	2 (1-5)	2 (2-3)	2 (1-5)	0.863
	(n/%)	**(n/%)**	**Total (n/%)**	
Gender				
Male	4/44.4	6/66.7	10/55.6	0.637
Female	5/55.6	3/33.3	8/44.4	
GMFCS (E&R) levels				
I	4/44.1	2/22.2	6/33.3	
II	4/44.1	7/77.8	11/61.1	0.666
III	1/11.1	0/0	1/5.6	
Children's clinical CP types				
Spastic diparetic	5/55.6	5/55.6	10/55.6	
Spastic hemiparetic	2/22.2	2/22.2	4/22.2	1.000
Ataxic	2/22.2	2/22.2	4/22.2	

Mann-Whitney U test, Pearson and Fisher's Chi-Square tests, *p <0.05, GMFCS: Gross Motor Functional Classification System (E&R) levels

A significant difference was found between the two groups in terms of MBSTET, PBT, MSBT (left), SUT, MPUT, 6MWT distance (m), 6MWT Blood Pressure (mmHg) (AW) (diastolic), 6MWT Blood Pressure (mmHg) (BW) (systolic), and 6MWT Blood Pressure (mmHg) (AW) (systolic) after comparing the intra-group results of the children BPT and APT ($p<0.05$). There was only a significant difference in the MPE group's MSBT right, AFT, 6MWT Respiration Rate (BW), and 6MWT Respiration Rate (AW) when the intra-group findings of the children BPT and APT were compared ($p<0.05$) (Table 2).

When the core stability performance measurements, 6MWT, and hemodynamic parameters of the children BPT and APT were compared between the groups, a significant decrease was detected in MSBT (right $p<0.05$, left $p<0.05$) and AFT ($p<0.05$) durations, a significant decrease was found in PBU test ($p<0.05$) measurements, and a significant increase was identified in SUT ($p<0.05$) in favor of the MPE group (Table 2). Diastolic blood pressure measured before 6MWT was significantly lower in favor of the MPE group ($p<0.05$) APT. Systolic blood pressure after 6MWT was significantly higher in the MPE group ($p<0.05$) APT (Table 2).

Table 2. Comparison of children's core stability performance measurements, 6MWT and hemodynamic parameters BPT and APT

		MPE group (n=9) Median (min-max)	NDT group (n=9) Median (min-max)	pa value
MBSTET (sec)	BPT	15.6 (3.93-47.94)	35 (15-66.83)	0.04*
	APT	54.6 (17-126)	36 (18-103.27)	0.796
p[b]		0.008*	0.008*	
PBT (sec)	BPT	10.96 (0-32.7)	31.51 (9.24-122.63)	0.024*
	APT	24.6 (8.5-92)	35.61 (9.45-127.89)	0.387
p[b]		0.008*	0.038*	
MSBT right (sec)	BPT	24.22 (0-60.5)	13.5 (0-96.7)	0.863
	APT	44.6 (10-130)	14.6 (0-103)	0.04*
p[b]		0.008*	0.093	
MSBT left (sec)	BPT	23.88 (0-52.4)	16.6 (4.01-126.27)	0.73
	APT	49 (8-119)	16.95 (4.05-128.2)	0.031*
p[b]		0.008*	0.021*	
AFT (sec)	BPT	19.3 (10.96-27.5)	14.96 (7.07-26.88)	0.436
	APT	32 (15-40)	14.5 (7.03-40)	0.014*
p[b]		0.008*	0.11	
PBU (mm hg)	BPT	77.20 (72.2-100.7)	91.5 (70-104)	0.258
	APT	71.20 (70-90.3)	87 (70-103)	0.024*
p[b]		0.066	0.138	
SUT	BPT	10 (6-14)	10 (0-19)	0.546
	APT	16 (12-23)	11 (1-21)	0.011*
p[b]		0.007*	0.034*	
MPUT	BPT	8 (0-17)	9 (0-23)	0.546
	APT	11 (6-20)	10 (1-24)	0.796
p[b]		0.011*	0.007*	
6MWT (m)	BPT	120 (0-204)	254 (80-267)	0.113
	APT	156 (18-204)	258 (82-290)	0.387
p[b]		0.012*	0.011*	
6MWT pulse (pulse/min) (BW)	BPT	97.33 (60-130)	94 (64-110)	0.478
	APT	97.66 (60-120)	92 (66-110)	0.150
p[b]		0.866	0.461	
6MWT pulse (pulse/min) (AW)	BPT	108.44 (90-135)	101 (67-120)	0.438
	APT	106.33 (90-125)	101 (70-125)	0.363
p[b]		0.160	1.00	

a Mann-Whitney U test, *$p<0.05$, **$p<0.001$, b Wilcoxon signed rank test, BW: before walk, AW: after walk, BPT: before physical therapy, APT: after physical therapy, MBSTET: modified biering sorensen trunk extensor test, PBT: prone bridge test, MSBT: modified side bridge test, AFT: abdominal fatigue test, PBU: pressure biofeedback unit test, SUT: sit ups test, MPUT: modified push ups test, mm hg: millimeter hg, sec: second, 6MWT: 6 minute walk test, m: meter, min: minute

Table 2. Comparison of children's core stability performance measurements, 6MWT and hemodynamic parameters BPT and APT				
		MPE group (n=9) Median (min-max)	NDT group (n=9) Median (min-max)	pa value
6MWT respiration rate (rr/min) (BW)	BPT	36 (30-42)	22 (21-28)	p<0.001**
	APT	32 (24-40)	21 (20-24)	p<0.001**
pb		0.01*	0.655	
6MWT respiration rate (rr/min) (AW)	BPT	40 (32-48)	23 (21-28)	p<0.001**
	APT	35 (32-40)	23 (21-26)	p<0.001**
pb		0.01*	1.00	
6MWT blood pressure (mmHg) (BW) (diastolic)	BPT	57 (50-60)	65 (50-100)	0.197
	APT	58 (50-70)	70 (50-80)	0.012*
pb		0.655	0.150	
6MWT blood pressure (mmHg) (AW) (diastolic)	BPT	58 (50-70)	60 (50-80)	0.958
	APT	57 (50-60)	67 (50-80)	0.169
pb		0.006*	0.005*	
6MWT blood pressure (mmHg) (BW) (sistolic)	BPT	122 (120-130)	121 (120-130)	0.903
	APT	131 (120-140)	128 (120-130)	0.331
pb		0.011*	0.029*	
6MWT blood pressure (mmHg) (AW) (sistolic)	BPT	124 (120-130)	120 (120-125)	0.081
	APT	131 (130-140)	128 (120-130)	0.006*
pb		0.007*	0.006*	

a Mann-Whitney U test, *p<0.05, **p<0.001, b Wilcoxon signed rank test, BW: before walk, AW: after walk, BPT: before physical therapy, APT: after physical therapy, MBSTET: modified biering sorensen trunk extensor test, PBT: prone bridge test, MSBT: modified side bridge test, AFT: abdominal fatigue test, PBU: pressure biofeedback unit test, SUT: sit ups test, MPUT: modified push ups test, mm hg: millimeter hg, sec: second, 6MWT: 6 minute walk test, m: meter, min: minute

When the percentage changes in all test parameters were compared BPT and APT, the MPE group showed a substantial significiant increase in MBSTET (p<0.001), MSBT (left) (p<0.05), AFT (p<0.05), SUT (p<0.001), MPUT (p<0.05) durations (Table 3). Also there was significiant decrease in the PBU (p<0.05), 6MWT Respiration Rate (BW) (p<0.05), 6MWT Respiration Rate (AW) (p<0.05), 6MWT Blood Pressure (mmHg) (AW) (systolic) (p<0.05) APT (Table 3).

Table 3. Comparison of the percentage changes in the two groups according to the initial measurements BPT of the tests			
	MPE group (n=9) Mean±SD (min-max)	NDT group (n=9) Mean±SD (min-max)	p value
MBSTET (sec)	212.57±118.77 (33-398)	12.65±20.25 (1.22-64.57)	p<0.001**
PBT (sec)	3681.42±2493.78 (1897-9100)	4831,66±4185.98 (845-12686)	0.71
MSBT right (sec)	5666.66±3905.68 (200-12950)	2399.37±3184.80 (545-10203)	0.05
MSBT left (sec)	5831.12±3236.96 (700-11800)	2806±3856.23 (305-12720)	0.034*
AFT (sec)	66.56±71.13 (9.19-222.35)	2.95 ±22.56 (-39.13-50.38)	0.002*
PBU (mm hg)	-8.04±14.95 (-27.11-25.07)	-0.94±1.85 (-4.92-1.13)	0.015*
SUT	79.27±55.85 (27.27-200)	5.37±5.80 (0-12.5)	p<0.001*
MPUT	44.51±35.72 (0-100)	8.51±5.04 (0-14.29)	0.018*
6MWT (m)	21.93±25.17 (0-72)	5.46±7.28 (-0.4-23)	0.132
6MWT pulse (Pulse/min) (BW)	0.33±7.82 (-10-18)	-2±6.06 (-18-2)	0.494
6MWT pulse (Pulse/min) (AW)	-2.11±8.59 (-14-17)	0±3.24 (-7-5)	0.058
6MWT respiration rate (rr/min) (BW)	-4±3.31 (-12-0)	-0.66±2.82 (-8-2)	0.007*
6MWT respiration rate (rr/min) (AW)	-5.11±4.13 (-12-0)	-0.33±1.80 (-5-1)	0.005*
6MWT blood pressure (mmHg) (BW) (diastolic)	1.11±7.81 (-10-10)	4.44±21.27 (-50-20)	0.075
6MWT blood pressure (mmHg) (AW) (diastolic)	8.88±6.0 (0-20)	7.22±6.66 (-10-10)	0.368
6MWT blood pressure (mmHg) (BW) (systolic)	72.22±6.66 (60-80)	68.88±7.81 (30-50)	0.695
6MWT blood pressure (mmHg) (AW) (systolic)	-66,66±7.07 (-80-(-60))	-52.77±7.54 (-70- (-45))	0.003*

Mann-Whitney U test, *p<0.05, **p<0.001, SD: standart deviation, BPT: before physical therapy, MBSTET: Modified biering sorensen trunk extensor test, PBT: prone bridge test, min: minute, MSBT: modified side bridge test, AFT: abdominal fatigue test, PBU: pressure biofeedback unit test, SUT: sit ups test, MPUT: modified push ups test, mm hg: millimeter hg, sec: second, 6MWT: 6 minute walk test, m: meter

DISCUSSION

This is the first study to investigate how children with CP respond hemodynamically to MPE exercises combined with the conventional NDT-Bobath method. The current study demonstrated that MPEs positively affected hemodynamic responses by reducing systolic blood pressure and respiratory frequency and increased the transversus abdominus (TrAb) and core stabilizer muscle strength more compared to NDT.

Children with CP are less physically fit due to their handicap, which is linked to the emergence of secondary illnesses such diabetes, obesity, and cardiovascular disease (9,11,13,24). In the current literature, it is remarkable that aerobic capacity training in children with CP is performed with adaptive cycling, arm ergometer, treadmill, aquatherapy, running, and swimming (10,15). In this study, unlike the literature, the preference for MPE and its positive effects on hemodynamic parameters will contribute to the literature.

Children with CP have inadequate aerobic capacity, one of the elements of physical fitness (26,27). According to studies, children with CP have much poorer cardiorespiratory capacities than their peers (9). Although decreased aerobic exercise responses are reported in such children, it is also indicated that reductions in respiratory capacity and aerobic exercise responses are not as severe as predicted by motor impairment (9).

Although improvements have been observed in maximum heart rate, resting heart rate, oxygen uptake, respiratory frequency, and muscle strength as a result of aerobic training with bicycle in studies, review studies emphasize conflicting results for improved cardiorespiratory fitness (10). In this study, the lower resting diastolic blood pressure in MPE before 6MWT compared to NDT indicates that MPE may positively affect hemodynamic responses in children with CP. It is contradictory that MPE increases systolic blood pressure after 6MWT following physiotherapy. However, upon comparing the percentage changes of the treatment groups, improvements in respiratory frequency with MPE before and after 6MWT following physiotherapy and improvements in systolic blood pressure after treatment were observed more. The above-mentioned development suggested that the TrAb muscle might be strengthened by MPE and positively affect the respiratory frequency and blood pressure in these children. These findings show that MPE training may be an alternative treatment for enhancing cardiorespiratory fitness in children with CP with high mobility levels.

Studies show that children with CP have significantly lower cardiorespiratory capacity than their peers (13,28). Consequently, for at least three days a week, the World Health Organization (WHO) advises engaging in at least 60 minutes of moderate-to-intense physical activity that involves bone- and muscle-strengthening activities (29). Studies have shown that muscle strength training is a safe and beneficial intervention for children with cerebral palsy, although the effectiveness of aerobic exercise is not entirely obvious (13,30). Studies indicating the effectiveness of Pilates exercises on gait, balance, and trunk control by increasing the core muscle strength in this group draw attention (16,31). It is noteworthy, however, that no assessment of cardiorespiratory fitness has been performed. In parallel to the literature, this study showed that MPE exercises increased the TrAb muscle activation by improving core strength and endurance tests. Hence, it is thought that using MPE training in strengthening training, compared to the traditional NDT approaches, may provide enhancements in hemodynamic responses by strengthening the core muscles more.

There is a mechanical and neuromuscular connection between respiration and postural control. Respiratory muscles and spinal stability are involved in both systems. Studies have demonstrated that core muscle training increases respiratory amplitude by causing a considerable alteration in the body position on the sagittal plane. Training of core stabilizer muscles increases trunk stabilization and enhances respiratory control (32). The present study showed that MPE exercises positively impacted hemodynamic responses by activating the TrAb muscle, with a significant reduction in respiratory frequency before and after 6MWT. Postural stability and trunk stabilization are primarily known to be accomplished by the abdominal muscles, which include the rectus abdominis (RA), TrAb, internal and external obliques, and TrAb (33). Accordingly, TrAb provides protection during activities that put the integrity of the lumbar spine in jeopardy. According to certain research, TrAb contributes more significantly than other muscles to the improvement of spinal stability (33,34). Via a variety of functional actions, all oblique muscles, including the TrAb muscle, maintain the stability of the trunk. Studies have indicated that core stabilization training and whole-body vibration therapy increase the TrAb muscle thickness and enhance muscle strength in children with CP (35,36). Although the TrAb muscle has an important duty as a stabilizer, it is also known to form the basis for respiration (37). There is a need for further research to reach a consensus in defining the functions of the respiratory muscles, particularly to understand the duty of the pelvic floor muscles in respiration and phonation (37). It has been shown that respiratory muscle training improves lumbopelvic stability by increasing the local core muscle activity in athletes (38). These results are compatible with the improvement of the respiratory system by training core muscles and the TrAb muscle in our study. The TrAb muscle and internal oblique muscles are much thicker toward the end of expiration than at inspiration, according to other research, and they are also much thicker than at full expiration or near the end of full expiration (39). These findings are consistent with our own, suggesting a cooperative relationship between the respiratory system and core muscle activation.

A decrease in systolic blood pressures measured after 6MWT following treatment in the study group compared to the control group demonstrates that MPE training not only increases core muscle activity but also positively

impacts blood pressure by increasing respiratory muscle activity. Hence, it is suggested that MPE can be used as an alternative therapy to enhance hemodynamic responses and increase cardiorespiratory compliance in children with CP.

The study's limitation is the small number of children who can walk at a low mobility level (GMFCS III) and the sample's comprising patients with spastic diparetic, hemiparetic, and ataxic types. In addition, the absence of outcomes from long-term follow-up poses a constraint in terms of the inability to assess treatment efficacy over time. Additional research with long-term follow-ups in various clinical settings and mobility levels is required. It is also advised to do more research comparing or combining MPE training with aerobic training.

CONCLUSION

It is concluded that MPEs were shown to increase the strength of core stability muscles and enhance cardiorespiratory fitness by increasing the TrAb muscle activity compared to NDT in children with CP. It was demonstrated that MPE training would positively impact hemodynamic responses, such as blood pressure and respiratory rate, in such children.

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MEDICAL RECORDS-International Medical Journal

Research Article

Investigation of the Effects of Physical Activity on Body Awareness, Posture and Anxiety in Smartphone Addicted Individuals

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Abstract

Aim: The aim of this study was to investigate the effect of physical activity on body awareness, posture and anxiety in smartphone addicted individuals.

Material and Method: The smartphone addiction level of 110 smartphone addicted young adult (20.27±2.25 years) included in the study was assessed with the Smartphone Addiction Scale-Short Version (SAS), physical activity level with the International Physical Activity Questionnaire Short Form (IPAQ), body awareness with the Body Awareness Questionnaire (BAQ), posture assessment with the New York Posture Rating Scale (NYPRS) and anxiety level with the Beck Anxiety Inventory (BAI). According to the IPAQ score, participants were categorised into three groups as inactive (I group), minimally active (M group) and active (A group). Body awareness, posture affectivity and anxiety levels of the groups were compared. The relationship between physical activity levels and body awareness, posture problems and anxiety levels of all participants was analysed.

Results: The BAQ score of the I group was lower than that of the M and A groups ($p<.05$), while the BAQ scores of the M and A groups were similar ($p>.05$). The BAI score of group I was higher than that of group A ($p=.039$). The NYPRS scores did not differ significantly between the groups ($p>.05$). There was a positive correlation between IPAQ score and BAQ score ($r=.283$, $p=.003$) and a negative correlation with BAI score ($r=.212$, $p=.043$). A negative correlation was found between sitting time and NYPRS score ($r=.214$, $p=.041$).

Conclusion: Physical activity has a positive effect on body awareness and anxiety in smartphone-addicted individuals. Physical activity can protect young adult from the negative physical and psychological effects of smartphones. In addition, it is important to pay careful consideration to the sitting time in order to prevent posture problems in these individuals.

Keywords: Smartphone addicted, physical activity, body awareness, posture, anxiety

INTRODUCTION

Mobile phones provide many different services in addition to providing communication technologies and internet use. Young people use mobile phones to express themselves, search for current information, follow videos, communicate with different communities (1). With the development of technology, smartphones have started to find more place in the lives of individuals with many advantages. Thus, it has a critical importance on human-machine interactions (2). With the use and widespread use of smartphones, it can be mentioned that they provide important benefits to the society and facilitate daily life (3). In addition to these benefits, the harms of smartphones are also mentioned. There is also the possibility that people can become addicted to their phones to the point of behavioural addiction (2).

Smartphone addiction refers to excessive and uncontrolled use of one's phone. An individual's addiction to the device is mentioned as a potential disorder leading to a psychological dependence. It is also categorised as a behavioural addiction, which can potentially cause negative physical, emotional and financial impact (4).

In studies on smartphone addiction in the young population, physical activity has been one of the topics investigated in related factors and interventions for

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prevention (5). The literature indicates an inverse relationship between physical activity and mobile phone addiction among adolescents and young adults (6). It is reported that smartphone addiction causes serious psychological and physical negative effects (7).

Among the physical health problems of smart phone users, postural effects are at the forefront. These factors can also lead to disorders related to body awareness (8). Body awareness includes a multifaceted concept such as knowledge, position perception and cognitive elements about the body parts of the individual in mobile and immobile posture. At a basic level, it refers to the level of knowledge about the body type of the individual (9). Body awareness is closely related to posture and musculoskeletal system. It is stated that body awareness may also be negatively affected due to posture disorders in smartphone users (8). Studies indicate that smartphone addicted individuals experience more posture-related symptoms than non-addicted individuals, as they experience a poor posture (10-13).

Smartphone addiction can lead to psychosocial problems such as depression and anxiety as well as physical health problems (14). Many studies emphasise the presence of anxiety in addicts and it is stated that anxiety-related problems in individuals affect mental health in a multidimensional way (15).

Recently, smartphone addiction has been the topic of current research in addiction types due to the increase in the frequency of smartphone use. Although the frequency of smartphone addiction is gradually increasing, it is stated that there are not enough studies on this subject (13). All of the above-mentioned factors seem to be absent in a comprehensive research on smartphone addiction. Based on this information, the aim of this study was to investigate the effect of physical activity on body awareness, posture and anxiety in smartphone addicted individuals. We think that determining the effects of physical activity in smartphone addicted individuals will be instructive in terms of approaches to be made for smartphone addiction.

MATERIAL AND METHOD

Design and Participants

This prospective cross-sectional study was conducted between January 2024 and April 2024 at the Department of Physiotherapy and Rehabilitation, Gaziantep İslam Science and Technology University. Data were collected in accordance with the Declaration of Helsinki. Participants were informed in writing and a consent form was obtained.

Participants over the age of 18, without structural scoliosis, without any neurological and orthopaedic disorders, with men scoring above 31 and women above 33 on the Smartphone Addiction Scale-Short Version (SAS) were included in the study. A total of 278 people were evaluated for the study. 168 people were not included in the study because they did not meet the cut off value of SASV and the study was completed with 110 young adult participants. Referring to the International Physical Activity Questionnaire Short Form (IPAQ), participants were grouped as inactive (I) with <600 MET-min/week, minimally active (M) with 600-3000 MET-min/week and active A) with more than 3000 MET-min/week.

Measurements

Demographic information, duration of daily-weekly phone use, primary purpose of smartphone use, and number of years of smartphone use were recorded. The level of smartphone addiction, physical activity level, body awareness, posture and anxiety level of the participants were also evaluated.

SAS was used to evaluate the risk of smartphone addiction. Scale scores range between 10-60. The higher the score obtained from the test, the higher the risk for addiction. The scale has one factor and no subscales. The cut-off score is 31 for men and 33 for women (16).

IPAQ: IPAQ was used to evaluate the physical activity level and exercise habits of individuals. The questionnaire, which consists of seven questions, evaluates the number of days and minutes of walking, moderate-to-vigorous and vigorous physical activities per week in the last week MET values by activity are calculated by multiplying MET values by minutes and days to obtain a total score in MET-minutes/week. Vigorous physical activity is assessed as 8 METs, moderate physical activity as 4 METs and walking as 3.3 METs. Daily sitting time is recorded as a separate parameter. The total physical activity score is grouped as inactive <600 minutes/min/week, minimally active 600-3000 MET-min/week and active over 3000 MET-min/week (17).

Body Awareness Questionnaire (BAQ): It is a questionnaire aimed at determining the level of normal or abnormal sensitivity of body composition. It consists of four subgroups (attention to changes and reactions in the body process, sleep-wake cycle, prediction at the beginning of the disease, prediction of body reactions) and a total of 18 statements. Rating in the questionnaire is done as a total score. The total score to be obtained from the questionnaire can be maximum 126 and minimum 18. The higher the total score, the better the body awareness. Total score was recorded (18).

New York Posture Rating Scale (NYPRS): It is an evaluation scale consisting of 13 items that evaluates static posture from the lateral and posterior aspects. For the assessment, the participant is assessed in a static position from the side and back in underwear. Each item in the evaluation sections is scored from 'good posture' to 'bad posture' (5-3-1) and the person receives a total score between 13-65. The higher the total score, the better the posture of the participant (19).

The Beck Anxiety Inventory (BAI): The scale assesses the state of anxiety in the last week. It consists of 21 items and each item is scored between 0-3. The total score in the scale takes a value between 0-63. A high total score is regarded as a high level of anxiety severity (20).

Statistical Analysis

SPSS 25 (IBM, Statistical Package for the Social Sciences) programme was used for data analysis. The normality of the variables was evaluated by Kolmogorov-Smirnov test. Numerical variables were presented as mean ± standard deviation (mean ± SD) and nominal values were presented as number (n). One-way analysis of variance (post hoc analysis Bonferroni correction) was used to evaluate the intergroup comparison of the participants grouped according to physical activity levels. Pearson correlation analysis was used to determine the relationship between two variables. P - values <.05 were considered statistically significant.

For power analysis, a 5% significance level, 80% power (1-b), and a medium effect size in the population (d=0.712) were assumed (8). G*Power analysis was used to estimate the minimum sample size required. The sample size was calculated as 28 participants in each group.

RESULTS

Comparison of demographic data and clinical characteristics of inactive (I), minimally active (M) and active (A) groups are presented in Table 1. The mean height of the inactive group was higher than the other two groups (Comparison of group A with group I, p=.034; comparison of group A with group M, p=.005). Considering that the IPAQ score was the discrimination parameter between the groups, there was a significant difference between the groups, as expected (p<.001 for pairwise comparisons between groups). The sitting time of group I was found to be longer than group A (p=.013). BAQ scores of group I were lower than those of groups M and A (p=.005, p=.002, respectively), whereas BAQ scores of groups M and A were similar (p>.05). The BAI score of group I was higher than that of group A (p=.039). No significant difference was found between the SAS and NYPRS scores between the groups (Table 1).

Table 1. Comparison of demographic characteristics, phone usage duration, smartphone addiction, physical activity, body awareness, posture status and anxiety levels of inactive, minimally active and active groups

	Inactive (I) (n=35)	Minimal active (M) (n=45)	Active (A) (n=30)	p	Group comparison
Age (years)	20.68±2.68	20.37±2.40	19.63±1.12	0.190	
Height (cm)	168.88±8.52	167.86±7.35	174.03±8.40	0.004*	I=M<A
Weight (kg)	61.65±10.68	62.04±12.8	67.7±12.42	0.083	
SUT (hours)	5.82±2.12	6.15±2.61	6.56±3.14	0.531	
SAS score	36.77±6.53	39.6±6.97	40.1±8.46	0.127	
IPAQ score	485.88±180.60	1734±656.61	3503.46±545.29	0.000*	I<M<A
ST (hours)	370.28±123.03	328±99.58	288±121.43	0.017*	I>A
BAQ score	73.68±20.9	87.8±18.99	90.5±17.84	0.001*	I<M=A
NYPRS score	54.91±5.86	55.17±5.87	55.23±5.40	0.970	
BAI score	17.25±13.96	15.28±12.3	9.6±9.37	0.036*	I>A
	n	**n**	**n**		
Gender (female/male)	27/8	34/11	11/19		
Purpose of using a smartphone					
Social media	30	39	19		
Gaming	3	4	2		
Music	1	1	5		
Shopping	1		2		
Communication		1	2		

*p<0.05 one-way analysis of variance (post hoc analysis Bonferroni correction); ST: sitting time, SUT: smartphone usage time, IPAQ: International Physical Activity Questionnaire, SAS: Smartphone Addiction Scale, BAQ: Body Awareness Questionnaire, NYPRS: New York Posture Rating Scale, BAI: Beck Anxiety Inventory

Table 2 presented the correlation analysis between the duration of smartphone use, IPAQ scores and SAS, BAQ, NYPRS and BAI scores. A positive correlation was found between IPAQ score and BAQ score, and a negative correlation was found with BAI score (Table 2A negative correlation was found between sitting time and NYPRS score (Table 2). A positive correlation was observed between the duration of smartphone use and SAS score. A positive correlation was found between SAS score and BAI score (Table 2).

Table 2. Analysing the correlation between physical activity, phone use, body awareness level, posture problem and anxiety

		IPAQ	ST	SUT	SAS	BAQ	NYPRS
IPAQ	**r**	1					
	p						
ST	**r**	**-0.250***	1				
	p	**0.032**					
SUT	**r**	0.119	0.050	1			
	p	0.215	0.604				
SAS	**r**	0.154	0.019	**0.446****	1		
	p	0.107	0.849	**0.000**			
BAQ	**r**	**0.283***	-0.029	0.044	0.095	1	
	p	0.003	0.766	0.646	0.325		
NYPRS	**r**	0.020	**-0.214***	-0.063	-0.077	0.050	1
	p	0.837	**0.041**	0.515	0.426	0.603	
BAI	**r**	**-0.212***	0.054	-0.005	**0.237***	-0.131	0.076
	p	**0.043**	0.575	0.957	**0.013**	0.173	0.427

*p<0.05, **p<0.001Pearson correlation analysis, IPAQ: International Physical Activity Questionnaire score, ST: sitting time, SUT: smartphone usage time, SAS: Smartphone Addiction Scale score, BAQ: Body Awareness Questionnaire score, NYPRS: New York Posture Rating Scale, BAI: Beck Anxiety Inventory score

DISCUSSION

The aim of this study was to investigate the effect of physical activity level on body awareness, posture problems and anxiety levels in smartphone addicted individuals. As a result of this study, it was found that individuals with high physical activity had higher body awareness and lower anxiety levels. In addition, physical activity level was positively correlated with body awareness and negatively correlated with anxiety level. It was observed that individuals with high sitting time had worse posture.

Physical activity is critical for maintaining health and preventing mortality (21). In the literature, there are many studies showing that there is a negative relationship between smartphone addiction and physical activity (5). In a study conducted on students, smartphone addiction and physical activity levels were examined and it was stated that participants with high smartphone addiction had lower physical activity levels (22). In another study, it was concluded that 67.8% of young people using smartphones had low physical activity levels (23). Similarly, we think that the reason why there was no relationship between physical activity level and duration of smartphone use in our study is that all participants were addicted to smartphones and the duration of phone use of all individuals was very high. For this reason, it can be thought that the participants in our study did not spend time for physical activity because of the high duration of smartphone use. The fact that 80 of the 110 students with smartphone addiction were inactive and minimally active in terms of physical activity supports this situation.

Body awareness is an indicator of the individual's ability to identify their body and sensory awareness and examines the individual in social, physical, emotional and psychological aspects (24). The number of studies examining the relationship between body awareness and physical activity level is limited in the literature (25). In a study investigating the relationship between physical activity and body awareness in athletes, it was reported that body awareness was higher than non-athletes (26). In other studies, it was found that those with low physical activity levels also had low body awareness (27,28). In our population of smartphone addicted individuals, the fact that the body awareness of the inactive group was different from the other groups and that the physical activity level was positively correlated with the body awareness level shows a mutual cause and effect relationship. In line with these findings, it can be hypothesised that physical activity relatively prevents body awareness in smartphone addicted individuals.

In the literature, there are studies on the beneficial effects of physical activity on mental health (30,31). However, when current studies are analysed, contradictory results are observed. In some studies, it is stated that there is a positive relationship between increased physical activity level and anxiety and depression symptoms (30,31), while in some studies, it is stated that there is a positive relationship between only moderate physical activity level and depression and anxiety (32). The possible reason for these contradictions may be methodological differences such as subject selection, characteristics of the subjects, and measurement methods used (33). One of the most common mental problems in university students is anxiety (34). In a study conducted in university students, high physical activity was found to be more effective in reducing anxiety than moderate physical activity (35). However, there was no relationship between the level of physical activity and depression and anxiety in secondary school students (36). In our study, it was observed that anxiety decreased with increasing physical activity level. This suggests that physical activity may be an important

method in the process of cope with anxiety, especially in a young population consisting of university students. Smartphone addiction may increase the level of anxiety. In our study, the fact that the anxiety level of the inactive group was higher than the active group may be considered that physical activity relatively protects the mental state.

Young adults with smartphone addiction showed a tendency to decrease in physical activity, which resulted in decreased muscle mass and different postural problems (22). In the study by Kee et al. it was emphasised that craniocervical posture and mobility were negatively affected in 16-17 year old individuals with smartphone addiction and this may cause temporomandibular joint pathologies (37). Similarly, in another study conducted in university students aged 18-32 years, an increase in nondominant side shoulder protraction, thoracic kyphosis, neck lateral flexion and pelvic obliquity was found in the posture evaluation performed before and after 5 minutes of smartphone use. It has been suggested that these disorders may cause low back pain, thoracic region pain and neck pain in the future (38). In our study, although the posture problems were not similar according to the physical activity groups, it was observed that individuals with high sitting time had worse posture. We think that this is due to the fact that all of the participants were addicted to smartphones and the mean NYPRS scores were close to the total score in all three groups. In addition, it is stated in the literature that long sitting time is an independent risk factor for deterioration of fitness, irrespective of physical activity level (39). In posture problems seen in smartphone addicts, parameters such as inappropriate sitting position and sitting time during smartphone use may be a more determining factor than physical activity level. Further comprehensive and controlled studies in this field may provide more accurate information about the level of physical activity and posture status. In addition, randomised controlled trials with physical activity interventions of different intensity may be important in knowing the effectiveness of approaches to prevent smartphone addiction.

There are some limitations of our study. Since the population of our study consisted of university students, anxiety level may be high in this age group. Accordingly, the level of anxiety in this age group may have increased independently of the smartphone. In addition, the fact that university students stay in a sitting position for a long time due to their academic studies may have affected the posture.

CONCLUSION

With the changing world, the increasing use of various technological devices such as smartphones by young people brings with it spine, shoulder, elbow and various postural problems. In addition, body awareness and mental state can be affected. In our study, physical activity had a positive effect on body awareness and anxiety in young people with smartphone addiction. We think that physical activity will be a method to protect young people from the harmful effects of smartphones. In addition, sitting time is an important factor in posture problems and even in young people with high physical activity level, to avoid various posture problems, attention should be paid to sitting time.

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Research Article

Evaluation of Stability and Stress Distribution on Plate and Bone for Correction of Anterior Open Bite with Le Fort I Osteotomy: New Plate Design

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Abstract

Aim: Many different fixation methods have been proposed in the literature for the treatment of open bite. Beginning with the use of plates and screws, rigid fixation methods have become commonplace, however, open bite is a disorder prone to relapse despite rigid fixation. In our study, we aimed to eliminate the need for guided split usage during surgery and to increase postoperative stabilization in open bite patients with a new personalized plate design.
Material and Method: For this purpose, a three-dimensional (3D) head model was created in the virtual environment. After the Le Fort I osteotomy on the model, the inferior segment of the maxilla was placed 1 cm forward and positioned to leave a space between the inferior and superior part of the maxilla. Different fixation methods were applied to fix the bone segments. In the first group, four plates with a thickness of 0.8 mm were fixed. In the other groups, we used three different thicknesses (0.4 mm, 0.6 mm, 0.8 mm) of the continuous plate we designed. The amount of movement and tension that occurred on the bone segments, plates, and screws were evaluated.
Results: The maximum movement in the study was observed with the standard 4-plate fixation method, and the minimum movement was observed with the custom plate system with 11-screw type with a thickness of 0.8 mm. As a result, it has been found that the custom-made continuous plates provide a more rigid fixation than the standard plates.
Conclusion: It may be possible to reduce the likelihood of a relapse problem by designing a plate with the appropriate thickness and form to spread the stress on the bone over a wider area.

Keywords: Orthognathic surgery, bone fixation, Le Fort I osteotomy

INTRODUCTION

Anterior open bite (AOB) is defined as non-contact between maxillary and mandibular anterior teeth (1). The incidence of AOB in the community ranges from 1.5% to 11%, and this ratio varies between races (2). The difficulty in the treatment of patients with anterior open bite closure is due to the fact that the etiology of the problem is multifactorial (skeletal, dental, soft tissue, bad habits, etc.) (3). Several studies have reported a tendency for relapse after conventional or surgical orthodontic treatment for this purpose (4). For this reason, it is considered one of the dentofacial deformities that are difficult to treat due to the difficulties of determining the etiology and the possibility of relapse after treatment.

The Le Fort I osteotomy became popular in the 1970s, and it has increasingly been used for correcting anterior open bite. This method allows the treatment of upper jaw hypoplasias that are in three planes. Recent studies have focused on the safety of maxillary movements in relation to long-term stability and relapse (5,6).

There are differences in the rates of relapses in the literature as the anomalies in different etiologies can be corrected by Le Fort I osteotomy. Dowling et al. identified only 14% of patients with clinically significant relapses (>2 mm) without a result, additional operations, or associated syndromes (7). In 1991, Proffit et al. reported a similar rate of recurrence (>2 mm) in the study they published (8). Additionally, rates of relapse in patients treated for vertical excesses are also similar (9,10). Studies have reported that relapse rates are between 0-18% for the anterior maxilla and 6-7% for the posterior maxilla when the maxilla is positioned in the superior position. Relapse rates for advancing the maxilla range from 5-15%. They

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reported that maxillaries positioned inferiorly (using bone grafts) could result in up to 28% of cases of anterior region relapse and up to 70% of posterior relapse (11). It has been reported that most of the relapses in open bite cases occurred during the first 6 months, and the amount of movement was the primary cause of relapse (7). After the correction of maxillary anterior open bite, the relapse rates in the sagittal direction increase to 37%, while the vertical relapse rates are as high as 65% of the total movement (12).

Preoperative planning is essential for the success of orthognathic procedures. In recent years, with the development of technology, preoperative planning - in addition to traditional methods - can be done by computer, and post-op results can be seen before the operation. Also, customized surgical guides or fixation plaques can be made using Computer-aided design/ Computeraided manufactur-ing (CAD/CAM) systems. In orthognathic surgery, the soft tissues are stretched due to the movement of the jaws. Existing lengths of muscle fibers and occlusal forces lead to relapse formation after postoperative functions. Studies in the literature indicate that the odds of relapse are increased by the amount of movement of the maxilla. The key factors that influence the relapses are fixation technique and resistance of the fixation material to occlusion forces. Relapse in anterior open bite patients is the most important problem because of the amount of movement made after the osteotomy. In our study, it is aimed to increase the rigid fixation stabilization and increase the resistance to occlusion forces by increasing the plate surface. In addition, it is thought that, in addition to the result obtained, added value can be achieved by shortening the operation time with preoperative digital adaptation.

To evaluate the stabilization, conventional 4-hole titanium plates, and a designed titanium plaque are modeled virtually. It is planned to compare the plaques in terms of stabilization and durability against occlusal forces (in the bone/plaque connection region) with the finite element analysis method and to evaluate the ideal plate/screw combination and the position where more successful retention is achieved.

MATERIAL AND METHOD

In our study, a new surgical plate design (Figure 1A) was developed to enhance stability when positioning the maxilla anteriorly and inferiorly. We evaluated the results obtained by comparing this designed plate with the conventional 4-plate fixation technique (Figure 1B). Our research employed static, linear analysis using the 3-dimensional finite element stress analysis method to ensure that comparisons were conducted under identical conditions.

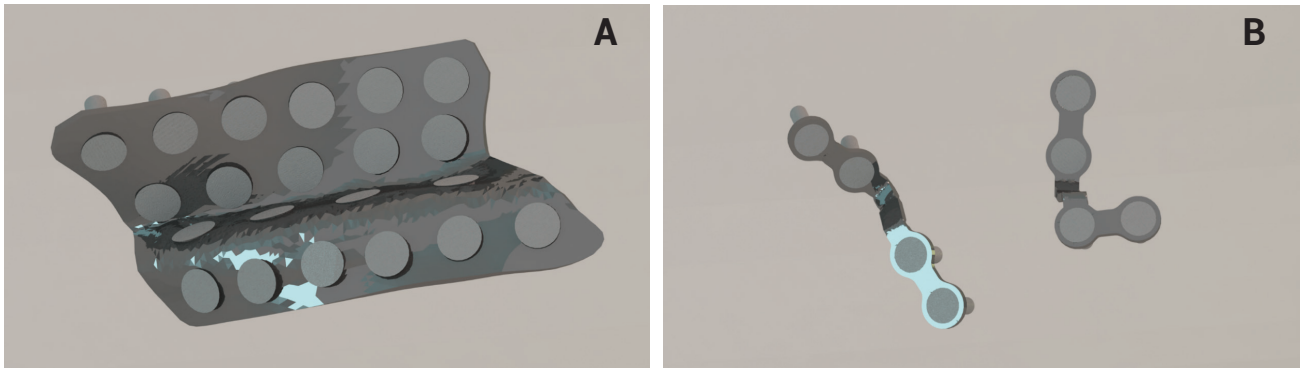


Figure 1. A. New le fort I plate design; **B.** 4 holes miniplate

Using the finite element analysis method, we simulated Le Fort I osteotomy in a three-dimensional (3D) skull model and separated the bone segments. The inferior segment was positioned 1 cm anteriorly and 6 mm inferiorly, with gap left between the segments. 120 Newton (N) force was applied with 60°to the Frankfurt horizontal plane on one side.

The plates we designed were intended to be continuous pieces extending from the zygomatic protrusion to the piriform area. These plates were manufactured in three different thicknesses: 0.4 mm, 0.6 mm, and 0.8 mm, constructed to match the patient's bone shape. During simulation, fixation was achieved using either 8 or 11 screws strategically placed through predefined screw holes on the plate. The objective was to compare both the thickness of the plate and the stabilizing effect of the number of screws used in plate fixation.

To ensure consistency, the locations of the screw holes on the plate were determined based on distances in the standard plate system. In alignment with the anatomical structure of the sampled patient, 11 screw holes were incorporated into the plate, aligning with the bone volume. This approach aimed to provide a comprehensive analysis of the impact of plate thickness and screw quantity on overall stability and performance in the simulated 3D network structure.

The workstation utilized for the 3-D network configuration, homogenization, 3-D solid model creation, and stress analysis in our study featured an Intel Xeon® R CPU 3.30 GHz processor, a 500 GB Hard Drive, 14 GB RAM, and Windows 7 Ultimate operating system. The software tools employed included Rhinoceros 4.0 (Robert McNell&Associates, USA) for 3D solid model creation and stress analysis, an optical scanner with a Version Service Pack 1 operating system, Activity 880 modeling software by smart optics Sensortechnik GmbH, VRMesh Studio by VirtualGrid Inc (USA), and Algor Fempro analysis program (ALGOR, Inc. USA).

Simulation

In our study, a stepped Le Fort I osteotomy was performed. With Le Fort I osteotomy, the anterior descent of the maxilla was placed 1 cm forward, leaving a 6 mm space between the bone segments, modeled as one of the orthognathic procedures with the most relapse. The inferior segment was positioned 1 cm anteriorly with a 6 mm gap between the superior segment. The simulation was conducted in 7 different ways:

- **Model 1:** 0.8 mm thick, 4 holes with 4 plates (8 screws),
- **Model 2a:** Fixed with 2 plates with 17 holes of 0.8 mm thickness (11 screws),
- **Model 2b:** Fixed with 2 plates of 17 holes with 0.8 mm thickness (8 screws),
- **Model 3a:** Fixed with 2 plates of 17 holes with 0.6 mm thickness (11 screws),
- **Model 3b:** Fixed with 2 plates with 17 holes of 0.6 mm thickness (8 screws),
- **Model 4a:** Fixed with 2 plates with 17 holes of 0.4 mm thickness (11 screws),
- **Model 4b:** Fixed with 0,4 mm thick 17 holes with 2 plates (8 screws).

RESULTS

Demographic and clinical data of the groups are shown in the least movement after the chewing force was applied to the model was observed in Model 2a. The maximum movement was determined in the standard Model 1 (Figure 2A).

The amount of movement observed in the X plane after applying the force to the model follows the sequence: Model 1 > Model 4b > Model 4a > Model 3b > Model 3a > Model 2b > Model 2a. There was no significant difference between the models, but most movements were observed in Model 1.

The motion of the Y plane followed a similar trend: Model 1 > Model 4b > Model 4a > Model 3b > Model 3a > Model 2b > Model 2a. Model 2a (Figure 3A) provided the most stable result with a move-ment of 0.438367 mm.

The minimum movement in the Z plane was observed in Model 2a (Figure 3B). The movement amounts of all models were significant, with Model 1 having the highest movement.

The total amount of movement was the highest in Model 1 with a total movement of 6.22 mm (Figure 2B). The minimum movement was determined in Model 2a (11 screws) with 0.6875734 mm (Figure 3B). The order of all models was Model 1 > Model 4b > Model 4a > Model 3b > Model 3a > Model 2b > Model 2a (Graph 1).

Stress analysis revealed that stress occurring in Model 1 is six times higher than the stress in Model 2 (Graph 2). In our custom-designed plates, the maximum stress, at a thickness of 0.4 mm, was observed in Model 4b, fixed with 8 screws. However, even the stress in Model 4b is only one-third of the stress in the standard 4-plate fixation technique (Model 1). Fixation of plates with the same thickness but a different number of screws has minimal impact on the stress on the plate.

Stresses in the screws are notably higher in Model 1 compared to other models. The stress distribution occurs in the same order in both the screws and the plates, and the resulting stresses can be listed as Model 1 > Model 4b > Model 4a > Model 3b > Model 3a > Model 2b > Model 2a. Moreover, the increase in the number of screws leads to a reduction in the stress on the screws (Figure 4A, Figure 4B).

When considering stresses on the bone, the greatest stress is found in Model 1. These stresses are listed in descending order as follows: Model 1 > Model 2b > Model 4b > Model 3b > Model 2a > Model 3a > Model 4a (Graph 3). Examining stresses in the bone, an increase in the number of screws results in a more balanced outcome in terms of strength distribution. Models with 11 screws are less desirable than those with 8 screws. Among the 8-threaded models, Model 3 with a thickness of 0.6 mm exhibited the least stress (Figure 5A, Figure 5B).

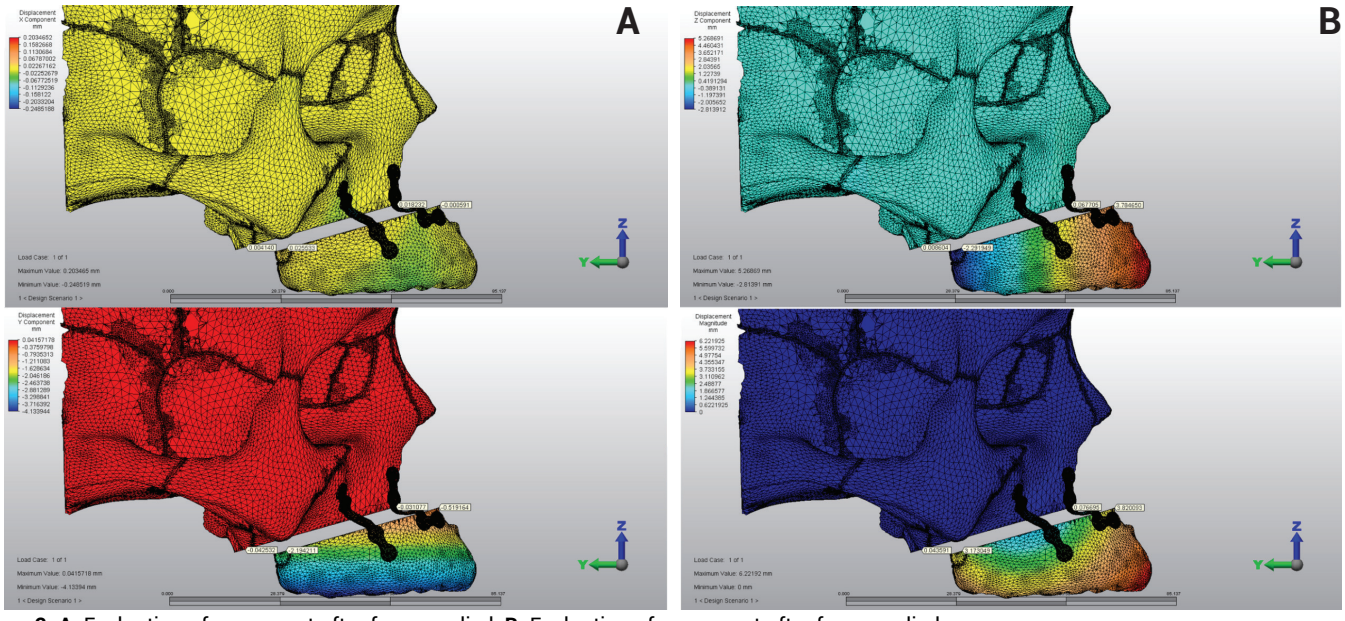


Figure 2. A. Evaluation of movement after force applied; **B.** Evaluation of movement after force applied

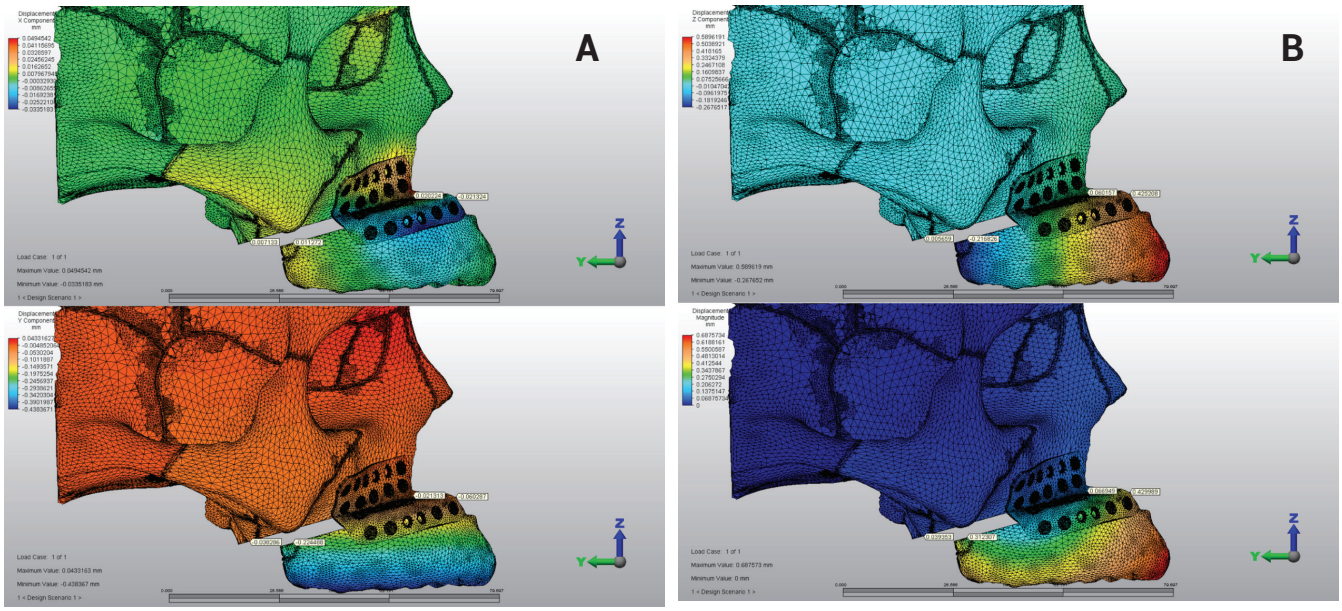


Figure 3. A. Evaluation of movement after force applied with design plate; **B.** Evaluation of movement after force applied with design plate

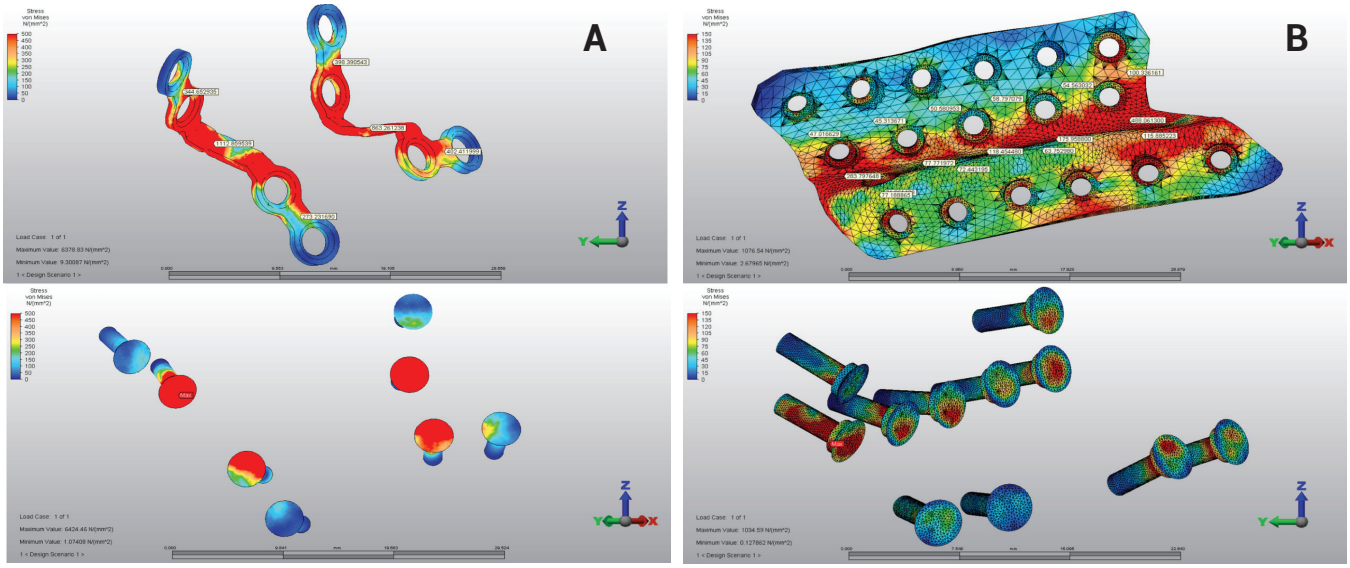


Figure 4. A. Stress distribution on plate and screw; **B.** Stress distribution on design plate and screws

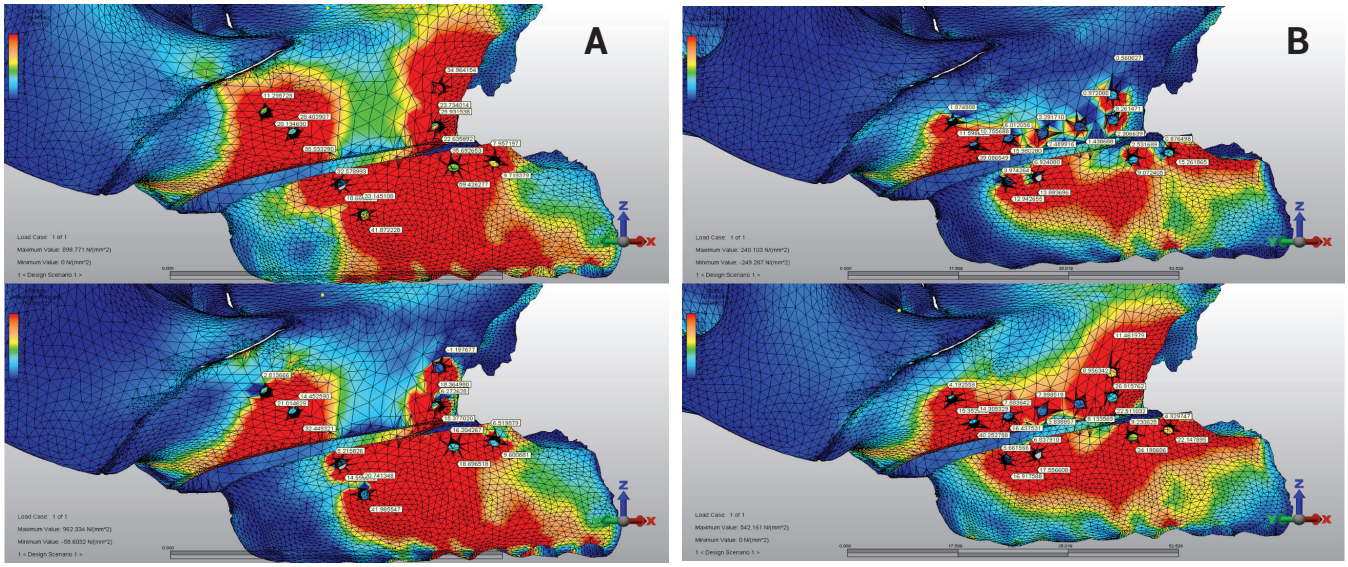
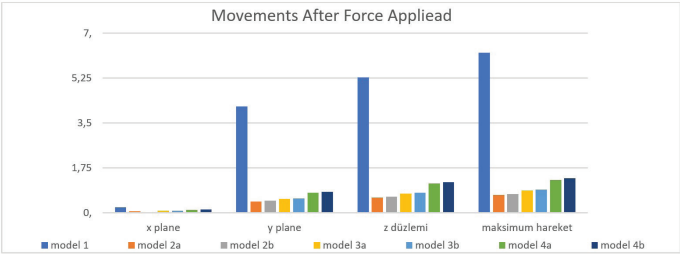
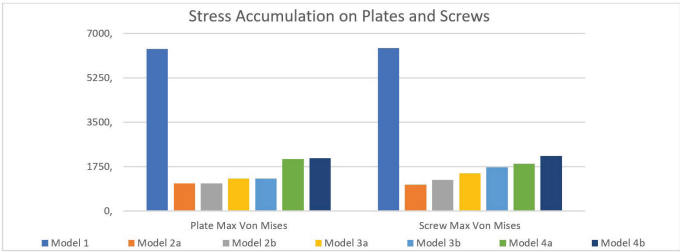


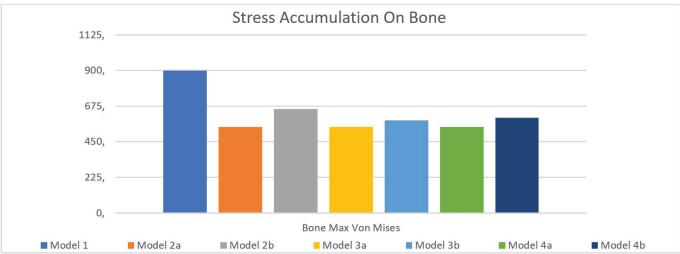
Figure 5. A. Stress distribution on bone; **B.** Stress distribution on bone with design plate



Graph 1. Movements at all plane



Graph 2. Stress accumulation on screws and plates



Graph 3. Stress accumulation on bone

DISCUSSION

The primary objective of Le Fort I surgery is to maintain the stability of the inferior segment in its new position after the separation of the superior and inferior segments.

There are differences in the rates of relapses in the literature as the anomalies in different etiologies can be corrected by Le Fort I osteotomy. Dowling et al. identified only 14% of patients with clinically significant relapses (>2 mm) without a result, additional operations, or associated syndromes (7). In 1991, Proffit et al. reported a similar rate of recurrence (>2 mm) in the study they published (8). Additionally, rates of relapse in patients treated for vertical excesses are also similar (9,10). Studies have reported that relapse rates are between 0-18% for the anterior maxilla and 6-7% for the posterior maxilla when the maxilla is positioned in the superior position. Relapse rates for advancing the maxilla range from 5-15%. They reported that maxillaries positioned inferiorly (using bone grafts) could result in up to 28% of cases of anterior region relapse and up to 70% of posterior relapse (11). It has been reported that most of the relapses in open bite cases occurred during the first 6 months, and the amount of movement was the primary cause of relapse (7). After the correction of maxillary anterior open bite, the relapse rates in the sagittal direction increase to 37%, while the vertical relapse rates are as high as 65% of the total movement (12).

Moldez et al. (2000) concluded that, in their study, Class III AOB patients who underwent bimaxillary surgery experienced 8.7 relapses at a 5-year follow-up. Additionally, for patients rotating clockwise in the palatal plane, the study reported that the inferior orientation of the anterior maxillary segment was more stable than for those undergoing frontal opening correction (13).

Espeland et al. (2008) reported negative overbite in 12 patients after a 3 year follow-up. This occurred with standard single-piece Le Fort I interstitials and fixation utilizing 2 L-shaped 1 mm thick miniplates for 2 sherds on each side (14).

Various studies have indicated that stabilization is compromised when the maxilla is positioned inferiorly with Le Fort I osteotomy in Class III AOB cases, leading to a gap between the inferior and superior segments (15-18).

The study of tissue and organs during the consideration of operative techniques, such as maxillary Le Fort I osteotomy and fixation, is particularly challenging due to ethical problems, difficulty of standardization and insufficiencies in measurement and analysis. Finite Element Analysis (FEA) effectively addresses these challenges, allowing for detailed mathematical study of complex numerical values such as displacement, stress, and compressive stresses caused by forces acting on structures with complex geometry. Transferring the structures to be examined with FEA to the computer ensures that stress values arising after force application are obtained pricesly. The complex calculations of FEA transform the studied model into a series of simple equations (19-22).

Nagasao et al. first utilized FEA in 2007 to demonstrate the relationship between the diameter and stability of fixation screws in Le Fort I osteotomy. They reported that stabilization was greater when the thickness of the fixation site bone equaled the size of the fixation screw (23).

In their study Atac et al. employed Le Fort I osteotomy in 2008 and 2009, using 4-hole plain plaques in the aperture priform rim area and posterior zygomatic support points in a study comparing 2 and 4 plate fixations with FEA after different maxillary postures. They reported that plaque fixation was less stressful than the 2-system (24, 25). In one of their studies, using Le Fort I osteotomy, 5 mm advancement in the upper cannula, 4 mm inferior positioning, and bone grafting to the gap between bone segments were performed (26). The plaques used were 2 mm thick, unlike our study. Comparison revealed that the data obtained indicated less stress on the plaque in the 4-plaque fixation than in our study. This difference may be attributed to the fact that in our study, both the inferior and anterior movements were greater, while the plaque thickness was less. It can be said that stability changes linearly with plate thickness, inversely proportional to the amount of movement.

Coşkunses et al. (2015) used FEA to evaluate Le Fort I osteotomy, employing mini-plates pre-bent for fixation in models. Pre-bent plates proved a good alternative to conventional two-plate systems for advances up to 5 mm,

but their predictability and feasibility in advances greater than 5 mm and in vertical position changes require further study (27).

Huang et al. (2016) investigated the biomechanical relations of different mini plate fixations in models made maxillary using Le Fort I osteotomy by FEA. They reported that more stable results were obtained with lateral fixation using L-shaped plaques, and maximal 5 mm advancements in the maxilla would increase plaque breakage and relapse risk (28).

To achieve desired aesthetic and functional results after orthognathic surgery, correct repositioning of the upper jaw is crucial. The method for 3D control of upper jaw movements during surgery is still controversial (29,30). Traditionally, the upper jaw is repositioned using surgical splints based on intraoral or extraoral measurements. There is a high probability of errors in such measurements, with splints typically prepared manually before surgery using surgical models. Errors of up to 5 mm in the upper jaw position have been reported after surgery according to preoperative planning (31).

During orthognathic surgery, when the upper jaw moves, only the mandible can be used as a reference point to determine the new position of the maxilla. To position the maxilla correctly, the mandible to which the surgical splint is inserted is directed to the top and back positions of the joint pit. However, during surgery, there is no anatomical point or chewing gauge to guide the placement of the mandible, other than the surgeon's experience. Additionally, an average of 2.4 mm of vertical movement of the condyle was reported in the patient under anesthesia in the supine position. Consequently, the mandible may have been directed farther than necessary, leading to incorrect mandibular posterior mandibular and causing the maxillary segment to move forward in the anteroposterior direction and rotate counterclockwise according to the preoperative plan (32).

Suojanen et al. (2016) conducted a study to evaluate the accuracy of personalized cutting guide and fixation plates in orthognathic procedures without using of surgical splints. They included 32 patients and Le Fort I osteotomy planned for all cases. In all cases, except one, the surgical application was done as planned. In one patient, the designed plaques did not conform to the bum, suggesting that this may be due to an incorrect design of the posterior osteotomy, possibly due to misdetection of the lower jaw position during computed tomography (33).

In a study focused on patients with Class III open bite, fixation was achieved by positioning the using upper jaw segment 6 mm inferiorly for 10 mm advancement and open-closing correction. The evaluation of plaque stability in vertical movements by leaving a gap between the bone segments was also a targeted aspect.

When designing a single-piece plaque, our goal was to enhance stabilization, considering the following points:

- Achieve minimum plate thickness,
- Ensure that the plaque is lightweight,
- Facilitate fixation (screws can be applied to each zone).

In our study, the plates were designed with 6 different thicknesses (0.4 mm, 0.6 mm, 0.8 mm) and numbers of screws (8 or 11). To reduce the weight of the designed plates, 17 screw holes were formed in the direction of the patient's anatomy on each plate by placing a screw hole in the appropriate range on the entire surface. This approach aimed to prevent the plaque from becoming unusable by allowing fixation through the appropriate hole at the end flap and to address possible complications during the operation. Furthermore, screw holes between the bone segments would allow intersegmental grafting during the operation if needed.

In our study, after Le Fort I osteotomy in Class III open closure patients, FEA was employed to stabilize specially designed individual fixation plates and movements in the segments using the standard 4-plate fixation method under 240 N occlusal force. In all models, the most significant part of the movement was observed in the anterior segment of the inferior segment of the maxilla. It is mentioned in the literature that stabilizing the anterior part of the upper jaw following the inferior direction after Le Fort I osteotomy, especially in front open closure cases, is challenging. This finding aligns with previous studies indicating that the region with the most movement in our study is the anterior part of the inferior segment of the maxilla (16-18).

When examining the total amount of motion across all planes, Model 1 exhibited the maximum movement, measuring 6.22 mm, while Model 2 displayed a movement amount of 0.68 mm. The order of movement in the models studied ranged from larger to smaller: Model 1 > Model 4b > Model 4a > Model 3b > Model 3a > Model 2b > Model 2a.

The maximum von Mises stress value formed on the plates and screws was found to be 6 times higher in Model 1 than in Model 2. Specifically, among the plaques designed, Model 1 showed about 3 times more stress accumulation than Model 4b, which had the highest stress accumulation value, with a thickness of 0.4 mm and 8 screws. Stresses on both plates and screws were considerably less than those of Model 1 in single-piece platters. Examining the single plate, it was observed that the stress on the plates and screws decreased as the thickness and the number of screws increased. A linear relationship between stress on plates and screws was identified, with the stress order being Model 1 > Model 4b > Model 4a > Model 3b > Model 3a > Model 2b > Model 2a. Comparatively, Huang et al. compared the standard 4-plate system with the plate produced specially for the work, reporting Von Mises stress values that were 67% less when using specially produced one-piece plates compared to the 4-plate system and 65% less when using the midevacuated optimum plates. In our study, Von Mises stress values showed a reduction of 83% on the plate compared to Model 2a, which represented the 4-plate standard system, and exhibited the most stable

results among the singlepiece plates produced specially for individuals (34).

When assessing stresses in the bone, the least stress accumulation was observed in Model 4a. The difference between Model 4a, Model 3a, and Model 2a at different thicknesses using 11 screws was negligible. Stress on 8-threaded plates was more pronounced and formed in Model 3b, which had a minimum stress of 0.6 mm on 8-threaded plates. Subsequently, Model 4b on 0.4 mm paper was followed by Model 2b on 0.8 mm thickness. A plate with a thickness of 0.6 mm was found to be more effective in terms of balanced distribution of stress on balanced bone. Moreover, the results indicated that screw numbers must be kept high during fixation to ensure a balanced distribution of stress to the bone. The models were designed to ensure perfect bone/plaque compatibility. Therefore, the use of thinner plaques was considered more crucial for balanced distribution of stress on bone, considering the discrepancies that may occur on the plates matched to bone contours during surgery.

The results obtained in our study showed that the plate designed for stabilization provided more stability than fixation with 4 plates at all thicknesses. When examining stresses on screws and plates, the stress on the plates we designed was considerably less than the standard method. When considering these parameters in addition to the measurement of stress on the bone, an ideal Le Fort I osteotomy fixation would be achieved with a single piece and a thin (0.4 mm) plate fitted with as many screws (11 screws) as possible.

CONCLUSION

Achieving the best aesthetic and functional result after orthognathic surgery requires preoperative planning, transferring the planned plan to the patient, ensuring patient comfort after the operation, and preserving the obtained result in the long term. The use of patient specific designed plates for the operation with the thinnest and most durable plates for the operation plan is expected to result in high bone/plaque compatibility and ease of use during the operation. This comprehensive approach aims to transfer the operation plan to the patient completely. It is anticipated that optimal plate design may lead to lead to a decline in relapse rates in the long term, ultimately benefiting patients.

Financial disclosures: *The authors declared that this study has received no financial support.*

Conflict of interest: *The authors have no conflicts of interest to declare.*

Ethical approval: *In this study, no questionnaires, interviews, focus groups, observations, experiments, or similar methods were employed, no experiments were conducted on humans or animals, and no violation of personal data protection laws occurred. It has been declared by the corresponding author that this is a study that does not require ethics committee approval.*

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MEDICAL RECORDS-International Medical Journal

Research Article

The Effects of Magnetic Fields Created by Mobile Phones on In Vitro Embryo Development

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Abstract

Aim: The risks to public health of radiofrequency signals emitted by mobile phones, an indispensable part of our daily lives, have begun to be questioned. For this reason, the magnetic field created by a third-generation mobile phone was applied to the embryos obtained by in vitro embryo culture technique during the organogenesis period of the rat embryo and its effect on development was examined.

Material and Method: In our study, 20 adult female rats weighing between 200-300 g and 30 male Wistar albino rats weighing over 300 g were used. The developmental morphology of embryos from the control and experimental groups exposed to magnetic fields for different periods (24 hours, 48 hours) was evaluated.

Results: When the morphological score, yolk sac diameter, crown-rump length and number of somites of embryos exposed to magnetic fields for different periods were compared, the experimental groups regressed compared to the control group.

Conclusion: As a result, it was shown that developmental delays and deformities may occur in embryos depending on the duration of exposure to the magnetic field.

Keywords: 3G mobile phone, embryo development, in vitro, magnetic field, rat

INTRODUCTION

With the development of technology, many electronic equipment that we commonly use in daily life, such as mobile phones, tablets, and Wireless Fidelity (Wi-Fi) communication devices, create Electromagnetic fields (EMF) at different levels (1, 2). While the lowest frequency of these EMFs is 3-30 Hertz (Hz), 50-60 Hz, which is frequently encountered in daily life, the frequency range of mobile phones, which are the most dangerous and widely used for humans, is hundreds of Megahertz (MHz) (3). Mobile phones, a part of the electromagnetic spectrum, are the most common sources of radiofrequency fields (4). Mobile communication services are a major concern for people as they are the fastest-growing area in the telecommunications industry (5,6). It has been stated that mobile phones operate between 300 MHz and 3 GHz (Gigahertz) within the Global Mobile Communications System (GSM) (7). Mobile phones with third-generation telephone (3G) technology are known to be in the frequency range of 1900 MHz to 2200 MHz (4).

The effect of EMF on living organisms began to be investigated in 1961 (8). The biological effects of exposure to EMF have been discussed for years (9). It has been reported that individuals using mobile phones may affect the nervous system due to EMF exposure, especially in the head area (10-13). Additionally, it has been reported that there are impairments in the synaptic transmission of pyramidal neurons in the prefrontal cortex of mice exposed to radiation generated by mobile phones in intrauterine life (14).

Studies have shown that mice exposed to 900 MHz mobile phone radiation for 1 hour stimulated tooth germ cells and caused teeth to erupt before the normal time (4). Studies conducted on living organisms have reported that both in vivo and in vitro studies in the 900-1800 MHz range cause Deoxyribonucleic acid (DNA) damage (15). Another study reported differences in the kidney, liver, and eye tissues of animals exposed to second-generation (2G) or 3G mobile phone radiation (16-19).

CITATION
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This study aims to investigate the systemic effects of radiation generated by 3G mobile phones on in vitro embryo development.

MATERIAL AND METHOD

Approval for this study was obtained with the decision of Erciyes University, Experimental Animals Ethics Committee, numbered 07/07 and dated 10.10.2007. In the study, 20 adult female rats weighing between 200-300 g and 30 male Wistar albino rats weighing over 300 g were used. Embryo culture was performed according to the procedures of New (20).

Embryo Culture

Female and male rats were kept in cages in groups of five, and their water and nutritional needs were provided in the normal order of the day. 4-10 month old females weighing 200-300 g were kept in a cage overnight (between 5.00 pm and 8.00 am) with males capable of fertilisation. In the morning, vaginal smears were taken from the females, and it was checked whether there was sperm. A vaginal smear was performed on females in the morning. Females in which sperm was seen were considered 0.5 days pregnant, fed normally, and kept for 9 days. Pregnant rats were anaesthetised using diethyl ether. When it was observed that the cornea and foot reflexes were absent, it was decided that anaesthesia had been achieved. The anterior abdominal walls of the rats were disinfected with 70% alcohol. A V-shaped incision was made over the pubis towards the arches of both ribs, and the anterior abdominal wall was opened. Blood was taken from the bifurcation of the visible abdominal aorta with a sterile syringe and centrifuged at 3500 revolutions per minute for 5 minutes. Thus, the serum to create the culture medium was obtained. At the same time, the embryo sacs located in the uterine horn were cut one by one and placed in a sterile petri dish containing Hanks' salt solution. Subsequent processes were carried out in a Lamin-air flow cabinet and under a stereo microscope for a sterile environment. With the help of sterile forceps, the muscle layer and decidua layer on the uterine wall were removed. A frontal section was made in the decidua tissue and carefully removed without damaging the embryo on one side. In the second stage, the Reicherts membrane was removed from the embryonal pole and transferred to a sterile petri dish containing embryo medium (Figure 1).

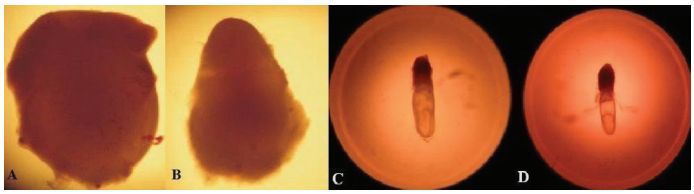

Figure 1: A. Endometrial tissue **B.** Decidua **C.** Embryo with Reicherts membrane D. Embryo with Reicherts membrane removed

Formation of Experimental Groups

Embryos obtained from pregnant rats were divided into one control and two experimental groups. Our study cultured embryos according to New's procedures (20).

Control group: Embryos in this group (n: 14) were cultured in rat serum for 48 hours without being subjected to any magnetic field.

Experimental group 1: Embryos in this group (n: 15) were exposed to a magnetic field created by a 3G mobile phone placed in an oven incubator with rollers inside and set at 37°C in the first 24 hours of the 48-hour culture period.

Experimental group 2: Embryos in this group (n: 15) were exposed to the magnetic field created by the mobile phone throughout the 48-hour culture period.

In the experimental groups, a third-generation mobile phone was placed vertically in the oven on a perforated mechanism with dimensions of 15x10 cm. The mobile phone was vibrated, the Wireless Local Area Network (WLAN) and Bluetooth settings were kept on, and an uninterrupted call was made for 2 minutes every hour. At the end of the 48-hour culture period, embryos were taken from the culture bottles and evaluated morphologically under a stereomicroscope, and the results were compared with the control group.

According to the morphological scoring system developed by Van Maele-Fabry et al. (21), respectively. The yolk sac vascularisation, allantois, flexion, heart, caudal neural tube, hindbrain, midbrain, forebrain, branchial bar, olfactory, otic and optic system, maxillary and mandibular processes, forelimbs, hindlimbs, and somites were examined. The development of 17 parameters was evaluated by giving points between 1 and 5. The yolk sac diameter, embryo crown-rump length, number of somites, and total morphological score values obtained from morphological scoring were recorded.

Statistical Analysis

Descriptive statistics were given as a unit number (n), mean ± standard deviation. The normal distribution of data belonging to numerical variables was evaluated with the Shapiro-Wilk normality test. The variance homogeneity of the groups was assessed using the Levene test. Comparisons between groups for numerical variables were made with a one-way analysis of variance. SSPS 15.0 package program was used for statistical analysis. $p<0.05$ was considered statistically significant.

RESULTS

As a result of our study, when the embryos grown in a culture environment for 48 hours were evaluated morphologically. The developmental disorder in the embryos kept for 48 hours in the magnetic field created by the mobile phone (Experimental Group 2) was more pronounced than the developmental disorder in the embryos kept for 24 hours (Experimental Group 1) compared to the control group.

In the experimental groups, it was determined that the embryos exposed to the magnetic field created by the mobile phone showed an increase in the average total morphological score, number of somites, yolk sac diameter and crown-rump length, depending on the duration of exposure to the magnetic field (Table 1).

Table 1. Effects of the magnetic field created by a mobile phone on in vitro embryonic rat embryo development

	N	Control group	Experimental Group 1 (Embryos exposed to magnetic field for 24 hours)	Experimental Group 2 (Embryos exposed to magnetic field for 48 hours)
Total morphological score	14	53.00±6.59	41.13±7.32***	37.26±5.92***
Number of somites	15	21.4±4.04	16.8±2.14***	15.4±1.72***
Yolk sac diameter (mm)	15	3.40±1.46	2.39±0.40**	1.88±0.36***
Embryo crown-rump length (mm)	15	2.77±1.21	2.06±0.41*	1.64±0.20***

Results show mean values±standard deviation; *P<0.05, **P<0.01, ***P<0.001 (compared to the control group)

In most of the embryos in the control group, many thin branches were seen on the main vessel on the yolk sac. While there were a few thin vessels in the yolk sac in experimental group 1, there were prominent blood islands in the yolk sac in experimental group 2 (Figure 2).

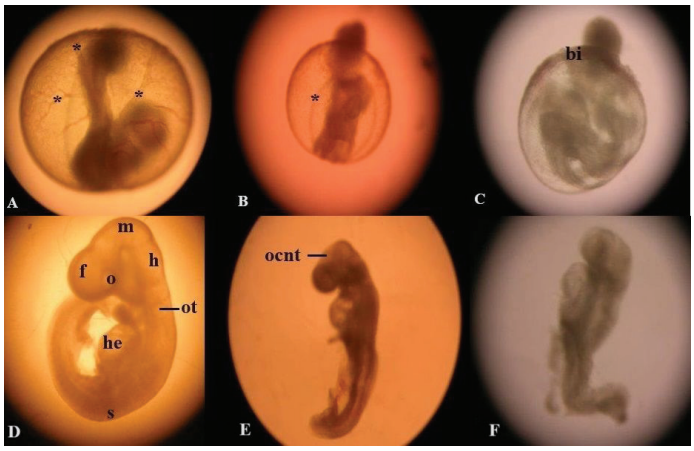

Figure 2. Embryos in the yolk sac; **A.** 11.5-day-old rat embryos growing in normal culture medium (* Blood vessels); **B.** 11.5-day-old rat embryos exposed to the EMF of a mobile phone for 24 hours (* Blood vessels); **C.** 11.5-day-old rat embryos exposed to the EMF of a mobile phone, for 48 hours (bi: blood island); Embryos with yolk sac dissected; **D.** 11.5-day-old rat embryos growing in normal culture medium; f: forebrain, m: midbrain, h: hindbrain, o: optic vesicle, ot: otic vesicle, he: heart, s: somit **E.** 11.5-day-old rat embryos exposed to mobile phone EMF for 24 hours, ocnt: open cranial neural tube **F.** 11.5-day-old rat embryos exposed to mobile phone EMF for 48 hours (Not fully developed)

When looking at heart development, the heart was mostly three-chambered in the control group embryos, while the bulbus cordis, atrium, and ventricle were separate and distinct in experimental groups 1 and 2 (Table 2). When the forebrain development of the embryos was examined, it was seen that the most development was in the control group (the prosencephalon of 6 embryos was united entirely). In comparison, there was a regression in experimental groups 1 and 2 (the prosencephalic fold was partially closed in 6 and 9 embryos, respectively). Caudal neural tube development was highest in the control group (there was a small opening in the posterior neuropore in 6 embryos, and the posterior neuropore was open and shaped in 8 embryos), in most of the embryos in experimental groups 1 and 2, it was observed that the neural fold was united at the level of 4-5 somites and the caudal neural tube was open (Table 3).

While optic vesicle development occurred in 12 embryos in the control group and the optic stalk was open, this was seen in 6 embryos in experimental group 1 and 2 embryos in experimental group 2. As for otic vesicle development, it was observed that the astrocyte was located dorsally in 2 embryos in the control group, and the otic vesicle was separated from the epidermis in 12 embryos. It was observed that the development of the embryos in experimental groups 1 and 2 did not reach this level. In addition, it was found that the otic vesicle was not separated from the epidermis in most experimental groups embryos (Table 4).

The highest improvement in the branchial bar and maxillary process, was observed in the control group, experimental group 1, and experimental group 2, respectively. In front limb development, all embryos in the control group had budded limbs; It was observed that the front extremities of some of the embryos in the experimental groups were budded, while some of them were curved outwards at the level of 9 to 13 somites. While the situation was the same in the development of the hind limb, the only difference was that the hind limb was curved outwards at the level of 26 to 30 somites (Table 5).

Table 2. Effects of the magnetic field generated by a mobile phone on the development of yolk sac vessels and heart of in vitro embryonic rat embryos

		Vitellus sac vessels development					Heart development			
Groups	**N**	**(0) Yolk sac vessels or blood islands are prominent**	**(1) Blood islands are evident around the ectoplacental cone.**	**(2) A few thin vessels on the yolk sac**	**(3) The vascular network is prominent in the yolk sac**	**(4) Many thin branches on the main vessel**	**(2) S-shaped heart tube**	**(3) Bulbus cordis, atrium and ventricle separate and distinct**	**(4) 3 chambered heart**	**(5) 4 chambered heart**
Control group	**14**	-	2	-	2	10	1	6	7	-
Experimental group 1	**15**	4	1	5	4	-	6	9	-	-
Experimental group 2	**15**	5	4	3	2	-	7	8	-	-

Table 3. Effects of the magnetic field generated by a mobile phone on the development of the forebrain and caudal neural tube of the in vitro embryonic rat embryo

Groups	N	Forebrain development				Caudal neural tube development			
		(2) U-shaped neural fold	(3) Prosencephalic fold partially fused	(4) Prosencephalon fully united	(5) Telencephalic evagination view	(1) The neural layer is closed and united with the neural layer	(2) Neural folds are united at the level of 4-5 somites	(3) Posterior neuropore open but unformed	(4) A small opening in the posterior neuropore
Control group	14	-	3	6	5	-	-	8	6
Experimental group 1	15	3	6	4	2	2	7	6	-
Experimental group 2	15	3	9	3	-	-	11	4	-

Table 4. Effects of the magnetic field generated by a mobile phone on the development of yolk sac vessels and heart of in vitro embryonic rat embryos

Groups	N	Eye development				Ear development			
		(1) Eye groove	(2) Elongated optical promordium	(3) Oval shaped optical promordium	(4) The optic vesicle has formed and the optic stalk is open.	(2) Otic fossa	(3) Otic vesicle closed but not separated from epidermis	(4) Otic vesicle separated from epidermis	(5) Autocyte settled dorsally
Control group	14	-	-	2	12	-	2	10	2
Experimental group 1	15	1	5	3	6	-	8	7	-
Experimental group 2	15	1	9	3	2	1	11	3	-

Table 5. Effects of magnetic field generated by mobile phone on branchial bar, maxillary process, forelimbs and hindlimbs extremity development of in vitro embryonic rat embryos

Groups	N	Branchial bar			Maxillary processes			Forelimb development			Hindlimb development		
		(1) 1 branchial bar	(2) 2 branchial bar	(3) 3 branchial bar	(1) Rudimentary bar separated from the anterior head	(2) Maxillary process with branchial bar processes inwards	(3) A layer between the mandibular process and the forebrain	(1) At the level of 9-13th somites	(2) Forelimbs bud shaped	(3) Forelimbs are paddle-shaped	(1) At the level of 26-30th somites	(2) Hindlimbs bud shaped	(3) Hindlimbs are paddle-shaped
Control group	14	1	13	-	-	11	3	-	14	-	8	6	-
Experimental group 1	15	7	8	-	3	12	-	8	7	-	9	6	-
Experimental group 2	15	13	2	-	7	8	-	11	4	-	12	3	-

DISCUSSION

It is stated that exposure to radiation in the 900 MHz frequency range affects the central nervous system (22, 23). In animal model studies, it has been reported that the number of cells in the hippocampus region of rats exposed to EMF before birth is significantly reduced (24). Another in vitro study reported differences in blood-brain barrier permeability at 900 MHz (25,26). In our study, the morphological scoring method, which includes 17 embryonic development parameters, was used to determine the total development levels of rat embryos. When the morphological score results showing total embryonic development were compared, it was seen that there was a significant regression in the experimental groups compared to the control group (morphological score: 61.7±1.75). It was determined that the developmental disorder was more in experimental group 2 (morphological score; 44.5±4.10), which was exposed to the magnetic field for a longer time (48 hours), and was relatively less in the embryos in experimental group 1 (morphological score: 57.6±2.64), which was exposed to the magnetic field for a shorter time.

The formation of the vascular system is very important in embryo development and growth processes. Because

disruption of this functional system will not be able to provide the necessary oxygen and nutrients to the organism or even remove waste products (27). A study reported that vascular occlusion, changes in vascular smooth muscles, thickening of the intima layer, and inflammation in the adventitia layer occurred after radiation exposure (28). In another study, the testicles of rats exposed to mobile phone radiation (1.58 Specific Absorption Rate (SAR)) for a long time were examined with electron and light microscopy. It has been reported that the capillaries of rats dilate after exposure (29). In his histopathological study, Mercantepe et al. (30) examined the kidney tissue of rat embryos. It has been reported that embryos exposed to 6-Gray (Gy) ionizing radiation (IR) have vascular occlusion in the intercellular space. In another study, thickening was reported in the renal vessel walls of rats exposed to EMF at 900/1800 MHz, 2400 MHz, and 8Gy x-ray frequencies (31). Our study observed that the experimental groups exposed to 3G mobile phones had a few thin vessels or prominent blood islands in the yolk sac, depending on the exposure time.

Türedi et al. (32) examined the heart tissue of male baby rats in the prenatal period to which 900 MHz radiation was applied. Another study analysed the heart tissue of rats exposed to 50 Hz radiation (33). In both studies, it was reported that EMF caused apoptosis in heart tissue. In one part of their study, Adebayo et al. (34) examined mice's heart muscles and fibres by exposing them to mobile phones for certain periods. It has been reported that in mice exposed to 900 MHz radiation, there is an increase in the gaps between heart fibres and irregular heart muscle and contractions. In our study, three-chambered heart development was observed only in the embryos of the control group. Although the scores of the embryos in the experimental group were similar to each other, only the development of the heart tube, bulbus cordis, atrium, and ventricle were seen to be separate/distinct. It was observed that exposure to magnetic fields affected heart development.

When using a mobile phone, the ear and brain are affected by EMF. It has been stated that the rate of tumours such as neuroma and glioma may increase as a result of exposure to EMF. In addition, it may cause effects such as irreversible hearing problems (35) and acoustic neuroma (36). In a study, it was reported that rat embryos irradiated with a dose of 1 Gy had a lack of fusion in the nerve folds, developmental delay in the otic vesicle, olfactory systems were not sufficiently developed, and the neural tubes remained open in the caudal and cranial regions (37). Similarly, in our study, while developmental delay was observed in the otic vesicle, the presence of open but unformed posterior neuropores of the caudal neural tubes showed that there was not sufficient development.

The study of D'Silva et al. (38) reported that the radiation emitted by the 2G mobile phone causes conditions such as deterioration in the lens fibres and epithelium of the chick embryo and the formation of cystic cells and cavities. In another study, male Wistar albino rats were exposed to radiation emitted by a 3G mobile phone for 20 days (exposure time 20 minutes a day), and their eye tissues were examined. It has been reported that such short-term exposure does not harm the eye tissue of rats (39). In addition, it has been stated that the radiation emitted by a mobile phone at a frequency of 900 MHz for four weeks causes oxidative stress in the cornea and lens tissues (16). In the study of Balcıoglu et al. (37), it was reported that there was a developmental delay in the otic vesicle of rats exposed to ionising radiation. In our study, delayed development of optical systems was detected in direct proportion to the duration of exposure to the magnetic field. We think the reason for the differences is not the duration of radiation exposure alone but may be related to the effect of the SAR value.

Limitations

Although we express the limitations of our study as sample size, duration of exposure to mobile phones, exposure conditions and the unknown effects of radiation created by the development of wireless technology in recent years on embryo development, we think this study will contribute to subsequent studies.

CONCLUSION

The embryos' development in our study's control group was better than in the experimental group. When compared, the experimental groups showed development directly proportional to the duration of radiation exposure. As far as we have found in the literature, many histopathological studies exist. Studies investigating the systemic effects of radiation generated by 3G mobile phones on embryos are quite limited. With the development of technology, more work is needed in this field.

This research was produced from Nihal Gürlek Çelik's Master's thesis, "The Effects of Magnetic Fields Created By Mobile Phones on In Vitro Embryo Development".

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Conflict of interest: *The authors have no conflicts of interest to declare.*

Ethical approval: *Erciyes University Experimental Animals Ethics Committee gave ethical approval (numbered 07/07 and dated 10.10.2007).*

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MEDICAL RECORDS-International Medical Journal

Research Article

Investigation of Aquaporin Molecules in the Placentas of Pregnant Women with Premature Rupture of Membranes

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Abstract

Aim: This study aimed to investigate the immunohistochemical expression of Aquaporin 3 (AQP3) in placentas of pregnant women with premature rupture of membrane (PROM) and to explore AQP3-related interactors and signaling pathways using in silico approaches.

Material and Method: Placental samples from 21 healthy (control) pregnant women and 21 pregnant women diagnosed with PROM were processed for routine histological tissue preparation. Sections were immunostained with AQP3 and analyzed under light microscope via ImageJ software. Protein-protein interaction (PPI) network of AQP3 was constructed with Cytoscape (version 3.10.2). Nodal centrality indexes (degree, closeness and betweenness) were computed through CentiScaPe plugin. The Enrichr tool was utilized to perform pathway enrichment analysis for 15 central genes.

Results: AQP3 immune activity was significantly decreased in the plasma membrane of the trophoblastic cell layer of the PROM group compared to control group. According to network centrality analysis, AQP subfamily proteins predominantly play central roles in the AQP3 network; Major Intrinsic Protein of Lens Fiber (MIP), Glycerol-3-Phosphate Dehydrogenase 2 (GPD2), Glyceraldehyde-3-Phosphate Dehydrogenase (GAPDH), Glycerol Kinase 2 (GK2), GK, and Actin Beta (ACTB) with additional central interactors including proteins. Peroxisome proliferator-activated receptors (PPAR) signaling pathway was obtained as the most significantly enriched pathway.

Conclusion: Alterations in AQP3 expression level in the PROM group compared with the control group may contribute to disturbances in water transport and cellular homeostasis in placental tissues and in silico potential interaction between AQP3 expression and PPAR signaling suggest the role of AQP3 in cell metabolism in PROM.

Keywords: Premature rupture of membranes, aquaporin 3, placenta, immunohistochemistry

INTRODUCTION

Premature rupture of membranes (PROM) a common obstetric complication causing perinatal mortality and morbidity, affecting 5-10 % of all pregnancies (1,2). PROM can significantly have adverse impacts on the health of neonates, comprising main reasons for neonatal survival and stay in the intensive care unit (3). Maternal, neonatal and environmental factors are etiologically risk factors. Many predisposing factors such as preeclampsia, cervical effacement, congenital malformations, autoimmunity, previous high-risk pregnancies, exposure to heavy metal poisoning, use of assisted reproductive techniques, and stress are strongly associated with PROM (4,5).

Water transport in the cell membrane structure is facilitated by integral membrane proteins called aquaporins (AQPs) (6). AQPs are channel proteins that use osmotic charge to help water transport (7). So far, 13 aquaporins have been discovered. Aquaporin 3 (AQP3) is one of the well-investigated of AQPs and it is mainly found in epithelial layer of the skin. Ear, eye, intestine and human placenta also have AQP3 expression. Although, AQPs has been known to take role in transport of water and various substances,

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recently, the role of AQPs has been a subject of curiosity in placentas. Damiano et al showed that AQP3 was located to on the apical surface of syncytiotrophoblasts since these cells played an important role in transport of metabolites, ions and water from mother to fetus (8). The authors speculated that AQP3 may be an important regulator of these changes. Another study also revealed that AQP3 level was decreased in placentas of preeclamptic patients. The authors claimed that the reduction in AQP3 level was an adaptive response to trophoblastic apoptosis (8,9).

There are many studies on AQP3 and placentas, yet none include association between AQP3 and placentas of patients with PROM. In this study, we examined the level of aquaporin 3 and investigated whether it is a possible regulator in the molecular mechanism of PROM.

MATERIAL AND METHOD

Study Design

Ethical approval was taken from Non-interventional Clinical Research Ethical Committee of Faculty of Medicine, Dicle University (approval no: 188). The placentas of 21 healthy (control) pregnant women and 21 pregnant women who diagnosed with PROM were collected. Small samples were dissected and objected to routine histological tissue preparation.

Tissue Preparation

The placenta tissues were placed in 10% neutral formalin solution for fixation. The tissues were then placed under running tap water for 12 hours and dehydrated by passing through increasing alcohol series (50%, 70%, 80%, 90%, 96% and absolute ethyl alcohol). Samples were kept in xylene for 3 x 15 minutes and placed in paraffin incubation. 5 µm thick sections were cut from paraffin blocks using a microtome (catalog number: LeicaRM2265, Wetzlar, Germany).

Immunohistochemical Staining

Placental sections were dewaxed, ran through a decreasing series of alcohol series, and then cleaned with distilled water. The endogenous peroxidase activity was inhibited by using hydrogen peroxide (H2O2). After being cleansed in PBS, the sections were treated with blocking solution. The sections were incubated with the primary antibody Aquaporin 3 (catalogue no: Santa Cruz 518001 Biotechnology Inc. CA, USA) for an overnight period at +4°C. The sections were incubated with a secondary antibody the next morning, and then were treated with streptavidin peroxidase reaction for 15 minutes. Diaminobenzidine (DAB) chromogen was applied following PBS washing. Sections were counter-stained with Hematoxylin. All sections were imaged by Zeiss Imager A2 light microscope.

ImageJ Analysis

ImageJ software was used to process and quantify each image. The AQP3 staining intensity was determined using the Image J software (version 1.53, http://imagej.nih.gov/ij). The measurement was computed using Crowe et al.'s approach (10). In order to record the quantification, ten fields from each specimen in each group were examined (11,12). In specimens, the color blue denotes a negative expression of the target antibody, whereas the color brown indicates a positive expression of the antibody. The calculation of signal intensity (expression) from a field involved dividing the intensity of the target antibody by the total area of the sample. For every sample from 10 fields, a staining area/whole area value was computed. Measured for each group, an average value was examined for semi-quantitative immunohistochemical scoring. Zeiss Imager A2 was used to image the slides.

Network Topology Analysis

Using Cytoscape (http://www.cytoscape.org/, version 3.10.2), we constructed the protein-protein interaction (PPI) network of AQP3 by querying the Search Tool for the Retrieval of Interacting Genes (STRING) database with a reliability threshold set to less than 0.4, and subsequently selecting 50 additional interactors. The network topology was analysed by calculating nodal centralities using the CentiScaPe 2.2 plugin. Degree centrality was computed to identify central regulator interactors, closeness centrality was calculated to assess functional relevance probability of interactors, and betweenness centrality was computed to evaluate organizational regulator characteristics of interactors (13). The nodes were colored based on closeness values, while node sizes were set according to degree values.

Pathway Enrichment Analysis

The proteins within the network were initially ranked according to their degree values. To include additional interactors beyond different AQPs, Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis was conducted using Enrichr for the top 15 proteins (14). It was conducted to observe which signaling pathways could be affected by the expression difference obtained in healthy and PROM pregnant women for AQP3. KEGG (https://www.kegg.jp), an extensively utilized repository, contains extensive information on human cell signaling and metabolic pathways, genomes, diseases, and pharmaceuticals. A significance threshold of $p<0.05$ was applied for statistical significance. Significant terms were ranked based on their p values, and a bar graph depicting the top ten enriched terms was generated.

Statistical Analysis

IBM SPSS 25.0 (IBM, Armonk, New York, US) was used for statistical analysis. The median (Quartiles 1–3) was used to record the data. Using the Shapiro-Wilk test, statistical distribution was assessed. The Mann-Whitney U test was used for binary group comparisons. $p<0.05$ were regarded as significant. Using G Power analysis (version 3.1), the number of patients for each group was determined. Alviggi et al.'s work served as the basis for the definition of Cohen's criterion (15).

RESULTS

Demographical Features

Maternal and fetal parameters belonging to control and PROM groups were listed in Table 1. Compared to control group, gestational age at delivery week was earlier and cesarean ration was higher in PROM group.

Table 1. Demographical properties of patients by groups

	Control (n=21)	PROM (n=21)
Maternal age, year	27.35±2.59	31.28±5.57
Gravida, n	1.36±0.85	2.93±1.58
Parity, n	1.13±0.92	1.73±1.84
Gestational age at delivery (week)	38.76±1.56	32.43±2.05
Birth week,	39.33±1.25	38.22 ±2.50
Birth weight, g	3462.29±287.28	3043.30±329.83
BMI, kg/m²	27.48±3.28	28.35±4.20
Cesarian birth, %	42	61

PROM: premature rupture of membranes, BMI: body mass index

Immunoexpression of AQP3

AQP3 immune staining of placental tissue sections is shown in Figure 1. In the images of the control group, AQP3 expression was abundant in plasma membrane of cytotrophoblast and syncytiotrophoblast and plasma membrane of cells of connective tissue in placental villi. (Figure 1a-c). When compared to control group, PROM group showed abundant negative AQP3 immune activity in plasma membrane of trophoblastic cell layer and in mesoderm of placental villi (Figure 1d-f). This alteration in AQP3 expression may have implications for water transport or homeostasis within these cells and tissues between groups, suggesting deterioration of cellular homeostasis in PROM group.

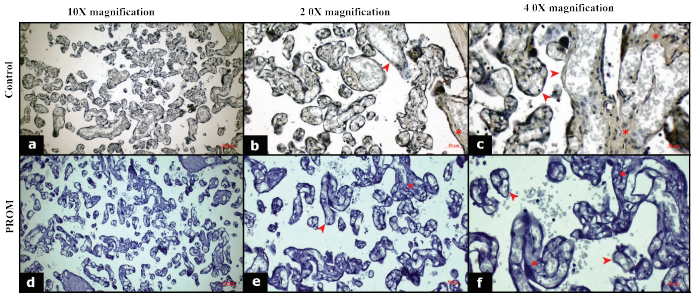

Figure 1. Placental sections of control group (a-c); positive expression of AQP3 in plasma membrane of cyto- and syncytiotrophoblast cells (arrowhead) and in plasma membrane of connective tissue cells (asterisk). Placental sections of PROM group (d-f); negative expression of AQP3 in plasma membrane of cyto- and syncytiotrophoblast cells (arrowhead) and in plasma membrane of connective tissue cells (asterisk); aquaproin3 immune staining, Scale Bar: 100 µm (10X), 50 µm (20X), and 50 µm (40X)

Table 2 displayed the semiquantitative measurement of AQP3 immune staining.

Table 2. AQP3 signal level in groups

	Control	PROM	p value
	Median (Q1-Q3)		
AQP3 signal	27 (25-31)	5.8 (5.3-6.7)	<0.0001*

* Mann Whitney U test, PROM: premature rupture of membrane

Figure 2 displayed a graphic representation of signal intensity and its importance.

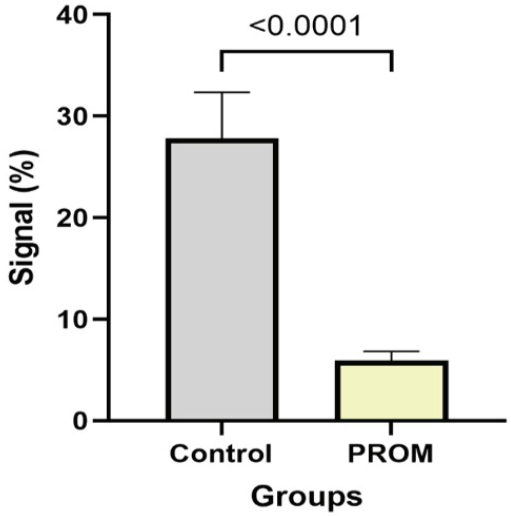

Figure 2. Graphical illustration of aqp3 signal intensity and significance between groups

In-silico findings

The AQP3 protein-protein interaction (PPI) network consists of a total of 51 nodes and 361 edges, as illustrated in Figure 3A. Using CentiScaPe, degree, closeness, and betweenness centrality values were calculated for the AQP3 PPI network, and the top 15 interactor proteins based on degree values were listed in Table 3. Closeness centrality values exhibited a similar pattern to degree values, decreasing from high to low for top central interactors. Additionally, betweenness centrality values, with some exceptions, revealed the same trend as degree and closeness centrality values. Centrality analysis revealed that members of the AQP subfamily (AQP9, AQP2, AQP1, AQP7, AQP10, AQP5, AQP8, AQP10, AQP6) were significant remarkable central genes within the AQP3 network. Additionally, proteins including Major Intrinsic Protein of Lens Fiber (MIP), Glycerol-3-Phosphate Dehydrogenase 2 (GPD2), Glyceraldehyde-3-Phosphate Dehydrogenase (GAPDH), Glycerol Kinase 2 (GK2), GK, and Actin Beta (ACTB) were identified as central interactors. Furthermore, KEGG pathway analysis indicated that the top 15 central genes are enriched in the peroxisome proliferator-activated receptors (PPAR) signaling pathway ($p<0.05$) (Figure 3B).

Table 3 degree, closeness, and betweenness values for the top 15 central interactors in the AQP3 PPI network.

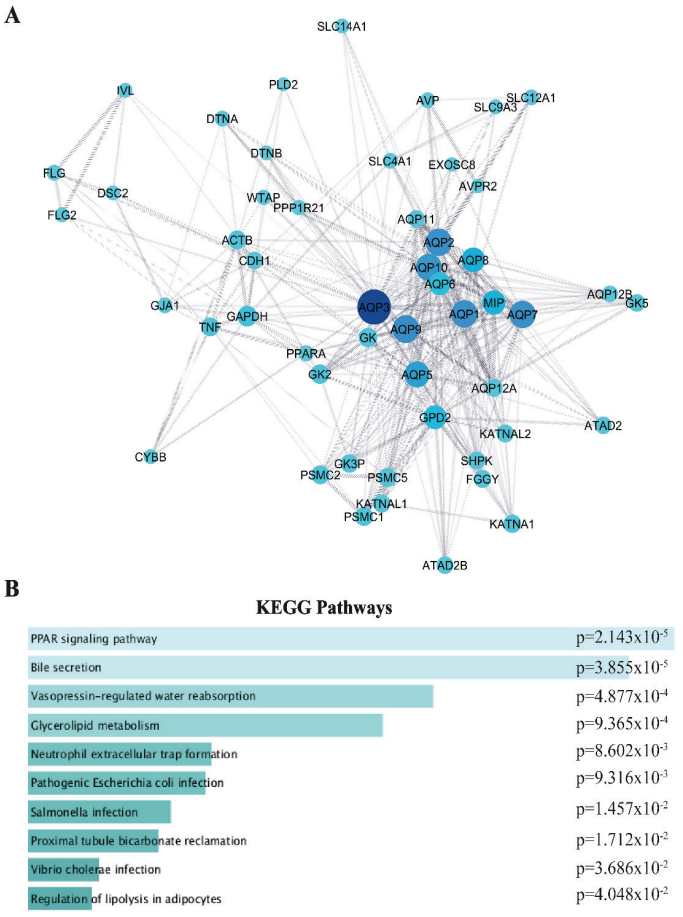

Figure 3. AQP3 PPI network and pathway enrichment; **A.** network centralities analysis was performed by computing degree, closeness and betweenness through CentiScape; the nodes were colored from light blue to dark blue, representing decreasing to increasing closeness values, respectively. Node sizes represent degree values, with larger nodes indicating higher degree values; **B.** significantly enriched KEGG pathway terms for the central 15 proteins of AQP3 PPI network (p<0.05)

Table 3. Degree, closeness, and betweenness values for the top 15 central interactors in the AQP3 PPI network

Gene symbol	Degree	Closeness	Betweenness
AQP3	50.0	0.02	866.97
AQP9	34.0	0.0151	128.84
AQP2	33.0	0.0149	141.32
AQP1	33.0	0.0149	130.65
AQP7	33.0	0.0149	100.39
AQP10	32.0	0.0147	88.42
AQP5	30.0	0.0143	71.93
AQP8	27.0	0.0137	25.72
MIP	26.0	0.0135	25.36
GPD2	25.0	0.0133	21.50
AQP6	23.0	0.0130	24.86
GAPDH	18.0	0.0122	62.29
GK2	15.0	0.0117	6.66
GK	15.0	0.0117	6.66
ACTB	14.0	0.0116	27.71

DISCUSSION

In this study, we reported AQP3 expression in placenta with PROM. The pathophysiology of PROM is multifactorial. The most important cause of term PROM is physiological changes occurring in the membranes (16). Membrane weakening is caused by an increase in local cytokines, collagenase and protease activity, an imbalance between matrix metalloproteinases and tissue inhibitors, and other factors that may lead to increased intrauterine pressure (17).

AQPs are small membrane proteins (30 kDa) found in different organs and responsible for permeability of water. Maternal-fetal fluid balance has critical importance during pregnancy. Therefore, many molecules, including AQPs, have been shown to play important roles in maternal-fetal fluid balance. When the homeostasis of maternal-fetal fluid exchange is disrupted, abortion, premature birth, abnormality in amniotic fluid volume, malformation and fetal growth restrictions may occur (18). Therefore, AQPs may involve in many cellular processes throughout placentation.

Studies demonstrated that AQP3 is present in the placenta and fetal membranes not only during normal pregnancy but also in pathological conditions such as polyhydramnios and oligohydramnios (19). In an animal model study of intrauterine growth restriction, Seo et al. (20) showed that AQP3 deficiency in placental componenets was associate with impared placental function, reduced amniotic fluid volume and fetal growth. Zhu et al. (7) examined the normal amniotic fluid and oligohydramnios patients to investigate role of AQP3.The authors found that APQ3 expression was localized in amnion, chorion and placental structures such as trophoblast cells. Moreover, AQP3 expression was significantly increased in oligohydramnios placentas compared to normal amniotic fluid volume patients.The authors suggest that alterations in AQP3 expression may be important in the pathophysiology of oligohydramnios. Another study indicated that AQP3 expression was significantly reduced in placentas of patients with preeclampsia compared to placentas from healthy pregnant women (21). Similarly, reduced AQP3 was found in gestational diabetes mellitus patient, causing increased risk for pregnancy anomalies such as cesarean section, macrosomia, fetal distress and neonatal asphyxia (22).

In our study, we analyzed AQP3 expression in the placentas of pregnant women with PROM comparing to placentas from healthy pregnant women. Consistent with previous studies, we detected AQP3 expression in syncytiotrophoblasts. Compared with the control group, we showed that AQP3 expression was decreased in the plasma membrane of the trophoblastic cell layer and mesoderm of the placental villi in the PROM group. This change in AQP3 expression may have effects on water transport or homeostasis in these cells and tissues between the groups, suggesting that cellular homeostasis was impaired in the PROM group.

In network topology analysis, it was observed that proteins belonging to the AQP subfamily predominantly play regulatory roles as central interactors associated with AQP3. Additionally, AQP3 was shown to be related to MIP, GPD2, GAPDH, GK, GK2, and ACTB proteins. The PPAR signaling pathway emerged as the most highly annotated pathway in the analysis of potential pathways affected by the expression difference observed for AQP3 in healthy and PROM pregnant women. PPARs play significant roles in regulating lipid and glucose metabolism, inflammation, and angiogenesis, facilitating the mother's adaptation to the nutritional and perfusion needs of the fetus. The regulation of the PPAR pathway has been shown to be involved in trophoblast invasion and placental development, and it is crucial in the risk of pregnancy-related conditions such as gestational diabetes mellitus, intrauterine growth restriction, and preeclampsia (23,24). Additionally, it influences apoptotic mechanisms implicated in fetal membrane rupture and may contribute to preterm delivery (25). One of the studies was demonstrated that mono-2-ethylhexyl phthalate reduces PPARγ activity and its anti-inflammatory properties. As a result, it has been emphasized that amniotic PPARγ disruptors could potentially cause premature rupture of fetal membranes (26). Based on the results of in silico analysis, we suggest that the potential regulation of PPAR, which is crucial in various aspects of maternal-fetal health, may be influenced by the effects of AQP3. This highlights the importance of further investigation of the interplay between AQP3 expression and PPAR signaling in the context of pregnancy-related conditions and pregnant women with PROM, as well.

CONCLUSION

The results strongly suggest that the changes in AQP3 expression in the PROM group compared to the control group may contribute to disruptions in water transport and cellular homeostasis within the placental tissues. This alteration in AQP3 expression could be a relevant factor in understanding the mechanisms underlying the pathophysiology of PROM, highlighting the importance of aquaporin-mediated water transport in maintaining placental health and function. Further research and exploration of the specific implications of AQP3 dysregulation in PROM may provide valuable insights into the development and progression of this condition.

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Ethical approval: *Ethics Committee of Dicle University Faculty of Medicine, Non-Interventional Clinical Researches with decision no. 188 on 2023/06.*

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MEDICAL RECORDS-International Medical Journal

Research Article

Comparison of Glucose Measurement Techniques Using Venous and Capillary Blood Samples in Diabetics Regarding Patient Satisfaction

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Abstract

Aim: This study was conducted to compare the satisfaction of patients diagnosed with diabetes mellitus regarding blood glucose measurement based on the blood glucose measurement techniques (intravenous and capillary) used.
Material and Method: A randomized controlled study was conducted with 110 patients with diabetes mellitus. Patients were randomized into the experimental group (n=55) and control group (n=55). Patient Information Form, Diabetes Fear of Injecting and Self-testing Questionnaire (D-FISQ), and Blood Glucose Measurement Patient Satisfaction Form were used in the study. The control group patients had their blood sugar measured using capillary blood from a finger prick. The experimental group patients had their blood glucose measured intravenously using venous blood, followed by capillary blood glucose measurement from a finger prick. Data analysis was conducted using chi-square test and independent t-test.
Results: There were statistically significant differences in the satisfaction of diabetic patients with the blood glucose measurement technique between the use of venous blood and intravenous blood glucose measurement by finger prick ($p<0.05$).
Conclusion: The measurement of blood glucose using venous blood obtained by an intravenous catheter positively affects patient satisfaction compared to the finger prick technique of measuring capillary blood glucose in patients with diabetes.

Keywords: Blood glucose, diabetes, patient satisfaction

INTRODUCTION

Diabetes is a chronic metabolic disease characterized by high blood glucose levels. It is reported that there are 537 million adults with diabetes worldwide (1). There are approximately 9 million diabetic patients in Türkiye, and the highest rate of diabetic patients in Europe lives in Türkiye (1,2).

The primary goal in diabetes treatment is to ensure blood glucose regulation, prevent acute and chronic complications that may develop due to the disease, and reduce the risk of complications (2). Therefore, blood glucose monitoring is critical in diabetes management. Blood glucose must be measured regularly to determine the insulin dose used in treatment and/or to prevent possible acute complications (3).

Nowadays, non-invasive technological developments for blood glucose measurement are increasing and alternative methods are being developed (4). However, venous or capillary blood samples are generally used to measure blood glucose in routine practices (5). In standard procedures applied in diabetes management, blood glucose monitoring is done based on taking capillary blood samples by pricking the fingertip (6). In clinical practice, measurements are usually made from a whole blood sample taken from a venous vein for routine laboratory tests required to monitor diabetic patients. In addition, a capillary blood sample can be used by pricking the fingertip to monitor the patient's blood glucose (2,5). Studies in the literature compare blood sugar

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measurements made from different blood samples. In these studies, it has been reported that the measurement results obtained from different blood samples are similar (7).

Diabetic patients may fear finger pricking while monitoring their blood glucose. It is reported in the literature that the fear of finger pricking due to blood glucose measurement in diabetic patients is 0.2-80% (8). This situation may negatively affect the compliance of individuals with diabetes with treatment (9). Individuals with diabetes may avoid insulin injections and self-measurement of blood sugar due to the fear of experiencing pain. In addition, an increase in the number of blood sugar measurements causes deformation of the fingertips of the diabetic individual and negatively affects patient satisfaction (10).

No study was found in the literature investigating patient satisfaction using glucose measurement techniques from venous and capillary blood samples in diabetic patients. This study was conducted to compare the satisfaction of patients diagnosed with diabetes mellitus with blood glucose measurement according to the applied blood glucose measurement technique (intravenous and capillary).

The study hypotheses were the following:

In comparisons made in terms of blood glucose measurement techniques in patients diagnosed with diabetes mellitus, according to the measurement made by taking a venous blood sample from the intravenous catheter and by pricking the fingertip;

- **H1:** creates less stress with a statistically significant difference,
- **H2:** causes less severe pain with a statistically significant difference,
- **H3:** lessens the ability to perform daily living activities, with a statistically significant difference,
- **H4:** provides a higher level of satisfaction with a statistically significant difference.

The study's results may significantly contribute to reducing multiple finger punctures and preserving fingertip skin integrity in patients with diabetes.

MATERIAL AND METHOD

This study was a single-center, prospective, randomized controlled trial. The study population consisted of adult patients with diabetes mellitus who were treated and followed up in the inpatient services of a hospital located within the borders of Zonguldak province from March 2023 to June 2023. The study's sample size was calculated using the G*Power Version 3.1.7 program. The study sample was determined as 110 patients at a significance level of 0.05 and an effect size of 0.50. Before capillary blood glucose measurements, blood glucose was measured from a venous blood sample via an intravenous catheter in the experimental group of patients, and satisfaction levels were compared in terms of both measurement techniques. The relevant EQUATOR guideline, the Consolidated Standards of Reporting Trials (CONSORT) checklist, was used for reporting this study, and a ClinicalTrials.gov registration number was obtained (NCT05976191 registered).

The research sample selection criteria were determined using the "purposeful sampling" method.

Criteria for inclusion in the study:

- Agreeing to participate in the study voluntarily,
- Patients whose blood sugar is monitored from fingertip capillary blood samples,
- Patients with an intravenous catheter,
- Patients who have been diagnosed with Diabetes Mellitus for at least one year.

Exclusion criteria from the study:

- Patients whose intravenous catheter insertion date has exceeded 24 hours,
- Patients who are unconscious, confused, apathetic.

To avoid bias in the patients to be included in the study, randomization was performed in accordance with the order of the patient protocol numbers assigned by the hospital during the hospitalization process. An internet program accessed via the "https://www.calculatorsoup.com" link was used to create the randomization table. Patients were matched with the randomization table and assigned to research groups.

Data Collection Tools

Patient Information Form

The researchers prepared the form, following the literature (2,9,11). It consists of 6 questions regarding the patients' socio-demographic characteristics (age, gender, marital status, educational status, employment status, income status) and two questions regarding their clinical characteristics (diabetes duration, type of drug treatment).

Diabetes Fear of Injecting and Self-testing Questionnaire (D-FISQ)

The scale was developed by Snoek et al. (1997) to measure the fear of self-injection and self-testing in diabetic individuals who need insulin (12). Celik, and Pınar conducted the Turkish reliability and validity study of the scale in 2016 (13). Cronbach's alpha coefficient of this study was calculated as 0.97 for the total scale score, 0.96 for the fear of injecting subscale, and 0.95 for the fear of self-testing subscale.

The scale consists of 15 items and two subscales. Each item on the scale is scored on a four-point Likert type. The scale is evaluated by calculating the total score of each subscale separately and/or the scale's total score. An increase in the score indicates an increase in fear (13).

Blood Glucose Measurement Patient Satisfaction Form

The form was prepared by the researchers using the literature (2,9). The form includes four questions examining the satisfaction level of the patients after their fasting blood sugar measurement. The answer to each question was evaluated as 0–10 points. The decrease in the answer score to questions "Does knowing that blood will be drawn for a blood glucose measurement cause stress for you?", "How severe is the pain you feel at the site where the blood sample was taken?" and "Does the site where the blood sample was taken limit you in performing daily living activities after the measurement?" indicates that patients' satisfaction with blood glucose measurement has increased. The decrease in the answer score to the question "How satisfied were you with this measurement technique?" indicates that blood glucose measurement satisfaction decreases.

Study Procedures

Patients who met the inclusion criteria for the study were identified by visiting inpatient services three days a week. In the study, the fasting blood glucose levels of the patients were measured. Blood glucose measurements were taken from 06:00 to 07:00 with devices used in the hospital. This study used two different blood glucose measurement techniques: 1) venous blood glucose measurement technique and 2) capillary blood glucose measurement technique. A 1cc venous blood sample drawn from the intravenous catheter into the syringe was used for venous blood glucose measurement. For capillary blood glucose measurement, the blood sample was obtained by pricking the tip of the patient's finger with a lancet. The fingertip pricking of the patients was performed with lancets routinely used in the hospital. Patient Information Form and D-FISQ were applied to the control group before blood glucose measurement. Then, the patients' capillary blood glucose was measured, and they were asked to fill out the Blood Glucose Measurement Patient Satisfaction Form. In the experimental group, venous blood glucose was measured first, and the participants were asked to fill out the Blood Glucose Measurement Patient Satisfaction Form. Then, the patient's capillary blood glucose was measured, and they were asked to fill out the Blood Glucose Measurement Patient Satisfaction Form again.

Data Analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 21.0. The chi-square test was used to compare the frequency distribution of the two groups and the homogeneity of categorical variables. The independent t-test was used to compare the mean scores. The data were analyzed at a significance level of $p<0.05$ within a 95% confidence interval. p-values less than 0.05 were considered statistically significant.

Ethical Considerations

The study was approved by the ethics committee of Istanbul University-Cerrahpaşa Social and Humanities Research Ethics Committee (Ethical date: 21 February 2023; Approval number 2023/67); institutional permission was received from Zonguldak Provincial Health Directorate Çaycuma State Hospital. Data were collected by obtaining verbal consent from the participants.

RESULTS

The patient was 61.11±12.07 (min: 28 – max: 81) years old. 51.8% of the patients were women, 82.7% were married and 70% were primary/secondary/high school graduates. Most of the patients were retired or unemployed (58.2%) and had a moderate income (70.9%). The duration of diabetes of the patients was 15.80±9.88 years, and most of them (71.8%) were receiving insulin treatment. When the experimental group and control group patients were compared in terms of socio-demographic and clinical characteristics, it was found that there was no statistically significant difference ($p>0.05$) (Table 1).

The D-FISQ scores of the patients were compared statistically. There was no statistically significant difference between the experimental and control groups ($t=0.442$; $p>0.05$), and the experimental group patients were similar to the control group patients in terms of fear of self-injection and testing (Table 2).

After measuring fasting blood glucose from the patients' fingertip capillary blood sample, the Blood Glucose Measurement Patient Satisfaction scores were compared statistically between the experimental and control groups. It was determined that there was no statistically significant difference between the experimental and control groups in terms of stress creation state, pain, limitation in activities of daily living, and satisfaction with the blood glucose measurement technique used ($p>0.05$) (Table 3).

In the experimental group, patient satisfaction score averages were compared statistically according to blood glucose measurement techniques. It was determined that there were statistically significant differences between the venous blood glucose measurement technique and capillary blood glucose measurement technique in terms of stress creation state, pain, limitation in activities of daily living, and satisfaction with the blood glucose measurement technique used ($p<0.05$) (Table 4). It was determined that the venous blood glucose measurement technique, according to other techniques, creates less stress, causes less pain intensity, limits daily living activities less, and provides greater patient satisfaction in diabetic patients.

In the experimental group, the venous blood glucose measurement value was 121.75±23.24 mg/dL, and the capillary blood glucose measurement was 124.8±24.10 mg/dL. There was a statistically significant difference between the averages of blood glucose values measured with both blood glucose measurement techniques ($t=3.643$; $p<0.01$), and a positive, very strong, and statistically significant relationship between both measurements. It was determined that there was a positive, very strong and statistically significant relationship between both measurements ($r=0.962$; $p<0.001$) (Table 5).

Table 1. Socio-demographic and clinical characteristics of patients (n=110)

Variables		Experimental group (n=55)		Control group (n=55)		Test	Significance
		n	%	n	%	χ^2	p
Age (years)	≤60	28	50.9	23	41.8	0.914	0.339
	≥61	27	49.1	32	58.2		
Gender	Female	26	47.3	31	56.4	0.910	0.340
	Male	29	52.7	24	43.6		
Marital status	Married	44	80.0	47	85.5	0.573	0.449
	Single	11	20.0	8	14.5		
Education level	Without formal education	12	21.8	10	18.2	0.390	0.823
	Primary/secondary/high school	37	67.3	40	72.7		
	University	6	10.9	5	9.1		
Employment status	Employed	29	2.7	17	30.9	5.477	0.065
	Unemployed/retired	26	47.3	38	69.1		
Income status	Low	11	20.0	13	23.6	2.218	0.330
	Moderate	38	69.1	40	72.7		
	High	6	10.9	2	3.7		
Duration of diabetes (years)	≤15	29	52.7	35	63.6	1.345	0.246
	≥16	26	47.3	20	36.4		
Diabetes treatment	Oral antidiabetic drug*	17	30.9	14	25.5	0.404	0.525
	Insulin	38	69.1	41	74.5		
Total		55	100	55	100		

χ^2: Chi-square test, p<0.05; *Patients whose diabetes treatment method is oral antidiabetic medication but who receive insulin injections if necessary during hospitalization

Table 2. Comparison of patients' D-FISQ scores (n=110)

D-FISQ and subscales	Experimental group (n=55)	Control group (n=55)	Test	Significance
	Mean±SD	Mean±SD	t	p
D-FISQ total score	31.47±14.30	30.31±13.32	0.442	0.660
Fear of injecting score	13.85±6.70	12.55±5.50	1.120	0.265
Fear of self-testing score	17.62±8.20	17.76±7.89	0.095	0.925

t: Independent samples t test, p<0.05; D-FISQ: Diabetes Fear of Injecting and Self-testing Questionnaire

Table 3. Comparison of patient satisfaction scores after capillary blood glucose measurement (n=110)

Blood glucose measurement patient satisfaction form questions	Experimental group (n=55)	Control group (n=55)	Test and significance
	Mean±SD	Mean±SD	
Does knowing that blood will be drawn for a blood glucose measurement cause stress for you?	4.64±3.83	5.02±3.70	z=0.590 p=0.555
How severe is the pain you feel at the site where the blood sample was taken?	4.87±3.42	5.71±3.24	z=1.358 p=0.175
Does the site where the blood sample was taken limit you in performing daily living activities after the measurement?	2.07±3.23	2.82±3.26	z=1.466 p=0.143
How satisfied were you with this measurement technique?	4.16±3.45	4.73±3.66	z=0.832 p=0.405

z: Mann Whitney U Analysis, p<0.05

Table 4. Comparison of patient satisfaction score means according to blood glucose measurement technique (n=55)

Blood glucose measurement patient satisfaction form questions	Blood glucose measurement techniques		Test and Significance
	Venous blood glucose measurement	Capillary blood glucose measurement	
	Mean±SD	Mean±SD	
Does knowing that blood will be drawn for a blood glucose measurement cause stress for you?	3.18±4.11	4.64±3.83	t=3.019 p=0.004*
How severe is the pain you feel at the site where the blood sample was taken?	0.24 ±1.40	4.87±3.42	t=9.334 p < 0.001**
Does the site where the blood sample was taken limit you in performing daily living activities after the measurement?	0.00±0.00	2.07±3.23	t=4.766 p<0.001**
How satisfied were you with this measurement technique?	9.64±1.63	4.16±3.45	t=-10.430 p<0.001**

t: Paired groups t-test, *p<0.01, **p<0.001

Table 5. Comparison of fasting blood glucose values in experimental group patients according to blood glucose measurement technique (n=55)

Blood glucose measurement techniques	Blood glucose value	Test and significance		Relationship and significance	
	Mean±SD	t	p	r	p
Venous blood glucose measurement	121.75±23.24	3.643	0.001*	0.962	< 0.001**
Capillary blood glucose measurement	124.98±24.10				

t: Independent samples t-test, r: Pearson Moment Correlation coefficient, *p<0.01, **p<0.001

DISCUSSION

This study was conducted to compare the satisfaction of patients diagnosed with diabetes mellitus regarding blood glucose measurement based on the blood glucose measurement techniques (intravenous and capillary) used. The homogeneity of the study was ensured by evaluating the socio-demographic characteristics, fear of self-injection and testing, and patient satisfaction scores of the patients participating in the study. Our research has shown that the venous blood glucose measurement technique via an intravenous catheter creates less stress, causes less pain intensity, limits daily living activities less, and provides greater patient satisfaction in diabetic patients.

In studies comparing different blood glucose measurement techniques, blood glucose levels are close to each other (7,10,11). It is also reported in the diabetes monitoring guide published by the Turkish Endocrinology and Metabolism Association that venous plasma blood glucose measurement and capillary blood glucose measurement values are equivalent to each other for fasting blood glucose value (2). In our study, blood glucose was measured using venous blood samples via an intravenous catheter and fingertip capillary blood samples. It was determined that there was a statistically significant difference in measurement values between the two techniques. However, this difference does not have any clinical significance. Literature supports the findings of our study.

In diabetes management, regular blood glucose monitoring is essential to ensure glycemic control. The fingertip blood glucose measurement creates a fear of needles, pain and discomfort in patients (14). It has been reported that patients receiving insulin therapy postpone or do not their blood glucose measurements due to pain and fear of needle/finger pricking. It is emphasized that patients avoid measuring blood glucose because they feel pain during fingertip puncture (15). Blood glucose monitoring of diabetic patients receiving treatment in inpatient services is a routine. The fingertip capillary blood glucose measurement technique can create a fear of needles in patients. Alternative ways to solve this problem need to be created for diabetic patients who have a fear of needles. It is thought that this requirement has an important place in terms of patient comfort and compliance with treatment (16).

Our study reveals that blood sugar measurement can create stress in diabetic patients, cause them to feel pain, and make it difficult for them to perform daily living activities. In our study, the dissatisfaction experienced by diabetic patients regarding blood sugar measurement is parallel to the literature (3,6,7). No studies were found in the literature where blood glucose measurement techniques were evaluated in terms of patient satisfaction. This study shows that patient satisfaction may vary depending on the blood glucose measurement technique. According to the fingertip capillary blood glucose measurement technique, the venous blood glucose measurement technique via an intravenous catheter can increase patient satisfaction. Notably, patients with diabetes are more satisfied with the venous blood glucose measurement technique than with other techniques. For routine blood glucose monitoring in inpatient services, it is recommended that patients

with diabetes measure blood glucose from venous blood samples. For routine blood glucose monitoring in inpatient services, it is recommended that diabetic patients' blood glucose measurements be made from venous blood samples via an intravenous catheter.

CONCLUSION

The fingertip capillary blood glucose measurement technique, which uses venous blood via an intravenous catheter, creates less stress, causes less pain intensity, limits daily living activities less, and provides greater patient satisfaction in patients with diabetes.

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Ethical approval: *The study was approved by the ethics committee of İstanbul University-Cerrahpaşa Social and Humanities Research Ethics Committee (Ethical date: 21 February 2023; Approval number 2023/67); institutional permission was received from Zonguldak Provincial Health Directorate Çaycuma State Hospital.*

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Research Article

Explainable Machine Learning Models for Predicting Recurrence in Differentiated Thyroid Cancer

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Abstract

Aim: Differentiated thyroid cancer (DTC) is a common type of cancer that originates in the thyroid gland. This study aimed to predict the recurrence of differentiated thyroid carcinoma, in patient with well-DTC, using explainable machine learning (XAI) models.
Material and Method: The study utilized a dataset from the UCI Machine Learning Repository, which included 383 patients and 13 candidate predictors. After a variable selection process using distance correlation, only four predictors (Response, Risk, T, and N) were retained for model building. Two XAI models, Fast Interpretable Greedy-Tree Sums (FIGS) and Explainable Boosting Machines (EBM), were employed.
Results: The EBM model slightly outperformed the FIGS model in terms of accuracy. The study found that the most influential predictors of Well-DTC recurrence were the response to DTC treatment, risk status according to the American Thyroid Association classification, tumor size (T), and lymph node metastasis (N).
Conclusion: In conclusion, this study successfully identified key risk factors for DTC recurrence using XAI models, providing interpretable insights for clinical decision-making and potential for personalized treatment strategies.

Keywords: Differentiated thyroid cancer, explainable machine learning, risk factors, explainable boosting machine, fast interpretable greedy-tree sums

INTRODUCTION

Thyroid cancer is a type of cancer that begins in the thyroid gland. The thyroid gland is a small gland located at the front of the neck that produces hormones that regulate metabolism (1,2). Thyroid cancer is increasingly common worldwide. The reasons for this increase are not fully known, but it is thought to be due to improvements in diagnostic methods and environmental factors. Thyroid cancer is more common in women than men and is usually diagnosed early-50s (3).

Differentiated Thyroid Cancer (DTC) is the general name for the types of cancer that develop in the thyroid gland. The most common types of thyroid cancer are papillary thyroid cancer and follicular thyroid cancer. DTC usually grows slowly and responds well to treatment when detected early (4,5). Well-DTC is a type of cancer that occurs in the thyroid gland and consists of well-differentiated cancer cells, meaning they look like normal thyroid cells. Well-DTC is the most common type of thyroid cancer and is usually slow-growing and responds well to treatment (6,7).

Explainable Machine Learning (XAI) is an approach that makes it easier to understand the decisions and predictions of machine learning models. Traditional machine learning models are often referred to as "black boxes" because their inner workings and decision-making processes can be difficult to understand. Thanks to XAI, revealing what factors the model relies on and how it reaches its conclusions. This is especially critical in sensitive fields such as medicine to understand and trust the treatment decisions of the models by clinicians (8,9).

It is observed that there is an increase in the number of studies in the literature where thyroid cancer is predicted/classified using XAI methods. In a study (10), 9 classical machine learning methods were considered together with 3 XAI tools (SHAP, Shapash, LIME). In the study where the XGBoost model gave the best performance, the outputs of the relevant model were interpreted with XAI tools and it was determined that the TSH hormone was the variable that

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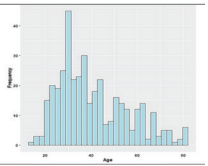
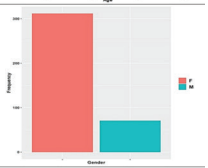
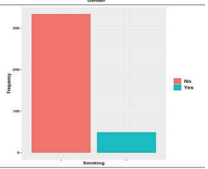
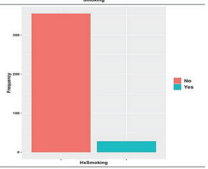
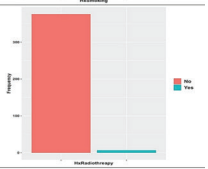
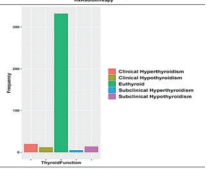
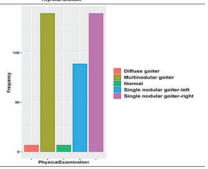
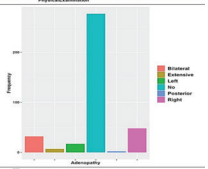
contributed the most to the model performance. In another study (11), the outputs of a rule-based machine learning model were interpreted with the SHAP XAI technique. The use of the rule-based machine learning model and the SHAP technique together in explaining the patterns in the data set resulted in a more reliable prediction of thyroid cancer.

This study aimed to identify candidate predictors of DTC recurrence using two XAI methods and to obtain explainable/interpretable results.

MATERIAL AND METHOD

Data Set

The data set analyzed in this study is titled "Differentiated Thyroid Cancer Recurrence" obtained from the UCI Machine Learning Repository (12) (https://archive.ics.uci.edu/dataset/915/differentiated+thyroid+cancer+recurrence). In addition, this dataset was originally generated in the study (13). Since this study was conducted on a publicly available clinical data set, Ethics Committee approval is not required. The dataset consisted of 13 candidate predictors for predicting well-DTC recurrence and 383 patients. In this dataset, collected over a 15-year period, each patient was followed up for 10 years. The mean age of the study participants was 40.86±15.13 years. The gender distribution was 312 (81.5%) females and 71 (18.5%) males. The distribution of the response variable well-DTC recurrence status (referred to as "Recurred") was 275 (71.8%) "No" and 108 (28.2%) "Yes". A comprehensive overview of the variables is given in Figure 1.

Features	Description of feature	Feature roles	Descriptive statistics	Distribution plots
Age	-	Predictor	N: 383 Mean: 40.87 Std. deviation: 15.13 Median: 37 Min: 15 Max: 82	
Gender	-	Predictor	F: 312 (%81) M: 71 (%19)	
Smoking	-	Predictor	No: 334 (%87) Yes: 49 (%13)	
HxSmoking	Smoking history	Predictor	No: 355 (%93) Yes: 28 (%7)	
lxRadiothreap	Radiation therapy history	Predictor	No: 376 (%98) Yes: 7 (%2)	
hyroidFunctio	-	Predictor	Clinical Hyperthyroidism: 20 (%5) Clinical Hypothyroidism: 12 (%3) Euthyroid: 332 (%87) Subclinical Hyperthyroidism: 5 (%1) Subclinical Hypothyroidism: 14 (%4)	
sicalExamina	-	Predictor	Diffuse goiter: 7 (%2) Multinodular goiter: 140 (%37) Normal: 7 (%2) Single nodular goiter-left: 89 (%23) Single nodular goiter-right: 140 (%37)	
Adenopathy		Predictor	Bilateral: 32 (%8) Extensive: 7 (%2) Left: 17 (%4) No: 277 (%72) Posterior: 2 (%1) Right: 48 (%13)	

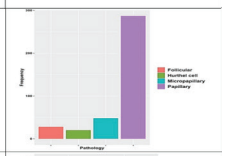
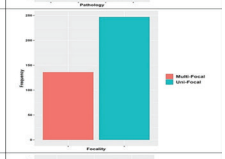
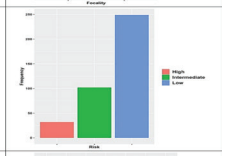
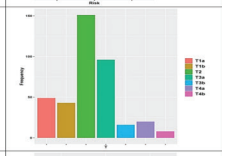
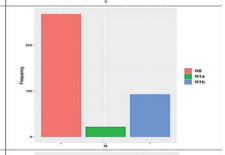
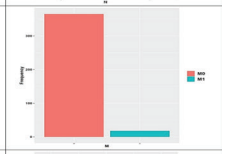
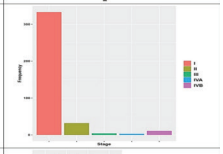
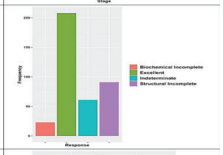
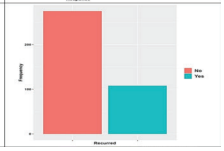
Features	Description of feature	Feature roles	Descriptive statistics	Distribution plots
Pathology		Predictor	Follicular: 28 (%7) Hurthel cell: 20 (%5) Micropapillary: 48 (%13) Papillary: 287 (%75)	
Focality		Predictor	Multi-Focal: 136 (%36) Uni-Focal: 247 (%64)	
Risk		Predictor	High: 32 (%8) Intermediate: 102 (%27) Low: 249 (%65)	
T	TNM grading (Primary tumor)	Predictor	T1a: 49 (%13) T1b: 43 (%11) T2: 151 (%39) T3a: 96 (%25) T3b: 16 (%4) T4a: 20 (%5) T4b: 8 (%2)	
N	TNM grading (Regional lymph nodes)	Predictor	N0: 268 (%70) N1a: 22 (%6) N1b: 93 (%24)	
M	TNM grading (Distant metastasis)	Predictor	M0: 365 (%95) M1: 18 (%5)	
Stage	-	Predictor	I: 333 (%87) II: 32 (%8) III: 4 (%1) IVA: 3 (%1) IVB: 11 (%3)	
Response	-	Predictor	Biochemical Incomplete: 23 (%6) Excellent: 208 (%54) Indeterminate: 61 (%16) Structural Incomplete: 91 (%24)	
Recurred	-	Response	No: 275 (%72) Yes: 108 (%28)	

Figure 1. A comprehensive overview of the variables

Basic Statistical Analyses Phase

The variables considered in the study were summarized as frequency (percentage). Pearson chi-square tests were used to determine whether there was a statistically significant difference between the "Recurred" response variable groups. $p \leq 0.05$ was accepted as the statistical significance level.

Machine Learning Modeling Phase

Data preprocessing

In this study, the distance correlation-based variable selection method was applied to reduce model complexity and filter out variables that are not expected to contribute to the predictive performance of the machine learning models. Distance correlation is a statistical method used to measure the dependence relationship between two random variables. Unlike the classical Pearson correlation coefficient, it can detect not only linear relationships but also non-linear relationships. Thanks to this feature, it can reveal complex dependency structures between variables (14). This analysis, interpreted as a classical Pearson correlation coefficient, is applied sequentially between response and predictor variables. The cut-off value was set at 0.5 and variables with correlation values below this value were removed from the data set. In addition, to test validation of the predictive performance of machine learning models, the data set was randomly divided into two parts as training (80%) and test (20%) data sets. While the model training process was performed on the training data set, learning performance was evaluated on the test data set.

Machine learning models

Fast Interpretable Greedy-Tree Sums (FIGS)

FIGS is a tree-based model that generalizes Classification and Regression Trees (CART) to reduce bias and unexplained variance and aims to be both fast and interpretable. FIGS takes a greedy approach to the training process, building trees quickly. This helps compensate for the weaknesses of a single tree and constructs a more powerful and generalizable model. The generated trees have a simple and understandable structure to make it easier to understand the reasons for the model's predictions and bring transparency to decision-making processes. It can be used in both classification and regression problems, i.e. it is suitable for predicting both categorical and continuous features (15).

Explainable Boosting Machines (EBM)

Explainable Boosting Machines (EBM) is a machine learning model that offers both high prediction performance and the ability to explain the reasons for the model's decisions. It combines the power of traditional gradient boosting and generalized additive models with interpretability. EBM can model complex relationships using gradient boosting and achieve high prediction accuracy, making it suitable for a variety of classification and regression problems. EBM provides interpretability by visualizing and quantifying the impact of each feature on the prediction, thus making it easier to understand what factors the model's decisions are based on and bringing transparency to decision-making processes. It can work with different types of features (numeric, categorical, ordinal) and model various binary interactions, making it adaptable to different types of data. Among its advantages are its combination of high predictive performance and interpretability, its ability to work with different data types and features, its fast training process and scalability, and its use of various techniques to reduce the risk of overfitting. EBM is especially used in areas such as credit risk assessment, medical diagnosis, etc., where it is important to explain the reasons for the model's decisions (16,17).

Metrics for evaluating the predictive performance of the models

In this study, accuracy (ACC), the area under the receiver operating characteristics curve (AUC), F1-score (F1), logarithmic loss (Log-Loss), and Brier score (Brier) metrics were used to evaluate the binary classification performance of the models. When the model prediction performance is evaluated in the range of 0 to 1, ACC, AUC and F1 metrics with values of 1 or close to 1 indicate that the model has a high level of predictive performance, while Log-Loss and Brier metrics with values of 0 or close to 0 indicate that the model has a high level of predictive performance.

The Environments Where the Analyses were Performed

In this study, R (version 4.1.2) was used for statistical analysis, and Python (version 3.10.0) was used for machine learning modeling. Python language-based XAI library PiML (18) was used to construct the modeling workflow.

RESULTS

There were no missing values in the data set. Since all variables except age are categorical, no transformation method was applied to the data set. After applying the distance correlation-based variable selection algorithm, 4 of the 13 predictor variables (Response, Risk, T, and N) were selected. The findings of the related variable selection analysis for the top 10 variables are given in Figure 2.

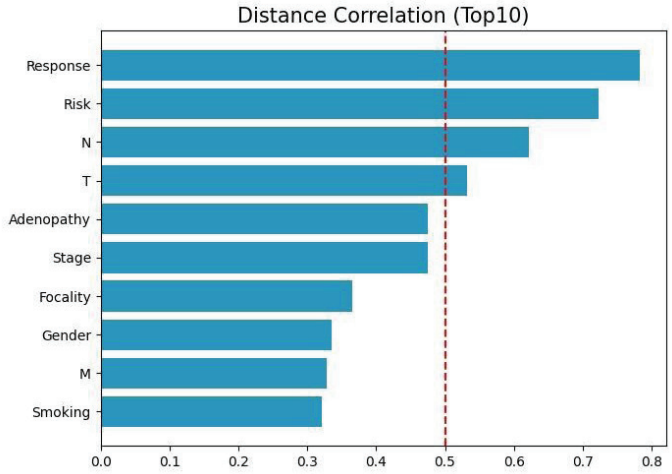


Figure 2. The findings of the related variable selection analysis for the top 10 variables

The inferential statistics results for the 4 variables obtained after the variable selection analysis are given in Table 1.

Table 1. Inferential statistics findings of Well-DTC groups in terms of predictor variables

Predictor		Well-DTC recurrence		Pearson chi square statistics	p
		No (n=275)	Yes (n=108)		
Risk	High	0 (0.0%)	32 (29.6%)	208.83	<0.001
	Intermediate	38 (13.8%)	64 (59.3%)		
	Low	237 (86.2%)	12 (11.1%)		
T	T1a	48 (17.5%)	1 (0.9%)	141.29	<0.001
	T1b	38 (13.8%)	5 (4.6%)		
	T2	131 (47.6%)	20 (18.5%)		
	T3a	55 (20.0%)	41 (38.0%)		
	T3b	2 (0.7%)	14 (13.0%)		
	T4a	1 (0.4%)	19 (17.6%)		
	T4b	0 (0.0%)	8 (7.4%)		
N	N0	241 (87.6%)	27 (25.0%)	153.19	<0.001
	N1a	12 (4.4%)	10 (9.3%)		
	N1b	22 (8.0%)	71 (65.7%)		
Response	Biochemical incomplete	12 (4.4%)	11 (10.2%)	309.47	<0.001
	Excellent	207 (75.3%)	1 (0.9%)		
	Indeterminate	54 (19.6%)	7 (6.5%)		
	Structural incomplete	2 (0.7%)	89 (82.4%)		

The overall accuracy (ACC) values obtained for both FIGS and EBM models as a result of training with Risk, T, N, and Response variables are presented in Figure 3. In addition, detailed classification performance metric values obtained from both training and test datasets for the two models are reported in Table 2.

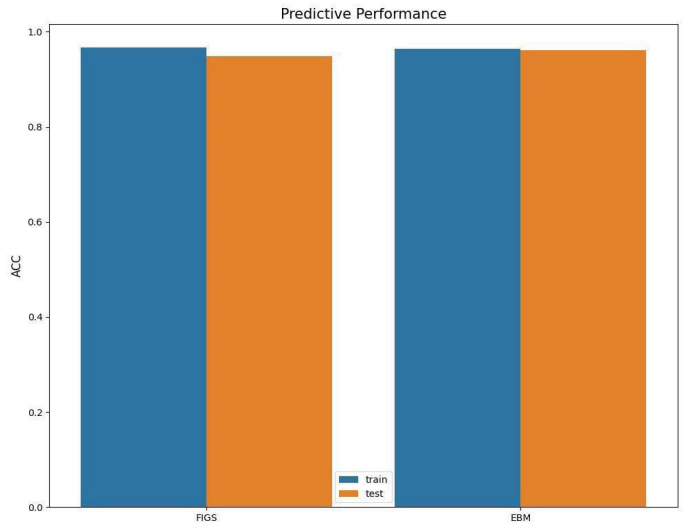


Figure 3. The overall accuracy (ACC) values obtained for both FIGS and EBM models

Table 2. Classification performance metrics for both EBM and FIGS models

Models	Data source	Performance metrics				
		ACC	AUC	F1	LogLoss	Brier
FIGS	Train	0.9673	0.9964	0.9444	0.1438	0.0283
	Test	0.9481	0.9964	0.9000	0.1534	0.0319
EBM	Train	0.9641	0.9922	0.9364	0.1015	0.0284
	Test	0.9610	0.9927	0.9189	0.0939	0.0268

Figure 4 shows the global effect importance levels of the single and binary interaction states of the variables obtained from the EBM model.

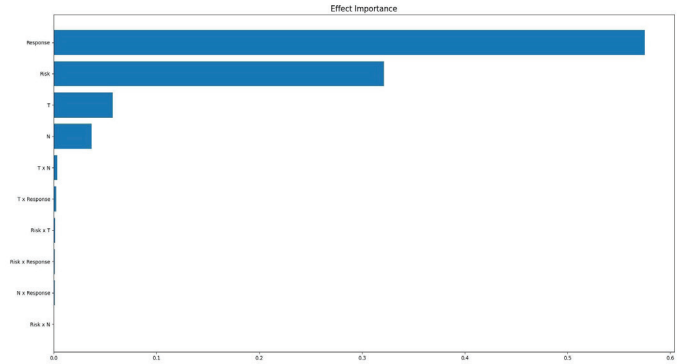


Figure 4. Global effect importance levels of the single and binary interaction states of the variables obtained from the EBM model

Figure 5 shows the local effect findings of the EBM model for two randomly selected patients with positive and negative recurrence labeling. Here,

- For the "Risk" variable, 0, 1, and 2 values indicate high, medium, and low risk respectively.
- For the "Response" variable, values 0, 1, 2, and 3 represent the categories Biochemical Incomplete, Excellent, Indeterminate, and Structural Incomplete, respectively.
- For the "T" variable, 0, 1, 2, 3, 4, 5, and 6 values indicate T1a, T1b, T2, T3a, T3b, T4a, and T4b categories, respectively.
- For the "N" variables values 0, 1, and 2 represent N0, N1a, and N1b categories, respectively.

The classification rules and uncalibrated recurrence risks based on the two samples shown in Figure 5 are presented in Table 3.

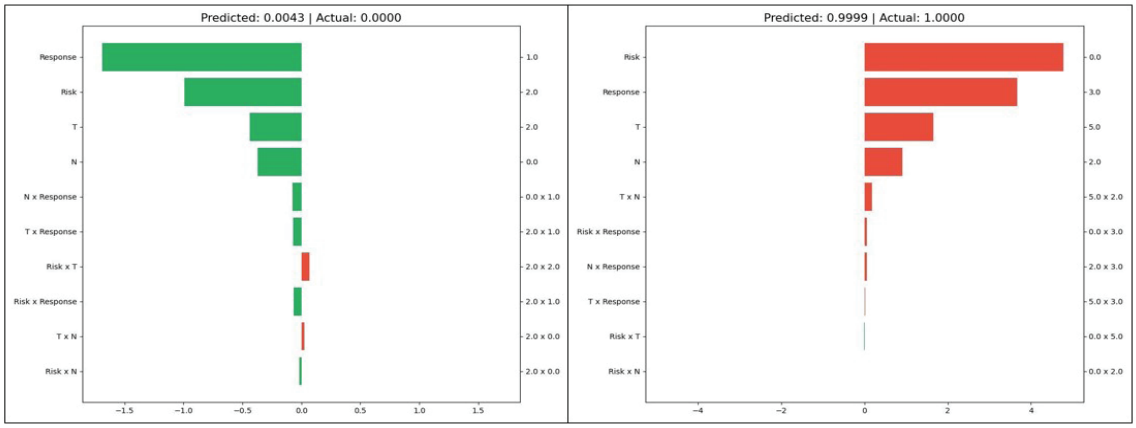


Figure 5. The local effect findings of the EBM model for two randomly selected patients with positive and negative recurrence labeling

Table 3. The classification rules obtained from the EBM model

Real case	Rules	Model prediction	Uncalibrated recurrence risk (%)
Recurrence positive	Risk = "High" & Response = "Structural Incomplete" & T= "T4a" & N = "N1b"	Recurrence positive	0.9999
Recurrence negative	Response = "Excellent" & Risk = "Low" & T = "T2" & N = "N0"	Recurrence negative	0.0043

DISCUSSION

In this study, we aimed to identify risk factors that can be used as decision support in the prediction of recurrence of well-differentiated thyroid carcinoma with XAI models such as FIGS and EBM, which have gained increasing popularity in recent years. The data set considered in the study consisted of 13 predictor variables in the first stage. This number decreased to 4 after the variable selection analysis. Statistically significant differences were observed between the replication groups in terms of the relevant variables (Table 1).

When the classification performances of the EBM and FIGS models are evaluated, it is observed that both models give similar results, but the EBM model performs slightly better than FIGS. Since the EBM model is the best-performing model, the prediction explanations of the relevant model have been considered. In fact, when the global effect importance graph in Figure 4 is evaluated, it is seen that the order of the predictors affecting the classification performance of the model is "Response", "Risk", "T" and "N". The variable pairs seen under the effect values of single variables and connected with the "x" symbol are interaction terms. As can be observed from Figure 4, the single effects of the relevant risk factors were more effective on the classification performance of the EBM model. It was observed that the effect of the binary interaction terms of the relevant variables on the classification performance remained weak.

When Figure 5 and Table 3 are examined together, it is observed that if the rule combination, Risk= "High" & Response= "Structural Incomplete" & T= "T4a" & N= "N1b" the risk of well-DTC recurrence has a high probability of occurring.

In the current study, the greatest contribution to the risk of recurrence occurred in patients at high risk according to the American Thyroid Association (ATA) classification (19). In thyroid cancer, the term "structural incomplete" is often used in a pathology report and refers to the fact that microscopic examination after surgical removal of the thyroid gland shows that there is uncertainty as to whether the tumor was completely removed (20). The prevalence of structural incomplete is correlated with thyroid cancer risk stratification (21). The T4a classification is part of the TNM system for staging thyroid cancer (22). This classification indicates that the cancer is at an advanced stage and treatment options may be more limited. One study (23) also reported that tumor sizes over 4 cm are a risk factor for recurrence of follicular thyroid cancer, a subtype of DTC. The N0, N1a and N1b classifications for thyroid cancer are part of the TNM staging system, which indicates the spread of cancer to lymph nodes (metastasis). N1b classification indicates that the cancer is at a more advanced stage and treatment options may be more limited. One study concluded that nodal involvement in DTCs may increase the risk of recurrence (24).

Similarly, if the resulting classification rule is such, *Response= "Excellent" & Risk= "Low" & T= "T2" & N= "N0"* the risk of well-DTC recurrence has a very low probability. As expected, this suggests that the risk of well-DTC is very low in the presence of a good response to treatment, low recurrence, tumors smaller than 2 cm, and no cancer in regional lymph nodes.

When other machine learning-based studies using this dataset are evaluated, the support vector machine model (SVM) showed better classification performance than other classification models (sensitivity=0.99, specificity=0.97, and AUC=0.99) in the study carried out by Borzooei et al. (13). The results obtained are close to the findings of the present study, and it is a disadvantage for clinicians that the SVM model is not within the scope of explainable models such as the EBM and FIGS models considered in this study.

Therefore, the results obtained from the model are only related to classification performance. Moreover, the high classification performance obtained in our study was achieved with only 4 variables, which may suggest that modeling the remaining 9 variables is unnecessary.

In another study (25) dealing with the same dataset, after various preprocessing analyses, the dataset was modeled with the ensemble stacking algorithm and the related model showed a classification accuracy of 97%. This finding is less than the EBM and FIGS models considered in this study.

CONCLUSION

In this study, candidate risk factors that can be used to predict the risk of recurrence in patients with well-DTC were determined by XAI methods such as EBM and FIGS. According to the outputs obtained from the EBM model, which has a better classification performance, the response to DTC treatment, risk status, tumor size, and location, and the spread of cancer to nearby lymph nodes were determined as the most important risk factors for recurrence. This study has some limitations. The use of data obtained from a single center with relatively small sample size and the absence of an external cohort to increase the generalizability of the results are the main limitations of this study. As further research, it is recommended that researchers construct a meta-model using more XAI models together to obtain outputs with higher validity and reliability.

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Conflict of interest: *The authors have no conflicts of interest to declare.*

Ethical approval: Since this study was conducted on a publicly available clinical data set, Ethics Committee approval is not required.

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MEDICAL RECORDS-International Medical Journal

Research Article

Impact of Mental Health Literacy on Mental Health and Renal Function in Dialysis Patients: A Cross-Sectional Study

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Abstract

Aim: This article aims to assess Mental Health Literacy (MHL) in dialysis patients and examine their impact on anxiety, depression and physical health.
Material and Method: The study was conducted in the Hemodialysis Unit of Karaman Training and Research Hospital between March and June 2024. A total of 87 patients who met the inclusion criteria and agreed to participate were included in the study. Data were collected using a semi-structured sociodemographic form, Mental Health Literacy Scale, Hamilton Depression Scale and Hamilton Anxiety Scale. Biochemical parameters were obtained from electronic patient records.
Results: The frequency of depression was 45%. There was no significant difference in MHL points among individuals with and without depression. Furthermore, no correlation was found between MHL and duration of disease or dialysis. A significant relationship was found between Total and Resource subscale scores of MHL and estimated glomerular filtration rate (eGFR).
Conclusion: The frequency of depression was higher in dialysis patients than in the general population. Albeit no significant difference in MHL was observed between patients diagnosed with depression and those without, the significant relationship between MHL and eGFR suggests that interventions to increase MHL may have positive effects on disease progression.

Keywords: Mental health literacy, depression, hemodialysis, creatinine, renal function

INTRODUCTION

Mental health literacy (MHL) encompasses a range of competencies, including the capacity to prevent the onset of mental illness, the ability to identify early signs of mental distress, effective self-management techniques for non-advanced problems, and the skills required to provide assistance to others (1). For example, in an Australian study, when participants were presented with a case study of a patient with depression, only 39% correctly identified the condition, and 11% incorrectly considered depression to be a physical ailment (2). These deficiencies in MHL result in impaired communication between patients and health professionals (3). This lack of knowledge also affects treatment response and the decision to seek medical help for mental disorders. In one study, the attribution of psychiatric illnesses to metaphysical causes was shown to lead to non-medical treatment seeking and impaired treatment collaboration (4). An important goal of MHL efforts is to reduce stigma against mental disorders. In one study, it was reported that stigmatisation not only affects the decision to seek medical help but also causes negative physical outcomes (5).

The experience of chronic illness has the potential to alter an individual's perspective on life, with the potential for significant psychological effects (6). Despite the encouraging developments in the treatment of chronic physical illnesses, the acceptance of certain consequences remains a significant challenge for the individual. This can result in adverse mental health outcomes, particularly depression and anxiety (7). For these reasons, it is pivotal that interventions are developed to enhance self-help skills in the context of chronic physical illnesses (8). In this context, a study conducted in Iran demonstrated that the provision of psychoeducation to patients with Type 2 Diabetes led to an increase in treatment compliance and MHL (7). Consequently, it is hypothesised that a range of psychosocial interventions can address the psychological needs associated with chronic physical diseases (9).

CITATION
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Mental health literacy is an issue that is becoming increasingly foremost in the field of health. A review of the literature showed that there is a lack of research examining the relationship among MHL, psychiatric illness and disease parameters in patients on dialysis. Given the evidence that psychoeducation has a beneficial effect on depression in dialysis patients (10) and also has a positive impact on treatment adherence(11), it is essential to assess MHL in this patient group. The goal of this research was twofold: first, to assess and improve the MHL of dialysis patients; second, to investigate the effect of MHL on depression, anxiety and renal function in dialysis patients.

In this context, the hypotheses to be tested in our study are as follows.

Hypothesis 1:

H0: MHL has no effect on depression and anxiety levels in dialysis patients,

H1: MHL affects depression and anxiety levels in dialysis patients.

Hypothesis 2:

H0: MHL has no effect on renal function in dialysis patients,

H1: MHL affects renal function in dialysis patients.

MATERIAL AND METHOD

This research was conducted at Karaman Training and Research Hospital Haemodialysis Unit, March-June 2024. In the specified time period, 112 patients were followed in the haemodialysis unit, undergoing haemodialysis 3 days a week. Patients were informed about the study procedure and the social, personal and scientific benefits of the study. Inclusion criteria: 1. Diagnosed end-stage renal disease, 2. age >18 years, 3. haemodialysis treatment more than 6 months. Exclusion criteria: 1. a lack of willingness to participate in the study, 2. severe cognitive, sensory and motor impairment, 3. illiteracy. G*Power was used to determine the sample size. Calculations using a 5% margin of error and an effect size of 0.3 to achieve 80% power showed that a minimum of 82 participants were required. Ethical approval was obtained from the Ethics Committee of Karamanoğlu Mehmetbey University Faculty of Medicine (dated 27.02.2024, no. 01.2024/03).

Patients who were not included in the study; 8 patients were excluded because they were illiterate, 6 patients were excluded because of severe cognitive impairment, 6 patients were excluded because of severe visual/ hearing impairment, 3 patients were excluded because they did not want to participate and 2 patients were excluded because they had not received dialysis treatment for more than 6 months". After assessments, written informed consent was obtained from patients meeting inclusion and no exclusion criteria (n=87). Interviews with participants to optimise completion of the scales and completion of the scales were conducted on the day after dialysis. Data were collected using a semi-structured socio-demographic data form. Participants were asked to complete the Mental Health Literacy Scale. Then, Hamilton Depression Scale and the Hamilton Anxiety Scale were administered. These scales have been shown to be valid and reliable in evaluating anxiety and depression in haemodialysis patients (12). In addition, biochemical parameters were recorded during the assessment from the patients' electronic records.

Data Collection Tools

Sociodemographic data form: The researcher-designed personal information form was administered face-to-face to obtain data on age, gender, educational status, employment status, presence of additional physical and psychiatric illnesses, and duration of dialysis. In addition, serum urea, creatine, sodium, haemoglobin, eGFR (estimated glomerular filtration rate), calcium and phosphorus levels were recorded from the patients' electronic records.

Hamilton Depression Scale (Ham-D): It is a 17-item self-report instrument for the assessment of depressive symptoms experienced over the past week (13). The maximum total score on the Hamilton Scale for Depression is 53. Points between 0 -7 are classified as "no depression," 8-15 as "mild depression," 16-28 as "moderate depression," and scores of >28 as "severe depression." The test-retest reliability, internal consistency, and inter-rater reliability coefficients for the Turkish version were .85, .75, .87, and .98, respectively (14).

Hamilton Anxiety Scale (Ham-A): The scale is interviewer-administered and comprises a total of 14 items, that ask about both mental and physical symptoms. The point for each item ranges between 0-4, while the total scale score ranges from 0-56. Items 1, 2, 3, 5 and 6 of the scale are designed to assess psychic anxiety, while items 4, 7-13 are designed to evaluate somatic anxiety. The validity and reliability study of the scale was conducted by Yazıcı et al. in Türkiye. In the Turkish version, the item-specific correlation coefficients were each 0.72, whereas the overall correlation coefficient was 0.94 (15).

Mental Health Literacy Scale (MHL): The Mental Health Literacy Scale, originally developed by Jung et al., underwent a Turkish validity and reliability assessment conducted by Göktaş et al. This scale includes three sub-dimensions and a total of 22 items. These sub-dimensions are designated as follows: Knowledge-Oriented MHL (items 1-10), Beliefs-Oriented MHL (items 11-18), and Resource-Oriented MHL (items 19-22). The scale's scores range from 0 to 22. The initial 18 questions, which cover the first two sub-dimensions, follow a six-point Likert format with the response options: 'strongly agree', 'agree', 'undecided', 'disagree', 'strongly disagree', and 'don't know'. The four questions within the Resource-Oriented MHL sub-dimension are answered with 'yes' or 'no'. In this scoring system, 'strongly agree', 'agree', and 'yes' responses are assigned 1 point, while all other responses receive 0 points. Additionally, items 11-18, which belong to the Belief-Oriented RSF subscale, are reverse scored. The internal consistency analysis coefficient of the Turkish version was 0.71 and the test-retest coefficient was 0.72 (16,17).

Collection of Blood Samples and Biochemical Analyses: Blood analysis to measure urea, creatinine, eGFR, calcium, haemoglobin, sodium, potassium and phosphorus levels was performed between 08:00 and 10:00 in the morning on a nondialysis day. Blood samples were taken from the antecubital vein with a sterile needle and immediately placed in two separate tubes, 2 ml with EDTA and 5 ml without anticoagulant, and immediately centrifuged. Serum samples were analysed for serum urea, creatinine, eGFR, calcium, sodium, potassium and phosphorus levels by spectrophotometry using a Beckman Coulter AU5800 analyser (Beckman Coulter, Nyon, Switzerland) and haemoglobin levels were measured using a BC-6800 (Mindray, Shenzhen, China).

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) version 25 Windows (SPSS Inc., Chicago, IL, USA) was used for statistical analyses. All participants were classified as depressed (45%) or non-depressed (55%) based on the cutoff score of the Ham-D (HamD>7, indicative of depression). The normality of the variables was evaluated using both visual methods (such as histograms and probability plots) and the Shapiro-Wilk test for analytical assessment. For comparing categorical data between the two groups, the chi-squared test was employed. Continuous variables were analyzed using the t-test for normally distributed data and the Mann-Whitney U test for data that did not follow a normal distribution. Relationships between variables were examined using the Spearman correlation test, considering p-values below 0.05 to be statistically significant.

RESULTS

The mean age of patients with depression (61.18±15.78) was higher than that of patients without depression (53.63±16.53) (p=0.033). The plurality of depressed patients were married (71.8%), had completed primary school (66.7%), whereas the majority of non-depressed patients were married (66.7%) and had completed primary school (58.3%) (p>0.05). The duration of disease and dialysis did not differ significantly between the two groups (p=0.09, p=0.982). The majority of the depressed group (61.5%) were unemployed, whereas the majority of the non-depressed group (52.1%) were retired (p=0.047) (see Table 1).

Table 1. Comparison of socio-demographic data between depressed and non-depressed patients

		Depressed (n=39)	Non depressed (n=48)	χ^2/t	df	p
Age mean(SD)		61.18 (15.78)	53.63 (16.53)	2.16	85	0.03[a]
Gender n (%)	**Male**	22 (56.4)	37 (77.1)	4.21	1	0.04[b]
	Female	17 (43.6)	11 (22.9)			
Marital status n (%)	**Married**	28 (71.8)	32 (66.7)	2.36	3	0.50[b]
	Single	6 (15.4)	12 (25.0)			
	Divorced	1 (2.6)	0 (0.0)			
	Widowed	4 (10.3)	4 (8.3)			
Education n (%)	**Primary school**	26 (66.7)	28 (58.3)	0.64	3	0.88b
	Middle school	5 (12.8)	8 (16.7)			
	High school	6 (15.4)	9 (18.8)			
	University	2 (5.1)	3 (6.3)			
Income n (%)	**Low**	12 (30.8)	7 (14.6)	4.22	2	0.12[b]
	Medium	25 (64.1)	40 (83.3)			
	High	2 (5.1)	1 (2.1)			
Psychiatric illness n (%)	**Yes**	8 (20.5)	6 (12.5)	1.02	1	0.31[b]
	No	31 (79.5)	42 (87.5)			
Disease duration n (%)	**<1 year**	4 (10.3)	0 (0.0)	6.48	3	0.09[b]
	≥1-<3 years	5 (12.8)	5 (10.4)			
	≥3-<6 years	7 (17.9)	6 (12.5)			
	≥6 years	23 (59.0)	37 (77.1)			
Dialysis duration n (%)	**<1 year**	6 (15.4)	7 (14.6)	0.17	3	0.98[b]
	≥1-<3 years	11 (28.2)	12 (25.0)			
	≥3-<6 years	8 (20.5)	10 (20.8)			
	≥6 years	14 (35.9)	19 (39.6)			
Employment status n (%)	**Employed**	2 (5.1)	6 (12.5)	6.12	2	0.047[b]
	Unemployed	24 (61.5)	17 (35.4)			
	Retired	13 (33.3)	25 (52.1)			
Living area n (%)	**City center**	30 (76.9)	38 (79.2)	4.65	2	0.09[b]
	District	5 (12.8)	1 (2.1)			
	Village/town	4 (10.3)	9 (18.8)			

a: independent T test, b: Chi square test

The comparison of the biochemical values of both groups is shown in Table 2. The mean eGFR of patients with depression (25.24±11.52) was higher than that of patients without depression (22.02±14.85) (p=0.044). The mean sodium level of patients with depression (133.02±21.25) was lower than that of patients without depression (137.38±2.79) (p=0.039). The two groups did not exhibit any statistically significant differences in the levels of urea, creatinine, calcium, hemoglobin, potassium, or phosphorus. No significant differences were observed in the overall and subscale scores of the MHL scale between the two groups (p>0.05) (Table 2).

Table 2. Comparison of biochemical data and MHL scores of patients with and without depression

Variable	Depressed (n=39) Mean (SD)	Non-depressed (n=48) Mean (SD)	t/df	p
Urea (mg/dL)	39.65 (19.01)	40.66 (20.05)	901/85	0.07[a]
Creatinine (mg/dL)	2.73 (1.21)	3.14 (1.16)	716/85	0.06[a]
eGFR	25.24 (11.52)	22.02 (14.85)	700/85	0.044[a]
Ca^{++} (mg/d)	8.80 (0.62)	8.85 (0.72)	855/85	0.48[a]
Hemoglobin(g/dL)	10.89 (1.41)	11.06 (1.61)	-0.517/85	0.60[b]
Na^{+} (mmol/L)	133.02 (21.25)	137.38 (2.79)	695/85	0.03[a]
K^{+} (mmol/L)	4.34 (1.13)	4.35 (1.02)	913/85	0.84[a]
P^{+} (mg/dL)	4.52 (1.26)	4.97 (1.28)	-1.63/85	0.10[b]
MHL-knowledge	6.31 (2.26)	7.08 (2.42)	762/85	0.13[a]
MHL-beliefs	3.28 (2.05)	3.06 (1.70)	0.545/85	0.58[b]
MHL-resource	2.87 (1.10)	2.92 (1.25)	885/85	0.64[a]
MHL-total	12.46 (4.06)	13.06 (4.05)	-0.687/85	0.49[b]

a: Mann Whitney U, b: independent T test; MHL: mental health literacy, eGFR: estimated glomerular filtration rate, Ca^{++}: calcium, Na^{+}: sodium, K^{+}: potassium, P^{+}: phosphorus

Table 3 illustrates the correlation among the psychometric test results for the participants and the duration of dialysis, disease duration and eGFR values. The results indicated that no statistically significant relationship was observed among the MHL scale and subscale scores and Ham-D, Ham-A scores, disease duration and dialysis duration (p>0.05). A statistically significant correlation was identified among eGFR and both MHL-Source and MHL-Total scores (r=0.282, p<0.01; r=0.217, p<0.01, respectively).

Table 3. Correlations between psychometric test scores and disease duration, dialysis duration and eGFR of all participants

		MHL-knowledge	MHL-beliefs	MHL-resource	MHL-total	Duration of Illness	Duration of dialysis	HamD	HamA	eGFR
MHL-knowledge	r	–								
MHL-beliefs	r	0.28**	–							
MHL-resource	r	0.44***	0.21*	–						
MHL-total	r	0.85***	0.67***	0.64***	–					
Duration of illness	r	-0.11	0.08	0.04	-0.01	–				
Duration of dialysis	r	-0.16	0.01	-0.14	-0.12	0.63***	–			
Ham-D	r	-0.10	0.03	-0.04	-0.04	-0.15	-0.01	–		
Ham-A	r	-0.11	-0.01	-0.04	-0.07	-0.11	0.02	0.88***	–	
eGFR	r	0.17	0.06	0.28**	0.21**	-0.10	-0.13	0.09	0.12	-

*p<0.05, **p<0.01, ***p<0.001; Spearman Correlation test was used; MHL: mental health literacy, eGFR: estimated glomerular filtration, Ham-D: Hamilton Depression Scale, Ham-A: Hamilton Anxiety Scale

DISCUSSION

This research aimed to assess the level of mental health literacy among individuals with end-stage renal failure who are undergoing hemodialysis therapy. Moreover, the research sought to determine the freuqency of depressive symtomps among these patients, as well as to examine the correlation between these psychological states and biochemical data related to the disease.

The findings showed that 45% of the participants were suffered from depression. No significant differences were observed in MHL levels among patients with and without depression. Furthermore, MHL was not associated with disease duration or dialysis duration. A correlation was identified between the MHL-Total,MHL-Source scores and the eGFR.

A comprehensive meta-analysis conducted by Palmer et al. revealed that 39% of dialysis patients exhibited depressive symptoms according to rating scales, with approximately one-quarter of them being diagnosed with depression following a diagnostic interview (18). A different study

determined that the frequency of depressive symptoms among patients undergoing dialysis treatment was 27% (19). Similarly, the frequency of depression in our study was found to exceed the general population prevalence (7.5%) (20). In this context, chronic physical conditions such as end-stage renal failure may be an element of risk for depression. It has been reported that factors such as disturbances in calcium metabolism, oxidative stress, increased amounts of pro-inflammatory cytokines, nutritional disturbances and disease-related disability may be the causes of depression in dialysis patients (21-24).

Gazmararian et al. (2005) found that people with reduced MHL were 2.7 times more prone to experiencing depression than those with elevated MHL (25). Similarly, Amone-P'olak et al. reported that MHL level predicts the occurrence of mental problems such as depression (26). A lack of adequate information about psychological health issues, stigmatisation and difficulties in accessing health services have been identified as risk factors for various psychiatric disorders, especially depression (27). A review of the literature reveals no studies that examine the association between MHL and psychiatric disorders in patients undergoing haemodialysis treatment. Consequently, although there is no data available for comparison with the results of our study, there are researches on the psychological effects of MHL in diabetes, which is one of the leading causes of end-stage renal failure. In one study, low MHL was demonstrated to be associated with diabetes-related burnout in participants with Diabetes Mellitus. Similarly, a research conducted in Poland demonstrated that brief psychological interventions were effective in reducing diabetes-related burnout and stress burden (28). However, a meta-analysis investigating the effect of psychological interventions in diabetes demonstrated that no psychological intervention was more efficacious than traditional methods in reducing diabetes-related distress (29). Similarly, our research did not identify a significant relationship among MHL, Ham-D and Ham-A scores. Although it remains challenging to elucidate these contradictory findings, potential explanations include discrepancies in study design, the psychological resilience of individuals, the assessment tools employed, and cultural variations. For instance, previous studies have reported that the effects of MHL have mostly been studied in Western societies, and that cultural values may influence beliefs about mental health and coping strategies for mental illness (30).

One of the most notable findings of our study was the significant relation between MHL-Total and the MHL-Source point and eGFR. A review of the literature revealed no studies investigating the association between MHL and disease-related parameters in haemodialysis patients. Given these findings, it can be postulated that interventions designed to enhance the MHL in haemodialysis patients may exert a beneficial influence on the progression of the disease. For instance, psychoeducational interventions in diabetic patients have been demonstrated to be linked with lower fasting glucose levels and enhanced treatment adherence (31). Furthermore, a reduction in MHL has been linked to a decline in self-care behaviours and an adverse impact on the progression of the illness (32). Given the positive effect of psychoeducational interventions on self-efficacy, adherence and mental well-being in dialysis patients (33), it is critical to develop practices that improve MHL in these patients. In this regard, it is important to increase mental health screening and services in dialysis centres. In addition, interventions such as psychoeducation (34) and cognitive behavioural therapy (35) for patients and their families can increase MHL levels and have a positive impact on disease prognosis.

While our study yielded noteworthy findings, it is substantial to acknowledge the presence of certain limitations. Limitations to the generalisability of our findings may be influenced by the fact that our study was conducted at a single site, the relatively small sample size, and the homogeneity of participants' socio-cultural backgrounds. In addition, the scale used to measure MHL is based on self-report, which may result in response bias. The lack of use of diagnostic tools such as the SCID may have led to undiagnosed psychiatric conditions being missed, thereby affecting the results obtained. Finally, it is not possible to establish a definitive cause-and-effect relationship due to the nature of a cross-sectional study.

CONCLUSION

To conclude, our results show a high frequence of depressive symptoms among dialysis patients. No significant difference was observed in MHL among patients with and without depression. However, a significant association was identified among MHL and estimated glomerular filtration rate (eGFR). These findings indicate that interventions aimed at enhancing MHL may have a beneficial impact on disease progression. Further large-scale and multicentre studies are required so as to gain a deeper understanding of the impacts of MHL on chronic disease management and outcomes.

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Research Article

Anxiety in Pregnancy: Comparing High-Risk and Normal Pregnant Women through the Beck Anxiety Inventory

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Abstract

Aim: Pregnancy is a critical life event that necessitates adaptation to numerous physical and psychological changes. While it often brings positive emotions, it can also induce significant stress and anxiety, especially in high-risk scenarios with potential maternal and fetal health concerns. This study aims to investigate whether there is a difference in anxiety levels between pregnant women under routine obstetric care and those under perinatology care for high-risk pregnancies.
Material and Method: This cross-sectional survey was conducted at the Giresun Training and Research Hospital Obstetrics and Gynecology Hospital. Ninety pregnant women aged 18-40 were divided into two groups: 45 women receiving routine obstetric care (Group I) and 45 women receiving perinatology care for high-risk pregnancies (Group II). Data were collected using a 20-question socio-demographic and medical characteristics questionnaire, along with the Beck Anxiety Inventory.
Results: The study found no significant difference in socio-demographic characteristics such as education, employment, and income status between the two groups ($p>0.05$). The Beck Anxiety Inventory scores indicated that both groups predominantly experienced low-level anxiety: 82.2% in Group I and 86.7% in Group II. Moderate anxiety was reported by 15.6% of Group I and 11.1% of Group II. Only 2.2% of participants in each group experienced severe anxiety. There was no significant difference in the overall anxiety levels between the two groups ($p>0.05$), although Group I reported higher heart palpitations ($p<0.05$).
Conclusion: The findings suggest that while high-risk pregnancies managed by perinatology specialists do not significantly differ in overall anxiety levels from normal pregnancies, specific anxiety symptoms like heart palpitations may vary. This underscores the need for targeted anxiety management interventions for pregnant women, regardless of risk status, to ensure better maternal and fetal outcomes.

Keywords: Pregnancy anxiety, Beck Anxiety Inventory, perinatology, anxiety management in pregnancy

INTRODUCTION

Pregnancy is a pivotal period of profound physiological, emotional, and psychological transformations. While it is often a time filled with anticipation and joy, it can also be fraught with significant stress and anxiety. Various factors, including hormonal changes, physical discomforts, and concerns about the health and well-being of the fetus and the impending responsibilities of motherhood, influence these psychological states during pregnancy (1).

The prevalence of anxiety during pregnancy is notably high, with studies indicating that approximately 15-23% of pregnant women experience clinically significant anxiety symptoms (2). Anxiety during pregnancy is not only distressing for the expectant mother but also has been associated with adverse outcomes for both the mother and the fetus. Elevated anxiety levels have been linked to complications such as preterm birth, low birth weight, and developmental issues in children. Additionally, high maternal anxiety can adversely affect maternal-infant bonding, potentially leading to long-term emotional and behavioural problems in children (3).

High-risk pregnancies, defined by the presence of medical or obstetric complications that may endanger the health of the mother or fetus, further amplify the psychological burden on expectant mothers. These complications can include conditions such as preeclampsia, gestational diabetes, and fetal growth restrictions, among others. Women with high-risk pregnancies are subjected to more frequent medical interventions and heightened monitoring, which can exacerbate feelings of anxiety and stress. The uncertainty surrounding the pregnancy outcome and the potential for adverse events create a significant psychological strain on these women (4,5).

Perinatology, a subspecialty of obstetrics, focuses on managing high-risk pregnancies. Perinatologists are crucial in identifying, monitoring, and managing risk factors

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to optimise maternal and fetal outcomes (6,7). However, the psychological support provided to these women is equally vital. Studies have shown that psychological interventions, including counselling, stress management techniques, and social support, can significantly alleviate anxiety and improve pregnancy outcomes (8).

The purpose of this study was to investigate the differences in anxiety status in pregnant women receiving routine obstetric care and pregnant women under the supervision of perinatologists for high-risk pregnancies. By utilising the Beck Anxiety Inventory (BAI), a widely recognised tool for assessing anxiety, this study seeks to provide a comprehensive comparison of anxiety levels in these two distinct groups of pregnant women. Understanding these differences is essential for developing targeted interventions to support the mental health of all pregnant women, especially those facing high-risk conditions.

Through this research, we aim to highlight the importance of addressing psychological well-being in prenatal care and underscore the need for comprehensive support systems for expectant mothers, ensuring both their mental health and optimal pregnancy outcomes.

MATERIAL AND METHOD

The local ethics committee of Giresun Training and Research Hospital approved the study protocol. Participants were recruited from the Obstetrics and Perinatology Outpatient Clinics. After obtaining informed consent, participants were asked to complete the socio-demographic and medical characteristics questionnaire, followed by the Beck Anxiety Inventory. The data was collected in a private and comfortable setting to ensure the participants' confidentiality and comfort. This study was conducted following the relevant ethical principles of the Declaration of Helsinki, which was revised in 2013.

The study included pregnant women aged 18-40 who were literate and had no communication barriers, ensuring they could understand and complete the questionnaire. Participants were required to be willing to participate in the study, as indicated by their informed consent. Exclusion criteria were multiple pregnancies, which presented different risk factors, psychological challenges, and refusal to participate in the study. These criteria ensured a focused and comparable study population, allowing for a clear assessment of anxiety levels in routine obstetric care versus high-risk perinatology care.

This cross-sectional survey was conducted at the Giresun Training and Research Hospital Obstetrics and Gynecology Clinic. The study population consisted of pregnant women attending the Obstetrics and Perinatology Outpatient Clinics for pregnancy follow-up. A total of 90 pregnant women aged 18-40 were included in the study. Participants were divided into two groups: 45 women receiving routine obstetric care (Group I) and 45 women under perinatology care for high-risk pregnancies (Group II).

The BAI consists of 21 questions, with each response rated on a scale from 0 (none) to 3 (severe). The standardised cut-off points are as follows: 0-7 indicates minimal anxiety, 8-15 indicates mild anxiety, 16-25 indicates moderate anxiety, and 26-63 indicates severe anxiety. The demographic data of the patients were obtained from patient records. The Beck anxiety inventory scale (9) is shown in Table 1.

Table 1. Beck anxiety inventory

	Not at all	Mildly, but it didn't bother me much	Moderately – it wasn't pleasant at times	Severely – it bothered me a lot
Numbness or tingling	0	1	2	3
Feeling hot	0	1	2	3
Wobbliness in legs	0	1	2	3
Unable to relax	0	1	2	3
Fear of worst happening	0	1	2	3
Dizzy or lightheaded	0	1	2	3
Heart pounding/racing	0	1	2	3
Unsteady	0	1	2	3
Terrified or afraid	0	1	2	3
Nervous	0	1	2	3
Feeling of choking	0	1	2	3
Hands trembling	0	1	2	3
Shaky/unsteady	0	1	2	3
Fear of losing control	0	1	2	3
Difficulty in breathing	0	1	2	3
Fear of dying	0	1	2	3
Scared	0	1	2	3
Indigestion	0	1	2	3
Faint/lightheaded	0	1	2	3
Face flushed	0	1	2	3
Hot/cold sweats	0	1	2	3
Column sum				

Statistical Analysis

Data were analysed using the Statistical Package for the Social Sciences (SPSS) 26.0 Statistics package programme. The categorical data of pregnant women who applied to the obstetrics outpatient clinic and perinatology outpatient clinic were given as numbers and percentages, and continuous variables were given as mean and standard deviation. The conformity of the patients' age, items of the Beck Anxiety Scale and total scores to normal distribution was determined by looking at the skewness and kurtosis values. It was decided that the items of the Beck anxiety scale, except for the items of loss of balance, shakiness, fear of losing control and fainting, complied with the rules of normal distribution. The reference value taken in a normal distribution is between ±1.96. The chi-square test was used to compare the demographic, social status, health and family status values of pregnant women who applied to the obstetrics outpatient clinic and perinatology outpatient clinic. Independent Sample T Test or Mann Whitney U Test was used to test whether there was a significant difference between the Beck anxiety levels of pregnant women who applied to obstetrics outpatient clinic and perinatology outpatient clinic. In the study, significance levels were carried out by considering 0.05 and 0.01 values.

RESULTS

The study included 90 pregnant women, divided equally into two groups: 45 women receiving routine obstetric care (Group I) and 45 women under perinatology care for high-risk pregnancies (Group II). The socio-demographic characteristics of the participants were generally similar between the two groups. In Group I, 60% of the women were high school graduates, and 40% were university graduates. In Group II, 46.7% were high school graduates, and 53.3% were university graduates. The employment rate was consistent across both groups at 60%. Most participants in both groups reported that their income and expenses were balanced. Social security coverage was reported by 73.3% of Group I and 88.9% of Group II participants. Most participants in both groups desired their pregnancies (Group I: 91.1%; Group II: 97.8%), and very few reported consanguineous marriages (Group I: 6.7%; Group II: 0%). These differences were not statistically significant (p>0.05).

The educational status of the participants' husbands showed some variation. In Group I, 22.2% of the husbands had education levels of secondary school or below, 46.7% were high school graduates, and 31.1% were university graduates. In Group II, 20% had education levels of secondary school or below, 24.4% were high school graduates, and 55.6% were university graduates. This difference in husbands' educational status was statistically significant (p<0.05).

The mean age of the pregnant women in Group I was 28.71 years, and in Group II, it was 29.84 years, showing no significant difference (p>0.05).

Table 2 compares the demographic and social status of pregnant women who applied to the obstetrics outpatient clinic and the perinatology outpatient clinic.

Table 2. Comparison of demographic and social status of pregnant women admitted to obstetrics outpatient clinic and perinatology outpatient clinic

Demographic and social situation		Gynaecology outpatient clinic (n: 45)		Perinatology outpatient clinic (n:45)		p
		Number	%	Number	%	
Education level	High school and below	27	60.0	21	46.7	0.291
	University	18	40.0	24	53.3	
Employment status	Working	18	40.0	18	40.0	1.000
	Housewife	27	60.0	27	60.0	
Income status	Income less than expenditure	8	17.8	10	22.2	0.801
	Income equal to expenditure	27	60.0	27	60.0	
	Income more than expenditure	10	22.2	8	17.8	
Presence of social security	Exist	33	73.3	40	88.9	0.106
	None	12	26.7	5	11.1	
Husband's education level	Secondary school and below	10	22.2	9	20.0	**0.043***
	High school	21	46.7	11	24.4	
	University	14	31.1	25	55.6	
Desire for pregnancy	Exist	41	91.1	44	97.8	0.357
	None	4	8.9	1	2.2	
Consanguineous marriage status	Exist	3	6.7	0	0.0	0.242
	None	42	93.3	45	100.0	
		Med.±S.D (Min.-Max.)		Med.±S.D (Min.-Max.)		
Age[t]		28.71±4.47 (18-38)		29.84±4.88 (21-42)		0.254

*p<0.05, **p<0.01, χ^2: Chi-square test (Categorical data), t: Independent Sample T Test; Med: median, S.D: standart deviation

Among the participants, 4.4% of Group I and 2.2% of Group II had a disabled child. The distribution of first pregnancies was largely similar in both groups. Stillbirths were reported by 13.3% of Group I and 11.1% of Group II participants. Both groups demonstrated regular doctor visits and reported having a good marital life. These health

and family status distributions showed no significant differences between the two groups (p>0.05).

Table 3 compares the health and family status of pregnant women who applied to the obstetrics outpatient clinic and the perinatology outpatient clinic.

Table 3. Comparison of health and family status of pregnant women who applied to obstetrics outpatient clinic and perinatology outpatient clinic

Health and family situation		Gynaecology outpatient clinic (n: 45)		Perinatology outpatient clinic (n: 45)		p
		Number	%	Number	%	
Presence of children with disabilities	Exist	2	4.4	1	2.2	1.000
	None	43	95.6	44	97.8	
Number of pregnancies	First pregnancy	18	40.0	20	44.4	0.887
	2-3rd pregnancy	22	48.9	21	46.7	
	4th and above	5	11.1	4	8.9	
Number of stillbirths	Exist	6	13.3	5	11.1	1.000
	None	39	86.7	40	88.9	
Regular medical check-ups	Not regular	5	11.1	1	2.2	0.203
	Regular	40	88.9	44	97.8	
Status of married life	Not bad	4	8.9	2	4.4	0.700
	Good	19	42.2	20	44.4	
	Very good	22	48.9	23	51.1	

*p<0.05, **p<0.01, χ^2: Chi-square test (Categorical data)

The BAI scores were used to assess anxiety levels. The mean BAI score for Group I was 13.53, while for Group II, it was 12.33. This difference was not statistically significant (p>0.05).

In Group I, 82.2% of participants exhibited low-level anxiety, 15.6% had moderate anxiety, and 2.2% had severe anxiety. In Group II, 86.7% of participants showed low-level anxiety, 11.1% had moderate anxiety, and 2.2% had severe anxiety. The distribution of anxiety levels between the two groups was not significantly different (p>0.05).

However, a significant difference was observed in the heart palpitations item of the BAI. Group I participants had a mean heart palpitations score of 0.91, compared to 0.51 in Group II (p<0.05), indicating that heart palpitations were more common in women receiving routine obstetric care than those under perinatology care.

The comparison of Beck anxiety scores of pregnant women who applied to the obstetrics outpatient clinic and perinatology outpatient clinic is shown in Table 4.

Table 4. Comparison of Beck Anxiety Scores of pregnant women admitted to obstetrics outpatient clinic and perinatology outpatient clinic

Questions and responses	Gynaecology outpatient clinic (n: 45)	Perinatology outpatient clinic (n: 45)	p
	Med.±S.D	Med.±S.D	
Numbness or tingling[t]	0.67±0.74	0.71±0.76	0.779
Feeling hot[t]	1.09±0.95	0.84±0.74	0.176
Wobbliness in legs[t]	0.69±0.87	0.62±0.78	0.703
Unable to relax[t]	0.51±0.76	0.56±0.66	0.767
Fear of worst happening[t]	0.73±1.01	1.04±0.88	0.122
Dizzy or lightheaded[t]	0.82±0.83	0.76±0.80	0.700
Heart pounding/racing[t]	0.91±1.04	0.51±0.69	**0.035***
Unsteady[z]	0.47±0.63	0.27±0.50	0.083
Terrified or afraid[t]	0.44±0.76	0.44±0.76	1.000
Nervous[t]	1.16±0.85	1.16±0.80	1.000
Feeling of chocking[t]	0.49±0.76	0.53±0.76	0.781
Hands trembling[t]	0.33±0.56	0.38±0.58	0.712
Shaky/unsteady[z]	0.20±0.46	0.11±0.38	0.228
Fear of losing control[z]	0.27±0.50	0.18±0.44	0.307
Difficulty in breathing[t]	0.76±0.83	0.56±0.62	0.200
Feel of dying[t]	0.44±0.76	0.49±0.66	0.767
Scared[t]	0.64±0.80	0.76±0.77	0.505
Indigestion[t]	1.36±0.93	1.27±1.01	0.665
Faint/lightheaded[z]	0.38±0.68	0.24±0.53	0.394
Face flushed[t]	0.44±0.66	0.40±0.62	0.742
Hot/cold sweats[t]	0.73±0.81	0.51±0.69	0.166
Beck Anxiety Score[t]	**13.53±9.52**	**12.33±8.17**	0.523

*p<0.05, **p<0.01, t: Independent Sample T Test; z: Mann Whitney U Test; Med: median, S.D: standart deviation

The Beck Anxiety Inventory scores for pregnant women attending the obstetrics outpatient clinic averaged 13.53, while those for women at the perinatology outpatient clinic averaged 12.33. These results indicate that there was no significant difference in the anxiety levels between the two groups (p>0.05). Figure 1 illustrates the Beck Anxiety Inventory scores for both the obstetrics and perinatology outpatient clinic groups.

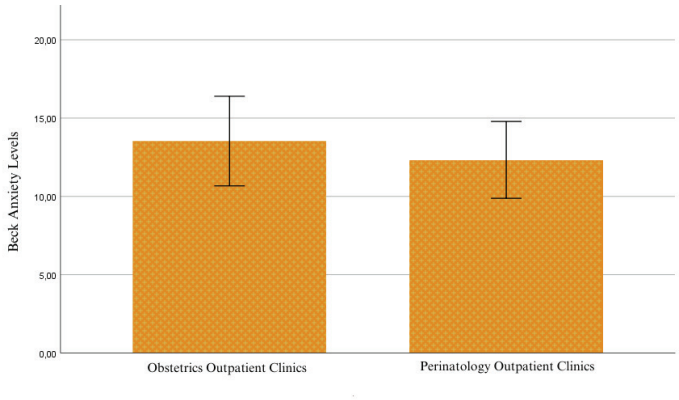

Figure 1. Beck anxiety levels of pregnant women admitted to obstetrics outpatient clinic and perinatology outpatient clinic

Of the pregnant women attending the obstetrics outpatient clinic, 82.2% exhibited low-level anxiety, 15.6% showed moderate anxiety, and 2.2% experienced severe anxiety. In comparison, among those at the perinatology outpatient clinic, 86.7% had low-level anxiety, 11.1% had moderate anxiety, and 2.2% had severe anxiety. The distributions of Beck Anxiety Inventory levels between the two groups did not differ significantly (p>0.05). Table 5 presents the comparison of Beck anxiety levels between pregnant women at the obstetrics and perinatology outpatient clinics.

Table 5. Comparison of Beck anxiety levels of pregnant women admitted to obstetrics outpatient clinic and perinatology outpatient clinic

Beck anxiety levels	Gynaecology outpatient clinic (n: 45)		Perinatology outpatient clinic (n: 45)		p
	Number	%	Number	%	
Low-level anxiety	37	82.2	39	86.7	0.877
Moderate anxiety	7	15.6	5	11.1	
Severe anxiety	1	2.2	1	2.2	

*p<0.05, **p<0.01, χ^2: Chi-square test (Categorical data)

DISCUSSION

The principal aim of this study was to assess and contrast the prevalence of anxiety disorders between pregnant women who received standard obstetric care and those who were under the care of a perinatologist for pregnancies deemed high-risk. This was achieved by utilising the BAI. The findings indicate that, although the overall anxiety levels were comparable between the two groups, specific symptoms, such as heart palpitations, were more prevalent among women receiving routine obstetric care.

These findings are in alignment with those of numerous studies that have investigated anxiety in pregnant populations. For example, Dunkel Schetter and Tanner have reported that approximately 15-23% of pregnant women experience clinically significant anxiety symptoms, thereby underscoring the pervasive prevalence of anxiety during pregnancy (10). In accordance with the aforementioned findings, our study revealed that a considerable proportion of participants from both groups exhibited low to moderate anxiety levels, with no notable discrepancy in the overall BAI scores.

Moreover, Field et al. have demonstrated that elevated anxiety levels during pregnancy are associated with adverse outcomes, including preterm birth and low birth weight (11). Although our study did not directly assess pregnancy outcomes, the comparable anxiety levels observed in both groups indicate that substantial psychological stress can impact both high-risk and normal pregnancies, emphasising the necessity for meticulous monitoring and prompt intervention. As evidenced by studies such as those conducted by Howard et al., antenatal anxiety has been identified as a predictor of adverse birth outcomes. This reinforces the importance of addressing anxiety during prenatal care (12).

In contrast, a study by Cumberbatch et al. reported that anxiety levels are typically higher among women with high-risk pregnancies than those with normal pregnancies (13). This discrepancy may be attributed to differences in the characteristics of the samples, the methods of anxiety assessment employed, or the specific risk factors present in the high-risk group. Our findings indicate that the prevalence of heart palpitations was higher in the routine obstetric care group, suggesting that anxiety symptoms may vary based on the type of care provided and the perceived level of risk. This is corroborated by recent findings from Pascal et al., who observed that anxiety manifestations, such as physical symptoms, were more pronounced in settings where perceived medical support was less specialised (14).

The notable discrepancy in heart palpitation scores between the two groups may suggest that women receiving routine obstetric care experience more pronounced physical manifestations of anxiety than those under perinatology care. This may be attributed to the enhanced surveillance and specialised management provided by perinatologists, which might offer high-risk pregnant women a greater sense of security and support. A study by McLeish and Redshaw similarly demonstrated that the provision of specialised care and continuous monitoring resulted in a notable reduction in anxiety symptoms among high-risk pregnant women, thereby underscoring the importance of specialised support in the management of anxiety (15).

Furthermore, Guardino and Schetter have highlighted the pivotal role of coping mechanisms and social support in the management of pregnancy-related anxiety, advocating for the implementation of targeted interventions tailored to both routine and high-risk pregnancy care contexts (16). Similarly, recent literature, such as that presented by

Manolova et al., has highlighted the benefits of integrating mental health support and stress-reduction strategies into prenatal care, particularly for women facing elevated medical risks (17).

In light of these findings, our study contributes to the understanding of prenatal anxiety by highlighting that while overall anxiety levels may not differ significantly between routine and high-risk pregnancies, the specific nature of anxiety symptoms can vary. This underscores the need for comprehensive, tailored approaches to anxiety management in both routine and specialised prenatal care settings. Further studies should explore these dynamics further, focusing on diverse populations and utilising multiple measures of anxiety to provide more nuanced insights into the psychological experiences of pregnant women.

Study Limitations

This study has several limitations. The small sample size and single-center design limit generalizability. The cross-sectional approach only provides a snapshot of anxiety levels, requiring longitudinal studies for a more comprehensive view. Reliance on self-reported data introduces potential biases, and the lack of detailed medical histories and control of confounding variables may affect the results. The specific cultural context may also influence applicability to other regions. While the BAI is validated, additional assessment methods could offer a broader perspective.

CONCLUSION

In conclusion, our study found no significant difference in overall anxiety levels between pregnant women receiving routine obstetric care and those under perinatology care for high-risk pregnancies, as measured by the Beck Anxiety Inventory. However, specific symptoms such as heart palpitations were more pronounced in the routine obstetric care group, highlighting the variability in anxiety manifestations. These findings underscore the importance of comprehensive psychological support for all pregnant women, regardless of risk status. Targeted interventions to manage anxiety symptoms can improve maternal well-being and pregnancy outcomes. Future research with larger, multi-centre, and longitudinal designs are necessary to confirm these results and explore the underlying mechanisms of prenatal anxiety. Addressing these aspects will contribute to better maternal and fetal health, ultimately enhancing the overall pregnancy experience.

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MEDICAL RECORDS-International Medical Journal

Research Article

Evaluation of Sclerotic Bordered Mandibular Pathologic Lesions with Cone Beam Computed Tomography

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Abstract

Aim: The aim of this study was to evaluate the radiologic features of intraosseous pathologic lesions with radiolucent and cortical borders in the unilateral posterior mandible using cone beam computed tomography (CBCT).
Material and Method: In the study, the largest size, cortical expansion, and relationship of the lesion to the teeth and mandibular canal were evaluated in radiolucent lesions with cortical borders in the posterior mandible on CBCT images of 36 patients. Mandibular cortical bone thickness was compared between the lesion side and the intact side. Mann Whitney U tests were used to compare the data ($p<0.050$).
Results: The mean size of the lesions was 16.41 mm. The lesions showed cortical expansion in 83.3%, relationship with teeth in 86.1%, and relationship with mandibular canal in 58.3%. The mandibular cortical thickness was 3.08 mm on the lesioned side and 3.49 mm on the intact side. There was no statistical difference between these two values ($p>0.05$).
Conclusion: Most of the corticated border mandibular posterior pathologic lesions were found to be associated with teeth and expansion occurred. Care should be taken before surgical procedures as these lesions may be associated with the mandibular canal. There was no change in mandibular cortical thickness on the lesion side.

Keywords: Mandibula pathology, sclerotic border, cone beam computed tomography

INTRODUCTION

Pathologic lesions of the jaws have a wide distribution, including benign, malignant, and locally aggressive. There is also a wide range of odontogenic and nonodontogenic lesions of the jaws. These lesions may be cysts, tumors, or tumor-like lesions. The clinical features of these multispecies lesions may be nonspecific. Radiologic evaluation may lead to a diagnosis of the lesion if a few specific findings are found or a few differential diagnoses can be made (1).

Conventional radiographs are still indispensable methods in the evaluation of the jaws. Intraoral and panoramic radiographs are the most commonly used techniques in the initial evaluation of jaw lesions. Intraoral radiographs provide a more detailed evaluation, while panoramic radiography evaluates larger areas. Intraoral radiographs are insufficient in the evaluation of lesions larger than 3 cm. In large lesions, panoramic radiography can be used to evaluate the relationship between the lesions and surrounding structures and teeth (2). Conventional radiographs allow two-dimensional evaluation of three-dimensional structures, so detailed information such as lesion size, margin characteristics, and extension are missing. For this, advanced imaging is needed. For this purpose, computed tomography (CT), magnetic resonance imaging and cone beam computed tomography (CBCT) can be used (1). The CBCT has widespread use in dentistry. CBCT provides faster imaging with a lower radiation dose than CT, but soft tissue resolution is poorer with CBCT. Jaw lesions can be evaluated in three dimensions and in detail with CBCT (3).

There have been numerous studies in the literature on intraosseous jaw lesions, but most of these studies have evaluated odontogenic or nonodontogenic cysts, odontogenic or nonodontogenic tumors, special cysts and tumors or specific groups such as pediatric groups and some geographical regions (1,4-9). However, to our knowledge, there is no study evaluating intraosseous radiolucent pathologic lesions with sclerotic borders

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in the mandible in the literature. The aim of this study was to evaluate the radiologic features of radiolucent intraosseous pathologic lesions with sclerotic (cortical) borders in the mandible on CBCT images.

MATERIAL AND METHOD

Ethical approval for the study was obtained from the İnönü University's health sciences non-interventional clinical research ethics committee (2024/5897).

In this study, CBCT images of 36 patients with unilateral intraosseous pathologic lesions located in the posterior mandible were retrospectively evaluated. The records with radiolucent pathologic lesions with regular cortical borders on reconstructive panoramic images obtained from CBCT were considered as sclerotic borders and included in the study (Figure 1). Images with artifacts due to motion and dense dental materials, and patients with previous surgical procedures in the relevant region were excluded from the study.

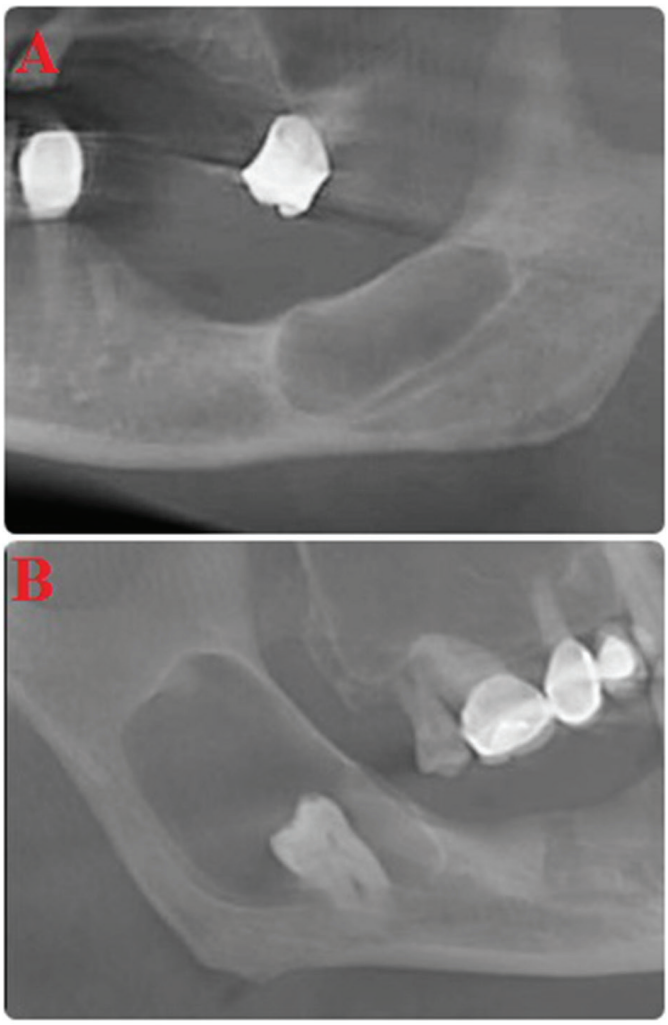

Figure 1. Mandibular posterior intraosseous pathologic lesions (A and B) with cortical borders on reconstructive panoramic images obtained from CBCT

In this study, CBCT images obtained from Newtom 5G (Verona, Italy) device. The device has a field of view (fov) between 8x8 and 18x16 cm, 110 kV, and 1-20 mA exposure factors. The images were evaluated with the NNT (New New Tom) program. Scanning time was 18 s, exposure time was 3.6 s and field of view was 15x12.

In the lesion images size measurements were made from different sections and the largest size was recorded. In axial sections, it was evaluated whether the lesion had cortical expansion or not. Evaluation of CBCT images for the presence of teeth associated with the lesion. The intact, root canal treatment and carious status of the teeth associated with the lesion were evaluated. The thickness of the mandibular basal cortical bone at the position corresponding to the midpoint of the lesion in the antero-posterior direction was measured (Figure 2) and compared with its symmetry on the intact side. In cases where the lesion progressed into the ramus, the cortical measurement corresponding to the middle part of the corpus section was performed.

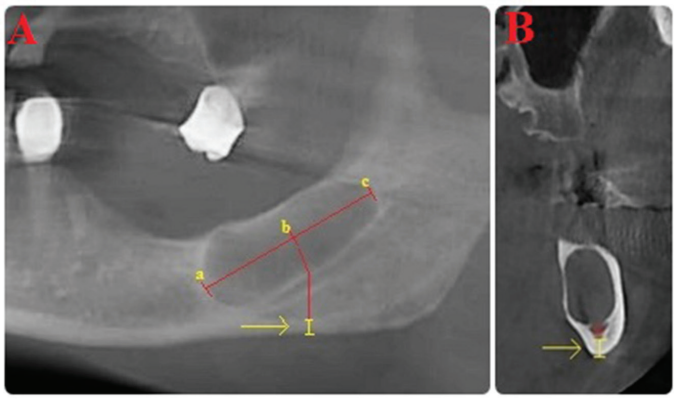

Figure 2. Determination of the cortical measurement region (arrow) in the basis cortex corresponding to the midpoint (ab=bc) of the antero-posterior dimension of the lesion on the reconstructed panoramic image (A); measurement of mandibular cortical thickness (B)

Data were analyzed with IBM SPSS V23. were used. The Mann-Whitney U test was used to compare the basis cortical thickness dimensions between the lesioned and non-lesioned sides. The significance level was accepted as $p<0.050$.

RESULTS

A total of 36 patients were evaluated in the study, 17 (47.2%) females and 19 (52.8%) males. The mean age of the women was 34.75 years (min: 13, max: 60, sd: 13.64) and the mean age of the men was 39.78 years (min: 14, max:69, sd: 16.59), with a total mean age of 37.39 years (min: 13, max: 69, sd: 15.27).

The mean maximum size of the lesions was 16.41 (min:7.9, max: 30.5, sd: 5.48) mm. Pathologic lesions showed cortical expansion in 30 (83.3%) and no expansion in 6 of them. In 21 (58.3%) of the lesions, a mandibular canal relationship was observed, while in 15 lesions there was no relationship with the mandibular canal. In 31 (86%) of the pathologic lesions, there was a relationship with the tooth, while in 5 (14%) lesions there was no tooth associated with the lesion. Of the teeth associated with these lesions, 17 (54.8%) were intact, 10 (32.2%) had root canal treatment and 4 (12.9%) were carious (Table 1).

Table 1. Frequency of radiologic features of mandibular posterior intraosseous pathologic lesions with cortical borders

Characteristics of lesions		Presence		
		Yes N (%)		No N (%)
Cortical expansion		30 (83.3)		6 (16.7)
Related to the mandibular canal		21 (58.3)		15 (41.7)
Related to teeth	Intact	17 (47.2)	31 (86)	5 (14)
	Root canal treatment	10 (27.7)		
	Caries	4 (11.1)		

The mandibular cortical bone thickness was 3.08 mm (min: 0.6, max: 4.8, sd: 0.86) on the side with a pathologic lesion. On the side without lesion, the mandibular cortical bone thickness was 3.49 (min: 1.6, max: 5.3, sd: 0.78). There was no statistically significant difference between these two values (p=0.116) (Table 2).

Table 2: Comparison of mandibular cortical thickness between the side with pathologic lesion and the side without pathologic lesion using Mann Whitney U test

Mandibular cortical thickness	Mean (mm)	Minimum	Maximum	Standard deviation	P value
Pathologic lesion side	3.083	0.6	4.8	0.86	0.116
Intact side	3.489	1.6	5.3	0.78	

DISCUSSION

The role of radiologists has increased not only in diagnosis but also in supporting the treatment process with the increased use of advanced imaging techniques (1). The use of CBCT is very important in the evaluation of radiolucent intraosseous pathologic lesions detected on conventional radiographs. Although these lesions can be inflammatory, developmental, and neoplastic, CBCT can be used to approach the diagnosis to a large extent by evaluating features such as multiple or single, well or ill-defined margins, location in the jaw, relationship with the tooth or crown, presence of septa, expansion, root resorption, and tooth mobility (10).

Radiologic features with other findings should be carefully evaluated in cases of intraosseous pathologic lesions. These features include location, periphery, shape, internal structure, and effects on other tissues. Some of these are important in distinguishing between benign and malignant lesions. The cortical border is a thin bony line at the periphery of the lesion, this type of border is observed in cysts and slow growing tumors (11). In a radiological study evaluating intraosseous benign jawbone lesions, 83.9% of cysts, 83.3% of benign tumors, and 33.3% of tumor-like lesions had good and regular cortical margins (12). According to a study evaluating odontogenic cysts, most of the lesions were found in the mandibular posterior region (13). In our study, unilateral intraosseous pathologic lesions with sclerotic (cortical) borders located in the posterior mandible were evaluated. The purpose of this study was to compare the thickness of the mandibular cortical bone at the bases between the non-lesioned side and the lesioned side. The mean value was 3.08 mm on the lesion side and 3.49 mm on the intact side. Although the mandibular cortical bone on the lesion side was dimensionally less than the intact side, no statistical difference was found. To our knowledge, there are no studies in the literature evaluating this feature in mandibular pathologic lesions.

The average age of patients with intraosseous pathologic lesions in both maxilla and mandible was found to be 36.5 years in a large series study in the Thai population (14). The mean age was found to be 24.59 and 68 years in some studies (15,16). In our study, only individuals with intraosseous pathologic lesions in the posterior mandible with sclerotic borders were evaluated and the mean age was found to be 37.39 years, which is compatible with the literature.

Gender distribution was found to be close to each other in a study evaluating odontogenic cysts and tumors (17). Also in our study, gender distribution was close to each other in males and females.

In a CBCT study performed to evaluate intraosseous pathologic lesions of the maxilla and mandible, the largest size was measured in the mesio-distal direction with a mean of 24.9 mm (3). In our study, the largest of these dimensions was measured in different directions and was found to be 16.41 mm.

It was found in a study that 83.9% of cysts, 83.3% of benign tumors, and 61.1% of tumor-like lesions were associated with teeth (12). In our study, 86.1% of the pathologic lesions were associated with teeth. However, 54.8% of these teeth were intact, 32.2% had root canal treatment and 12.9% were carious.

The frequency of cortical expansion in cyst and tumor-like lesions was found to be 51.6% and 44.4% in some studies (13,18). The frequency of cortical expansion in sclerotic bordered lesions was found to be 83.3% in our study.

CT and CBCT are used in the preoperative evaluation of cysts in the mandible to assess the association of the

lesion with the mandibular canal as well as the integrity of the cortical margin (2). In our study, 58.3% of the lesions were associated with the mandibular canal. Because of the relationship with the mandibular canal, intraosseous lesions located in the posterior mandible should be careful to avoid complications during surgery.

CONCLUSION

Mandibular posterior intraosseous pathologic lesions with sclerotic borders had no effect on the mandibular cortical bone. The majority of these lesions were found to have cortical expansion and relationship with the teeth. In the surgery of this type of pathologic lesion, the possibility that it is related to the mandibular canal should not be ruled out.

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MEDICAL RECORDS-International Medical Journal

Research Article

Unveiling the Nexus: Is Iron and Sodium Deficiency in Children with Febrile Seizures Risk Factor?

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Abstract

Aim: To examine the connection between the brain and sodium and iron levels in children under age 6.
Material and Method: This retrospective cohort study at Karabuk University Faculty of Medicine included 121 patients divided into three groups: Febril seizure (FS) patients, only fever children without FS, and healthy children. Our study distinguishes itself from other research in this field by its distinctive approach. Various laboratory parameters including sodium, Urea, Creatinine, AST, ALT, RDW, RDW Index, Mentzer Index, Hb, MCV, Ferritin and iron were compared among the groups. Statistical analysis used SPSS software and significance tests.
Results: Significantly lower sodium levels were observed in FS patients and iron levels were notably lower in children with FS. This findings suggest a potential association between lower sodium and iron levels in children with febrile seizures. Thus contributing to unveiling the nexus of brain. Additionaly, elevated AST levels in FS may signify liver function changes. findings suggest a connection between the liver function and brain function. However, urea and creatinine variations were non-significant.
Conclusion: Our findings suggest a potential association between electrolyte levels in children with febrile seizures. Iron plays a crucial role in brain metabolism and is necessary for the activity of certain enzymes involved in neurotransmitter functions. The low levels of sodium and particularly iron in the serum biochemistry of FS patients suggest a connection between these minerals and brain function. Moreover, the observed association between liver function markers and febrile seizures warrants further investigation into the link between liver health and brain function.

Keywords: Febrile seizures, brain connectivity, nexus, iron, sodium

INTRODUCTION

Febrile seizures (FS) are associated with the effect of fever on the brain (1). The increased regional connections are associated with seizures in childhood (2,3). The most prevalent seizure disorder in children is febrile seizures. Predominantly affecting children aged 1 month to 5 years with no prior history of afebrile seizures, arise during febrile illnesses (4). The rise in body temperature can increase electrical activity in the brain, thus accelerating abnormal neuronal responses (5). Understanding the biochemical relationship with the brain may unveil the truth behind these connectivity (6).

The role of iron is essential, especially in facilitating the connectivity of the brain with neurochemical processes. In addition to its role in brain metabolism, iron is also necessary for the activity of certain enzymes involved in neurotransmitter functions (7). Although there have been numerous studies investigating the link between seizures and iron deficiency, the bulk of these researches have been carried out in the Middle East (7). However, this issue continues to be a topic of contention, as conflicting findings persist in the literature. Some studies have suggested a higher prevalence of iron deficiency, in children experiencing febrile seizures (5-7), while others have found no significant association between iron deficiency and febrile seizures (8).

Notably, it is well-established that sodium plays a critical role in regulating nerve transmission and electrical activity in the brain. Research suggests that a decrease in sodium levels may contribute to increased depolarization in nerve cells, potentially leading to seizures (9,10). Therefore, this inference underscores the importance of sodium in neural communication within the brain (11,12). However, there are also studies suggesting contrary findings, which can lead to confusion (13).

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Despite extensive research, the mechanisms underlying febrile seizures remain incompletely understood. Conflicting results and uncertainties have been noted in the literature, contributing to the confusion surrounding this topic. Our study aims to address this gap by investigating the potential relationship between electrolyte imbalances, particularly iron and sodium deficiency, and febrile seizures. Specifically, we aimed to investigate the connection between electrolytes such as sodium and iron with the brain in order to provide further insights into the mechanism of febrile seizures, and to achieve clearer and more reliable results. Additionaly, most studies in the literature have primarily involved comparing two groups, febrile convulsion patients and healthy children (5-8,10). In contrast, our study stands out by comparing three groups (febrile seizure patients, fever-only cases, and healthy children). As far as we know, our study distinguishes itself from other research in this field by its distinctive approach, thereby providing a unique contribution.

MATERIAL AND METHOD

Data Design

The medical records of patients under the age of 6 who presented to the Karabuk University Faculty of Medicine Training and Research Hospital, Department of Pediatric emergency were retrospectively reviewed. We meticulously reviewed medical records, focusing on patients with FS who presented at the pediatric emergency department. The laboratory results and outcomes were systematically detected. Specifically, patients with an R56.0 (Febril seizures) diagnosis code were included in the analysis, encompassing the following International Classification of Diseases (ICD) codes: R56, and R56.9 (Convulsions, other unspecified). Accordingly, initially, 186 patients were identified. However, upon detailed review of the records, patients with afebrile seizures and those aged over 60 months were excluded from the study. Thus, by removing those with incorrect diagnoses, 110 patients with corrected diagnoses were identified. Then, laboratory records of patients with a confirmed diagnosis of FS were examined. We excluded patients with missing laboratory data to ensure data transparency. Subsequently, the e-Nabız patient information system of the Ministry of Health (https://enabiz.gov.tr/) was accessed to identify and exclude patients with chronic illnesses. Thus, an additional 70 patients were excluded from the study. Consequently, a total of 39 patients, confirmed to have febrile seizures without any underlying conditions, were included in the study.

Cohort Classification and Study Groups

The study divided into three groups

Group 1 comprised 42 healthy individuals, Group 2 included 40 patients with fever but no seizures, and Group 3 consisted of 39 patients aged under 60 mounths experienced fever and seizures (total cohort: 121 patients) (female:57; male: 64).

Cohort Classification Strategy

Segmentation for comparative analysis

In a two-group study consisting of patients with fever and seizures (FS) and patients with fever only (Only fever), the variable distinguishing the groups is the presence or absence of seizures, as both groups have fever. Therefore, such a study could investigate how changes in brain electrical activity are affected by iron and sodium levels and explore the relationship between them. However, since it cannot be determined whether changes in iron and sodium levels are due to fever or seizures, the relationship with febrile convulsions may not be conclusively elucidated. This is because the hallmark of febrile convulsion is the occurrence of seizures in conjunction with fever (5). Hence, a third group comprising both febrile and non-seizure patients (healthy children) was added to the study. Patients in this third group were children attending yearly routine health check-ups, diagnosed with Z00.1 (Routine child health examination) according to the ICD coding system, and were matched in age, gender, and number to the FS patient group. This approach allows for a more accurate assessment of the specific effects of FS on various laboratory indicators and outcomes.

Inclusion and Exclusion Criteria

1. **Inclusion criteria of the first group of FS cases:**

- Aged between 6 months and 5 years,
- Experiencing fever and with their first episode of FS,
- Patients who had undergone serum electrolyte and hemogram assessments during febrile seizures, as well as those who had their serum ferritin and iron levels assessed within the last 2 months before and after the onset of seizures.

2. **Exclusion criteria of the first group of FS cases:**

- Recurren FS, the presence of cerebral palsy, electrolyte imbalance caused convulsion, central nervous system infection, chronic and/or genetic disease, metabolic disease, and antibiotic therapy. Patients with seizures lasting >15 minutes were considered to have status epilepticus and were excluded from the study. We initially identified 186 cases of febrile seizures (FS); however, after applying the specified inclusion and exclusion criteria, the number of eligible cases was narrowed down to 39.

3. **Inclusion criteria of the second group of fever without seizures (only fever):**

- The second group was selected from patients diagnosed with R50.9 (Fever, unspecified) and R50.8 (Other specified fever) according to the ICD coding system. They were matched in age, gender, and number to the FS patient group.

4. **Exclusion criteria of the second group of fever without seizures (only fever):**

- FS, Recurren FS, Status epilepticus, the presence of cerebral palsy, Electrolyte imbalance occurred

concomitantly with the disease, the disease triggered the convulsion, central nervous system infection, chronic and/or genetic disease, metabolic disease, and under antibiotic therapy patients.

5. **Inclusion criteria of the third group of healty children:**

- Similar age-gender-number groups admitted to the pediatric outpatient clinics, and had no acute no chronic and no genetic diseases [Diagnosed with Z00.1 (Routine child health examination) according to the ICD coding system].

6. **Exclusion criteria of the third group of healty children:**

- FS, Recurren FS, Status epilepticus, the presence of cerebral palsy, Electrolyte imbalance occurred concomitantly with the disease, the disease triggered the convulsion, central nervous system infection, chronic and/or genetic disease, metabolic disease, and under antibiotic therapy patients.

Statistical Analysis

The data obtained in the study were analyzed using SPSS for Windows (Version 20.0, Statistical Package for Social Sciences) software. Data distribution was assessed based on Skewness and Kurtosis values, confirming a normal distribution. Descriptive statistics for blood parameters in the study included mean and standard deviation values. The relationship between groups and blood parameters was examined using the One-Way ANOVA test with Bonferroni correction, followed by Post Hoc analysis using Tukey and Tamhane tests. Comparisons with p-values less than 0.05 were considered statistically significant.

RESULTS

Changes in sodium, urea, and creatinine values among children in the study, grouped accordingly, are presented in Table 1. Upon analysis, a significant difference was observed only in sodium values among the groups (p=0.00). This significant difference in sodium values was attributed to children with febrile seizures, as their sodium values were found to be lower than both the fever without FS group and the healthy child group. No significant differences were observed in urea and creatinine values (Table 1).

Table 1. Comparison of serum sodium, urea and creatinine values of children

Laboratory parameter	Group-1 (healthy child)	Group-2 (fever-without FS)	Group-3 (febril seizure)	Test* (ANOVA)	p
	mean±SD	mean±SD	mean±SD		
Sodium	138.48± 3.2[a]	138.42± 2.07[a]	136.38±2.07[b]	11.35	0.00
Urea	24.33±8.18	23.55±8.13	25.1±7.38	31.37	0.68
Creatinine	0.33±0.09	0.3±0.1	0.32±0.13	1.14	0.33
ALT	17.57±8.94	16.45±6.13	22.28±23.87	1.69	0.19
AST	36.83±19.44	34.35±9.57	45.03±27.73	3.01	0.05

*One Way ANOVA a-b=there is no difference between values with the same letter; a: results for sodium in group-1 and group 2, b: results for sodium in group-3

The variations in ALT and AST values among the children in the study according to the groups are presented in Table 1. Upon analysis, a borderline significant difference was observed between the groups and ALT and AST values (ANOVA, p: 0.05). It was noted that the group with febrile seizures exhibited higher AST values compared to the other two groups (Table 1).

In Table 2, changes in RDW and MENTZER values of children in the study are presented according to their respective groups. The analysis revealed a significant difference among groups in RDW values (p=0.00). However, this significant difference was attributed to children with only fever group (without febrile seizures), as there was no significant difference in RDW values among children who had experienced febrile seizures. No significant differences were observed in MENTZER and RDW Index values between the groups (with p-values of 0.16 and 0.19, respectively).

Table 2. Comparison of serum RDW, Mentzer and RDW Index values of children

Laboratory parameter	Group-1 (healthy child)	Group-2 (fever-without FS)	Group-3 (febril seizure)	Test* (ANOVA)	p
	mean±SD	mean±SD	mean±SD		
RDW	13.85±0.99[a]	15.49±2.47[b]	14.04±1.4[a]	7.62	0.00
MENTZER	17.13±2.05	16.24±2.46	16.99±2.13	1.87	0.16
RDW INDEX	236.6±27.73	236.2±25.31	211.47±82.1	1.69	0.19
Hb	12.15±1.13	11.85±1.16	12.07±0.9	0.81	0.44
MCV	78.77±4.61	76.4±7.34	78.01±4.62	1.85	0.16
FERRITIN	21.94±12.97	28.01±24.95	19.5±13.9	2.34	0.10
IRON	66.99±34.72[a]	63.23±41.36[a]	51.25±20.75[b]	3.65	0.03

*One Way ANOVA a-b=there is no difference between values with the same letter; a: results for RDW in Group 1 and Group 3; Results for IRON in Group 1 and Group 2, b: results for RDW in Group 2; Results for IRON in Group 3

Changes in iron values among children in the study, categorized by groups, are presented in Table 2. The analysis showed a significant difference among groups in iron values (p=0.03). This significant difference was found to be associated with children who had experienced febrile seizures, as their iron values were lower compared to healthy children. No significant differences were observed between children with fever but without febrile seizures and healthy children (Table 2).

DISCUSSION

The literature on the relationship between low sodium levels and febrile seizures has been characterized by conflicting findings, contributing to ambiguity (11-13). Nevertheless, our study findings, which reveal a significant decrease in sodium levels among children who experienced febrile seizures (FS) compared to both the fever-only (without FS) group and healthy children, are consistent with previous research (6,9,10). This consistency highlights the potential correlation between lower sodium levels and an increased risk of febrile seizures. However, despite these findings, further investigations are warranted to elucidate the precise mechanisms underlying the relationship between sodium levels and seizures, thus contributing to unveiling the nexus of brain.

Our investigation revealed a significant discrepancy among the groups concerning iron values (p=0.03). Specifically, children who experienced febrile seizures exhibited significantly lower iron levels compared to their healthy counterparts. However, no substantial differences were observed between the group of children with only fever (without febrile seizures) and the healthy children group. These findings suggest a potential relationship between iron levels and the occurrence of febrile seizures, consistent with earlier research findings (5,7). Interestingly, upon examining ferritin levels, we found no significant disparities among the groups, aligning with the results of a previous study conducted by Yousefichaijan et al. (8). The observed discrepancy in iron levels between children who experienced febrile seizures and healthy counterparts supports the hypothesis that iron deficiency may contribute to the pathogenesis of febrile seizures. However, the lack of significant differences in ferritin levels suggests that ferritin alone may not be a reliable indicator of iron status in the context of triggering convulsions. Further research is warranted to elucidate the complex relationship between iron metabolism and febrile seizure susceptibility.

Our analysis revealed a significant difference among the groups regarding RDW values (p=0.00). Interestingly, this notable difference was primarily observed in children with only fever (without FS) group. Surprisingly, there was no significant difference in RDW values among children who had experienced febrile seizures. Additionally, no substantial disparities were detected in MENTZER and RDW Index values between the all groups (by the p-values of 0.16 and 0.19, respectively). These research outcomes closely align with the findings reported in a study (7). The significant difference in RDW values in the children-only fever group (without FS) suggests that the elevation in body temperature increases heterogeneity in the size and shape of erythrocytes, to unveiling the nexus of hematologic system. However, the lack of significant difference in RDW values in children who experienced febrile seizures (FS group) suggests that alterations in erythrocyte distribution may not directly influence cerebral electrical activity. Therefore, the original inference drawn is as follows: Fever alters the size and shape of erythrocytes; however, these changes may not directly impact cerebral electrical activity.

Our analysis unveiled a noteworthy trend in AST values among the groups, approaching borderline significance. Significantly, children experiencing febrile seizures displayed elevated AST levels compared to the other two groups. This observation aligns with a similar study where the significance value of AST, which we found to be on the verge of significance, reached statistical significance (10). The elevation in AST levels may potentially signify alterations in liver function associated with febrile seizures. This finding suggests a potential connection between liver function and brain function, indicating the need for further comprehensive investigations to explore this relationship.

In our investigation, variations in urea and creatinine values were observed; however, these differences did not reach statistical significance among the groups (p>0.05). Consistent with our findings, similar studies have also reported no significant differences in these parameters (10,14,15). This implies that urea and creatinine may not play a direct role as contributors to febrile seizures within our study population. Nevertheless, it is imperative to acknowledge the multifaceted nature of febrile seizures and to delve deeper into the exploration of potential contributing factors.

Limitations of the Study

The main limitation of our study is its retrospective nature, which relies on the review of patients' past records. Consequently, imaging techniques that are supported by MRI and enhanced by signal changes could not be utilized.

CONCLUSION

In conclusion, our study sets itself apart by comparing three distinct groups: febrile seizure patients, those with fever alone, and healthy children. Our findings suggest a potential association between lower sodium and iron levels in children with febrile seizures. Thus contributing to unveiling the nexus of brain. Additionaly, our findings suggest a connection between the liver function and brain function, as evidenced by elevated AST levels in FS. Overall, our study enhances our understanding of the complex factors related to febrile seizures.

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Ethical approval: *The study strictly adhered to the ethical principles outlined in the Declaration of Helsinki. This study was approved by the Ethics Committee of Karabük University (Ethical Approval Date: 27/02/2023, Ethic Decission No: 2023/1273).*

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Research Article

Evaluation of Dysphagia and Associated Factors in Patients with Neuromuscular Disorders: Do the Oral Factors Deserve Some Focus too?

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Abstract

Aim: Dysphagia may occur during neuromuscular disorders. As it may cause serious morbidity and mortality, it is important to define the characteristics and burden of this problem among these individuals. This study aimed to evaluate the dysphagia status and associated factors in patients with neuromuscular disorders in a tertiary care center.
Material and Method: Two-hundred fifty-two patients in the three groups were included in this study (59 Duchenne or Becker muscular dystrophies (DMD-BMD), 130 other muscular diseases, and 63 neuropathies). The patients were carefully assessed clinically, and their dysphagia status was evaluated using the EAT-10 questionnaire. Dysphagia prevalence was defined for each diagnosis, and patients in each group were compared in terms of their clinical characteristics, depending on the presence of dysphagia.
Results: The prevalence of dysphagia was 17%, 18.4%, and 47.6% in the DMD-BMD, other muscular diseases, and neuropathy groups, respectively. Moreover, dysphagia was associated with worse ambulatory status, poor oral hygiene, dry mouth, dental implants, and pneumonia ($p<0.05$).
Conclusion: Dysphagia is an important problem in neuromuscular diseases and requires inquiry and assessment by caregivers and clinicians. Studies focusing on more detailed evaluations, especially for oral health status, and the effectiveness of possible treatment methods will improve this problem.

Keywords: Neuromuscular disorders, dysphagia, muscular dystrophy, neuropathy, oral health

INTRODUCTION

Neuromuscular disorders are a group of diseases that impair the function of the locomotor system, which consists of the nervous and muscular systems (1). These include polyneuropathies, motor neuron diseases, spinal muscular atrophy, neuromuscular junction diseases, myopathies, muscular dystrophies, and inflammatory muscle diseases. While there have been great efforts to search for a cure or prevent the disabilities they bring, the majority of these disorders are progressive with no definitive cure (2).

While neuromuscular disorders mainly cause impairments in physical functioning and movement, these diseases usually result in problems beyond locomotion (3). One of these problems is dysphagia, which is defined as discomfort or difficulty while swallowing (4). It can range from mild discomfort while swallowing to a swallowing disorder that prevents oral intake. Swallowing dysfunction in neuromuscular disorders is attributed to the lack of synergy between or weakness in oropharyngeal muscles, as these diseases may affect the nerves and muscles (5). Dysphagia may result in a reduction in quality of life, dietary restrictions, nutritional problems, and complications such as pneumonia (5,6).

Several methods can be used to assess the presence of dysphagia. Although videofluoroscopy (VFS) and oropharyngeal examination with videofibrolaryngoscopy provide the best insight into the presence and mechanisms of dysphagia, these methods are expensive and time-consuming (7). Moreover, their results may vary between assessors and carry risks for complications. The recent opinion for the evaluation of dysphagia in neuromuscular disorders such as muscular dystrophy does not recommend routine evaluation with invasive methods unless there are signs or symptoms of dysphagia (6). Thus standardized questionnaires have been developed to screen and evaluate dysphagia, including EAT-10 (Eating Assessment tool-10) (8). These tools were found to be

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strong indicators of dysphagia, and are widely used in both clinical settings and studies (8,9).

The presence of dysphagia in neuromuscular disorders has been shown in several studies in the literature (4,10,11). These studies relied on medical history, with or without face-to-face interaction, rather than standardized assessments. Although other studies use extensive methods such as VFSS, they are hindered by a small number of patients (12,13). Finally, little is known about the features and prevalence of dysphagia in some uncommon or rare neuromuscular disorders, which underlines the importance of studies or reports on these patients.

Oral health problems are known to contribute to the presence and severity of dysphagia in many groups of patients, and a healthy process of mastication and delivery of food with adequate consistency to the pharynx is a requirement for all individuals, regardless of their risk of dysphagia (14,15). Although it can be inferred that the maintenance of oral health applies to patients with neuromuscular disorders, none of the studies focused on the effects of oral problems on dysphagia in this group of patients.

This study aimed to evaluate the prevalence of dysphagia in patients with different types of neuromuscular disorders at a specialized center. Another aim was to investigate the factors associated with dysphagia and determine whether they correlated with the EAT-10 score, which is an indicator of dysphagia.

MATERIAL AND METHOD

Two-hundred and fifty-two patients who were admitted to the outpatient clinics of the Neuromuscular Diseases Center of a Training and Research Hospital were included in this study (59 Duchenne or Becker muscular dystrophies (DMD-BMD), 130 other muscular diseases and 63 neuropathies). Written informed consent was obtained from all patients and their caregivers, and the study was approved by the Institutional Review Board for Ethics before initiation (number: 2019/11-16).

The inclusion criteria were as follows:

- Patients with a definite diagnosis of neuromuscular disease based on clinical, genetic, and biopsy findings,
- Those aged 8 and over,
- Women and men,
- Those who did not use nasogastric or PEG,
- Those who can understand and speak Turkish.

The exclusion criteria were as follows:

- Patients without a diagnosis of neuromuscular disease,
- Age under 8 years,
- Presence of percutaneous gastrostomy/jejunostomy and nasogastric catheter,
- Those who do not understand or speak Turkish,
- Gastrointestinal, rheumatic, rheumatological, and malignant diseases that cause dysphagia.

After being evaluated by a team of physicians experienced in this field to confirm their diagnosis through history, physical examination, and laboratory/imaging, clinical and demographic data were obtained from the eligible patients. The patients were then questioned about their dysphagia status and problems with oral intake or swallowing, including a history of pneumonia. Physical activity levels of the patients were recorded by a self-reported measure, being either sedentary, seldomly exercising or regularly exercising. The same team also obtained a history of oral health and performed a physical examination of the mouth, teeth, and periodontal tissues, and gave an overall score ranging from 1 to 4, with lower scores being worse.

Functional Ambulation Classification (FAC): Patients were evaluated for their physical functioning and ambulatory status using the FAC. It consists of 6 stages, ranging from 0 to 5. Non-functional ambulation corresponds to 0, while independent ambulation corresponds to 5 (16).

EAT-10: The Eating Assessment Tool in 10 questions (EAT-10) was used to assess the swallowing function. First described by Belafsky et al. in 2008 (17), the EAT-10 is widely used to assess symptom severity and treatment response in dysphagia. The questionnaire consists of 10 multiple-choice questions, each of which is marked from 0 to 4. Although there are different cutoffs described in various patient groups, scores ≥3 are associated with the present risk of oropharyngeal dysphagia (17). The Turkish version of the test was also shown to be valid and reliable (18).

Using this EAT-10 score cut-off (≥3), patients were grouped as having dysphagia (Dysphagia +) or not (Dysphagia -). The factors associated with swallowing disorders and ambulatory status were analyzed to determine whether there was a correlation between them and the EAT-10 scores in patients with neuromuscular disorders.

Statistical Analysis

Statistical analyses were conducted using the Statistical Package for the Social Sciences (IBM Corporation, Armonk, NY, USA), version 23 for Windows. The demographic and clinical characteristics of the participants were analyzed using descriptive statistics. Categorical variables were analyzed using Pearson's chi-square test and Fisher's Exact Test. The normality of the data was tested using the Shapiro-Wilk test. As the numerical variables did not meet the criteria for normality, the Mann-Whitney U test was used to compare numerical variables among the groups. Correlation analysis was performed using Spearman's rank-order correlation test. The homogeneity of variances was tested using the Levene's test. As the variances could not meet the criteria for a parametric covariance test, non-parametric covariance analysis (Quade's test) was used (19). Statistical significance was defined as $p<0.05$.

RESULTS

Demographic and clinical data of the groups are shown in Table 1. 73 patients (30.1%) of the 242 recruited were under 19 years old. The DMD-BMD group constituted a special population among the other patient groups, since this group consisted of only males and was younger. They also had worse ambulatory status compared to the

other groups (p<0.05). Moreover, as most of them were already using corticosteroids and other supplementary drugs, they had a higher number of prescription drugs (p<0.05). Dysphagia was worse in the neuropathy group (p<0.05), mostly due to the inclusion of amyotrophic lateral sclerosis and other motor neuron diseases, which are known to affect swallowing function immensely. The dysphagia prevalence measured using the EAT-10 scores (cutoff: ≥3) in different diagnoses is given in Table 2. The prevalence of dysphagia was 17% in the DMD-BMD group, 18.4% in the other muscular diseases group, and 47.6% in the neuropathy group.

A comparison of the clinical characteristics and ambulatory status of patients with and without dysphagia is shown in Table 3. Ambulatory status was worse in patients in the DMD-BMD and neuropathy groups (p<0.05). Although the prevalence of pneumonia was higher in patients with dysphagia in all groups, statistical significance was obtained only in the DMD-BMD group (p<0.001). Problems in maintaining oral hygiene were significant in patients with dysphagia in both groups (p<0.05). Moreover, all groups reported a higher presence of dry mouth and limitations for certain types of food in patients with dysphagia (p<0.05). Muscular disorders other than the DMD-BMD and neuropathy groups also had higher numbers of dental implants in the dysphagia + group, while the DMD-BMD group, which consisted of younger patients, did not report any presence of dental implants at all.

The correlations between EAT-10 scores and clinical characteristics commonly associated with swallowing disorders and ambulatory status are shown in Table 4. These results show that poor ambulatory status, poor oral hygiene, dry mouth, food limitations dental implants, and pneumonia are correlated with higher EAT-10 scores (p<0.05).

We performed covariance analysis to determine whether oral factors were independent factors for the presence of dysphagia and pneumonia. When a model where FAC and age were used as covariates to show the progression of the disease, oral hygiene was not shown to be an independent factor for dysphagia and pneumonia (F (3.248)=0.51, p=0.67, and F (3.248)=0.23, p=0.87, respectively).

Table 1. Demographical and clinical characteristics of the participants (n%) or mean (SD)

	DMD/BMD (n: 59)	Other muscle diseases (n: 130)	Neuropathy (n: 63)	p
Gender (male)	59 (100)	58 (44.6)	30 (47.6)	**<0.001**
Education				0.38
Elementary	41 (70.7)	74 (56.9)	39 (61.9)	
High school	14 (24.1)	34 (26.2)	14 (22.2)	
University	3 (5.2)	17 (13.1)	7 (11.1)	
Mastery or higher	0 (0)	5 (3.8)	3 (4.8)	
Marital status (married)	1 (1.7)	62 (47.7)	32 (50.8)	**<0.001**
Physical activity level				**0.001**
Sedentary	26 (44.1)	76 (58.5)	41 (65.1)	
Seldom	3 (5.1)	21 (16.2)	3 (4.8)	
Regular exercise	30 (50.8)	33 (25.4)	19 (30.2)	
Comorbidities (yes)	17 (28.8)	47 (36.2)	33 (52.4)	0.057
FAC				**<0.001**
0	33 (55.9)	18 (13.8)	12 (19)	
1	2 (3.4)	10 (7.7)	9 (14.3)	
2	0	7 (5.4)	2 (3.2)	
3	3 (5.1)	7 (5.4)	8 (12.7)	
4	5 (8.5)	24 (18.5)	10 (15.9)	
5	16 (27.1)	64 (49.2)	22 (34.9)	
Swallowing problems (yes)	12 (20.3)	31 (23.8)	35 (55.6)	**<0.001**
Pneumonia	5 (8.5)	6 (4.6)	3 (4.8)	0.53
Number of drugs used	0-9 (1)	0-15 (0)	0-10 (2)	**0.006**
Food limitations				0.016
None	52 (88.1)	116 (89.2)	44 (69.8)	
Solid	4 (6.8)	8 (6.2)	9 (14.3)	
Liquid	3 (5.1)	3 (2.3)	8 (12.7)	
Semi-solid	0	3 (2.3)	2 (3.2)	
EAT-10 scores	1.3 (3.2)	1.96 (5)	6.5 (9.9)	**<0.001**
EAT-10 (>=3)	10 (17)	24 (18.4)	30 (47.6)	**<0.001**

Pearson's Chi Square and Fisher's Exact test, Student's T test; FAC: functional ambulation categories; significance: p<0.05

Table 2. Dysphagia prevalences according to EAT-10 (Cut-off >=3) (n%)

Diagnosis	Dysphagia (+)	Total
Duchenne muscular dystrophy	9 (19.6)	4
Becker muscular dystrophy	1 (7.7)	13
Limb-girdle muscular dystropy	2 (8)	25
Facioscapulohumeral muscle dystrophy	0 (0)	10
Myotonic dystrophy	3 (18.8)	16
Myotonia congenita	0 (0)	11
Congenital myopahty	1 (33.3)	3
Myopathy (other)	11 (28.9)	38
Non-inflammatory myopathy	0 (0)	7
Mitochondrial myopathy	3 (42.9)	1
Other muscle diseases	4 (21)	19
Polyneuropathy	9 (33.3)	27
Spinal muscular atrophy	3 (37.5)	8
Amyotrophic lateral sclerosis/motor neuron disease	15 (62.5)	24
Metabolic neuropathy	3 (75)	4

Table 3. Comparison of clinical characteristics between patients with and without dysphagia (n%)

	DMD-BMD			Other muscular diseases			Neuropathy		
	Dysphagia- (n: 49)	Dysphagia+ (n: 10)	p	Dysphagia- (n: 106)	Dysphagia+ (n: 24)	p	Dysphagia- (n: 33)	Dysphagia+ (n: 30)	p
Age (years)			0,56			0,43			0,29
10 to 19	32 (65.3)	7 (70)		18 (17)	1 (4.2)		10 (30.3)	5 (16.7)	
20 to 29	12 (24.5)	3 (30)		20 (18.9)	5 (20.8)		5 (15.2)	1 (3.3)	
30 to 39	5 (10.2)	0 (0)		25 (23.6)	5 (20.8)		4 (12.1)	4 (13.3)	
40 to 49	0 (0)	0 (0)		24 (22.6)	6 (25)		5 (15.2)	3 (10)	
50 to 59	0 (0)	0 (0)		15 (14.2)	7 (29.2)		6 (18.2)	10 (33.3)	
60 to 69	0 (0)	0 (0)		3 (2.8)	0 (0)		2 (6.1)	5 (16.7)	
70+	0 (0)	0 (0)		1 (0.9)	0 (0)		1 (3)	2 (6.7)	
FAC			**0.01**			0.9			**0.008**
<4	28 (57.1)	10 (100)		34 (32.1)	8 (33.3)		11 (33.3)	20 (66.7)	
>=4	21 (42.9)	0 (0)		72 (68)	16 (66.7)		22 (66.7)	10 (33.3)	
Swallowing problems (yes)	4 (8.2)	8 (80)	**<0.001**	15 (14.2)	16 (66.7)	**<0.001**	7 (21.2)	28 (93.3)	**<0.001**
Pneumonia	1 (2)	4 (40)	**<0.001**	4 (3.8)	2 (8.3)	0.3	0 (0)	3 (10)	0.06
Comorbidities	13 (26.5)	4 (40)	**0.45**	34 (33)	13 (54.2)	0.12	13 (39.4)	20 (66.7)	0.076
Oral hygiene problems	7 (14.3)	3 (30)	**0.04**	23 (21.7)	12 (50)	**0.048**	7 (21.3)	9 (30)	0.67
Dry mouth	3 (6.1)	5 (50)	**<0.001**	15 (14.2)	12 (50)	**0.001**	5 (15.2)	15 (50)	**0.003**
Dental implants (+)	0 (0)	0 (0)	**NA**	5 (4.7)	6 (25)	**0.001**	3 (9.1)	8 (26.7)	0.098
Food limitations			**<0.001**			**<0.001**			**<0.001**
None	47 (95.9)	5 (50)		102 (96.2)	14 (58.3)		31 (93.9)	13 (43.3)	
Solid	1 (2)	3 (30)		2 (1.9)	6 (25)		1 (3)	8 (26.7)	
Liquid	1 (2)	2 (20)		2 (1.9)	1 (4.2)		1 (3)	7 (23.3)	
Semi-solid	0 (0)	0 (0)		0 (0)	3 (12.5)		0 (0)	2 (6.7)	

Pearson's Chi Square and Fisher's Exact test; FAC: functional ambulation categories; significance: p<0.05

Table 4. Correlation of EAT-10 scores with the clinical characteristics		
FAC	**R**	-0.242
	p	**<0.001**
Oral hygiene	**R**	-0.189
	p	**0.003**
Dry mouth	**R**	-0.416
	p	**<0.001**
Food limitation	**R**	0.546
	p	**<0.001**
Dental implants	**R**	-0.27
	p	**<0.001**
Pneumonia	**R**	0.243
	p	**<0.001**

Spearman's rank correlaton test; FAC: functional ambulation categories; significance: p<0.05

DISCUSSION

The results of this study show that dysphagia is a significant problem in patients with neuromuscular disorders. Even in the absence of food administration routes other than oral administration, a considerable number of patients across all groups showed signs of dysphagia. Moreover, dysphagia was correlated with pneumonia in these patients. The severity of dysphagia was found to scale with worse ambulatory status, probably due to the progressive course of many of these pathologies, which affect motor functions, as well as swallowing.

In recent decades, the prevalence of dysphagia in neuromuscular disorders has been the focus of research. A case-control study by Jaffe et al. focused on patients with DMD and reported that upper gastrointestinal functional problems were prevalent in these patients (20). A study that used a survey with questions regarding swallowing in various neuromuscular disorders by Willig et al. was among the first studies (4). While the prevalence of dysphagia is reported to be around 25-45% in patients with myotonic dystrophy (21,22), which is an adult-onset form of muscular disease, it is difficult to estimate the actual prevalence of many of these disorders due to their progressive nature, especially in patients with DMD, motor neuron disease, some forms of polyneuropathies, or other progressive muscular diseases (6,7,12). Thus, although our study reports prevalence from our spectrum of patients, these findings may be drastically different if these patients are in different stages of their pathologies. In addition, the study involved only a few patients with some of the rarer diseases. While these reports can be valuable in estimating the potential impact of swallowing disorders, low numbers may cause overestimation or underestimation of this problem in these populations. As our groups, especially those other than DMD-BMD, involved diverse pathologies with different involvement of swallowing function, the group with neurological involvement had the highest rate of dysphagia, partly due to the considerable proportion of patients with motor neuron disease (23).

The link between limited ambulation and dysphagia is a relatively novel focus of research in the general population. It has been shown that poor ambulatory status is associated with dysphagia (24,25). This link is mostly thought to originate from the presence of lower muscle mass and strength and sarcopenia, which contributes to both ambulation and swallowing functions, as the impairment of muscle mass and strength also affects muscles in the oropharynx as well (26,27). Moreover, in patients whose movements are severely limited, the inability to adjust posture and compensate for neck maneuvers or scoliosis of cervical and upper-thoracic levels may contribute to swallowing disorders as well (28). Our findings suggest that a possible link between ambulatory status and swallowing disorders may be valid in patients with neuromuscular disorders. However, the mechanisms of this association may not be the same as that in the general population. While sarcopenia, comorbidities, and frailty might be the main predictors of dysphagia in the general population, neuromuscular disorders have different characteristics. As many neuromuscular disorders are progressive and affect both neuromuscular systems involved in swallowing and ambulation, the actual progress of the disease may be the main mechanism for the severity of dysphagia and limited ambulation. As our findings were more robust in the DMD-BMD and neuropathy groups, which consisted solely of progressive disorders or had a large number of them, this assumption can be true. The cross-sectional design of our study makes it impossible to make a cause-effect relationship in this issue, though. Nevertheless, it might be interesting to study whether interventions for strength training that can improve ambulation or posture can also alleviate dysphagia in patients with neuromuscular diseases as well (29).

The findings of our study suggest that dysphagia was also correlated with higher rates of pneumonia, worse oral hygiene, dryness of the mouth, and the presence of dental implants. The link between pneumonia and dysphagia is well established, and dysphagia, especially when not treated properly, can cause aspiration pneumonia in both the general population and patients with neuromuscular disorders (6,30). Our findings confirm this link, especially in patients with DMD or BMD. We could not show this association for muscular disorders other than DMD-BMD, which involved myopathies or myotonic dystrophies. While the association between pneumonia and dysphagia is clearer in cases with neuropathies or DMD in the literature (6,31), it is not always possible to show this link in some muscular disorders with milder involvements, such as myotonic dystrophy (32). However, the lack of findings in this particular group should not undermine the importance of addressing dysphagia in these patients.

Disturbances in oral hygiene are among the most important issues affecting swallowing and nutrition. Studies have shown that oral health is associated with dysphagia and malnutrition (33,34). Poor oral hygiene is also known to contribute to pneumonia, and maintaining good oral health can help reduce pneumonia in susceptible

populations (35,36). Our findings underscore the importance of oral health in patients with neuromuscular disorders. Thus, maintaining good oral hygiene in these patients may improve their swallowing problems and help reduce the incidence of pneumonia. Our data showed that oral hygiene status is not an independent factor that contributes to pneumonia and dysphagia. As neuromuscular diseases progress, the maintenance of oral health encounters many problems, including the loss of manual dexterity to perform self-care tasks such as brushing teeth and impaired control of the saliva and head and neck muscles, resulting in xerostomia. These factors may have shadowed the possible contribution of oral hygiene to dysphagia since these problems are encountered more commonly in patients with progressive disease. Since the effects of oral health problems are well known in other patient groups susceptible to aspiration pneumonia, proper oral and dental care should be provided to these patients, especially in the advanced stages of the disease. Dental implants were found to be common in patients with neuropathy in the group that included patients over 50 years of age. Dental problems and implant applications are known to be more prevalent in older age (37). As dysphagia is more common in older patients with neuropathy, this finding can be attributed to the progression of oropharyngeal muscle weakness with increasing age in this population (38).

This study is the first to evaluate the dysphagia status in patients in a neuromuscular disease clinic in Türkiye. Moreover, this is the first study to highlight the importance of oral health in swallowing problems in patients with neuromuscular disorders. The strengths of this study include its considerable number of patients. We also used a validated tool, EAT-10, to screen for dysphagia. All patients were evaluated face-to-face, without a remote tool such as telephone or e-mail, which reduces the potential problems in clinical evaluations.

The main limitation of this study was the lack of objective tests to evaluate dysphagia in detail, such as videofluoroscopic swallowing studies. However, the use of such a test in a large number of patients is not possible, especially when we consider a large number of asymptomatic patients with no apparent problems in the early stages. It is not routinely recommended to perform such invasive tests to screen for dysphagia, such as muscular diseases, in some of our patient groups, such as muscular diseases (6). However, the use of such tests after screening at-risk patients can drastically improve future studies. Another limitation was the lack of additional tools and questionnaires to evaluate dysphagia and nutritional status in greater detail. Screening for nutrition would allow us to determine the potential impact of dysphagia in these patient groups. Although these patients underwent an oral examination by a team of physicians, there were many composite and organized assessment scores and validated questionnaires to determine the oral health status of the patients, and this study was unable to employ them (39). While the results can hold a light for the future studies in these rare groups of patients, this is a study which enrolled patients from a single tertiary care center. Since these results may vary from center to center, or may not be the same for other countries, the generalizability of the results should be evaluated with caution. Finally, the patients in the defined groups other than the DMD-BMD group were quite heterogeneous, which raises questions about the validity of reported differences between groups.

CONCLUSION

Dysphagia is a common neuromuscular disorder. Dysphagia can lead to significant complications. When evaluating patients, they should be questioned absolutely and directed to further investigations in their presence. The evaluation should also include inquiry and assessment of oral health status, and further studies should focus on a more detailed examination and use validated tools to evaluate this problem. Moreover, patients should be informed of the importance of regular oral examinations and maintenance of oral hygiene.

Studies that include a more detailed examination through the use of specialized methods and assessment of treatment methods for dysphagia in neuromuscular diseases may help clinicians alleviate swallowing disorders.

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MEDICAL RECORDS-International Medical Journal

Research Article

The Relationship Between Nutritional Status and Self-Esteem in Adult Women with Type 2 Diabetes: A Cross-Sectional Study

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Abstract

Aim: This study was aimed to determine the relationship between nutritional knowledge level and self-esteem in adult women with type 2 diabetes.
Material and Method: The sample of this descriptive cross-sectional study consisted of 387 participants. Data were collected in an endocrinology outpatient clinic via face-to-face interviews. The data collection form consisted of a 'Personal Information Form', 'Nutrition Habits Section', 'Nutrition Knowledge Level and Food Preference Scale', 'Rosenberg Self-Esteem Scale'. Number and percentage were used in the SPSS package program. Results that were not normally distributed were evaluated according to non-parametric tests.
Results: The mean age of the participants was 42.00±11.35 years and the educational level of 31.2% was primary school. The mean total score of the scales obtained by the participants was average. In the study, no relationship was found between basic nutrition knowledge level and food preference and self-esteem in adult women with type 2 diabetes.
Conclusion: Basic nutrition knowledge and food preferences of women with Type 2 Diabetes were moderate and their self-esteem was adequate. It is important for health professionals to plan individual trainings by determining the nutritional knowledge levels and food preferences of women, and to ensure that diabetes control and self-esteem are increased in the effective management of diabetes and in the promotion of women's health.

Keywords: Diabetes, nutrition, self-esteem, woman

INTRODUCTION

Diabetes Mellitus (DM) is a chronic disease that develops as a result of the absence or insufficiency of insulin secretion and/or insulin resistance. According to the Diabetes Atlas (2021) data, half a million adults worldwide have DM. This number is estimated to increase to 643 million in 2030 and 783 million in 2045 (1). DM has a high prevalence in Türkiye, which increases mortality and morbidity (2). DM increases the risk of heart disease approximately fourfold in women, but only twofold in men (3,4).

Medical nutrition therapy, pharmacologic agents, and insulin therapy can be applied in the treatment of DM (5). In individuals with type 2 diabetes, especially dietary compliance plays an important role in the treatment (6). A healthy diet is an important part of the management of blood glucose levels and also helps prevent DM (4).

Different results have been reported in the literature regarding the nutritional knowledge level of patients with DM. Özkarabulut et al. (2021) found that the nutritional knowledge level of patients with DM was moderate (7). In the study in which participants with DM participated, it was found that most of the patients had a moderate level of nutritional knowledge (8). Thewjitcharoen et al. (2018) found that the nutritional knowledge scores of 213 patients with type 2 diabetes were at a moderate level (9). Han et al. (2020) said that the level of nutritional knowledge in patients with diabetes was inadequate (10).

Nutritional behaviors help manage chronic diseases (such as diabetes and heart disease), increase energy, promote vitality, and improve an individual's mental health by reducing symptoms of anxiety and depression (11).

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Nutrition affects the mood and behavior of individuals (12). At the same time, nutritional behaviors play a significant role in self-esteem (13). Because nutrition affects the correct functioning of body functions and indirectly affects body weight.

In a study, the inverse relationship between body mass index (BMI) and self-esteem is more important in women than in men. Among women, higher and increasing BMI is associated with lower and slower increasing self-esteem (14,15). This relationship is not limited to the teenage years but continues into adulthood. However, studies in the literature mostly concern adolescents. There are a limited number of studies conducted on women over a certain age. In our study, the relationship between the nutritional status and self-esteem of women with diabetes, which can cause significant complications, is examined.

Research Questions

- What are the individual characteristics of the participants?
- What are the dietary habits of the participants?
- What are the nutrition knowledge levels of the participants?
- Is there any relationship between participants' level of nutritional knowledge and self-esteem?

MATERIAL AND METHOD

Design

This is a descriptive-cross-sectional study.

Participants and Settings

The population of the study consisted of patients with type 2 DM applied to the Diabetes Education Unit between 15.01.2023 and 15.07.2023. According to the records of the diabetes education unit, an average of 80 women with Type 2 diabetes applied monthly. At the time of the study, a total of 486 women who met the research inclusion criteria applied. All patients were wanted to be reached within the scope of the sample, but 387 people were reached due to reasons such as not wanting to participate in the research and time problems.

Inclusion Criteria

- Having type 2 DM
- Aged 18-64 years
- Being female
- Volunteering to participate in the research
- Applying to the diabetes education unit within the study recruitment period
- Being able to communicate and cooperate

Data Collection Form

A data collection tool consisting of 5 sections was used. These sections consisted of 'Introductory Information' including questions (age, income level, marital status), 'Nutrition Habits', 'Level of Nutrition Knowledge Level Scale (LNKAS) and Food Preference Scale', 'Basic Nutrition and Food-Health Knowledge', 'Food Preference Scale (FPS)' and 'Rosenberg Self-Esteem Scale (RSES)'.

Introductory Information Section: This section included characteristics such as age, income level, and marital status.

Nutrition Habits Section: It consists of questions about skipping meals and snack/main meal consumption habits.

LNKAS/Basic Nutrition and Food-Health Knowledge: The scale was developed by Batmaz and Güneş (2019). The scale consists of 20 items assessing food preference and 12 items including Basic Nutrition and Food Health Relationship. Items 1, 3, 6, 8, 13, 16, 19, and 20 of the scale are scored in reverse. The scale is scored on a 5-point Likert scale between 4-significantly agree and 0-significantly disagree. Cronbach's Alpha values for the Basic Nutrition Knowledge scale and the Nutrition Preference scale were .72 and .70, respectively. According to the cut-off points for Basic Nutritional Knowledge, the nutritional knowledge level of those who scored less than 45 points is evaluated as "poor", those who scored between 45-55 points as "moderate", those who scored between 56-65 points as "good", and those who scored above 65 points as "very good". For Food Preference, those who scored below 30 points were considered to have "poor" food preference, those who scored between 30-36 points were considered to have "moderate" food preference, those who scored between 37-42 points were considered to have "good" food preference, and those who scored above 42 points were considered to have "very good" food preference. The minimum score on the Basic Nutrition Knowledge scale is 0 and the maximum score is 80, and the minimum score on the Food Preferences scale is 0 and the maximum score is 48 (16).

Rosenberg Self-Esteem Scale (RSES): 0-1 points are scored as high self-esteem, 2-4 points as moderate self-esteem, and 5-6 points as low self-esteem. The RSES consists of twelve sub-domains and the first ten items measure self-esteem. The positively and negatively loaded items are ordered consecutively. Items 1, 2, 4, 6, and 7 are positively loaded and items 3, 5, 8, 9 and 10 are negatively loaded. In scale scoring, a low score indicates high self-esteem and a high score indicates low self-esteem (17).

Data Collection

Data was collected through face-to-face interviews with participants applied to the Diabetes Education Unit and met the inclusion criteria. The data collection time was approximately 15 minutes.

Ethical Aspects of the Research

Ethics committee permission was obtained from Karamanoğlu Mehmetbey University Scientific Research and Publication Ethics Committee (01-2023/13). Verbal and written consents of the participants were obtained. Permission was obtained via e-mail for the scales used in the study.

Data Analysis

SPSS 21 package program was used. Descriptive measures were used in the analysis. Since the data was not normally distributed, non-parametric groups were used to determine whether there was a difference between more than groups. Characteristics such as marital status, smoking and alcohol use were measured with the Mann Whitney U Test, and characteristics such as physical activity and body mass index were measured with the Kruskall Wallis H Test.

A p value below 0.05 was accepted as significant. The Spearman correlation test (r coefficient) was used to examine the relationship between scale ratings.

r=<0.2-Very weak relationship or no correlation,

r=0.2-0.4-Weak correlation,

r=0.4-0.6-Moderate correlation,

r=0.6-0.8-High correlation,

r=>0.8-Very high correlation (18).

RESULTS

The mean age of the participants was 42.00±11.35 years and 79.6% were married. Having any chronic disease other than DM was found to be 31.9% (Table 1).

Table 1. Descriptive characteristics of the participants

		Number (n=387)	Percent
Age Minimum: 18, Maximum: 82, 42.00±11.35 years			
Marital status	**Single**	79	20.4
	Married	308	79.6
Education status	**Primary school**	121	31.2
	Middle school	42	10.9
	High school	117	27.7
	University	107	30.2
Income status	**Income less than expense**	134	34.6
	Good income	253	65.4
Smoking	**Yes**	113	25.3
	No	274	74.7
Alcohol use	**Yes**	31	9.3
	No	356	90.7
Regular physical activity status	**Yes**	73	18.9
	No	193	49.9
	Partially	121	31.2
Having a chronic disease other than type 2 diabetes	**Yes**	128	31.9
	No	259	68.1
Chronic diseases	**Kidney failure**	6	4.7
	Heart failure	18	14.0
	Asthma	28	21.8
	Hypertension	67	52.3
	Other (such as depression and goiter)	9	7,.2
Drug use	**Yes (such as oral antidiabetics, antihypertensives, and anticoagulants)**	184	47.5
	No	203	52.5
Body mass index	**Normal overweight**	59	15.2
	Overweight	135	34.9
	Fat	193	49.9
Vitamin-mineral use	**Yes**	132	34.1
	No	255	65.9
Size: Minimum: 52, Maximum: 150, 83.44±17.759			
Height (cm): Minimum: 140, Maximum: 196, 162.21±8.543			
Body mass index	**Normal**	81	20.9
	Slightly overweight	121	31.3
	Fat	185	47.8

According to the dietary habits of the participants, the frequency of milk and milk group consumption was 59.4% and the frequency of vegetable consumption was 34.4%. The mean relationship between nutrition and health was determined as 7.00±1.48 and the total mean score of food preference was 5.98±1.80 (Table 2).

The mean total score of the participants on the LNKAS was 48.35±6.26, the mean total score on the FPS was 31.06±8.47, and the mean total score on the RSES was 18.60±5.84 (Table 3).

Table 2. Distribution of participants' dietary habits

		Number (n=387)	Percent
Frequency of main meal consumption	One	23	5.9
	Two	142	36.7
	Three	222	57.4
Frequency of snack consumption	One	120	31.0
	Two	124	31.9
	Three	143	37.1
Meal skipping status	Yes	256	66.1
	No	131	33.9
Distribution of meals skipped	Morning meal	41	16.1
	Lunch	64	25.0
	Evening meal	22	8.5
	Snacks	129	50.4
Milk and milk group consumption status	Yes	230	59.4
	No	157	40.6
Walnut consumption status	Yes	148	38.2
	No	239	61.8
Fruit consumption status	Yes	201	51.9
	No	186	48.1
Bread consumption status	Yes	292	75.5
	No	95	24.5
Vegetable consumption	Yes	133	34.4
	No	254	65.6
Cheese consumption status	Yes	77	19.9
	No	310	80.1
Coffee consumption status	Yes	51	13.2
	No	336	86.8
Consumption of carbonated drinks	Yes	22	5.7
	No	365	94.3
Chips consumption status	Yes	13	3.4
	No	374	96.6
Chocolate consumption status	Yes	28	7.2
	No	359	92.8
Consumption of sweet biscuits	Yes	26	6.7
	No	361	93.3
Consumption of salty biscuits	Yes	30	7.8
	No	357	92.2
Consumption of dietary products	Yes	13	3.4
	No	374	96.6
Nutrition Health Relationship Minimum (Min): 2, Maxium (Max): 10, 7.00±1.48			
Food Preference Min: 1, Max: 10, 5.98±1.80			

Table 3. Total mean scores, standard deviations, and minimum and maximum values of the scales				
Scale	**n**	**Mean±SD**	**Min.**	**Max.**
LNKAS	387	48.35±6.26	11.00	78.00
FPS	387	31.06±8.47	2.00	48.00
RSES	387	18.60±5.84	10.00	36.00
SD: standard deviation				

According to income status, those who expressed their income status as good had a higher mean total score on the LNKAS and RSES than those who expressed their income status as low. It was found that those who had any chronic disease other than DM had higher mean scores on the LNKAS than those who did not. It was determined that those who had any chronic disease other than DM had a higher mean total score on the RSES than those who did not have any chronic disease. The mean total score of those who performed regular physical activity was found to be higher than those who never or partially performed physical activity. There was a statistically significant difference according to variables such as BMI, frequency of main meal consumption, and marital status (p≥0.05) (Table 4).

Table 4. Comparison of the mean total scale scores according to the socio-demographic characteristics of the participants				
		LNKAS	**FPS**	**RSES**
Income level	**Less than expenditure**	154.50	187.28	185.92
	Good income	199.48	194.23	211.13
	U	11097.000	15410.000	14182.000
		p=.000	p=.565	p=.018
Marital status	**Single**	191.26	201.84	204.22
	Married	184.06	189.44	191.38
	U	10525.500	11231.000	11359.000
		p=.603	p=.374	p=.362
Smoking status	**Yes**	184.76	184.46	203.28
	No	185.79	210.25	190.17
	U	13674.000	13132.000	14432.000
		p=.934	p=.038	p=.293
Having a chronic disease other than type 2 diabetes	**Yes**	193.57	190.86	184.16
	No	166.43	194.77	216.99
	U	1222.500	14866.000	13051.500
		p=.025	p=.752	p=.008
Frequency of main meal consumption	**One**	169.31	240.43	196.50
	Two	180.81	193.40	204.88
	Three	190.27	186.04	186.78
	KW	1.171	5.092	2.291
		p=.557	p=.078	p=.318
Vitamin-mineral use	**Yes**	195.87	194.76	174.78
	No	180.15	190.58	203.95
	U	14065.500	16086.000	14293.500
		p=.179	p=.726	p=.015
Body mass index	**Normal**	164.85	194.46	172.17
	Slightly overweight	199.46	180.85	195.12
	Overweight	185.80	198.26	202.82
	KW	4.897	1.850	4.272
		p=.086	P=.397	p=.118
Physical activity	**Yes**	179.49	197.15	223.41
	No	190.37	189.70	165.45
	Partially	181.27	192.54	186.36
	KW	0.793	0.245	14.104
		p=.673	p=.885	p=.001
Mann Whitney U test= U; Kruskal Wallis test: KW				

It was observed that there was very weak or no correlation between the scales (p≥0.05) (Table 5).

Table 5. The relationship between the scales

	2. FBS	3. RSES
1. LNKAS	r=.214	
2. FBS		r=-.145
3. RSES		

r=correlation

Multiple linear regression analysis method was used to determine the effect of nutrition knowledge level and food preference on women's self-esteem. There are assumptions in this parametric method. The predicted (dependent) variable should be continuous and normally distributed, and the continuous predictive (independent) variables should also be normally distributed. In addition, there should be no multicollinearity problem among the independent variables in the multiple regression equation (19). This assumption is an important one and is examined with tolerance and VIF values. If VIF values are less than 10 and tolerance values are greater than 0.10, there is no multicollinearity (20). The tolerance value obtained between nutritional knowledge level and food preference is 0.984, which is greater than 0.10, and the VIF value is 1.016, which is less than 10. Therefore, there is no multicolinearity. The regression model examined according to the effect of nutrition knowledge level and food preference on women's self-esteem is significant (F (2,363)=3.111, p<.05). R square value is a statistic that shows how much of the variability in the predicted variable is explained by the independent variables (Pallant, 2017). 2.7% of the variability in self-esteem scores is explained by nutritional knowledge level and food preference scores. LNKAS (B=-0.08, t=-2.689, p<.05) significantly predicts the self-esteem levels of women's children in a negative direction. Since there is a 1 unit increase in LNKAS scores, there is a 0.08 unit decrease in women's self-esteem scores. In this regression model examined, food preference (FBT) is not a significant predictor for women's self-esteem (p>.05). The established regression equation is; Self Esteem=24.195-0.08* LNKAS (Table 6).

Table 6. Reggession table

IV	B	S.E.	β	t	p
Constant	24.195	2.434		9.939	0
FPS	-0.057	0.035	-0.085	-1.611	0.108
LNKAS	-0.08	0.047	-0.089	-2.689	**0.042**
Mod. statistics			$F_{(2.363)}$=3.111; p<.05 R^2=0.027		

IV: independent variable, S.E.: standard error

DISCUSSION

Women are the most affected by nutritional problems in society due to their various physiological periods of major hormonal changes such as pregnancy, breastfeeding and menopause (21). In addition, the nutrition of the children and family is generally the accountability of women and they have an important role in decisions related to nutrition in the society (22,23). The findings obtained from the study conducted to determine whether there is any relationship between nutritional knowledge level and self-esteem in adult women with type 2 DM were discussed in line with the literature.

In the study, it was found that the average scores of primary nourishment and food option of women were both at an intermediate level. In previous studies, it has been found that the nutritional wont and knowledge levels of teachers were inadequate (24,25) and Akgöz et al. (2021) found that the nutritional knowledge equalitys of students in the faculty of sport sciences were poor, unlike our study (26). In Karakuş Kayalı et al.'s (2023) with physical education teachers, similar to our study, it was found that the mean scores of basic nutrition and food preference sub-dimensions of nutrition knowledge levels of teachers were at a moderate level (27). In Önen and Güngör's (2023) study, nutritional knowledge and food preference knowledge of women were at an intermediate level. Although the nutritional knowledge of the women was at an intermediate level in the present study, it was determined that half of them were obese, they did not perform regular physical activity and the majority of them skipped their meals. Inadequate and unbalanced nutrition leads to many chronic diseases, especially obesity (23,27). Nutritional knowledge also influences the nutritional status and habits of families, especially women (28). It is important that women are given practical trainings on adequate and balanced nutrition by health professionals. On the other hand, the fact that women stated that there was a relationship between nutrition and health above the average can be seen as a positive finding of the study.

Studies have shown that individuals with higher income levels have higher BMI (29-31). The basic nutrition knowledge levels and self-esteem of those with good income status are higher than those with low-income status. However, the majority of the women were in the study were in the overweight and obese group according to BMI. It can be thought that higher income leads to obesity by causing more food consumption and calorie intake with increased purchasing power of individuals. Socioeconomic status is one of the factors affecting an individual's self-esteem (32). Döğücü and Başer

(2021) found that self-esteem increased as income level increased in women. It is thought that a person's high financial income level, meeting their needs, changes in their eating and drinking habits may lead to an increase in self-confidence and self-esteem (33).

In the development of healthy lifestyle behaviors in women, it is important to indicate the negative effect of smoking on diabetes (34). In a study, it was found that smokers had more inadequate and unbalanced eating habits than non-smokers (35). Smoking affects adequate and balanced nutrition and nutritional knowledge (36). In this study, food preferences of non-smokers were better than those of smokers. It can be considered as a natural finding of the study that non-smoking women have better food preferences than smokers due to their better healthy lifestyle behaviors.

Those with any chronic disease other than type 2 diabetes had better basic nutrition knowledge. In the study, hypertension was found to be the most common chronic disease in addition to diabetes in women. Chronic diseases such as diabetes and hypertension are closely related to the weight and nutrition of individuals (37). Having both diseases may have increased women's search for information about nutrition, thus increasing their level of basic nutritional knowledge.

In the study, it was observed that those who had any chronic disease other than DM had lower self-esteem than those who did not. Self-esteem is the state of liking and respecting the characteristics that the individual uses to define themselves. Self-esteem is also closely related to how satisfied the individual is with themselves and how much they value themselves. Self-esteem is affected by many conditions such as physical appearance, health status, and illness (38).

Herring et al. (2014) found that participation in physical activity had positive effects on physical self-concept and self-esteem in young women. In the study conducted with Ouyang et al. (2020) with students, it was observed that participation in sports had a positive effect on self-esteem (39). The study found that women who regular physical activity had higher self-esteem than those who did no or partial physical activity. Our study findings were similar to the literature. Physical activity is thought to have positive effects on women's self-esteem.

In the study, it was determined that there was no relationship between the basic nutrition knowledge level of adult women with type 2 DM and their food preferences and self-esteem. No relevant study was found in the literature. Unlike our study, Durak and Yılmaz (2022) determined that there was a relationship between nutritional literacy and self-efficacy and self-care behaviors in their study where the majority of the participants were women (40). Basic nutritional knowledge and food preference may be an important variable for women to manage their medical nutrition treatments correctly, develop healthy eating behaviors, make decisions for their own health, develop self-confidence, and use health services effectively, especially in diseases such as DM.

The current study has several limitations. The data was based on parcipitants's self-reports. It was studied on a limited sample.

CONCLUSION

It was found that basic nutrition knowledge and food preferences of women with DM were at a moderate level and their self-esteem was adequate. Women's basic nutritional knowledge levels were affected by income status and having another disease; their food preferences were affected by smoking status; and their self-esteem was affected by income status, having another disease, vitamin and mineral use, and performing regular physical activity. The main finding of the study was that there was no relationship between basic nutrition knowledge, food preferences, and self-esteem in adult women with DM.

For this purpose, diabetes schools and trainings are organized for patients in health institutions. It is important for health professionals to plan individual trainings by determining the nutritional knowledge levels and food preferences of women and to ensure that their self-esteem is increased with diabetes control in the effective management of diabetes and in the promotion of women's health.

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Research Article

Investigation of the Relationship Between Bruxism Symptoms and Restless Leg Syndrome

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Abstract

Aim: This study aims to examine the relationship between bruxism symptoms and restless legs syndrome (RLS), focusing on the frequency and severity of RLS symptoms in patients with bruxism.

Material and Method: A total of 134 patients (50 males, 84 females) diagnosed with bruxism out of 212 patients presenting with jaw pain between April 10 and July 6, 2019, were included in the study. The average age of the participants was 47. Patients completed the Bruxism Determination Questionnaire and the RLS Severity Scale. Data were analyzed using SPSS (IBM SPSS for Windows, version 26). Relationships and correlations were determined using descriptive statistics and various statistical tests. Statistical significance was set at ($p<0.05$).

Results: No statistically significant difference was found between bruxism symptoms and RLS severity ($p>0.05$). However, a significant positive correlation was found between the number of bruxism symptoms and the RLS severity score (19.3%, $p=0.025$). Additionally, smoking was found to affect bruxism symptoms but not RLS severity.

Conclusion: Bruxism symptoms increase with the severity of RLS, but no significant inverse relationship was observed. While smoking affects bruxism symptoms, it does not affect RLS severity. Further research with larger sample sizes and more objective evaluation criteria is needed to better understand the relationship between these two conditions.

Keywords: Bruxism, sleep bruxism, restless leg syndrome, cigarette smoking

INTRODUCTION

Bruxism is a condition of significant interest in dentistry, neurology, and psychiatry, attracting the attention of both clinicians and researchers due to its impact on the temporomandibular joint. While various definitions exist in the literature, bruxism is generally characterized as a set of non-functional, pathological jaw movements, such as teeth grinding and clenching, that occur outside the normal physiological functions of the mandible, such as chewing and speaking (1,2). The prevalence of bruxism varies between 6% and 91%, depending on the age groups studied and the types of bruxism considered (3,4). The consequences of bruxism include wear on the occlusal surfaces of teeth, fractures of teeth and implants, hyperkeratotic areas in the buccal mucosa, indentations on the tongue and lips, displacement of the temporomandibular joint (TMJ) disk, pain and hypertrophic appearance in the masticatory muscles.

Restless Leg Syndrome (RLS) was first described by Ekbom in 1945 as a neurological disorder causing varying degrees of discomfort in the legs (5). Initially considered a rare disorder, a 2006 study reported the prevalence of moderate to severe RLS in the general population to be 4.4% (6).

The current literature presents mixed findings regarding the relationship between bruxism symptoms and RLS. The main objective of this study is to investigate the potential relationship between the increase in bruxism symptoms and the severity of RLS. This study is distinctive in that it examines not only the presence of RLS but also the extent to which the severity of RLS correlates with bruxism symptoms.

MATERIAL AND METHOD

This study received the necessary ethical approval from the Non-Invasive Clinical Research Ethics Committee of Recep Tayyip Erdoğan University (Protocol No: 2019/66). A total of 212 patients who presented with jaw pain to the Department of Oral and Maxillofacial Surgery at Recep Tayyip Erdoğan University Faculty of Dentistry between April 10, 2019, and July 6, 2019, were evaluated based on

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the clinical parameters listed in Table 1. Among these, 134 patients (50 males and 84 females) exhibiting bruxism symptoms were included in the study. The average age of the participants was 47 years, ranging from 21 to 69 years.

All patients were provided with an oral and written informed consent form. Those who consented were given the 'Bruxism Determination Questionnaire' listed in Table 2, which was developed based on the diagnostic criteria of the American Academy of Sleep Medicine (3). In this questionnaire, 'yes' answers were scored as '1', 'no' as '0', and 'unknown' as '2'. A score of '1' from any question was considered sufficient for a diagnosis of bruxism.

Patients diagnosed with bruxism were then assessed using the RLS Assessment Scale published by the International RLS Study Group in 2003, as listed in Table 3. This scale includes ten questions, each rated on a scale from 'very severe (4)' to 'none (0)'. The scores were categorized as 'Mild (1-10)', 'Moderate (11-20)', 'Severe (21-30)', and 'Very severe (31-40)'. Data obtained were analyzed using SPSS (IBM SPSS for Windows, version 26).

Table 1. Bruxism clinical parameters

- **Is there abnormal wear on the occlusal surfaces of the teeth?**
- **Is there hypertrophy of the masticatory muscles?**
- **Do you feel fatigue and pain in the masticatory muscles?**
- **Do you have cold sensitivity in your teeth or tooth?**
- **Is there any sound from the TMJ during function?**
- **Are there teeth marks on the buccal mucosa and lateral sides of the tongue?**

Table 2. Bruxism identification questionnaire

	Yes	No	Don't know
Do you grind your teeth while sleeping?			
Do your relatives hear you grinding your teeth while sleeping?			
Do you wake up with your teeth clenched?			
Do you experience jaw pain or fatigue upon waking?			
Do you feel your teeth are loose when you wake up?			
Do you experience sensitivity in your teeth or gums upon waking?			
Do you feel pain in your temples upon waking?			
Do you feel your jaw is locked upon waking?			

Table 3. Restless legs syndrome (RLS) assessment scale

Overall, how would you evaluate the discomfort of RLS in your arms or legs?	(4) Very severe (3) Severe (2) Moderate (1) Mild (0) None	**Overall, assess the severity of your RLS**	(4) Very severe (3) Severe (2) Moderate (1) Mild (0) None
Overall, how do you evaluate the urge to move due to RLS symptoms?	(4) Very frequent (3) Frequent (2) Moderate (1) Infrequent (0) None	**Evaluate how often your RLS symptoms occur**	(4) Very often (6-7 days/week) (3) Often (4-5 days/week) (2) Occasionally (2-3 days/week) (1) Rarely (1 day/week) (0) Never
Overall, how would you rate the relief of your RLS symptoms with movement?	(4) No relief (3) Slight relief (2) Moderate relief (1) Complete/nearly complete relief (0) No discomfort	**Evaluate the average severity of your RLS symptoms**	(4) Very severe (8 hours or more/24 hours) (3) Severe (3-8 hours/24 hours) (2) Moderate (1-3 hours/24 hours) (1) Mild (less than 1 hour/24 hours) (0) None
Evaluate your sleep disturbance due to RLS	(4) Very much (3) Much (2) Moderate (1) Little (0) None	**Evaluate how much RLS symptoms negatively impact your daily life (social, familial, work/school)**	(4) Very much (3) Much (2) Moderate (1) Little (0) None
Evaluate your fatigue and insomnia due to RLS	(4) Very much (3) Much (2) Moderate (1) Little (0) None	**Evaluate your psychological changes due to RLS symptoms (irritability, depression, sadness, anxiety, etc.)**	(4) Very much (3) Much (2) Moderate (1) Little (0) None
Scoring criteria: mild (1-10); moderate (11-20); severe (21-30); very severe (31-40)			

RESULTS

The sample size for this study was calculated to ensure a power of at least 80% and a Type-1 error of 5% for each variable. The normality of continuous measurements was assessed using the Kolmogorov-Smirnov (n>50) and Skewness-Kurtosis tests, and parametric tests were applied as the measurements were normally distributed. Descriptive statistics for the variables were expressed as mean, standard deviation, number (n), and percentage (%). The Independent T-test and One-Way ANOVA were used to compare continuous measurements based on categorical factors, followed by the Duncan test for group comparisons. Multiple Correspondence Analysis was performed to examine the relationships between categorical variables, and the Chi-square (Fisher's exact) test was used to determine relationships between categorical variables. Pearson correlation coefficients were calculated to assess relationships between scales, with a significance level (α) of 5%. Data were analyzed using SPSS (IBM SPSS for Windows, version 26).

Table 4 presents the general descriptive statistics of the 'Demographic, RLS, and Bruxism' measurements of the patients. According to these statistics, 17.9% of patients were categorized as having 'Mild' and 'Moderate' RLS severity; 21.6% were smokers. Additionally, the average RLS severity score was 6.3, and the mean number of Bruxism Symptoms was 3.9.

Table 4. General descriptive statistics of data

		Count	Percentage (%)
Severity of RLS	None	73	54.5
	Mild	24	17.9
	Moderete	24	17.9
	Severe	10	7.5
	Very severe	3	2.2
Smoking status	Non-smoker	105	78.4
	Smoker	29	21.6
		Mean	Std. Dev.
Severity of RLS		6.31	8.83
Bruxism symptoms		3.92	1.88

Table 5 compares the 'Bruxism symptoms' according to the 'RLS severity range'. No statistically significant difference was observed between 'Bruxism symptoms' and the 'RLS severity range' (p>0.05). Although there was a trend of increasing 'Bruxism Symptoms' with increasing 'RLS severity', this increase was not significant.

Tablo 5. Comparison of bruxism symptoms and RLS severity levels

	RLS severity	N	Mean	Std. dev.	Min.	Max.	F	*p
Bruxism Symptoms	None	73	3.62	2.05	1.00	9.00	1.597	0.179
	Mild	24	3.92	1.28	1.00	6.00		
	Moderate	24	4.42	1.89	2.00	9.00		
	Severe	10	4.90	1.66	2.00	7.00		
	Very severe	3	4.00	1.00	3.00	5.00		

* Significance levels according to one-way ANOVA results; a,b,c: Shows the difference between groups (Tukey post-hoc test)

Table 6 presents the correlation analysis between the 'number of Bruxism symptoms' and 'RLS severity scores'. A statistically significant positive correlation of 19.3% was found between the 'Number of Bruxism Symptoms' and 'RLS severity score' (p=0.025). This indicates that as 'Bruxism Symptoms' increase, 'RLS severity score' also increases.

Table 6. Correlation analysis between bruxism symptoms and RLS severity

		RLS severity
Bruxism symptoms	r	.193
	p	**.025**
	n	134

r: pearson correlation coefficients, p: significance levels for the correlation coefficient, n: participant count

Table 7 compares 'Bruxism symptoms' and 'RLS severity' scores according to 'Smoking status'. No statistically significant difference was observed in the 'RLS severity score' based on 'Smoking status' (p>0.05). However, a significant difference was found in 'Bruxism symptoms' based on 'Smoking status' (p=0.011), with lower 'Bruxism symptoms' observed among smokers.

Table 7. Comparison of bruxism and RLS scores by smoking status

	Cigarette	N	Mean	Std. Dev.	t	*p
RLS severity	None	105	6.97	9.07	1.672	.097
	Yes	29	3.90	7.52		
Bruxism symptoms	None	105	4.13	1.90	2.571	.011
	Yes	29	3.14	1.62		

*Independent sample t-test results indicating significance levels

DISCUSSION

This study set out to evaluate the relationship between 'Bruxism Symptoms' and 'RLS' through three different research questions. The first aimed to measure the incidence of RLS in patients with bruxism symptoms. The second investigated the effect of increased bruxism symptoms on RLS scores. The final research question explored the impact of smoking on the number of bruxism symptoms and RLS scores.

Bruxism is characterized by parafunctional habits such as teeth grinding and clenching, leading to tooth wear, hypertrophy, and pain in the masticatory muscles (7). Clinical studies report a bruxism prevalence ranging from

6.5% to 88%, while epidemiological studies typically report lower figures (6-8%) (8-14).

The etiology of bruxism is multifactorial. Historically, it was thought to result primarily from maladaptive prosthetic and restorative rehabilitations applied to the dentition, occlusal discrepancies from tooth tissue damage, and anatomical deviations due to congenital/acquired factors. However, it is now accepted that these factors play a minimal role, with stress, social life, genetics, personality traits, exogenous factors (smoking), and central nervous system dysfunctions being the primary etiological factors (15).

There is no consensus on specific diagnostic criteria or grading systems for bruxism in the literature. Lobezzo et al. advocated for the use of electromyography (EMG) to assess chewing activity and polysomnography (PSG) records for diagnosing sleep bruxism to obtain more objective results (16). Conversely, some studies argue that patient questionnaires, verbal and written anamnesis records, intraoral and extraoral examination findings are preferred diagnostic tools despite their relatively subjective results, due to their clinical applicability, ease of access, short application time, no need for additional equipment, and cost-effectiveness (17,18).

RLS is a neurological disorder causing an urge to move the legs due to unpleasant sensations, primarily at rest, which is alleviated by movement and worsens in the evening or night. Epidemiological studies using diagnostic criteria report an RLS prevalence between 5% and 15% (19,20).

Since its definition, various subjective and objective diagnostic tools have been used for RLS. Clinical findings such as an urge to move the legs due to unpleasant sensations, onset during periods of rest or inactivity, relief with movement, and worsening of symptoms in the evening or night are crucial for diagnosis (21). Additional parameters include periodic limb movements during wakefulness and sleep, functional MRI recordings of neuronal activation in the CNS, and low ferritin levels in serum and cerebrospinal fluid (22-25). In 2003, the International RLS Study Group standardized RLS diagnosis and grading with a 10-question scale (26).

Although many studies have investigated the relationship between these two conditions, few have compared the incidence of RLS in patients with bruxism. Lavigne et al. reported that 9.6% to 10.9% of patients with bruxism symptoms exhibited RLS symptoms in a study of 2019 patients. In another experimental group of 93 individuals diagnosed with RLS, they found that 12.2% had bruxism symptoms (11). Saletu et al. conducted a control study using polysomnography and found a higher PLMS index in patients with sleep bruxism (SB) compared to controls (27). However, these studies only evaluated the presence of symptoms, not the severity of RLS. In our study, this rate varied between 2.2% and 17.9%, inversely proportional to the severity of RLS, partially supporting the literature.

There are some physiological and electrochemical similarities between bruxism and RLS. These similarities are seen in genetic factors, stress, anxiety, poor sleep quality, and various drug effects. Genetic predisposition is an important risk factor for both conditions. RLS often follows an autosomal dominant inheritance pattern, making it more likely to be passed from parent to child. Some genetic markers associated with RLS have been identified (e.g., MEIS1 and BTBD9 genes). These genes might contribute to symptoms by affecting the dopamine system. Although genetic markers for bruxism are less clear, similar inheritance patterns have been observed. Genetic predisposition, combined with environmental factors, may increase the risk of developing bruxism or RLS. This suggests that gene-environment interactions may play a key role in the development of both conditions (28,29).

Psychological factors such as stress, anxiety, and depression can trigger or worsen both conditions. Chronic stress disrupts the balance of dopamine and other neurotransmitters, increasing symptoms of bruxism and RLS. Stress raises hormones like cortisol, which affects dopamine activity in the brain. Bruxism during sleep is often seen as a result of stress. Psychological treatments (e.g., cognitive behavioral therapy) can help manage both bruxism and RLS. Stress management techniques and relaxation therapies may help reduce symptoms (30,31).

Bruxism usually occurs during sleep and is more common in certain stages of the sleep cycle, especially REM sleep. Increased muscle activity during these stages is linked to bruxism. RLS typically occurs when falling asleep or throughout the night and can severely affect sleep quality. People with RLS often experience insomnia and frequent awakenings. Good sleep hygiene is important for both conditions. Regular sleep schedules, a comfortable sleep environment, and limiting caffeine and alcohol can significantly help control symptoms (32,33).

Medications like antidepressants and antipsychotics can trigger symptoms of both bruxism and RLS. SSRIs (selective serotonin reuptake inhibitors) may increase the risk of bruxism, while antipsychotics, which block dopamine receptors, can worsen RLS. Caffeine and alcohol can both worsen symptoms; caffeine stimulates the central nervous system, which can aggravate bruxism and RLS. Alcohol may initially help with falling asleep but can decrease sleep quality and worsen symptoms. Stopping substances like nicotine or alcohol suddenly can also worsen symptoms. Nicotine withdrawal, in particular, can increase RLS symptoms by affecting dopamine levels (34,35).

Both conditions are known to be related to dopamine. While RLS responds positively to dopamine-containing drugs, the role of dopamine in bruxism is still debated (36). Despite these similarities, no consensus exists on the causative role of dopamine in either condition. Our study did not reveal a significant effect of increased bruxism symptoms on RLS scores, but we observed an increasing

trend, although it was not statistically significant. Additionally, we found a significant correlation between the number of bruxism symptoms and RLS severity score, indicating that as bruxism symptoms increase, RLS severity score also increases. These results suggest a potential relationship between the two conditions, with shared pathophysiological mechanisms possibly involving dopaminergic pathways.

Regarding smoking, our study found a significant difference in bruxism symptoms based on smoking status, with smokers exhibiting lower bruxism symptoms. However, no significant difference was observed in RLS severity score based on smoking status. This finding contrasts with previous studies suggesting that smoking may exacerbate bruxism and RLS symptoms (37,38). Further research is needed to explore the complex interactions between smoking, bruxism, and RLS.

CONCLUSION

This study provides insights into the relationship between bruxism symptoms and RLS. While no significant difference was observed between bruxism symptoms and RLS severity range, a significant positive correlation was found between the number of bruxism symptoms and RLS severity score. Additionally, a significant difference in bruxism symptoms was observed based on smoking status, with smokers exhibiting lower bruxism symptoms. These findings suggest a potential relationship between bruxism and RLS, with shared pathophysiological mechanisms possibly involving dopaminergic pathways. Further research is needed to elucidate the complex interactions between these conditions and to explore the role of smoking in their manifestation.

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Research Article

The Effects of Muscular Strength and Biochemical Parameters on Mallampati Classification in Elite Athletes and Non-athletes

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Abstract

Aim: This study aimed to undertake an anthropometric assessment and to compare the muscular strength of elite athletes with that of a control group to predict Mallampati classification.
Material and Method: The study group consisted of elite track athletes, and the control group consisted of volunteers with similar characteristics. Anthropometric measurements of the hand, fingers, and wrist were made; handgrip strength and the pinch strength of the fingers were also measured. A serum biochemical analysis was then performed. Participants were divided into two groups: those with Modified Mallampati Scores (MMS) I and II, and those with III and IV. A partial correlation test was used to examine the correlations of the variables according to the MMS groups.
Results: The study included 32 elite athletes and 42 volunteer participants. Serum Na level, fingertip to root digit 3 (FTR3), and FTR4 were significantly lower in males in MMS groups 3-4. Among all cases, wrist extension angle (WEA) was found to be significantly lower in MMS group 3-4. However, hand breadth at thumb (HBT), hand depth radial (HDR), breadth at the first joint of digit 2 (BFJD2), pinch strength of thumb (PST), and PSLF were significantly higher in MMS groups 3-4. Among these variables, HBT, BFJD2, PST, and PSLF were significantly higher in elite athletes, but HDR was similar between the study groups. MMS groups showed the highest correlation with the pinch strength of the thumb.
Conclusion: The pinch strength of the thumb and little finger was determined as the most important predictors for the MMS group rather than the handgrip strength (HGS).

Keywords: Modified Mallampati scores, handgrip strength, anthropometric measurements, elite athletes, difficult airway

INTRODUCTION

The unanticipated difficult airway is one of the worst scenarios in practice in anesthesia and reanimation due to potentially life-threatening events during anesthesia or acute airway management (1,2). A failed airway attempt is associated with several morbidity and mortality. Various office methods were suggested to use predicting the risk of the difficult airway in clinical evaluation before anesthesia intervention, but the accuracy and benefits of these remain unclear. Leading and well-studied tests included the Mallampati test, the modified Mallampati test, the Wilson risk score, the Cormack-Lehane test, thyromental distance, sternomental distance, mouth opening test, upper lip bite test, or any combination of these (1,3). A difficult airway means difficult facemask ventilation, difficult laryngoscopy, difficult tracheal intubation, and failed intubation. Unfortunately, all of these investigated index tests had relatively low sensitivities with high variability according to the current meta-analysis (2,4).

Although there have been significant developments and innovations with respect to airway management, such as video laryngoscopee and flexible fiberoptic intubation, difficult or failed intubation incidents are neither predictable norpreventable nor preventable (1). In addition to the physiological and metabolic characteristics of the case, the anthropometric evaluation of the airway and the associated factors that change anatomy affect airway management (5). Apart from the direct upper

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airway anatomy, individual characteristics such as age, gender, rare syndromes, and body mass index (BMI) that will indirectly affect this anatomy can make standard airway evaluation methods useless in some cases (6,7). Therefore, new diagnostic methods with higher sensitivity and specificity continue to be investigated (8,9). Lee et al. showed an inconsistency between the two most commonly used classificationsin obesity, Mallampati and Cormack-Lehane grades, and they indicate additional approaches or classification systems for the prediction of airway screening (8). Except for the head, neck, and upper airway, the relationship of some obesity-related anthropometric measurements with Mallampati scores has been previously studied (10). Weight and height are important parameters in the preoperative evaluation and these parameters differ significantly in elite athletes compared to the general population. Lean body mass, total muscle mass, and muscle strength are the most important features that can affect the airway and anesthesia intervention (11). Peck et al. (12) compared the risk for sleep-disordersbetween football linemen and other types of athletes and they detected a higher Mallampati index in the linemen group (2.2±0.8 vs 1.1±0.3). But, American football players are a specific group of athletes and the increased BMI is remarkable in this group (13). Track or endurance athletes have a higher lean body mass (muscle) so, it can be thought that Mallampati scores will be lower, or that the risk of a difficult airway may be lower (14). The negative effect of sarcopenia or the lossof muscle strength his seenin airway disease, andin chronic obstructive pulmonary diseases (15,16). Handgrip strength (HGS) is a standardized measure for assessing overall muscle strength and has been associated with restricted airflow in lung diseases (17). It can be predicted that airway management in track or endurance athletes will be simpler, but there are no studies in the existing literature on airway assessment or sleep disorders based on anthropometric measurements or muscle strength. This study aimed to conductanthropometric assessment and to compare the muscular strength of elite athletes withthat of the control group via Mallampati classification.

MATERIAL AND METHOD

Ethical Approval and Participants

An observational study was designed. The study was conducted in the Department of Anesthesiology, Faculty of Medicine, Ahi Evran University. Institutional ethics committee approval was obtained (2023-06/41). After written informed consent was obtained, 100 participants were enrolled in the study. The study group consisted of elite track athletes, while the control group consisted of volunteers with similar characteristics.

Eligibility Criteria

Elite athletes between the ages of 18-22 and volunteer participants in the same age range, of similar height and weight were included in the study. Participants with an inability to sit, macroglossia, a short frenulum, recent surgery of the head and neck, patients with severe cardiorespiratory disorders, patients with a dental prosthesis, or those who refused or were unable to give informed consent, were excluded from the study.

Outcome Parameters

In anthropometrics measurements height and weight were measured without shoes or heavy clothing to the nearest centimeter and 100 g, respectively. BMI was calculated as body weight in kilograms divided by height squared in meters. HGS tests were performed with a JAMAR® branded hand dynamometer to assess muscle power. Patients were placed seated on a chair with their hands were placed on a table. Their arms were held in a 90-degree flexion, parallel to the floor. Measurements of the dominant hand were then taken three times at 1-minute intervals. The average of three measurements was taken as the "low muscle strength",which was below 15 kg for males and 10 kg for females.

The modified Mallampati score (MMS; 1 to 4) was made by a single anesthetist with 5 years' clinical experience. The patients were divided into two groups: one group for MMS classes 1 and 2, and another group for MMS classes 3 and 4.

Hand anthropometric and muscle strength measurements (mm and kg) were as follows (18-21): hand length (HL), hand breadth at thumb (HBT), hand grip strength (HGS), wrist thickness, dorsal volar diameter (WTDVD), hand circumference (HC), wrist circumference (WC), hand depth radial (HDR), hand depth ulnar (HDU), fist circumference (FC), breadth/depth of digits 1 to 5 at the first and second joint (BFJD1-5, DFJD1-5, BSJD1-5, DSJD1-5), height of digits 1 to 5 (H1-5), palmar height of 1 to 4 (PH1-5), fingertip to root digit 1 to 5 (FTR1-5), total Length of digit 1 to 5 (TL1-5), span length of thumb-Index/middle/ring/little (SLTI-TM-TR-TL), pinch strength of thumb/index/middle/ring/little fingers (PST-M-R-LF), wrist radial abduction angle (WRAA), wrist ulnar abduction angle (WRAA), wrist flexion angle (WFA), wrist extension angle (WEA), thumb metatarsophalangeal flexion angle (TMFFA), and thumb interphalangeal flexion angle (TIFFA).

Laboratory Tests

Venous blood samples were collected for analysis after anthropometric measurements. Atomic absorption spectrometry and enzymatic / colorimetric methods were used for the serum biochemical analysis;copper (Cu, mg/dl), potassium (K, mEq/L), alanine aminotransferase (ALT, IU/L), aspartate aminotransferase (AST, IU/L), creatine kinase (CK, IU/L), high density lipoprotein (HDL, mg/dL), low density lipoprotein (LDL, mg/dL) lactate dehydrogenase (LDH, IU/L), triglyceride (TRIG, mg/dL), zinc (Zn, mg/dL), magnesium (Mg, mg/dL), iron (Fe, ug/dL), sodium (Na, mEq/L), and calcium (Ca, mg/dL).

Statistical Analysis

SPSS 25.0 and Modeler 18.0 (IBM Corporation, Armonk, New York, United States) programs were used in the analysis

of the variables. The conformity of the data to the normal distribution was evaluated with the Shapiro-Wilk Francia test, while the homogeneity of variance was evaluated with the Levene test. Participants were divided into two groups, those with Mallampati scores I and II, and those with III and IV. The Independent-Sample t-test was expressed with Bootstrap results in the comparison of normally distributed quantitative variables according to Mallampati groups, and the Mann-Whitney U test was expressed with Monte Carlo results in the analysis of non-normally distributed variables. Pearson Chi-square and Fisher exact tests, and the Monte Carlo Simulation technique were used to comparethe Mallampati groups with each other according to gender and study groups. After controlling for the gender and study groups of the variables, the Partial Correlation test was used to examine the correlations of the variables according to the Mallampati score. For finding and estimating the variable with the highest significance of the Mallampati groups, supervised machine learning methods, Logistic regression, Support vector machine, Random forest, K-nearest neighbor algorithm, Simple (Naïve) Bayes Classification, C5 algorithm from decision trees and Neural network (Multilayer Perceptron-Radial) Basis was used. The results of the Neural Network (Multilayer Perceptron) analysis, which is the most successful model among these methods, were used. Gradient descent was used for the optimization algorithm, hyperbolic tangent was used as the hidden layer activation function, and Softmax was used as the output layer activation function. While quantitative variables were expressed as mean (standard deviation) and Median (Minimum-Maximum) in the tables, categorical variables were shown as n (%). The variables were analyzed at a 95%-confidence level and a p-value of less than 0.05 was considered significant.

RESULTS

The study included 32 (43.2%) elite athletes and 42 (56.8%) volunteer participants. Thirty-eight (51.4) of the participants were male. MMS was found to be MMS=1 in 31 (41.9) participants, MMS=2 in 22 (29.7%) participants, and MMS=3 in 20 (27.0%) participants. HGS was 37.5±12.6 kg in MMS 1 group, 44.2±15.0 kg in MMS group 2, and 45.5±12.9 kg in MMS group 3 (p=0.077). While WEA (0.010) was found to be significantly lower in MMS groups 3-4 in women, WC (0.049), HDR (0.021), PSLF (0.046) and TIFFA (0.004) were significantly higher. In males BMI (0.036) was found to be significantly higher in MMS groups 3-4, while Na (0.010), BSJD4 (0.030), H2 (0.049), FTR2 (0.030), FTR3 (0.022) and FTR4 (0.030) were significantly lower. Among all cases, WEA (0.010) was found to be significantly lower in MMS groups 3-4. Otherwise, BMI (0.021), HBT (0.049), FC (0.043), WC (0.013), HDR (0.010), BFJD2 (0.030), PST (0.003), PSLF (0.016) and TIFFA were significantly higher in MMS groups 3-4. Among these variables, HBT (<0.001), FC (0.002), WC (0.001), BFJD2 (0.001), PST (<0.001), and PSLF (<0.001) were significantly higher in elite athletes, but WEA (0.537), HDR (0.416) and TIFFA (0.528) were similar between study groups. All of the comparisons are given in Table 1. In addition, MMS groups showed the highest correlation with the pinch strength of the thumb (r=0.392, p=0.001, Table 2). According to the Multilayer Perceptron analysis, the most important factor for MMS groups in females was PSLF (100%), in males, fingertip to root digit 3 (FTR3) (100%) and among all participants, HBT (100%). According to this model, the variable with the lowest significance in the estimation of Mallampati in women, men or in total was determined as the study group (elite athlete vs. control, Table 3).

Table 2. The order of importance of the variables in MMS estimation, by gender and in total (%)

Total		Female		Male	
Variables	**Importance (%)**	**Variables**	**Importance (%)**	**Variables**	**Importance (%)**
HBT	100.0	**PSLF**	100.0	**FTR3**	100.0
WC	81.1	**TIFFA**	81.6	**Na**	96.5
PST	77.2	**HDR**	77.2	**CSJD4**	91.8
WEA	74.8	**WEA**	63.2	**H2**	87.1
BFJD2	61.6	**WC**	13.6	**FTR2**	85.4
PSLF	55.2	**Study group**	9.9	**BMI**	45.7
HDR	35.4			**FTR4**	11.4
Gender	15.5			**Study group**	6.1
Study group	14.3				

Mallampati	**Predicted**								
	I+II	**III+IV**	**Correct (%)**	**I+II**	**III+IV**	**Correct (%)**	**I+II**	**III+IV**	**Correct (%)**
I+II	50	3	94%	28	1	97%	18	6	75%
III+IV	1	20	95%	1	6	86%	5	9	64%
Total	**69%**	**31%**	**95%**	**81%**	**19%**	**94%**	**61%**	**39%**	**71%**

HBT: hand breadth at thumb, WC: wrist circumference, PST: pinch strength of thumb, WEA: wrist extension angle, BFJD2: breadth at the first joint of digit 2, PSLF: pinch strength of little finger, HDR: hand depth radial, TIFFA: thumb interphalangeal flexion angle, FTR3: fingertip to root digit 3, CSJD4: circumference at the second joint of digit 4, H2: height 2, FTR2: Fingertip to root digit 2, BMI: body mass index, FTR4: fingertip to root digit 4

Neural Network (Multilayer Perceptron), Hidden layer activation function: Hyperbolic tangent output layer activaction function: Softmax, Dependent Variable: Mallampati

Table 1. Multi-layered comparison of variables by study group (control and elite athlete) and gender

	Female		p	Male		p	Total		p
	(I+II)	(III+IV)		(I+II)	(III+IV)		(I+II)	(III+IV)	
	n (%)			n (%)			n (%)		
Gender (male)	-	-	-	-	-	-	24 (45.3)	14 (66.7)	0.125[c]
Elite athlete	7 (24.1)	2 (28.6)	0.999[f]	14 (58.3)	9 (64.3)	0.746[c]	21 (39.6)	11 (52.4)	0.436[c]
	Mean (SD.) or Median (min-max)			Mean (SD.) or Median (min-max)			Mean (SD.) or Median (min-max)		
Height	1.65 (0.05)	1.65 (0.02)	0.784[t]	1.74 (1.66-1.94)	1.74 (1.65-1.85)	0.244[u]	1.68 (1.52-1.94)	1.70 (1.62-1.85)	0.501[u]
Weight	59.06 (6.68)	59.51 (9.56)	0.883[t]	82.05 (17.22)	83.86 (7.45)	0.713[t]	64.20 (44-129)	78.10 (47-98.70)	0.052[u]
BMI	20.98 (18.78-29.72)	21.30 (17.47-28.65)	0.872[u]	24.66 (19.84-43.10)	28.05 (22.82-33.75)	**0.036[u]**	22.27 (18.78-43.10)	25.50 (17.47-33.75)	**0.021[u]**
Age	20 (19-22)	20 (18-21)	0.345[u]	20 (18-27)	20 (18-26)	0.473[u]	20 (18-27)	20 (18-26)	0.281[u]
HL	173.23 (6.32)	173.32 (9.31)	0.990[t]	191.26 (169.17-201.58)	185.52 (172.63-198.99)	0.100[u]	177.62 (157.02-201.58)	181.92 (156.82-198.99)	0.532[u]
HBT	74.85 (4.93)	75.90 (5.85)	0.640[t]	87.34 (5.18)	87.69 (4.02)	0.812[t]	80.50 (8.02)	83.76 (7.29)	**0.049[t]**
HGS	28.68 (5.02)	29.61 (4.40)	0.630[t]	54.36 (5.84)	53.52 (5.44)	0.634[t]	34.90 (19.60-72.10)	50.30 (23.40-67)	0.173[u]
Zn	0.78 (0.57-1.11)	0.66 (0.57-0.96)	0.216[u]	0.84 (0.51-1.92)	0.90 (0.54-1.84)	0.292[u]	0.81 (0.51-1.92)	0.88 (0.54-1.84)	0.567[u]
Cu	0.93 (0.63-1.90)	0.96 (0.78-1.17)	0.608[u]	0.78 (0.57-1.09)	0.80 (0.36-1.08)	0.985[u]	0.84 (0.57-1.90)	0.87 (0.36-1.17)	0.913[u]
Mg	24.90 (16.65-54.60)	22.50 (20.85-28.95)	0.636[u]	26.73 (4)	26.69 (2.82)	0.970[t]	26 (16.65-54.60)	25.80 (20.85-30.75)	0.879[u]
Fe	1.50 (0.56)	1.56 (0.46)	0.810[t]	1.89 (0.47)	2.01 (0.60)	0.475[t]	1.67 (0.55)	1.86 (0.59)	0.218[t]
K	142.50 (88.50-300)	160.50 (93-248)	0.874[u]	241 (115-264)	234 (105-260)	0.522[u]	165 (88.50-300)	174 (93-260)	0.791[u]
Na	2946.81 (97.52)	2916.77 (146.54)	0.560[t]	2927.47 (83.92)	2862.76 (84.85)	**0.010[t]**	2938.05 (91.27)	2880.76 (108.64)	0.059[t]
Ca	126.75 (57.88-382.75)	91.13 (46.63-147)	0.121[u]	113.19 (26.87)	120.58 (25.88)	0.396[t]	121 (57.88-382.75)	120.75 (46.63-182)	0.550[u]
AST	17 (10-42)	14 (13-27)	0.623[u]	22.33 (5.04)	20.79 (5)	0.317[t]	18 (10-42)	18 (10-29)	0.721[u]
ALT	15 (9-43)	14 (7-25)	0.541[u]	20 (12-61)	17.50 (10-53)	0.375[u]	16 (9-61)	17 (7-53)	0.945[u]
CHO2	152.90 (28.08)	146.29 (16.78)	0.450[t]	131 (90-241)	128.50 (109-206)	0.895[u]	140 (90-241)	137 (109-206)	0.739[u]
CK	70 (43-727)	75 (46-772)	0.977[u]	119 (61-437)	113 (79-648)	0.216[u]	102 (43-727)	102 (46-772)	0.727[u]
HDL	60 (39.90-86.40)	57.60 (42.60-86.30)	0.931[u]	53.95 (32-70.70)	55.75 (33.20-68)	0.982[u]	55.85 (11.74)	56.05 (12.73)	0.941[t]
LDL	97.68 (26.43)	83.93 (13.01)	0.070[t]	88.78 (30.58)	90.39 (22.29)	0.871[t]	93.65 (28.45)	88.24 (19.58)	0.356[t]
LDH	155 (120-325)	148 (120-346)	0.744[u]	189 (127-391)	145.50 (133-268)	0.145[u]	157 (120-391)	147 (120-346)	0.237[u]
TRİG	78 (34-271)	96 (47-143)	0.537[u]	69 (50-232)	71 (64-452)	0.268[u]	73 (34-271)	76 (47-452)	0.155[u]
WTDVD	51.91 (48.91-77)	53.06 (44.74-58.04)	0.994[u]	58.21 (51.23-67.72)	58.92 (52.58-63.58)	0.693[u]	54.23 (48.91-77)	57.70 (44.74-63.58)	0.101[u]
HC	73.19 (4.56)	73.57 (5.16)	0.900[t]	83.50 (21-94)	85 (79-92)	0.957[u]	79 (21-94)	81 (65-92)	0.096[u]
WC	77.62 (6.30)	80.86 (3.13)	**0.049[t]**	90.50 (22.50-107)	90 (72-106)	0.971[u]	82 (22.50-107)	87 (72-106)	0.089[u]
FC	94 (64-107)	94 (88-110)	0.567[u]	109 (27-124)	110.50 (102-123)	0.730[u]	99 (27-124)	107 (88-123)	**0.043[u]**

HL: hand length, HBT: hand breadth at thumb, HGS: hand grip strength, WTDVD: wrist thickness, dorsal volar diameter, HC: hand circumference, WC: wrist circumference, FC: fist circumference

t: Independent t-test (Bootstrap), u: Mann-Whitney U test (Monte Carlo), f: Fisher exact test (Exact), c: Pearson Chi-square test (Monte Carlo, Exact)

Table 1. Multi-layered comparison of variables by study group (control and elite athlete) and gender

	Female		p	Male		p	Total		p
	(I+II)	(III+IV)		(I+II)	(III+IV)		(I+II)	(III+IV)	
	Mean (SD.) or Median (min-max)			Mean (SD.) or Median (min-max)			Mean (SD.) or Median (min-max)		
WC2	61 (54-69)	63 (59-71)	0.401[u]	70 (17.50-83)	71.50 (64-78)	0.240[u]	63 (17.50-83)	70 (59-78)	**0.013[u]**
HDU	24.64 (2)	25.13 (2.92)	0.750[t]	29.47 (2.51)	28.56 (1.69)	0.178[t]	26.82 (3.29)	27.42 (2.67)	0.455[t]
HDR	41.68 (33.61-52.56)	47.33 (37.71-49.07)	**0.021[u]**	51.93 (4.62)	53.38 (3.30)	0.307[t]	46.57 (6.72)	51.01 (4.85)	**0.010[t]**
BFJD1	17.91 (1.11)	17.81 (1.59)	0.850[t]	20.95 (18.84-23.69)	20.73 (19.16-24.26)	0.549[u]	19.33 (1.97)	19.81 (1.97)	0.436[t]
DFJD1	15.18 (1.02)	15.40 (1.36)	0.760[t]	17.42 (1.32)	17.07 (1.27)	0.386[t]	16.20 (1.61)	16.52 (1.50)	0.485[t]
BFJD2	16.84 (12.54-19.09)	16.57 (14.96-20.08)	0.830[u]	19.04 (1.69)	19.48 (1.23)	0.376[t]	17.85 (1.85)	18.69 (1.81)	**0.030[t]**
DFJD2	14.87 (10.52-16.77)	15.48 (14.02-16.92)	0.484[u]	17.42 (1.27)	17 (0.95)	0.277[t]	16.09 (1.72)	16.49 (1.24)	0.347[t]
BSJD2	14.26 (13.09-15.79)	14.73 (13.09-17.23)	0.999[u]	16.19 (1.07)	16.23 (1.02)	0.931[t]	15.38 (13.09-17.96)	15.70 (13.09-18.17)	0.187[u]
DSJD2	11.58 (1.29)	11.50 (1.50)	0.900[t]	12.56 (11.49-15.23)	12.71 (9.93-14.80)	0.572[u]	12.26 (1.43)	12.21 (1.31)	0.950[t]
BFJD3	16.72 (0.94)	16.91 (1.88)	0.780[t]	19.33 (1.13)	19.06 (1.06)	0.545[t]	17.90 (1.66)	18.35 (1.69)	0.347[t]
DFJD3	15.34 (0.98)	15.93 (1.38)	0.340[t]	17.67 (1.61)	17.42 (0.94)	0.584[t]	16.40 (1.74)	16.93 (1.29)	0.178[t]
BSJD3	14.28 (0.90)	14.36 (1.60)	0.910[t]	16.45 (0.93)	16.19 (0.93)	0.396[t]	15.26 (1.42)	15.58 (1.45)	0.426[t]
DSJD3	11.69 (1.28)	11.73 (1.61)	0.970[t]	13.60 (1.16)	13.01 (0.82)	0.119[t]	12.55 (1.55)	12.59 (1.27)	0.960[t]
BFJD4	15.61 (0.76)	15.58 (1.42)	0.950[t]	18.22 (1.20)	18.23 (1.16)	0.990[t]	16.79 (1.63)	17.34 (1.77)	0.218[t]
DFJD4	14.37 (1.07)	14.65 (1.42)	0.710[t]	16.71 (1.18)	16.44 (1.23)	0.554[t]	15.43 (1.62)	15.84 (1.53)	0.347[t]
CFJD4	13.34 (9.49-15.32)	13.93 (12.16-16.13)	0.589[u]	15.25 (13.93-19.72)	15.41 (14.32-17.76)	0.588[u]	14.49 (1.82)	14.94 (1.35)	0.287[t]
BSJD4	10.63 (0.98)	10.76 (1.37)	0.850[t]	12.43 (1.01)	11.88 (0.67)	**0.030[t]**	11.45 (1.34)	11.50 (1.07)	0.911[t]
BFJD5	13.94 (1.23)	13.68 (1.76)	0.670[t]	15.64 (14.35-18.64)	15.92 (14.41-18.11)	0.450[u]	14.93 (1.63)	15.07 (1.63)	0.782[t]
DFJD5	12.47 (0.91)	12.29 (1.09)	0.800[t]	14.78 (1.17)	14.70 (1.31)	0.871[t]	13.52 (1.55)	13.90 (1.68)	0.455[t]
BSJD5	11.94 (0.73)	12.15 (1.18)	0.660[t]	13.76 (11.23-17.06)	13.89 (13-16.24)	0.932[u]	12.69 (9.96-17.06)	13.62 (10.55-16.24)	0.089[u]
DSJD5	9.44 (0.84)	9.54 (1.73)	0.890[t]	11.34 (1.30)	11.16 (0.99)	0.634[t]	9.93 (8.22-15.13)	10.99 (7.22-12.62)	0.193[u]
H1	81.34 (11.53)	76.66 (16.56)	0.450[t]	79.78 (12.15)	74.95 (9.99)	0.198[t]	80.63 (11.73)	75.52 (12.16)	0.129[t]
H2	163.51 (6.81)	161.15 (13.84)	0.670[t]	177.56 (9.54)	170.76 (7.55)	**0.049[t]**	169.87 (10.73)	167.56 (10.77)	0.495[t]
H3	173.37 (6.45)	173.74 (9.21)	0.930[t]	189.77 (8.80)	185 (4.18)	0.079[t]	180.80 (11.16)	181.25 (8.15)	0.881[t]
H4	164.50 (7.53)	161.99 (9.43)	0.490[t]	182.40 (161.41-192.39)	175.83 (165.72-183.75)	0.123[u]	170.91 (11.09)	169.96 (9.08)	0.733[t]
H5	134.07 (11.34)	129.68 (11.11)	0.360[t]	147.78 (10.78)	144.18 (9.52)	0.267[t]	140.28 (12.96)	139.34 (12.04)	0.772[t]
PH1	55.16 (4.25)	52.39 (8.27)	0.430[t]	55.81 (40.20-69.96)	61.81 (47.93-78.60)	0.115[u]	55.27 (5.60)	59.43 (11.47)	0.158[t]
PH2	97.41 (4.07)	96.65 (7.54)	0.780[t]	108.65 (95.62-155)	105.24 (98.28-111.09)	0.205[u]	101.43 (88.45-155)	104.45 (85.77-111.09)	0.427[u]

WC2: wrist circumference, HDU: hand depth ulnar, HDR: hand depth radial, BFJD1: breadth at the first joint of digit 1, DFJD1: depth at the first joint of digit 1, BFJD2: breadth at the first joint of digit 2, DFJD2: depth at the first joint of digit 2, BSJD2: breadth at the second joint of digit 2, DSJD2: depth at the second joint of digit 2, BFJD3: breadth at the first joint of digit 3, DFJD3: depth at the first joint of digit 3, BSJD3: breadth at the second joint of digit 3, DSJD3: depth at the second joint of digit 3, BFJD4: breadth at the first joint of digit 4, DFJD4: depth at the first joint of digit 4, CFJD4: circumference at the first joint of digit 4, BSJD4: breadth at the second joint of digit 4, BFJD5: breadth at the first joint of digit 5, DFJD5: depth at the first joint of digit 5, BSJD5: breadth at the second joint of digit 5, DSJD5: depth at the second joint of digit 5, H1: height1, H2: height2, H3: height3, H4: height4, H5: height5, PH1: palmar height of 1, PH2: palmar height of 2

t: Independent t-test (Bootstrap), u: Mann-Whitney U test (Monte Carlo), f: Fisher exact test (Exact), c: Pearson Chi-square test (Monte Carlo, Exact)

Table 1. Multi-layered comparison of variables by study group (control and elite athlete) and gender

	Female		p	Male		p	Total		p
	(I+II)	(III+IV)		(I+II)	(III+IV)		(I+II)	(III+IV)	
	Mean (SD.) or Median (min-max)			Mean (SD.) or Median (min-max)			Mean (SD.) or Median (min-max)		
PH3	97.98 (4.76)	98.59 (6.16)	0.840[t]	107.69 (6.21)	106.79 (3.41)	0.673[t]	102.38 (7.29)	104.06 (5.88)	0.188[t]
PH4	87.01 (6.01)	86.41 (6.92)	0.840[t]	97.67 (82.56-196.80)	95.05 (87.62-103.57)	0.533[u]	90.65 (73.23-196.80)	93.25 (77.79-103.57)	0.495[u]
FTR1	60.38 (4.28)	61.46 (5.49)	0.710[t]	68.45 (5.12)	66.08 (3.78)	0.149[t]	64.03 (6.16)	64.54 (4.83)	0.703[t]
FTR2	69.93 (61.99-81.93)	71.18 (63.76-75.47)	0.297[u]	74.79 (4.52)	71.37 (2.41)	**0.030[t]**	71.82 (5.04)	71.12 (3.06)	0.455[t]
FTR3	75.33 (3.36)	75.60 (3.29)	0.840[t]	84.04 (72.64-91.45)	78.39 (73.01-80.83)	**0.022[u]**	77.09 (65.36-91.45)	78.21 (69.74-80.83)	0.784[u]
FTR4	70.01 (3.82)	70.07 (4.11)	0.970[t]	76.39 (4.72)	73.07 (3.05)	**0.030[t]**	72.90 (5.29)	72.07 (3.64)	0.337[t]
FTR5	57.66 (3.43)	58.80 (5.13)	0.580[t]	62.57 (3.84)	61.06 (3.30)	0.208[t]	59.88 (4.36)	60.31 (4.02)	0.733[t]
TTL1	124.33 (5.18)	126.14 (8.01)	0.490[t]	134.23 (6.10)	134.09 (5.34)	0.960[t]	128.81 (7.46)	131.44 (7.25)	0.079[t]
TL2	169.36 (7.19)	169.94 (10.03)	0.890[t]	182.75 (8.47)	178.89 (5.40)	0.089[t]	175.43 (10.24)	175.90 (8.23)	0.782[t]
TL3	174.35 (6.49)	173.38 (9.97)	0.880[t]	189.26 (9.56)	184.90 (6.76)	0.129[t]	181.10 (10.92)	181.06 (9.51)	0.990[t]
TL4	164.86 (6.66)	164.24 (9.52)	0.930[t]	179.45 (9.45)	176.71 (6.48)	0.386[t]	170.24 (151.57-190.96)	172.25 (147.50-190.01)	0.449[u]
TL5	142.61 (6.72)	141.70 (8.49)	0.790[t]	155.30 (8.98)	153.97 (6.50)	0.634[t]	148.36 (10.03)	149.88 (9.18)	0.495[t]
SLTI	113.75 (10.94)	120.22 (15.57)	0.240[t]	134.85 (114.03-174.60)	127.40 (114.14-155.25)	0.208[u]	121.80 (91.06-174.60)	127.01 (99.96-155.25)	0.287[u]
SLTM	149.78 (104.80-414.80)	161.04 (129.32-184.70)	0.113[u]	177.59 (19.19)	168.55 (12.53)	0.079[t]	159 (104.80-414.80)	164 (129.32-197.62)	0.335[u]
SLTR	165.58 (12.29)	174.97 (17.38)	0.160[t]	194.12 (21.28)	185.82(13.98)	0.228[t]	175.54 (141.11-247)	185.70 (140.97-208.96)	0.205[u]
SLTL	181.29 (13.21)	190.26 (17.83)	0.190[t]	202.76 (16.99)	199.71 (10.05)	0.554[t]	188.42 (148.29-233)	201.91 (157.07-212)	0.075[u]
PST	10.25 (4.01)	14.40 (7.32)	0.290[t]	19.42 (6.68)	24.09 (7.42)	0.119[t]	13.60 (2.40-29)	19.80 (7.70-35)	**0.003[u]**
PSIF	7 (2.34)	7.47 (2.79)	0.720[t]	12.70 (4.60-22.70)	12.30 (9.10-22.30)	0.807[u]	7.90 (3.50-22.70)	10.70 (3.20-22.30)	0.078[u]
PSMF	6.96 (2.51)	7.66 (3.73)	0.660[t]	12.47 (4.15)	12.19 (4.17)	0.839[t]	8.40 (2.50-21.70)	10.40 (1.20-17)	0.175[u]
PSRF	5.07 (1.45)	6.16 (2.54)	0.310[t]	9.12 (4.14)	8.21 (2.21)	0.436[t]	6.20 (1.70-19.60)	7.50 (2.30-11.60)	0.107[u]
PSLF	2.60 (1.20-6.50)	3.90 (2.50-6.10)	**0.046[u]**	5.87 (2.34)	6.03 (1.98)	0.851[t]	3.40 (1.20-10.70)	5.50 (2.50-9)	**0.016[u]**
WRAA	30.07 (5.97)	29.29 (6.37)	0.860[t]	32.50 (24-46)	39 (16-45)	0.362[u]	31.45 (5.91)	32.79 (9.37)	0.594[t]
WRAA	33 (21-50)	34 (20-42)	0.746[u]	40 (25-50)	43 (20-49)	0.983[u]	40 (21-50)	40 (20-49)	0.886[u]
WFA	60 (44-89)	65 (42-70)	0.886[u]	69.55 (10.62)	76.22 (14.42)	0.168[t]	65.08 (10.22)	70.43 (15.53)	0.139[t]
WEA	78.06 (9.54)	67.14 (10.09)	**0.010[t]**	70.75 (9.56)	67.53 (9.59)	0.386[t]	74.75 (10.14)	67.40 (9.50)	**0.010[t]**
TMFFA	55 (40-76)	55 (50-70)	0.469[u]	60 (45-70)	62 (45-67)	0.895[u]	60 (40-76)	60 (45-70)	0.312[u]
TIFFA	78 (60-90)	87 (85-90)	**0.004[u]**	85 (60-96)	84 (70-90)	0.831[u]	80 (60-96)	85 (70-90)	**0.013[u]**

PH3: palmar height of 3, PH4: palmar height of 4, FTR1: fingertip to root digit 1, FTR2: fingertip to root digit 2, FTR3: fingertip to root digit 3, FTR4: fingertip to root digit 4, FTR5: fingertip to root digit 5, TTL1: total thumb length, TL2: total length 2, TL3: total length 3, TL4: total length 4, TL5: total length 5, SLTI: span length thumb-index, SLTM: span length thumb-middle, SLTR: span length thumb-ring, SLTL: span length thumb-little, PST: pinch strength of thumb, PSIF: pinch strength of index finger, PSMF: pinch strength of middle finger, PSRF: pinch strength of ring finger, PSLF: pinch strength of little finger, WRAA: wrist radial abduction angle, WRAA: wrist ulnar abduction angle, WFA: wrist flexion angle, WEA: wrist extension angle, TMFFA: thumb metatarsophalangeal flexion angle, TIFFA: thumb interphalangeal flexion angle

t: Independent t-test (Bootstrap), u: Mann-Whitney U test (Monte Carlo), f: Fisher exact test (Exact), c: Pearson Chi-square test (Monte Carlo, Exact)

Table 3. Partial correlation table of MMS groups with variables

Mallampati*	r	p	Mallampati*	r	p	Mallampati*	r	p
Height	-0.200	0.092	**HDU**	-0.136	0.254	**PH3**	-0.091	0.448
Weight	0.010	0.936	**HDR**	**0.246**	0.037	**PH4**	-0.057	0.635
BMI	0.110	0.357	**BFJD1**	-0.071	0.551	**FTR1**	-0.129	0.281
Age	-0.043	0.717	**DFJD1**	-0.006	0.959	**FTR2**	-0.171	0.150
HL	-0.133	0.266	**BFJD2**	0.092	0.442	**FTR3**	-0.213	0.073
HBT	0.037	0.760	**DFJD2**	0.027	0.819	**FTR4**	-0.209	0.078
HGS	-0.052	0.665	**BSJD2**	0.037	0.758	**FTR5**	-0.031	0.793
Zn	0.025	0.833	**DSJD2**	-0.112	0.351	**TTL1**	-0.016	0.891
Cu	0.102	0.393	**BFJD3**	-0.058	0.630	**TL2**	-0.149	0.211
Mg	-0.125	0.296	**DFJD3**	0.069	0.564	**TL3**	-0.157	0.188
Fe	0.037	0.759	**BSJD3**	-0.009	0.943	**TL4**	-0.162	0.173
K	-0.010	0.931	**DSJD3**	-0.037	0.758	**TL5**	-0.093	0.436
Na	**-0.246**	0.037	**BFJD4**	-0.024	0.840	**SLTI**	-0.109	0.364
Ca	-0.129	0.281	**DFJD4**	0.013	0.915	**SLTM**	-0.003	0.983
AST	-0.048	0.687	**BSJD4**	0.041	0.731	**SLTR**	-0.056	0.641
ALT	-0.050	0.674	**CSJD4**	-0.101	0.398	**SLTL**	0.039	0.746
CHO2	0.007	0.952	**BFJD5**	-0.087	0.466	**PST**	**0.392**	0.001
CK	0.106	0.376	**DFJD5**	-0.079	0.512	**PSIF**	0.231	0.051
HDL	0.090	0.453	**BSJD5**	-0.028	0.814	**PSMF**	0.052	0.663
LDL	-0.138	0.249	**DSJD5**	-0.001	0.996	**PSRF**	0.006	0.958
LDH	-0.017	0.889	**H1**	-0.232	0.049	**PSLF**	0.131	0.273
TRİG	0.190	0.110	**H2**	-0.253	0.032	**WRAA**	-0.053	0.656
WTDVD	-0.038	0.751	**H3**	-0.128	0.285	**WRAA**	-0.077	0.520
HC	0.007	0.953	**H4**	-0.225	0.057	**WFA**	0.048	0.689
WC	0.051	0.671	**H5**	-0.196	0.099	**WEA**	**-0.277**	0.019
FC	0.066	0.581	**PH1**	0.095	0.429	**TMFFA**	0.145	0.225
WC2	0.053	0.656	**PH2**	**-0.240**	0.042	**TIFFA**	0.156	0.191

HL: hand length, HBT: hand breadth at thumb, HGS: hand grip strength, WTDVD: wrist thickness, dorsal volar diameter, HC: hand circumference, WC: wrist circumference, FC: fist circumference, WC2: wrist circumference, HDU: hand depth ulnar, HDR: hand depth radial, BFJD1: breadth at the first joint of digit 1, DFJD1: depth at the first joint of digit 1, BFJD2: breadth at the first joint of digit 2, DFJD2: depth at the first joint of digit 2, BSJD2: breadth at the second joint of digit 2, DSJD2: depth at the second joint of digit 2, BFJD3: breadth at the first joint of digit 3, DFJD3: depth at the first joint of digit 3, BSJD3: breadth at the second joint of digit 3, DSJD3: depth at the second joint of digit 3, BFJD4: breadth at the first joint of digit 4, DFJD4: depth at the first joint of digit 4, CFJD4: circumference at the first joint of digit 4, BSJD4: breadth at the second joint of digit 4, BFJD5: breadth at the first joint of digit 5, DFJD5: depth at the first joint of digit 5, BSJD5: breadth at the second joint of digit 5, DSJD5: depth at the second joint of digit 5, H1: height1, H2: height2, H3: height3, H4: height4, H5: height5, PH1: palmar height of 1, PH2: palmar height of 2, PH3: palmar height of 3, PH4: palmar height of 4, FTR1: fingertip to root digit 1, FTR2: fingertip to root digit 2, FTR3: fingertip to root digit 3, FTR4: fingertip to root digit 4, FTR5: fingertip to root digit 5, TTL1: total thumb length, TL2: total length 2, TL3: total length 3, TL4: total length 4, TL5: total length 5, SLTI: span length thumb-index, SLTM: span length thumb-middle, SLTR: span length thumb-ring, SLTL: span length thumb-little, PST: pinch strength of thumb, PSIF: pinch strength of index finger, PSMF: pinch strength of middle finger, PSRF: pinch strength of ring finger, PSLF: pinch strength of little finger, WRAA: wrist radial abduction angle, WRAA: wrist ulnar abduction angle, WFA: wrist flexion angle, WEA: wrist extension angle, TMFFA: thumb metatarsophalangeal flexion angle, TIFFA: thumb interphalangeal flexion angle

Partial Correlation Test, Control Variables: Study group & gender, r: Correlation Coefficient

DISCUSSION

The main findings of the study indicate that WEA was significantly lower in high MMS groups. In addition, BMI, HBT, FC, WC, HDR, BFJD2, PST, PSLF, and TIFFA were significantly higher in MMS groups. MMS groups showed the highest correlation with the PST. The most important factor for MMS groups in females was PSLF (100%), FTR3 in males, and HBT among all participants.

The Mallampati classification of the upper airway is based on the anatomical relation of the palatoglossal and palatopharyngeal arches, uvula, and the posterior part of the tongue. As such, if the volume or size of the base of the

tongue is large, this limits the capacity of the oropharyngeal cavity (22). In addition, increased tongue thickness (TT), demonstrated even by neck ultrasonography, is an independent, proven risk factor for an increased risk of a difficult airway (Odd's Ratio=4.525 for TT>67 mm) (23,24). Wang et al. demonstrated strong correlations between tongue fat reduction and improvement in the apnea-hypopnea index (AHI), and they indicated that areduction in tongue fat affects tongue volume, increases the upper airway passage, improves tongue function, increased muscle strength, reduced and collapsibility of the tongue. The tongue is formed by extrinsic and intrinsic muscles, and the extrinsic muscles (the genioglossus, the hyoglossus, the styloglossus, and the palatoglossus) determine and change the position of the tongue in the oropharyngeal space (25). Current studies showed the efficacy of hypoglossal nerve stimulation as a major reason for hypopharyngeal obstruction with collapsed tongue base of the upper airway due to reduced genioglossus muscle tone (26). Similarly, myofunctional exercises of the local oropharynx region increase the mobility, endurance, and strength of the related muscles, and thus prevent the hypopharyngeal collapsing, especially the tongue base by forced repositioning (27). We could not find a study that directly assessed tongue/oropharyngeal muscle strength and mallampati scores or the risk of difficult airway intervention. However, with a general approach, a hypothesis such as 'Increasing muscle strength affects upper airway anatomy and functions similar to the effect achieved by reducing fat volume (decreased fat volume, and increased muscle function)' can be established. HGS has been suggested as a beneficial index for diagnosing overall muscular strength and sarcopenia in various conditions including nutritional status, muscle mass, walking performance, disabilities, and pulmonary function (15,17,28-31). Moreover, pinch strength reflects hand dexterity and is a more limited and specific issue. Pinch strength capabilities are generally associated with a response to rehabilitation after injuries, medicolegal reports with industrial accidents, specific athletic abilities, special sports branches, musculoskeletal and neurological diseases affecting dexterity, and industrial occupations/ergonomics (32). In the present study, contradictory to each other, PST and PSLF were found to be independent and important factors for difficult airway while the more commonly known HGS values did not show a significant relationship with MMS groups. Behavioral and neurophysiological studies support that the most stable grasp was obtained by jointly placing the index and middle finger as counterparts on the thumb (33,34). Furthermore, these three fingers constituted different types of pinch strength such as lateral pinch strength, key pinch strength, three-jaw chuck pinch strength, and tip-to-tip pinch, and both HGS with pinch strength of the fingers correlate to common anthropometric features including hand circumference, hand span, hand length, and palm length (35).

HGS and PSF are significantly higher in males and elite athletes, in keeping with the existing literature,with samples containing the same and different populations (36,37). HGS and PSF correlate with gender, age, height, weight, hand dominance, and BMI, and reach their peak between 25-29 years of age (38). Serum levels of CK, LDH, AST, and ALT are the most related markers of muscle volume and injury, so it is an expected finding that they are high in athletes and males. LDH is an important enzyme of the anaerobic metabolic pathway as oxidoreductase, and it catalyzes the reversible conversion of the lactate to pyruvate (39). Thus, increased serum levels have been demonstrated in sleep apnea and other ischemic conditions (40). However, given the association of OSAS or ischemic events with higher Mallampati classes in this situation, it would be expected that increased LDH levels would be associated with a higher MMS score. In this study, contrary to expectations, although a significant relationship between LDH and lower Mallampati scores was found, there is not enough evidence in the literature, and it is not realistic to declare LDH as a predictor for MMS with a limited sample size.

Limitations of the Study

The most important limitation of the study is the very small number of cases per sub-study group, for example, there was only one patient in the Mallampati class 4 group. In addition, it can be expected that the participants were not selected according to exercise intensity in the elite athlete group, and this would affect the laboratory parameters. Furthermore, ultimately, difficult airway is a clinical intervention, and planning a cohort study would be more appropriate for the methodology of such a study.

CONCLUSION

Clinically, PST and PSLF, which are variables expressing muscle strength, and FTR3 and HBT, which are anthropometric measurements, may be more useful because they both indicate elite athletes and correlate with high MMS groups. Contrary to the literature, the HGS muscle was not usable in this study because the analysis was made by controlling for gender and professional occupation affecting muscle strength.

In our study, the pinch strength of the thumb and little finger was determined as the most important predictor for the MMS group rather than HGS. Despite conflicting results, it may be recommended that elite athletes must be evaluated separately in their own groups in terms of anesthesia applications compared to other groups (for example, in the case of obesity).

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University. Institutional ethics committee approval was obtained (2023-06/41). After written informed consent was obtained, 100 participants were enrolled in the study. The study group consisted of elite track athletes, while the control group consisted of volunteers with similar characteristics.

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Research Article

Prognostic Importance of PTEN, p53, and MDM2 Expressions in Endometrioid and Serous-Type Endometrial Carcinomas

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Abstract

Aim: Endometrial carcinomas (ECs) are neoplasms with the highest rate of change in the phosphatidylinositol 3-kinase (PI3K)/AKT/mammalian target of rapamycin (mTOR) pathway. In this study, the relationship among PTEN, MDM2, and p53 protein expression in the PI3K/AKT/mTOR pathway with clinicopathological data in endometrioid endometrial carcinomas (EECs) and serous-type endometrial carcinomas (SECs) was evaluated.

Material and Method: A hundred and twenty cases of patients who underwent hysterectomy for EC between 2009 and 2021 were included in the study. Thirty cases of SEC and 90 cases of EEC were evaluated. EEC cases consist of grades 1-3 tumors, and each group includes 30 patients. p53 was examined in two groups as normal/wild type and abnormal/mutant type. PTEN and MDM2 were examined in two groups: positive and negative. The relationship among p53, PTEN, and MDM2 immunohistochemical expression status with histological grade, myometrial invasion, cervical invasion, lymphovascular invasion (LVI), metastatic lymph nodes, presence of tumor in peritoneal fluid, tumor stage, and overall and progression-free survival was evaluated.

Results: Loss of PTEN was associated with EEC compared to SEC (p<0.001). PTEN loss is mostly associated with p53 normal/wild type (p=0.038). MDM2 expression was associated with a lower histological grade (p<0.001) and stage (p=0.002). MDM2 expression was inversely associated with lymphovascular invasion (p=0.017), cervical invasion (p=0.040), and peritoneal fluid retention (p=0.018). In most cases showing MDM2 expression, p53 was found to be normal/wild type (p=0.011). p53 mutation was found to be associated with advanced age (p=0.002), SEC (p<0.001), high grade (p<0.001), high risk (p<0.001), advanced stage (p=0.002), adjuvant therapy (p=0.002), and peritoneal fluid involvement (p=0.002) and low overall (p=0.014) and progression-free survival (p=0.050).

Conclusion: MDM2 expression was found to be associated with positive prognostic parameters. PTEN loss can be used to distinguish between EEC and SEC. p53 remains a critical determinant of prognosis in ECs.

Keywords: Endometrial carcinomas, PTEN, MDM2, p53, immunohistochemistry

INTRODUCTION

ECs are the most common gynecological malignancy in the United States (1). Unlike most cancers, the incidence rates of ECs have been increasing over the past two decades and are expected to increase significantly. This increase has been attributed to obesity rates, the aging of the population, and the decreased use of combined menopausal hormone therapy (2).

Bokhman's classification system classifies ECs as type I (endometrioid type) or type II (serous type) based on clinical, demographic, and endocrine characteristics (3). Type I ECs have a good prognosis and are associated with hyperestrogenism and obesity. Type II ECs have a poor prognosis and are not associated with hyperestrogenism or obesity (4).

The PI3K/AKT/mTOR pathway is involved in numerous cancers. Endometrial cancers exhibit the highest frequency of alterations in this pathway, occurring in 80% of cases. Specifically, alterations in this pathway are observed in 92% of type I endometrial cancers and 60% of type II endometrial cancers. Loss of phosphatase tensin homolog (PTEN) and/or PI3K mutations are seen in type I ECs, whereas type II ECs are associated with a high

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mTOR expression and less PTEN loss (5). PTEN, a tumor suppressor gene found on chromosome 10, produces a protein that influences various cellular functions such as cell death and proliferation via the PI3K/AKT/mTOR pathway (6). PTEN enhances both the levels and activity of p53 by suppressing MDM2's transcription and its ability to bind to p53 (7). It also inhibits MDM2 from entering the nucleus, thus detaching it from p53 (8).

MDM2 functions as an oncoprotein regulating tumorigenesis. Its mRNA level is subject to transcriptional control by p53 following DNA damage, including oxidative stress (9). MDM2, functioning as a ubiquitin ligase, attaches ubiquitin to both p53 and itself when situated in the cytoplasm, consequently directing both proteins for proteasomal degradation. AKT regulates both the MDM2 protein itself and its cellular localization (10). PTEN suppresses MDM2 transcription, while PI3K/AKT signaling facilitates MDM2 translocation. When PTEN is absent in cells, MDM2 promoter activity becomes apparent, leading to elevated MDM2 expression. MDM2 plays a crucial role as the regulator of p53 (8).

The most prevalent somatic gene alteration observed in neoplasms is the mutation of p53 (11). The p53 protein is a stress-activated transcription factor that positively regulates the gene products required for cell cycle arrest or apoptosis (9).

This study will evaluate the relationship of PTEN, MDM2, and p53 expression with prognostic factors and other clinicopathological data in endometrioid and serous-type endometrial carcinomas. The importance of this pathway in treatment will be questioned, and this pathway may guide the development of targeted therapy agents.

MATERIAL AND METHOD

Following local ethics committee approval on November 18, 2020, reference number 2020/22, 120 consecutive cases diagnosed with EEC or SEC were included in the study. These cases were selected from specimens obtained after total abdominal hysterectomy + bilateral salpingo-oophorectomy (TAH+BSO) and/or regional lymphadenectomy performed between 2009 and 2021. EECs constitute 90 of these cases and SECs constitute 30 of them. Cases of EECs consisted of grades 1, 2, and 3 tumors, and each group included 30 patients (Figure 1). Data pertinent to patient records, including age, tumor size, tumor stage, lymph node metastasis, affected lymph node area, total number of lymph nodes, prognostic category, treatment status, involvement of peritoneal fluid, recurrence status, and survival, were extracted. Two pathologists reviewed hematoxylin-eosin-stained pathology slides to assess pathological prognostic factors including histological subtype, tumor grade, myometrial invasion, cervical invasion, and lymphovascular invasion.

The clinical and pathological staging of the cases were re-evaluated according to the WHO 2019 TNM and FIGO staging system.

The cases were examined in five groups as low, moderate, moderate-high, high, and advanced metastatic, according to the prognostic risk groups recommended by the International Society of Gynecological Pathologists (ISGyP) guidelines.

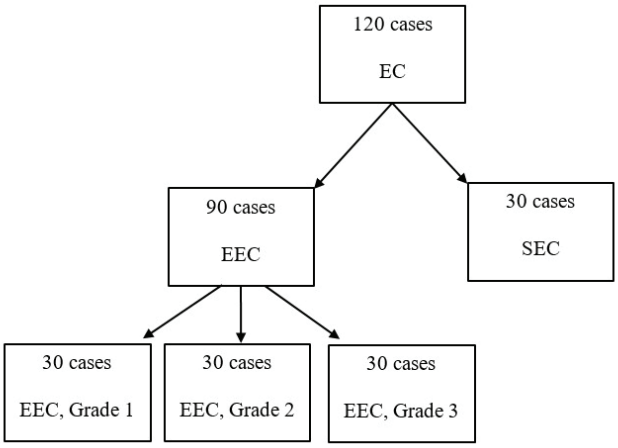

Figure 1. Flow chart of the distribution of groups

Evaluation and Scoring of Immunohistochemically Stained Slides

While evaluating PTEN immunohistochemical staining, a comparison with stroma was made. If there was no staining in the tumor, the score was 0; less than stroma, light brown staining, score 1 (+); less intense than stroma and moderate brown staining, score 2 (++); equal or more severe staining with the stroma was evaluated as score 3 (+++). A score of 0 was defined as PTEN negative and a score of 1–3 as PTEN positive (12).

In the evaluation of MDM2, the rate of positive staining were determined by photographing the cases with the most intense staining in a high-magnification area (with the AxioCam MRc5 camera connected to the Zeiss Imager.D1 brand microscope). Ten percent or more staining was accepted as positive expression and less than 10% staining as negative expression (11,13).

p53 staining is evaluated as normal/wild type and abnormal/mutant type. In the normal/wild type, heterogeneous staining is seen in the cells. In the abnormal/mutant type, there are three different staining patterns. The first is the overexpression pattern of p53, in which more than 80% of tumor cells show strong and diffuse nuclear staining. Another pattern is the null pattern, in which no staining is seen in the tumor cells. Internal control is essential when evaluating this pattern. The last pattern is the pattern in which cytoplasmic staining is seen in tumor cells. In this pattern, nuclear staining should be of the same or less intensity than the cytoplasm. If the nuclear staining is more intense than

the cytoplasm, this cannot be considered a cytoplasmic pattern. In addition to these staining patterns, the presence of a normal pattern with one or more abnormal patterns is called a subclonal staining pattern. The threshold for subclonal staining is the presence of a population of at least 12 cells with an abnormal staining pattern (14).

Statistical Analysis

The data underwent analysis within a computerized setting utilizing the SPSS 25.0 software. When the expected value was less than 5 in over 20% of cells within multi-well tables, Fisher's exact test was employed. The normal distribution of continuous data was assessed through Q-Q plots, skewness, and kurtosis. The multiple Cox proportional hazards model was used to examine the parameters affecting the survival time of the patients, and the Kaplan–Meier method was used to examine the lifetime curves. A significance level of $p<0.05$ was considered for all analytical findings.

RESULTS

One hundred and twenty patients diagnosed with EC were evaluated in this study. The mean age of the patients was 60 years (25–87). The mean follow-up period of the patients was 66.0±46.6 (1.0–140.0) months. At the end of the follow-up period, 72.5% (n=87) of the patients included in the study were alive and 27.5% (n=33) were dead. The mean tumor size was 4.8±2.1 (0.5–11.0) cm. The clinicopathological characteristics of the patients are summarized in Table 1.

Immunohistochemical analysis of p53, PTEN, and MDM2 is shown in Figures 2-4.

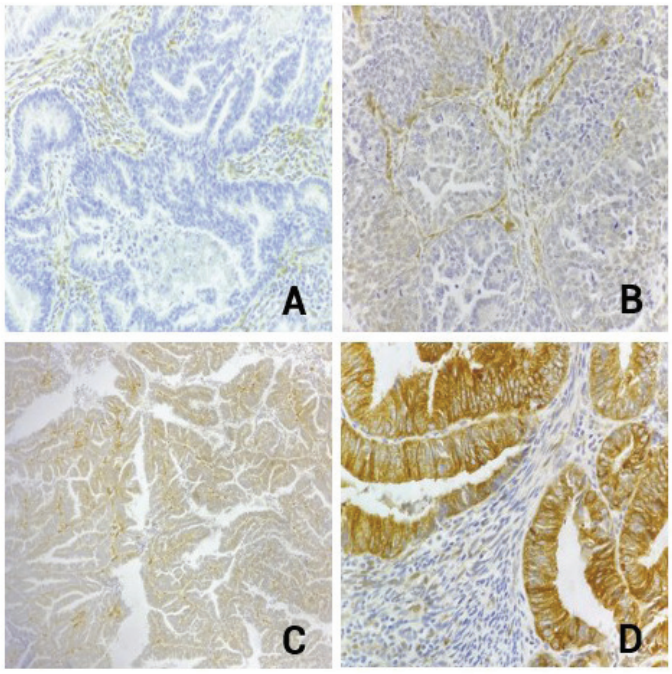

Figure 2. PTEN staining scores: A. Score 0 (x200); B. Score 1 (x100); C. Score 2 (x100); D. Score 3 (x400)

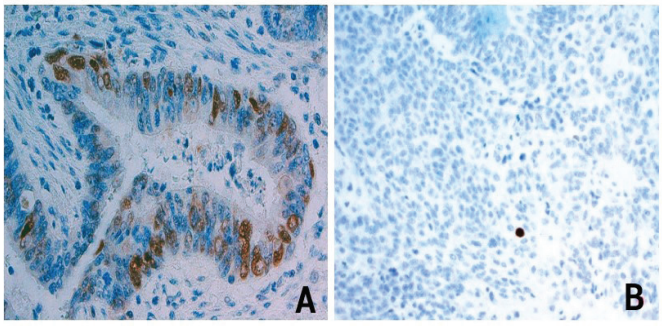

Figure 3. Positive (A) and negative (B) expression in tumor cells by MDM2 (x400)

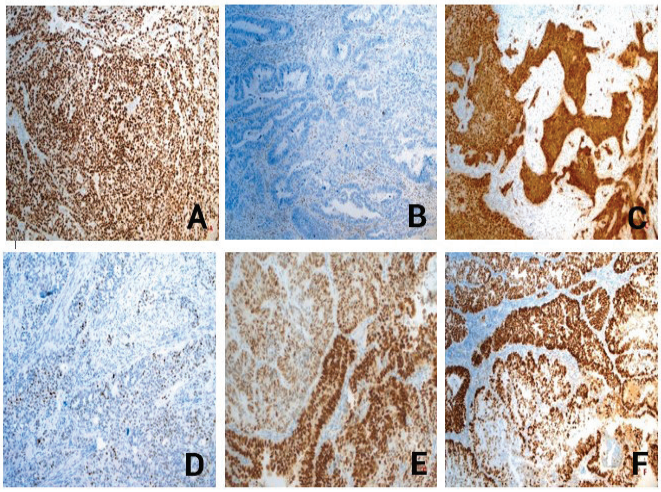

Figure 4. A. abnormal/mutant p53 overexpression pattern (x100); B. abnormal/mutant p53, null pattern (x200); C. abnormal/mutant p53, cytoplasmic pattern (x400); D. p53 normal/wild type (x100); E and F. subclonal pattern (x200).

Relationship between p53, PTEN, and MDM2 Expressions with Clinicopathological Data

p53 abnormal/mutant-type staining was higher in patients over 60 years of age ($p=0.002$), in SEC ($p<0.001$), in the high and advanced metastatic risk group, ($p<0.001$), in stage 4, ($p=0.002$), in those with retained peritoneal fluid ($p=0.002$) and in those receiving adjuvant therapy ($p=0.015$). No statistically significant correlation was found between p53 expression and other clinicopathological data ($p>0.05$) (Table 1).

Loss of PTEN was found to be higher in EEC than in SEC ($p<0.001$). No statistically significant correlation was found between PTEN expression and other clinicopathological data ($p>0.05$) (Table 1).

MDM2 expression was observed in grade 1 EEC ($p<0.001$), and low-risk group ($p=0.002$). MDM2 expression was inversely associated with adjuvant therapy ($p<0.001$), LVI ($p=0.017$), cervical invasion ($p=0.040$), and peritoneal fluid retention ($p=0.018$). No statistically significant correlation was found between MDM2 expression and other clinicopathological data ($p>0.05$) (Table 1).

Table 1. Relationship among PTEN, P53, and MDM2 expressions with clinicopathological data

			p53			PTEN			MDM2		
		(n/%)	N/W	A/M	p*	Negative	Positive	p*	Negative	Positive	p*
Age	**≤60 (n/%)**	59 (49.1)	45 (76.3)	14 (23.7)	**0.002**	31 (52.5)	28 (47.5)	0.713	41 (69.5)	18 (30.5)	0.25
	>60 (n/%)	61 (50.9)	30 (49.2)	31 (50.8)		30 (49.2)	31 (50.8)		48 (78.7)	13 (21.3)	
Histological type	**EEC (n/%)**	90 (75.0)	71 (78.9)	19 (21.1)	**<0.001**	54 (60.0)	36 (40.0)	<0.001	64 (71.1)	26 (28.9)	0.185
	SEC (n/%)	30 (25.0)	4 (13.3)	26 (86.7)		7 (23.3)	23 (76.7)		25 (83.3)	5 (16.7)	
Grade	**Grade 1 EEC (n/%)**	30 (25.0)	29 (96.7)[a]	1 (3.3)a	**<0.001**	20 (66.7)[a]	10 (33.3)[a]	0.005	12 (40.0)[a]	18 (60.0)[a]	**<0.001**
	Grade 2 EEC (n/%)	30 (25.0)	25 (83.3)[a.b]	5 (16.7)[a.b]		17 (56.7)[a.b]	13 (43.3)[a.b]		24 (80.0)[b]	6 (20.0)[b]	
	Grade 3 EEC (n/%)	30 (25.0)	17 (56.7)[b]	13 (43.3)[b]		17 (56.7)[a.b]	13 (43.3)[a.b]		28 (93.3)[b]	2 (6.7)[b]	
	SEC (n/%)	30 (25.0)	4 (13.3)[c]	26 (86.7)[c]		7 (23.3)b	23 (76.7)[b]		25 (83.3)[b]	5 (16.7)[b]	
Risk groups	**Low (n/%)**	29 (24.2)	27 (93.1)[a]	2 (6.9)[a]	**<0.001**	18 (62.1)	11 (37.9)	0.299	14 (48.3)[a]	15 (51.7)[a]	**0.002**
	Middle (n/%)	21 (17.5)	15 (71.4)[a.b]	6 (28.6)[a.b]		12 (57.1)	9 (42.9)		15 (71.4)[a.b]	6 (28.6)[a.b]	
	Middle-high (n/%)	15 (12.5)	11 (73.3)[a.b]	4 (26.7)[a.b]		6 (40.0)	9 (60.0)		14 (93.3)[b]	1 (6.7)[b]	
	High (n/%)	40 (33.3)	19 (47.5)[b.c]	21 (52.5)[b.c]		16 (40.0)	24 (60.0)		32 (80.0)[a.b]	8 (20.0)[a.b]	
	Advanced metastatic (n/%)	15 (12.5)	3 (20.0)[c]	12 (80.0)[c]		9 (60.0)	6 (40.0)		14 (93.3)[b]	1 (6.7)[b]	
Stage	**1 (n/%)**	68 (56.7)	49 (72.1)[a]	19 (27.9)[a]	**0.002**	34 (50.0)	34 (50.0)	0.844	45 (66.2)	23 (33.8)	0.092**
	2 (n/%)	9 (7.5)	7 (77.8)[a]	2 (22.2)[a]		5 (55.6)	4 (44.4)		8 (88.9)	1 (11.1)	
	3 (n/%)	28 (23.3)	16 (57.1)[a.b]	12 (42.9)[a.b]		13 (46.4)	15 (53.6)		22 (78.6)	6 (21.4)	
	4 (n/%)	15 (12.5)	3 (20.0)[b]	12 (80.0)[b]		9 (60.0)	6 (40.0)		14 (93.3)	1 (6.7)	
Survival	**Alive (n/%)**	87 (72.5)	59 (67.8)	28 (32.2)	0.051	45 (51.7)	42 (48.3)	0.751	62 (71.3)	25 (28.7)	0.238
	Ex (n/%)	33 (27.5)	16 (48.5)	17 (51.5)		16 (48.5)	17 (51.5)		27 (81.8)	6 (18.2)	
Recurrence	**No (n/%)**	112 (93.4)	72 (64.3)	40 (35.7)	0.131	57 (50.9)	55 (49.1)	0.961**	83 (74.1)	29 (25.9)	0.956
	Yes (n/%)	8 (6.6)	3 (37.5)	5 (62.5)		4 (50.0)	4 (50.0)		6 (75.0)	2 (25.0)	
Adjuvant therapy	**No (n/%)**	31 (25.8)	25 (80.6)	6 (19.4)	**0.015**	19 (61.3)	12 (38.7)	0.176	14 (45.2)	17 (54.8)	**<0.001**
	Yes (n/%)	89 (74.2)	50 (56.2)	39 (43.8)		42 (47.2)	47 (52.8)		75 (84.3)	14 (15.7)	
LVİ	**No (n/%)**	89 (74.2)	59 (66.3)	30 (33.7)	0.146	45 (50.6)	44 (49.4)	0.92	61 (68.5)	28 (31.5)	**0.017**
	Yes (n/%)	31 (25.8)	16 (51.6)	15 (48.4)		16 (51.6)	15 (48.4)		28 (90.3)	3 (9.7)	
Cervix invasion	**No (n/%)**	83 (69.2)	54 (65.1)	29 (34.9)	0.386	43 (51.8)	40 (48.2)	0.749	57 (68.7)	26 (31.3)	**0.04**
	Yes (n/%)	37 (30.8)	21 (56.8)	16 (43.2)		18 (48.6)	19 (51.4)		32 (86.5)	5 (13.5)	
Peritoneal fluid retention	**No (n/%)**	98 (83.1)	67 (68.4)	31 (31.6)	**0.002**	48 (49.0)	50 (51.0)	0.624	68 (69.4)	30 (30.6)	**0.018**
	Yes (n/%)	20 (16.9)	6 (30.0)	14 (70.0)		11 (55.0)	9 (45.0)		19 (95.0)	1 (5.0)	
Pelvic lymph node involvement	**No (n/%)**	87 (73.7)	56 (64.4)	31 (35.6)	0.348	44 (50.6)	43 (49.4)	0.834	62 (71.3)	25 (28.7)	0.308
	Yes (n/%)	31 (26.3)	17 (54.8)	14 (45.2)		15 (48.4)	16 (51.6)		25 (80.6)	6 (19.4)	
Paraaortic lymph node involvement	**No (n/%)**	96 (81.4)	62 (64.6)	34 (35.4)	0.204	48 (50.0)	48 (50.0)	>0.999	70 (72.9)	26 (27.1)	0.675
	Yes (n/%)	22 (18.6)	11 (50.0)	11 (50.0)		11 (50.0)	11 (50.0)		17 (77.3)	5 (22.7)	
Myometrium invasion	**<1/2 (n/%)**	65 (54.2)	41 (63.1)	24 (36.9)	0.887	33 (50.8)	32 (49.2)	0.988	45 (69.2)	20 (30.8)	0.179
	≥1/2 (n/%)	55 (45.8)	34 (61.8)	21 (38.2)		28 (50.9)	27 (49.1)		44 (80.0)	11 (20.0)	

* chi-square test; N/W: normal/wild; A/M: abnormal/mutant

Interrelationship of p53, PTEN, and MDM2 Expression

When the relationship among p53, PTEN, and MDM2 expressions was evaluated, it was observed that p53 normal/wild type staining was higher in those with MDM2 staining than in those without (p=0.005). In those with PTEN loss, p53 normal/wild-type staining was found to be high (p=0.038). It was observed that PTEN staining and MDM2 staining did not differ according to each other (p>0.999) (Table 2).

When the patients were grouped as EEC and SEC and the relationship between PTEN, p53, and MDM2 staining status was evaluated, it was observed that p53 normal/wild type staining was higher in those with MDM2 staining than in those without MDM2 staining (p=0.011). (Table 3).

Table 2. Interrelationship among p53, PTEN, and MDM2 expressions in whole patients

			p53		X^2	p*
			N/W	A/M		
MDM2	Negative	n (%)	49 (55.1)	40 (44.9)	8.145	**0.005**
	Positive	n (%)	26 (83.9)	5 (16.1)		
PTEN	Negative	n (%)	44 (72.1)	17 (27.9)	4.91	**0.038**
	Positive	n (%)	31 (52.5)	28 (47.5)		
			MDM2			
			Negative	Positive		
PTEN	Negative	n (%)	45 (73.8)	16 (26.2)	0.01	>0.999
	Positive	n (%)	44 (74.6)	15 (25.4)		

* chi-square test; N/W: normal/wild; A/M: abnormal/mutant

Table 3. Interrelationship of p53, PTEN, and MDM2 expression in separate groups of EEC and SEC

				p53		X^2	P
				N/W	A/M		
EEC	PTEN	Negative	n (%)	44 (81.5)	10 (18.5)	0.545	0.46*
		Positive	n (%)	27 (75.0)	9 (25.0)		
	MDM2	Negative	n (%)	46 (71.09)	18 (28.1)	6.544	**0.011***
		Positive	n (%)	25 (96.2)	1 (3.8)		
				MDM2			
				Negative	Positive		
	PTEN	Negative	n (%)	39 (60.9)	25 (39.1)	0.81	0.776*
		Positive	n (%)	15 (57.7)	11 (42.3)		
				p53			
				N	A/M		
SEC	PTEN	Negative	n (%)	0 (0.0)	7 (100.0)	-	0.548*
		Positive	n (%)	4 (17.4)	19 (82.6)		
	MDM2	Negative	n (%)	3 (12.0)	22 (88.0)	-	0.538**
		Positive	n (%)	1 (20.0)	4 (80.0)		
				MDM2			
				Negative	Positive		
	PTEN	Negative	n (%)	6 (24.0)	1 (76.0)	-	0.999**
		Positive	n (%)	19 (80.0)	4 (20.0)		

*chi-square test, ** Fisher's exact test

Effects of PTEN, p53, and MDM2 Expression on Overall and Progression-Rree Survival

It was observed that the survival time of patients with p53 normal/wild staining was higher than those with p53 abnormal/mutant staining (log-rank χ^2=8.438, p=0.004). It was observed that the progression-free survival time of patients with p53 normal/wild staining was higher than that of patients with p53 abnormal/mutant staining, but this difference closed toward the end of the observation period (log-rank χ^2=8.438, p=0.050; Breslow=3.964, p=0.046) (Figure 5). Among the low-grade patients, those with p53 normal/wild staining had a higher survival time than those with p53 abnormal/mutant staining (log-rank χ^2=6.053, p=0.014). When we observed the effect of p53 staining on overall survival in high-grade patients, the survival times did not differ between the groups (log-rank χ^2=5.070, p=0.079).

It was observed that the overall (log-rank χ^2=0.242, p=0.623) and progression-free survival times (log-rank χ^2=0.005; p=0.944) of patients with normal PTEN and loss of PTEN did not differ (Figure 6). It was observed that PTEN staining status did not affect overall survival in low- (log-rank χ^2=0.178, p=0.673) and high-grade (log-rank χ^2=0.021, p=0.885) patients.

It was observed that the overall (log-rank χ^2=2.354, p=0.125) and progression-free survival times (log-rank χ^2=0.050; p=0.824) of patients with and without MDM2 staining did not differ (Figure 7). It was observed that MDM2 staining status did not affect overall survival in low- (log-rank χ^2=0.538, p=0.463) and high-grade (log-rank χ^2=0.342, p=0.559) patients.

When the effects of risk group (log-rank χ^2=35.778, p<0.001) and grade (log-rank χ^2=19.661, p<0.001) on overall survival times were evaluated, it was seen that mean survival differed significantly between groups.

Eleven parameters that can be used to predict overall survival are age at diagnosis, p53, PTEN, MDM2, tumor grade (G1+G2=low-grade tumors; G3+serous=high-grade tumors), cervical invasion, myometrial invasion, peritoneal fluid involvement, pelvic lymph node involvement, paraaortic lymph node involvement, and LVI. The Cox regression model was found to be significant (log-rank x2=45.505, p<0.001). Age at diagnosis (B=0.056; p=0.002), peritoneal fluid involvement (HR=4.836; 95% CI=1.651–14.162; p=0.004), and pelvic lymph node involvement (HR=4.660; 95% CI=1.401–15.500; p=0.016) were found to be effective on survival (Table 4).

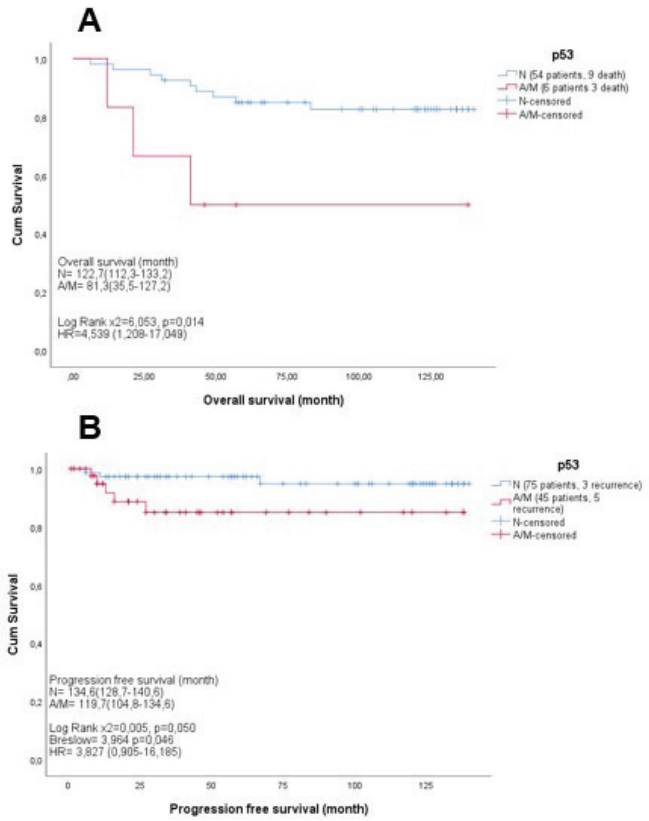

Figure 5. Effect of p53 expression on overall and progression-free survival

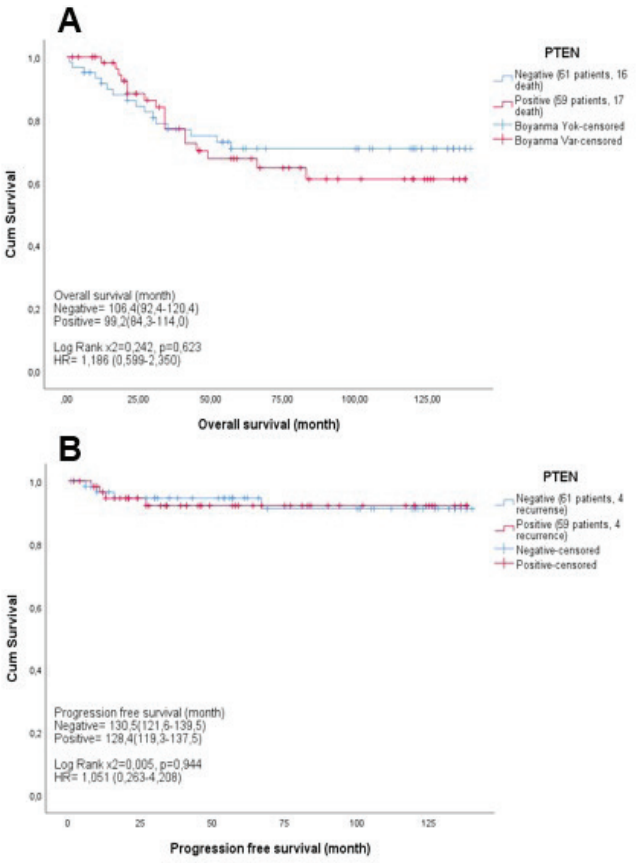

Figure 6. Effect of PTEN expression on overall and progression-free survival

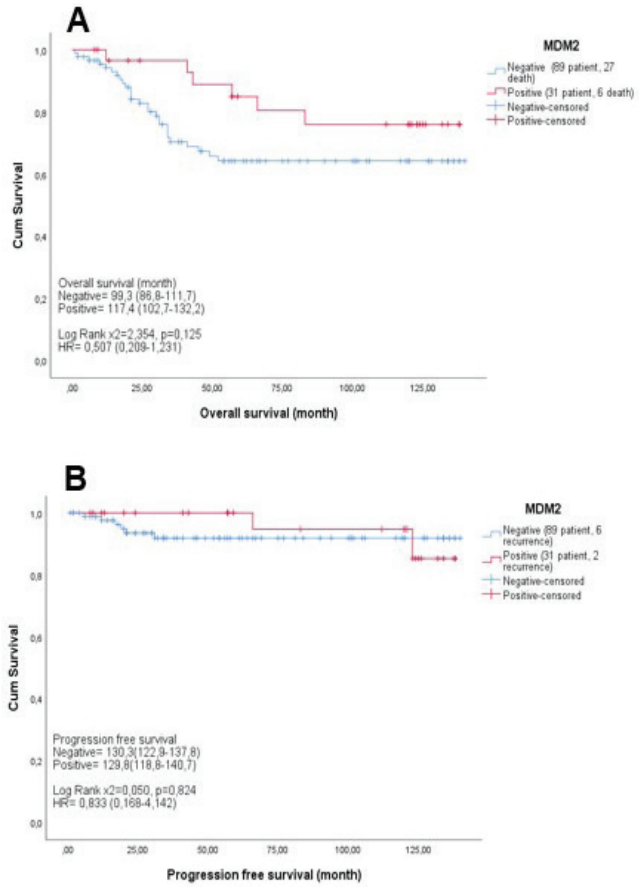

Figure 7. Effect of MDM2 expression on overall and progression-free survival

Table 4. Regression model to analyse the factors affecting the overall survival time of the patients.

							95.0% CI for Exp(B)	
	B	S.E.	Wald	df	p*	Exp (B)	Lower bound	Upper bound
Age	0.056	0.017	10.465	1	0.002	1.057	1.022	1.093
P53 (abnornal/mutant)	0.267	0.512	0.273	1	0.602	1.306	0.479	3.56
PTEN	-0.269	0.406	0.439	1	0.508	0.764	0.345	1.693
MDM2	-0.292	0.571	0.262	1	0.609	0.747	0.244	2.285
Grade (high)	0.238	0.631	0.142	1	0.706	1.268	0.368	4.371
Myometrium invasion	0.676	0.399	2.87	1	0.09	1.966	0.899	4.297
Lymphovascular invasion	-0.766	0.514	2.22	1	0.136	0.465	0.17	1.273
Cervix invasion	-0.587	0.498	1.385	1	0.239	0.556	0.209	1.477
Peritoneal fluid involvement	1.576	0.548	8.264	1	0.004	4.836	1.651	14.162
Pelvic lymph node involvement	1.539	0.613	6.3	1	0.012	4.66	1.401	15.5
Paraaortic lymph node involvement	-0.107	0.586	0.034	1	0.855	0.898	0.285	2.831

*Cox regression analysis

DISCUSSION

Loss of PTEN expression is associated with EEC rather than SEC in the literature (12). Djordjevic et al. and Sal et al. revealed no significant differences between the grades of EEC in terms of PTEN expression and PTEN mutation (15,16). In a study by Tao et al., the presence of the PTEN mutation was higher under 60 years of age than above 60. PTEN mutation was found to be more common in patients with EEC than SEC in patients with EC, in stages 1–2 than in stages 3–4, and in low grade than in high grade. In survival analyses, progression-free and overall survival times were found to be higher in cases with PTEN mutation (17). In a study by Sal et al., although PTEN expression was not associated with stage, LVI status, adjuvant therapy, metastasis, recurrence, survival status, or progression-free and overall survival, positive staining of PTEN was positively correlated with myometrial invasion (16). Akiyame-Abe et al. investigated the relationship among PTEN expression and age, LVI status, tumor stage, myometrial invasion, and histological type and found that PTEN loss was associated with EEC and inversely associated with LVI status. In survival analyses, the loss of PTEN expression was found to be an important and independent prognostic determinant of favorable survival in EC (18). Li et al. found that loss of PTEN was associated with EEC and that the overall survival time of these cases was higher than that of cases with PTEN expression (19). In a study by Stavropoulos et al., the relationship among PTEN expression and age, histological type, stage, histological grade, myometrial invasion, LVI, tubal-ovarian involvement, and tumor necrosis was not found (20). In a study by Daniilidou et al., PTEN staining was associated with grades 1 and 2 and stage 1B tumors, and PTEN loss was associated with grade 3 and stages 1C and 2C tumors (21). In this study, PTEN loss was more common in EECs than in SECs. It was concluded that PTEN loss can be used for diagnostic purposes in the differentiation of EEC and SEC. However, it should be kept in mind that PTEN loss can also be seen in SECs. We observed that PTEN expression did not affect survival. There is no common scoring system to evaluate PTEN expression in studies. This may explain the different results of PTEN expression on survival. A common scoring system should be established by looking at PTEN mutation and expression status in larger series.

In the series of 114 cases of high-grade endometrial cancer analyzed by Edmondson et al., it was observed that patients with high MDM2 expression had poorer overall survival compared to those with low or negative MDM2 expression. A study by Jeczen et al., consisting of 39 patients diagnosed with metastatic EC, found MDM2 overexpression to be more common in high grade tumors than low grades. No significant difference was found between overall survival and MDM2 overexpression alone. However, cases with both p53 and MDM2 overexpression had worse overall survival rates compared to those negative for both p53 and MDM2 (14). Soslow et al. found that MDM2 expression was associated with higher p53 expression in EEC than in SEC in a study of 41 patients diagnosed with high-grade EC (22). In a study by Ambros et al., p53 overexpression in EC was frequently associated with MDM2 overexpression. Liu et al. found MDM2 expression to be higher in EC than in the normal endometrium. It has been reported that MDM2 expression is associated with histological grade and lymph node metastasis but not with patient age, tumor size, and histological type. It was observed that MDM2 expression was higher in patients with stage 3 and 4 tumors and lymph node metastases (13). In the study by Buchynska et al. consisting of cases diagnosed with EC and endometrial hyperplasia, high p53 levels were found to be associated with low MDM2 levels. Their conclusion suggested that poorly differentiated endometrial cancer may be characterized by low MDM2 expression and high p53 expression levels (23). Soslow et al. found an inverse relationship between p53 and MDM2 expression in high-grade EEC versus SEC. In SEC, strong p53 immunoreactivity correlated with low MDM2 expression, while in EEC, weak p53 expression was linked with moderate MDM2 expression (22). In this study, MDM2 expression was observed more frequently in grade

1 EECs and the low-risk group. In contrast, no staining was observed in cases with cervical invasion, peritoneal fluid retention, and adjuvant treatment. We observed no effect of MDM2 expression on survival.

P53 mutations are almost exclusively present in high-grade tumors (24-26). Khalifa et al. determined that p53 positivity was associated with the non-endometrioid type (27). In a series of 100 cases diagnosed with EC by Lukes et al., p53 was found to predict recurrent or persistent disease (28). In the 221 cases of endometrial cancer studied by Hamel et al., strong p53 expression was linked to various prognostic factors, including stage, grade, depth of myometrial invasion, histological subtype, cytological findings, DNA ploidy, and HER-2/neu expression (29). Kohlberger et al. examined p53 overexpression in 92 cases diagnosed with stage 1 EC. In the study, it was concluded that immunohistochemically detected p53 protein overexpression in early-stage EC may have an impact on adjuvant and adjuvant therapy in predicting prognosis (30). p53 expression is associated with non-endometrioid, advanced high-grade, lymph node metastasis (31-33), peritoneal cytology (31,34), and deep myometrial invasion (35). Consistent with the literature, P53 abnormal/mutant type was associated with advanced age, SEC, high-grade EEC, high and advanced metastatic risk group, stage 3-4 tumor, adjuvant treatment, and peritoneal fluid retention.

CONCLUSION

MDM2 expression was found to be associated with positive prognostic parameters. This result can be clarified with further studies with larger series. PTEN loss can be used for diagnostic purposes differentiation of EEC and SEC. However, it should be noted that PTEN loss can also be seen in SECs. p53 remains a critical determinant of prognosis in ECs.

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Research Article

The Effect of Controlled Hypotensive Anesthesia on Postoperative Sore Throat

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Abstract

Aim: Postoperative sore throat (POST) is a commonly encountered and significant complication following anesthesia, which can adversely affect the quality of a patient's recovery. Many factors contribute to the development of POST. Controlled hypotension (CH) is a surgical technique used to reduce blood flow, improve visibility, and shorten procedure time by safely lowering blood pressure. In this study, we aimed to investigate the effects of CH on POST, coughing, hoarseness, and vomiting in patients undergoing surgery in a supine position with a fixed endotracheal cuff pressure.
Material and Method: A total of 124 patients, aged between 18 and 65 years, classified as American Society of Anesthesiologists (ASA) class I-II and scheduled for elective surgical procedures, were included in the study. The patients were divided into two groups: Group N (n=65), consisting of normotensive individuals, and Group H (n=59), which included patients subjected to CH. In both groups, the endotracheal cuff pressure was manually set to 25 cmH2O using a cuff pressure manometer. CH was achieved in Group H by administering glyceryl trinitrate (nitroglycerin) infusion, maintaining the mean arterial pressure (MAP) within the range of 55-65 mmHg. Patients were assessed for POST, coughing, hoarseness, and vomiting at postoperative 15 minutes, 2, 6, 12, and 24 hours.
Results: Demographic data, smoking status, ASA scores, surgical and anesthesia durations were similar between the groups. Statistically significant differences were observed between the groups in the numeric rate scores (NRS) for throat pain at 15 minutes and 2 hours, as well as hoarseness scores at 2 and 6 hours. The groups were similar regarding vomiting rates and cough scores.
Conclusion: In this study investigating the impact of CH on sore throat, we observed an increased incidence of POST and hoarseness in patients subjected to CH.

Keywords: Sore throat, intubation, hoarseness, controlled hypotension

INTRODUCTION

Postoperative sore throat (POST) is a commonly encountered and significant complication that often disrupts the quality of a patient's recovery following anesthesia. Airway devices such as endotracheal tubes (ETT) and laryngeal masks, which are used to maintain airway patency in patients undergoing general anesthesia, play a crucial role in the development of POST by affecting mucosal blood flow (1,2). The occurrence of POST after endotracheal intubation has been documented to be between 14.5% and 50%, while after laryngeal mask insertion, it ranges from 14.4% to 34% (3,4). Controlled hypotension (CH) is a technique applied during surgery to reduce blood flow within the surgical field, improve visibility and shorten the procedure duration, while safely lowering the patient's blood pressure to a level that does not compromise perfusion indices. It has been widely employed for many years in various surgical procedures, including otolaryngology, ophthalmology, neurosurgery, plastic and reconstructive surgery, among others (5,6).

Under anesthesia, the placement of devices required to maintain airway patency results in prolonged external pressure on the airway structures. When this pressure exceeds capillary-arteriolar blood pressure, it can lead to complications ranging from tissue ischemia, inflammation, ulcer development, granulation, and even stenosis. While the inflation of the cuffs of airway devices is the most significant factor contributing to this condition, it is also

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believed that hypotension may potentially contribute by reducing mucosal blood flow (7,8). However, while the relationship between endotracheal cuff pressure and sore throat under anesthesia is established the clinical impact of CH applied during surgery on this sore throat hasn't been definitively determined. In this study, our objective was to examine the hypothesis that CH administered during surgery affects the incidence of sore throat.

MATERIAL AND METHOD

This study was carried out on orthopedic patients scheduled for elective surgery in a supine position under general anesthesia in a university hospital, following approval from the Clinical Research Ethics Committee (Approval No: 17-KAEK-049). Patients were informed about the study prior to surgery, and written consent was acquired. A total of 150 patients aged between 18 and 65 years with an American Society of Anesthesiologists (ASA) score of I or II, who consented to participate in the study, were included. Patients who declined to participate, those with ASA scores of III-IV, a history of hypertension, use of antihypertensive, opioid, or steroid medications, preoperative sore throat, known anatomical abnormalities in the airway anatomy, requirements for intubation lasting more than 4 hours, tracheostomy, patients undergoing head-neck or laparoscopic surgery, and pregnant patients were omitted from the study. Patients who underwent multiple laryngoscopy procedures for intubation, those with procedures lasting more than 4 hours, those who developed complications during surgery, those who received steroids, and those who used another airway device for airway management were also excluded. After excluding 26 patients who did not meet the study criteria, the study was completed with 124 patients, who were randomly allocated to Group N (Normotensive) and Group H (Hypotensive) using a sealed envelope method.

After patients were positioned on the operating table and standard monitoring was initiated, preoxygenation was administered. Anesthesia induction for the patients was achieved with intravenous 2 mg/kg of propofol, 1 mcg/kg of fentanyl, and 0.6 mg/kg of rocuronium bromide. Following at least 2 minutes of ventilation with a mask, endotracheal intubation was performed by the same anesthetist using an appropriate endotracheal tube (ETT) (female: 7.0-7.5 mm cylindrical cuff, male: 8.0-8.5 mm cylindrical cuff). Anesthesia maintenance was provided with a flow of 2 liters/min of 50% oxygen, 50% air, and 1 MAC sevoflurane. Throughout the procedure, a moisture and bacteria filter (Altech® Bacterial/Viral Filter) was used between the expiratory limb and the ETT breathing circuit. The intubation duration and the intubation difficulty scale (IDS) scores were measured and documented during the intubation procedure.

Group N (Normotensive) (n: 75): After standard monitoring, patients underwent intubation with an appropriate ETT following anesthesia induction. The ETT cuff pressure was adjusted to 25 cmH2O using a standard cuff pressure gauge and was checked every 5 minutes. If there were any increases or decreases in cuff pressure, it was readjusted to 25 cmH2O.

Group H (Hypotensive) (n:75): After standard monitoring, patients underwent intubation with an appropriate ETT following anesthesia induction. The ETT cuff pressure was adjusted to 25 cmH2O using a standard cuff pressure gauge and was readjusted to 25 cmH2O if there were any changes in cuff pressure. CH was achieved by infusing a solution prepared by diluting glyceryl trinitrate (nitroglycerin) (TRINITY 10mg/10mL I.V infusion solution) with 40 ml of 0.9% sodium chloride to achieve a dose of 0.25-2 µg/kg/min, targeting a mean arterial pressure (MAP) within the range of 55-65 mmHg. If MAP fell below 55 mmHg, the drug infusion was temporarily stopped. In cases of persistent hypotension, intravenous ephedrine (5 mg) was administered in increasing doses. Bradycardia, defined as a heart rate <50 beats/min, was treated with intravenous atropine (0.5-1.0 mg), and the infusion of the drug was discontinued.

All patients received 0.05 mg/kg of morphine and 8 mg of ondansetron intravenously within the case. Following 0.02 mg/kg of atropine administration, decurarization was achieved by administering 0.04 mg/kg of neostigmine or 2 mg/kg of sugammadex.

After the completion of surgery, extubated patients were monitored in the recovery unit at 15 minutes and in the follow-up ward at 2, 6, 12, and 24. hours. If patients experienced pain, 1 mg/kg of tramadol and/or 1 g of intravenous paracetamol were administered.

Postoperative sore throat was assessed using the numeric rating scale (NRS), while vomiting was evaluated as present or absent. Coughing and hoarseness were assessed using 4-point verbal scales.

Cough Score:

0: No cough at all,

1: Mild; only occurred 1 or 2 times or in an annoying manner,

2: Moderate; 3 or 4 times,

3: Severe; 5 or more coughs.

Hoarseness Score:

0: Never present,

1: Mild; not present during conversation but previously experienced and resolved,

2: Moderate; hoarseness present during conversation that the patient can feel,

3: Severe; hoarseness present during conversation.

Statistical Analysis

In calculating the sample size, another study was used as a reference for our primary outcome, which is the

incidence of postoperative sore throat, and it was assumed that hypotensive anesthesia would increase this rate by 50%. Taking into consideration a power of 80% and a significance level of 5%, it was determined that 58 patients per group would be sufficient to detect this change. To account for potential data losses, a total of 150 patients were planned to be included in the study.

The normal distribution of the data was examined using the Kolmogorov-Smirnov test. Categorical data were presented as percentages, while quantitative data were presented as mean±standard deviation (SD) (minimum-maximum). For the comparison of categorical data, the Chi-square test and Fisher's exact test were used. The Mann-Whitney U test was employed to compare numerical data that did not follow a normal distribution, while the Student's t-test was used for numerical data that did follow a normal distribution. All data were analyzed using the Statistical Package for Social Sciences 20.0 (SPSS Inc. Chicago, IL) program. The threshold for statistical significance was set at $p<0.05$.

RESULTS

The study included a total of 150 patients. However, 12 patients could not achieve controlled hypotension with nitroglycerin, 4 patients had multiple laryngoscopy attempts, 8 patients had surgery durations of less than 60 minutes, and 2 patients received steroids, leading to their exclusion from the study. As a result, the study was completed with 124 patients. There were no statistically significant differences between the groups in terms of demographic data of the patients (Table 1).

Table 1. Comparison of demographic data

	Group N (n: 65)	Group H (n: 59)	p value
Age (years); mean±SD	38.89±13.98	36.08±12.80	0.247
Gender (F/M); n (%)	25/40 (38.5/61.5)	31/28 (52.5/47.5)	0.116
BMI (kg/m²); median (min-max)	27.00 (18.52-41.21)	26.95 (18.92-36.89)	0.584
ASA (1/2); n (%)	20/45 (30.8/69.2)	22/37 (37.3/62.7)	0.444
Smoking (yes/no)	28/37	20/39	0.295
Intubation duration (sec); median (min-max)	10.00 (5-15)	8.00 (5-15)	0.350
Mallampati (1/2); n (%)	24/41 (36.9/63.1)	20/39 (33.9/66.1)	0.725
IDS; median (min-max)	1 (0-3)	0 (0-3)	0.341
Anesthesia duration (min); median (min-max)	105.00 (60-240)	105.00 (75-240)	0.972
Paracetamol (gr); median (min-max)	2.00 (0-4)	2.00 (1-4)	0.221
Tramadol (mg); median (min-max)	200 (0-300)	200 (0-400)	0.618
Atropine-neostigmine/sugammadex; n (%)	31/34 (47.7/52.3)	21/38 (35.6/64.4)	0.173

IDS: intubatin difficulty scale, BMI: boddy mass index, SD: standard deviation

There was a statistically significant difference in favor of Group H in terms of throat pain NRS scores at 15 minutes and 2 hours between the groups (p=0.001, p=0.021, respectively).

There was no statistically significant difference between the groups regarding throat pain NRS scores at 6, 12, and 24 hours (p=0.050, p=0.177, p=0.107, respectively) (Table 2).

Table 2. NRS scores for throat pain in the groups

	Group N	Group H	p value
15. min. median (min-max)	0 (0-5)	2 (0-5)	0.001*
2. hr. median (min-max)	0 (0-5)	2 (0-6)	0.021*
6. hr. median (min-max)	0 (0-5)	1 (0-6)	0.050
12. hr. median (min-max)	0 (0-5)	0 (0-7)	0.177
24. hr. median (min-max)	0 (0-2)	0 (0-6)	0.107

*p<0.05

The scores for hoarseness at 2 and 6 hours between the groups showed a statistically significant difference in favor of Group H (p=0.049, p=0.005) (p<0.05).

There was no statistically significant difference in hoarseness scores between the groups at 15 minutes, 12 hours and 24 hours (p=0.398, p=0.071, p=0.017) (Table 3).

Table 3. Hoarseness scores between groups			
Median (min-max)	**Group N**	**Group H**	**p value**
15. min.	0 (0-2)	0 (0-2)	0.398
2. hr.	0 (0-2)	0 (0-3)	0.049*
6. hr.	0 (0-1)	0 (0-2)	0.005*
12. hr.	0 (0-1)	0 (0-2)	0.071
24. hr.	0 (0-0)	0 (0-2)	0.017
*p<0.05			

There was no statistically significant difference between the groups in terms of cough scores of patients at 15 minutes, 2, 6, and 12 hours (p=0.311, p=0.109, p=0.823, p=0.888, p=0.945).

The total number of patients who had vomiting at least once within 24 hours was similar between the groups (p=0.847).

DISCUSSION

In our study examining the effect of CH anesthesia on POST, we observed an increased incidence of POST and higher hoarseness scores.

POST is a significant side effect that affects the quality of postoperative recovery in patients undergoing general anesthesia. Studies have reported a high incidence of POST, ranging from 14.5% to 50% after endotracheal intubation and from 14.4% to 34% after the use of a laryngeal mask (3,4). The mechanism behind the development of POST is primarily associated with local trauma-induced inflammation, resulting in edema and congestion of the pharyngeal mucosa (9-11). While cuff pressure is considered one of the major factors contributing to POST, the impact of impaired mucosal blood flow on throat pain has not been clearly elucidated (12-16).

CH anesthesia is widely used in many surgical procedures, but it carries certain risks, especially when prolonged hypotension is applied. Prolonged hypotension can lead to organ damage, tissue perfusion disorders, cognitive changes due to cerebral hypoperfusion, myocardial ischemia due to decreased coronary circulation, and even conditions like postoperative oliguria or anuria in cases of reduced kidney blood flow. Extended periods of hypotension may result in hemiplegia, acute tubular necrosis, cerebral thrombosis, myocardial infarction, blindness, and even death. Therefore, while CH anesthesia is safely employed in many surgeries, its reliability is a subject of debate in some procedures (17,18). Recent studies have found an association between CH anesthesia and postoperative neurological deficits in arteriovenous malformation surgeries (19). To minimize complications, it is essential to carefully select patients for CH anesthesia, pay attention to the duration of hypotension, and closely monitor patients during and after the procedure.

Hypotension has adverse effects on cellular damage, ischemia, and tissue perfusion. In a study (20), induced hypotension in normotensive rats using L-arginine resulted in mild arteriolar obstruction in glomeruli and mild ischemic damage in tubular areas of kidney tissue. Another study (21) demonstrated that hypotension induced by isoflurane significantly caused neuronal damage in the hippocampal CA1 region. Severe hypotension can lead to neuronal endoplasmic reticulum stress and apoptosis (22). Prolonged hypotension due to trauma-related hemorrhage has been shown to significantly affect mitochondrial function, endoplasmic reticulum stress markers, and free iron levels (23). O'Meara et al. (24) reported a significantly higher percentage of iron-laden histiocytes in tracheobronchial secretions of patients who underwent CH, suggesting an association with decreased tissue perfusion. Although our study did not investigate cellular-level effects, we believe that CH may have increased the sensitivity of pharyngeal structures to the accepted safe levels of intracuff pressure. This could have led to more cellular ischemia, edema, and damage in this area, ultimately resulting in an increased incidence of sore throat and hoarseness.

To our most current knowledge, this is the first study to investigate the effect of CH on sore throat. However, our study has several limitations. First, the relatively small sample size, and second, the lack of confirmation of ETT cuff placement using fiberoptic visualization. The ETT tube was placed based on a standard size of 21 cm for females and 23 cm for males, and its position was verified by feeling the cuff at the suprasternal notch and listening to breath sounds in 5 quadrants.

CONCLUSION

In conclusion, we found that CH increased the incidence of POST and hoarseness. Anesthesiologists should prioritize patient monitoring, effectively regulate intraoperative cuff pressure, and develop strategies to reduce POST occurrence in patients undergoing CH anesthesia.

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MEDICAL RECORDS-International Medical Journal

Research Article

Prevalence of Hepatitis B Serology and Reactivation in Rheumatology Patients Receiving Biologic or Targeted Synthetic Disease-Modifying Antirheumatic Drugs

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Abstract

Aim: This study sought to assess hepatitis B virus (HBV) serology and the incidence of HBV reactivation (HBVr) in rheumatology patients with resolved hepatitis B infection (HBsAg negative and HBcAb positive) who were undergoing treatment with biologic or targeted synthetic disease-modifying anti-rheumatic drugs (b/tsDMARDs).
Material and Method: Data from rheumatology patients treated with b/tsDMARDs were retrospectively reviewed from the electronic records. The demographic data, the anti-rheumatic drugs used, and the hepatitis serologies (HBsAg, anti-HBc IgG, anti-HBs, and anti-HCV) of the patients were analyzed.
Results: The study included a total of 316 patients, of whom 217 (68.7%) were diagnosed with ankylosing spondylitis, 74 (23.4%) with rheumatoid arthritis, and 25 (7.9%) with psoriatic arthritis. Evaluation of the patients' viral serologies revealed that four (1.2%) were HBsAg positive, and 18 (5.7%) were HBsAg negative and HBcAb positive. Anti-HCV positivity was observed in one (0.3%) patient. All serologies were negative in 153 (48.4%) patients. No HBVr was detected during the follow-up of the patients.
Conclusion: The rate of resolved hepatitis B infection is relatively high in patients under rheumatologic follow-up. However, the use of biologics in these patients poses a low risk of HBVr.

Keywords: Biologic therapy, b/tsDMARD, hepatitis B virus reactivation, rheumatologic diseases

INTRODUCTION

Both rheumatic inflammatory diseases and viral hepatitis are serious health issues. It is known that approximately one in three people in the world is infected with hepatitis B virus (HBV) (1). In Türkiye, it is estimated that around 3.3 million people are HBV carriers, with an overall prevalence rate of 4.57% (2).

The pathogenesis of rheumatologic diseases is based on autoimmunity, necessitating the use of immunosuppressive agents in their treatment. Immunosuppressive therapy encompasses corticosteroids, conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), biologic disease-modifying antirheumatic drugs (bDMARDs), and targeted synthetic disease-modifying antirheumatic drugs (tsDMARDs) (3). CsDMARDs include drugs like azathioprine, sulfasalazine, leflunomide, hydroxychloroquine, minocycline and methotrexate. bDMARDs consist of interleukin (IL)-1 inhibitors (canakinumab and anakinra), tumor necrosis factor (TNF) inhibitors (adalimumab, infliximab, etanercept, certolizumab and golimumab), IL-17 inhibitors (ixekizumab and secukinumab), IL-6 inhibitors (tocilizumab), and IL-23 inhibitors (guselkumab and ustekinumab). TsDMARDs include JAK kinase inhibitors such as tofacitinib, filgotinib, peficitinib, upadacitinib, and baricitinib (4). In recent years, b/tsDMARDs used in the treatment of rheumatic diseases have revolutionized rheumatology. However, these treatments have strong immunosuppressive effects (5). Extended use of b/tsDMARDs has been linked to a higher frequency of activation of opportunistic infections, tuberculosis, herpes zoster and infections caused by HBV or Hepatitis C virus (HCV) (6). Recent guidelines recommend hepatitis screening before starting biologic therapy (5,7). For

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patients who are HBsAg positive, prophylactic antiviral treatment is advised before initiating b/tsDMARD therapy. However, recommendations for HBsAg negative and HBcAb positive patients differ, and there is no agreed-upon guideline for prophylactic treatment (1). However, although the risk of HBVr in HBsAg negative and HBcAb positive patients is lower compared to HBsAg positive patients, the prevalence of HBcAb positive patients is higher than that of HBsAg positive patients (8). The general strategy is to handle HBsAg negative and HBcAb positive patients with detectable HBV DNA in a manner similar to HBsAg positive patients. For those with negative HBV DNA, regular monitoring of aminotransferase and HBV DNA levels is recommended, or they may be given prophylactic antivirals like lamivudine (9).

In this study, our goal was to evaluate the seroprevalence of HBV in patients diagnosed with ankylosing spondylitis (AS), rheumatoid arthritis (RA), and psoriatic arthritis (PsA) who were treated with various b/tsDMARDs at our center, and to assess the risk of HBV reactivation in patients with HBsAg negative and HBcAb positive serology.

MATERIAL AND METHOD

This retrospective study involved the electronic review of the data from a total of 316 patients diagnosed with AS, RA, and PsA who visited the physical therapy and rehabilitation outpatient clinic and the pulmonary diseases outpatient clinic for drug safety monitoring between January 1, 2018, and December 31, 2023, and were treated with b/tsDMARDs. The recorded data included patients' age, gender, diagnosis, b/tsDMARD therapy, hepatitis serology (HBsAg, HBsAb, HBcAb, and anti-HCV), and serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels. An anti-HBs value above 10 mIU/mL was considered positive.

Inclusion and Exclusion Criteria

The inclusion criteria were being aged 18 or over, being diagnosed with AS, RA, or PsA, undergoing b/tsDMARD therapy, having hepatitis serology (HBsAg, HBsAb, HBcAb and anti-HCV) tests annually, and having AST and ALT levels measured every three months. Patients who did not meet these criteria and those with incomplete data were excluded. The study received approval from the local ethics committee at Ordu University Faculty of Medicine (decision number: 2024/56).

Statistical Analysis

All statistical analyses were conducted using the SPSS software (version 22.0, Inc., Chicago, Illinois, USA). Comparative statistical tests were not used. Simple descriptive statistics, such as percentages and means, were utilized.

RESULTS

A total of 316 patients diagnosed with AS, RA, and PsA who were being followed up at our hospital under any of the b/tsDMARD therapies were retrospectively evaluated. The mean age of the patients was 47.87±12.59 years, with 160 (50.6%) males and 156 (49.4%) females. Among the patients, 217 (68.7%) had AS, 74 (23.4%) had RA, and 25 (7.9%) had PsA. Regarding the b/tsDMARDs used, 100 patients were on adalimumab, 89 on etanercept, 35 on secukinumab, 34 on certolizumab, 27 on golimumab, 16 on infliximab, nine on tofacitinib, three on tocilizumab, and three on baricitinib. Concerning the viral serologies, four (1.2%) patients were HBsAg positive, 18 (5.7%) were HBsAg negative and anti-HBc IgG positive, and 52 (16.5%) were HBsAg positive and anti-HBc IgG positive. Anti-HCV positivity was found in one (0.3%) patient. The number of patients with negative serologies for all markers was relatively high, at 153 (48.4%). Tenofovir was used prophylactically in 4 HBsAg positive patients. None of the other patients were receiving antiviral treatment. No reactivation was detected in any of the patients (Table 1).

Table 1. Clinical characteristics of the patients

Clinical characteristics	n (%)
Age, mean±SD	47.87±12.59 (19-77)
Gender	
Male	160 (50.6%)
Female	156 (49.4%)
Disease diagnosis	
Ankylosing spondylitis	217 (68.7%)
Rheumatoid arthritis	74 (23.4%)
Psoriatic arthritis	25 (7.9%)
B/tsDMARD	
Adalimumab	100 (31.6%)
Etanercept	89 (28.2%)
Secukinumab	35 (11.1%)
Certolizumab	34 (10.8%)
Golimumab	27 (8.5%)
Infliximab	16 (5.1%)
Tofacitinib	9 (2.8%)
Tocilizumab	3 (0.9%)
Baricitinib	2(0.6%)
Abatacept	1 (0.3%)
Viral serology	
HBsAg positive	4 (1.2%)
HBsAg negative and anti-HBc IgG positive	18 (5.7%)
HBsAg positive and anti-HBc IgG positive	52 (16.5%)
Anti-HCV positive	1 (0.3%)
All serologies negative	153 (48.4%)
HBV reactivation	0

DISCUSSION

Globally, more than 2 billion individuals are estimated to have been exposed to HBV, with approximately 292 million suffering from chronic infections (10). It is known that

immunosuppressive therapies increase the risk of HBV. These treatments can cause reactivation in patients with HBsAg negative and HBcAb positive, causing various liver problems that can result in death (11). The risk of HBVr is affected by host factors, HBV viral status, as well as the type and duration of immunosuppressive therapy (12). A systematic review showed that 6.5% of HBsAg negative and HBcAb positive patients receiving immunosuppressive therapy had HBVr. In the same study, when patients were grouped, the HBVr rate was reported as 10.9% in those with hematological disease, while this rate was reported as 3.6% in those without hematological disease. The findings also indicated that the risk of HBVr was lower in patients with non-hematologic conditions and those not on rituximab-containing regimens. As a result, it was concluded in the study that anti-HBV prophylaxis may not be necessary for patients who are HBsAb positive and HBV DNA negative (8).

In rheumatic diseases like RA and AS, the risk of reactivating viral infections is heightened by immunosuppressive therapy. The frequency of HBV infection in these patients is thought to be the same as in the general population, with an estimated HBsAg positive prevalence ranging from 3% to 3.5% and a past infection rate of 13% to 50% (12). Therefore, it is recommended that patients with rheumatologic diseases receiving immunosuppressive therapy, such as DMARDs, undergo appropriate screening and treatment to mitigate the risk of HBVr (11). In a study conducted by Fidan et al. with 272 HBsAg negative and HBcAb positive patients, no HBVr was observed in the 31 patients receiving antiviral prophylaxis, while only one (0.4%) of the 241 patients not receiving prophylaxis experienced HBVr (13). Similarly, a multicenter study by Çapkın et al. found a reactivation rate of 11.4% in HBsAg positive rheumatology patients receiving biologics, compared to a reactivation rate of 0.82% in HBsAg negative and HBcAb positive patients (14). A recent study reported that HBV DNA development was at a very low rate of 0.9% for all biological agents in HBsAg negative and HBcAb positive patients using biological agents, thus posing a very low risk of reactivation (15). In another study, all HBsAg positive or HBsAg negative and HBcAb positive patients were given prophylactic antiviral treatment with entecavir or tenofovir before starting b/tsDMARD therapy, and no HBVr was observed during the study period. The absence of reactivation was attributed to the antiviral treatment administered (1). A recent meta-analysis included 26 studies involving a total of 2252 HBsAg negative and HBcAb positive patients with RA receiving b/tsDMARD therapy. IL-6, TNF-a and JAK inhibitors were found to have low HBVr rates of 0%, 0% and 1%, respectively. The study shows that each of these three agents is safe for patients with RA and prophylactic antiviral treatment may not be necessary due to low reactivation rates and cost-effectiveness (16). In our study, four patients were HBsAg positive and all were using tenofovir prophylactically. Additionally, 18 patients were HBsAg negative and HBcAb positive, and 52 were HBsAg positive and HBcAb positive. None of these patients were receiving prophylactic antiviral treatment, and no reactivation was detected during follow-up.

Studies have presented conflicting information on the HBVr risk in HBsAg negative and HBc Ab positive rheumatologic patients receiving biologic therapy, with the prevalence ranging from 0 to 5.5% (6). In our study, no HBVr was observed in AS, RA, and PsA patients receiving different b/tsDMARD therapies. The discrepancy in reactivation incidence among different studies may be due to variations in follow-up duration and/or the number of patients included. Studies indicate that the HBVr rate is very low, especially in patients with resolved HBV infection; thus, prophylactic antiviral treatment for these patients remains a topic of discussion.

In our study, we observed that 153 (48.4%) patients had negative serologies for all markers, highlighting gaps in patient management. Türkiye is considered an intermediate endemic region, and mandatory HBV vaccination at birth commenced in 1998, indicating that individuals born before this date are at risk (17). Ideally, hepatitis markers should be requested from all rheumatology patients after diagnosis, especially in areas with high HBV prevalence. HBV vaccination should be administered before starting anti-TNF therapy or within the first six months of treatment due to potential reductions in vaccine efficacy associated with these drugs (18).

The limitations of this study involve the relatively brief follow-up period and the retrospective nature of the design. However, the study's strength lies in the inclusion of patients receiving various b/tsDMARD therapies with regular three-month follow-ups.

CONCLUSION

Although HBc IgG positivity is highly prevalent in RA, AS, and PsA patients, the HBVr rate is very low. Additionally, a significant portion of rheumatology patients in Türkiye have not been vaccinated against HBV. Despite the low HBVr rate, it would be beneficial to screen and vaccinate these patients before initiating immunosuppressive therapy, given the potential need for lifelong immunosuppressive treatment.

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MEDICAL RECORDS-International Medical Journal

Research Article

Evaluation of the Turkish Population's Knowledge about Dental Implants

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Abstract

Aim: Dental implants have become the most preferred treatment method for tooth loss. The aim of this study is to evaluate the knowledge and preferences of individuals living in Türkiye regarding dental implants.
Material and Method: In this research, a multiple-choice questionnaire was administered to assess individuals' knowledge levels and reasons for preference concerning dental implants. The survey was conducted online among men and women aged 18-79 who had never undergone implant treatment, residing in various provinces of Türkiye. The statistical analysis of the obtained data was performed using the SPSS program and the chi-square test.
Results: A total of 429 individuals participated in the study, including 196 men (45.7%) and 233 women (54.3%). Of the participants, 47.9% learned about the concept of dental implants from dentists, and 57.6% reported having partial knowledge. A majority of 67.7% preferred to have implant treatment performed by a specialist dentist. 87.8% believed that dental implants are not harmful to health after treatment. Most participants indicated that the most crucial factor in the preference for implants is the dentist's recommendation (54.2%).
Conclusion: This study provides significant data for understanding the knowledge levels and factors influencing the preferences of individuals regarding dental implants. While highlighting the critical role of dentists in providing information and guidance, it also underscores the need to increase awareness about dental implants among the general population. Accordingly, broader informational and educational efforts are necessary to promote more widespread and correct application of dental implant treatments.

Keywords: Dental implants, patient knowledge level, implant treatment, implant preferences

INTRODUCTION

Dental implant procedures were introduced into dental practice with the description of osseointegration by Branemark and his team in the early 1980s (1). Osseointegration is a critical process that enables dental implants to integrate biologically with bone, making them a reliable and long-lasting treatment option for individuals with tooth loss (1). This development has led to the rapid adoption of dental implants in clinical practice (1).

Dental implant applications have a wide distribution network, and patient demand, influenced by the information provided by physicians and the media, plays a significant role in expanding this network (2). Physicians' patient education, including the advantages and disadvantages of dental implants, increases the acceptance of implant procedures (2). The media is also an important factor in increasing the popularity and awareness of dental implants in society (2). There is extensive literature on dental implants, with most studies providing information on the clinical success of dental implants (2,3). Topics such as factors affecting implant success, surgical techniques, materials used, and long-term clinical outcomes have been extensively researched (2,3).

Dental implant treatment is one of the primary treatment options for both edentulous and partially edentulous patients (3). In this treatment process, the patient's expectations and preferences are as important as the physician's choice (3,4). Patient-related factors include not only physical conditions such as bone volume but also psychosocial conditions, expectations, and economic means (5). Particularly, patients' aesthetic expectations, functional needs, and psychological approaches to treatment play a significant role in implant treatment planning. (6). Economic factors also directly affect patients' preferences for implant treatment, as dental implants are generally among the high-cost treatments

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(3-7).

Physicians' education and guidance of their patients are highly effective in planning dental implant treatments (7). Factors contributing to this influence include the physician's knowledge and experience, ability to explain the planning, and good communication with the patient (8). Physicians' knowledge and experience are critical for gaining patients' trust and fostering a positive attitude towards treatment (9). Additionally, the educational materials provided by the physician help patients make informed decisions (7-11).

A review of the literature reveals that although there are many studies focusing on the clinical success of dental implants, there are relatively few studies on patient awareness and knowledge levels (10-12). Increasing patient awareness and knowledge is essential for the success of implant treatment, as informed patients can be more compliant with the treatment process and more careful about post-treatment care (10). Some researchers have conducted various studies to evaluate patients' awareness of dental implants in different countries (10). These studies reveal how cultural and socioeconomic differences affect patient awareness and attitudes towards implant treatment (10).

This research aims to evaluate the awareness levels regarding implants, ways of accessing information about implants, and the factors influencing implant preferences among patients living in various provinces of the country who have never undergone implant treatment. This study will reveal the knowledge levels of patients about dental implants and help dentists develop more effective patient education and information strategies in this area. Additionally, our study aims to emphasize the importance of patient education in dental practice and shed light on future research in this field.

MATERIAL AND METHOD

Ethical Approval

The study was conducted over a three-month period (December 2022- February 2023) in accordance with the principles of the Declaration of Helsinki. Ethical approval for the study was obtained from the Non-Interventional Clinical Research Ethics Committee of Karamanoğlu Mehmetbey University on December 16, 2022, with decision number 11-2022/06.

Survey Design

This cross-sectional study, which aims to evaluate the knowledge and awareness of individuals regarding implant application, was designed as a survey study consisting of open-ended and multiple-choice questions. The survey forms were prepared using Google Forms (Google, Inc., 2017, California, USA). Before the survey questions, a section explaining the nature and purpose of the study and including a consent form for participants was prepared. The voluntary nature of participation and the confidentiality of responses were assured. Individuals who selected the option "I do not wish to participate" were excluded from the study. Following a literature review, a 12-question survey was prepared based on previous studies and evaluated for face and content validity through a pilot study on three randomly selected volunteers (13). To ensure the accuracy and confidentiality of the data, participants were asked to use nicknames instead of their names and to respond with the same nickname during a follow-up test two weeks later. Data from the pilot study were not included in the final analysis. Subsequently, all validated questions were evaluated for validation by sending a five-point Likert scale evaluation form via email to two oral surgeons and one periodontologist. All questions were revised and finalized based on expert feedback. The self-administered, online 12-question survey, consisting of two sections, was distributed to 450 volunteers via email and messages. The study included 429 volunteers who agreed to participate. No personal information, including email addresses, was requested from participants. Demographic information, professional experience, and institutional affiliations of the participants were collected. Only volunteers who had not previously undergone implant treatment and agreed to participate were included in the study. The survey consisted of two sections. The first section inquired about demographic characteristics such as age, gender, education, and income level. The second section, comprising eight questions, examined participants' preferences regarding dental implants. The survey investigated how patients accessed information about dental implants, whether they considered their knowledge sufficient, the institution they preferred for treatment, whether they believed dental implant treatment was harmful to health, their preference for domestic or imported products, and the reasons for these preferences. The relevant link (URL) to the survey was sent to individuals who had never undergone implant treatment. Participants were informed that they could contact the researcher with any questions or issues they might encounter at any stage of the study. The data obtained were transferred to Microsoft Excel by the researcher, and percentage/frequency values for each item in the survey form were calculated.

Participants

Individuals who had never undergone implant treatment were included in the study. The aim was to reach 450 individuals. Those under the age of 18, those who had previously undergone implant treatment, and individuals with conditions such as mental retardation were excluded from the study. Online consent forms were obtained from participants, and they were allowed to participate voluntarily.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics (Version 26.0. Armonk, NY: IBM Corp.). Categorical data were expressed as numbers and percentages. The chi-square test was used to evaluate responses to the questions according to participants' gender, age, education level, and monthly income. A p-value of <0.05 was considered statistically significant in the study.

RESULTS

The demographic characteristics of the individuals participating in the study are as shown in Table 1. These findings indicate that the participants of the study are from a broad demographic spectrum.

Table 1. Demographic characteristics of participants

		f	%
Gender	Male	196	45.7
	Female	233	54.3
Age	Under 30	73	17.0
	30-40	212	49.4
	40-50	67	15.6
	50-60	45	10.5
	Over 60 years old	32	7.5
Education level	Primary school	35	8.2
	Middle school	41	9.6
	High school	66	15.4
	Associate degree	52	12.1
	Licence	145	33.8
	Graduate	90	21.0
Income rate	Low income	80	19.5
	Middle income	188	45.7
	High income	143	34.8

When examining the findings regarding where participants first learned about the concept of dental implants, 47.9% (n=205) reported learning about it from dentists, 32.2% (n=138) from relatives or friends, 11.7% (n=50) from social media (Facebook, Instagram, etc.), 5.1% (n=22) from visual media (TV, billboard, etc.), and 3.0% (n=13) from print media (newspaper, magazine, brochure, etc.). When evaluating the levels of knowledge about dental implants, 57.6% (n=247) reported having partial knowledge, 27.3% (n=117) sufficient knowledge, and 15.2% (n=65) no knowledge at all. When asked where they would prefer to have dental implant treatment, 67.7% (n=289) preferred a specialist dentist's clinic, 23.0% (n=98) a university hospital, and 9.4% (n=40) any dentist. While 87.8% (n=374) did not believe that dental implants are harmful to health after treatment, 12.2% (n=52) had concerns about this. When asked if they knew someone who had undergone dental implant treatment, 81.1% (n=346) answered yes and 18.9% (n=81) answered no. Of the participants, 66.3% (n=283) considered getting a dental implant to be a difficult procedure, while 33.7% (n=144) did not. In implant preferences, 55.7% (n=235) preferred imported implants, while 44.3% (n=187) preferred domestic implants. Among the factors determining implant preferences, 54.2% (n=230) cited the recommendation of their dentist, 19.1% (n=81) cited recommendations they had heard, 16.5% (n=70) cited price, 9.7% (n=41) cited the country of manufacture/national preference, and 0.5% (n=2) cited social media.

In the evaluation by gender, it was found that female participants were more likely than male participants to learn about implants first from dentists, to consider themselves sufficiently knowledgeable about implants, to think that getting a dental implant is a difficult procedure, and to have the recommendation of their dentist as the determining factor in their implant preference ($p<0.05$). There were no statistically significant differences between male and female participants' responses to other questions ($p>0.05$) (Table 2).

In the evaluation by age, it was found that as age increases, participants are more likely to have first learned about the concept of dental implants from a dentist. The age group most likely to prefer any dentist for their dental implant treatment was those under 30, while the age group most likely to prefer a university hospital was those over 60. As age increases, the proportion of participants who believe that dental implants are not harmful to health after treatment also increases. The participants who were most likely to prefer imported implants were those aged 30-40, while those who preferred domestic implants were most likely over 60. The highest proportion of participants who preferred a national brand for implant preference were over 60, whereas the highest proportion of participants who preferred recommendations they had heard were those under 30 ($p<0.05$). There were no statistically significant differences in responses to other questions based on age ($p>0.05$) (Table 3).

In the evaluation by educational status, it was found that participants with postgraduate education were more likely to have first learned about dental implants from a dentist, while those who preferred the answer "I learned from relatives/friends" were most likely primary school graduates. Participants who answered "I have sufficient knowledge about implants" were most likely postgraduate individuals. Regarding the institution where they would prefer to have implant treatment, the highest proportion of participants who chose any dentist were primary school graduates, while the highest proportion of participants who chose university hospitals were postgraduate individuals. Participants who believed that dental implants are harmful to health after treatment were primary school graduates. Those who preferred domestic implants were also most likely primary school graduates. The highest proportion of participants who cited price as the determining factor in their implant preference were primary school graduates, while those who cited their dentist's recommendation were most likely postgraduate individuals ($p<0.05$). There were no statistically significant differences in responses to other questions based on educational status ($p>0.05$) (Table 4).

In the comparison by income level, it was found that participants with high income were more likely to have first learned about the concept of dental implants from a dentist, and these individuals consider themselves to have sufficient knowledge about dental implants. Participants with low income were more likely to choose any dentist when asked about the institution where they would prefer to have implant treatment, while those with high income were more likely to choose university hospitals and specialist dentist clinics. Participants with low income were more likely to believe that dental implants

are harmful to health after treatment and consider the procedure to be difficult, and they were also the group most likely to prefer domestic implants. Regarding the factors determining implant preference, participants with low income were more likely to cite implant price, while those with high income were more likely to cite their dentist's recommendation ($p<0.05$). There were no statistically significant differences in responses to other questions based on income level ($p>0.05$) (Table 5).

Table 2. Questions showing statistical differences in comparison by gender

Questions			Gender		Total	p
			Male	Female		
Where did you first learn about the concept of dental implants?	Relative/friend	n	65	73	138	0.018
		%	33.2	31.5	32.2	
	Dentist	n	87	118	205	
		%	44.4	50.9	47.9	
	Visual media (TV, billboard, etc.)	n	11	11	22	
		%	5.6	4.7	5.1	
	Social media (Facebook, Instagram, etc.)	n	21	29	50	
		%	10.7	12.5	11.7	
	Print media (newspaper, magazine, brochure, etc.)	n	12	1	13	
		%	6.1	0.4	3.0	
Do you have any knowledge about dental implants?	I have no knowledge	n	39	26	65	0.007
		%	19.9	11.2	15.2	
	Partially	n	115	132	247	
		%	58.7	56.7	57.6	
	I have sufficient knowledge	n	42	75	117	
		%	21.4	32.2	27.3	
Do you know someone who has had a dental implant?	Yes	n	152	194	346	0.140
		%	77.9	83.6	81.0	
	No	n	43	38	81	
		%	22.1	16.4	19.0	
Which type of implant would you prefer in your implant choice?	Imported implant	n	105	130	235	0.551
		%	54.1	57.0	55.7	
	Domestic implant	n	89	98	187	
		%	45.9	43.0	44.3	
Which of the following factors determines your implant preference?	Recommendations I have heard	n	44	37	81	0.019
		%	22.8	16.0	19.1	
	Price	n	28	42	70	
		%	14.5	18.2	16.5	
	My dentist's recommendation	n	94	136	230	
		%	48.7	58.9	54.2	
	Social media	n	2	0	2	
		%	1.0	0.0	0.5	
	Country of manufacture/national preference	n	25	16	41	
		%	13.0	6.9	9.7	

Table 3. Questions showing statistical differences in comparison by age

Questions			Age					Total	p
			Under 30	30-40	41-50	51-60	Over 60		
Where did you first learn about the concept of dental implants?	Relative/friend	n	34	73	16	10	5	138	0.032
		%	46.6	34.6	23.9	22.2	15.6	32.2	
	Dentist	n	27	97	35	24	22	205	
		%	37.0	46.0	52.2	53.3	68.8	47.9	
	Visual media (TV, billboard, etc.)	n	1	10	6	4	1	22	
		%	1.4	4.7	9.0	8.9	3.1	5.1	
	Social media (Facebook, Instagram, etc.)	n	7	25	10	6	2	50	
		%	9.6	11.8	14.9	13.3	6.3	11.7	
	Print media (newspaper, magazine, brochure, etc.)	n	4	6	0	1	2	13	
		%	5.5	2.8	0.0	2.2	6.3	3.0	
Do you have any knowledge about dental implants?	I have no knowledge	n	19	14	2	5	0	40	0.001
		%	26.0	6.6	3.0	11.1	0.0	9.4	
	Partially	n	45	140	51	34	19	289	
		%	61.6	66.4	77.3	75.6	59.4	67.7	
	I have sufficient knowledge	n	9	57	13	6	13	98	
		%	12.3	27.0	19.7	13.3	40.6	23.0	
Do you know someone who has had a dental implant?	Yes	n	17	24	6	4	1	52	0.018
		%	23.3	11.4	9.0	8.9	3.2	12.2	
	No	n	56	186	61	41	30	374	
		%	76.7	88.6	91.0	91.1	96.8	87.8	
Which type of implant would you prefer in your implant choice?	Imported implant	n	33	137	37	17	11	235	0.001
		%	45.8	65.9	56.1	37.8	35.5	55.7	
	Domestic implant	n	39	71	29	28	20	187	
		%	54.2	34.1	43.9	62.2	64.5	44.3	
Which of the following factors determines your implant preference?	Recommendations I have heard	n	18	40	12	8	3	81	0.001
		%	24.7	19.0	17.9	18.2	10.0	19.1	
	Price	n	22	34	6	4	4	70	
		%	30.1	16.2	9.0	9.1	13.3	16.5	
	My dentist's recommendation	n	28	117	41	28	16	230	
		%	38.4	55.7	61.2	63.6	53.3	54.2	
	Social media	n	0	0	1	1	0	2	
		%	0.0	0.0	1.5	2.3	0.0	0.5	
	Country of manufacture/ national preference	n	5	19	7	3	7	41	
		%	6.8	9.0	10.4	6.8	23.3	9.7	

Table 4. Questions showing statistical differences in comparison by educational status

Questions			Education level						Total	p
			Primary school	Middle school	High school	Associate degree	Undergraduate	Graduate		
Where did you first learn about the concept of dental implants?	Relative/friend	n	21	13	26	18	40	20	138	0.037
		%	60.0	31.7	39.4	35.3	27.6	22.2	32.2	
	Dentist	n	10	20	26	21	72	56	205	
		%	28.6	48.8	39.4	41.2	49.7	62.2	47.9	
	Visual media (TV, billboard, etc.)	n	1	2	1	4	12	2	22	
		%	2.9	4.9	1.5	7.8	8.3	2.2	5.1	
	Social media (Facebook, Instagram, etc.)	n	3	4	11	7	16	9	50	
		%	8.6	9.8	16.7	13.7	11.0	10.0	11.7	
	Print media (newspaper, magazine, brochure, etc.)	n	0	2	2	1	5	3	13	
		%	0.0	4.9	3.0	2.0	3.4	3.3	3.0	
Do you have any knowledge about dental implants?	I have no knowledge	n	10	11	13	8	14	9	65	0.001
		%	28.6	26.8	19.7	15.4	9.7	10.0	15.2	
	Partially	n	15	25	41	34	92	40	247	
		%	42.9	61.0	62.1	65.4	63.4	44.4	57.6	
	I have sufficient knowledge	n	10	5	12	10	39	41	117	
		%	28.6	12.2	18.2	19.2	26.9	45.6	27.3	
Where do you prefer to have dental implant treatment?	Any dentist Specialist dentist's clinic	n	10	5	10	6	4	5	40	0.001
		%	28.6	12.2	15.4	11.8	2.8	5.6	9.4	
	University hospital Any dentist	n	21	25	39	34	111	59	289	
		%	60.0	61.0	60.0	66.7	76.6	65.6	67.7	
	Specialist dentist's clinic	n	4	11	16	11	30	26	98	
		%	11.4	26.8	24.6	21.6	20.7	28.9	23.0	
Do you think dental implants are harmful to health after treatment?	Yes	n	10	3	11	4	16	8	52	0.025
		%	28.6	7.5	16.7	7.8	11.1	8.9	12.2	
	No	n	25	37	55	47	128	82	374	
		%	71.4	92.5	83.3	92.2	88.9	91.1	87.8	
Which type of implant would you prefer in your implant choice?	Imported implant	n	5	13	29	28	99	61	235	0.001
		%	14.7	31.7	44.6	54.9	69.7	68.5	55.7	
	Domestic implant	n	29	28	36	23	43	28	187	
		%	85.3	68.3	55.4	45.1	30.3	31.5	44.3	
Which of the following factors determines your implant preference?	Recommendations I have heard	n	4	10	11	13	26	17	81	0.012
		%	11.4	24.4	16.9	25.5	18.3	18.9	19.1	
	Price	n	11	4	18	11	15	11	70	
		%	31.4	9.8	27.7	21.6	10.6	12.2	16.5	
	My dentist's recommendation	n	16	19	27	26	85	57	230	
		%	45.7	46.3	41.5	51.0	59.9	63.3	54.2	
	Social media	n	0	0	0	0	1	1	2	
		%	0.0	0.0	0.0	0.0	0.7	1.1	0.5	
	Country of manufacture/ national preference	n	4	8	9	1	15	4	41	
		%	11.4	19.5	13.8	2.0	10.6	4.4	9.7	

Table 5. Questions showing statistically significant differences in comparisons based on income level

Questions			Income rate			Total	p
			Low income	Middle income	High income		
Where did you first learn about the concept of dental implants?	Relative/friend	n	43	54	36	133	0.001
		%	53.8	28.7	25.2	32.4	
	Dentist	n	29	89	79	197	
		%	36.3	47.3	55.2	47.9	
	Visual media (TV, billboard, etc.)	n	1	15	6	22	
		%	1.3	8.0	4.2	5.4	
	Social media (Facebook, Instagram, etc.)	n	6	24	16	46	
		%	7.5	12.8	11.2	11.2	
	Print media (newspaper, magazine, brochure, etc.)	n	1	6	6	13	
		%	1.3	3.2	4.2	3.2	
Do you have any knowledge about dental implants?	I have no knowledge	n	14	31	18	63	0.012
		%	17.5	16.5	12.6	15.3	
	Partially	n	44	120	72	236	
		%	55.0	63.8	50.3	57.4	
	I have sufficient knowledge	n	22	37	53	112	
		%	27.5	19.7	37.1	27.3	
Where do you prefer to have dental implant treatment?	Any dentist	n	21	12	5	38	0.001
		%	26.3	6.5	3.5	9.3	
	Specialist dentist's clinic	n	45	130	101	276	
		%	56.3	69.9	70.6	67.5	
	University hospital	n	14	44	37	95	
		%	17.5	23.7	25.9	23.2	
Do you think dental implants are harmful to health after treatment?	Yes	n	19	18	11	48	0.001
		%	23.8	9.7	7.7	11.8	
	No	n	61	167	132	360	
		%	76.3	90.3	92.3	88.2	
Do you consider getting a dental implant to be a difficult procedure?	Yes	n	60	137	75	272	0.001
		%	75.0	73.7	52.4	66.5	
	No	n	20	49	68	137	
		%	25.0	26.3	47.6	33.5	
Which type of implant would you prefer in your implant choice?	Imported implant	n	19	107	103	229	0.001
		%	23.8	57.8	73.0	56.4	
	Domestic implant	n	61	78	38	177	
		%	76.3	42.2	27.0	43.6	
Which of the following factors determines your implant preference?	Recommendations I have heard	n	22	31	24	77	0.001
		%	27.5	16.8	17.0	19.0	
	Price	n	23	34	10	67	
		%	28.8	18.4	7.1	16.5	
	My dentist's recommendation	n	24	102	94	220	
		%	30.0	55.1	66.7	54.2	
	Social media	n	0	0	2	2	
		%	0.0	0.0	1.4	0.5	
	Country of manufacture/ national preference	n	11	18	11	40	

DISCUSSION

In this study, where individuals first learned about the concept of dental implants and the factors influencing their implant preferences were examined. The findings show that the majority of participants learned about dental implants from dentists (47.9%). This highlights the significant influence and critical role of dentists in informing patients (14). It was also found that gaining information through relatives or friends (32.2%) is common, which indicates the influence of social circles in informing and guiding dental health decisions.

Regarding the level of knowledge about dental implants, 57.6% of participants had partial knowledge, 27.3% had sufficient knowledge, and 15.2% had no knowledge. This finding suggests that the overall level of knowledge about dental implants in society is insufficient, although the majority have some knowledge. Therefore, it can be said that more extensive information and educational efforts are needed to increase awareness about dental implants across the general population. A survey study (15) found that 43.5% of participants with similar educational backgrounds had sufficient knowledge, compared to 26.8% in our study. This discrepancy is thought to be due to differences in the educational levels of the individuals. Studies conducted in different countries have shown a higher level of knowledge about implants among participants, which may be attributed to socioeconomic differences (8,9).

The findings regarding where participants preferred to have dental implant treatment show that 67.7% preferred a specialist dentist's clinic, 23.0% preferred a university hospital, and 9.4% preferred any dentist. These results underscore the high level of trust in specialist dentists and the importance placed on the quality of treatment. The preference for university hospitals indicates that patients value academic and reliable treatment environments. A survey study (16) found that 40.6% of patients learned about implants from their dentists, compared to 47% in our study. These similar rates are thought to be due to similar patterns of dental visits. The finding that dentists are the primary source of information aligns with similar studies (17,18). Our study observed that as education and income levels increase, individuals are more likely to obtain information about implants from their dentists.

When examining perceptions of whether dental implants are harmful to health post-treatment, 87.8% believed that the treatment is not harmful, while only 12.2% had concerns. Other studies in the literature have shown that individuals have less knowledge about implants (15). This indicates a generally positive perception of dental implant treatment among the participants. However, for the minority with concerns, informational and confidence-building efforts may be beneficial. The study found that 81.1% of participants knew someone who had undergone dental implant treatment, and 66.3% considered implant treatment to be a difficult procedure. These findings suggest that implant treatment is common in society, but there are some perceptions about its difficulty. Detailed information is needed to change this perception and make the process more understandable.

In terms of implant preference, 55.7% of participants preferred imported implants, while 44.3% preferred domestic implants. The higher preference for imported implants may be due to a higher perception of quality and reliability. However, to increase preferences for domestic implants, it is important to emphasize the quality and reliability of local productions.

Finally, among the factors determining implant preference, 54.2% of participants cited the recommendation of their dentist, 19.1% cited recommendations they had heard, 16.5% cited price, 9.7% cited the country of manufacture/national preference, and 0.5% cited social media. This finding shows that the dentist's recommendation is the most determining factor in implant preference. While other factors are also important, it can be said that the authority and expertise of the dentist have a dominant influence on patients. The cost is less influential than the dentist's recommendation, which is consistent with a similar study (16). However, for individuals with lower income levels, cost is a significant determinant of implant preference, highlighting the relationship between cost and dental implant treatment.

This study provides important data for understanding the knowledge levels and factors influencing individuals' preferences regarding dental implants. The results emphasize the critical role of dentists in informing and guiding patients and also highlight the need to increase awareness about dental implants across society. The findings clearly demonstrate the significant role of dentists in patient education and guidance regarding dental implants. The majority of participants learned about the concept of dental implants from dentists, highlighting the critical role of dentists in patient education.

Limitations of the Study

This study has several important limitations. First, the sample size is limited and data were collected from 429 individuals who had not undergone implant treatment. This limits the generalizability of the results and may not be representative of the larger population. In addition, the cross-sectional design of the study does not allow for the assessment of time-varying factors. Longitudinal studies are needed to examine long-term effects. The study is limited by demographic data and participants' knowledge of dental implants. Additional variables such as participants' health status, dental history, psychosocial factors, and economic conditions should be examined for a more comprehensive assessment. These factors may help to better understand preferences for dental implants and attitudes toward treatment.

CONCLUSION

As a result, data were collected from a wide demographic spectrum of participants, including age, gender, education

level, and income. This increased the generalizability of the results across different demographic groups and allowed for the examination of differences in knowledge levels and preferences for dental implants across these groups. The results demonstrated the critical role of dentists in informing and guiding patients and highlighted the need to increase public awareness of dental implants. Accordingly, broader informative and educational efforts are needed to encourage more widespread and appropriate implementation of dental implant treatments.

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MEDICAL RECORDS-International Medical Journal

Research Article

The Impact of Olaparib on Metabolic Pathways in Triple Negative Breast Cancer: A Bioinformatics Approach

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Abstract

Aim: Triple-negative breast cancer (TNBC) is a highly aggressive subtype of breast cancer (BC) characterized by the lacking estrogen receptors, progesterone receptors, and HER2 expression, making it challenging to treat with targeted therapies. Olaparib, a PARP inhibitor, has shown promise in treating TNBC, particularly in patients with BRCA1 or BRCA2 mutations. This study aims to elucidate the metabolic pathways affected by olaparib in TNBC using bioinformatics analysis.

Material and Method: For bioinformatics analysis, mRNA microarray data of control MDA-MB-468 cells (non-treated) and OlaR MDA-MB-468 (3μM olaparib-treated MDA-MB-468 cells) with the study numbered GSE165914 were downloaded from Gene Expression Omnibus (GEO) database. GEO2R was used to analyze and identify differentially expressed genes (DEGs). Gene ontology (GO) and Kyoto gene and genome encyclopedia (KEGG) analysis were carried out for DEGs to determine significant genes and the biological pathways influenced by olaparib treatment. Protein-protein interaction (PPI) network analysis further identified key proteins and interactions within these pathways.

Results: For GEO2R analysis adjusted P-value<0.05 and |log2FC|>1.0 were selected. The results revealed the upregulation of 2277 genes and downregulation of 2298 genes in olaparib-treated cells compared to the controls. It was reported that DEGs enriched in pathways including, metabolic pathways, pathways in cancer, chemical carcinogenesis - reactive oxygen species, cell cycle, autophagy - animal, Efferocytosis and TNF signaling pathway. Both upregulated and downregulated DEGs were associated with metabolic pathways. Moreover, NDUFA5, NDUFA6, NDUFS6, NDUFB3, NDUFB10, NDUFB7, NDUFA7, NDUFA9, H2AC8, H2AC13, H2AC17, H4C11, H4C12, H2BC12, H2BC21 and H2BC4 were identified as the most significant candidate genes.

Conclusion: This comprehensive bioinformatics approach provides insights into the molecular mechanisms of olaparib's action and identifies potential targets for combination therapies to enhance treatment efficacy in breast cancer.

Keywords: Triple-negative breast cancer, olaparib, bioinformatics, gene expression omnibus, gene expression

INTRODUCTION

Breast cancer (BC) is the most prevalent malignant tumor and cause of cancer-related mortality among women all around the world. It is a heterogeneous disorder with various molecular subtypes representing distinct biological, histological and clinical evidences (1,2).

Based on the presence of molecular biomarkers, BC can be classified into 3 subtypes including, BC expressing hormone receptor (progesterone receptors (PR+), estrogen receptors (ER+)), BC expressing human epidermal receptors 2 (HER2+) and Triple-negative breast cancer (TNBC) (ER−, PR−, HER2−) (2,3). TNBC is a very complex malignancy with a wide variety of molecular subgroups (4). It is one of the most aggressive type of BC, with early metastasis, a quick recurrence, and a dismal prognosis (5). The past few decades have seen little advancement in therapy due to the TNBC's high heterogeneity (5). Roughly 20-30% of TNBC patients are reported to have a proven BRCA1/2 mutation (5).

The therapeutic strategies should be based on the molecular properties of BC. It is a challenge to clinicians to manage TNBCs due to the limited availability of targeted therapies and unfavorable results (6).

Many clinical trials, such as a phase 3 trial of veliparib, phase 1/2 trials of niraparib and talazoparib, and phase 2/3 trials of olaparib, are investigating the use of PARP

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inhibitors (PARPi) in the treatment of early-stage BC (7).

Olaparib, an oral PARPi, suppresses both PARP catalytic activity and traps the PARP enzymes at damaged DNA (8). Olaparib also represents promising anti-tumor effects in patients with germline BRCA-positive HER-negative metastatic BC (9). The cytotoxic and apoptotic effects of olaparib in combination with chemotherapy, immunotherapy, and targeted therapies were reported in the recent studies (10-12). Sinha and colleagues reported that olaparib increased the Resveratrol-mediated apoptosis in BC cells by suppressing the homologous recombination repair pathway (11).

Despite the therapeutic potential of olaparib, the number of studies investigating its molecular mechanisms and effects in BC is relatively limited. Therefore, studies to analyze the underlying mechanisms in olaparib therapy for BC are ongoing.

In this study, we focused on analyzing genes expression profiles in BC cell lines (MDA-MB-468 cells). Recently, bioinformatics analysis has become a prevalent tool for investigating the potential molecular mechanisms and therapeutic targets of various diseases. The identification of novel biomarkers that can be used for diagnostic and prognostic purposes is very important. In this study, we aimed to investigate the genes and mechanisms which are involved in olaparib therapy. For this purpose, we used bioinformatics tools to investigate target genes and interaction networks between these genes to get deeper insight into the mechanisms underlying olaparib treatment in BC.

MATERIAL AND METHOD

Microarray Data

For genome-wide gene expression profiling between control MDA-MB-468 cells (non-treated) and OlaR MDA-MB-468 (3μM olaparib-treated MDA-MB-468 cells), we conducted a microarray analysis using the study numbered GSE165914. The high-throughput gene expression microarray datasets (GSE165914) were obtained and downloaded from the freely accessible GEO database (https://www.ncbi.nlm.nih.gov/geo/).

Screening and Identification of Differentially Expressed Genes (DEGs)

DEGs were screened and identified by comparing OlaR MDA-MB-468 cells with control MDA-MB-468 cells. The DEGs from the datasets were analyzed by using the GEO2R online statistical tool (https://www.ncbi.nlm.nih.gov/geo/geo2r). The adjusted P-value and |log2FC| were calculated, and genes meeting the criteria of an adjusted P-value<0.05 and |log2FC|>1.0 were considered DEGs.

Gene Ontology (GO) and KEGG Pathway Enrichment Analysis

For functional annotation of GO and analysis of KEGG pathway enrichment, we utilized the web-based DAVID 6.8 tool (DAVID; https://david.ncifcrf.gov). To observe the functional enrichment of the DEGs, the results obtained from DAVID were imported into GO. The DEGs were enriched with 3 categories including, molecular function (MF), cell components (CC) and biological processes (BP) (13).

Construction of Protein-Protein Interaction (PPI) Network

To predict the constructed PPI network and the connections between the DEGs, STRING was utilized. The PPI network were extracted using a total interaction score greater than 0.9. The PPI interactions between the statistically significant DEGs were then interpreted using the Cytoscape software (www.cytoscape.org) (14).

Screening of Hub Gene and Module Analysis

Based on the PPI network of DEGs, five topological algorithms (Maximal Clique Centrality, Radiality Centrality, Edge Percolated Component, and Stress Centrality and Density of Maximum Neighborhood Component) in the cytoHubba plugin of Cytoscape were used to identify hub genes.

RESULTS

Identification of Up-Regulated and 2298 Down-Regulated Genes

We carried out gene expression profile analysis of OlaR MDA-MB-468 cells in comparison with the control MDA-MB-468 cells. We used GSE165914 GEO datastes. In the comparison of olaparib treated cells to the control group, olaparib enhanced the expression of 2277 genes and reduced the expression of 2298 genes (Figure 1).

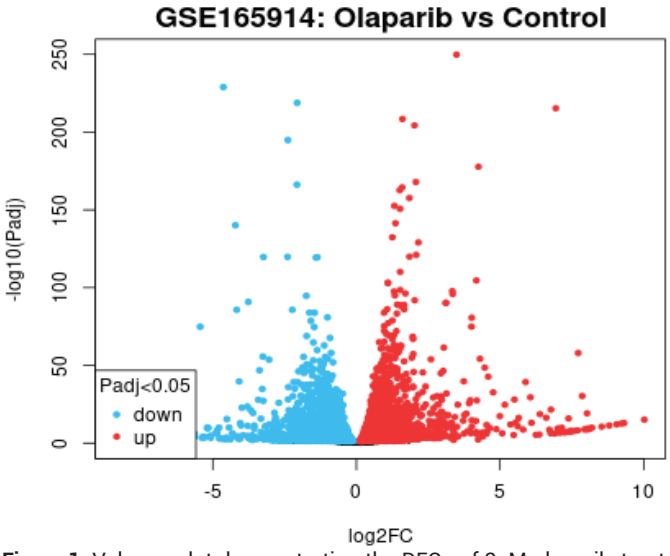

Figure 1. Volcano plot demonstrating the DEGs of 3μM olaparib-treated MDA-MB-468 vs.control, each dot in the volcano map shows a gene; (red = upregulated, blue = downregulated)

GO Functional and KEGG Pathway Enrichment Analysis of the DEGs

Terms related to molecular activities, biological processes, and signaling pathways were used to identify KEGG pathway-enriched genes and potential Gene Ontology categorization.

Base on the GO analysis, the molecular function (MF) mediated by upregulated DEGs were mostly concentrated in ATP binding, ATP hydrolysis activity, unfolded protein binding, nuclear receptor activity, DNA helicase activity and ATP-dependent protein folding chaperone ($p<0.05$). The results of cellular component (CC) were mainly concentrated in proteasome complex, U2-type precatalytic spliceosome, vesicle membrane, U4/U6 x U5 tri-snRNP complex and ciliary tip ($p<0.05$). Moreover, the results of the biological processes (BP) represented that cell division, DNA repair, cilium assembly, ubiquitin-dependent protein catabolic process, protein folding, protein polyubiquitination, proton transmembrane transport, chromosome segregation, DNA duplex unwinding, protein K48-linked ubiquitination, cellular respiration, regulation of macroautophagy, proton motive force-driven mitochondrial ATP synthesis, DNA-templated DNA replication, mitochondrial electron transport, NADH to ubiquinone and DNA unwinding involved in DNA replication were significant enrichment items (Figure 2A) ($p<0.05$).

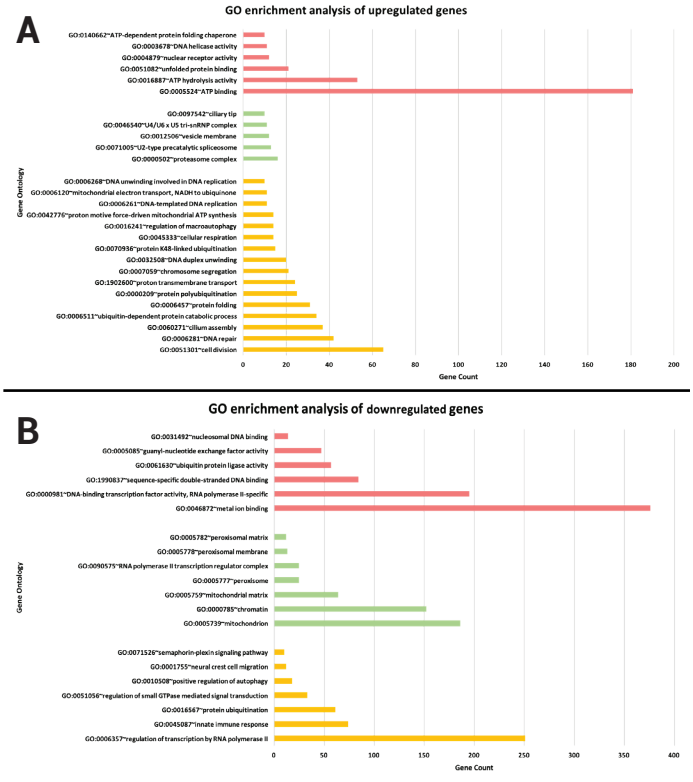

Figure 2. GO enrichment analysis of upregulated and downregulated genes; **A.** OlaR MDA-MB-468 cells compared to the control MDA-MB-468 cells upregulated DEGs; **B.** OlaR MDA-MB-468 cells compared to the control MDA-MB-468 cells downregulated DEGs; Pink: MF, Green: CC and orange: BP

Furthermore, the results of MF mediated by downregulated DEGs were mainly concentrated in ion binding, DNA-binding transcription factor activity, RNA polymerase II-specific, sequence-specific double-stranded DNA binding, ubiquitin protein ligase activity, guanyl, nucleotide exchange factor activity and nucleosomal DNA binding ($p<0.05$). The results of CC showed that mitochondrion, chromatin, mitochondrial matrix, peroxisome, RNA polymerase II transcription regulator complex, peroxisomal membrane, peroxisomal matrix were important enrichment items ($p<0.05$). Moreover, the results of BP were enriched in regulation of transcription by RNA polymerase II, innate immune response, protein ubiquitination, regulation of small GTPase mediated signal transduction, positive regulation of autophagy, neural crest cell migration and semaphorin-plexin signaling pathway (Figure 2B) ($p<0.05$).

KEGG pathway analysis represented that upregulated DEGs were correlated to pathways including metabolic pathways, pathways in cancer, chemical carcinogenesis - reactive oxygen species, cell cycle. Moreover, downregulated DEGs were involved in metabolic pathways, autophagy - animal, Efferocytosis and TNF signaling pathway. Both upregulated and downregulated DEGs were associated with metabolic pathways (Table 1).

Table 1. Results of KEGG pathway enrichment analysis of common genes by David ($p<0.05$)

Category	Term
Upregulated genes	
KEGG_PATHWAY	hsa01100: Metabolic pathways
KEGG_PATHWAY	hsa05200: Pathways in cancer
KEGG_PATHWAY	hsa05208: Chemical carcinogenesis - reactive oxygen species
KEGG_PATHWAY	hsa04110: Cell cycle
KEGG_PATHWAY	hsa00190: Oxidative phosphorylation
KEGG_PATHWAY	hsa04015: Rap1 signaling pathway
KEGG_PATHWAY	hsa04218: Cellular senescence
KEGG_PATHWAY	hsa04150: mTOR signaling pathway
KEGG_PATHWAY	hsa04120: Ubiquitin mediated proteolysis
KEGG_PATHWAY	hsa01232: Nucleotide metabolism
KEGG_PATHWAY	hsa03013: Nucleocytoplasmic transport
KEGG_PATHWAY	hsa00230: Purine metabolism
KEGG_PATHWAY	hsa04350: TGF-beta signaling pathway
KEGG_PATHWAY	hsa04721: Synaptic vesicle cycle
KEGG_PATHWAY	hsa05222: Small cell lung cancer
Downregulated genes	
Category	**Term**
KEGG_PATHWAY	hsa01100: Metabolic pathways
KEGG_PATHWAY	hsa04140: Autophagy - animal
KEGG_PATHWAY	hsa04148: Efferocytosis
KEGG_PATHWAY	hsa04668: TNF signaling pathway
KEGG_PATHWAY	hsa00230: Purine metabolism
KEGG_PATHWAY	hsa03083: Polycomb repressive complex
KEGG_PATHWAY	hsa04146: Peroxisome
KEGG_PATHWAY	hsa00310: Lysine degradation
KEGG_PATHWAY	hsa01230: Biosynthesis of amino acids
KEGG_PATHWAY	hsa04330: Notch signaling pathway

Construction of the PPI Network and Identification of Hub Genes

To analyze the interactions of DEGs and identify hub genes involved in olaparib therapy for breast cancer, we used the STRING database to create PPI networks. Further analysis was conducted using cytoHubba, plugins of the Cytoscape software. Ten hub genes were ranked based on the MCC score, which demonstrated the number of gene interactions in the PPI network. The hub genes with increased expression, NDUFA5, NDUFA6, NDUFS6, NDUFB3, NDUFB7, NDUFB10, NDUFA7 and NDUFA9 had the highest node degree in olaparib treated cells (Figure 3A). The hub genes with the lowest expression levels were: H2AC8, H2AC13, H2AC17, H4C11, H4C12, H2BC21 and H2BC4 (Figure 3B).

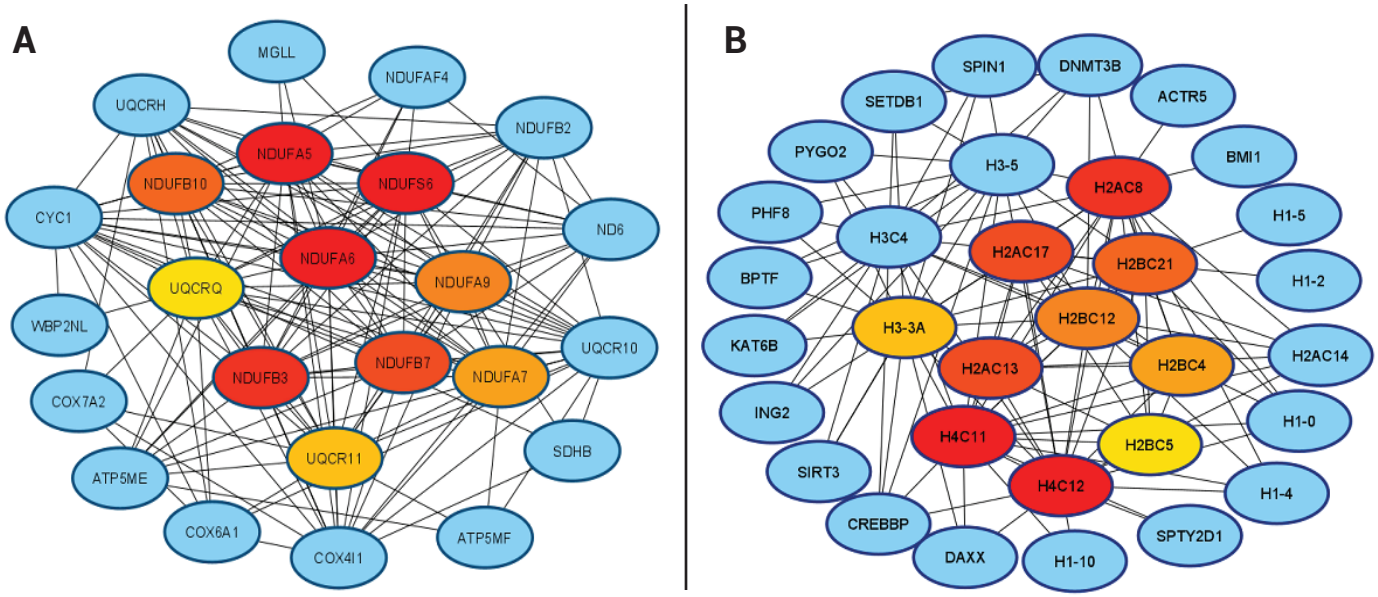

Figure 3. Top 10 hub genes screened by degree according to cytoHubba plug-in; **A.** upregulated genes OlaR MDA-MB-468 cells vs control MDA-MB-468 cells; **B.** downregulated genes OlaR MDA-MB-468 cells vs control MDA-MB-468 cells. The top 10 hub genes ranked by the MCC algorithm and their neighbors in the blue nodes. The red nodes represent genes with a high MCC score, while yellow nodes represent genes with a low MCC score

DISCUSSION

BC is a significant health concern, and scientists looked for novel biomarkers for predicting the disease's prognosis (15). Differential expression of many molecular biomarkers together with genetic, epigenetic, and phenotypic changes describe BC, a complicated disease (15,16). TNBC, a subtype of BC, is negative for PRs, ERs, and HER2 expressions. Due to its strong metastatic character, invasive nature, and high recurrence rate, it is the BC type with the worst prognosis (17,18). Treatment of TNBC is difficult by the lack of these biomarkers, and the disease has a poor survival rate and a high metastasis rate in comparison to other BC types (17). A variety of treatment approaches, such as immunotherapy, chemotherapy and targeted therapy have been used to treat TNBC (17). All these therapeutics have their own side effects.

Thus, it is essential to find out novel, trustworthy diagnostic biomarkers and develop distinctive BC immunotherapeutic targets.

In the current study, we investigated the significant pathways and genes which were upregulated and downregulated in olaparib-treated MDA-MB-468 cells compared to the control MDA-MB-468 cells. According to the KEGG pathway analysis, both upregulated and downregulated DEGs were associated with metabolic pathways. These results represented the importance of metabolic pathways underlying olaparib effect mechanisms.

Based on the bioinformatics analysis, there are upregulated (NDUFA5, NDUFA6, NDUFS6, NDUFB3, NDUFB10, NDUFB7, NDUFA7 and NDUFA9) and downregulated (H2AC8, H2AC13, H2AC17, H4C11, H4C12, H2BC12, H2BC21 and H2BC4) hub genes which showed higher node degree in PPI network.

NADH dehydrogenase 1 alpha subcomplex 5 (NDUFA5) contributes to the development of the electrochemical potential required to produce (19). In the study by Shimada and colleagues, NDUFA5 was significantly overexpressed in HPV-positive cervical cancer, therefore, they suggested the possible role of NDUFA5 in the multi-step carcinogenesis in human cervical cancer (20).

NDUFA6 and NDUFB3 genes which were found to be overexpressed in olaparib-treated cells. The NDUFA6 is a gene connected to mitochondrial translation process (21) and encoded a protein which is localized to the mitochondrial inner membrane (22). Zhao and colleagues reported NDUFA6 as a novel prognostic biomarker in multiple myeloma (MM) and suggested its association with the progression of MM (23). According to their study,

MM patients represented higher expression of NDUFA6 than healthy group, and the expression of NDUFA6 enhanced with the tumor stage (23). Upregulation of NDUFB3 (NADH:ubiquinone oxidoreductase subunit B3) protein lead to activation of NLRP3 inflammasome and cell pyroptosis in Nasopharyngeal Carcinoma (NPC) (24).

In contrast to the upregulated genes, H2AC8 is among the genes which was downregulated in olaparib-treated BC cells compared to the untreated cells.

There are not enough studies to explain the roles of the genes proposed in our study in many cancers, especially breast cancer. Therefore, the roles of these genes in breast cancer have not been clearly explained and needs further studies to determine these genes roles.

CONCLUSION

In conclusion, this study aimed to identify genes and pathways associated with olaparib therapy in TNBC. These genes were identified and could be considered as potential biomarkers for TNBC. Additional experimental and clinical researches are required to validate and confirm the biological roles and clinical relevance of these genes in TNBC prognosis and progression. One possible therapeutic approach for the treatment of TNBC is targetting the elevated genes or inducing the downregulated genes.

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Conflict of interest: *The authors have no conflicts of interest to declare.*

Ethical approval: *Not applicable. This paper does not involve human or animal subjects.*

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Research Article

Comparison of the Female Sexual Function Index, Beck Depression Inventory, and Patient Satisfaction Scale in Patients Undergoing Total Abdominal Hysterectomy and Single-Port Laparoscopic Hysterectomy for Benign Conditions

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Abstract

Aim: The uterus is widely accepted as a sexual organ, children-making body, secretory organ, youth, charm, or power supply by women. By hysterectomy, psychosocial problems such as fear of losing sexual identity occur, and depression may arise as a result of this. In this study, we investigated the effects of surgery on female sexual function and psychosocial situation according to the methods of Total Abdominal Hysterectomy (TAH) and Single Port Laparoscopic Hysterectomy (SPLH).
Material and Method: This prospective surgical study included 60 patients, including 30 SPLH and 30 TAH patients with benign reasons. The demographic data of patients, Female Sexual Function Inventory (FSFI) score, Beck Depression Inventory (BDI) score, and Patient Satisfaction Scale (PSS) score results were all assessed according to TAH and SPLH methods.
Results: In the FSFI questionnaire, significant differences were found between SPLH and TAH groups for all "desire frequency," "desire level," "stimulation frequency," "stimulation level," and "stimulation trust" subquestions (p=0.004, p=0.0001, p=0.003, p=0.011 and p=0.011, respectively). In the BDI, the TAH score (4.4±3.25) was significantly higher than the SPLH score (2.77±2.97) (p=0.047). TAH had 7.97±3.6 points, and SPLH had 3.73±1.1 points regarding treatment results (p=0.00017). Similarly, TAH had 14±4.4 points, while SPLH had 6.1±1.3 points regarding the functionality of hysterectomy (p<0.0001).
Conclusion: FSFI's results for SPLH were more effective than TAH's, as it was a more effective method for all the treatment processes, functionality, and treatment scores. SPLH instead of TAH will be powerfully influential in eliminating the postoperative negative impacts of hysterectomy.

Keywords: Female Sexual Function Index, Beck Depression Inventory, Patient Satisfaction Scale, Total Abdominal Hysterectomy, Single-Port Laparoscopic Hysterectomy

INTRODUCTION

Hysterectomy is the most commonly performed major surgical procedure by gynecologists (1). It is used to address various indications such as dysfunctional uterine bleeding, uterine fibroids, endometriosis, adenomyosis, pelvic inflammatory disease, pelvic pain, gynecological cancers, and obstetric complications (2). The removal of the uterus not only affects an individual's body image and psychosocial status but also jeopardizes their reproductive capacities and sexual functions (3). Cultural beliefs regarding the importance of genital organs and the meanings attributed to the uterus influence women's perceptions of the implications of its removal (4).

Patients undergoing removal of any organ experience fears and anxieties related to pain, death, disability, and changes in body image (5). Specifically, women facing hysterectomy have additional concerns regarding loss of sexual function, fertility, and their role as women (6). The removal of the uterus often leads to physical symptoms as well as psychological distress, including feelings of weakness, loss of

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sexual identity, and fears about their partners' fidelity, resulting in depression (7). Neurological implications are also significant, as autonomic nerve fibers originating from the pelvic region play crucial roles in stimulating sexual functions and facilitating orgasm through uterine contractions (8). Over the past decade, there has been a shift in surgical techniques towards minimally invasive procedures, which have become the standard treatment for various benign and malignant gynecological conditions (9,10). Gynecological laparoscopic surgery has seen a growing preference for single-port laparoscopic surgery (SPLH), which has shown promising results (11). However, there is limited information in the literature regarding the impact of SPLH on postoperative female sexual function (4,7,10). Given the uterus's perceived role as an organ of sexuality, fertility, and strength by women, the fear of losing one's sexual identity after a hysterectomy can lead to psychosocial issues, including depression.

This study aims to explore the effects of Total Abdominal Hysterectomy (TAH) and SPLH on female sexual function and psychosocial status. The Female Sexual Function Index (FSFI), Beck Depression Inventory (BDI), and Patient Satisfaction Scale (PSS) will be used to provide a comprehensive overview of these surgical impacts.

MATERIAL AND METHOD

Study Design and Ethical Approval

This prospective, randomized study was conducted at the Kocaeli Derince Education and Research Hospital, Department of Obstetrics and Gynecology. The research focused on women aged 35 to 70 years, diagnosed with benign gynecological conditions, who underwent elective hysterectomy procedures, either TAH or SPLH. A total of 60 patients (30 undergoing TAH and 30 undergoing SPLH) were included in the study.

Data Collection & Assessment Instruments

Patient data were meticulously collected and anonymized, including demographic information, preoperative and postoperative clinical records, anesthesia logs, and surgical notes. A questionnaire developed based on existing literature was used to assess sociodemographic characteristics, obstetric history, and potential risk factors for sexual dysfunction. FSFI: A 19-item Likert scale to assess sexual dysfunction among women. BDI: This 21-item scale measures the severity of depression. The scale has demonstrated high reliability and validity. PSS: Employed to assess patient satisfaction during and after treatment, consisting of questions ranging from symptom management to satisfaction with the treatment outcomes.

Statistical Analysis

Data were analyzed using the IBM-SPSS-16.0 software. The initial step in the analysis involved examining the normality of the distribution for each variable using the Shapiro-Wilk test. For two independent groups, the following methods were employed depending on the data distribution: An independent samples t-test was used to compare the means of the two groups for normally distributed numerical data. The Mann-Whitney U test was utilized for non-normally distributed numerical data. This non-parametric test compares two independent groups when the data does not follow a normal distribution. The Chi-square was applied to evaluate the differences in categorical variables. At the same time, Fisher's exact test was used when the expected frequencies were too low for reliable Chi-square computation. It provides a precise p-value calculation without requiring large sample sizes. To ensure robustness in the findings, a multiple regression analysis was also performed to adjust for potential confounding variables and to assess the independent effects of various predictors on the outcomes of interest. All tests were two-tailed, and the results were considered significant at a p-value less than 0.05.

RESULTS

Demographic Data

The average age was comparable between the two groups (TAH: 46.9±6.1; SPLH: 47.7±4.8; p=0.41). Most patients had a primary or secondary education level (TAH 29/30; SPLH 24/30), with no significant difference in education levels between groups. All operated patients were married, and most were housewives (29/30). None of the patients consumed alcohol, and a small proportion smoked (TAH: 6/30; SPLH: 7/30). There was a difference in height between groups (p=0.001) but no difference in BMI and weight (p=0.859 and p=0.071, respectively). There were no differences in the number of births, pregnancies, or miscarriages between the groups. Among all patients, 34 (56.7%) had no miscarriages, 22 (36.7%) had one, and 4 (6.6%) had two or more miscarriages. Thus, the demographic characteristics of both groups were similar.

Sexual Function

Analysis of FSFI responses revealed differences between the TAH and SPLH in questions 1 (Desire frequency), 2 (Desire level), 3 (Arousal frequency), 4 (Arousal level), and 5 (Arousal confidence) with p-values of 0.004, 0.0001, 0.003, 0.011, and 0.011, respectively (Table 1). Despite significant differences in the first five questions of the FSFI, there were no significant differences in the subcategories of desire, arousal, lubrication, orgasm, satisfaction, and pain (Table 2).

Table 1. Comparison of groups based on the Female Sexual Function Index

Test questions	TAH (SD)	SPLH (SD)	p-value
1. Desire: frequency	2.80 (1.25)	1.97 (0.84)	0.004
2. Desire: level	3.67 (1.11)	2.00 (0.82)	0.0001
3. Arousal: frequency	3.67 (1.11)	2.87 (0.81)	0.0003
4. Arousal: level	3.50 (1.18)	2.83 (0.69)	0.011
5. Arousal: confidence	3.33 (1.22)	2.57 (0.99)	0.011
6. Arousal: satisfaction	3.07 (1.31)	2.80 (0.87)	0.366
7. Lubrication: frequency	3.03 (1.25)	2.87 (0.72)	0.536
8. Lubrication: difficulty	3.37 (1.22)	3.40 (0.71)	0.9
9. Lubrication: maintenance frequency	3.07 (1.31)	2.67 (0.79)	0.165
10. Lubrication: difficulty	3.30 (1.13)	3.20 (0.91)	0.712
11. Orgasm: frequency	2.97 (1.38)	2.80 (0.79)	0.574
12. Orgasm: difficulty	3.33 (1.32)	3.30 (0.82)	0.909
13. Orgasm: satisfaction	2.80 (1.25)	2.63 (0.84)	0.553
14. Satisfaction: intimacy level with partner	2.20 (1.17)	2.63 (0.84)	0.109
15. Satisfaction: sexual intercourse	2.50 (1.18)	2.57 (0.76)	0.799
16. Satisfaction: overall sexual life	2.80 (1.25)	2.53 (0.76)	0.331
17. Pain: frequency during vaginal penetration	3.67 (1.11)	3.40 (0.99)	0.336
18. Pain: frequency after vaginal penetration	3.67 (1.11)	3.60 (0.92)	0.803
19. Pain: level during or after vaginal penetration	3.50 (1.18)	3.60 (0.80)	0.706

TAH: Total abdominal hysterectomy, SPLH: Supracervical laparoscopic hysterectomy, SD: Standard deviation

Table 2. Analysis of patients' FSHI test results by categorical score

Category	TAH±SD	SPLH±SD	p-value
Desire	5.27±2.71	3.97±1.6	0.009
Arousal	1.27±4.75	11.07±3.0	0.021
Lubrication	1.27±1.96	12.13±1.4	0.012
Orgasm	0.91±1.58	8.73±0.9	0.026
Satisfaction	0.75±3.37	7.73±2.3	0.092
Pain	1.08±3.31	1.06±2.6	0.051
TOTAL	**58.07±3.19**	**5.42±2.4**	**0.084**

TAH: Total abdominal hysterectomy, SPLH: Supracervical laparoscopic hysterectomy, SD: Standard deviation, FSHI: Female Sexual Health Inventory

Depression and Satisfaction

FSHI total scores were higher in the TAH (58.1±10.4) compared to the SPLH (54.23±6.45), but this difference was not significant (p=0.084). The average FSFI score was higher in the TAH group (9.6) compared to the SPLH (9.01), but again, this difference was not significant (p=0.084). However, the BDI score was higher in the TAH (4.4±3.25) compared to the SPLH (2.77±2.97) (p=0.047), indicating a higher tendency towards depression in the TAH. According to the BDI, the majority of patients in both groups had no depression, with only one patient in each group scoring ten or above (Table 3).

Table 3. FSHI, BDI, and Treatment Process Assessment Survey scores

Category	TAH±SD	SPLH±SD	p-value
FSHI Sexual Dysfunction Survey	5.81±1.04	54.23±6.45	0.084
BDI	4.4±3.25	2.77±2.97	0.047
Treatment Process and Post-Treatment Assessment	3.52±1.19	16.77±3.57	0.000001

TAH: Total abdominal hysterectomy, SPLH: Supracervical laparoscopic hysterectomy, SD: Standard deviation, FSHI: Female Sexual Health Inventory, BDI: Beck Depression Inventory

Patient Satisfaction

Significant differences were observed in responses to treatment-related questions between the TAH and SPLH groups. TAH responses to "Did the same doctor continue treatment?" (23.3%+16.7% vs. 56.7%+40%; p=0.0004), "Was the doctor knowledgeable about my condition?" (36.7%+16.7% vs. 60%+40%; p=0.001), "Did I have the opportunity to talk to my doctor about my condition?" (33.3%+16.7% vs. 76.7%+23.3%; p=0.002), "Did my doctor listen and understand me?" (p=0.004), and "Did I receive regular information about my treatment and progress?" (p=0.00003) were significantly lower compared to the SPLH.

Postoperative Pain and Aesthetics

Postoperative pain and aesthetic assessments showed

differences between the TAH and SPLH groups. The SPLH group reported higher satisfaction regarding sexual life post-surgery (p=0.002), frequency of pain during intercourse (p=0.0001), and absence of pain at the surgical site (p=0.00004). Additionally, the SPLH group reported higher aesthetic satisfaction with the surgical site (p=0.00001). The Patient Satisfaction Survey results showed that the average scores for treatment process, functionality, and treatment outcomes were significantly lower in the SPLH group than in the TAH group, indicating higher satisfaction in the SPLH. The overall satisfaction score was lower in the SPLH (16.77±3.57) compared to the TAH group (35.2±11.9) (p=0.00001), demonstrating that the SPLH method provided better patient satisfaction.

Correlation Analysis

Pearson correlation showed a positive correlation between patient satisfaction scores and both FSFI (r=0.452, p=0.0001) and BDI (r=0.265, p=0.041) scores, indicating a solid association with FSFI. A stronger positive correlation was found between BDI and FSFI (r=0.619, p=0.00001). A weak positive correlation was found between FSFI and age (Table 4). No correlation was found between BMI and any scale. These results suggest that patient satisfaction is closely associated with sexual function and depression scores. The results of this study indicate that SPLH is associated with higher patient satisfaction, lower depression scores, and better postoperative pain and aesthetic outcomes compared to TAH.

Table 4. Pearson correlation analysis for HMS, FSHI, BDI, age, and BMI

Tests	HMS	FSHI	BDI	Age	BMI
HMS	1	0.452**	0.265*	0.039	-0.089
		0.00001	0.041	0.769	0.5
FSHI	0.452**	1	0.619**	0.264*	-0.083
	0.00001		0.000001	0.041	0.52
BDI	0.265*	0.619**	1	0.239	0.219
	0.041	0.00001		0.066	0.09

HMS: Hysterectomy-related menopausal symptoms, FSHI: Female Sexual Health Inventory, BDI: Beck Depression Inventory, BMI: body mass index

DISCUSSION

The impact of hysterectomy on sexual functionality is a matter of paramount concern. Our study reveals that women undergoing TAH experience a more protracted recovery period and a heightened risk of developing abdominal adhesions, which can detrimentally affect sexual function. Comparing the sexual functionality and predisposition to depression in patients undergoing TAH and SPLH were essential issues, as our findings underscore the significant role played by choice of surgical technique in influencing these outcomes.

Hysterectomy is a commonly performed surgical procedure primarily intended for nonmalignant conditions, but it carries considerable physical and psychosocial consequences for women (12). The findings are congruous with the results reported by Weber et al., which indicate a greater incidence of sexual dysfunction following TAH (13). Conversely, patients undergoing SPLH report less pain during intercourse and better overall sexual health. These findings lend support to the notion that the minimally invasive nature of SPLH helps to preserve sexual function (14). This is consistent with the findings of Rhodes et al., who observed that less invasive procedures tend to lead to fewer sexual complications (1).

The psychological aspect of sexual health after hysterectomy is also worthy of note (15). Women frequently associate their uterus with their femininity and sexual identity, and this can have a significant impact on their postoperative sexual satisfaction (16). The findings of our study indicate that the superior sexual outcomes experienced by SPLH may be attributed to the less invasive nature of the procedure, which leads to less disruption to their psychological and sexual well-being (11). Depression is a commonly observed issue following a hysterectomy, as it is influenced by the physical and mental stress associated with the procedure (17). Utilizing the BDI, our study reveals that TAH patients exhibit higher depression scores compared to SPLH, indicating a greater predisposition to depression (18). This finding concurs with the research conducted by Goktas et al., which reported an increase in depression after hysterectomy (7). The less invasive SPLH procedure is likely to contribute to lower depression rates due to its swifter recovery and reduced physical trauma, thereby enhancing overall psychological well-being.

Demographic factors such as educational level, employment status, and marital status exert an influence on the assessment of sexual function and psychological health after surgery (10). Most participants in our study were married housewives with primary or middle school education, which aligns with the findings of previous studies (19, 20). This demographic homogeneity highlights the importance of providing tailored educational and psychological support to these women, addressing their unique needs and concerns. Patient satisfaction is a critical indicator of surgical success in an academic context (13). Our study discovered that patients who underwent SPLH reported higher satisfaction levels. This can be attributed to several factors, including

reduced hospital stays, decreased intraoperative blood loss, diminished postoperative pain, and faster recovery times associated with SPLH (21). These benefits of SPLH align with the findings of Ayoubi et al., indicating a growing preference for minimally invasive techniques in gynecological surgeries (22). Given the higher satisfaction rates among SPLH, it suggests that this technique better aligns with patient expectations and needs, ultimately resulting in improved overall outcomes.

Despite this study's strengths, such as utilizing validated assessment tools and carefully considering demographic factors, some limitations need acknowledgment. The absence of preoperative FSFI scores limits a comprehensive evaluation of the impact on sexual function, as pre-existing conditions are not taken into account. Additionally, the sample size and the need for a control group restrict the generalizability of the findings. Future research should include more extensive and diverse populations while incorporating preoperative assessments to understand the effects of different hysterectomy techniques better.

CONCLUSION

Hysterectomy significantly impacts the sexual and psychological well-being of women, with the chosen surgical technique playing a critical role in determining these outcomes. Our study suggests that SPLH is associated with more remarkable preservation of sexual function and a lower risk of depression compared to TAH. These findings support the increased utilization of SPLH in clinical practice to enhance postoperative outcomes and patient satisfaction. Given the multifaceted nature of sexual health and psychological well-being, further research is necessary to delve deeper into these relationships and develop comprehensive strategies for undergoing hysterectomy. Through such research, healthcare providers can better support their patients during surgical and postoperative recovery, ensuring physical and psychological needs are adequately addressed.

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Research Article

Oxidative Stress and Anti-Carbonic Anhydrase Antibody Levels in Early Preeclampsia: A Clinical Investigation

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Abstract

Aim: Preeclampsia (PE) is a dangerous condition that affects 3–5% of pregnancies and has a substantial risk of death and morbidity for both mothers and newborns. The processes behind the etiology of PE are not entirely known, despite the fact that it is the primary cause of illness and death among mothers globally. In order to further understand the correlations between these parameters, this study will look at the levels and presence of anti-carbonicanhydrase (CA) I and II antibodies, total oxidant capacity (TOC), total antioxidant capacity (T-AOC), and malondialdehyde (MDA) in early PE.
Material and Method: The research analyzed 30 pregnant women with early PE and 30 normal pregnant women as the control group. Serum levels of anti-CAI (pg/mL), anti-CAII (ng/mL), MDA (nmol/mL), TOS (U/mL), T-AOC (U/mL) were measured and compared between the two groups.
Results: Significant variations were noted in the amount of anti-CA I, anti-CA II, MDA, TOS, and T-AOC (both $p<0.05$) between the control group and the early PE group. More specifically, oxidative stress indicators were changed and increased levels of anti-CA I and anti-CA II were seen in the early PE group in comparison with the control group.
Conclusion: The findings show that elevated amounts of anti-CAI and anti-CAII antibodies may serve as predictive markers for early PE. The significant differences in oxidative stress parameters further support the oxidative stress involvement in the pathogenesis of early PE. However, more extensive Research is required to validate these results and clarify the mechanisms underlying PE.

Keywords: Antioxidants, carbonic anhydrase, malondialdehyde, oxidants, oxidative stress, preeclampsia

INTRODUCTION

Preeclampsia (PE) is a hypertensive condition that affects 3-5% of women during the second half of pregnancy, posing significant risks to fetal, perinatal, and maternal health, especially in nations with poor and moderate incomes (1). Clinically, PE is categorized based on its onset: early PE, which happens before the thirty-fourth week of pregnancy, and late PE, which happens after the thirty-fourth week (2). Early PE, although less common, is a more severe form associated with abnormal placentation and intrauterine growth restriction (3). It affects approximately 0.5% of all pregnancies, accounting for 10% of all PE cases, and is linked to higher maternal and neonatal morbidity and mortality compared to late-onset PE.

Understanding the etiology of early PE is crucial due to its severity. The primary source of stress in early PE is uteroplacental malperfusion, which is secondary to abnormal remodeling of the uterine spiral arteries (4). Studies have shown that oxidative stress is more pronounced in early PE in comparison with late PE. The pathogenesis of PE is thought to originate in the utero-placental unit and is exacerbated by oxidative stress until it impacts the maternal endothelium (5). Free oxygen radicals and peroxides build up as a result of an imbalance between the body's natural antioxidant defense mechanisms and the oxidative chemicals that are produced. This imbalance is known as oxidative stress.

Oxidative stress evidences have been observed in both the placenta and the maternal circulation in cases of PE (6). It has been discovered that placentas from women with PE have lower antioxidant capacities than placentas from pregnancies that are typical. Additionally, blood tests on

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females with PE have shown increased levels of oxidative alterations of proteins and lipoprotein particles and decreased levels of antioxidants (7).

The carbonic anhydrase (CA) enzyme, which plays a versatile role in metabolism, has been identified as a potential contributor to the pathogenesis of adverse prenatal outcomes. The CA enzyme (EC 4.2.1.1) is a zinc-containing metallo enzyme. Antibodies against CA-I and CA-II enzymes have been proved to inhibit CA catalytic activity and disrupt placental and endometrial functions, potentially contributing to PE (8,9). Despite the importance of CA in metabolic processes, there are few studies investigating its role in the etiopathogenesis of hypertensive diseases in pregnancy.

In this study, we measured oxidative stress markers and levels of anti-CAI and anti-CAII antibodies in pregnant females with early PE to explore potential correlations. The focus is to find out if anti-CA I and II antibodies are present in PE and to examine the connections between these autoantibodies and parameters measuring MDA, TOC and T-AOC. This study aims to provide insight into the role of CA and oxidative stress in the pathogenesis of early PE, potentially contributing to better understanding and management of the condition.

MATERIAL AND METHOD

Ethical Approval

The Inonu University Faculty of Medicine Clinical Research Ethics Committee granted the project approval (Approval No. 2021/113). The research adhered to the World Medical Association Declaration of Helsinki (including the amendments made in 2013) and followed Good Clinical Practices (GCP) guidelines throughout the study.

Study Population

All pregnant women who attended the Prenatal Diagnosis and Treatment Unit of the Department of Gynecology and Obstetrics at Inonu University Faculty of Medicine Hospital between May 1, 2021, and May 1, 2022, and were diagnosed with early preeclampsia were included in the research. The research group was made up of 30 individuals having early preeclampsia, while 30 normotensive pregnant females, matched for age, gestational week, and body mass index (BMI), set up the control group. Gestationaliage was confirmed by first-trimester ultrasonography measurements.

Exclusion and Inclusion Criteria

Inclusion criteria for the research were as follows:

- Pregnant females aged 18-45,
- Singleton, live pregnancies,
- Diagnosed with early-onset PE,
- BMI; 35kg/m^2,
- Normal medical and obstetric history.

Exclusion criteria were as follows:

- Multiple pregnancies,
- Gestational diabetes,
- Preterm premature rupture of membranes,
- Presence of maternal systemic diseases (dyslipidemia, asthma, malignancy, chronic renal failure, chronic hypertension, pulmonary or cardiac diseases),
- Abnormali karyotype or fetal malformations,
- Alcohol and tobacco use.

Diagnosis of Preeclampsia

PE was diagnosed following the criteria established by the American College of Obstetricians and Gynecologists (ACOG). PE was defined as high blood pressure (140/90 mmHg) beginning after the 20th week of pregnancy in a previously normotensive female who also had proteinuria and/or end-organ dysfunction (ACOG Practice Bulletin, Number 222).

Blood Sample Collection and Processing

Following an overnight fast, participants; blood samples were drawn in the morning and placed into gel separator (serum) tubes. After 30 minutes of clotting at room temperature, the samples were centrifuged for 10 minutes at 1200 g. The serum was then separated and transferred to micro-volume eppendorf tubes and kept at -80°C until biochemical analysis.

Biochemical Analysis

ELISA for serum anti-CA I and II antibodies: Serum levels of anti-CA I and anti-CA II antibodies were determined using commercial enzyme-linked immunosorbent assay (ELISA) kits (Bioassay Technology Laboratory, Cat. No: E1371Hu, China). Total Antioxidant Capacity (T-AOC): T-AOC levels in serum samples were measured using a commercial ELISA kit (Sunredbio, Cat. No: 201-12-2200, China). Total Oxidant Capacity (TOC): TOC levels were measured using a commercial ELISA kit (Sunredbio, Cat. No: 201-12-5539, China). Malondialdehyde (MDA): MDA values were measured using a commercial ELISA kit (Bioassay Technology Laboratory, Cat. No: E1371Hu, China).

Sample Size Calculation

A power analysis was conducted to ascertain the necessary sample size for the research. The investigation was predicated on the finding that pregnant women with early PE had a statistically significant drop in the anti-carbonic anhydrase II ratio of 1.0 pg/mL with a 1.7 standard deviation. The calculation indicated that to achieve 80% statistical power at a 5% significance level (two-tailed), a minimum of 30 participants per group was required.

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) software, version 22.0 (SPSS Inc., New York, USA), was used to conduct statistical analyses. Means, standard deviations, minimum and maximum values were used to describe continuous variables, while medians with interquartile ranges were used to show baseline characteristics of the study and control groups. The distribution of the data was examined for normalcy using

the Shapiro-Wilk test. Two-sample t-tests were used to examine differences between the study and control groups for normally distributed data. The Mann-Whitney U test was applied to data that were not regularly distributed. Frequencies and percentages were used to summarize the categorical variables, and Pearson exact chi-square test and continuity-corrected chi-square test were used to make comparisons. A p-value of less than 0.05 on both sides was deemed statistically significant.

RESULTS

Demographic and Clinical Characteristics

The demographic and clinical characteristics of the participants are summarized in Tables 1 and 2. There were no statistically significant differences between the control and study groups regarding parity, gravidity, BMI, maternal age, ethnicity, and smoking habits (Table 1).

Obstetric History and Placenta-Mediated Disease

A statistically significant difference was observed among the study and control groups with regard to early PE and the presence of placenta-mediated diseases in the obstetric history ($p<0.05$). Additionally, a significant difference was observed in the need for neonatal intensive care unit (NICU) admission between the groups ($p<0.05$) (Table 1).

Maternal and Fetal Characteristics

Table 2 presents maternal and fetal characteristics. No significant differences were found between groups concerning gestational age, number of pregnancies, parity, weight, height, BMI, 24-hour urine protein, platelet count (PLT), alanine amino transferase (ALT), cord blood pH value, and cord blood base excess ($p>0.05$).

Table 1. Demographicand clinical characteristics

Variable	Group	n/%	Groups		Total	p value
			Study	Control		
Early PE	(-)	n	26	30	56	0.016*
		%	86.7	100.0	93.3	0.016*
	(+)	n	4	0	4	0.016*
		%	13.3	0.0	6.7	0.016*
The presence of placenta-mediated diseases in the obstetric history	(-)	n	12	17	29	0.005*
		%	40.0	56.7	48.3	0.005*
	IUGR	n	15	6	21	0.005*
		%	50.0	20.0	35.0	0.005*
	PE	n	0	1	1	0.005*
		%	0.0	3.3	1.7	0.005*
	OLIGO	n	0	4	4	0.005*
		%	0.0	13.3	6.7	0.005*
	PPROM	n	0	2	2	0.005*
		%	0.0	6.7	3.3	0.005*
	LGA	n	2	0	2	0.005*
		%	6.7	0.0	3.3	0.005*
	IUEF	n	1	0	1	0.005*
		%	3.3	0.0	1.7	0.005*
Gender	Female	n	11	13	24	0.598*
		%	36.7	43.3	40.0	0.598*
	Male	n	19	17	36	0.598*
		%	63.3	56.7	60.0	0.598*
Need for neonatal intensive care unit (NICU)	(-)	n	4	20	24	0.001*
		%	13.3	66.7	40.0	0.001*
	(+)	n	26	10	36	0.001*
		%	86.7	33.3	60.0	0.001*
Total		n	**30**	**30**	**60**	
		%	**100.0**	**100.0**	**100.0**	

n: number of samples, %: percent, test value: chi-square test value ($\chi 2$), p value: statistical significance, *p<0.05: There is a statistically significant difference between the groups

Table 2. Maternal and fetal characteristics

Variable	Study		Control		Sig. (p)
	Mean±SD	M (Min-Max)	Mean±SD	M (Min-Max)	
Number of pregnancies	32±2.96	31.5 (28-37)	32.57±4.08	32 (24-40)	0.721[a]
Age	31.83±5.98	31 (20-42)	29.33±5.8	29.5 (18-41)	0.125a
G	2.7±1.34	2.5 (1-6)	2.73±1.57	3 (1-6)	0.964[a]
P	1.13±1.2	1 (0-4)	1.2±1.19	1 (0-4)	0.799[a]
A	0.57±0.86	0 (0-4)	0.53±0.94	0 (0-4)	0.607[a]
Weight	77.03±16.41	77 (52-110)	69.45±15.62	73.25 (8-90)	0.216[a]
Height	161.8±5.71	162 (150-175)	160.4±5.86	160 (145-170)	0.238[a]
BMI	29.37±5.83	29.73 (20.83-42.97)	27.02±6.1	26.98 (3.13-35.16)	0.304[a]
PE diagnosis pregnancy week	32±2.96	31.5 (28-37)	0±0	0 (0-0)	
Systolic blood pressure	157±23.84	159.5 (109-207)	110.97±11.55	107.5 (90-135)	**<0.001*[a]**
Diastolic blood pressure	99.03±13.29	100 (70-130)	72.93±8.59	72.5 (60-89)	**<0.001*[a]**
24 H MTP	3371.31±5009.35	1170 (150-21986.25)	210.7±62.6	215 (70-310)	**<0.001*[a]**
PLT	219.37±78.65	222 (83-383)	232.33±77.23	221.5 (95-364)	0.549[a]
AST	46.07±55.18	22 (9-240)	19.57±5.96	18 (13-35)	**0.038*[a]**
ALT	36.53±48.93	15.5 (6-236)	14.67±5.86	13 (3-34)	0.177[a]
BUN	12.06±6.29	10.64 (3-29.91)	7.43±2.58	7.01 (3.74-14.95)	**0.001*[a]**
CRE	0.7±0.16	0.68 (0.44-1.19)	0.6±0.13	0.6 (0.4-1.1)	**0.002*[a]**
LDH	350.6±168.15	293 (163-886)	210.81±75.23	202.5 (7.4-403)	**<0.001*[a]**
Uric acid	5.82±1.4	5.71 (3.1-8.6)	4.41±1.12	4.2 (2.7-7.8)	**<0.001*[a]**
Birth weight	1818.17±603.27	1780 (500-3240)	2755.9±640.35	2851 (850-3700)	**<0.001*[a]**
Cord blood PH	7.27±0.12	7.3 (6.9-7.38)	7.31±0.1	7.33 (7.1-7.56)	0.222[a]
Cord blood LB	-5.93±5.24	-6.15 (-22.4-2.6)	-4.91±2.8	-4.4 (-13.6--1)	0.460[a]
Birth type	Cesarean (n/%)		Vaginal (n/%)		0.236[b]
	30 (100.0)	0(0.0)	27 (90.0)	3 (10.0)	

Cover: mean, sd: standard deviation, min: the smallest value taken is max: the highest value taken, a: Mann Whitney Test Value p value, n: number of samples, %: percent, a: chi-square test($\chi 2$) p value, *p<0.05; There is a statistically significant difference between the groups.

Blood Pressure and Biochemical Parameters

Significant differences were detected between the groups regarding systolic and diastolic blood pressure, as well as levels of aspartate amino transferase (AST), blood urea nitrogen (BUN), lactate dehydrogenase (LDH), creatinine (CRE), uric acid, and birth weight (p<0.05) (Table 2).

OxidativeStress Markers and Anti-CA Antibodies

The oxidative stress markers and values of anti-carbonic anhydrase (CA) antibodies were significantly different between the groups. anti-CA I (pg/mL) (Figure 1) and anti-CA II (ng/mL) antibodies (Figure 2), MDA (nmol/mL) (Figure 3), TOC (U/mL) (Figure 4), and T-AOC (U/mL) (Figure 5) were significantly greater in the study group in comparison with the controlgroup (Both p<0.05) (Table 3).

Table 3. Oxidative stress markers and anti-CA antibodies

Valuable	Study		Control		Mann Whitney Sig. (p)
	Mean ±SD	M (Min-Max)	Mean±SD	M (Min-Max)	
Anti-CAI (pg/mL)	23797.1±7503.95	22889.82 (14903.33-40890.61)	11977.99±2998.27	11108.87 (8440.97-18696.39)	<0.001*
Anti-CAII (ng/mL)	24.47±9.2	26.7 (12.05-37.81)	20.06±7.93	19.49 (9.46-35.91)	0.037*
MDA (nmol/mL)	64.64±9.9	65.09 (42.75-94.61)	20.83±8.13	19.2 (10.55-45.62)	<0.001*
TOC (U/mL)	287.46±62.3	289.44 (146.25-373.4)	50.41±14.02	48.47 (25.02-91.94)	<0.001*
T-AOC (U/mL)	14.67±3.98	13.8 (8.72-25.46)	50.48±9.08	49.77 (36.18-77)	<0.001*

Cover: mean, sd: standard deviation, *p<0.05: There is a statisticallysignificant differenc between the groups

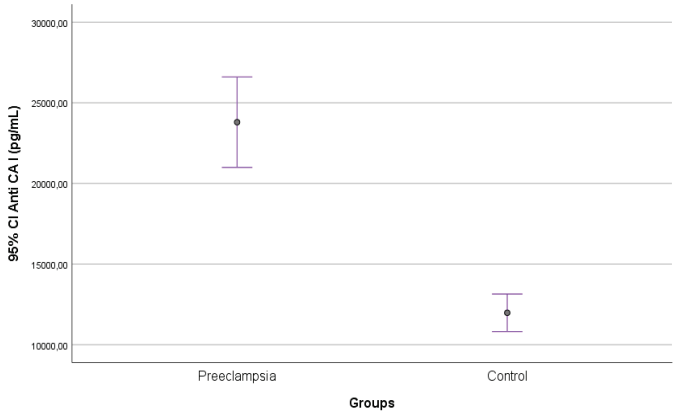

Figure 2. Boxplot in groups for Anti CA I (pg/mL)

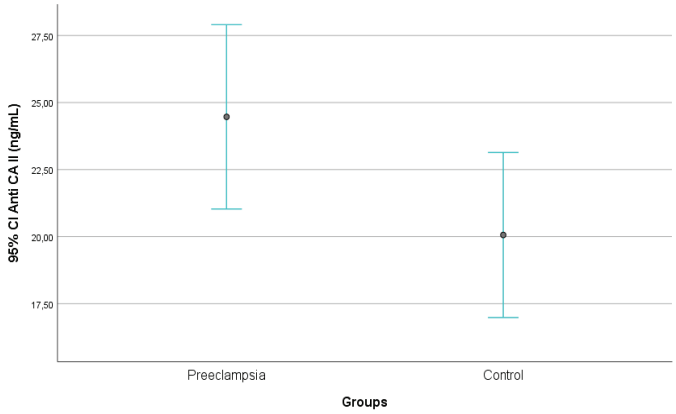

Figure 3. Boxplot in groups for Anti CA II (ng/mL)

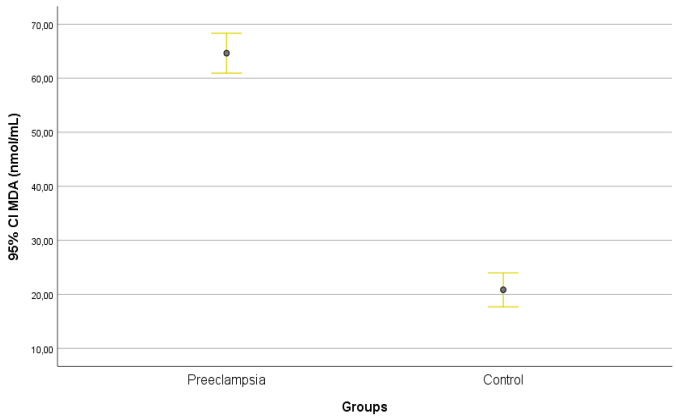

Figure 4. Boxplot in groups for MDA (nmol/mL)

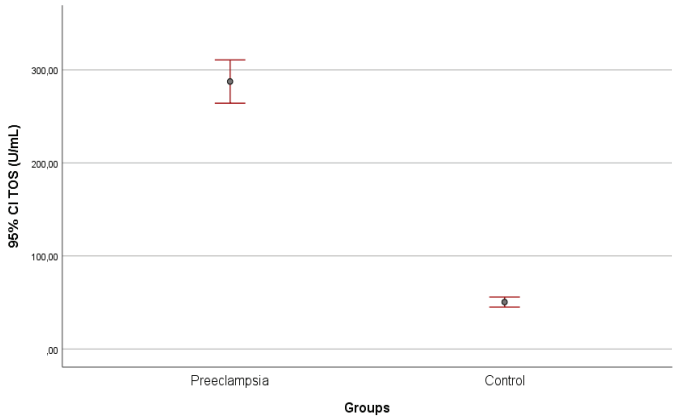

Figure 5. Boxplot in groups for TOC (U/mL)

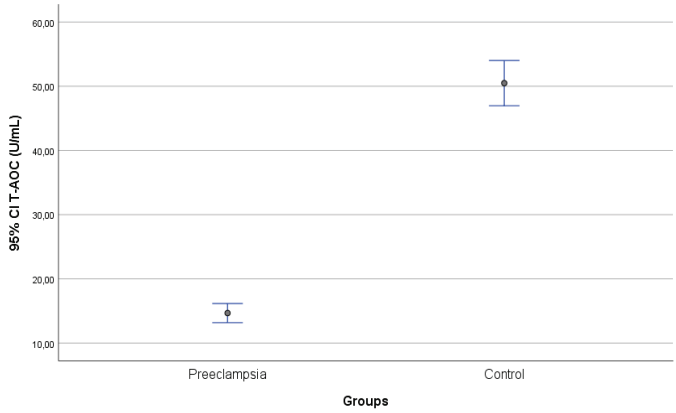

Figure 6. Boxplot (U/mL) in groups for T-AOC

DISCUSSION

In this research, we investigated the existence of CA I and II antibodies in early PE and examined the relation between these auto antibodies and various oxidative stress parameters, including T-AOC, TOC and MDA. Our results demonstrated significant differences between pregnant females with early PE and healthy pregnant females across all measured values. These findings are crucial as they provide a comprehensive evaluation of the antioxidant system and oxidative stress, which are integral to understanding the pathogenesis of early PE.

Our study revealed significantly higher levels of anti-CA I and anti-CA II auto antibodies in pregnant women with early PE in comparison with the control group. This result shows that the autoimmune response against CA I and CA II enzymes may have a part in the pathogenesis of early PE. The presence of CA autoantibodies is known to be linked with auto immune diseases, but there are limited studies focusing on their presence in early PE patients (10). The relationship between early PE and oxidative stress has been well-documented, with several studies indicating that uteroplacental hypoxia/reoxygenation during PE elevation maternal and fetal oxidative stress. Free radicals stemming from an inadequately perfused fetoplacental unit trigger oxidative stress in placental cells, further exacerbating the condition (11).

MDA, a product of lipid peroxidation, acts as a marker for oxidative stress. Our study found elevated MDA levels in the early PE group, indicating on going excessive lipid peroxidation, a marker of oxidative stres (12). This finding is consistent with previous research that have reported higher plasma MDA levels in women with PE compared to normal pregnancies. Lipid peroxidation, driven by free radicals attacking poly unsaturated fatty acids in cell membranes, leads to increased membrane fluidity and permeability (13). This process is toxic and damages endothelial cells, increasing peripheral vasoconstriction, promoting thromboxane synthesis, and decreasing prostacyclin synthesis, all of which are critical for the pathogenesis of PE (14).

Our research also revealed lower T-AOC and higher TOC

levels in pregnant women with early PE compared to normal pregnant women. This imbalance indicates that oxidative stress has a significant part in PE pathogenesis. Previous studies have reported similar findings, suggesting that decreased antioxidant capacity and increased oxidant levels contribute to the development of PE. The relationship between serum T-AOC and PE has been extensively investigated, with studies suggesting that decreased T-AOC is linked with a higher rate of maternal complications and PE (15). The imbalance between free radical production and the antioxidant defense system appears to play a crucial role in PE's pathogenesis, as indicated by lower T-AOC activity in our research in the early PE group in comparison with the normal group (16,17).

Early PE is mostly dependent on the placenta, and increasing oxidative stress during pregnancy may cause tissue damage (18). When oxidative stress in the placenta exceeds antioxidant defenses, oxidative damage can spread to distal tissues, contributing to the pathogenesis of PE. Placentas from women with PE have been shown to have lowered antioxidant capacity in comparison with normal placentas, and females with PE have lower blood levels of antioxidants and oxidatively modified proteins and lipoprotein particles (19). The placental barrier may burst due to oxidative stress and tissue damage, enabling fetal and placental-derived substances to enter the mother's blood and causing endothelial damage in the mother as well as increased oxidative stress and systemic inflammation (15). These findings highlight the importance of further research into the potential effects and mechanisms of antioxidant treatments in early PE.

Evaluating the carbonic anhydrase enzyme, which has a versatile effect on metabolism, alongside oxidative stress markers can significantly contribute to the literature on PE. Our study found that anti-CA I and anti-CA II autoantibody levels were significantly higher in pregnant women with early PE compared to the control group, suggesting an autoimmune response against CA I and CA II enzymes may play a role in early PE's pathogenesis. MDA values were also observed to be geater in the early PE group, indicating increased lipid peroxidation and oxidative stress. These results confirm that increased lipid peroxidation may be associated with the pathogenesis of PE. The imbalance between T-AOC and TOC further supports the notion that oxidative stress is a critical factor in early PE.

Strengths and Limitations

Our research has many strengths. Firstly, it provides a comprehensive analysis of the relationships between auto antibodies and oxidative stress parameters in early PE, offering valuable insights into the pathogenesis of the condition. Secondly, by investigating novel biomarkers (anti-CA I and anti-CA II antibodies) that have not been extensively studied in the context of early PE, we contribute to the limited literature on this topic. This novel approach can help in understanding the potential role of autoimmunity in PE and open new avenues for research.

However, there are limitations to our study that should be acknowledged. The relatively small sample size may limit the generalizability of our findings. Larger studies with more participants are needed to validate our results and confirm the observed associations. Additionally, as a single-center study, our findings may not be representative of the broader population. Multi-center studies would enhance the external validity of our results and provide a more comprehensive understanding of early PE. Furthermore, our study did not include molecular analyses, which could provide deeper insights into the mechanisms underlying the observed associations. Future research incorporating molecular techniques is warranted to elucidate the etiopathogenesis of early PE further.

CONCLUSION

Our study found that anti-CA I and anti-CA II antibody levels, along with oxidative stress markers, were significantly higher in pregnant women with early PE compared to healthy controls. These results suggest that the autoimmune response against CA I and CA II enzymes and increased oxidative stress play crucial roles in the pathogenesis of early PE. Understanding these mechanisms could lead to the development of new diagnostic and therapeutic strategies for early PE. Future studies should focus on larger, multi-center cohorts and incorporate molecular analyses to further elucidate the etiopathogenesis of this complex condition. The presence and levels of anti-CA I and II antibodies and antioxidant parameters discussed in our study highlight the need for further research in this field. Our findings underscore the importance of comprehensive maternal-fetal health approaches to minimize the risks associated with early PE for maternal, fetal, and neonatal individuals. As PE's prevalence and high treatment follow-up and costs necessitate biomarker studies, it seems possible that panels consisting of both biochemical and molecular markers may be clinically useful in predicting this disease.

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MEDICAL RECORDS-International Medical Journal

Review Article

Use of Silver Diamine Fluoride: Past to Present

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Abstract

Bacteria in the oral cavity have a great impact on caries formation by demineralizing tooth enamel. Bacterial infection should be prevented before restorative treatments. Rather than invasive treatment of existing caries, arresting bacterial activity in carious lesion and remineralizing dental tissue have become the goal of contemporary caries management philosophy. Silver compounds with antimicrobial effects have been developed over time and have taken their place in dentistry. 'Silver Diamine Fluoride' was created by combining the remineralizing effect of fluoride with the cariostatic effect of silver. Its popularity has increased because it appeals to the general population. It's application is painless, simple, and affordable. Our aim in this review is to provide a general perspective on the usage areas of Silver Diamine Fluoride from past to present and to create a guide for its use in pediatric patients.

Keywords: Silver diamine fluoride, preventive dentistry, conservative treatment

INTRODUCTION

The most common chronic disease, affecting people in all countries and age groups, is tooth decay. It imposes a heavy economic burden on families and the health care system. Many factors, such as microbial, behavioral, genetic and environmental determinants, affect the formation of caries (1). Regular use of medications, high sugar consumption, poor oral hygiene, low socioeconomic conditions, income rate, and parental education are high risk factors for tooth decay. It is often very difficult to obtain children's cooperation during dental treatment, and high-risk treatments such as general anesthesia or sedation for behavior management are common. In addition to its cost, it requires advanced skills of clinicians. Therefore, minimally invasive techniques have been recommended for caries treatment (2).

The philosophy of contemporary caries treatment has altered from the traditional to a minimally invasive approach that containes using of fluoride and antimicrobial agents (3). Traditionally, the treatment of dental caries has consisted of less conservative treatments that require removing of extra healthy dental tissue to increase surface areas for the mechanical retention of the restorative material. It has been proposed that minimally invasive treatments are alternative treatment options to traditional treatments with the emergence of new biomaterials (4,5). Beyond just focusing on restorative treatment, strategies should be developed to eliminate the bacterial factors that cause caries and prevent further bacterial infections. The aim should be to remineralize the decay rather than merely eliminate it. By using professionally applied fluoride-based materials, caries lesions can be both arrested and prevented (3-6).

The Historical Journey of Silver Compounds

Silver has been used for a long time due to its material properties and effects (5,7). It was started to use in dentistry and medicine due to its anti-cavity, antimicrobial and antirheumatic traits in 1800s. Silver compounds gotten popularity in the treatment of tetanus and rheumatism in the 1900s. Before antibiotics were discovered, silver compounds began to be used by some physicians in the treatment of colds and gonorrhea (8,9). The use of silver nitrate (SN) solution, a silver compound, as eye drops in newborns has become widespread in the treatment of venereal diseases such as umbilical granuloma and warts, and to prevent the transmission of Gonorrhea from the mother to the baby's eyes during birth (5,10).

Silver compounds have been started to use in dentistry at nearly 659 AD. SN was used to arrest dental caries as the first silver compound because it was used in the early

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1840s to reduce the incidence rate of caries in children with primary dentition (6). It was reported that SN could arrest dental caries in both dentition (11). In the 1960s, a combined beneficial the idea of combining silver with fluoride as an anti-caries agent was put forward to create the effect (7,11).

Today, a new silver compound named 'Silver Diamine Fluoride (SDF)' has been improved, which has the remineralizing feature of fluoride along with the cariostatic effect of the silver (5). SDF, which is its commonly used form at 38% concentration, contains of 25% silver and 5% fluoride ions dissolved in 8% amine, which is structurally like to SN, and sodium fluoride (NaF), which is a fluoride varnish. The cariostatic and biochemical effects of SDF on tooth structure and bacteria are like to SN. Both reinforce the structure of the tooth by creating fluorapatite crystals and reduce bacterial DNA and proteins with the effect of silver ion (12).

It is not necessary to remove the bruise before applying silver compounds. Their application is simple and painless. They do not require advanced instruments or techniques, so they are cost-effective agents in caries management. Its use is suitable for the general population (2).

Silver Diamine Fluoride

It is a colorless solution with antimicrobial properties and remineralizing ability. A 38% solution of SDF containing 253,900 ppm silver and 44,800 ppm fluoride ions is widely used (13). Because of an alkaline solution, silver and fluoride in SDF act synergetically to arrest caries lesions (14). Due to silver is an antimicrobial agent,it inhibits the development of cariogenic biofilm by denatured enzymes that destroys collagenous dentin. Fluoride stimulates remineralization and prevents demineralization of teeth under acid attack (15,16). The fluoride in SDF supports the accumulation of fluorapatite crystals, that are more resilient to acidic attack on the tooth structure (17). Silver fluoride inhibits Streptococcus mutans, a primer pathogen in caries. It has been shown that a thinner biofilm layer is formed on teeth treated with SDF (18). Systematic reviews have reported that SDF is an efficacious cariostatic agent in arresting caries (2,19). SDF promotes calcium absorption and increases the mineral content of dental hard tissues. Therefore, it is known that the surface microhardness of carious lesions treated with SDF increases significantly (20-22).

SDF was confirmed for using as a therapeutic agent in Japan in the 1960s (23). In 2014, the United States Food and Drug Administration (FDA) approved the first SDF product for use in the USA (24). SDF has so far been used to arrest caries lesions of primary teeth in children (20), to inhibit pit and fissure caries of erupting permanent molars (25), and root caries in older people. It has taken its place in the literature with its various usage areas (26).

There are solutions containing SDF in different concentrations in the market, such as 3.8% (Saforide RC, Japan), 10% (Cariostatic, Brazil), 12% (Cariestop and Ancarie, Brazil), 30% (Cariestop and Ancarie, Brazil) and 38% (Advantage Arrest (USA), Bioride (Brazil), Fagamin, Fluoroplat (Argentina), Saforide (Japan), e-SDF, Dengen Caries Arrest (India), Topamine (Thailand), Riva Star (Australia)) (27). Studies have shown that the amount of fluoride and silver in SDF solutions can vary from brand to brand and even from bottle to bottle within the same brand. For example, it is thought that the difference between studies is due to the fact that the content of a 38% SDF solution consists of silver, fluoride and ammonia ions, which will be 38% in total, and that it is within certain average ranges (28).

Atraumatic restorative treatment (ART) is a minimally invasive approach that was initiated by Jo Frencken in Tanzania in the 1980s, where the restoration is completed after cleaning the carious tissue using hand instruments. Literature studies show that it is not necessary to completely remove the infected dentin in deep carious lesions if a sealed restoration is made. This procedure, which uses SDF and glass ionomer cement (GIC) with the ART method, is called silver modified atraumatic restorative technique (SMART). This technique provides children with the opportunity to restore the tooth by stopping the carious lesion without creating aerosols as an alternative to traditional restorative treatment methods and reduces dentist anxiety in children (29).

Uses of Silver Diamine Fluoride

Treatment of SDF is basic, non-invasive, painless, unexpensive and does not generate aerosols. The unit can also be used for treatment of children who are non-cooperative or too young to accept traditional restorative treatment (30). The SDF application using technique can be individually arranged according to needs of the patients in the clinic. A recommended SDF application technique for patients with cooperation problems is drying, applying and protecting. It is recommended that physicians check one to three weeks after application to see whether the carious lesion has been stopped. If the caries lesion has not arrested, SDF should be applied all over. If it has arrested, the agent should be renewed every three to six months (24).

- The manufacturer's recommendation is that the bottle in which SDF is stored should not transmit light, and since it can dissolve metal and glass, it should be placed in a plastic container during application and used as soon as possible after removal. Because if SDF is exposed to light, it can become unstable and break down into silver ions.
- SDF is an agent that is applied topically to the involved tooth surface only. Avoid using more than one drop of SDF solution per patient in a single visit (28).
- Vaseline should be applied around the mouth. Gingival barrier and rubber dam should be applied to inhibit accidental contact and staining with the skin, gums, mucosa and lips. The areas to be treated should be isolated with cotton rolls (8,31).

- Superficial debris can be removed to increase the contaction area between the solution and carious lesion. It is not necessary to remove carious dentin; however, the rate of arrested caries lesions that turn black when removed can be reduced and can be taken into account for aesthetic purposes.
- The lesion should be dried with compressed air; because it is thought to increase the effectiveness of the process.
- It should be applied by dipping the brush into the solution and scrubbing it directly into the lesion for 1 minute.
- It should be waiting for 1-3 minutes for reaction between the solution and carious lesion.
- It should be applied a light compressed airflow until the solution dries (31).
- To minimize systemic absorption, it is recommended to remove excess SDF with a cotton roll or sterile sponge after application and continue isolation for at least 3 more minutes.
- According to the manufacturer's recommendations; it can then be air dried for 30-60 seconds. Washing is not required after the application.
- Finally, a thin layer of 5% NaF varnish is applied to the SDF applied surface.
- It is recommended that the patient does not eat or drink anything for an average of one hour after the procedure.

It has been reported that application times can vary between 10 seconds and 3 minutes in clinical studies. Although no correlation has been found between application time and the effectiveness of SDF in clinical studies, it is recommended to pay attention to the time, especially when applied for the first time. It has been stated that a longer application time may reduce the possibility of removing SDF from the lesion in case of washing after treatment (28).

Advantages

SDF is widely used worldwide to treat dentin hypersensitivity and carious lesions (2,32). It supposed that SDF has a multiple effect of preventing caries and cariogenic biofilm, protecting collagen from degradation, and increasing dentin microhardness (33). SDF It is a practical and low-cost remedy to stop the growth of decayed layers in both dentition (34). It is a simple treatment option that is cost-effective, minimally invasive, and easily clinically applicable for most patients. Due to its advantages, it has become a promising strategy for caries treatment in children who are very young or have behavioral or medical treatment difficulties due to their special needs, have a high caries risk, have multiple cavitations, and have difficulty accessing dental treatment. In a meta-analysis review, it was stated that active caries decreased by 71% after 30 months in patients receiving SDF treatment in the primary dentition (2). Another clinical study reported that using of 38% SDF every six months succeed a 74% caries arresting ratio in primary teeth (35). However, there are also studies that say approximately 11-32% of caries lesions remain active after SDF treatment4. A study on 976 school-age Nepali children reported that a one practition of SDF was efficacious in preventing caries at 6, 12, and 24-month follow-ups (36). Another research found that using of 38% SDF every 6 months was efficient in arresting carious dentin lesions. It has been shown to be more effective than 5% NaF application (37). In another study, similarly, annual 38% SDF application was more efficient than 5% NaF application every three months. A research with 375 preschool children showed that the practition of SDF once in a year was better than application of 5% NaF every three months. However, many researches have shown that the use of SDF is more efficient than glass ionomer cement or fluoride varnish in inhibiting the growth of primary tooth decay (22).

Disadvantages and Limitations

The most evident disadvantage of using silver compounds in dentistry is that silver-containing solutions permanently dye carious lesions black (5). SDF solution is colorless and odorless; but it can blot skin, clothing, countertops, flooring, and appliances (2). The reason of this discoloration is oxidation of ionized silver to metallic silver; This restricts the clinical utilizzation of silver compounds in patients with aesthetic demands (8). Some researchers have recommended applying a tooth-colored material, like glass ionomer cement, on the black colored and stalled caries lesion to solve this aesthetic problem (5).

It is very significant to explain the disadvantages to the patient before application to prevent displeasure and complaints. A study conducted in New York found that coloring on their children's premolar and molar teeth treated with silver compounds was more admissible to parents than becoming stain on the anterior teeth, that parental acceptance of children with more difficulty in receiving treatment increased with socioeconomic status, and that parents with lower levels of education reported that the acceptability rate was higher (38).

When solutions containing silver come into contact with the skin, a temporary henna stain appears. If silver does not pass through into the dermis, skin pigmentation disappears within 7 to 14 days (8). When exposed to a small amount of the solution, there are no immediate or side effects other than coloring of the skin. If a stain occurs on the skin, it is recommended to wash it immediately with water or wipe it with a salty slurry. If exposure is repeated, undesirable effects may become more evident. Long time exposure to large amounts of silver on parts of the body exposed to light can cause irreversible pigmentation of the skin or eyes (32). Another disadvantage is that desquamative processes such as ulcerative gingivitis may occur if adequate soft tissue isolation is not performed. However, these symptoms are

temporary and disappear within 48 hours (39). In order to prevent and reduce the discoloration effect of SDF, compounds such as glutathione (GSH) or potassium iodide (KI) have been introduced to the market. GSH is an antioxidant and reducing agent commonly found in the human body. It forms a layer around silver ions and restricts their release. It is mixed with SDF and applied to the relevant tooth surface (28).

A new approach proposed in 2005 to prevent unwanted staining is the application of saturated KI immediately after the application of SDF. The most important reason for the reversal of the black stain is suggested to be the formation of a white powder from tripotassium phosphate. Another product formed by the reaction of silver with iodide ions is silver iodide. It is a light-sensitive yellowish-white powder that darkens when exposed to light (39).

The recommended usage protocol for KI is as follows:

- A sufficient amount of KI should be put into a disposable medicine container.
- It should be applied to the relevant tooth surface with the help of a micro brush saturated with KI, like SDF application. Reaction products are formed immediately.
- The restoration should then be completed with resin-modified glass ionomer or composite (39).

The SDF/KI combination has been shown to not prevent fluoride uptake into demineralized tooth tissue and to significantly increase the microtensile and shear bond strength of GIC and dentin. Recently, a commercial SDF/KI agent (Riva Star; SDI, Bayswater, Australia) consisting of a KI solution saturated with 30–35% SDF has been introduced for the treatment of dentin hypersensitivity. The SDF/KI protocol has been found to be less anticariogenic and more effective in reducing staining compared with SDF alone. Insignificant color change has been reported when used under GIC compared with irrigation with deionized water. The use of KI should be restricted in pregnant and lactating women because it has been reported to cause fetal harm, thyroid abnormalities, and goiter (39).

The toxicity of solutions containing silver compounds is about the dose used; however, the dosage for use in the treatment of dental caries is excessively low (32). It is reported that accumualtion of excess silver is in the skin, liver, kidneys, spleen, corneas, gums, mucous membranes and nails. There is little data reporting possible toxic effects of the use of silver compounds. In general, it has been reported about low cell toxicity of silver ions. Few reports about silver allergy have been reported (8).

A bibliometric analysis revealed that global attention in SDF has shown an increase exponentially (40). However, SDF is not available in every country. When using the 25% SN + 5% NaF varnish, that is currently convenient throughout the world, it is possible to achieve similar results, although the silver and fluoride concentrations are lower than 38% SDF (22). The same applies to the treatment cost. So, first 25% SN then 5% NaF varnish using may be more suitable for using in young children, considering availability and cost throughout the world (34).

CONCLUSION

Using of silver compounds have became widespread in many areas from past to present with their healing properties. Silver diamine fluoride has become popular with silver's antimicrobial and fluoride's remineralizing feature. Since caries removal is not required and its cost is low, it has taken an important place in caries management in dentistry.

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