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Contents / İçindekiler

Research Articles / Araştırma Makaleleri

RESEARCH ARTICLE

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Comparing Personal Risk Communication with Generic Information on Breast Cancer Screening Attendance: A Randomized Controlled Trial

ABSTRACT

Objective: This study sought to discern the differential impacts of communicating individualized breast cancer risk versus disseminating generic breast cancer information on women's proclivity towards breast cancer screenings.

Method: A structured experimental design was used, including 300 female volunteers aged between 40-69, who had not previously been diagnosed with breast cancer, in Erzincan. Data collection entailed a face-to-face administration of a 22-item questionnaire complemented by the ASSISTS scale. Participants were randomized into two conditions: one receiving a standardized briefing on breast cancer screening modalities, and the other being apprised of their lifetime risk of breast cancer development based on the modified Gail model.

Results: Post-intervention, 55.8% (n=72) of the risk-informed cohort and 40.5% (n=41) of the generic information cohort expressed a willingness to undergo screening (p=0.022). Notably, the group informed of their personalized risk exhibited a more pronounced uptick in requests for breast self-examination, clinical breast examination, and mammography screening compared to their counterparts.

Conclusions: The communication of personalized breast cancer risk proves to be a more efficacious and time-efficient strategy than generic information dissemination in bolstering screening participation rates.

Keywords: Breast Neoplasms, Breast Cancer, Mammography, Secondary Prevention, Early Diagnosis of Cancer.

Meme Kanseri Taramasına Katılmada Kişisel Risk Bildirimi ile Genel Bilgilendirmenin Etkisinin Karşılaştırılması: Randomize Kontrollü Bir Çalışma

ÖZET

Amaç: Bu çalışma, bireyselleştirilmiş meme kanseri riski bildirimi ile genel meme kanseri hakkında bilgilendirme yapmanın kadınların kanser taramasına katılım eğilimleri üzerindeki etkilerini anlamayı amaçlamaktadır.

Yöntem: Bu çalışma, Erzincan ilinde, daha önce meme kanseri teşhisi konmamış 40-69 yaş arasındaki 300 kadın gönüllü üzerinde yapılandırılmış bir deneysel tasarım kullanılmıştır. Veri toplama, 22 maddelik bir anketin yüz yüze uygulanması ve ASSISTS ölçeğinin kullanılması ile gerçekleştirilmiştir. Katılımcılar iki gruba ayrılmıştır: bir grup standart meme kanseri tarama yöntemleri hakkında bilgilendirilmiş, diğer grup ise modifiye Gail modeline dayalı olarak ömür boyu meme kanseri geliştirme riskleri hakkında bilgilendirilmiştir.

Bulgular: Müdahaleden sonra, risk bilgilendirilmiş grubun %55.8'i (n=72) ve genel bilgi grubunun %40.5'i (n=41) tarama yaptırmaya istekli olduklarını ifade etmiştir (p=0.022). Özellikle, kişiselleştirilmiş riskleri hakkında bilgilendirilen grup, genel bilgilendirme yapılan gruba kıyasla daha fazla meme kendi kendine muayene, klinik meme muayenesi ve mamografi taraması talebinde bulunmuştur.

Sonuç: Kişiselleştirilmiş meme kanseri riski bildiriminin, genel bilgi verilmesine göre tarama katılım oranlarını artırmada daha etkili ve zaman açısından daha verimli bir strateji olduğu görülmektedir.

Anahtar Kelimeler: Meme Neoplazmları, Meme Kanseri, Mamografi, Sekonder Koruma, Kanserin Erken Teşhisi.

INTRODUCTION

Breast cancer has recently become more prevalent than lung cancer worldwide according to the International Agency for Research on Cancer (IARC) 2020 data (1, 2). It is not only the most commonly diagnosed cancer in women but also the primary cause of cancer related deaths among them responsible, for 15.5% of such cases (1). Currently, there is no established methodology for the outright prevention of breast cancer. Nonetheless, routine screenings and examinations can significantly enhance life expectancy and even facilitate full recovery if the diagnosis occurs during the early stages of the disease(3, 4). This highlights the need to combat this disease with successful prevention methods especially through early detection and screening known to enhance survival rates and decrease mortality.

In Turkey the number of cases of breast cancer is quite high with the Global Cancer Observatory (GLOBOCAN) stating a rate of 46.6 per 100,000 women in 2020 higher than the 45.6 reported in 2016 by the Ministry of Health of Turkey (1, 5). Despite this rate not many women are getting screened for breast cancer according to the Health Statistics Yearbook (HSY) from 2016 which shows that 71.1% of women aged 15 and above have never had a mammography screening (6). This concerning data points out a gap, in the healthcare systems efforts to promote and facilitate these potentially life saving screenings.

Existing strategies aimed at increasing breast cancer screening rates in Turkey have shown mixed results, necessitating a detailed evaluation to identify where these approaches fall short (7). This assessment is essential for crafting interventions that can more effectively bridge the gap between availability and utilization of screening services, particularly mammography. Despite the proven effectiveness of mammography in decreasing breast cancer mortality, its adoption among Turkish women remains insufficiently widespread (8, 9). This gap highlights a crucial need for targeted educational and outreach programs that can overcome cultural, logistical, and informational barriers to screening participation.

Building on the findings from previous studies, our research further explores the dynamics between breast cancer risk perception and screening participation. Earlier research has highlighted the crucial role of effective communication in enhancing screening uptake, indicating a need for clearer conveyance of breast cancer risk to improve engagement (10-12). Additionally, studies have identified gaps in healthcare professionals' perspectives on risk stratification versus disease screening, suggesting that there may be an underutilization of screening appointments as opportunities for risk assessment and tailored prevention advice (12). Our study aims to address these gaps by comparing the effectiveness of personalized risk information versus general health advice, aiming to determine which method more effectively motivates women to participate in breast cancer screenings, thereby refining communication strategies to increase screening rates effectively.

This study aims to delve into the perceptions and attitudes of Turkish women towards breast cancer screenings. We seek to identify not only the barriers to participating in these screenings but also to explore how different communication strategies might influence women's decisions to undergo mammography. Specifically, the research will compare the impact of general health information versus personalized risk assessments on the willingness of women to participate in breast cancer screenings, aiming to pinpoint more effective methods for increasing screening rates among this target demographic.

In this context, our objectives are twofold: to clarify the factors that deter women from participating in breast cancer screenings and to determine whether tailored interventions based on personalized risk or general information are more effective in motivating them to engage in such preventive measures. By addressing these points, the study will contribute valuable insights into enhancing breast cancer screening rates and, consequently, reducing mortality from the disease in Turkey.

MATERIAL AND METHODS

Study Design and Population: This study was designed as a randomized controlled trial. The target population comprised female patients aged 40-69 years, residing in the central district of Erzincan, Turkey. Participants were recruited during their scheduled visits as well as opportunistically when they visited the family health center for other health concerns, ensuring a broad representation of the target demographic. These participants visited a family health centre between December 1, 2022, and April 1, 2023, and had no prior diagnosis of breast cancer.

Sample Size Determination: Utilizing the confidence interval method with a type 1 error of 0.05 and a power of 0.95, and anticipating a 20% difference between the two groups with a sensitivity of 0.05, the sample size was estimated to be 264. This anticipated difference was based on clinical expectations and expert opinion regarding the potential impact of personalized risk communication versus generic information dissemination on screening participation rates. As no similar studies were found in the literature to provide a basis for this estimate, we relied on our clinical expectations and expert judgment. To account for an approximate 10% data attrition, the study ultimately included 300 participants, with 150 individuals in each group.

Data Collection Instruments: A comprehensive questionnaire was formulated by the research team after an extensive literature review. This questionnaire encompassed demographic details, inquiries about participants' perspectives on breast cancer screenings, and questions derived from the modified Gail risk scoring system. The Gail risk model, which originated from the Breast Cancer Detection and Demonstration Project (BCDDP) data, incorporates various risk factors to provide a lifetime breast cancer development risk as a percentage(13).

Subsequently, the ASSISTS scale, a 33-item instrument developed by Khazaee et al. in 2016 and later validated in Turkish by Turan et al., was administered(14, 15). This scale, devoid of a specific cut-off, operates on the premise that higher scores indicate heightened awareness of breast cancer preventive behaviors. Each item on the ASSISTS scale is rated on a Likert scale ranging from 1 (Strongly Disagree) to 5 (Strongly Agree). The scale is designed to gauge women's attitudes, knowledge, and perceptions related to breast cancer and its screening practices. The total score is calculated by summing the responses to all items, with potential scores ranging from 33 to 165. A higher score indicates a greater awareness and understanding of breast cancer preventive behaviors. In terms of internal consistency, the ASSISTS scale has demonstrated a Cronbach's alpha of 0.81 in previous studies, indicating good reliability.

Prior to and immediately following the interventions, participants responded to three Likert-scale items, which ranged from 1 (indicating 'Strongly Disagree') to 10 (indicating 'Strongly Agree'). These items gauged their inclination towards undergoing mammography, BSE (breast self-examination), and CBE (clinical breast examination) in the subsequent year.

Randomization Procedure: People were split into two groups depending on the order of their visits to the health center. One group was for those with odd visit numbers and the other was for those with even numbers. This strategy of using visit numbers to assign groups was an effective way to randomize making sure that each person had a fair shot at being placed in either group and reducing the risk of bias, in selection. One cohort received concise information, a 212-word text derived from the "Breast Cancer Prevention, Screening, Diagnosis, Treatment and Follow-up Clinical Guide" by the Cancer Department of the Ministry of Health. Conversely, the other group was informed solely about their lifetime risk percentage of developing breast cancer, as determined by the modified Gail risk model(8). Information and risk communication were administered orally by the same researcher, who read from a previously standardized script to ensure consistency and accuracy. This method was chosen to guarantee that all participants received the same information in a controlled manner, facilitating a uniform understanding across the study. This approach also helped maintain the integrity of the intervention by ensuring that the delivery was uniform and unvarying, thus supporting the reliability of the study's findings. Upon study conclusion, all participants were provided both the standard information text and their Gail risk score (Figure 1).

Ethical Considerations: The study secured ethical approval from the Erzincan University Faculty of Medicine Clinical Research Ethics Committee on October 27, 2022, under the reference number 04/10. Additionally, permission was granted by the Erzincan Provincial Health Directorate to administer the questionnaire in family health centres. Informed consent, both verbal and written, was obtained from all willing participants. Participants' data were stored anonymously, ensuring no identifiers or personal information that could lead to disclosure were used. There were no conflicts of interest associated with this study. To ensure the well being of the participants all interviews and conversations took place in spaces, within each family health center to maintain confidentiality and privacy. The study followed the guidelines laid out in the updated Helsinki Declaration diligently. CONSORT guideline rules were followed in all phases of the trial study.

Statistical Analysis: Data were inputted and analyzed using IBM SPSS Statistics 25 (SPSS, Chicago, IL). Quantitative data were summarized using either mean ± standard deviation for normally distributed variables or median (minimum – maximum) for non-normally distributed variables. Categorical variables were expressed as frequency (%). The Kolmogorov-Smirnov test was utilized to verify the assumption of normality, and the Levene test assessed the homogeneity of variances.

For comparing two groups, the Student's t-test was applied to normally distributed data, while the Mann-Whitney U test was used for non-normally distributed data to analyze differences in median values. For comparisons involving more than two groups, one-way ANOVA was employed for normally distributed data to compare means, and the Kruskal-Wallis test was used for non-normally distributed data to compare medians. The relationship between two categorical variables was examined using the Chi-Square test.

A p-value of less than 0.05 was deemed statistically significant.

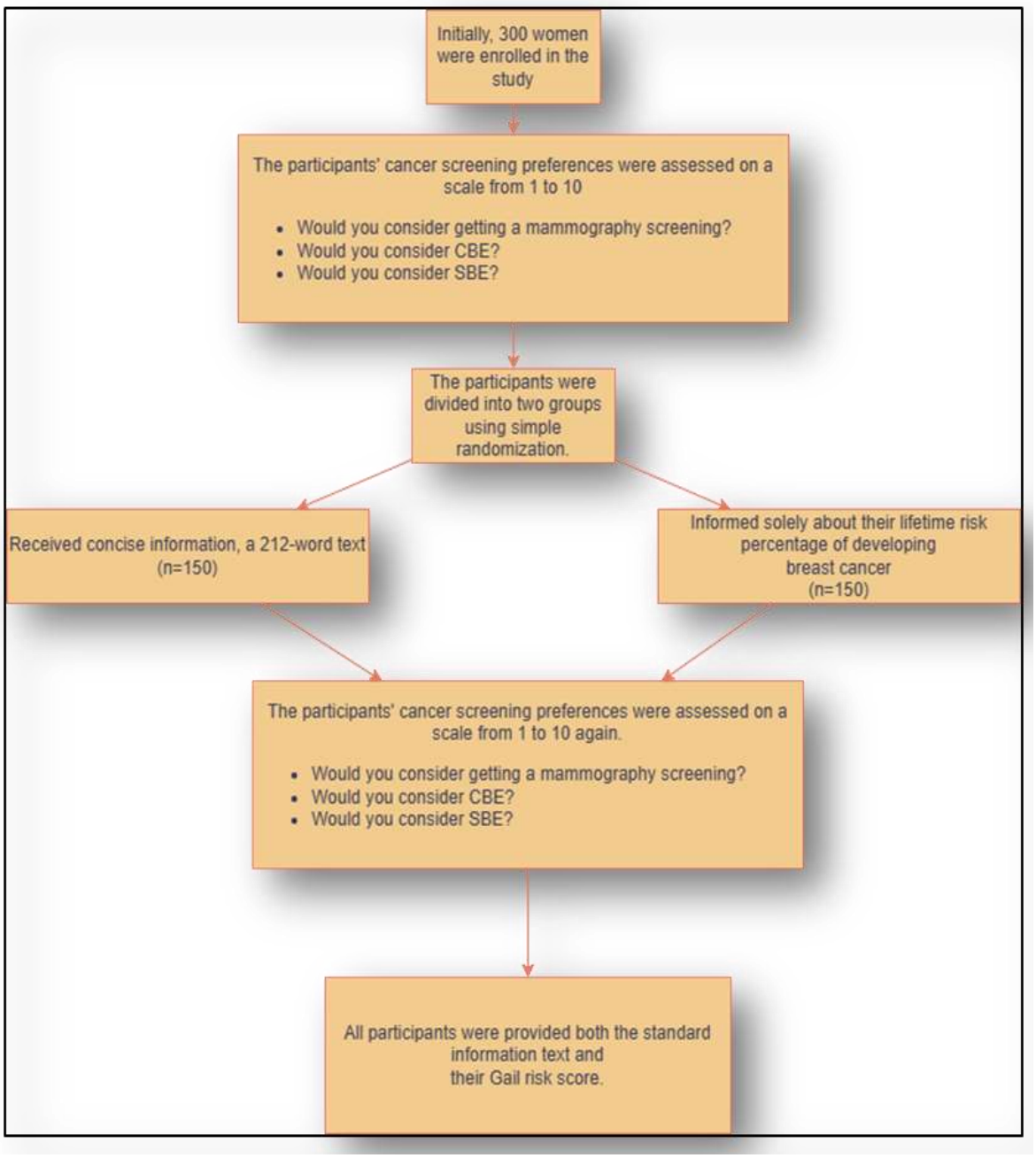


Figure 1. Flowchart of the study.
* SBE (self breast examination); **CBE (clinical breast examination)

RESULTS

Demographic Characteristics: A total of 300 participants were enrolled in this study, with an average age of 53.49±8.03 years (min=40, max=69). The participants reported a mean age of menarche at 13.25±1.60 years (min=9, max=20). Among those who had experienced childbirth, the mean age at first live birth was 21.27±4.68 years (min=15, max=44). The mean score achieved by participants on the ASSISTS scale, which has a maximum attainable score of 165, was 123.92±11.318 (min=97, max=162). Detailed demographic characteristics of the participants and their relationship with the ASSISTS scale are presented in Table 1.

Cancer Screening Status: The cancer screening behaviors of the participants are delineated in Table 2. The primary reason cited for not conducting CBE, by participants was a lack of knowledge as reported by 90.3% (n=254) with a minority of 4.3% (n=13) attributing it to feeling healthy. Similarly when it came to reasons for skipping BSE the majority of non performers mentioned lack of awareness at 68.3% (n=115). Feeling healthy at 21% (n=63). In the case of mammography similar trends emerged; 52.7% (n=158) highlighted knowledge as the deterrent, followed by 24.7% (n=74) citing good health and 4.7% (n=14) stating they did not see the necessity, for screening.

Table 1. Demographic data of participants and comparison of participants' scores on the ASSISTS scale

		n	%	Avg	p
Marital status	Married	260	86.67	124.51 ± 11.38	**0.048**
	Single	8	2.67	123.25 ± 11.26	
	Widowed	32	10.66	123.92 ± 9.95	
Do any of your first-degree relatives have breast cancer?	No	288	96	123.84 ± 11.33	0.551
	Yes	12	4	125.83 ± 11.27	
Do you have a friend who has breast cancer?	No	109	36.33	120.17 ± 10.44	**p<0.001**
	Yes	191	63.67	126.06 ± 11.26	
Do you do BSE*	No	84	28	116.43 ± 9.14	**p<0.001**
	Yes	160	53.33	129.04 ± 10.53	
	Partly	56	18.67	120.54 ± 8.69	
Have you had a mammogram before?	No	102	34	119.16 ± 10.05	**p<0.001**
	Yes, regularly every two years	37	12.33	135.49 ± 12.35	
	Yes... years ago	161	53.67	124.28 ± 9.78	
Have you been CBE** before?	No	158	52.67	119.35 ± 9.84	**p<0.001**
	Yes, regularly, once a year	20	6.67	140.25 ± 10.79	
	Yes... years ago	122	40.66	127.16 ± 9.52	
Source of information	Media	106	35.33	120.20 ± 9.92	**p<0.001**
	Family	11	3.67	133.55 ± 9.33	
	Friend	27	9	119.96 ± 11.99	
	Internet	18	6	126.50 ± 11.73	
	Doctor	138	46	126.45 ± 11.16	
Requesting a mammogram screening	Have had a mammogram screening within the last two years	70	23.33	129.69 ± 11.97	**p<0.001**
	Eligible but do not want	117	39	119.87 ± 9.65	
	Eligible and Want	113	37.67	124.67 ± 10.90	

* BSE (breast self-examination)
**CBE (clinical breast examination)

Table 2. Breast cancer screening status of participants

		n	%
Have you had a mammogram screening before?	No	102	34
	Yes, regularly every two years	37	12.3
	Yes, I have had it before	161	53.7
Do you do breast self-examination?	No	116	38.7
	Yes, regularly	95	31.7
	Partly	89	29.7
Have You Had a Clinical Breast Examination Before	No	158	52.7
	Yes, regularly, once a year	19	6.3
	Yes, I have been before	123	40.7

* SBE (self breast examination)
**CBE (clinical breast examination)

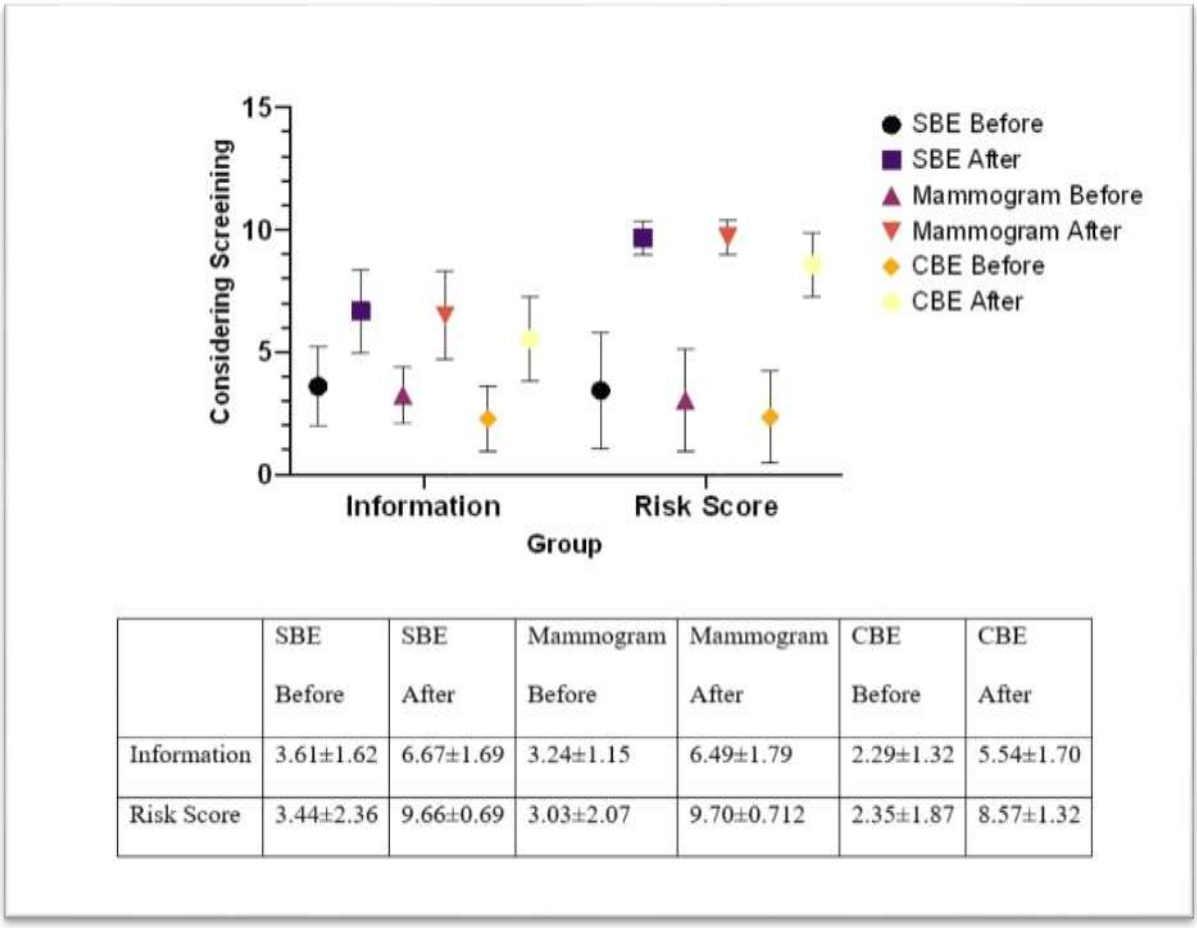
Sources of Breast Cancer Knowledge: When participants were queried about their primary sources of information regarding breast cancer, 46% (n=138) cited physicians, 35.3% (n=106) attributed it to media, 9% (n=27) to friends, 6% (n=18) to the internet, and 3.7% (n=11) to family members.

Gail Lifetime Risk Assessment: For participants subjected to the Gail risk-scoring model, the average lifetime risk of developing breast cancer was determined to be 8.12±3. In comparison to the general population, 82.7% (n=124) were categorized as having a low risk, 4.7% (n=7) an equivalent risk, and 12.6% (n=19) a heightened risk.

Mammography Screening Post-Intervention: At the outset of the study, the mammography screening rate among the cohort was relatively low, with only 23.3% (n=70) of participants having undergone mammography within the previous two years, and of these, just 12.3% (n=37) were doing so on a regular basis. Following the disclosure of cancer risks or when pertinent information was provided to those needing screening, participants were asked about their willingness to undergo mammography. Of those informed, 40.5% (n=41) expressed a

willingness to undergo screening, and this percentage increased to 55.8% (n=72) among those who were informed of their specific risk level (p=0.022). This marks a significant increase from the baseline screening behavior observed at the start of the study.

Attitudinal Shift Post-Intervention: A comparative analysis of the differential in scores pre- and post-intervention, pertaining to attitude-related questions among groups informed of their risk or provided with general information, is elucidated in Figure 2. According to the results, providing information based on risk scores led to a statistically significant increase in demand across all screening methods when compared to standard information provision (all p<0.001). When examining the effectiveness of interventions among groups that had previously undergone mammography screening and those that had not, the same result was observed (all p<0.001). On the other hand, whether the Gail score was low, equal, or high, it did not influence the desire for mammography screening (p=0.690).



	SBE Before	SBE After	Mammogram Before	Mammogram After	CBE Before	CBE After
Information	3.61±1.62	6.67±1.69	3.24±1.15	6.49±1.79	2.29±1.32	5.54±1.70
Risk Score	3.44±2.36	9.66±0.69	3.03±2.07	9.70±0.712	2.35±1.87	8.57±1.32

Figure 2. Participants' willingness to undergo cancer screening according to information and risk score groups.
* SBE (self breast examination); **CBE (clinical breast examination)

DISCUSSION

Breast cancer, despite its global prevalence, lacks a definitive preventive measure. However, early diagnosis through regular screenings can significantly improve prognosis and even facilitate complete recovery. Consequently, the importance of breast cancer screening programs cannot be overstated(5, 8). Early detection through screening not only reduces mortality rates but also lessens the burden on healthcare systems by enabling less aggressive treatment options and better patient outcomes. Our findings underscore the efficacy of communicating an individual's lifetime risk of developing breast cancer over generic information dissemination in guiding them towards breast cancer screenings.

Mammography is considered the gold standard due to its high sensitivity and ability to detect early-stage cancers, thus reducing mortality rates. However, it is not untouched by controversies the problems of overdiagnosis and false positives that complicate the picture and may actually lead to unnecessary treatment and anxiety. CBE and BSE are preferred choices, especially in settings with low access to mammography (16). On one hand, while some studies have raised questions on the role of CBE and BSE in decreasing mortality, others have emphasized their role in increased breast awareness and detection early, particularly in resource-constrained settings (16). Differences aside, all the three in combination, as a part of comprehensive screening, can optimize early

detection and better the outcome of the breast cancer patient. Acknowledging the disparities in empirical foundations, it is crucial to consider the context in which each method may be appropriate. For example, in low-resource settings, CBE and BSE can be vital tools for early detection when mammography is not readily available.

Our study highlights significant discrepancies in adherence rates to regular mammography compared to national averages and global benchmarks. Compliance rates in our group are below the national average (18.7%) reported by the Ministry of Health for mammography and, unfortunately, still fall far short of global standards and the domestic target of 70% mammography coverage (6). Notably, the national data from the Ministry of Health reflect mammography rates over the past two years without accounting for regularity. This implies that individuals may have undergone mammography in the past two years but not consistently before, suggesting that the true rate of regular mammography could be lower than reported. Our findings align with existing literature that highlights challenges in implementing organized screening programs, such as those reported in Brazil and Germany, indicating that similar issues may be present in our cohort (17, 18). Emphasizing these comparisons is crucial for understanding the broader implications of our study and advocating for strategies to enhance screening adherence rates.

Moreover, our study revealed that social and psychological determinants such as marital status, personal connections to breast cancer, and primary sources of information significantly influence breast cancer screening behaviors. Addressing these factors is essential in designing effective screening promotion strategies, as they play a pivotal role in shaping individuals' attitudes and decisions towards screening. A salient observation from our study was the pivotal role of information accessibility in influencing breast cancer screening behaviors, a finding corroborated by existing literature (19, 20). The imperative of enlightening women about the merits of cancer screening for early detection and management is evident. Prior research indicates a direct correlation between heightened awareness of cancer screening and increased participation rates (21). Given that 46% (n=138) of our participants cited physicians as their primary source of breast cancer information, healthcare professionals are uniquely positioned to champion cancer prevention and control strategies.

Our study further revealed that the ASSISTS scores were significantly influenced by factors such as adherence to regular breast cancer screening methods, marital status, having a friend diagnosed with breast cancer, and family being the primary information source. These findings underscore the intricate interplay of social and psychological determinants in shaping breast cancer screening behaviors. To bolster screening participation, it is paramount to equip women with accurate and up-to-date breast cancer information, elucidate the advantages and limitations of screening tests, and ensure their accessibility and affordability(22). Additionally, the role of spouses, family, friends, and healthcare professionals in guiding women towards screening cannot be overstated(23).

Our intervention demonstrated a marked shift in participants' inclination towards BSE, CBE, and mammography post-intervention, with the most pronounced change observed in the cohort informed of their lifetime cancer risk. This group also exhibited a significantly higher proclivity for mammography screening compared to their counterparts provided with generic information. These findings advocate for the efficacy of personalized risk communication over generic information dissemination, especially considering its time efficiency, making it a potentially preferable approach for clinicians.

However, the mode of risk communication warrants consideration. Digital platforms, such as web-based tools or applications, could be harnessed to facilitate breast cancer risk estimation, thereby reaching a broader audience. While this method offers the advantage of enhanced comprehension and recall, it presupposes technological accessibility and literacy, potentially excluding certain demographics.

It's imperative to acknowledge that enhancing breast cancer screening participation is multifaceted, necessitating considerations beyond mere information dissemination. Factors encompassing cost, availability, quality, and the structural organization of screening programs can significantly influence screening decisions(24). The pivotal role of healthcare professionals in this endeavor cannot be overstated, necessitating their active involvement in guiding, educating, and advising women on breast cancer screening(24). A holistic, multi-pronged strategy is indispensable to optimize breast cancer screening participation.

Study Limitations: This study is not without limitations. Its single-center design, reliance on participant self-reporting, and cross-sectional nature potentially limit the generalizability of the findings. Furthermore, behavioral intentions do not always predict actual behaviors, and our study did not facilitate the longitudinal tracking of participants' cancer screening behaviors. These limitations highlight the need for cautious interpretation of the results. Future research should consider conducting multi-center studies with extended follow-up periods to track participants' screening behaviors longitudinally. Such studies could provide more comprehensive insights into the long-term effectiveness of different breast cancer screening strategies and address the current study's limitations by offering a broader and more diverse

sample, reducing bias, and enhancing the generalizability of the findings.

CONCLUSION

Breast cancer, as the foremost global cancer type, necessitates community-centric screening programs to mitigate its morbidity and mortality. Enhancing patient motivation for screenings is pivotal, and our findings suggest that communicating individualized lifetime breast cancer risk is more efficacious than protracted information dissemination. This approach could potentially address the time constraints faced by clinicians in guiding patients towards screenings. However, a comprehensive strategy, encompassing both personalized risk communication and generic information provision, could further elevate screening participation rates. Policymaking that incentivizes physicians in this regard is imperative.

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RESEARCH ARTICLE

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Child Sexual Abuse in Boys: A Retrospective Investigation

ABSTRACT

Objective: Although recent studies have increased public awareness of child sexual abuse, certain aspects of the issue remain unclear. While research on sexual abuse in girls is abundant, there is limited focus on boys in our country. This study aims to explore the characteristics of cases involving sexual abuse of boys in the province of Türkiye.

Methods: The study is descriptive and retrospective in nature. A total of 245 boys who underwent forensic interviews for alleged sexual abuse between September 2017 and March 2023 at the Child Advocacy Center in the province of Türkiye were retrospectively examined.

Results: The study included 245 boys aged 3-18 with a mean age of 11.04±3.39. The most common type of sexual abuse was non-penetrative contact (57.6%). Delayed disclosure was primarily attributed to factors such as threat, fear, and shame. Sexual abuse predominantly occurred in public places (56.5%). There were significant among age groups concerning the identity of the reporters, initial disclosure persons, the existence of abuse, and reporting time. However, no significant differences were found in the presence of multiple suspects, recurrent abuse, and the incident location. Post-abuse behavioral changes in children included fear of the perpetrator (15.5%), emotional changes (15.5%), physiological changes (9.4%), and the displaying of risky behaviors (4.1%).

Conclusions: The study emphasized the importance of not overlooking sexual abuse among male children. The findings underscore the need for enhanced awareness and intervention strategies to address sexual abuse in boys within the country.

Keywords: Sexual Abuse, Male, Child, Adolescent, Child Advocacy Center.

Erkek Çocuklarda Cinsel İstismar: Retrospektif Bir Araştırma

ÖZET

Amaç: Son yıllarda yapılan çalışmalar çocuk cinsel istismarı konusunda toplumsal farkındalığı artırmış olsada, konunun bazı yönleri hala belirsizliğini korumaktadır. Ülkemizde kız çocuklarına yönelik cinsel istismar araştırmaları oldukça fazla iken, erkek çocuklarına yönelik araştırmalar sınırlıdır. Bu çalışma, Türkiye'de erkek çocuklara yönelik cinsel istismar vakalarının özelliklerini araştırmayı amaçlamaktadır.

Yöntem: Çalışma tanımlayıcı ve retrospektif niteliktedir. Türkiye'nin bir ilindeki Çocuk İzlem Merkezi'nde Eylül 2017 ile Mart 2023 tarihleri arasında cinsel istismar iddiasıyla adli görüşme yapılan toplam 245 erkek çocuk retrospektif olarak incelenmiştir.

Bulgular: Çalışmaya yaşları 3-18 arasında değişen ve yaş ortalaması 11,04±3,39 olan 245 erkek çocuk dahil edilmiştir. En yaygın cinsel istismar türü penetratif olmayan dokunmadır (%57,6). Bildirimin gecikmesi öncelikle tehdit, korku ve utanç gibi faktörlere bağlanmıştır. Cinsel istismar ağırlıklı olarak kamuya açık yerlerde gerçekleşmiştir (%56,5). Bildirimde bulunanların kimliği, ilk bildirimde bulunan kişiler, istismarın varlığı ve bildirim süresi açısından yaş grupları arasında anlamlı farklılıklar bulunmuştur. Ancak, birden fazla şüphelinin varlığı, tekrarlayan istismar ve olayın gerçekleştiği yer açısından anlamlı bir farklılık bulunmamıştır. Çocuklarda istismar sonrası davranış değişiklikleri arasında failden korkma (%15,5), duygusal değişiklikler (%15,5), fizyolojik değişiklikler (%9,4) ve riskli davranışlar sergileme (%4,1) yer almaktadır.

Sonuç: Çalışma, erkek çocukların da cinsel istismar açısından ihmal edilmemesinin önemini vurguladı. Bulgular, ülke içinde erkek çocuklarda cinsel istismarı ele almak için gelişmiş farkındalık ve müdahale stratejilerine duyulan ihtiyacın altını çiziyor.

Anahtar Kelimeler: Cinsel İstismar, Erkek, Çocuk, Ergen, Çocuk İzlem Merkezi.

INTRODUCTION

Child sexual abuse (CSA) is a global public health issue that disrupts the physical and mental well-being of children (1). Children who are victims of sexual abuse experience a range of short and long-term physical, social, psychological, and behavioral problems (2,3). Major depression, suicidal tendencies, substance abuse, post-traumatic stress disorder, anxiety disorders, antisocial personality disorder, and sexual dysfunction are among the observed adverse outcomes in victims of sexual abuse (4,5).

The prevalence rates of child sexual abuse vary, with approximately 18-20% in girls and 8-10% in boys (6). While it is suggested that boys are affected by sexual abuse two times less than girls, it is believed that male victims are underreported, and there is insufficient research on this matter (7,8). Incidence studies on sexual abuse in boys indicate that a significant proportion of abuse victims are male: 37% in Canada and 47.5% in the United States (9,10).

Despite an increase in national and international studies on child sexual abuse, there are still aspects of this issue that remain incompletely understood (11). Aspects such as the extent of sexual abuse against boys, disclosure, the identity of perpetrators, and observed behaviors in children are among the areas that need further exploration (12). While scientists have extensively examined sexual abuse in girls, there are indications that sexual abuse of boys has been overlooked (7). Describing the experiences of sexual abuse is often a complicated, complex, and painful process for victims. Previous research has shown that some male victims of CSA may delay disclosing their experiences for years, while others may never disclose at all (8,13). Factors such as fear of re-victimization, the stigma of being labelled as homosexual, and feelings of shame reduce the likelihood of reporting by boys (14,15). This negatively impacts the motivation of boys to report and complicates the acquisition of accurate data. Furthermore, failure to make an official report can lead to the continuation of abuse, further victimization, and the abuse of other children (16). Making an official report is crucial for ending the abuse and ensuring that victimized children receive the necessary therapeutic interventions (15–17).

In our country, sexuality is generally considered taboo, and while cases of sexual abuse against girls are increasing, those against boys are not being reported sufficiently. Prejudices about homosexuality and perceptions of boys being strong contribute to the overlooking of sexual abuse against boys (18).

Comparisons between child and adolescent periods have been limited in a few of studies. A recent study highlighted that the perpetrators were familiar during adolescence, while they were strangers before adolescence (19). Another study reported differences in the type, number, onset, method, and proximity of the perpetrator based on the child's developmental stage (20). Most studies on child sexual abuse have relied on mixed-gender samples to compare the prevalence of sexual abuse between the two genders (21,22). Additionally, there have been limited studies explicitly focusing on sexual abuse in boys, and these studies have mainly concentrated on the general characteristics of children. The present study aimed to compare the sociodemographic, clinical, and abuse-related characteristics of boys who were victims of sexual abuse during pre-adolescence and adolescence. We hypothesized that family characteristics, type of abuse, perpetrator profile, and reporting characteristics would differ between pre-adolescence and adolescence.

MATERIAL AND METHODS

This retrospective descriptive study was conducted at the Child Advocacy Center in the Turkish province. Researchers created a data form specific to the study's objectives. The data form included variables such as demographic information of the child and the suspect, type of sexual abuse, location of the incident, the status of repeated abuse, the time elapsed between the occurrence of sexual abuse and its reporting, factors delaying the reporting of abuse, and observed behaviors in the child. The study received approval from the local ethics committee (Approval No: 321/05.12.2022).

Between September 1, 2017, and February 28, 2023, the files of 245 boys who underwent forensic interviews were retrospectively reviewed. Victim statements, forensic interview reports, and information notes were thoroughly examined and recorded in the data form.

Cases were analyzed in two age groups, pre-adolescence (3-11 years) and adolescence (12-18 years), following the literature and based on the developmental stages of children (20). The suspects were classified according to the provisions of article 103/3/c-d-e of the Turkish Penal Code (23). Accordingly, individuals known to the child but without any familial relationship, such as friends, acquaintances, partners, teachers, and dormitory staff are categorized as "extra-familial abuse"; biological or stepfathers, biological or step-siblings, uncles, aunts, grandfathers, and their children are categorized as "domestic abuse"; and individuals unknown to the child without any kinship relationship were categorized as "strangers". The time elapsed between the occurrence of the incident and its reporting was categorized as early reporting (0-72 hours) and delayed reporting (4 days and above) per the literature (24).

The study was analyzed using SPSS 24.0 software. Continuous variables were expressed as mean and standard deviation, while categorical variables were presented as numbers and

percentages. Chi-square tests were used for descriptive analyses of frequency and percentage values and to compare categorical variables. Statistical significance was set at $p<0.05$.

RESULTS

Between September 15, 2017, and March 31, 2023, 1395 cases were referred to the Child Advocacy Center. Of the forensic cases evaluated for alleged sexual abuse, 17.6% were boys (n=245). The age range of boys was 3-18 years, with a mean age of 11.04±3.39. The number of cases in the pre-adolescent and adolescent groups was similar. Moreover, 64.9% of the participants (n=159) had a nuclear family structure. There was a significant difference in family characteristics between the pre-adolescent and adolescent periods. According to post-hoc analyses, fragmented families were significantly more common during adolescence compared to pre-adolescence. Peer abuse was significantly higher in the adolescent period compared to the pre-adolescent period. The age of the suspect was significantly different between groups. Post-hoc analyses indicated that adult suspects were significantly higher during adolescence compared to pre-adolescence. Extra-family suspects were predominant in both age groups (n=162). No statistically significant difference existed in the suspects' identities among the victim age groups (Table 1).

Table 1. Relationship between the child's developmental stage and demographic characteristics

	Pre-adolescent group (n=124)	**Adolescence group (n=121)**	***p*[1]**	***Post-hoc p-values***	
	n (%)	**n (%)**			
Family characteristics					
Elementary	88 (71.0)	71 (58.7)	**.019**	El vs. Ex	.860
Extended	16 (12.9)	12 (9.9)		El vs. Fr	**.007**
Fragmented	20 (16.1)	38 (31.4)		Ex vs. Fr	**.046**
Age of the suspect					
6-12 years (pre-adolescent)	31 (28.4)	14 (12.3)	**<.001**	6-12 vs. 13-18	.191
13-18 years (adolescent)	35 (32.1)	27 (23.7)		6-12 vs. >18	**<.001**
> 18 years (adult)	43 (39.4)	73 (64.0)		13-18 vs. >18	**.013**
Profile of the suspect					
Extra-family[2]	82 (66.1)	80 (66.1)	.359		
Domestic[3]	28 (22.6)	21 (17.4)			
Strangers	14 (11.3)	20 (16.5)			

[1] $p<0.05$; [2] Extra-family: Friends, acquaintances, partners, teachers, dormitory staff, etc.
[3] Biological or stepfathers, biological or step-siblings, uncles, aunts, grandfathers, and their children.

The incidence of sexual abuse occurred in public settings for 33.9% of adolescents (n=41) and in outdoor settings for 33.9% of pre-adolescents (n=42). There was no significant difference between the groups regarding the location of the incidents. However, there was a statistically significant difference in the reporting profile of those reporting the incidents before and after adolescence. According to post-hoc analyses, family reporting was significantly higher during pre-adolescence compared to adolescence.

There was a statistically significant difference between age groups regarding the person to whom the incident was first disclosed. The pre-adolescent group more frequently disclosed the abuse to family members (n=77; 62.1%), while the adolescent group disclosed the abuse more often to non-family members (n=80; 66.1%). Characteristics specific to sexual abuse are presented in Table 2. In our study, multiple suspects were relatively rare (n=28; 11.4%), and nearly half of the cases (n=111; 45.3%) involved recurrent abuse. However, the majority of sexual abuse cases involved non-penetrative contact (n=141; 55.5%). Factors such as threats, fear, shame, mutual sexual activity, or receiving money or gifts contributed to delayed reporting. There was no statistically significant difference between age groups regarding the type of sexual abuse, number of suspects, repetition of abuse, and factors delaying reporting. However, there was a statistically significant difference in the reliability of statements about abuse between the groups. Statements from the pre-adolescent group were less reliable than those from the adolescent group. Male adolescents reported sexual abuse later than pre-adolescent boys. Physical, emotional, and psychological changes in children who are victims of sexual abuse are presented in Table 3.

Table 2. Comparison of Characteristics of Sexual Abuse among Groups

	Pre-adolescent	**Adolescent**			
	n (%)	**n (%)**	***p***	***Post-hoc p-values***	
Scene of the incident					
Victim's own home	30 (24.2)	23 (19.0)			
Public places (school, place of worship, Quran course, dormitory)	28 (22.6)	41(33.9)	.166		
Outdoor areas (park, garden, forest)	42 (33.9)	31 (25.6)			
Perpetrator's home	24 (19.4)	26 (21.5)			
The person reporting the abuse					
Parents	71 (57.3)	49 (40.5)	**.026**	Pa vs. Te	**.048**
Teachers	34 (27.4)	42 (34.7)		Pa vs. Ot.	**.016**
Others[1]	19 (15.3)	30 (24.8)		Te vs. Ot.	.051
The first person to whom the child disclosed the abuse					
Domestic	77 (62.1)	41 (33.9)	**<.001**		
Extra-family[2]	47 (37.9)	80 (66.1)			
Type of sexual abuse					
Contact with penetration	43 (34.6)	38 (31.4)	.715		
Non-penetrating contact	71 (57.3)	70 (57.9)			
Verbal (non-contact)	10 (8.1)	13 (10.7)			
Repetition of abuse					
None	70 (56.5)	64 (52.9)	.333		
Present	54 (43.5)	57 (47.1)			
Multiple suspects					
None	110 (88.7)	107 (88.4)	.552		
Present	14 (11.3)	14 (11.6)			
Time elapsed until the incident's disclosure					
Early reporting (first 72 hours)	49 (55.1)	35 (36.8)	**.013**		
Delayed reporting (>72 hours)	40 (44.9)	60 (63.2)			
The factors delaying the disclosure					
Reported immediately	36 (36.4)	36 (40.4)			
Threat	21 (21.2)	16 (18.0)			
Fear (fear of harm to oneself or being misunderstood)	19 (19.2)	13 (14.6)			
No abuse, just an allegation	9 (9.1)	5 (5.6)	.645		
Shame	3 (3.0)	7 (7.9)			
Mutual sexual activity	6 (6.1)	4 (4.5)			
Receiving money/gifts	3 (3.0)	5 (5.6)			
Reported but not believed	2 (2.0)	3 (3.4)			
Procedures performed in the center					
Only foresic examination	29 (23.4)	30 (24.8)			
Only mental examination	7 (5.6)	4 (3.3)	.267		
Both forensic and mental examination	9 (7.3)	3 (2.5)			
No consultation requested (only forensic interviews)	79 (63.7)	84 (69.4)			

[1] Others: Hospital reports, law enforcement identifications, neighbor reports, witness statements

[2] Extra-family: friends, neighbors, state empleyees

Table 3. Observed behavioral changes in child victims of sexual abuse

	n	%
No data	154	55.5
Fear of the suspect	38	13.8
Emotional changes[1]	38	13.8
Physiological changes[2]	23	8.3
Displaying risky behaviors[3]	10	3.6
Reluctance to go to school/Decreased academic performance	7	2.5
Increased interest in males/Sexual orientation uncertainty	6	2.1
Total	276***	100

*** More than one behavioral change can be observed in a child. Therefore, the number n exceeds the sample size.

[1] Aggression, emotionally withdrawn, social withdrawal, inertia, feel unwell, shame, hyperactivity

[2] Sleep problems, eating problems, enurezis/encopresis;

[3] Increased interest in sexuality, self-destructive behavior, alcohol/substance abuse, suicide attempt

DISCUSSION

While awareness of child sexual abuse has been increasing in our country, studies explicitly focusing on boys remain scarce. This research explores the sociodemographic and abuse-related characteristics of boys who are victims of sexual abuse, comparing pre-adolescent and adolescent periods. The present study contributes to understanding the characteristic features of sexual abuse among preadolescent and adolescent boys. Although the subset of boys who are victims of sexual abuse in our study represents only a tiny portion of all abuse victims, the results provide significant insights into the experiences of boys, adding valuable data to the existing body of knowledge.

The study found statistically significant differences between preadolescent and adolescent boys regarding family characteristics, the suspect's age, the person reporting the incident, the initial disclosure recipient, and the reporting time to authorities. Furthermore, factors such as threat, fear, and shame contributed to the delayed reporting of incidents.

In our investigation, the age group most susceptible to sexual abuse was the pre-pubertal stage. A comprehensive study focusing on sexual abuse of boys highlighted that this form of abuse was predominantly prevalent among children aged 8 to 12 years (25). Similarly, another study indicated that boys faced a higher risk of sexual abuse during the ages of 9 to 12 years (18,26–28). Notably, the average age of the cases in our study was 11.04±3.39 years. These findings align with the existing body of literature, underscoring the vulnerability of pre-adolescent children to sexual abuse.

Our study revealed that boys predominantly experienced non-penetrative contact. While some studies suggest that boys are more often subjected to acts involving penetration (18,25), others have indicated frequent exposure to non-penetrative acts (28). The variation in findings across studies could stem from differences in sample size, age distribution within the sample, or the location from which the sample was drawn.

In the study, most suspects were found to be non-family members. Some studies have reported that perpetrators are mostly known to the victim or the victim's family (29). However, there are also studies suggesting that perpetrators from outside the family are predominant (30). The findings underscore the complexity of perpetrator-victim relationships and highlight the need for further research to better understand the dynamics of familial and non-familial perpetration.

Adolescents who are victims of sexual abuse tend to disclose their negative experiences to peers (31) or professionals (31,32). As adolescents' language and cognitive abilities develop, they become less reliant on their parents, contributing to interactions with individuals outside the family, such as teachers, friends, police, neighbors, and others. In our study, the adolescents' initial disclosure of their experience of sexual abuse to someone outside the family was associated with this developmental shift.

It has been noted that only a small percentage of sexual abuse victims can immediately articulate their negative experiences, with a significant time gap often existing between the occurrence of abuse and its disclosure (18,33). Early reporting rates in children and adolescents vary between 26.4% and 58.5%, while delayed reporting rates range from 15% to 65.4% (12,32,34). The literature attributes this variability in reporting time to individual, familial, and cultural factors (24), as well as age, gender, the identity of the perpetrator, and the severity of the abuse (35). Our study revealed that adolescents tend to report later than children. The fear of being stigmatized as homosexual or the experience of threats might have contributed to the delayed reporting by adolescents. On the other hand, disclosing in public places may facilitate disclosure when there are multiple victims. However, if the victim is alone or unaware of other victims, they may choose not to disclose, contributing to delayed reporting.

There is an emphasis on the underreporting of sexual abuse experienced by boys (36). Reasons for non-disclosure by boys include the fear of re-victimization, threats, the stigma of being labelled as gay, fear of not being believed, and feelings of guilt and shame (24,29,37). Another study revealed

that perpetrators gave gifts or money to male victims to keep their interactions secret, threatening harm to them and their families (38). In our study, although no significant difference was observed between groups, factors such as threats, fear, and delayed realization of the abuse hindered reporting. In the study, the primary barriers to disclosure were threat and fear. Boys may have delayed reporting to prevent harm to themselves and their families.

Child sexual abuse can lead to various physical, emotional, and psychological impairments in the child. Studies have reported that boys who have experienced sexual abuse exhibit lower academic performance and engage in riskier behaviors (such as running away from home, suicide attempts, alcohol, and substance use) compared to those who have not experienced abuse (26,39). The study identified that victims experienced fear of the perpetrator, withdrawal, and shame and exhibited sleep and eating disturbances. Furthermore, victims showed academic underachievement, suicide attempts, and alcohol/substance use. The results of our study align with the existing literature. Accurately detecting changes in behavior in children can expedite the disclosure of the incident.

A comprehensive study on male child sexual abuse reported that the most common locations of incidents were the home of the victim or perpetrator, followed by outdoor settings such as parks, gardens, or forests (27). Another large-scale study demonstrated that boys were more likely to experience sexual abuse in their own homes or the perpetrator's home (30). In our study, however, the majority of the abuse incidents occurred in outdoor settings like parks, gardens, or forests. Our findings differed from other results in the literature. This discrepancy may be attributed to the predominance of non-family suspects in our study.

The age factor is crucial in the occurrence of sexual abuse and the reliable expression of victims (40,41). It has been reported that in forensic interviews, younger children may provide less detailed and shorter answers compared to older children, negatively impacting the reliability of their statements (42). Another study suggested that younger children might lack the language and cognitive development skills to understand or convey what happened to them (43). In our study, statements from adolescents were generally deemed reliable, while in the pre-adolescent group, the presence of abuse was considered doubtful. The better ability of adolescents to express themselves, coupled with higher knowledge, perception, and awareness levels regarding sexual abuse, may have positively influenced the reliability of their statements.

Limitations and Strengths: The study should be interpreted considering its limitations. This research includes cases from the Child Advocacy Center in the Turkish province, where forensic interviews were conducted. Therefore, the results may be limited to children who sought services at this center, and more data might be required for generalizations. Additionally, subjective assessments, such as observed behavior changes, may impact the interpretation of research results. Furthermore, the study cannot encompass the perspectives of the children. Finally, cases of child sexual abuse are often subject to reporting issues, and therefore, the results of this study may not reflect the entirety of actual cases.

Studies in the literature often focus on adult samples investigating experiences of childhood sexual abuse. Studies specifically targeting the child and adolescent group, mainly focusing on males, are limited in Turkey. This comprehensive retrospective study, conducted at the local Child Advocacy Center and encompassing the files of 245 boys, represents a significant database. The study provides valuable information about the demographic characteristics of sexually abused boys, the type of abuse, locations of incidents, reporting times, and other critical factors. Moreover, by comparing different age groups, specifically pre-adolescence and adolescence, the study aids in understanding the experiences of children in different age ranges. This research not only contributes significantly to the literature on sexual abuse in boys but also outlines potential limitations for future research in this field.

CONCLUSION

The current study underscores the importance of considering factors such as the suspect's age, the victim's family structure, the individuals to whom the incident was first disclosed, the reporters of the forensic notification, and the duration until forensic reporting, particularly during the critical developmental stages of pre-adolescence and adolescence. Moreover, our findings shed light on the significant role of threat and fear as primary factors contributing to the delay in disclosure. This study contributes valuable insights into understanding the dynamics of child sexual abuse, highlighting the need for targeted interventions and support systems tailored to the unique needs of victims during different developmental stages, thus enriching the existing literature on this pressing public health issue.

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RESEARCH ARTICLE

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The Prevalence of Anxiety, Depression, Insomnia, and Post-Traumatic Stress Symptoms Among Healthcare Workers After the COVID-19 Vaccinations

ABSTRACT

Objective: The purpose of this study was to determine the frequencies of depression, anxiety, insomnia, and post-traumatic stress disorder (PTSD) symptoms among healthcare workers (HCWs) in Turkey after the COVID-19 vaccinations and to evaluate the associated factors.

Methods: A cross-sectional online survey was conducted in Turkey between November and December 2021. We used a demographic data form, COVID-19 vaccination status, the Patient Health Questionnaire-9, General Anxiety Disorder-7, the Insomnia Severity Index, and the National Stressful Events Survey post-traumatic stress disorder (PTSD) Short Scale.

Results: A total of 1013 HCWs participated in the study. Women constituted 68.5% of the participants, 65.4% were physicians, 32.5% had histories of COVID-19, and 98.0% had received at least one dose of the COVID-19 vaccine. Depressive symptoms were exhibited by 50.3% of the HCWs, while 35.7% exhibited anxiety, 44.6% insomnia, and 12.0% PTSD symptoms. Nurses reported significantly greater depression ($p<0.001$), anxiety ($p<0.001$), insomnia ($p<0.001$), and PTSD ($p<0.001$) symptoms than physicians did. No statistically significant association was determined in terms of the reporting of depression, anxiety, insomnia, and PTSD symptoms and receipt of COVID-19 vaccination.

Conclusions: The prevalence of depression, anxiety, insomnia, and PTSD symptoms among health workers decreased from the beginning of the pandemic, although the prevalence of these symptoms was still high. Nurses exhibited greater depressive, anxiety, insomnia, and PTSD symptoms than physicians. Receipt or non-receipt of vaccination, or the number of doses involved, caused no difference in terms of mental health.

Keywords: COVID-19, Physicians, Nurses, Anxiety, Depression, Insomnia, PTSD.

COVID-19 Aşılamaları Sonrasında Sağlık Çalışanları Arasında Anksiyete, Depresyon, Uykusuzluk ve Travma Sonrası Stres Bozukluğu Semptomlarının Sıklığı

ÖZET

Amaç: Bu çalışmanın amacı, COVID-19 aşılamaları sonrasında Türkiye'deki sağlık çalışanları arasında depresyon, anksiyete, uykusuzluk ve travma sonrası stres bozukluğu (TSSB) semptomlarının sıklığını belirlemek ve ilişkili faktörleri değerlendirmektir.

Yöntem: Kasım ve Aralık 2021 tarihleri arasında Türkiye'de kesitsel bir çevrimiçi anket gerçekleştirilmiştir. Demografik veri formu, COVID-19 aşılama durumu, Hasta Sağlığı Anketi-9, Genel Anksiyete Bozukluğu-7, Uykusuzluk Şiddet İndeksi ve Ulusal Stresli Olaylar Anketi Travma Sonrası Stres Bozukluğu (TSSB) Kısa Ölçeği kullanılmıştır.

Bulgular: Çalışmaya toplam 1013 sağlık çalışanı katılmıştır. Katılımcıların %68,5'ini kadınlar, %65,4'ünü doktorlar, %32,5'ini COVID-19 geçmişi olanlar ve %98,0'ını en az bir doz COVID-19 aşısı olanlar oluşturmuştur. Sağlık çalışanlarının %50,3'ü depresif semptomlar gösterirken, %35,7'si anksiyete, %44,6'sı uykusuzluk ve %12,0'si TSSB semptomları sergilemiştir. Hemşireler doktorlara göre anlamlı derecede daha fazla depresyon ($p<0,001$), anksiyete ($p<0,001$), uykusuzluk ($p<0,001$) ve TSSB ($p<0,001$) semptomları bildirmiştir. Depresyon, anksiyete, uykusuzluk ve TSSB semptomlarının bildirilmesi ile COVID-19 aşısının alınması arasında istatistiksel olarak anlamlı bir ilişki tespit edilmemiştir.

Sonuç: Sağlık çalışanları arasında depresyon, anksiyete, uykusuzluk ve TSSB semptomlarının yaygınlığı pandeminin başlangıcından itibaren azalmakla birlikte, bu semptomların yaygınlığı hala yüksektir. Hemşirelerde depresyon, anksiyete, uykusuzluk ve TSSB semptomları hekimlere göre daha yüksekti. Aşı olup olmama ya da aşı dozu sayısı ruh sağlığı açısından bir fark yaratmamıştır.

Anahtar Kelimeler: COVID-19, Doktorlar, Hemşireler, Anksiyete, Depresyon, Uykusuzluk; PTSD.

INTRODUCTION

During the COVID-19 pandemic, healthcare workers (HCWs) encountered significant stress concerning exposure to the disease, anxiety regarding the transmission of the infection to their families, insufficient personal protective equipment, new shifts, working areas, and difficult decisions concerning the allocation of limited resources. Almost half of the HCWs encounter potentially morally injurious events (1). Working conditions were found to play an important role in COVID-19 deaths, particularly in occupations requiring contact with patients or the public (2). Higher rates of infection, hospitalization, and admission to the intensive care unit were found among HCWs with COVID-19 than those without (3). In one systematic review examining COVID-19 infection and deaths among HCWs in 195 countries, the general infection and mortality rates among HCWs were comparable to those of the general population. Infections were largely observed among women, although deaths occurred primarily among men. COVID-19-related infections occurred mostly in nurses, while deaths occurred mostly in doctors (4).

Effective vaccines or drugs were required in order to reduce COVID-19-related mortality. The first vaccines were applied worldwide by the end of 2020. One study performed at the beginning of the COVID-19 vaccination campaign described the idea that the COVID-19 vaccine would put an end to the pandemic among health workers as an important source of motivation (5). COVID-19 vaccination in Turkey was first administered to HCWs in the high-risk group in January 2021. HCWs began receiving CoronaVac and, subsequently, BioNTech vaccines. Homogenous and heterologous vaccinations are safe and effective (6-9). Although protection against infection and mild disease decreased in the months following vaccination, the effectiveness against severe disease and hospitalization remained high. However, declining immunity and circulation of SARS-CoV-2 variants have revealed the need for booster doses (10-14).

Although nurses exhibited lower levels of anxiety and depression following the COVID-19 vaccination compared to the pre-vaccination period, the COVID-19 vaccine was found to exhibit only a minimal association with nurses' mental health (15). A survey study repeated 12 times between January and July 2021 revealed small but significant associations between COVID-19 vaccination and mental health difficulties in adults. Initially, the non-vaccinated group reported more anxiety symptoms, but over time, anxiety symptoms decreased and became similar in the vaccinated and non-vaccinated groups Similarly, while there was a difference in depressive symptoms at first, there was no difference in depressive symptoms between vaccine and non-vaccine recipients over time (16).

HCWs on the frontline in the fight against the pandemic experienced considerable physical, psychological, and mental exhaustion during this period. The severity of mental health problems among HCWs increased between January and September 2020 (17). The first step in the provision of mental health and effective psychological interventions involves screening the mental health status of at-risk groups. One study performed in Turkey in the early stage of the COVID-19 pandemic reported prevalences of depressive, anxiety, insomnia, and post-traumatic stress disorder (PTSD) symptoms among HCWs of 77.6%, 60.2%, 50.4%, and 76.4%, respectively (18). These rates are considerably higher than those reported in several other studies from across the world (19-22). Limited numbers of studies have evaluated the psychological status of HCWs during this period when problems experienced at the outset of the pandemic decreased, the rate of COVID-19-related deaths decreased, protective measures such as lockdowns were discontinued, and COVID-19 vaccination coverage rates increased significantly. Determining the frequency of psychological problems among HCWs in light of the changing dynamics during the ongoing pandemic in Turkey will be useful in clarifying the long-term support needs of the healthcare workforce. This is because different conditions have emerged in all countries during the pandemic. It will therefore be useful to identify the factors capable of resulting in differences in the psychological status of HCWs in Turkey. For example, although not all HCWs were on the frontline, they enjoyed priority access to the COVID-19 vaccines. It will, therefore, be useful, in terms of the planning of future psychological interventions, to determine whether this priority access resulted in any difference among HCWs in psychological terms. The present study aimed to determine the frequencies of depression, anxiety, insomnia, and PTSD among HCWs in Turkey after the COVID-19 vaccinations and to evaluate the associated factors.

MATERIAL AND METHODS

This cross-sectional study was performed in Turkey between October 15 and November 15, 2021. Approximately 120,000 HCWs are employed in public, university, and private hospitals in Turkey. A minimum sample size of 385 individuals was calculated at 95% reliability, 5% margin of error, and 50% likelihood. HCWs (physicians, nurses, physiotherapists, audiologists, dieticians, language and speech therapists, radiotherapy technicians, anesthesia technicians, medical laboratory technicians, emergency medical technicians, psychologists, and medical secretaries) aged over 18 years and consent to participate were included. Permission for this study was obtained from the Turkish Ministry of Health Scientific

Research Platform. This study was approved by the Ondokuz Mayıs University Clinical Research Ethics Committee (OMUKAEK 2021/473).

The study data were collected using a questionnaire via Google Forms. The questionnaire was sent to e-mail groups via WhatsApp groups. Data were collected using the snowball method, which is generally used for unknown populations. A section at the beginning of the questionnaire provided information concerning the aim of the research, length of the survey, identities of the authors, and confidentiality of the data. Informed consent was obtained online before participants completed the questionnaire. The 'only permit one reply per user' option was selected in order to prevent the same individual from completing it more than once. There were no missing data since every question had to be answered.

The questionnaire contained questions on sociodemographic characteristics (age, sex, marital status, working years, and history of chronic disease), history of COVID-19, death among loved ones due to COVID-19, working on the frontline at any time during the COVID-19 pandemic, COVID-19 vaccination status, the effect of COVID-19 vaccination on mental state, the Patient Health Questionnaire-9, General Anxiety Disorder-7, the Insomnia Severity Index, and the National Stressful Events Survey PTSD Short Scale.

Patient Health Questionnaire-9 (PHQ-9): This questionnaire was used to perform a psychological evaluation of the problems experienced by individuals in the previous 12 weeks and the extent to which they were distressed. This four-point Likert-type scale consisted of nine items. Depression severity was classified as none or minimal (scores of 0-4), mild (scores of 5-9), moderate (score of 10-14), moderately severe (scores of 15-19), or severe (scores of 20-27). The cut-off score was 10. Depression should be investigated and confirmed among individuals scoring 10 or higher (23, 24).

General Anxiety Disorder-7 (GAD-7): This short self-report form was used to evaluate generalized anxiety disorders. It consists of seven items scored on a four-point Likert-type scale. Anxiety severity was categorized as none or minimal (scores of 0-4), mild (scores of 5-9), moderate (scores of 10-14), or severe (scores of 15-21). The cut-off score was 10. Anxiety should be investigated and confirmed in individuals scoring 10 or higher (25, 26).

Insomnia Severity Index (ISI): This short self-report questionnaire was used to evaluate insomnia. It contains seven items scored on a five-point Likert scale. The severity of insomnia was classified as none or minimal (scores of 0-7), mild (scores of 8-14), moderate (scores of 15-21), or severe (scores of 22-28). The cut-off score was 10. Insomnia should be investigated and confirmed in individuals scoring 10 or more (27-29).

National Stressful Events Survey PTSD Short Scale (PTSD-SS): This scale was developed by Kilpatrick et al.. and adapted into Turkish by Evren et al. This scale was employed to evaluate PTSD and measure its severity. It consists of nine items rated on a five-point Likert-type scale. Possible scores range between 0 and 36, with scores of 24 or higher being regarded as significant for PTSD (30, 31).

Statistical Analysis: Data were analyzed using IBM SPSS Statistics version 22 software and expressed as numbers, percentages, means, and standard deviations. Age and working years were categorized according to previous studies (32, 33). The chi-square test was used to compare categorical data. Data were evaluated using normality tests and charts. Non-normally distributed data were compared using the Kruskal-Wallis test. Multivariate logistic regression analysis was also performed. Odds ratios (OR) and 95% confidence intervals (CIs) were presented. Statistical significance was set at $p < 0.05$.

RESULTS

One thousand thirteen HCWs took part in this study. Analysis showed that 60.4% were aged 26-40, 68.5% were women, 68.0 were married, 76.5% had been working for 20 years or less, and 12.5% had a history of chronic disease. In addition, 32.5% of HCWs had histories of COVID-19 infection, 34.8% had lost a loved one to the disease, and 67.8% had worked on the frontline during the COVID-19 pandemic. In addition, 58.7% of HCWs believed that COVID-19 vaccination had a positive impact on health workers' mental states. Ninety-eight percent of HCWs received at least one dose of the COVID-19 vaccine (Table 1).

The analysis showed that 50.3% of the HCWs exhibited symptoms of depression, 35.7% had symptoms of anxiety, 44.6% had insomnia, and 12.0% had PTSD. Depressive symptoms were reported by 63.6% of nurses, 51.8% of allied health professionals (AHPs), and 45.9% of physicians. Physicians reported a lower rate of depressive symptoms than nurses did ($p<0.001$). A higher rate of severe depression was reported by nurses and AHPs ($p<0.001$). The nurses' mean PHQ-9 scores were significantly higher than those of physicians ($p<0.001$). Anxiety symptoms were reported by 45.0% of the nurses, 36.2% of the AHPs, and 32.7% of the physicians. A higher rate of severe anxiety symptoms was reported by physicians compared to nurses ($p<0.006$). A higher rate of anxiety symptoms was reported by nurses and AHPs ($p<0.001$). Nurses registered significantly higher mean GAD-7 scores than physicians ($p<0.001$). Insomnia symptoms were reported by 61.2% of the nurses, 47.5% of the AHPs, and 38.8% of the physicians. Physicians reported a lower rate of insomnia symptoms than nurses ($p<0.001$).

Table 1. Characteristics of the participants (n=1013)

Variables	Categories	n(%)
Age group	≤25 years	95(9.4)
	26-40 years	612(60.4)
	>40 years	306(30.2)
Sex	Male	319(31.5)
	Female	694(68.5)
Marital Status	Unmarried	324(32.0)
	Married	689(68.0)
Occupation	Nurses	209(20.6)
	Allied Health Professions	141(13.9)
	Physicians	663(65.4)
Working years	≤20 years	775(76.5)
	>20 years	238(23.5)
History of chronic disease	No	886(87.5)
	Yes	127(12.5)
History of COVID-19 diagnosis	No	684(67.5)
	Yes	329(32.5)
Having a loved one who died due to COVID-19	No	660(65.2)
	Yes	353(34.8)
Working on the frontline at any time during the COVID pandemic	No	326(32.2)
	Yes	687(67.8)
Believing that COVID-19 vaccination has a positive effect on the mental state of HCWs	No	418(41.3)
	Yes	595(58.7)
Receipt of COVID-19 vaccination	No	20(2.0)
	Yes	993(98.0)
COVID-19 vaccine doses	Not vaccinated	20(2.0)
	1 dose Sinovac	5(0.5)
	1 dose Biontech	10(1.0)
	1 dose Sinovac+1 dose Biontech	4(0.4)
	2 doses Sinovac	70(6.9)
	2 doses Biontech	92(9.1)
	1 dose Sinovac+2 doses Biontech	14(1.4)
	2 doses Sinovac+1 dose Biontech	346(34.2)
	3 doses Sinovac	97(9.6)
	2 doses Sinovac+2 doses Biontech	355(35.0)

A higher rate of severe insomnia symptoms was observed among nurses and AHPs ($p<0.001$). Nurses registered higher mean ISI scores than physicians ($p<0.001$). PTSD symptoms were reported by 18.7% of the nurses, 17.0% of the AHPs, and 8.9% of the physicians. Physicians reported a lower rate of PTSD symptoms than nurses and AHPs ($p<0.001$). Nurses' mean PTSD-SS scores were significantly higher than those of physicians ($p<0.001$) (Table 2).

Higher rates of depressive symptoms were observed among participants aged ≤25 years ($p<0.001$), women ($p<0.001$), unmarried individuals ($p=0.023$), those with ≤ 20 years of working experience ($p=0.019$), and those who thought that COVID-19 vaccination had no positive effect on HCWs' mental state ($p=0.002$). Higher rates of anxiety symptoms were reported among participants aged ≤25 years ($p=0.002$), women ($p=0.002$), those with 20 years' or less working experience ($p=0.02$), and those who had worked on the frontline at any time during the COVID-19 pandemic ($p=0.014$). Higher rates of insomnia symptoms were reported by individuals who had lost a loved one due to COVID-19 ($p=0.01$), those who had worked on the frontline at any time during the COVID-19 pandemic ($p=0.013$), and those who stated that COVID-19 vaccination had no positive impact on HCWs' mental state ($p=0.012$). Finally, higher rates of PTSD symptoms were reported by women ($p=0.030$), individuals with a chronic disease ($p=0.025$), individuals who had lost a loved one due to COVID-19 ($p=0.034$), and those who stated that the COVID-19 vaccination had no positive impact on HCWs' mental state ($p<0.001$). No statistically significant association was found between COVID-19 vaccination and the reporting of depression, anxiety, insomnia, or PTSD symptoms (Table 3).

Table 2. The presence of symptoms and the severity thereof according to PHQ-9, GAD-7, ISI, and PTSD-SS, and a comparison of those scores

			Nurses	AHPs	Physicians	Total	
			n=209	n=141	n=663	n=1013	
Variables	**Categories**	**Cut-off**	**n(%)**	**n(%)**	**n(%)**	**n(%)**	**p**
Depression Symptoms	Absent	<10	76(36.4)	68(48.2)	359(54.1)	503(49.7)	**<0.001***
	Present	≥10	133(63.6)	73(51.8)	304(45.9)	510(50.3)	
Depressive Symptom Severity	Minimal or none	0-4	22(10.5)	27(19.1)	135(20.4)	184(18.2)	**<0.001***
	Mild	5-9	54(25.8)	41(29.1)	224(33.8)	319(31.5)	
	Moderate	10-14	59(28.2)	28(19.9)	163(24.6)	250(24.7)	
	Moderately severe	15-19	37(17.7)	24(17.0)	99(14.9)	160(15.8)	
	Severe	20-27	37(17.7)	21(14.9)	42(6.3)	100(9.9)	
PHQ-9 (Mean±SD)			12.6 ± 6.6^{a}	11.1 ± 7.0^{ab}	9.7 ± 5.9^{b}	10.5 ± 6.3	**<0.001****
Anxiety Symptoms	Absent	<10	115(55.0)	90(63.8)	446(67.3)	651(64.3)	**0.006***
	Present	≥10	94(45.0)	51(36.2)	217(32.7)	362(35.7)	
Anxiety Symptom Severity	Minimal or none	0-4	39(18.7)	34(24.1)	221(33.3)	294(29.0)	**<0.001***
	Mild	5-9	76(36.4)	56(39.7)	225(33.9)	357(35.2)	
	Moderate	10-14	45(21.5)	23(16.3)	145(21.9)	213(21.0)	
	Severe	15-21	49(23.4)	28(19.9)	72(10.9)	149(14.7)	
GAD-7 (Mean±SD)			9.8 ± 6.0^{a}	8.6 ± 5.9^{ab}	7.5 ± 5.4^{b}	8.1 ± 5.7	**<0.001****
Insomnia Symptoms	Absent	<10	81(38.8)	74(52.5)	406(61.2)	561(55.4)	**<0.001***
	Present	≥10	128(61.2)	67(47.5)	257(38.8)	452(44.6)	
Insomnia Symptom Severity	Minimal or none	0-7	63(30.1)	62(44.0)	343(51.7)	468(46.2)	**<0.001***
	Mild	8-14	69(33.0)	43(30.5)	208(31.4)	320(31.6)	
	Moderate	15-21	54(25.8)	23(16.3)	87(13.1)	164(16.2)	
	Severe	22-28	23(11.0)	13(9.2)	25(3.8)	61(6.0)	
ISI (Mean±SD)			12.2 ± 7.1^{a}	9.8 ± 7.4^{b}	8.4 ± 6.4^{b}	9.4 ± 6.8	**<0.001****
PTSD Symptoms	Absent	<24	170(81.3)	117(83.0)	604(91.1)	891(88.0)	**<0.001***
	Present	≥24	39(18.7)	24(17.0)	59(8.9)	122(12.0)	
PTSD-SS (Mean±SD)			14.9 ± 9.1^{a}	13.4 ± 9.3^{a}	10.9 ± 8.4^{b}	12.1 ± 8.8	**<0.001****

[a-b]: a-b: For all variables with the same letter, the difference between the means is not statistically significant.
*Chi-sqaure test, ** Kruskal-Wallis test
AHPs= Allied Health Professionals, SD=standart devaiation, PHQ-9 = Patient Health Questionnaire-9, GAD-7 = General Anxiety Disorder-7, ISI = Insomnia Severity Index, PTSD-SS = Post-Traumatic Stress Disorder Short Scale

Multivariate logistic regression analysis (forward LR) was performed with factors exhibiting significant variation in the univariate analysis. Factors affecting depression symptoms were identified as age, sex, and occupation. The factors affecting the reporting of anxiety symptoms were age, sex, occupation, and having worked on the frontline during the COVID-19 pandemic. The factors affecting the reporting of insomnia symptoms were losing a loved one due to COVID-19 and working on the frontline during the pandemic. Finally, factors affecting the reporting of PTSD symptoms were occupation, presence of chronic disease, and belief that COVID-19 vaccination had no positive effect on HCWs' mental state (Table 4).

DISCUSSION

In this study, in which coverage rates of COVID-19 vaccination among HCWs were high, 50.3% of HCWs exhibited symptoms of depression, 35.7% symptoms of anxiety, 44.6% symptoms of insomnia, and 12.0% symptoms of PTSD. One meta-analysis, including 239 workers from the beginning of the pandemic to March 2021, stated that 33% of HCWs exposed to COVID-19 reported depressive symptoms, 42% anxiety symptoms, 32% PTSD symptoms, and 42% insomnia symptoms (34). Cases of the major depressive disorder increased by 28% and cases of anxiety disorder increased by 26% in 204 countries and regions due to the COVID-19 pandemic. Daily SARS-CoV-2 infection rates and decreased human mobility were found to be associated with an increasing prevalence of major depressive disorder and anxiety disorder (35).

Women were more affected by the epidemic than men, and younger age groups were more affected than the older age group (35, 36).

Table 3. A comparison of depression, anxiety, insomnia, and post-traumatic stress according to the characteristics of the HCWs

Variables	Categories	Depressive Symptoms		p*	Anxiety Symptoms		p*	Insomnia Symptoms		p*	Posttraumatic Stress Symptoms		p*
		Absent	Present		Absent	Present		Absent	Present		Absent	Present	
		n(%)	n(%)		n(%)	n(%)		n(%)	n(%)		n(%)	n(%)	
Age group	≤25 years	30(31.6)	65(68.4)	**<0.001**	50(52.6)	45(47.4)	**0.002**	43(45.3)	52(54.7)	0.067	80(84.2)	15(15.8)	0.179
	26-40 years	297(48.5)	315(51.5)		384(62.7)	228(37.3)		338(55.2)	274(44.8)		534(87.3)	78(12.7)	
	>40 years	176(57.5)	130(42.5)		217(70.9)	89(29.1)		180(58.8)	126(41.2)		277(90.5)	29(9.5)	
Sex	Male	187(58.6)	132(41.4)	**<0.001**	227(71.2)	92(28.8)	**0.002**	189(59.2)	130(40.8)	0.093	291(91.2)	28(8.8)	**0.030**
	Female	316(45.5)	378(54.5)		424(61.1)	270(38.9)		372(53.6)	322(46.4)		600(86.5)	94(13.5)	
Marital Status	Unmarried	144(44.4)	180(55.6)	**0.023**	196(60.5)	128(39.5)	0.086	175(54.0)	149(46.0)	0.548	280(86.4)	44(13.6)	0.303
	Married	359(52.1)	330(47.9)		455(66.0)	234(34.0)		386(56.0)	303(44.0)		611(88.7)	78(11.3)	
Working years	≤20 years	369(47.6)	406(52.4)	**0.019**	483(62.3)	292(37.7)	**0.020**	423(54.6)	352(45.4)	0.356	674(87.0)	101(13.0)	0.081
	>20 years	134(56.3)	104(43.7)		168(70.6)	70(29.4)		138(58.0)	100(42.0)		217(91.2)	21(8.8)	
History of chronic disease	No	446(50.3)	440(49.7)	0.250	577(65.1)	309(34.9)	0.132	502(56.7)	384(43.3)	0.031	787(88.8)	99(11.2)	**0.025**
	Yes	57(44.9)	70(55.1)		74(58.3)	53(41.7)		59(46.5)	68(53.5)		104(81.9)	23(18.1)	
History of COVID-19 diagnosis	No	351(51.3)	333(48.7)	0.127	443(64.8)	241(35.2)	0.631	391(57.2)	293(42.8)	0.100	606(88.6)	78(11.4)	0.367
	Yes	152(46.2)	177(53.8)		208(63.2)	121(36.8)		170(51.7)	159(48.3)		285(86.6)	44(13.4)	
Having a loved one who died due to COVID-19	No	340(51.5)	320(48.5)	0.105	432(65.5)	228(34.5)	0.280	385(58.3)	275(41.7)	**0.010**	591(89.5)	69(10.5)	**0.034**
	Yes	163(46.2)	190(53.8)		219(62.0)	134(38.0)		176(49.9)	177(50.1)		300(85.0)	53(15.0)	
Caring for patients with COVID-19 at any time during the pandemic	No	175(53.7)	151(46.3)	0.077	227(69.6)	99(30.4)	**0.014**	199(61.0)	127(39.0)	**0.013**	293(89.9)	33(10.1)	0.196
	Yes	328(47.7)	359(52.3)		424(61.7)	263(38.3)		362(52.7)	325(47.3)		598(87.0)	89(13.0)	
Believing that COVID-19 vaccination has a positive effect on the mental state of HCWs	No	183(43.8)	235(56.2)	**0.002**	256(61.2)	162(38.8)	0.093	212(50.7)	206(49.3)	**0.012**	348(83.3)	70(16.7)	**<0.001**
	Yes	320(53.8)	275(46.2)		395(66.4)	200(33.6)		349(58.7)	246(41.3)		543(91.3)	52(8.7)	
Receipt of COVID-19 vaccination	No	13(56.5)	10(43.5)	0.505	17(73.9)	6(26.1)	0.329	16(69.6)	7(30.4)	0.166	20(87.0)	3(13.0)	0.751
	Yes	490(49.5)	500(50.5)		634(64.0)	356(36.0)		545(55.1)	445(44.9)		871(88.0)	119(12.0)	

*Chi-square

Table 4. Risk factors for depression, anxiety, insomnia, and post-traumatic stress among HCWs

Variables	Categories	p-value*	aOR (95% CI)
Depressive Symptoms			
Age groups	>40 years		Reference
	≤25 years	**<0.001**	2.553 (1.550-4.206)
	26-40 years	**0.002**	1.564 (1.174-2.085)
Sex	Male		Reference
	Female	**0.015**	1.419 (1.071-1.880)
Occupation	Physicians		Reference
	Nurses	**<0.001**	1.905 (1.353-2.684)
	AHPs	0.273	1.234 (0.848-1.796)
Anxiety Symptoms			
Age groups	>40 years		Reference
	≤25 years	**0.008**	1.927 (1.188-3.123)
	26-40 years	**0.016**	1.463 (1.075-1.991)
Sex	Male		Reference
	Female	**0.030**	1.394 (1.033-1.881)
Occupation	Physicians		Reference
	Nurses	**0.004**	1.664 (1.182-2.342)
	AHPs	0.103	1.414 (0.933-2.145)
Caring for patients with COVID-19 at any time during the pandemic	No		Reference
	Yes	**0.006**	1.547 (1.136-2.106)
Insomnia Symptoms			
Occupation	Physicians		Reference
	Nurses	**<0.001**	2.660 (1.919-3.688)
	AHPs	**0.005**	1.772 (1.190-2.638)
Having a loved one who died due to COVID-19	No		Reference
	Yes	**0.030**	1.343 (1.028-1.754)
Caring for patients with COVID-19 at any time during the pandemic	No		Reference
	Yes	**<0.001**	1.699 (1.265-2.282)
Posttraumatic Stress Symptoms			
Occupation	Physicians		Reference
	Nurses	**0.001**	2.161 (1.399-3.430)
	AHPs	**0.006**	2.080 (1.357-3.928)
History of chronic disease	No		Reference
	Yes	**0.015**	1.881 (1.056-2.962)
Believing that COVID-19 vaccination has a positive effect on the mental state of HCWs	Yes		Reference
	No	**0.001**	1.985 (1.313-2.873)

* multivariate logistic regression
aOR= Adjusted odds ratio, AHPs= Allied Health Professionals

A meta-analysis including studies from China determined a prevalence of insomnia symptoms of 37.0% before April 2020, during the early period of COVID-19, and of 41.8% after April 2020. No significant difference was found in terms of the prevalence of insomnia symptoms between the early and late stages of COVID-19. The prevalence of insomnia symptoms was higher among HCWs, patients with COVID-19, patients with chronic medical disorders, and those with mental disorders (37). In another meta-analysis, the prevalence of sleep problems during the COVID-19 pandemic was 24% in women and 27% in men. Although the highest prevalence was exhibited by COVID-19 patients of both sexes, HCWs, and the general population, no statistically significant differences were observed (38). Similarly, in the present study, insomnia symptoms were greater among women, although no significant gender differences were observed. Insomnia symptoms were significantly greater among nurses, individuals who had lost their loved ones due to COVID-19, and frontline workers. Younger age, female gender, working on the front line, fear or

risk of infection, the nursing profession, existing or previous mental health problems, and a low level of social support have been associated with a risk of sleep disorder and adverse psychological outcomes (39). Similarly, in the present study, anxiety, depression, insomnia, and PTSD symptoms were greater among nurses than physicians. Depression and anxiety were greater in young age and female gender. Anxiety levels were higher among individuals who worked with COVID-19 patients. PTSD symptoms were greater among individuals with chronic disease and those reporting that COVID-19 vaccination had no positive effect on their mental state. A meta-analysis, including cohort studies, reported a rapid increase in mental health problem symptoms at the onset of the pandemic, followed by a significant decrease in March-April 2020, and a subsequent statistically insignificant increase (40). Psychological distress among HCWs during the first wave of COVID-19 increased from March to May 2020, but remained high, at the same level, in August and November 2020, when there was no fluctuation in the pandemic (41). A study investigating the longitudinal effects of exposure among physicians (residents and clinical fellows) to patients tested for COVID-19 on stress, anxiety, depression, and burnout in three surveys conducted during the early phase of the pandemic (April-June 2020) reported that mean stress, anxiety, and burnout decreased by 21%, 25%, and 13%, respectively. However, mean stress, anxiety, and burnout increased in line with the number of patients tested for COVID-19 to whom participants were exposed (42). In another study, the prevalence of PTSD increased from 12.5% in 2019 to 18.0% in April 2020 and 22.0% in May, decreasing to 17.6% in December 2020 (43). A time-dependent decrease was observed in the high PTSD rates in the early period of the pandemic. A study from Turkey performed in the early period of the COVID-19 pandemic reported a prevalence of depression, anxiety, insomnia, and PTSD symptoms among HCWs of 77.6%, 60.2%, 50.4%, and 76.4%, respectively (18). Although the longitudinal effects could not be evaluated in the present study, it may be concluded that despite a decrease compared to the early periods of the pandemic, the symptoms of psychological problems still persist with a high frequency. Similar to the onset of the pandemic, the rate of reporting psychological symptoms was significantly higher among nurses than among physicians. However, it would not be appropriate to account for these rates, which are higher than those in many countries in terms of the pandemic. This is because there are more complex factors, including the increase in violence against HCWs in Turkey in recent years, physician murders, the very high number of cases treated on a daily basis, low salaries, and overseas-bound brain drains. The COVID-19 pandemic has been found to exhibit a deleterious effect on the mental health of individuals with existing psychiatric disorders, although no significant increase in symptom severity was observed compared to pre-pandemic levels (44). Although individuals with depressive, anxiety, or obsessive-compulsive disorder scored higher on the four-symptom scale than individuals without these psychological disorders both before and during the COVID-19 pandemic, they still reported no significant increase in symptoms during the pandemic. Individuals without depression, anxiety, or obsessive-compulsive disorder exhibited a greater increase in symptoms during the COVID-19 pandemic; individuals with the greatest burden on their mental health tended to exhibit a mild decrease in symptoms (45). The pandemic and the methods adopted because of it led to changes in individuals' daily routines, limited social interactions and tensions in families in lockdown together, and to a fear of catching the disease and/or spreading the virus. All of these factors result in adverse psychological outcomes. COVID-19 vaccines represent a source of hope that these processes will end. However, the effect of the COVID-19 vaccination on mental health remains controversial. COVID-19 vaccination has been lined to decreased anxiety and perceived infection, and a lower risk of mortality and hospitalization (46). A study from Bangladesh reported a lower frequency of general health problems, depression, PTSD, insomnia, and isolation symptoms among vaccinated HCWs compared to unvaccinated staff (47). However, COVID-19 vaccination appeared to have no effect on mental health among Japanese workers in the early stages of vaccination. There was no difference between healthcare and non-HCWs (48). Another study reported that while the association between vaccination and psychological distress was more pronounced in the early period of vaccine introduction, this difference subsequently disappeared (16). Although no long-term evaluation was performed in the present study, conducted on days when booster doses were administered, vaccination appeared to make no difference in terms of mental problems. This may be due to the expectation that COVID-19 vaccination would entirely eliminate the disease not having been met, the emergence of complementary vaccine doses, and the ongoing lack of an effective treatment. Additionally, factors such as COVID-19 case numbers, expected to rise in line with increased mobility, uncertainties concerning the protection afforded by the vaccine against COVID-19 mutations, and information pollution may also have prevented potential improvement in mental states.

Limitations: It is particularly important to collect high-quality data regarding the effects of the COVID-19 pandemic on mental health in the entire population and vulnerable groups. However, difficulties in data collection arising from the nature of the pandemic, the desire to access information

quickly by means of online questionnaires, and difficulties in collecting data traditionally from pre- and post-pandemic cohorts make it difficult to draw definitive conclusions concerning mental health (49). This represents a principal limitation of the present study. Due to the nature of survey studies, there is always the possibility of no-response bias. Other limitations can be sampling bias (the sample was not representative of all HCWs in Turkey), social desirability bias, potentially recall bias (severity dependent on the phrasing of questions), and other potential confounders (including the time-specific trajectory of the pandemic and degree of involvement in the workforce). Despite its advantages in terms of cost and productivity, it also has the disadvantage of being a nonrandom sampling technique (50). Finally, the participants did not attend clinical interviews about their mental states and were only evaluated based on their declarations made on the scales.

CONCLUSION

The frequency of depression, anxiety, insomnia, and PTSD symptoms among HCWs decreased compared to the beginning of the pandemic, although the prevalence of these symptoms is still high. Nurses exhibited greater depressive, anxiety, insomnia, and PTSD symptoms than physicians. Being vaccinated or unvaccinated or the number of doses of the vaccine received associated with no significant difference in terms of mental health.

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RESEARCH ARTICLE

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Effects of Walnut Septum on The Enzyme Pathways Associated with Plasma Cholesterol Level

ABSTRACT

Objective: Cholesterol is crucial compound that plays pivotal role in cellular function in living organisms. Its excess or deficiency in plasma can lead to destruction and disintegration of cell membrane structure. Maintaining balanced intake of cholesterol in diet and seeking medical treatment, if necessary, can help prevent these negative effects. Furthermore, people often resort to natural and herbal remedies, such as walnut septum. Due to dearth of scientific data regarding effects of walnut septum on cholesterol metabolism, this research was undertaken to explore its potential effects.

Methods: Analysis was begun by extracting septum using various solvents. Resulting extracts were then analyzed using GC-MS, and compounds were identified by using an integrated library database. To detect effects of extracts on cholesterol esterase and HMG-CoA reductase, a colorimetric method was employed.

Results: Monophenol, 2,4-Di-tert-butylphenol, 2,6-Di-tert-butylphenol, ethyl linoleate, and butyl linoleate were some of compounds detected by GC-MS scanning. The highest inhibitions were observed in the enzymatic analysis, with a rate of 3.2% (acetone) in the HMG-CoA reductase analysis and 13.6% (water) in the cholesterol esterase analysis.

Conclusions: Although the walnut septum extract contains various chemical compounds, our in vitro analysis data suggest that there is no inhibitory effect at therapeutic level on enzyme pathways that regulate plasma cholesterol levels, namely HMG-CoA reductase and cholesterol esterase. We believe that further research is necessary to comprehensively evaluate its effects on other pathways.

Keywords: Walnut Septum, HMG-CoA Reductase, Cholesterol Esterase, GC-MS.

Ceviz Septumunun Plazma Kolesterol Düzeyi ile İlişkili Enzim Yolakları Üzerine Etkileri

ÖZET

Amaç: Kolesterol, canlı organizmaların hücresel fonksiyonunda rol oynayan önemli bir bileşiktir. Kan plazmasındaki fazlalığı veya eksikliği, hücre zar yapısının tahribine ve parçalanmasına neden olabilmektedir. Diyette, dengeli kolesterol alımını sürdürmek ve gerekirse tıbbi tedavi almak, bu olumsuz etkilerin önlenmesine yardımcı olabilir. Ayrıca, halk arasında genellikle ceviz septumu gibi doğal ve bitkisel tedavilere başvurulmaktadır. Ceviz septumunun kolesterol metabolizması üzerindeki etkilerine ilişkin bilimsel verilerin yetersizliği nedeniyle, bu araştırma potansiyel etkilerini araştırmak için yapılmıştır.

Yöntem: Analiz, çeşitli çözücüler kullanılarak septumun ekstrakte edilmesiyle başlatıldı. Elde edilen ekstraktlar daha sonra GC-MS'te analiz edildi ve bileşikler, entegre kütüphane veri tabanı kullanılarak tanımlandı. Ekstraktların kolesterol esteraz ve HMG-CoA redüktaz üzerindeki etkilerini saptamak için kolorimetrik yöntem kullanıldı.

Bulgular: GC-MS taraması ile tespit edilen belirgin bileşikler arasında monofenol, 2,4-Di-tert-bütilfenol, 2,6-Di-tert-bütilfenol, etil linoleat ve bütil linoleate bulunmaktadır. HMG-CoA redüktaz analizinde en yüksek inhibisyon %3,2 oranıyla aseton ekstraktında gözlenirken kolesterol esteraz analizinde %13,6 oranıyla sulu ekstrakta gözlendi.

Sonuç: Ceviz septum ekstraktı, çeşitli kimyasal bileşikler içermesine rağmen, plazma kolesterol seviyelerini düzenleyen enzim yolaklarından HMG-CoA redüktaz ve kolesterol esteraz üzerinde, in vitro olarak, terapötik seviyede inhibitör etkisinin olmadığını göstermektedir. Diğer yollar üzerindeki etkilerini kapsamlı bir şekilde değerlendirmek için daha fazla araştırmanın gerekli olduğuna inanmaktayız.

Anahtar Kelimeler: Ceviz Septum, HMG-CoA Redüktaz, Kolesterol Esteraz, GC-MS.

INTRODUCTION

Recently, new cholesterol drugs have been investigated by screening inhibitors of transmembrane protein Hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase, which facilitates transformation of HMG-CoA to mevalonate the critical point of control in cholesterol production (1). In addition, research on inhibitors of cholesterol esterase (CE), which plays a role in absorption of cholesterol and other lipids from the intestines, is also underway (2). One of the most critical factors in exploring these drugs; cholesterol is an essential molecule for stability of cell membrane structure. Thus, its amount must be kept within narrow limits (3). When there is excess or deficiency of cholesterol in plasma and other tissues, it can lead to destabilization of the cell membrane and disruption of apoptosis and necrosis mechanisms (4). Hypercholesterolemia leads to decrease in membrane viscosity, impairs selective permeability of the membrane by preventing pore closure, and causes formation of necrotic cell masses and tissue damage by affecting matrix metabolism (5). Amount of extrinsic cholesterol intake can be lessened by diminishing activity of pancreatic cholesterol esterase, which facilitates passage of cholesterol and lipids from diet from intestines into bloodstream (2). Internal balance of cholesterol levels is maintained by regulating the activity of HMG-CoA reductase, the enzyme involved in intracellular cholesterol synthesis. Despite their side effects, statins, which were initially derived from fungi but can now be synthesized, are the most effective class of drugs for inhibiting HMG-CoA reductase activity. To avoid negative effects associated with side effects, drugs with fewer side effects are preferred for regulating cholesterol levels (1). Based on this, there has been examination and analysis of new natural and herbal products that may offer safer response. Walnut, which has been recommended for medicinal use for a long time, is one of the plants that has been investigated. Various parts of the plant, such as fruit, seed, oil, leaf, and bark, have been subject of research for their diverse therapeutic effects (6). The therapeutic effects of walnut have been attributed to presence of unsaturated fatty acids, plant sterols, and polyphenols in its structure, according to reports (6-8). There are studies on the effects of walnut kernel (9), leaf (10) and green husk (11) on disorders related to cholesterol and lipid metabolism. However, although there is a belief among people that the walnut septum is effective, there is no literature data available on its potential effects on cholesterol metabolism, except for antibacterial (12), antitumoral (13), antidiabetic (14), and antioxidant (12) studies. In this study, various solvents (water, ethanol, methanol, acetone, hexane, and cyclohexane) were used to extract the walnut septum, followed by gas chromatography mass spectrometry scanning to identify its compounds. In the study was aimed to investigate whether the walnut septum had inhibitory effect on both CE and HMG-CoA reductase enzymes.

MATERIAL AND METHODS

Extract Preparation: The septum of walnuts acquired from local vendor was separated and solutions of 10% (w/v) were prepared with distilled water, ethanol, methanol, acetone, hexane and cyclohexane, and, then extracted at room temperature for 24 hours. One of aqueous solutions was separately boiled for one hour. All solutions were filtered and stock powder extracts were obtained.

GC-MS Analysis: Analysis was carried out on an Agilent 7890A GC System equipped with an Agilent 5975C inert Mass Selective Detector (MSD) with Triple Axis Detector (TAD). The mass spectrometry ion source was electron ionization (EI), and its source temperature was set to 230˚C. The carrier gas helium was used in the GC chromatography column (Agilent HP5-MS, 30m × 0.25mm × 0.25µm), and injector temperature was fixed at 200˚C. For splitless mode, 5mg/ml samples (distilled water powder extracts were dissolved in methanol and then injected) were injected into device with injection volume of 1.0 µL. Oven temperature was held at 40˚C for 5 minutes before being incremented to 100˚C at a rate of 5˚C per minute (5˚C/min). It was kept at 100˚C for 5 minutes and then increased to 225˚Cat a rate of 20˚C (20˚C/min) and maintained at 225˚C for 8 minutes in gradient mode. The analysis time was 33.25 minutes. The components' mass spectra in scanned samples were identified through comparison with integrated library database, such as the Wiley Registry of Mass Spectral Data, 7th Edition, and the NIST (National Institute of Standards and Technology 98 Library).

Analysis of the HMG-CoA Reductase Enzyme Activity: In the analysis performed according to instructions of HMG-CoA reductase commercial kit (Bio Vision K588-100), lyophilized HMG-CoA reductase, HMG-CoA, and NADPH were dissolved in 550 µL, 1300 µL and 440 µL distilled water, respectively. Extracts were dissolved in distilled water on a water bath, and solutions of 10 mg/ml were prepared, which were then diluted 1:5, 1:10 and 1:50. To run experiment in a 96-well plate, a reaction mixture (for one well; HMG-CoA 12 µL, NADPH 4 µL, and HMG CoA reductase assay buffer 174 µL) was prepared. Atorvastatin (10 mM) was transferred to inhibitor control well and 2 µL of extract to test wells. Then 3 µL of HMG-CoA reductase assay buffer, 5 µL of HMG-CoA reductase and 190 µL of the reaction mixture were transferred onto them. For enzyme well; 5 µL of HMG-CoA reductase, 5 µL of HMG-CoA reductase assay buffer, and 190 µL of the reaction mixture were transferred. After all transfers

were performed, they were kept at 37°C for 10 minutes and absorbances of 340 nm were read spectrophotometrically. Percent inhibition values were determined according to equation that "% inhibition= [(A (enzyme)- A (enzyme + extract))/ A(enzyme)] x 100".

Analysis of the Cholesterol Esterase Enzyme Activity: Volumes of 50 µL, 30 µL, 20 µL and 10 µL of the previously prepared 1:5 dilution were used for in vitro analysis performed according to reference method (15). Reaction, in which enzyme activity was measured without using the extracts, was taken as "control". Activator sodium taurocholate (12mM) (Sigma) was dissolved in 100 mM sodium phosphate and 100 mM NaCl (pH=7) assay buffer and kept at 0°C. Pancreatic cholesterol esterase (Sigma 26745) stock solution (0.018 U/mL) was prepared with 100 mM sodium phosphate buffer (pH=7), and diluted with same buffer and kept at 0 °C. Substrate para-nitrophenyl butyrate (Sigma), which was prepared as 4 mM with acetonitrile, was diluted 1:4 with assay buffer. Amounts were transferred to 96-well plate as shown in Table 1. The well-plate without substrate was kept at 30°C for 10 minutes, and at end of time, the substrate was added, and reaction was started. Absorbance was read at 408 nm, and percent inhibition values were determined using the equation "% inhibition= [(A (enzyme)- A (enzyme + extract))/ A(enzyme)] x 100".

Table 1. Content of cholesterol esterase enzyme analysis

Group	Test buffer	Distilled water	Sodium taurocholate	Para-Nitrophenyl butyrate	Cholesterol esterase	Extract
Enzyme (control)	80 µL	100 µL	100 µL	20 µL	10 µL	0
100 µg sample	80 µL	50 µL	100 µL	20 µL	10 µL	50 µL
60 µg sample	80 µL	70 µL	100 µL	20 µL	10 µL	30 µL
40 µg sample	80 µL	80 µL	100 µL	20 µL	10 µL	20 µL
20 µg sample	80 µL	90 µL	100 µL	20 µL	10 µL	10 µL

RESULTS

The compounds and the percentages data obtained by GC-MS scanning of walnut septum extracts prepared in different solvents are given in Table 2. Percentages of monophenol, 2,4-Di-tert-butylphenol, 2,6-Di-tert-butylphenol, ethyl linoleate and butyl linoleate were higher than other compounds. In colorimetrically measured enzyme data, inhibition rate of septum extracts on the HMG-CoA reductase enzyme was 3.2%, while rate of atorvastatin was 88.7% (Table 3). Inhibitory effect on the cholesterol esterase enzyme was seen in the distilled water extract with 13.6, but no inhibiting effect was observed in the other samples except for acetone (Table 4).

DISCUSSION

A parallel relationship is observed between deterioration of cholesterol balance in a body and increase in lipid metabolism-dependent disorders (16). Statins are the most common drugs used to restore balance (1). Additionally, it is outlined that walnut species are recommended because of their unsaturated fatty acid which has a therapeutic effect on disorders related to lipid metabolism (17). Presence of secondary metabolites such as phenolic compounds, which play a role as antioxidants in oxidative stress, makes the walnut species even more valuable (18).

Unsaturated fatty acids, one of chemical components in structure of walnut plant, have been seen in seed part (kernel) (19). According to a study by Pei et al, oleic acid, linoleic acid, and linolenic acid were common fatty acid components in the kernels (20). In a 1998 study that analyzed septum compounds, triacyl-glycerides predominated among the lipid components. It was reported that the fatty acids included in their formation were palmitic, stearic, oleic, linoleic, and linolenic (21). When the fatty acid content of the septum was examined in a thesis study, it was found that linoleic acid was the most abundant, followed by lesser amounts of oleic acid, gamma-linolenic acid and alpha-linolenic acid (22). Through our GC-MS scanning (Table 2), we identified that ethyl and butyl esters of linoleic acid (ethyl linoleate and butyl linoleate) stood out from fatty acid profiles of septum extracts.

The phenolic fractions of septum analyzed by Bezhuashvifi and Kurashvili were rich in low molecular mass aromatic substances, involving gallic, syringic, 4-hydroxybenzoic, protocatechuic, p-coumaric, ferulic, and vanillic acids (21). In the work of Rusu et al., gallic acid, protocatechuic acid, gentisic acid, catechin, syringic acid, epicatechin, vanillic acid, ferulic acid, p-coumaric, hyperoside, isoquercitrin, chlorogenic acid, and quercitrin were identified (23). Liu et al. found 75 phenolic compounds, including phenolic acids, tannins, and flavonoids, among which were quercetin-rhamnose-hexoside, kaempferol-rhamnoside quercetin-3-O-glucoside first identified (24). Fourteen phenolic compounds (gallic acid, catechin, phthalic acid, vanillin, ethyl gallate, kaempferol, dihydroquercetin, taxifolin-3-o-α-L-arabinofuranoside, quercetin-3-rhamnoside, quercetin-3-o(4-o-acetyl)-α-L-rhamnopyranoside, propyl gallate, blumenol B and vanillic acid) were reported by Hu et al. in the septum content analysis (25).

Table 2. Retention time and percentage values of the compounds seen as a result of scanning the extracts in GC-MS.

	A		B		C		D		E		F		G	
Compound name	R.T. min	% of total	R.T. min	% of total	R.T. min	% of total	R.T. min	% of total	R.T. min	% of total	R.T. min	% of total	R.T. min	% of total
1-Hexadecene	-	-	-	-	22.641	1.745	18.107	0.005	24.297	4.542	-	-	-	-
1-P-Menthene	-	-	-	-	-	-	21.220	0.060	-	-	-	-	-	-
1-Tetradecene	-	-	-	-	-	-	-	-	22.647	4.144	-	-	-	-
2,4-Di-tert-butylphenol	23.757	1.012	-	-	23.757	5.503	-	-	23.757	5.460	23.752	68.028	-	-
2,6-Di-tert-butylphenol	-	-	-	-	-	-	-	-	-	-	-	-	23.767	42.945
3-Carene	-	-	-	-	-	-	13.245	0.109	-	-	-	-	-	-
4-Vinylphenol	20.192	6.631	20.307	0.901	-	-	-	-	-	-	-	-	-	-
9-Hexadecenoic acid	-	-	16.213	2.111	-	-	-	-	-	-	-	-	-	-
Acrylic acid	-	-	-	-	-	-	-	-	25.236	23.194	-	-	-	-
Alpha terpinolene	-	-	-	-	-	-	15.772	0.118	-	-	-	-	-	-
Arachidonic acid trimethylsilyl ester	8.082	0.342	-	-	-	-	-	-	-	-	-	-	-	-
Butyl linoleate	-	-	-	-	25.744	84.769	25.583	55.128	-	-	-	-	-	-
Butylated hydroxytoluene	-	-	-	-	-	-	-	-	-	-	-	-	26.543	5.996
Carane	-	-	-	-	-	-	21.962	0.041	-	-	-	-	-	-
Caryophyllene	18.314	0.361	14.869	0.688	-	-	16.675	0.005	-	-	-	-	-	-
Citronellol	-	-	15.009	0.707	-	-	-	-	23.513	2.523	-	-	-	-
Cyclopentolate	23.363	1.086	-	-	-	-	-	-	-	-	-	-	-	-
Dinoseb acetate	22.833	0.366	-	-	-	-	-	-	-	-	-	-	-	-
Docosahexaenoic acid	-	-	17.712	0.481	-	-	17.603	0.008	-	-	-	-	-	-
Docosane	20.976	1.281	-	-	21.458	0.143	-	-	22.413	0.330	23.592	3.566	29.143	1.943
Dodecane	19.590	6.101	19.585	6.570	19.580	0.336	-	-	21.547	0.840	19.590	0.687	11.865	1.656
Eicosane	-	-	-	-	23.591	1.543	-	-	26.668	21.137	29.215	3.306	4.149	3.017
Ethinamate	22.242	0.633	17.884	0.464	-	-	17.297	0.004	-	-	-	-	-	-
Ethyl linoleate	-	-	-	-	-	-	25.755	22.345	-	-	-	-	-	-
Ethyl linolenate	13.966	0.324	-	-	-	-	-	-	-	-	-	-	-	-
Eugenol	22.309	0.964	-	-	-	-	-	-	-	-	-	-	-	-
Farnesane	-	-	-	-	22.102	0.092	-	-	21.251	0.683	14.973	0.197	-	-
Gamma terpinene	23.638	9.094	23.633	15.483	-	-	14.838	0.064	-	-	-	-	-	-
Gamma terpineol	-	-	-	-	-	-	-	-	7.278	0.884	-	-	-	-
Geranial	-	-	-	-	-	-	21.106	0.106	-	-	-	-	-	-
Geranyl acetate	-	-	-	-	-	-	22.569	0.082	-	-	-	-	-	-
Geranyl linalool isomer B	6.572	0.367	-	-	-	-	-	-	-	-	-	-	-	-
Guaiacol	15.808	10.734	-	-	-	-	-	-	-	-	-	-	-	-
Hemimellitene	-	-	-	-	-	-	-	-	12.607	3.666	-	-	-	-
Heneicosane	-	-	-	-	23.264	0.264	-	-	21.899	0.652	27.975	1.873	27.991	2.975
Heptadecane	-	-	-	-	23.352	0.274	-	-	-	-	23.357	0.455	26.398	2.146
Hexadecane	-	-	-	-	21.541	0.122	-	-	-	-	24.343	2.306	22.730	2.323

(Notes; R.T. : Retention time, "-": No detection, Extracts= A: Macerated in distilled water, B: Boiled in distilled water, C: Macerated in acetone, D: Macerated in ethanol, E: Macerated in methanol, F: Macerated in hexane, G: Macerated in cyclohexane)

Table 3. Percentage of inhibition of walnut septum extracts on the HMG-CoA reductase enzyme

Extracts	% Inhibition	In-well concentration
A	0.8	20 µg/mL
	1	5 µg/mL
	1.4	2 µg/mL
B	0.7	20 µg/mL
	1.6	5 µg/mL
	2.3	2 µg/mL
C	2.4	20 µg/mL
	1.8	5 µg/mL
	3.2	2 µg/mL
D	1.9	20 µg/mL
	2	5 µg/mL
	2.4	2 µg/mL
E	0.2	20 µg/mL
	2.7	5 µg/mL
	1.6	2 µg/mL
F	1.8	20 µg/mL
	2.3	5 µg/mL
	2.2	2 µg/mL
G	2.6	20 µg/mL
	3.1	5 µg/mL
	2.7	2 µg/mL
H	88.7	56 µg/mL

Notes; Extracts= A: Macerated in distilled water, B: Boiled in distilled water, C: Macerated in acetone, D: Macerated in ethanol, E: Macerated in methanol, F: Macerated in hexane, G: Macerated in cyclohexane, H: Atorvastatin

Table 4. Percentage of inhibition of walnut septum extracts on the cholesterol esterase enzyme

Extracts	% Inhibition	In-well concentration
A	No inhibition	333 µg/mL
	No inhibition	200 µg/mL
	8.1	133 µg/mL
	13.6	67 µg/mL
B	No inhibition	333 µg/mL
	2.7	200 µg/mL
	6.3	133 µg/mL
	7.2	67 µg/mL
C	1.8	333 µg/mL
	No inhibition	200 µg/mL
	No inhibition	133 µg/mL
	No inhibition	67 µg/mL
D	No inhibition	333 µg/mL
	No inhibition	200 µg/mL
	No inhibition	133 µg/mL
	No inhibition	67 µg/mL
E	No inhibition	333 µg/mL
	No inhibition	200 µg/mL
	No inhibition	133 µg/mL
	No inhibition	67 µg/mL
F	No inhibition	333 µg/mL
	No inhibition	200 µg/mL
	No inhibition	133 µg/mL
	No inhibition	67 µg/mL
G	No inhibition	333 µg/mL
	No inhibition	200 µg/mL
	No inhibition	133 µg/mL
	No inhibition	67 µg/mL

Notes; Extracts= A: Macerated in distilled water, B: Boiled in distilled water, C: Macerated in acetone, D: Macerated in ethanol, E: Macerated in methanol, F: Macerated in hexane, G: Macerated in cyclohexane

The phenolic compounds in the septum extracts we prepared using solutions of different polarities and identified by GC-MS scanning (Table 2) have a higher percentage distribution of substances such as 2,4-Di-tert-butylphenol (in hexane extract), 2,6-Di-tert-butylphenol (in cyclohexane extract) and monophenol (in distilled water extract).

These findings suggest that the reason for differences in results obtained from the aforementioned studies was due to differences in procedures used and habitats of septum.

Synthesis rate of cholesterol is determined by its level in cell. Cellular synthesis of cholesterol can be prevented by inhibiting HMG-CoA reductase, which is rate-limiting enzyme in cholesterol synthesis (26). As a result of the inhibition of HMG-CoA reductase, expression of LDL receptors, which lowers plasma concentration of cholesterol, is induced. Thus the amount of cholesterol can be regulated (27).

In our study, we investigated ability of walnut septum to obstruct HMG-CoA reductase using in vitro method. We observed that septum extracts prepared using solvents of different polarity were less effective than atorvastatin which inhibited HMG-CoA reductase by 88.7%. The highest inhibition in extracts at concentrations of 20 µg/mL and 5 µg/mL was determined in cyclohexane, at 2.6% and 3.1%, respectively, while the highest inhibition in 2 µg/mL extract was determined in acetone extract at 3.2% (Table 3). To our knowledge, there is no literature investigating inhibitory effect of walnut septum on HMG-CoA reductase activity, except for our study.

A study conducted by Oriakhi and Uadia (2020) investigated the effects of African walnut oil on HMG-CoA reductase enzyme activity in liver cells. It was reported that extract may inhibit HMG-CoA reductase activity, based on comparison of HMG-CoA reductase activity in liver cell lysates of animals fed normal diet and animals fed with African walnut oil. However, when the inhibition rate of walnut oil and atorvastatin on HMG-CoA reductase was compared after feeding with high cholesterol diet, the oil was not as effective as atorvastatin (28). Several studies investigating effects of different species on HMG-CoA reductase activity have reported that *Basella alba* (29), *Amaranthus viridis* (29) and *Piper sarmentosum* (29) species had anti-HMG-CoA reductase activity over 50% and that *Quercus infectoria* (30), *Rosa damascene* (30), *Myrtus communis* (30) and *Citrus aurantium* (31) flowers were strong inhibitors of HMG-CoA reductase. In another research on effectiveness of *Salvia* species on HMG-CoA reductase enzyme, researchers found that eight different *Salvia* species had inhibitory effect, although not as much as atorvastatin (32).

Pancreatic cholesterol esterase (CE) activity is one of the enzyme pathways associated with

plasma cholesterol level. It catalyzes cholesterol esters in intestinal lumen and mediates their entry into mucosal cells. These products are then transported into circulation via lymph, causing an increase in plasma cholesterol levels and contributing to develop and progress of atherosclerosis, a cardiovascular disease (3). To further this contribution, researchers are studying different plant species, their active ingredients, and chemical agents to investigate their potential to inhibit cholesterol esterase. In our study, we investigated effects of extracts prepared with solvents of different polarities on cholesterol esterase activity. We compared "normal enzyme activity of 100% " with "decreased enzyme activity" after treatment with the extracts. The highest inhibition rate (13,6 %) was observed in the extract that was kept in distilled water overnight, while we did not see any inhibition in the extracts prepared with ethanol, methanol, hexane and cyclohexane (Table 4). To the best of our knowledge, there are no previous studies on effects of walnut septum on cholesterol esterase activity, although there are studies on effects of other plant species on the enzyme. Thus, we have provided first record of its effectiveness of walnut septum extracts in inhibiting cholesterol esterase activity.

In one of these, it has been reported that effects on cholesterol esterase of clove (*Syzygium aromaticum*), which has an inhibitory effect as much as simvastatin, may be due to its phenolic content. Thus, it may contribute to prevention of hyperlipidemia by inhibiting cholesterol esterase activity and avoiding digestion and absorption of fats and cholesterol (33). According to another study, safflower (*Carthamus tinctorius*) and cassia (*Cassia angustifolia*) plants have a good inhibitory effect on CE, although not as much as simvastatin (34). Meanwhile there was no inhibitory effect of main bioactive component obtained from leaves of *Mangifera indica* (35) against CE, it was reported in literature that flower extracts of *Camellia nitidissima* (36), leaves of *Ecballium elaterium* (37), the bark of *Pinus brutia* (37), leaves of *Hedera helix* (37), *Dendrobium nobile* (38), *Citrus grandis* (39), grape seeds (40), hawthorn (38) and wolfberry (38) extracts had an inhibitory effect.

CONCLUSIONS

To clarify claims of cholesterol regulation by consuming walnut septum, we investigated effects of septum extracts on enzymes that are involved in enzyme pathways associated with plasma cholesterol levels. We determined that the septum did not have a noticeable inhibitory effect on either cholesterol esterase, which is responsible for absorption of cholesterol from intestines, or HMG-CoA reductase, which is responsible for intracellular cholesterol production, in vitro. Low rate of inhibitions led us to consider effects of various substances that emerged in content of walnut septum based on extraction method used.

Consequently, this research yielded worthy of note data indicating that the walnut septum extracts prepared in solvents of different polarities, despite having various chemical components, did not have a therapeutic level inhibitory effect on two different enzyme pathways that regulate the plasma cholesterol level. We consider that further research will be needed to evaluate its effects on other pathways deeply.

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RESEARCH ARTICLE

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Evaluation of the Effectiveness of Otorhinolaryngology Examination and Hearing Evaluation Training for Family Physicians

ABSTRACT

Objective: In our study, it is aimed to investigate the level of knowledge of family physicians working in primary health care organizations about Ear Nose and Throat (ENT) diseases, to examine how they manage frequently admitted ENT patients, to identify the problems they experience during examination and to examine the effect of the training given.

Methods: Participants were first administered a 30-question pre-test created by the researcher based on the literature. Then, a collective training lasting 2 days and 1.5 hours per day was given by an ENT specialist from the researchers and a post-test was applied. Afterwards, the topics in which the researchers made the most mistakes or remained uninterpreted were recorded and a training program including these topics was created and training was given.

Results: Of the 21 family physicians over 30 years of age, 2 (14,29%) were male and 18 (85,71%) were female. When the time of graduation from medical school of the family physicians in the study was analyzed, the number of family physicians with 5-10 years of medical school graduation was 4 (19,05%), 10 (47,62%) with 10-20 years of medical school graduation, and 7 (33,33%) with more than 20 years of medical school graduation. All of the family physicians who participated in the study think that ENT education is important for primary care medicine.

Conclusions: ENT diseases are common in primary care. In order for family physicians to manage their patients more comfortably, we believe that rotations in the field of ENT diseases in the postgraduate period would be appropriate.

Keywords: Family Physicians, ENT, Education.

Aile Hekimlerine Yönelik Kulak Burun Boğaz Muayenesi ve İşitme Değerlendirme Eğitiminin Etkinliğinin Değerlendirilmesi

ÖZET

Amaç: Biz çalışmamızda birinci basamak sağlık kuruluşlarında çalışan aile hekimlerinin Kulak Burun Boğaz (KBB) hastalıkları ile ilgili bilgi düzeylerini araştırmayı, sıklıkla başvuran KBB hastalarını nasıl yönettiklerini incelemeyi, muayene sırasında yaşadıkları sorunları tespit edip verilen eğitimin etkisini incelemeyi amaçladık.

Yöntem: Katılımcılara öncelikle araştırmacı tarafından literatür baz alınarak oluşturulmuş 30 soruluk bir ön test uygulandı. Ardından araştırmacılardan KBB uzmanı tarafından 2 gün süren ve günlük 1.5 saatlik toplu bir eğitim verildi ve son test uygulandı. Daha sonra araştırmacıların en çok hata yaptıkları veya yorumsuz kaldıkları konular kaydedildi ve bu konuları içeren bir eğitim programı oluşturularak eğitim verildi.

Bulgular: Çalışmaya alınan 30 yaş üzeri 21 aile hekiminden 3 (%14,29)'si erkek 18 (%85,71)'i kadındır. Çalışmadaki aile hekimlerinin tıp fakültesinden mezun olma süresi incelendiğinde, 5-10 yıl aralığında olanların sayısı 4 (%19,05), 10-20 yıl aralığında olanların sayısı 10 (%47,62), 20 yıldan fazla bir zamana sahip olanların sayısı ise 7 (%33,33)'dir. Çalışmaya katılan aile hekimlerinin tamamı birinci basamak hekimliği için KBB eğitiminin önemli olduğunu düşünmektedir.

Sonuç: KBB hastalıkları birinci basamakta sık görülen hastalıklardandır. Aile hekimlerinin daha rahat hastalarını yönetebilmeleri için mezuniyet sonrası dönemde KBB hastalıkları alanında rotasyonlarının uygun olacağı kanaatindeyiz.

Anahtar Kelimeler: Aile Hekimi, KBB, Eğitim.

INTRODUCTION

Family medicine is a medical discipline that provides comprehensive and continuous medical care to individuals of all ages, genders, and diseases. It offers services in the context of their own family, society, and culture while respecting patient autonomy. Specialist physicians trained in line with the principles of family medicine discipline are responsible for this care. To ensure quality and qualified family medicine specialty training, the curriculum must meet certain standards and adequately address the patient profile encountered in primary care. Although ENT diseases are prevalent in primary health care, they are not included in the core curriculum of family medicine. The aim of family medicine residency training is to provide suitable conditions for the development of a physician's clinical knowledge, skills, attitudes, and behaviors. Additionally, it aims to develop the ability to provide health education, conduct research, and possess management qualities in accordance with the basic principles of family medicine. To achieve this goal, a family medicine resident gains the necessary theoretical and practical knowledge and experience through rotations and practice in various areas of family medicine during their residency training (1).

In this study, we aimed to investigate the knowledge level of family physicians working in primary healthcare settings regarding ENT diseases, to examine how they manage frequently presenting ENT patients, and to observe whether their knowledge level and attitude towards patient management change after receiving ENT education.

MATERIAL AND METHODS

Study Design: This study is an interventional study. It was conducted between 22.08.2022 and 22.05.2023. The population of the study consisted of 24 family physicians who accepted to participate among the contracted family medicine residents who were trained in our department. The main places of service of these residents are family medicine units in Malatya province and districts and they receive 6 years of training in our department. The design of our study was explained to the contracted family medicine residents who were actively practicing family medicine in the field and their voluntary consent was obtained. Exclusion criteria were not participating in the training, providing incomplete or incorrect information in any of the questionnaires, or voluntarily leaving the study.

Method of Application of the Research and Collection of Data: First, a pre-test of 30 questions, created by the researcher based on the literature, was administered to the participants. The first 10 questions of the pre-test survey consist of questions regarding sociodemographic data and educational status. The last 20-question section consists of knowledge level questions about ENT diseases frequently encountered in primary care, prepared by an ENT specialist physician. Each question was determined as 5 points and the participants were evaluated out of 100 points. A total of 24 people were pre-tested via Google survey and their answers were recorded. Then, a 2-days, 1,5-hour daily collective training was given by the ENT specialist from the researchers. The training was interactive and in addition to theoretical information, practical information on otoscope use was given. After the two-days training period was completed, a post-test consisting of 30 questions was administered to the participants and the answers were recorded again. At this stage, 3 people were excluded from the study because they did not want to do the post-test. By comparing the results of both tests, it was compared whether the ENT training made any changes in the participants' knowledge levels and attitudes towards patient approach. Then, the topics where the researchers made the most mistakes or left no comment were recorded and a training program was created including these topics. Additional practices such as correct application of otoscope examination, normal ear examination with otoscope, and correct diagnosis of ear diseases are also included in the training program. It was found out whether the physicians felt competent after the training.

Ethical Approval: Ethical approval was received from İnönü University Health Sciences Non-invasive Clinical Research Ethics Committee on April 20, 2022, with decision number 2022/46.

RESULTS

Among the 21 family physicians over 30 years of age, 3 (14,29%) were male and 18 (85,71%) were female. When the time of graduation from medical school of the family physicians in the study was analyzed, the number of family physicians who had graduated from medical school between 5-10 years was 4 (19.05%), between 10-20 years was 10 (47.62%), and more than 20 years was 7 (33.33%). Similarly, among the 21 family physicians, 6 (28.57%) had a tenure between 1-5 years, 7 (33.33%) between 5-10 years, and 8 (38.10%) more than 10 years. Among the family physicians included in the study, there were 2 (9.52%) who did ENT internship for less than 2 weeks, 18 (85.71%) who did ENT internship for 2-4 weeks and 1 (4.71%) who did not do any ENT internship. Among the family physicians who did ENT internship in their pre-graduate education, 3 (15%) followed up patients, while 17 (85%) did not follow up patients. After graduation, 10 (47.62%) family physicians received ENT training after in-service training or seminars, while 11 (52.38%) family physicians did not receive such training. In addition, there were 5 (20.81%) family physicians who had sufficient knowledge about the correct use of the otoscope and the diseases that could be

diagnosed by otoscopic examination, 14 (66.66%) family physicians who had partial knowledge, and finally 2 (12.53%) family physicians who did not have this knowledge (Table 1).

Table 1. Sociodemographic data of the participants

		Count	Percent (%)
Gender	Male	3	14.29
	Female	18	85.71
How many years has it been since you graduated from medical school?	5-10 years	4	19.05
	10-20 years	10	47.62
	>20 years	7	33.33
How long was the ENT internship during your pre-graduation education?	No	1	4.76
	<2 week	2	9.52
	2-4 weeks	18	85.71
Did you follow up with patients during your ENT internship as an intern?	Yes	3	14.29
	No	18	85.71
Have you received ENT training after graduation, during in-service training or seminars?	Yes	10	47.62
	No	11	52.38
Do you have sufficient knowledge about the correct use of the otoscope and the diseases that can be diagnosed with otoscopic examination?	Yes	5	23.81
	Partially	14	66.67
	No	2	9.52

All of the family physicians who participated in the study thought that ENT education was important for primary care medicine. The accuracy rates of the answers given before and after the training to the 20 questions asked to 21 family physicians within the scope of the study are given in Table 2. The p values for the results of the two ratio test performed with the basic function of the R programming language (prop.test) are given in Table 2. Translated with DeepL.com (free version).

Table 2. Comparison of participants' correct guess rates before and after training

Questions	**Number of Correct Answers Before Training**	**Number of Correct Answers After Training**	***p*-value**
1	8 (38.10%)	20 (95.24%)	**<0.001**
2	3 (14.29%)	14 (66.67%)	**0.001**
3	18 (8.71%)	21 (100.00%)	0.23
4	21 (100.00%)	21 (100.00%)	1.000
5	18 (85.71%)	21 (100.00%)	0.23
6	9 (42.86%)	17 (80.95%)	**0.026**
7	9 (42.86%)	20 (95.24%)	**<0.001**
8	11 (52.38%)	18 (85.71%)	**0.045**
9	7 (33.33%)	20 (95.24%)	**<0.001**
10	12 (57.14%)	21 (100.00%)	**0.002**
11	3 (14.29%)	13 (61.90%)	**0.004**
12	17 (80.95%)	21 (100.00%)	0.114
13	8 (38.10%)	19 (90.48%)	**0.001**
14	9 (42.86%)	21 (100.00%)	**<0.001**
15	7 (33.33%)	19 (90.48%)	**<0.001**
16	9 (42.86%)	19 (90.48%)	**0.003**
17	7 (33.33%)	17 (80.95%)	**0.005**
18	7 (33.33%)	18 (85.71%)	**0.001**
19	1 (4.76%)	15 (71.43%)	**<0.001**
20	6 (28.57%)	18 (85.71%)	**<0.001**

Looking at the results in Table 2, the questions with a statistically significant increase in the rate of correct answers:

Question 1. "Which of the following is wrong about otoscopic examination?"

Question 2. "Which of the following is incorrect about the structures that can be seen with an otoscope?"

Question 6. "Which of the following statements about a patient with long-standing discharge and itching in the right ear whose otoscopic examination is as shown in the figure is incorrect?

Question 7. “A 4-year-old child was brought to the hospital by his family with suspicion of hearing loss because he remained unresponsive to his parents' calls and did not turn around, and got too close to the screen while watching television. The patient also has symptoms such as snoring at night and sleeping with his mouth open. Which of the following is incorrect about the patient whose otoscopic examination is as shown in the figure?

Question 8. “Which of the following is an ENT emergency?”

Question 9. “A 22-year-old female patient applied with the complaint of bleeding in her left ear. The patient states that he had severe pain and a feeling of fullness in his ear two days ago, and the pain decreased with bleeding. "Which of the following is your preliminary diagnosis in the patient whose otoscopic examination is as shown in the figure?"

Question 10. “A 42-year-old male patient applied with the complaint of yellow, foul-smelling discharge in the ear that has been going on for about four months. "Since the patient's otoscopic examination is as shown in the figure, what should be your preliminary diagnosis for this patient?"

Question 11. “A 40-year-old female patient applied with complaints of decreased hearing and a disturbing ringing sensation in both ears, which increased over time. The patient states that he hears better in environments where there is a lot of noise, and that he occasionally experiences dizziness and balance disorders. "Since the patient's otoscopic examination is as shown in the figure, which of the following statements about this patient is incorrect?"

Question 13. “Which of the following is not recommended for treatment in a patient with suspected acute otitis externa?” Question 14. “Which of the following approaches to treatment is correct in a patient presenting with acute otitis media?”

Question 15. “Which of the following is true regarding the treatment approach in a patient who is considered to be diagnosed with otomycosis in primary care?”

Question 16. “Which of the following is your treatment approach for a patient with a preliminary diagnosis of serous otitis media?”

Question 17. “Which of the following is incorrect about sudden hearing loss?”

Question 18. “Which of the information given about bullous myringitis is incorrect?”

Question 19. “What should be the most appropriate treatment approach in primary care for a patient diagnosed with chronic otitis media?” and

Question 20. “Which of the following is incorrect about Bening Paroxysmal Positional Vertigo?” It was observed that the rate of correct answers to the questions increased statistically significantly with the ear, nose and throat diseases training given to family physicians within the scope of the project.

The questions for which there is no statistically significant increase are;

Question 3: “A 20-year-old male patient applied with complaints of itching, pain and sensitivity in the left ear and said that these complaints appeared after swimming. The patient's physical examination revealed tragus tenderness and otoscopic examination revealed edematous and tender external auditory canal. “What is your preliminary diagnosis of the patient?”

Question 4. “The otoscopic examination of the patient who applied with complaints of decreased hearing and fullness in the ear after getting out of the shower is as shown in the figure. “What is the preliminary diagnosis of the patient?”

Question 5. “A 12-year-old male patient applied with complaints of pain in the right ear, decreased hearing, fever, and loss of appetite for the last four or five days. "Since the patient's otoscopic examination appearance is as shown in the figure, what is your preliminary diagnosis?" and

Question 12. “Which of the following is not a disease caused by vestibular system disorders?” Although the number of correct answers given before and after the training increased relatively, it was not found to be statistically significant.

DISCUSSION

Family physicians, who are at the central point of primary health care services, gain knowledge and equipment regarding the diagnosis and treatment of ENT diseases during ENT internships during their medical school education. When the patient profiles coming to family medicine are examined, it is seen that individuals mostly apply due to complaints related to ENT diseases (2,3).

Many studies show that ENT diseases have an important place in primary care medicine. However, it appears that the training provided on ENT diseases during medical school and family medicine specialty training is insufficient. In a study, more than 20% of the patients applying to primary health care institutions were found to be people with complaints about ENT diseases; Despite this, it has been claimed that adequate ENT training is not received during the medical faculty

and family medicine specialty education process (4). In another study, 7-25% of the patients coming to family medicine were found to be ENT patients (5). In a multi-center study conducted in Turkey, it is observed that the most common reason for applications to family medicine is ENT diseases, and when the consultations requested from other branches are examined, ENT diseases are again in the first place (2).

In our study, we investigated the current knowledge and attitudes of family physicians regarding ENT diseases. It was aimed to observe and reveal whether their knowledge and attitudes change when they receive adequate training on ENT diseases. First of all, a survey consisting of questions about ENT diseases and otoscopic examination, which are frequently encountered in family medicine, was created and this survey was applied to 21 family physicians working in the field before the training. Then, the participants were given two-day theoretical and practical training by an ENT specialist. After the training, the same survey was applied to the physicians again and it was seen that the training was effective.

The majority of our participants have practiced medicine for an average of 10 to 20 years, and the majority of them have been serving in family medicine for more than 10 years. The majority of our physicians stated that their knowledge of ENT diseases and otoscopic examination was partially sufficient, and all our participants stated that ENT diseases have an indisputable importance in primary health care.

When the data obtained from our study was evaluated, it was observed that the correct answer rate of the questions in the pre-training survey was lower, while this rate increased significantly in the post-training survey. It was also seen that the participants mostly answered the four questions asked about the diagnosis and treatment of otosclerosis, bullous myringitis, and serous otitis media correctly before the training. This shows that the physicians had sufficient knowledge and experience in these areas. In the other 16 questions, it was determined that the participants' correct answer rates increased significantly after the training. Additionally, it was observed in the individual post-training feedbacks that their knowledge levels had increased considerably.

In a similar study conducted by Kucheria et al., a survey was applied to family physicians working in primary care regarding their attitudes towards ENT diseases. Afterwards, a 10-days ENT training was given and their post-training status was evaluated again with a survey. As a result, it was observed that the participants' confidence in managing patients with ENT complaints increased significantly after the training. This study showed that adding ENT diseases to the family medicine residency curriculum will enable family physicians to examine their patients more confidently and reduce the workload of ENT clinics in secondary and tertiary care (6). In our study, we also emphasized the importance of ENT disease education in line with the literature.

The primary objective of rotations is to enable family physicians to gain the skills to see and manage patients that they are responsible for managing in primary care settings, but which they encounter less frequently in their own practice areas. In this context, one of the key factors in determining the curriculum of the training program is the primary care patient profile. To this end, many studies have been conducted in our country and around the world. Studies conducted in our country have examined patients who apply to family medicine and found that the most common reasons for application are cough, fever, headache, and sore throat; the most common diseases seen in patients are upper respiratory tract infection, musculoskeletal system diseases, hypertension, headache, and gastrointestinal system diseases (7-9). The most common diagnoses made in primary care are upper respiratory tract infections (viral-bacterial tonsillitis, otitis, influenza infections). For this reason, it is observed that family physicians frequently request consultation for ear, nose and throat diseases.

In other studies conducted around the world, a significant proportion of patients who apply to primary care health institutions are patients with complaints related to ENT diseases. However, the training in ENT diseases is inadequate both in pre-graduation medical school education and in family medicine specialization training (4,10).

CONCLUCION

In conclusion, when we look at the data obtained from many studies and our own study, ENT diseases have an undeniable importance for primary care health services. Despite this, ENT diseases are not given sufficient attention in both undergraduate medical school education and family medicine specialization training, which can put our physicians in a difficult position. The fact that family physicians feel inadequate in managing ENT patients also causes unnecessary workload and increase in workforce in secondary and tertiary care services.

For all these reasons, we believe that giving more importance to ENT diseases in the medical school education process and making ENT diseases a compulsory rotation in the family medicine specialization training process can eliminate the mentioned problems.

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RESEARCH ARTICLE

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Comprehensiveness and Instructional Quality of YouTube Videos on Clinical Record-Keeping Training in Medical Education

ABSTRACT

Objective: Clinical record-keeping is recognized as a core competency in medical education. This study aimed to evaluate comprehensiveness and instructional quality of videos available on the YouTube platform for teaching clinical record-keeping.

Methods: YouTube was searched by using relevant keywords. Based on eligibility criteria, 59 videos were included in the study. Videos were assessed for country of origin, video length, number of likes, dislikes, comments, daily views, like ratio, and video power index. Tools to measure the quality of clinical notes, which are QNOTE and RED Checklist, have been used to assess comprehensiveness of the videos. Instructional quality was assessed using the instructional video quality checklist (IVQC).

Results: The comprehensiveness score was 60.4±17.89 (out of 100), while instructional quality score was 11.19±3.61 (out of 27). IVQC scores were significantly higher in the university/professional organizations and academics compared to the others ($p<0.001$). However, there was no significant difference between the groups in comprehensiveness scores ($p=0.131$).

Conclusions: YouTube videos missing important rate of components of clinical record-keeping. Moreover, the instructional quality of the videos falls below the expected levels. These problems still persist in the videos uploaded by universities/professional organizations and academics. Therefore, YouTube videos should be used cautiously for clinical record-keeping training by medical students and medical educators.

Keywords: Medical Documentation, Clinical Records, Medical Education, Youtube, Video Quality, Online Education.

Tıp Eğitiminde Klinik Kayıt Tutma Eğitimine Yönelik YouTube Videolarının Kapsamlılığı ve Eğitimsel Kalitesi

ÖZET

Amaç: Klinik kayıt tutma, tıp eğitiminde temel bir yetkinlik olarak kabul edilmektedir. Bu çalışma, klinik kayıt tutma konusunda eğitim veren YouTube platformundaki videoların kapsamlılığını ve eğitimsel kalitesini değerlendirmeyi amaçlamaktadır.

Yöntem: İlgili anahtar kelimeler kullanılarak YouTube'da arama yapıldı. Uygunluk kriterlerine göre, çalışmaya 59 video dahil edildi. Videoların yüklendiği ülke, video süresi, beğeni sayısı, beğenmeme sayısı, yorum sayısı, günlük izlenme sayısı, beğeni oranı ve video güç endeksi açısından değerlendirilmiştir. Videoların kapsamlılığını değerlendirmek için QNOTE ve RED Checklist adlı klinik notlar kalitesini ölçen araçlar kullanılmıştır. Eğitimsel kalite ise Eğitim Videosu Kalite Kontrol Listesi (IVQC) kullanılarak değerlendirilmiştir.

Bulgular: Kapsamlılık puanı 60.4±17.89 (100 üzerinden), eğitimsel kalite puanı ise 11.19±3.61 (27 üzerinden) olarak bulunmuştur. IVQC puanları, diğer gruplarla karşılaştırıldığında üniversite/profesyonel kuruluşlar ve akademisyenler tarafından yüklenen videolarda anlamlı derecede yüksek bulunmuştur ($p<0,001$). Bununla birlikte, gruplar arasında kapsamlılık puanlarında anlamlı bir fark bulunmamıştır ($p=0,131$).

Sonuç: YouTube videoları, klinik kayıt tutmanın önemli bileşenlerini eksik bırakmaktadır. Ayrıca, videoların eğitimsel kalitesi beklenen seviyenin altında kalmaktadır. Bu sorunlar, hâlâ üniversiteler/profesyonel kuruluşlar ve akademisyenler tarafından yüklenen videolarda da devam etmektedir. Bu nedenle, tıp öğrencileri ve tıp eğitimcileri tarafından klinik kayıt tutma eğitimi için YouTube videolarının dikkatlice kullanılması gerekmektedir.

Anahtar Kelimeler: Tıbbi Dokümantasyon, Klinik Kayıtlar, Tıp Eğitimi, Youtube, Video Kalitesi, Online Eğitim.

INTRODUCTION

Clinical records include all materials related to patients who receive healthcare service, whether as outpatients or inpatients, for any reason (1). Clinical records can be generally defined as the notes of health professionals who record a patient's symptoms, medical history, laboratory and imaging results, and treatments. Clinical record-keeping serves as a foundation for numerous activities involved in delivering and researching healthcare services (2). Due to the importance of medical records and the fact that younger professionals spend substantial portion of their working hours to managing these records (3), many recommendations from both national and international authorities have been put forth regarding the need for clinical record-keeping training in medical education (4, 5). For instance, among the core entrustable professional activities (EPAs) that medical students are expected to achieve by graduation, medical students are expected to be able to "document a clinical encounter in the patient record" (5).

However, some studies in the literature showed that adequate education in clinical record-keeping has not been provided (6-9). More specifically, there are studies showed that up to 18.2% of interns feel that they were not adequately prepared for documenting a clinical encounter and they cannot perform this core EPA without direct supervision (10, 11). There is a lack of alignment between this EPA and milestones of several specialties (12).

Amidst the challenges associated with teaching clinical record-keeping, it is reasonable to assert that learners have attempted to bridge this training gap through their own efforts. One of the first sources that medical students refers to is the internet. YouTube is the leading video-broadcasting platform on the internet today. According to 2023 data, 2.5 billion people access this site monthly, spending an average of 19 minutes per day (13). As a meta-analysis and systematic review pointed out (14), it also has been commonly used by medical students for educational purposes. Studies showed that not only medical students but also physicians and educators frequently use YouTube videos related to their fields (15-18) for various educational purposes (19). If we consider that clinical record keeping is a clinical skill, YouTube is seen as a useful source to improve clinical skills (20). However, the content in YouTube videos may suffer from lack of verification or review, raising questions about the comprehensiveness and instructional quality of the information (21-24).

There are many studies that evaluated quality of YouTube videos as information source for patients (23, 24). However, evaluation of videos regarding medical education lacks. The most recent scoping review on the educational value of YouTube videos in medical education showed that there is a lack of evaluative studies on the effectiveness of YouTube videos (22). The comprehensiveness of content and instructional quality are among the essential factors in the effectiveness of videos. Considering the importance of clinical record-keeping, the content of YouTube videos on this core skill needs to be evaluated. In this respect, the purpose of the study was to evaluate comprehensiveness and instructional quality of the videos on teaching clinical record-keeping on YouTube.

MATERIAL AND METHODS

Study Design: This is a descriptive study.

Search: The process of keyword-based searches on the YouTube platform was carried out from September 25, 2023, to September 28, 2023. The searches were performed without signing in to YouTube by using a private browsing window in the web browser. Since the objective of this study was to assess the comprehensiveness and instructional quality of videos recorded for educational purposes for medical students and professionals in clinical record-keeping, the chosen keywords for the searches included "patient history", "clinical history", "patient notes", "progress notes", "consultation notes", and "discharge report". A separate search was performed for each keyword. The total number of results obtained from these searches was 1298. Out of 1298 videos, 213 videos were duplicates. Therefore, 986 videos obtained from these instances of search were evaluated considering the eligibility criteria.

Eligibility Criteria: In the initial analysis, videos considered irrelevant were eliminated by reading the video titles and description sections.
The excluded videos were:

- not on teaching clinical record-keeping,
- recorded in a language other than English,
- recorded for other healthcare professionals,
- recorded for informing general public.

Following this process, 287 videos remained for watching the content of the videos. In this process, 228 videos were excluded for reasons, which are aligned with eligibility criteria, presented in Figure 1. Finally, 59 videos that met eligibility criteria were included in the study. All these processes were carried out by one reviewer (EE).

Data Collection: Data collection was carried out by one reviewer (EE). Data collection form consisted of five parts:

- Video statistics
- Video source
- Type of clinical record-keeping
- Comprehensiveness
- Instructional Quality

Video Statistics: Descriptive statistics, including the country of origin, video length, likes

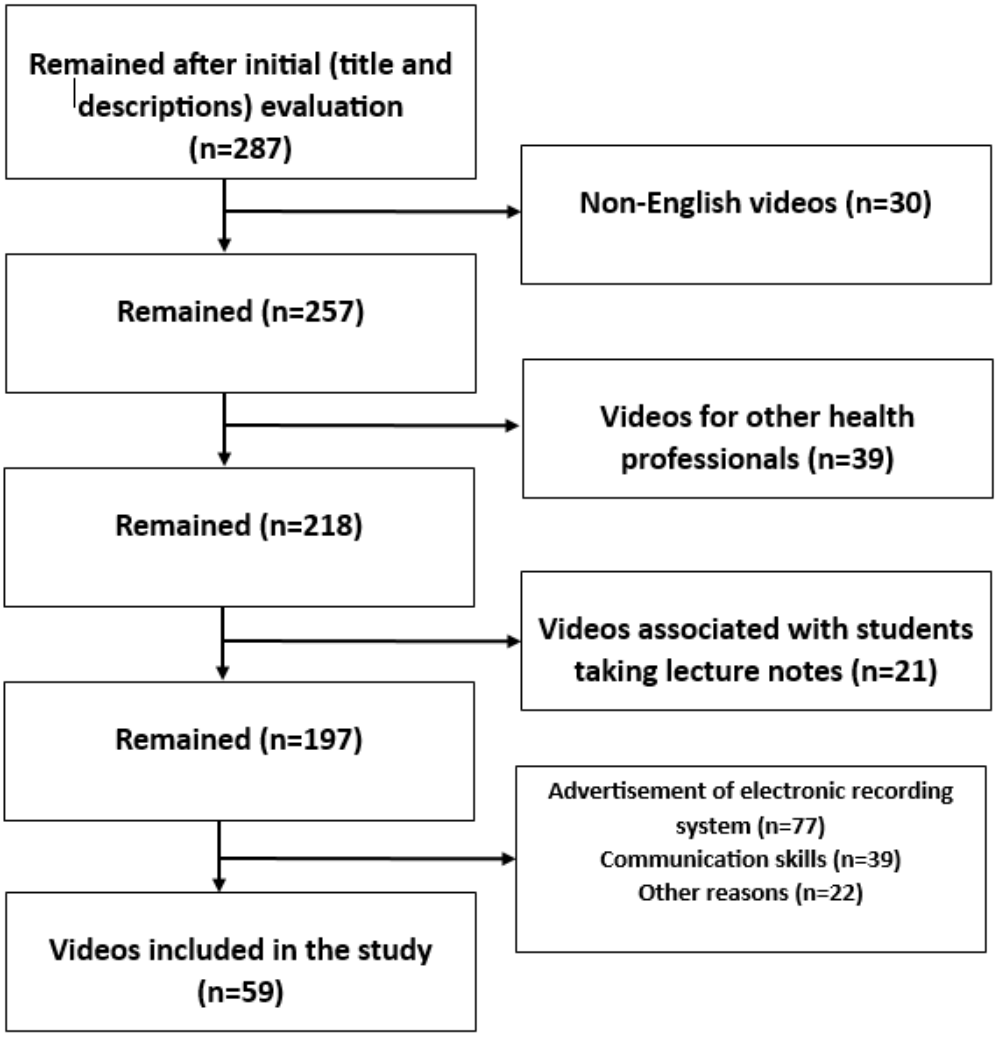

Figure1. Flowchart for video selection.

and dislikes count, comment count, and upload date, were documented. To present the videos' popularity, the number of views per day (number of views/days) and the like ratio (number of likes*100 / number of dislikes + number of likes) were calculated from this data. Lastly, the Video Power Index (VPI) was calculated as like ratio × view ratio/100 (25). In cases where videos consisted of multiple parts, they were treated as a singular entity by computing the view counts as the average of the view counts across the video parts. Regarding likes and dislikes, the highest counts from the various video parts were considered.

Video Source: The videos were assigned to these five categories according to their source (uploaders):

- Universities / professional organizations
- Individual academics (individuals who has academic titles)
- Non-academic physicians and medical students
- Non-physician healthcare professionals
- Non-healthcare professionals.

During the search for video sources, information from video descriptions, YouTube profiles, and, the video content itself, was utilized to identify the source. The decision not to present doctors and medical students as different categories was made because some videos were of older origin, making it challenging to distinguish whether the content was created during their student years or after transitioning into a professional role as a doctor. This approach was particularly necessary when considering cases where the uploader, although originally a student, is now practicing as a doctor. Lastly, if the video content includes information relevant to a particular medical specialty, such information was also recorded.

Type of Clinical Record-keeping: The assessment included determining the relevance of the videos to specific fields within clinical record-keeping. To achieve this, each video was assigned to one of these categories: “Patient history” and “Progress note”.

Comprehensiveness: Comprehensiveness of the videos were evaluated based on the specific categories regarding the type of clinical record-keeping they belong. QNOTE, an instrument for measuring the quality of notes, was used for videos on clinical record-keeping of patient history (26). In

the assessment of the videos on progress notes, a checklist developed for this type of documentation that consists of 18 items was used utilized (27). For the videos that include both patient history and progress notes, both of these tools were utilized and a comprehensiveness score (ComScore) was calculated by taking the average of the scores.

Instructional Quality: The instructional video quality checklist (IVQC) was used to evaluate the quality of the videos as educational materials, which was calculated over 27 points (28).

Statistical Analysis: Statistical analysis was performed using SPSS version 22.0 (IBM, Chicago, IL, USA). The descriptive data of the videos were presented by calculating descriptive statistics as mean ± standard deviation (SD) for continuous variables and percentages for categorical variables. Mann-Whitney U test was used in the analyses comparing two groups. $p<0.05$ was considered statistically significant.

Ethical Considerations: Since this study did not include any human participants but only involved publicly accessible videos, it does not require to obtain an ethical approval.

RESULTS

Among 59 videos were included in the study, 52 (88.14%) were on patient history, nine (15.24%) were on progress notes, and two (3.39%) were on both patient history and progress notes. Some descriptive statistics of the videos included in the study are shown in Table 1. Five videos reached more than 90% of comprehensiveness, while only one of them included all aspects of clinical record-keeping(https://www.youtube.com/watch?v=j0MsR-1e9ww).

Table 1. Descriptive findings of the videos

	Mean	SD	Minimum	Maximum
ComScore (n=59)	60.4	17.89	22.22	100
IVQC (n=59)	11.19	3.61	3	18
Duration on YouTube (days) (n=59)	1480.69	1067.78	76	4309
Video length (second) (n=59)	608.15	321.09	56	1305
Number of daily views (n=59)	41.49	55.1	0	217.68
Comment (n=57)	36.26	52.04	0	259
Like (n=58)	1136.28	1612.15	0	6015
Dislike (n=58)	23.24	37.89	0	156
Like ratio (n=59)	93.32	21.63	1	100
VPI(n=59)	40.45	54.24	0	213.04

ComScore: comprehensiveness score (out of 100), IVQC: instructional video quality checklist (out of 27), VPI: video power index

Of 59 videos, 14 (23.72%) specifically utilized the SOAP (subjective, objective, assessment, plan) note-taking method.

In the evaluation of the videos' affiliation with specific specialties, the number of videos related to specialties are as follows: Pulmonology (three videos), obstetrics (three videos), psychiatry (two videos), surgery (two videos), neurology, ophthalmology, clinical pharmacology, and intensive care (one video for each). Remained 45 (76.27%) videos were not specific to any specialty.

Upon evaluating the characteristics of the uploaders, it was found six (10.17%) videos were uploaded by universities or professional associations/organizations, five (8.47%) by individual academics, 33 (55.93%) by non-academic physicians or medical students, 11 (18.64%) by non-physician healthcare professionals, and three (5.08%) by non-healthcare professionals. The uploader of one (1.69%) video could not be classified. Group-based descriptive statistics are presented in Table 2.

Table 2. Descriptive information according to the uploader of the videos

	University / Professional Organization (n=6)	Academician (n=5)	Doctor / Medical student (n=33)	Non-doctor Healthcare Professionals (n=11)	Non-healthcare Professionals (n=3)
ComScore	62.96±22.48	67.78±25.80	57.37±16.15	62.5±17.945	61.11±17.35
IVQC	15.17±1.17	14±3.39	10.76±3.24	9.45±4.08	10.33±3.06
Duration on YouTube (days)	1430.5±898.14	2118.4±869.59	1324.42±984.24	1280.18±1083.95	2177±1714.15
Video length (second)	751.5±476.67	373.8±189.1	645.64±296.99	609.36±324.16	290±199.02
Number of daily views	51.05±44.77	89.01±63.38	42.82±61.94	23.29±26.15	7.99±2.60
Comment (n=57)	17.2±13.76	134.8±82.64	32.72±43.54	22.27±27.55	4.33±5.13
Like (n=58)	924.2±568.27	3579.8±2241.66	1170.09±1630.43	376.45±365.5	138±365.52
Dislike (n=58)	15±17.10	74.2±57.16	23.97±39.11	8.73±12.05	4±3.60
Like ratio	65.9±50.28	97.93±1.06	95.43±17.06	98.28±1.98	97.34±3.31
VPI	47.79±47.55	87.14±61.83	41.98±60.74	22.89±25.87	7.82±2.78

ComScore: comprehensiveness score (out of 100, IVQC: instructional video quality checklist (out of 27), VPI: video power index

In the examination of the countries from which the videos were uploaded, it was observed that 18 (30.51%) videos were from India, 15 (25.42%) from the United States, eight (13.56%) from the United Kingdom, four (6.78%) from Canada, three (5.08%) from Pakistan, two (3.39%) from the Philippines, and one (1.69%) each from Egypt, Nigeria, and South Africa. The origin countries of six (10.17%) videos could not be found. In a video uploaded by a university/professional organization, we excluded evaluation of likes, dislikes, and comments. Additionally, in a video uploaded by an individual academic, comments were not assessed. The reason was that these features were disabled in the videos.

Due to the limited number of uploaders in certain groups, group-based comparison was made by combining "universities or professional associations/organizations" and "individual academics" as the first group, others as the second group, which has been shown in Table 3. When uploader groups were divided into these two group, there was no significant difference in comprehensiveness score (p = 0.131). However, the first group (14.64±2.38) outperformed the second group (10.43±3.41) in IVQC score, and the difference was significant (p<0.001).

Table 3. Comparison of university/professional organization, academic uploaders group and others

	University / Professional Organization / Academician (n=11)	**Doctor / Medical student / Non-doctor Healthcare Professionals / Non-healthcare Professionals (n=47)**	**p-value**
ComScore	65.15±22.92	58.81±16.42	0.131
IVQC	14.64±2.38	10.43±3.41	**<0.001**
Duration on YouTube (days)	1743.18±913.71	1368.49±1050.22	0.168
Video length (second)	579.82±408.43	614.45±305.77	0.585
Number of daily views	68.3±54.79	36.03±54.23	**0.028**
Comment (n=57)	76±83.43	28.37±39.20	**0.036**
Like (n=58)	2252±2082.27	918.47±1426.44	**0.016**
Dislike (n=58)	44.6±50.55	19.13±33.97	**0.045**
Like ratio	80.46±39.30	96.22±14.33	0.081
VPI	65.67±55.52	35.34±53.20	0.090

ComScore: comprehensiveness score (out of 100, IVQC: instructional video quality checklist (out of 27), VPI: video power index Bolds are significant at <0.05 level.

DISCUSSION

Educational materials must meet high standards in terms of comprehensiveness and instructional quality. In this context, considering the extensive accessibility of YouTube and its use by medical students and medical educators, it is important to assess these aspects of YouTube videos. Therefore, educational videos on clinical record-keeping, which is one of the core competencies, were evaluated in terms of comprehensiveness and instructional quality.

In our study, the mean comprehensiveness score of the videos was 60.4±17.89 out of 100. This finding shows that video content on YouTube falls short in including the necessary components of clinical record-keeping. A student or physician watching the videos would only be able to obtain information about 60% of clinical record-keeping, missing a significant portion of the essential components of this core skill. This finding is similar to the previous studies that have highlighted the lack of quality in YouTube videos as a source for patients (23, 24). However, our findings pertain to the educational context specificatablelly for medical students and physicians. The finding is also in line with the scoping review on YouTube as an educational source that revealed many videos do not include sufficient content (22).

While the comprehensiveness of the videos did not meet the required standards, the instructional quality score was 11.19±3.61 out of 27. This implies that the quality of educational materials falls below half of the expected levels. Notably, our study revealed that the instructional quality score was higher among the university/professional organizations and individual academics compared to the other groups, aligning with expectations. Consistent with existing literature, similar studies have demonstrated that videos uploaded by academics or healthcare professionals tend to exhibit higher scores in terms of educational content and quality (25, 29-31). On top of these studies, two review studies found that quality of YouTube videos was superior if they were uploaded by the academics or reputable organizations compared to other uploaders (22, 24), even if the quality scores range within these groups varied widely across studies (24). Moreover, an

important finding in our study is the absence of a significant difference in the comprehensiveness score between both groups (university/academic 65.15±22.92, other 58.81±16.42). This suggests that even academics fall short in covering approximately 35% of the components of clinical record-keeping.

In a time where medical students ignore the curriculum and refer to alternative sources (32), it becomes imperative for medical educators to promote the use of reliable learning resources. Encouraging students to prefer videos uploaded by professional organizations or academics can be beneficial in ensuring a more comprehensive understanding of clinical record-keeping. Establishing a curated list of reliable sources for this purpose can guide learners toward more comprehensive materials. However, it is essential to advise students to approach each content with critical thinking skills, because even the videos uploaded by reputable sources do not include all components of clinical record keeping. Addition to that, in order to improve instructional quality of the videos, medical educators may benefit from quick tips and recommendations on this topic (33, 34).

Upon comparing the university/professional organizations and academic group with other uploaders, we found no significant difference between the two groups in terms of like ratio and VPI. These results indicate that there is no difference in popularity between these groups, aligning with similar findings in existing literature (24). However, it is noteworthy that the number of daily views was higher in the university/professional organizations and academician group. From these findings, one might infer that viewers, at the very least, show a preference for videos from uploaders they perceive as more reliable.

The study has several limitations. First, the evaluation of videos was confined to the most widely used video viewing platform, and videos from other sources might yield different conclusions. Second, as the study focused only on clinical record-keeping videos, it is necessary to recognize that generalizing conclusions to entire medical education cannot be warranted. Third, involving multiple reviewers for video evaluation would enhance the reliability of the findings. Last, while established data collection tools were utilized in the study, the potential impact of variations in clinical record-keeping education across diverse countries could influence our findings.

CONCLUSION

YouTube videos should be used cautiously for clinical record-keeping training by medical students and medical educators. For educators in the process of creating video materials, producing quality content with checklists and scales can be an important step in overcoming these obstacles. Additionally, although it may be challenging, enabling medical school students to identify and use videos with sufficient content quality in their online education materials and raising awareness on this matter will be beneficial.

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RESEARCH ARTICLE

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Impact of Subcutaneous Fat Thickness on Biochemical Recurrence and Recurrence-Free Survival in Patients Undergoing Radical Prostatectomy

ABSTRACT

Objective: Aim of this study is to evaluate the association between subcutaneous fat thickness (SCFT) and biochemical recurrence (BCR) in patients who have undergone radical prostatectomy (RP).

Methods: Study included 52 patients who had non-metastatic prostate cancer (PCa), underwent RP at our center between April 2015 and January 2020. All patients had a full abdomen computed tomography (CT) scan within six months prior to surgery. Measurements of fat, muscle, and tissue were evaluated by two radiologists, and binary logistic regression analysis was performed to determine factors influencing BCR. SCFT was identified as the only radiological factor influencing recurrence. A cut-off value (25.6) was determined using an ROC curve, and patients were divided into two groups based on this value.

Results: In Group 1 (SCFT < 25.6), the median recurrence time was 39 (3-65) months, and the median follow-up time was 40.5 (17-65) months. In Group 2 (SCFT ≥ 25.6), the median recurrence time was 20.5 (3-58) months, and the median follow-up time was 43 (12-69) months. The one-year and three-year recurrence-free survival rates were 82.1% and 78.4% for Group 1, respectively, while they were 62.5% and 52.2% for Group 2, respectively (p=0.047).

Conclusions: The ability to predict recurrence in PCa is crucial for the management and treatment of the disease. Our study, which demonstrates a significant relationship between SCFT and BCR, suggests that radiological evaluation and measurements will be further utilized in the diagnosis, treatment, and follow-up of the disease.

Keywords: Biochemical Recurrence, Prostate Cancer, Subcutaneous Fat Thickness.

Radikal Prostatektomi Uygulanan Hastalarda Deri Altı Yağ Kalınlığının Biyokimyasal Nüks ve Nükssüz Sağkalım Üzerine Etkisi

ÖZET

Amaç: Bu çalışmanın amacı radikal prostatektomi (RP) uygulanan hastalarda deri altı yağ kalınlığı (DAYK) ile biyokimyasal nüks (BKN) arasındaki ilişkiyi değerlendirmektir.

Yöntem: Çalışmaya Nisan 2015 ile Ocak 2020 tarihleri arasında merkezimizde RP uygulanan toplam 52 metastatik olmayan prostat kanseri tanılı hasta dahil edildi. Tüm hastalara ameliyattan önceki altı ay içinde tüm batın bilgisayarlı tomografi (BT) taraması yapıldı. Yağ, kas ve doku ölçümleri iki radyolog tarafından yapıldı ve BKN'yi etkileyen faktörleri belirlemek için ikili lojistik regresyon analizi uygulandı. DAYK, nüksü etkileyen tek radyolojik faktör olarak tanımlandı. ROC eğrisi kullanılarak kesme değeri (25,6) belirlendi ve hastalar bu değere göre iki gruba ayrıldı.

Bulgular: Grup 1'de (DAYK < 25,6) ortanca nüks süresi 39 (3-65) ay, ortanca takip süresi ise 40,5 (17-65) ay idi. Grup 2'de (DAYK ≥ 25,6) ortanca nüks süresi 20,5 (3-58) ay, ortanca takip süresi ise 43 (12-69) ay idi. Bir yıllık ve üç yıllık nükssüz sağkalım oranları Grup 1'de sırasıyla %82,1 ve %78,4 iken Grup 2'de sırasıyla %62,5 ve %52,2 idi (p=0,047).

Sonuç: Prostat kanserinde nüksü tahmin edebilmek hastalığın yönetimi için çok önemlidir. DAYK ile BKN arasında anlamlı bir ilişki olduğunu ortaya koyan çalışmamız; hastalığın tanı, tedavi ve takibinde radyolojik değerlendirme ve ölçümlerden daha fazla yararlanılacağını düşündürmektedir.

Anahtar Kelimeler: Biyokimyasal Nüks, Prostat Kanseri, Deri Altı Yağ Kalınlığı.

INTRODUCTION

Prostate cancer (PCa) is the second most common cancer and the fifth leading cause of cancer-related deaths among men globally, with around 1.4 million new cases and 375,000 deaths in 2020 (1).

Patients with biochemical recurrence (BCR) are known to be at an increased risk of developing distant metastases, experiencing death from PCa, and having higher overall mortality rates (2). Nomograms have been developed to predict the likelihood of BCR following local treatment of PCa. Some nomograms are based solely on pre-treatment factors, while others incorporate histopathological examination (3-5). Due to the growing use of multiparametric prostate magnetic resonance imaging (mpMRI), recent nomograms have begun to include variables like maximum tumor diameter. mpMRI provides a detailed assessment of PCa and facilitates a more accurate tumour classification. It enables the determination of precise measurements regarding the size, location, margins and invasiveness of tumors (6).

There are hypotheses which propose potential protective effects of subcutaneous adiposity in cancer patients. Possible explanations include energy metabolism, signaling from adipose tissue, and a higher frequency of medical visits among obese individuals (7).

This study aims to examine the correlation between subcutaneous fat thickness before surgery and BCR in patients who undergo radical prostatectomy (RP).

MATERIAL AND METHODS

The study was conducted according to the regulations of the institutional research ethics board. The study was approved by Ethics Committee of University (Approval No: 2022/0067, Date: 09/02/2022) and conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all patients participating in study.

Our center evaluated 230 patients who underwent preoperative mpMRI followed by RP between April 2015 and January 2020. Our study included 52 PCa patients who received primary RP and underwent an additional abdominal computed tomography (CT) scan within 6 months before surgery, meeting the criteria of non-metastatic disease, no androgen deprivation therapy, and no other malignancies. Exclusions from the analyses encompassed patients with insufficient imaging data or those who were lost to follow-up.

The definition for biochemical recurrence (BCR) was characterized by two consecutive postoperative PSA values exceeding 0.2 ng/ml. Metastases were considered as any lesions detected on postoperative systemic imaging. PSA surveillance was conducted every three months during the initial two years, followed by biannual monitoring in the subsequent year, and subsequently on an annual basis during the follow-up period. The frequency of PSA measurements was adjusted based on the patient's risk group and the adjuvant treatments received.

Two experienced radiologists assessed the patients' fat, muscle, and tissue measurements, and performed binary logistic regression analysis to determine the factors that influence BCR. The study concluded that subcutaneous fat thickness (SCFT) is the only radiological factor that influences recurrence. Using ROC curve analysis, a prediction value of 25.6 mm was determined. Patients were categorized into two groups according to this predictive value.

The average cross-sectional area of muscle and fat tissue was obtained from two axial images in the same series at the third lumbar vertebra (L3) using Horos v4.0 (Nimble Co LLC d/b/a Purview, Annapolis, MD, USA) and OsiriX v5.0 (Pixmeo, Geneva, Switzerland). Manual outlining was done to trace different tissue compartments, and the tissue of interest was segmented based on Hounsfield Unit (HU) thresholds. Selected areas were manually adjusted if necessary, and the total cross-sectional area of the segmented tissue was automatically calculated (Figure 1).

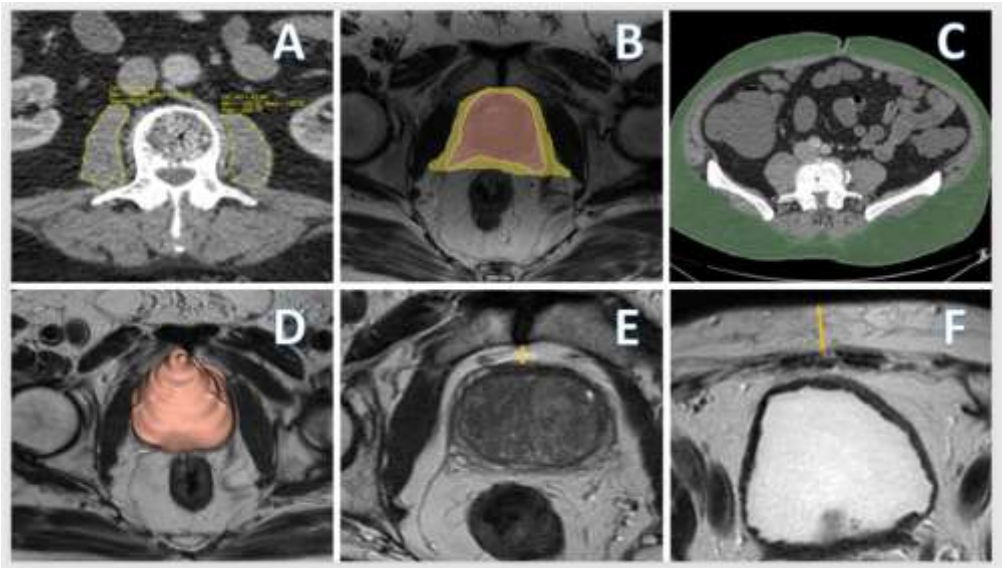

Figure 1. Parameters via MRI (A- Prostate volume, B- Periprostatic fat tissue area, C- Periprostatic fat tissue thickness, D- Psoas muscle density, E- Subcutaneous fat area, F- Subcutaneous fat thickness)

Statistics Analysis: The data were analyzed using SPSS version 22 (IBM, NY, USA). Binary logistic regression identified factors influencing BCR. An ROC curve assessed predictive value. Patients were grouped below and above the threshold. Categorical variables were compared using Pearson chi-square or Fisher's exact tests for non-normally distributed data. Kolmogorov-Smirnov tested distribution normality. Student's t-test analyzed normally distributed variables, while Mann-Whitney U test assessed others. Kaplan-Meier calculated survival rates; differences were log-rank tested. Statistical significance: $p<0.05$.

RESULTS

Tables 1 and 2 show the demographic, clinical, pathological, and radiological characteristics of the groups. Group 1 (SCFT <25.6) had a median time to recurrence of 39 months (range: 3-65) and a median follow-up time of 40.5 months (range: 17-65).

Table 1. Demographic, clinical and radiological characteristics of the groups

	Group 1 (n=28)	Group 2 (n=24)	p value
Age at diagnosis (years)	66 ± 5.7	63.8 ± 6.7	0.188
Body mass index (kg/m^2)	26.5 ± 3.2	28.1 ± 3.7	0.087
Charlson Comorbidity Index	4.96 ± 0.2	5.33 ± 0.39	0.842
Prostate-specific antigen (ng/ml)	11.9 ± 2.9	24.1 ± 8.2	0.139
Periprostatic adipose tissue area (cm^2)	14.6 ± 5.9	14.3 ± 5	0.821
Subcutaneous fat thickness (mm)	18.9 ± 3.8	30.1 ± 4.7	**<0.001**
Subcutaneous area of adipose tissue (cm^2)	196.9 ± 65.8	244.1 ± 52.6	**0.007**
Visceral adipose tissue area (cm^2)	172.8 ± 71.4	178.8 ± 44	0.726
Periprostatic adipose tissue thickness (mm)	7.6 ± 3.5	7.6 ± 2.9	0.964
Periprostatic adipose tissue area / Prostate volume	33 ± 30.8	31.5 ± 16	0.830
Periprostatic adipose tissue thickness / Subcutaneous fat thickness	0.41 ± 0.25	0.25 ± 0.13	**0.007**
Psoas muscle density (HU)	46 ± 8.3	51.8 ± 6.8	**0.010**
Skeletal muscle density (L3 vertebra level) (HU)	31.1 ± 9.3	34.8 ± 9.1	0.163
Prostate volume on mpMRI (cm^3)	56.8 ± 28.3	52.2 ± 22.6	0.529

Table 2. Preoperative patient history, pathology evaluation and postoperative clinical features

	Group 1 (n=28)	**Group 2 (n=24)**	**p value**
Family history of prostate cancer, n (%)	4 (% 14.3)	4 (%16.7)	0.556
pT			0.187
2	15	9	
3	13	15	
RRP-ISUP Grade			0.218
1	6	1	
2	5	10	
3	7	1	
4	7	4	
5	3	8	
EPE +, n (%)	13 (% 46.4)	15 (% 62.5)	0.246
LNI +, n (%)	0	0	
Biochemical recurrence, n (%)	6 (% 21.4)	11 (% 45.8)	0.061
Progression, n (%)	1 (% 3.6)	2 (% 8.3)	0.590

RRP: retropubic radical prostatectomy, ISUP: The International Society of Urological Pathology, EPE: extraprostatic extension, LNI: lymph node invasion

Group 2 (SCFT ≥25.6) had a median time to recurrence of 20.5 months (range: 3-58) and a median follow-up time of 43 months (range: 12-69). Group 1 had one-year and three-year recurrence-free survival rates of 82.1% and 78.4%, respectively, while for Group 2, they were 62.5% and 52.2%, respectively (p=0.047) (Figure 2).

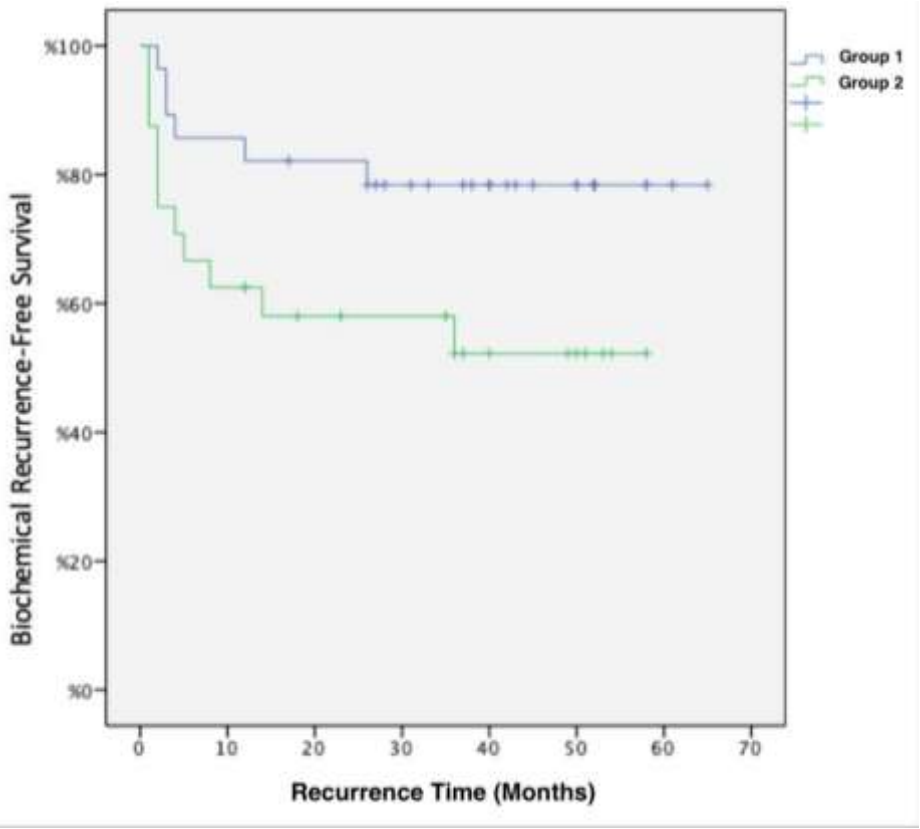

Figure 2. Kaplan-Meier curve for biochemical recurrence-free survival

In terms of RP ISUP grades, pathologic stages, extraprostatic extension, and lymph node involvement, there was no significant difference between the two groups. Regarding BCR, although there was no significant difference, Group 2 showed a higher rate of BCR that was almost statistically significant (p=0.061) (Table 2). In univariate analysis, subcutaneous fat thickness, TRUS biopsy ISUP grade, pT, RRP ISUP grade, and extraprostatic extension were all associated with BCR risk. In multivariate analysis, the presence of extraprostatic extension was the only factor that remained significantly associated with BCR risk (HR: 30.667; 95% CI: 3.617-259.986; p<0.002) (Table 3).

Table 3. Univariate and multivariate regression analysis of biochemical recurrence.

	Univariate Model					**Multivariate Model**				
	HR	(95% CI)			p value	HR	(95% CI)			p value
Age	0.938	0.850	-	1.036	0.206					
Body Mass Index	1.125	0.948	-	1.336	0.178					
Family history of prostate cancer	0.644	0.116	-	3.590	0.616					
CCI	1.480	0.986	-	2.220	0.058					
Diagnosis PSA	1.015	0.993	-	1.037	0.195					
Periprostatic adipose tissue area	1.001	1.000	-	1.002	0.206					
Subcutaneous fat thickness	1.100	1.004	-	1.206	0.042					
Subcutaneous adipose tissue area	1.000	1.000	-	1.000	0.180					
Visceral adipose tissue area	1.000	1.000	-	1.000	0.484					
Periprostatic fat thickness	0.988	0.821	-	1.189	0.900					
Skeletal muscle area	1.000	1.000	-	1.000	0.131					
Psoas muscle area	1.000	0.998	-	1.001	0.687					
Prostate volume MRI	0.997	0.974	-	1.020	0.792					
TRUS biopsy ISUP Grade	2.662	1.563	-	4.533	0.001					
pT	11.572	2.274	-	58.883	0.003					
RRP ISUP Grade	3.439	1.741	-	6.793	0.001					
EPE	30.667	3.617	-	259.986	0.002	30.667	3.617	-	259.986	0.002

HR: hazard raito, CI: confidence interval, CCI: Charlson Comorbidity Index, PSA: prostate-specific antigen, MRI: magnetic resonance imaging, TRUS: transrectal ultrasound, ISUP: The International Society of Urological Pathology, RRP: retropubic radical prostatectomy, EPE: extraprostatic extension

DISCUSSION

The association between body composition and PCa prognosis has been extensively studied, particularly concerning the obesity paradox. Numerous literature studies suggest that obesity (BMI ≥30 kg/m²) is linked to higher risks of high-grade PCa and recurrence following prostatectomy (8,9). In patients with advanced disease, some articles suggest that obesity may have a protective effect. Observations have shown that men with metastatic hormone-sensitive PCa who are obese tend to demonstrate improved progression-free survival and overall survival (10). The role of BMI as a prognostic marker for adiposity remains uncertain. A meta-analysis of 16 studies, which monitored 26,479 PCa patients post primary treatment, indicated that a 5 kg/m² increase in BMI was associated with a 21% higher risk of BCR (11). Multiple studies in the literature do not conclusively establish a connection between high BMI and the risk of BCR. The correlation between BMI and PCa outcomes may exhibit variations among studies, leading to contradictory findings. These differences in results could be attributed to factors such as study design, patient characteristics, duration of follow-up, and statistical adjustments. As a result, the relationship between high BMI and the risk of BCR in PCa remains a subject of continuous research and discussion (12-14). Thus, researchers are examining adiposity-related parameters other than BMI, which are linked to prognosis.

Studies have demonstrated that visceral fat is linked inversely to bioavailable testosterone and displays a more pronounced correlation with insulin resistance and pro-inflammatory cytokines compared to subcutaneous fat (15,16). In contrast to subcutaneous depots, visceral adipose tissue presents greater expression of glucocorticoid and androgen receptors, possesses a higher metabolic activity, and demonstrates elevated levels of lipolysis (15). In the regression analysis, the study did not discover a link between visceral fat area and BCR. However, subcutaneous fat thickness was identified as the only radiological parameter that influenced BCR. Identifying adiposity phenotypes with the greatest risk of developing aggressive PCa can contribute to uncovering the mechanisms connecting obesity to the onset of aggressive disease. Additionally, this identification can assist in targeting appropriate intervention strategies (17).

In vitro research has established a correlation between periprostatic adipose tissue and the development of an aggressive phenotype in PCa cells (18). Multiple clinical studies have confirmed a connection between periprostatic adipose tissue and the degree of aggressiveness displayed by PCa (19). A retrospective analysis of pelvic MRI was carried out by Woo et al. in 190 patients prior to RP (20). The study revealed a significant correlation between the Gleason score in RP specimens and periprostatic fat thickness. In a study conducted by Qiang et al., involving 184 men who underwent RP, a positive correlation was discovered between periprostatic fat area and the aggressiveness of PCa (21). Our study did not find any association between periprostatic fat area and BCR in the regression analysis. Obesity and its associated metabolic alterations play a substantial role in the occurrence of BCR, metastatic progression, and mortality among men with PCa. As per a study by Lopez et al., a link between overall survival in PCa patients and total adiposity is absent (22). Nonetheless, the study indicated that elevated levels of subcutaneous adipose tissue are linked to enhanced survival (HR 0.68, 95% CI: 0.54-0.84, p=0.001). There is a strong correlation between the area of fat tissue measured in a single axial abdominal image and the total volume of body fat tissue (23). The radiodensity of adipose tissue has recently been identified as a novel imaging biomarker that is closely associated with various adipokines (24). McDonald et al. conducted a study that involved 171 radiotherapy patients with high-risk PCa (25). Their findings indicate no statistically significant correlation between the area of subcutaneous fat tissue and BCR. Qiang et al. conducted a retrospective study and found no significant differences in subcutaneous fat thickness between clinical stages, Gleason scores, or risk groups (21). Similarly, our study did not find any significant association between subcutaneous fat tissue area and BCR in the regression analysis.

Study Limitations: The study has limitations. The study's retrospective design may have introduced biases and limitations in data collection. The study results may not be applicable to other ethnic groups as there may be variations in body composition attributed to ethnicity and race. Variations in the results may occur among patients with different PCa stages. It is crucial to consider the limitations when interpreting and applying the findings of the study. Prospective studies with diverse populations are necessary to validate and generalize the results.

CONCLUSION

Predicting recurrence in prostate cancer (PCa) is crucial for disease monitoring and treatment. Our study data demonstrated a significant correlation between subcutaneous fat thickness and BCR, indicating that radiological evaluation and measurements may become more common in the diagnosis, treatment, and follow-up of PCa in the future. The morphometric examination of mpMRI imaging can aid in pinpointing patients who are at an elevated risk of experiencing an unfavorable prognosis. In the future, body composition parameters determined by mpMRI data could offer objective prognostic factors to guide personalized treatment decisions. Supporting existing data with multicenter prospective studies is crucial.

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RESEARCH ARTICLE

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Improving the Knowledge, Skill, and Attitudes of Medical Faculty Students on the Breast Cancer

ABSTRACT

Objective: In this study, it was aimed for third-year medical school students to improve their knowledge, examination skills and attitudes about breast cancer, and to experience the skills of taking a disease history, communicating effectively and giving bad news.

Methods: The present study was carried out with 406 3rd-year medical faculty students from Akdeniz University and a semi-experimental method was employed. The content of implementation consists of improving the students' skills in receiving disease history from the patient and "clinical breast examination" on breast model, as well as informing the patient about the examination findings. Before the application, all students were given theoretical information about the subject and practiced with a learning guide on clinical breast examination. The pretest-posttest results of surveys received from the participating students and the standardized patient practice feedback form were analyzed.

Results: Examining the surveys conducted before and after the implementation with 406 students, it was found that the students learned what the risk factors related with breast cancer are and they could question them while receiving the patient history ($p<0.05$). Their ability to perform breast examination was improved and they could detect the lump in breast ($p<0.05$). They gained experience about informing the patients and referring them to the departments related with preliminary diagnosis of breast cancer, as well as giving bad news ($p<0.05$).

Conclusions: With a suitable scenario and planned educations, "Standardized Patient Practice" can be successfully used in preclinical educations.

Keywords: Breast Examination, Breast Cancer, Simulation Applications, Standardized Patient, Feedback.

Tıp Fakültesi Öğrencilerinin Meme Kanserine İlişkin Bilgi, Beceri Ve Tutumlarının Geliştirilmesi

ÖZET

Amaç: Bu çalışmada tıp fakültesi dönem üç öğrencilerinin meme kanseri ile ilgili bilgi, muayene becerisi ve tutum düzeylerini geliştirmeleri ayrıca hastalık hikayesi alma, etkili iletişim kurma ve kötü haber verme becerisini deneyimlemeleri amaçlanmıştır.

Yöntem: Çalışma Akdeniz Üniversitesi Tıp Fakültesindeki 406 dönem üç öğrencisi ile yapılmış, yarı deneysel bir yöntem uygulanmıştır. Uygulamanın içeriği standart hastadan hastalık hikayesi alma ve meme maketi üzerinde "klinik meme muayene" becerisinin geliştirme ve muayene sonucunun hastaya bilgi verilmesinden oluşmaktadır. Uygulama öncesi tüm öğrencilere konu hakkında teorik bilgi verilmiş ve klinik meme muayenesi konusunda öğrenim rehberiyle uygulama yaptırılmıştır. Uygulamalara katılan öğrencilerden alınan anketlerin öntest- sontest sonuçları ve standart hasta uygulaması geribildirim formu değerlendirilmiştir.

Bulgular: Çalışmaya katılan 406 öğrenciye uygulama öncesinde ve sonrasında uygulanan anketler değerlendirildiğinde, öğrenciler meme kanseri ile ilgili risk faktörlerinin neler olduğunu öğrenmiş ve hasta hikayesi alırken bunları sorgulayabildikleri belirlendi ($p<0,05$). Meme muayenesi yapma becerisini geliştirmiş ve memede kitle varlığını saptayabilmişlerdir ($p<0,05$). Hastalara bilgilendirme ve meme kanseri ön tanısı ile ilgili branşlara yönlendirme yaparak kötü haber verme becerisi deneyimi kazandılar ($p<0,05$).

Sonuç: Uygun bir senaryo ve planlı eğitimlerle "Standart Hasta Uygulamaları" klinik öncesi dönem eğitimlerinde başarıyla kullanılabilir.

Anahtar Kelimeler: Meme Muayenesi, Meme Kanseri, Simülasyon Uygulamaları, Standart Hasta, Geribildirim.

INTRODUCTION

Nowadays, the breast cancer is the most frequently detected type of cancer among the women around the world. In our country, the increase in the number of breast cancer diagnosis and the decrease in the age of diagnosis emphasize how important the breast cancer screening is important. Whereas the worldwide incidence of breast cancer among all the cancers is 25.1% (1), it is 24.9% in our country (2).

The social awareness is necessary in order for cancer screening programs to be effective. Raising awareness by making use of sustainable education strategies and determining the examination and screening methods most suitable for our country are very important for early diagnosis of breast cancer (3). Main risk factors for breast cancer are female gender, elderliness, and white race. Breast cancer is 70-80% sporadic, 15% familial, and 5-10% genetic. Estrogen hormone plays an important role in its etiology and most of the risk factors are directly or indirectly related with the effects of estrogen. The risk of breast cancer is higher among women giving their first birth at the ages older than 30 years when compared to those giving their first birth at the ages younger than 18 years. The risk of breast cancer is higher among the women having menarch at younger ages since their exposure to estrogen is longer. Obesity, exposure to radiation at the thoracic region during developmental period, having no birth history, and no lactation history are among the factors increasing the risk of breast cancer (4).

Among the breast cancer screenings, mammography is known to be the most important scanning method decreasing the mortality (5). Besides the advanced-level examinations, the breast examination is a very important scanning and diagnosis method for early diagnosis in our country. The breast examination plays an important role in early diagnosis of breast cancer since it can be applied anytime, it requires no additional cost, and it is a guide for further examinations (6).

Breast examination is one of the important competences in medical education program. In medical education in our country, a medical faculty graduate is supposed to make a provisional diagnosis of breast disease and tumors within the scope of fundamental medical practice, to refer them to relevant specialist, and to apply suitable one among primary, secondary, and tertiary protection to the patient (7).

In medical faculties, various methods are used in teaching this skill. One of them is the simulation-based “Standardized Patient Practice”. This method enable the students to have a contact with patients in a realistic clinical environment, to communicate with them, and to have a learning experience in a reliable and real-like clinical environment, which is not risky for the patients, under the supervision and guidance of lecturers/faculty members (8, 9). In this study, it is anticipated that students will acquire experience in various breast diseases through the combined utilization of standard patient applications and breast models. Through interaction with these simulation tools, students acquire clinical skills by mastering correct examination techniques and learning how to effectively communicate examination findings to patients. This practice affords students the chance to assess clinical scenarios and develop decision-making skills in the diagnostic process. It also allows for an understanding of and empathy towards patients' emotional needs. Furthermore, it provides students with the opportunity to practice and subsequently receive feedback without the risk of making errors, thereby enhancing their capacity to learn from mistakes and continuously refine their skills. The content of this educational program consists of introduction to the education method in preliminary interviews with students, informing the students, answering the questions, and having them meet with patients.

Breast cancer remains a prevalent and pressing health concern within society, warranting heightened awareness and education, particularly among medical faculty students. The present study endeavors to address this imperative by focusing on enhancing the understanding and proficiency of breast cancer and breast examination skills among 3rd-year medical faculty students. Through the implementation of a dedicated breast cancer education module, the study seeks to contribute towards empowering future healthcare professionals with the knowledge and skills necessary to effectively combat this widespread disease.

MATERIAL AND METHODS

This study consists of 3rd-year students studying at the Medical Faculty of Akdeniz University in education year 2017-2018 (n=406). All the students were contacted. The study was carried out with pretest-posttest model. The Standardized Patient (SP) application was integrated into the training program, scheduled for two days a week, four hours per day, at regular intervals throughout the program, totaling 20 days. Hybrid method was used for teaching the breast examination skill. The method covers receiving the history from patient by using SP practice and using a model for examination skills. Ethics committee approval for the study was received from Akdeniz University Faculty of Medicine Clinical Research Ethics Committee number 2017-281.

The education program consists of 4 steps (Figure 1). In the first step, without giving any education to the students, a knowledge, skill, and attitude survey on breast cancer and giving bad news was conducted. In the second step, the definition and incidence of breast cancer, risk

groups, what to do for early diagnosis, screening tests, and the importance and application of breast self-examination (BSE) and clinical breast examination (CBE) were explained to the students by using breast models. In this step, the breast examination was standardized with models by using education guidelines. The educational guidelines were exactly followed until students acquired the skill, and they were let correct their errors by performing repetitive examinations. In the third step, the students met with SP practice. It consists of interview with SP, performing CSE on models, and explaining the patients how to perform BSE. In the fourth step, the posttest was conducted. Moreover, the students were also asked to fill the feedback forms.

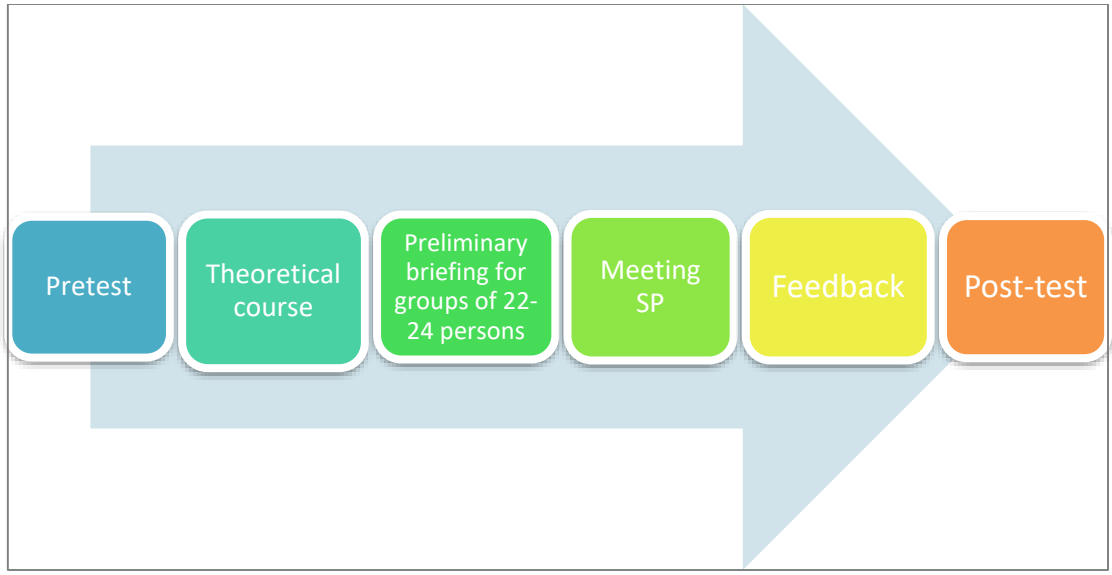

Figure 1. Flowchart of the research

The survey form used before and after the courses contains items about most frequently seen symptoms of breast cancer, risk factors, frequency of BSE, communication skills, and giving bad news.

The statistical analyses were performed using SPSS 18.0 package software. In statistical analyses, the descriptive tables were used and Chi-Square test was conducted. The level of significance was set to be $p< 0.05$.

RESULTS

The study was carried out with 406 3rd-year medical faculty students consisting of 227 (55.9) women and 179 (44.1%) men. Before the education, the students were asked if they have any knowledge about the breast cancer. Of the students, 83.7% (n=340) responded that they had knowledge on the SP practice, whereas the portion of these students increased to 96.8% (n=393) after meeting a SP (p=0.002).

Most of the answers given to the question "What are the most frequently seen symptoms of breast cancer" were the lump in breast, the pain in breast, the sunken nipple, and the leakage from nipple. While 88.6% of participating students stated that one of the most frequently seen symptoms is a lump in breast, the same rate increased to 94.8% after the education (p=0.001). When compared to the results obtained before the education, it was found that the number of students having higher level of knowledge on pain in breast, leakage from nipple, and sunken nipple that are the other most frequently seen examination findings statistically significantly increased (p<0.05) (Table 1).

Table 1. The distribution of most frequent symptoms of breast cancer as reported by the participating students before and after the education

Most frequent symptoms seen in breast cancer	Before education (n)	%	After education (n)	%	P
Pain in breast	120	29.5	95	23.3	0.00
Lump in breast	360	88.6	385	94.8	0.001
Leakage from nipple	99	24.3	120	29.5	0.00
Sunken nipple	109	26.8	112	27.5	0.00

The answers (before and after the educational program) of participating students to the questions about the effects of risk factors in breast cancer are summarized in Table 2. According to these studies, when compared to the results obtained before the educational program, the rate of knowing that not having lactated, not having given birth, using oral contraceptive, obesity, and the first

menstruation before the age of 11 years increases the risk of breast cancer and the first delivery at the age younger than 30 years decreases the risk of breast cancer statistically significantly increased after the education.

The portion of those giving right answer to the question "How frequently should BSE be performed" after the education was approx. 2 folds of the rate before education (Table 3).

Table 2. Participating students' level of knowledge on the relationship between risk factors and breast cancer, before and after the education

Questions	Before education			After education		
	R % (n)	**W % (n)**	**R/W**	**R % (n)**	**W % (n)**	**R/W**
Lactating in any period of live decreases the risk of breast cancer	54.43 (221)	45.56 (185)	1.19	81.77 (332)	18.22 (74)	4.48
Having no delivery history increases the risk of breast cancer	46.3 (188)	53.69 (218)	0.86	72.9 (296)	27.09 (110)	2.69
Use of oral contraceptive increases the risk of breast cancer	54.18 (220)	45.81 (186)	1.18	83.49 (339)	16.5 (67)	5.06
The familial history of breast cancer increases the risk of breast cancer	97.04 (394)	2.95 (12)	32.89	99.26 (403)	0.73 (3)	135.9
The incidence of breast cancer increases at later ages	88.66 (360)	11.33 (46)	7.82	96.3 (391)	3.69 (15)	26.09
Obesity increases the risk of breast cancer	45.81 (186)	54.18 (220)	0.84	85.22 (346)	14.77 (60)	5.76
The menarch at the age younger than 11 years increases the risk of breast cancer	46.05 (187)	53.94 (219)	0.85	86.2 (350)	13.79 (56)	6.25
First delivery at the age younger than 30 years decreases the risk of breast cancer	40.39 (164)	59.6 (242)	0.67	69.7 (283)	30.29 (123)	2.3
Breast cancer history of person's own increases the risk of breast cancer	90.88 (369)	9.11 (37)	9.97	97.78 (397)	2.21 (9)	44.24

R: Right. W: Wrong. R/W: Right/Wrong

The feedbacks obtained from the students right after the education were positive. After the SP practice, 91.4% of students were satisfied with SP and history, 93.3% were satisfied with the contribution of interview to the learning, and 92.8% were satisfied with the contribution of feedback to the learning. Moreover, 87.6% of students were satisfied with their performance. The overall rate of satisfaction was 99%.

Table 3. Distribution of participating students' answers to "how frequently should the BSE be performed" before and after the education

How frequently should the BSE be performed	**Before education (n)**	**%**	**After education (n)**	**%**	**p**
Whenever remembered	44	11	14	3.52	0.01
Once every bath	82	20.6	7	1.7	
Once a week	39	9.82	6	1.5	
Once a month	184	46.3	362	91.1	
Once every three months	48	12	8	2	
Total	397		397		

DISCUSSION

The present study is an interventional study and it was observed that, when compared to the pre-education period, the present study improved the students in terms of knowledge of breast examination, knowledge of most frequent symptoms seen in breast cancer, and BSE skills. Most of the studies in literature are cross-sectional ones. No interventional study carried out with medical students could be found. In the present study, the use of model, SP practice, and theoretical courses positively contributed to the improvement in skills, knowledge, and attitudes of students.

Among the answers of students regarding the most frequently seen symptoms in breast cancer, the lump in breast was ranked first. The same rate among the students in High School of Nursing was found to be 54.6% (10). It might be because there is no relevant subject in curricula of medical students.

When compared to the period before the educational program, the students' knowledge about the factors increasing and decreasing the risk of breast cancer significantly increased after the education.

In literature, there are studies reporting similar results. According to the study carried out by Aslan et al., 85% of students in high school of nursing know that lactation decreases the incidence of breast cancer (10). In the study of Seidel et al., it was reported that the level of students' knowledge increased after the education (11). In Karayurt et al.'s study, it was determined that 76.2% of women do not know how the use of OKS affects the breast cancer (12). The present study is seen to have significantly contributed to the students' knowledge of risk factors of breast cancer such as having no birth-giving history, obesity, first menstruation before the age of 11, and familial breast cancer history. Since they play an important role in the delivery of protective medical services to the society, it might be considered as a good educational practice for the physicians to well know these risk factors and use them in their professional lives. Moustafa et al. emphasized that education is a positive predictor for improving the knowledge, skill, and attitudes of students (13).

Breast cancer is the most common type of cancer among women and has the highest mortality rate (14, 15). For this reason, the early diagnosis is very important in breast cancer. BSE and CSE play an important role in early diagnosis of breast cancer among women aged <40 years. However, in the previous studies, it was reported that the women and the students studying in medical sciences and non-medical departments do now sufficiently know BSE and CSE (16). In the present study, although only half of the students correctly answered the question "how frequently should BSE be applied" before the education, this rate increased to 91.1% after the education. In the study of Karayurt et al., it was reported that only 6.7% of university students were regularly performing BSE on monthly basis (12). The rate of women stating that they perform BSE on regular basis was reported to be 28.9% by Göçgeldi et al., 32.7% by İtilli, and 42.3% by Yıldırım et al. (17-19). The education on breast examination positively changes the attitudes of students. In a study carried out in a high school of nursing located in İstanbul, it was determined that the group that had education performed BSE and CSE more than the group having no education (16). Similar results were also reported by Uzun et al. Based on these results, it can be stated that educations related with BSE change the behaviors and attitudes (20). In the study of Maurer, it was reported that the health promoting education given to young women increased their knowledge of BSE and improved their BSE skills (21).

In summary, the fact that there is a significant lack of knowledge about breast cancer among third-year medical students suggests that this lack of knowledge will be at a higher level in the general population. Therefore, these results show that it is necessary to develop and implement educational programs for breast cancer. There are various studies using different methods such as individual study, group study, and peer education. The common result of all studies is that education provides changes in knowledge and behavior (22-24).

CONCLUSION

After participating in this educational intervention, medical students exhibited enhanced knowledge of breast cancer risk factors and improved proficiency in breast examination. The training program also promoted the development of basic communication skills, enabling students to effectively communicate with patients about their condition and guide them towards appropriate diagnostic pathways. The statistically significant improvements observed underscore the effectiveness of Standardized Patient Practice in preclinical educational settings. Moving forward, concerted efforts should be made to disseminate and implement such educational programs, aiming to bolster breast cancer awareness and enhance outcomes across diverse populations.

A limitation of the study may be its regional focus due to being conducted solely within a medical school. Enhancing the overall validity of the results could be achieved by conducting multicenter studies and implementing the model in the education of medical students across diverse geographical regions.

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RESEARCH ARTICLE

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Investigation of Pneumococcus, Influenza, Covid-19 Vaccination Rates and Affecting Factors in Patients Aged 65 and Over

ABSTRACT

Objective: This study was planned to determine the vaccination rates and related factors with Pneumococcal, Influenza and Covid-19 vaccines in adults aged 65 and over who applied to the Family Medicine Outpatient Clinic.

Methods: The sample of the descriptive study consisted of 200 volunteer adult patients aged 65 and over who applied to the Family Medicine outpatient clinic between May and October 2021. The data were collected by applying a face-to-face interview with descriptive features.

Results: The mean age of the participants was 71.21±5.97 years. Influenza vaccination rate of all participants in the last 1 year was 24.50%, Pneumococcal vaccination rate in the last 5 years was 42%, and Covid-19 vaccination rate was 86%. In our study, having a chronic disease was the factor that increased the rate of influenza vaccination, it was determined that the factor determining the pneumococcal vaccination rate was affected by the habit of going to the family doctor regularly ($p<0.05$). Individuals who did not receive the Covid-19 vaccine stated that they did not have the vaccine because they were afraid of the side effects of the vaccine and did not find the vaccine safe.

Conclusions: Our study revealed that adult vaccination rates are low and they do not have enough information about their vaccinations. Health professionals, especially family physicians, have important duties to determine the factors affecting the level of knowledge about immunization in adults, to increase awareness and to make preventive medicine reach more people.

Keywords: COVID-19, Pneumococ, Influenza.

65 Yaş ve Üzeri Hastalarda Pnömokok, Grip, Covid-19 Aşılama Oranları ve Etkileyen Faktörlerin Araştırılması

ÖZET

Amaç: Bu çalışma, Aile Hekimliği Polikliniğine başvuran 65 yaş ve üzeri erişkinlerin Pnömokok, İnfluenza ve Covid-19 aşıları ile aşılanma oranları ve ilişkili faktörleri belirlemek amacıyla planlandı.

Yöntem: Tanımlayıcı olarak yapılan araştırmanın örneklemini Mayıs -Ekim 2021 tarihleri arasında Aile Hekimliği polikliniğine başvuran 65 yaş ve üzeri 200 gönüllü erişkin hasta oluşturdu. Veriler tanıtıcı özellikleri içeren anket yüz yüze görüşme şeklinde uygulanarak toplandı.

Bulgular: Katılımcıların ortalama yaşı 71.21±5.97 yıldı. Tüm katılımcıların son 1 yıl içinde İnfluenza aşılanma oranı 24.50%, son 5 yıl içinde Pnömokok aşılanma oranı 42%, Covid-19 aşılanma oranı 86% olarak bulunmuştur. Çalışmamızda kronik hastalığa sahip olmanın influenza aşılanma oranını arttıran faktör olduğu, Pnömokok aşılanma oranını belirleyen faktörün ise düzenli aile hekimine gitme alışkanlığından etkilendiği belirlenmiştir($p<0.05$). Covid-19 aşısı yaptırmayan bireyler ise aşının yan etkilerinden korktuğu ve aşıyı güvenli bulmadıkları için yaptırmadıklarını ifade etmiştir.

Sonuç: Çalışmamız erişkin aşılanma oranlarının düşük olduğunu ve aşıları hakkında yeterli düzeyde bilgi sahibi olmadıklarını ortaya koymuştur. Erişkinlerde bağışıklama ile ilgili bilgi düzeyini etkileyen faktörlerin belirlenmesi, farkındalığı arttırmak ve koruyucu hekimliğin daha çok kişiye ulaşabilmesi için sağlık profesyonellerine özellikle aile hekimlerine önemli görevler düşmektedir.

Anahtar Kelimeler: COVID-19, Pnömokok, İnfluenza.

INTRODUCTION

Among preventive health services, immunization has an important place in terms of both individual health and public health. Many infectious diseases have been brought under control and eradicated with vaccination in the world. Implemented vaccination policies and Expanded Programme on Immunization are important factors in increasing childhood vaccination rates (1). Despite all vaccine studies in our country, the same rates have not been achieved in adult immunization yet. Adult vaccination rates and awareness is low, especially in individuals aged 65 and over (2).

Infections are an important cause of mortality in the elderly. Approximately 80% of the elderly population has at least one chronic disease and 25% has three or more chronic diseases. Chronic diseases of the elderly population cause worsening of the existing disease and increase in morbidity and mortality (3). During life, humans come into contact with various viruses such as Influenza, Herpes simplex, Varicella zoster, Epstein-barr and Cytomegalovirus, and latent infections may occur. Influenza infections also increases susceptibility to pneumococcal infections in elderly individuals. The effectiveness of vaccination has been demonstrated in the prevention of pneumococcal infections (such as meningitis, acute otitis media and invasive pneumococcal disease) and complications Vaccination is very important in the elderly in terms of preventing diseases and complications caused by these factors, and enabling the elderly to continue their daily activities in a healthier way (4).

Immunization programs for elderly individuals are carried out in 75 different countries around the world. Our country also carries out a program in accordance with current guidelines, and conjugated pneumococcal vaccine and influenza vaccine, which are included in the adult vaccination calendar, have an important place in adult immunization. Studies have shown that pneumococcal vaccination in adult hood is a cost-effective way against pneumococcal diseases. In addition, the pneumococ vaccine is an important immune defense tool that we can use in the fight to reduce job losses, disease-related complications and hospitalizations that may occur due to influenza (3).

The Covid-19 pandemic has been one of the most important problems of our century. Among the populations at high risk of Covid-19 identified by the American Center for Disease Control and Prevention [Center for Disease Control (CDC)]; There are also adults 65 years of age and older with underlying comorbidities. Today, Covid-19 vaccines are a very important tool in the fight against the Covid-19 virus (5). Vaccination has gained a much more important place in the fight against the COVID-19 epidemic, which has affected all countries of the world. The implemented vaccine policies, obligations and the epidemic showed that people are encouraged to get the Covid-19 vaccine, but they do not have the same attitude and knowledge towards other necessary vaccines. Based on this, our study aimed to determine the rates of Pneumococcal, Flu and COVID-19 vaccines in the vaccination calendar of adults aged 65 and over and the factors affecting them. As primary care physicians, we aim to inform our patients about the vaccines included in the adult vaccination guide, to reach people who are hesitant about vaccination and provide information about vaccines and their side effects, and to increase vaccination rates by contributing to activities.

MATERIAL AND METHODS

This study was conducted prospectively with 200 volunteer adults aged 65 and over. All patients aged 65 and over who applied to the family medicine outpatient clinic between May and October 2021 and agreed to participate in the study were included. Local ethics committee approval was obtained for this study Namık Kemal University Faculty of MedicineScientific Research Ethics Committee within accordance with the Declaration of Helsinki (Date: 13.04.2021, number: 2021.91.04.09)

We were informed partipicans about the study, written and verbal consent was obtained. Inclusion criteria for the study were determined as seeing to Namık Kemal University Faculty of Medicine, Hospital Family Medicine Polyclinic, have 65 years old and over, and volunteering for the study. In order to collect data, a questionnaire was filling out face to face to measure the sociodemographic characteristics of the participants and their attitudes and knowledge levels about adult immunization, which was prepared by us in accordance with the literature research. With the questionnaire filled out, data were collected about habits of going to the family physician and attitudes, sources of information and vaccination status about influenza, pneumococcal, Covid-19 vaccines.

Statistical Analysis: SPSS (IBM SPSS Statistics 24) program was used for statistical analysis of the study.Variables that didn't show normal distribution were presented as median, min-max. Variables with normal distribution were presented as mean and standard deviation, and categorical variables were presented as numbers and percentages. Pearson-$\chi 2$ cross tables were used to analyze the relationships between two qualitative variables. $p<0.05$ wereconsidered statistically significant.

RESULTS

A total of 200 people participated in our study, 53.50% (n=93) male and 46.50% (n=107) female, the mean age was 71.21±5.97 years. Details of sociodemographic characteristics of the participants are shown in Table 1.

Table 1. Distribution of sociodemographic characteristics of the participants

Variable (N=200)	N	%
Age groups		
[$\bar{X} \pm$ S.S.→71.21±5.97 (year)]		
≤65	39	19.50
66-70	70	35.00
71-75	44	22.00
>75	47	23.50
Gender		
Famale	107	53.50
Male	93	46.50
Marital status		
The married	151	75.50
Single	49	24.50
Level of education		
Illiterate	22	11.00
Literate	21	10.50
Primary school	96	48.00
Middle School	13	6.50
High school	20	10.00
University	28	14.00
Monthly income level		
Below minimum wage	58	29.00
Minimum wage	60	30.00
Above minimum wage	82	41.00
Living place		
Provincial center	137	68.50
District	40	20.00
Village	23	11.50
Total	200	100

When the participants habits of going to the family doctor were questioned, it was seen that 50.50%(n=101) did not go to the family doctor regularly for health check-ups. When we questioned the reasons why they seen to the family physcian,we were seen that 91.50% of the participants (n=183) went to the family doctor to have the drugs re-prescribed fortheir use chronic diseases. It was observed that 41.50% (n=83) of the participants seen to their family physician to be examined. It was observed that only 6.50% (n=13) of the participantswent to the family physician for preventive health care.

The influenza vaccination rate in the last 1 year and the pneumococcal vaccination rate in the last 5 years were 24.50%(n=49) and 42%(n=84), respectively. We were determined that 14% (n=28) of participants who were not vaccinated for Covid-19. Details of the habits of seeing family physcians and the distribution of findings regarding adult vaccinations are shown in Table 2.

Table 2. Distribution of the participants' rates of going to Family Medicine and the findings regarding adult vaccinations

Variable (N=200)	N	%
Going to a regular family doctor for a health checkup		
Yes	99	49.50
No	101	50.50
Reasons for going to the family doctor*		
Printing medicine	183	91.50
To be examined	83	41.50
Obtaining preventive health service	13	6.50
Known vaccines*		
Influenza vaccine	163	81.50
Pneumococcal vaccine	156	78.00
Covid-19 vaccine	199	99.50
Influenza vaccination in the last 1 year		
Yes	49	24.50
No	151	75.50
Pneumococcal vaccination in the past 5 years		
Yes	84	42.00
No	116	58.00
Getting a Covid-19 vaccine		
Yes	172	86.00
No	28	14.00

* More than one answer was given to the question. Percentages were determined based on the total number of samples on a column basis

93.87% of 49 people who get influenza vaccine in the last 1 year get their vaccine in the primary healthcare centre(PHC). 90.47% of 84 people who get pneumococcal vaccines in thelast 5 year get their vaccine in the PHC. 39.53% of 172 people who get Covid 19 vaccine gettheir vaccine in the PHC (Table 3).

Table 3. Vaccination place preferences of the participants

Variable (N=200)	Influenza vaccine		Pneumococcal vaccine		Covid-19 vaccine	
	N	%	N	%	N	%
Vaccination places*						
Family health center	46	93.87	76	90.47	68	39.53
Public Hospital	1	2.04	6	7.14	40	23.25
University Hospital	-	.	-	-	54	31.39
Private hospital	-	-	1	1.19	10	5.81
Pharmacist	2	4.08	1	1.19	-	-
Total	49	100	84	100	172	100

* More than one answer was given to the question. Percentages were determined based on the total number of samples on a column basis.

When the information sources of the participants for the influenza vaccines are analyzed, 38.43% obtained information from the mass media, and 26.52% from the social environment.The rate of participants who learned influenza vaccines from their family physcians is 17.68%, and the rate of

those who learned from other types of physician specialist 8.84%. We were seen that the participants obtained information about pneumococcal vaccine from massmedia (37.61%), social environment (25.10%), family physicians (17.86%), and other types ofphysician specialist (10.34%). The sources of information about the Covid-19 vaccine are rateof 41.78% mass media and rate of 25.92% social environment. Participants who didn't get the influenza vaccine didn't get because 30.14% rates of they didn't need, 17.34% doctors didn't recommend it and 11.04% they were not aware of the vaccine. Inaddition, we were observed that participants who didn't get the pneumococcal vaccine didn'tget because 29.03% rates of they didn't need, %20.73they were not aware of the vaccine and%19.81 doctors didn't recommend it. When we look at the hesitancy of the Covid-19 vaccine, partipants who didn't get the Covid-19 vaccines didn't get, because 26.78% they think thatthe vaccines is not safe, 23.21% it's not their turn, 21.42% were afraid of the side effects of the vaccines (Table 4).

Table 4. Information sources and attitudes of the participants about adult vaccines

Variable (N=200)Vaccine	**Influenza**		**Pneumococcal**		**Covid-19**	
	N	**%**	**N**	**%**	**N**	**%**
Information about the vaccine*						
Television-Internet	111	33.84	105	32.91	184	37.86
Books, magazines	15	4.59	15	4.70	19	3.92
Family doctor	58	17.68	57	17.86	59	12.13
Otherbranch physicians	29	8.84	33	10.34	30	6.19
Due to the pandemic	19	5.79	23	7.21	59	12.13
Chemist	9	2.74	6	1.88	9	1.85
Social environment	87	26.52	80	25.10	126	25.92
Reason for vaccination*						
Caused by chronic disease	15	13.15	33	16.25	62	14.51
For the benefits	35	30.74	53	26.13	131	30.69
Doctor's recommendation	35	30.68	63	31.03	66	15.45
Environmental advice	17	14.91	25	12.31	71	16.64
Post pandemic	12	10.52	29	14.28	97	22.71
Reason for not getting vaccinated*						
Not informed	37	11.04	45	20.73	-	-
Not feeling the need	101	30.14	63	29.03	1	1.78
Lack of knowledge	29	8.65	29	13.36	6	10.71
Allergy/side effects	12	3.58	4	1.84	12	21.42
The vaccine is not safe	15	4.47	5	2.30	15	26.78
Lack of protection from the vaccine	38	11.34	9	4.14	3	5.40
Doctor's disapproval	58	17.34	43	19.81	-	-
Vaccine causing disease	11	3.28	2	0.94	6	10.70
Failure to vaccinate	14	4.19	11	5.09	13	23.21
To be paid	20	5.97	6	2.76	-	-

* More than one answer was given to the question. Percentages were determined based on the total number of samples on a column basis.

Education level, level of education of spouse, monthly household income, place of residence,live together with aged 65 and over individuals, live together with chronic diseaseindividuals, number of respiratory tract infections per year,habits of regular health check werenot statistically significant between the getting a influenza vaccines in the last 1 year ($p<0.05$). İnfluenza vaccination behavior in last 1 year was statistically significant betweenthe have a chronic diseases that requires continued medication use ($\chi2=4.746$; $p=0.029$).Education level, level of education of spouse, place of residence, live together with aged 65 and over individuals, live together with chronic disease individuals, number of respiratorytract infections were not statistically significant between the getting a pneumoccocal vaccination in the last 5 year ($p<0.05$). Monthly household income, habits of regular health check were significantly associated with pneumoccocal vaccination behavior [respectively($\chi2=10.703$;$p=0.005$),($\chi2=4.521$; $p=0.033$)].

Education level, level of education of spouse, monthly household income, place of residence,live together with aged 65 and over individuals, live together with chronic diseaseindividuals, number of respiratory tract infections per year,habits of regular health check werenot statistically significant between the Covid-19 vaccination behavior ($p>0.05$).Covid-19vaccination behavior was statistically significant between the have a chronic diseases thatrequires continued medication use ($\chi2=10.631$; $p=0.0001$).

DISCUSSION

The mean age of the participants was 71.21±5.97 years, with a minimum age of 65 and a maximum age of 95. In another study investigating the rate of vaccination in adults of 65 years and over, the mean age was found to be 71.36 ±5.30 years, which is consistent with our study (2). We were observed that most of the participants primary school education, and only a little amount had university education or higher. In many related studies, when theeducation level is investigated, lower secondary education and below education levelsconstitute the majority, and similar results were obtained in our study (2). In our study it was determined that the majority of the participants lived with their family. This ratio is a point that should be considered interms of approaching the geriatric population, which is a especially risky group. In our study, it was determined that majority of participants had at least one chronic disease that required continuous drug use.

The participants habits of going to the family physicians were questioned. It has been observed that half of participants, that is, 1 out of 2 people, do not go to the family physician regularly for health check-ups, which is a high rate. When we questioned the reasons why they seen to the family physcian,we were seen that majority of the partipicans went to the family doctor to have the drugs re-prescribed for their use chronic diseases. It was observed that less than half of the participants seen to their family physician to be examined. It was observed that only a small amount of the participants went to the family physician for preventive health care.

In a study conducted in Erciyes University in 2018, it was observed that 58.4% of people went to their family physician to re-prescribe their used medications and to be examined with 45.3%(6). The reason for the higher rate of represcribing the drugs they used in our study can be attributed to the fact that only individuals aged 65 and over were included in the study. As the average age increases, the rate of chronic diseases increases and the average age of our study is higher.

The fact that the majority of participants who have get the vaccines have gotten vaccinated in the PHC shows us that PHC are more easy accessible to people. PHC have an important place in obtaining information and preventive health care, and it is obvious that adult immunization studies conducted by PHC will make great contributions to the solution of public health issues.

In our study, rate of influenza vaccination in the last 1 year and rate of pneumococcal vaccination in the last 5 years were found to be 24.50% and 42.00%, respectively. When we investigate the rate of pneumococcal and influenza vaccination in developed countries; the highest rate of influenza vaccination for 65 years and over was found to be 74.7% in the USA, 65.5% in the Netherlands, and 57.4% in Spain (7,8). In 2019, this rate is 69.9% in Canada(9).

Many studies have been carried out on adult vaccination in our country. In a study conducted with 303 people 65 years and older who saw to the Family Medicine outpatient clinic inIstanbul in 2017, it was seen that 33.94% of the elderly got influenza vaccine and 9.91% got pneumococcal vaccine (2). In studies on adults, the most frequently heard, learned, and administered vaccines were influenza, tetanus, and hepatitis B vaccines, respectively (10,11). In our study, the influenza vaccination rate was lower than the pneumococcal vaccination rate. This is because many global influenza epidemics have occurred over the years, and these recurrent outbreaks have affected people's view of the efficacy of influenza vaccines. In addition, the fact that mass media coverage on influenza vaccinesand speculative news in the media can be shown as another reason.

When we asked the participants who knew about influenza, pneumococcal and Covid-19 vaccines their sources of information, it was seen that for all 3 vaccines, they obtained information from the mass media with the highest rate and then from the social environment. Different rates have been obtained in studies conducted in our country. For example, in another study conducted with geriatric patients receiving home health care services in 2018, it was seen that people who were aware of vaccines learned about vaccines mostly from physicians and health workers (10,11). This may be due to the fact that the population of receiving home health care services is in closer contact with health workers. In another study conducted with adults, it was determined that the information sources of participants who know about vaccines are mostly mass media and social environment, and the results are consistent with our study (12).

In our study, it was shown that 26.52% of the individuals who knew the influenza vaccine and 28.20% of the individuals who knew the pneumococcal vaccine learned the information from the doctors. Unfortunately, these rates are lower than the rate of participants who learn the vaccines from the mass media and social environment. The results which demonstrated once again that the importance of physicians providing more counseling and information to people about vaccines.

We were questioned the reasons of the participants whom get vaccinated and don’t get vaccinated. It was observed that 30.74% of the individuals who get the influenza to get it because they believed it would be beneficial, 30.68% as recommended it by doctors, and 10.52% decided to get it due to the Covid-19 pandemic. Again in this study; less than half of the participants stated that they weren’t informed about the vaccines as the

reason for don't getting vaccinated and didn't vaccinated because they thought that the they didn't need to get the vaccines (12).

Our study has some limitations. The research conducted within the scope of the study is limited to those aged 65 and over, and future studies can be carried out with the entire adult age group and more general conclusions can be reached by comparing the results with this study. The superiority of our study is that it is an important study conducted during the pandemic period and reveals the importance of adult immunization.

In our study, it was observed that 31.03% of those who had the pneumococcal vaccine had the vaccine on the recommendation of a doctor. In addition, it was observed that 14.28% of those who had the pneumococcal vaccine decided to have it after the pandemic. The effect of the pandemic is great in both vaccines.

In our study Covid-19 vaccines vaccination rate was found to be 86%. Our study has shown that having a chronic diseases has an impact on getting vaccinated with Covid-19 vaccines. A statistically significant relationship was found between the getting Covid-19 vaccines and the having a chronic disease. It was determined that one third of the participants who got the covid-19 vaccine got it because they thought thevaccine would be beneficial. It was determined that 16.64% of the participants who got the covid-19 vaccine got it because social environment recommended it. In addition, the fact that the Covid -19 disease is more severe in individuals with chronic diseases may have increased the vaccination rates by raising awareness about the vaccine in these people. Considering the reasons for not getting the Covid-19 vaccines, 26.78% of the participants said that they thought the vaccine was not safe and 21.42% said they didn't get it because they were afraid of the side effects of the vaccine. In another study on the Covid-19 vaccines in our country, participants reported that they was afraid of the side effects of the vaccines, didn't trust the producing companies and thought that the vaccine could not protect against COVID-19 as the reason for not getting vaccinated. Our results are similar to this study (13). We think that the newly developed Covid-19 vaccines and the speculative journalism in the mass media have animpact on the rate of getting this vaccine. As seen in all three vaccines, it is seen that the highest rate among the reasons for the participants to have these vaccines is their own attitudes about vaccines and it is obvious that the rate of vaccination will increase if they are informed correctly. The fact that the rate of those who have been vaccinated at the recommendation of a doctor is relatively low, shows us that physicians should attach importance to the issue of immunization, inform and encourage individuals to get vaccinated.

CONCLUSION

Familyp hysicians have an important role to play that healthy aging of individuals aged 65 and over,who are quite fragile, in increasing the vaccination rates of the target population and informing them about adult immunization. In addition, health care professionals and the media should act together on the prejudices and fears of the society about vaccines, ensuring that people reach the right information and aiming to increase adult immunization rates.

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RESEARCH ARTICLE

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Long-term Outcomes of Children with Myelomeningocele and the Quality of Life in Survivors

ABSTRACT

Objective: Myelomeningocele, a condition that causes chronic health conditions and diminished quality of life, affects not just the children but also their families. Therefore, we comprehensively evaluated the data of 101 children with MMC (myelomeningocele) and aimed to compare the quality of life between children with MMC and their siblings. It is crucial to understand that children with MMS have a diminished quality of life with social and behavioral aspects and health issues, which can be emotionally challenging for them and their families.

Methods: In this retrospective study, we collected data from electronic files, ensuring a comprehensive and accurate representation of the participants' medical history. To measure the quality of life, we used the KIDSCREEN 10 instrument, a widely recognized and validated tool in pediatric research.

Results: Of the 101 children, 93 were survivors. Comparing the survivors (n=93) with their siblings, survivors had lower HRQoL (health-related quality of life) scores in subdimensions of physical well-being ($p<0.001$), relationships with family ($p<0.001$) and friends ($p<0.001$), school performance and attention ($p<0.001$). On the other hand, the psychological wellness score was higher in survivors than in siblings ($p<0.001$). Most 44 (43.5%) had average mental capacity. The HRQoL score, a measure of the impact of health conditions on a person's overall well-being, was lower in the Chiari type 2 group than in the other survivors ($p=0.035$). Serum and folic acid levels did not correlate with HRQoL measures.

Conclusions: This study illuminates the quality of life measures in MMC survivors and the Chiari type 2 group and utilizes new MRI findings, which provide groundbreaking insights into the health conditions and well-being of these populations. These findings are of utmost importance for medical professionals, researchers, and healthcare providers specializing in pediatric care and neurology, as they can significantly impact the treatment and care of these patients.

Keywords: Myelomeningocele, Quality Of Life, Chiari Type 2 Malformation, Magnetic Resonance

Miyelomeningoselli Çocukların Uzun Dönem Sonuçları ve Hayatta Kalanların Yaşam Kalitesi

ÖZET

Amaç: Kronik sağlık sorunlarına ve yaşam kalitesinin düşmesine neden olan miyelomeningosel, sadece çocukları değil ailelerini de etkilemektedir. Bu nedenle MMC'li (miyelomeningosel) 101 çocuğun verilerini kapsamlı bir şekilde değerlendirdik ve MMC'li çocuklar ile kardeşleri arasındaki yaşam kalitesini karşılaştırmayı amaçladık. MMS'li çocukların sosyal ve davranışsal yönleri ve sağlık sorunları nedeniyle yaşam kalitesinin düştüğünü ve bunun kendileri ve aileleri için duygusal açıdan zorlayıcı olabileceğini anlamak çok önemlidir.

Yöntem: Bu retrospektif çalışmada elektronik dosyalardan veri toplayarak katılımcıların tıbbi geçmişinin kapsamlı ve doğru bir şekilde temsil edilmesini sağladık. Yaşam kalitesini ölçmek için pediatrik araştırmalarda yaygın olarak tanınan ve doğrulanan bir araç olan KIDSCREEN 10 cihazını kullandık.

Bulgular: Meningomyeloselli 101 çocuktan 93'ü hayatta kaldı. Hayatta kalanlar (n=93) kardeşleriyle karşılaştırıldığında, hayatta kalanların fiziksel iyilik hali ($p<0,001$), aileyle ilişkiler ($p<0,001$) ve arkadaşlarla ilişkiler ($p<0,001$) alt boyutlarında HRQoL (sağlıkla ilişkili yaşam kalitesi) puanları daha düşüktü ($p<0,001$), okul performansı ve dikkat ($p<0,001$). Öte yandan hayatta kalanlarda psikolojik iyilik puanı kardeşlere göre daha yüksekti ($p<0,001$). Çoğu 44 (%43,5) ortalama zihinsel kapasiteye sahipti. Sağlık koşullarının kişinin genel refahı üzerindeki etkisinin bir ölçüsü olan HRQoL puanı, Chiari tip 2 grubunda diğer hayatta kalanlara göre daha düşüktü ($p=0,035$). Serum ve folik asit düzeyleri HRQoL ölçümleriyle korelasyon göstermedi.

Sonuç: Bu çalışma yalnızca MMC'den sağ kurtulanlarda ve Chiari tip 2 grubundaki yaşam kalitesi ölçümlerini aydınlatmakla kalmıyor, aynı zamanda bu popülasyonların sağlık koşulları ve refahı hakkında çığır açıcı bilgiler sağlayan yeni MRI bulgularını da kullanıyor. Bu bulgular, bu hastaların tedavi ve bakımını önemli ölçüde etkileyebileceğinden, pediatrik bakım ve nöroloji alanında uzmanlaşmış tıp uzmanları, araştırmacılar ve sağlık hizmeti sağlayıcıları için son derece önemlidir.

Anahtar Kelimeler: Meningomyelosel, Chiari Tip 2 Malformasyonu, Manyetik Rezonans.

INTRODUCTION

Spina bifida is a development and closure defect of the neural tube. Myelomeningocele

(MMC), Alternatively, open spina bifida is the most severe spina bifida associated with malformations (Chiari tip two malformations, hydrocephalus, brainstem, and midbrain abnormalities). Spinal cord injury and brain abnormalities may cause paralysis, sensory dysfunction, and bladder and bowel incontinence. These abnormalities have neurobehavioral consequences (1,2). Other impairments include learning disabilities, memory difficulties, depression, anxiety, and impulsive behaviors. The children with MMC have survival rates increasing up to %70-80. These advances led to the need to research disabilities and their effects on daily life.

Spina bifida, a chronic health condition, significantly affects an individual's quality of life. This term encompasses their position within their cultural and value systems, goals, expectations, and concerns. The impact of spina bifida extends across multiple domains, including psychosocial, physical, and cognitive issues, as well as school attendance and performance. Understanding and addressing these issues is crucial for improving the lives of those with spina bifida (3,4,5).

The study aims to compare these parameters of individuals with or without Chiari malformations, providing a comprehensive understanding of the unique challenges and needs of those with this specific form of spina bifida.

MATERIAL AND METHODS

Our study, which drew data from the Duzce University School of Medicine database, focused on children with myelomeningocele (n=101). The HRQoL questionnaire was administered to MMC survivors aged between 2 and 18 years, with non-completion of the questionnaire being the only exclusion criterion. Data from the questionnaires were collected via phone calls, and the patients' parents were duly informed about this retrospective study, ensuring the reliability and relevance of our findings.

Our study adhered to the highest ethical standards per the 1964 Helsinki Declaration. The Bioethics Committee of the Medical University of Duzce University approved the study (date: 18.03.2022 number), further attesting to the ethical soundness of our research.

We present all demographics and laboratory and clinic data (sex, age, hydrocephalus, mobility, urinary incontinence, mental status, cranial malformations, serum Vitamin B12, folic acid, and ferritin levels) with MMC. A child and adolescent psychiatrist evaluated the cognitive capacities of the patients as a result of psychometric tests and psychiatric interviews. Some of the participants' (n=58) psychometric examination files were available in the study and were evaluated with a detailed psychiatric examination by a child and adolescent psychiatrist based on a medical board report. When the retrospectively examined files of the cases were examined, it was found that the Denver II developmental screening test was applied to children between the ages of 0-6, and the Kent-EGY intelligence test - Porteus Labyrinths Tasti and Wisc-R Intelligence tests were applied to children and adolescents between the ages of 6-18 to evaluate the cognitive development of some cases. As a result of all these examinations, the cognitive capacity and accompanying psychiatric disorders of the cases were evaluated. The Kent EGY test is applied to evaluate the verbal intelligence skills of individuals based on knowledge and language; there is no time limit, and it is used individually in a single session. We used The Porteus Maze Test and The Denver Developmental Screening Test (DDST) for cognitive capacity. The Porteus Maze Test was used as a nonverbal intelligence test to measure planning and adaptation to new conditions, as well as some competent functions such as making decisions, prescience, impulsivity, and the ability to delay contentment (6). DDST was used to detect developmental retardation in infants and children below 6 years of age. The parameters of this test detect properties such as; gross motor, language, fine motor-adaptive, and personal-social (7).

We also compared the HRQoL between several groups [Chiari Type 2 group vs. non-Chiari Type 2 group) (MMC survivors vs. their siblings)]. The questionnaire included eleven questions, revealing physical, psychological, social status, and school performance. Questions 1-2 are related to general health, and 3 and 4 show emotional levels. Questions 4-9 include social accordance (lifestyle, relationships with family and friends). Finally, questions 10-11 show school attendance, success, and attention (Table 1) (8).

Our data analysis was comprehensive and rigorous. We used IBM SPSS V23 to analyze the data, calculating HLQoL scores by T scores (a mean value of 50 ± a standard deviation of 10). The Kolmogorov-Smirnov test confirmed the normal distribution, and the Mann-Whitney U test was used to compare the groups. Spearman's rho correlation coefficient was employed to analyze the relationship between folate and quality of life. We presented the quantitative data as mean, deviation, median, minimum, and maximum, and categorical data was shown as frequency and percentage. A p-value below 0.05 was considered significant, ensuring the thoroughness and reliability of our findings.

RESULTS

Out of 101 children with MMC, 93 (92.08%) survived, resulting in a cumulative survival rate of 92%. The average age of the children at the time of the study was 9.2±6.1 years. Fifty-five percent of the children (n=51) were male.

Table 1. Kidscreen 10 instrument (6)

No	Question	Answer				
1.	Has your child felt fit and well?	Not at all	Slightly	Moderately	Very	Extremely
2.	Has your child felt full of energy?	Never	Seldom	Quite often	Very often	Always
3.	Has your child felt sad?	Never	Seldom	Quite often	Very often	Always
4.	Has your child felt lonely?	Never	Seldom	Quite often	Very often	Always
5.	Has your child enough time for him or herself?	Never	Seldom	Quite often	Very often	Always
6.	Has your child been able to do things in her/his free time?	Never	Seldom	Quite often	Very often	Always
7.	Has your child felt that her/his parents treated him/her fairly?	Never	Seldom	Quite often	Very often	Always
8.	Has your child had fun with his or her friends?	Never	Seldom	Quite often	Very often	Always
9.	Has your child had fun with his or her friends?	Never	Seldom	Quite often	Very often	Always
10.	Has your child got on well at school?	Not at all	Slightly	Moderately	Very	Extremely
11.	Has your child been able to pay attention?	Never	Seldom	Quite often	Very often	Always

Ninety-two children underwent surgery within one week after birth, and unfortunately, one child passed away on the first day of life. The most common complications found were shunted hydrocephalus (n=71, 70.3%) and Chiari type 2 malformation (n=20, 25.32%). Of the 101 children, 58 (57.8%) were unable to walk, while 21 (20.79%) were able to walk unaided. Approximately 56.4% of the children required clean intermittent catheterization. Most families had 4 (n=27) or 5 (n=20) members.

Cognitive evaluation revealed that 20 (19.8%) had cognitive impairment, and 38 had average cognitive capacity (Table 2). Psychiatric disorders included one (1.8%) adjustment disorder, 6 (10.9%) specific learning disability, and one (1.8%) selective mutism. Also, we report that three (5.5%) had attention deficit hyperactivity disorder, two (3.6%) had an anxiety disorder, two (3.6%) had conduct disorder, and one (1.8%) had a depressive attack.

Table 2. Demographics

	n=101	%
Survival		
Live	93	92.08
Dead	8	7.92
Sex		
Male	51	50.50
Female	50	49.50
Hydrocephalus	71	70.30
Chiari type 2 malformation	20	25.32
Mobility		
Unable to walk	58	57.43
Walking with sticks or crutches	22	21.78
Walking unaided	21	20.79
Urinary continence		
Always dry	12	11.8
Always wet	31	30.6
Clean intermittent catheterizations	57	56.4
Unknown	1	0.9
Family size (number of individuals)		
<4	6	9.67
4	27	43.55
5	20	32.26
≥6	9	14.52
Cognitive function		
Average mental capacity	38	37.6
Mild cognitive impairment	7	6.9
Moderate cognitive impairment	4	4
Severe cognitive impairment	5	5
Mild-moderate cognitive impairment	1	1
Moderate-severe cognitive impairment	2	1.98
Borderline mental retardation	1	1
Unknown	43	42.5

The median (minimum-maximum) levels of Vitamin B12, folic acid, and ferritin were approximately 302.2 (47-1500), 26.9 (3.8-518), and 8.5 (1.7-172.6), respectively. The study found no correlation between folate levels and HRQoL (r=-0.122; p=0.519). The most common brain MRI findings were inferior cerebellar vermis and tonsils (n=45, 54.2%), corpus callosum dysgenesis, agenesis (n=37, 44.5%), and colpocephaly (n=27, 32.5%). Spinal MRI findings included tethered cord (n=16, 19%), syringohydromyelia (n=13, 16%), and scoliosis (n=3, 3.75%) (Table 4). Additionally, one case involved situs inversus abdominis, and two involved renal agenesis (Table 3).

Table 3. Cranial and spinal malformations

	n=101	%
Cranial findings:		
Inferior cerebellar tonsils and vermis	45	54.22
Corpus callosum disgenezis, agenezis	37	44.58
Colphocephaly	27	32.5
Inferior fourth ventricle	17	20.48
Interdigitation of posterior and midline structures	13	15.85
Inferior tentorium	12	14.46
Pecking in the tectum	8	9.64
Brainstem atrophy	5	6.02
Cerebellar atrophy	2	2.41
Vermian hypoplasia	1	1.20
Third ventricle's superiority	1	1.20
Leukomalacia	2	2.41
Tower cerebellum	1	1.20
Septal dysplasia	2	2.41
Absent Septum Pellicidum	1	1.20
The cerebellum migrating to the upper cervical canal	2	2.41
Inferior Medulla oblongata	1	1.20
Evert hippocampus	1	1.08
Superior tentorium	1	1.20
Posterior fossa hypoplasia	2	2.41
Spinal findings:		
Tethered cord	16	19.05
Syringohydromyelia	13	16.05
Medullar Spur	6	7.1
Scoliosis	3	3.75

Our study, involving a sibling group (n=73) with a mean age of 11.58 and a standard deviation of 7.43, revealed some unexpected findings. Fifty-six percent (n=41) of the siblings were male. When comparing the HRQoL between the siblings and MSS survivors, we found that the siblings had a significantly higher median total score than the survivors (57.61 vs. 43.58, respectively) (p<0.001). This difference was also evident in the median scores of physical well-being (58.23 vs. 41.83, p<0.001), social functioning (55.86 vs. 43.27, p<0.001), friends relations (56.67 vs. 41.31, p<0.001), and school performance (58.81 vs. 44.72, p<0.001). Even the mean HRQoL score of relations with family was higher in siblings (53.81±5.05) than in survivors (46.81±12.14) (p<0.001). However, it was surprising to find that the psychologic status was better in the survivors (median score of 54.8) than in the siblings (median score of 42.68)(p<0.001)(Table 4). This unexpected finding opens up new avenues for research and warrants further investigation.

The Chiari type 2 group (median of 44.64) had lower HRQoL scores than the non-Chiari type 2 group (median of 50.16) in the MMC survivors group (p=0.035). This finding suggests that individuals with Chiari type 2 malformations may experience more significant impairments in their quality of life than those without this specific condition (Table 5). The psychological evaluation of the health status of some of the patients with myelomeningocele (n=55) was available from the medical records.

Table 4. Comparing the HRQoL of MMSS and their siblings

	MMSS (n=71)		Siblings (n=73)		ES	TS*	p
	Median (Min-Max)	Mean SD	Median (Min-Max)	Mean SD			
Total	43.58 (23.33 – 70.07)	43.4 ± 9.9	57.61 (49.82 – 62.28)	56.4 ± 4.4	1.634	619.5	<**0.001**
Physical well-being	41.83 (25.43 – 58.23)	42 ± 8.53	58.23 (50.03 – 58.23)	57.78 ± 1.88	2.372	295.5	<**0.001**
Psychological well-being	54.8 (42.68 – 91.14)	56.59 ± 10.31	42.68 (42.68 – 66.91)	43.59 ± 3.3	2.202	368.5	<**0.001**
Social functioning	43.27 (22.29 – 55.86)	44.1 ± 11.56	55.86 (47.47 – 55.86)	55.74 ± 0.98	1.207	1039.5	<**0.001**
Relationships with family	55.44 (4.35 – 55.44)	46.09 ± 12.14	55.44 (38.41 – 55.44)	53.81 ± 5.05	0.657	1654.5	<**0.001**
Relationships with friends	41.31 (25.95 – 56.67)	44.23 ± 11.34	56.67 (41.31 – 56.67)	55.61 ± 2.95	1.135	1109	<**0.001**
School functioning	44.72 (37.67 – 65.85)	46.6 ± 8.71	58.81 (37.67 – 65.85)	53.31 ± 10.12	0.695	1605.5	<**0.001**

ES: Effect Size; T.S.: Test statistics, * Mann Whitney U test, MMSS: Myelomeningocele survivors, HRQoL: Health-related quality of life

Table 5. The comparison of HRQoL of the Chiari type 2 malformation group with the non-Chiari type 2 malformation group

	Non-Chiari type 2 malformation group (n=45)		Chiari type 2 malformation group (n=16)		ES	TS*	p
	Median (Min-Max)	Mean SD	Median (Min-Max)	Mean SD			
Total	50.16 (31.27 – 76.91)	51.41 ± 9.84	44.64 (29.70-61.17)	45.24 ± 8.30	0.560	231.5	**0.035**

ES: Effect Size; T.S.: Test statistics, * Mann Whitney U test, MMSS: Myelomeningocele survivors, HRQoL: Health-related quality of life

DISCUSSION

Myelomeningocele causes both physical and mental sequela. The underlying aetiologies are the brain and spinal malformations (mostly hydrocephalus and Chiari type 2 malformations (. Paschereit et al. reported that the histopathological data of the patients with MMC is variable. The malformations were hydrocephalus (71%), Chiari II malformation (36%), heterotopia (34%), cerebellar anomalies (36%), gyrification defects (33%), ependymal denudation (29%), abnormality of corpus callosum (19%). These findings indicate a wide range of brain and spinal cord structural abnormalities, likely contributing to the observed differences in HRQoL scores. Rare anomalies were dysplastic cranial nerves, hypoplasia/aplasia of the mesencephalon, aplasia of olfactory bulbous, atresia of the 4th ventricle, aqueductal stenosis, anomalies of the limbic system, hippocampal anomaly, aplasia of the fornix, nuclear anomalies, dysplastic olives, diminution of pontine nuclei, and the meningeal malformations. Some of these histopathological findings were not present in MRI findings. They concluded that cerebellar malformations and cerebral heterotopias accompany MMC (9). In the literature, cerebellar dysplasia, abnormal gyrus structure in the cerebral hemispheres, colpocephaly, corpus callosum dysgenesis or agenesis, large massa intermedia, small third ventricle, aqueductal anomalies, absent tentorium, displacement of the cerebellum towards the upper cervical canal, pons, herniation of the cerebellar vermis and tonsils into the upper cervical canal are well documented (9, 10). These findings further support the hypothesis that the observed differences in HRQoL scores are due to the underlying structural abnormalities in the brain and spinal cord.

In our study, of 101 patients with MMC, the most common malformations were inferior cerebellar tonsils and vermis (n=45, 54.2%), corpus callosum dysgenesis, agenesis (n=37, 44,5%), colpocephaly (n=27, 32,5%), inferior fourth ventricle (n=17, 20.48%), interdigitation of posterior and midline structures (n=13, %15.85), pecking in the tectum (n=8, 9.64%), brainstem atrophy (n=5, %6.02). More common than the literature, we detected interdigitation of the structures, pecking in the septum, and brainstem atrophy.

Our patients' rare malformations, which were not reported before, were vermian hypoplasia (n=1), third ventricle's superiority (n=1), leukomalacia (n=2), tower cerebellum (n=1), septal dysplasia (n=2), absent septum pallidum (n=1), evert hippocampus (n=1), superior tentorium (n=1), posterior fossa hypoplasia (n=2). In our study, these findings were reported in the literature before: cerebellar atrophy (n=2), cerebellum migrating to the upper cervical canal (n=2), and inferior medulla oblongata (n=1).

Various studies measured the HRQoL in MMC survivors. Buoro et al. reported that myelomeningocele harmed the caregiver's or mother's quality of life, functional capacity, emotional status, and mental health. Bladder catheterization, general care, and financial

limitations are the main problems. They used the World Health Organisation Quality of Life, BREF questionnaire (11). Karmur et al. found that age, level of myelomeningocele, and socioeconomic factors were related to health status outcomes (12). Hydrocephalus Outcome Questionnaire and Health Utility Index scores revealed higher scores of HRQOL associated with lower age, lower anatomical level of myelomeningocele, better family functioning, and higher family income in patients with myelomeningocele and shunted hydrocephalus (12). Previous studies revealed impairment of HRQOL in the domains of health, relationships, esteem and sexuality, bladder, bowel, and bathroom use (13), family and freedom, bladder and bowel esteem, and independence (14).

In another study using Health Utilities Index 3 from Uganda, carer predictions didn't correlate with the child's reported score. Urinary incontinence, essentially family size, male sex, and the presence of hydrocephalus altered the HRQoL in children with MMC. As a component of the WHO QOL index, the Vas score achieved more accurate results than the Health Utilities Index 13) (15). Abanoz et al. compared the HRQoL of children with MMC (n=50) and healthy children (n=50) using the Child Health Questionnaire Parent Form 50. The patients with MMC had significantly lower QOL scores (general health, physical functioning, role/social limitations, emotional/behavioral, mental health, family activities, and family cohesion) than those of the healthy group (14).

Our investigation demonstrated the impairment in MMS survivors' total HRQoL scores and domains (physical well-being, social functioning, friendly relations, family relations, and school performance). Inconsistent with the literature, psychological functioning was significantly better in the MMC survivors than in the siblings. Among the cases whose psychiatric files were accessed, we found that the most common psychiatric diagnoses were mental retardation, specific learning disability and conduct disorder, and attention deficit hyperactivity disorder.

While few studies have examined the impact of Chiari type 2 malformations on quality of life, our study focused on MMC survivors' vision, speech, hearing, dexterity, ambulation, cognition, emotions, and pain. The Chiari type 2 group had worse overall cognition and speech scores, indicating potential cognitive and communication challenges associated with this malformation. We also found a worse total score, including subdimensions of physical well-being, psychological well-being, relationships with family and friends, and school performance in the Chiari Type 2 group, suggesting a broader impact on various aspects of HRQoL.

Our study reveals that HRQoL scores, particularly in the subdimensions of physical well-being, relationships with family and friends, school performance, and attention, are significantly lower in MMS survivors than their siblings. However, MMS survivors surprisingly exhibit higher psychological wellness scores than their siblings. Furthermore, Chiari type 2 malformations significantly exacerbate the already compromised HRQoL scores.

We discovered novel MRI findings in MMS survivors, including vermian hypoplasia, superiority of the third ventricle, leukomalacia, tower cerebellum, septal dysplasia, and absent septum pallidum. These unique findings add a new dimension to our understanding of MMC and its impact on HRQoL. New health policies, home care services and social assistance should be developed to improve the quality of life of meningomyelocele patients.

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REVIEW

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Family Physicians' Knowledge, Attitudes, and Practices Regarding Adult Immunization in Turkey: A Systematic Review

ABSTRACT

Objective: This systematic review aims to investigate the knowledge, attitudes, thoughts, and behaviors of family physicians (family medicine specialists, family doctors, family medicine assistants) in Türkiye regarding adult vaccinations.

Methods: In this systematic review, data were obtained through a retrospective search of descriptive studies published in Turkish and English between 2013-2023 in the databases of " PubMed, Google Scholar, National thesis center." The PICOS method was used to determine the eligibility of included studies, and the methodological quality of the studies within the systematic review was assessed using the The Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols Checklist (PRISMA) checklist flow diagram.

Results: 177 selected by title for abstract analysis; among which 55 articles and theses were considered to be examined for the full-text review. As a result of the detailed examination of them, a total of 23 articles and theses were selected to be included in the study. Influenza vaccine and HPV vaccine knowledge of family doctors were higher and followed by hepatitis B. COVID-19, hepatitis B, tetanus, influenza were the mostly recommended vaccines by family doctors to adults.

Conclusions: In conclusion, this systematic review emphasizes the critical role of family physicians in promoting vaccination among adult populations. By addressing knowledge gaps, addressing concerns of family doctors, promoting a culture of vaccination within the healthcare community, we can enhance vaccine uptake and ultimately contribute to improved public health outcomes and disease prevention efforts.

Keywords: Family Physician, Family Medicine, Adult Immunization, Systematic Review

Türkiye'deki Aile Hekimlerinin Erişkin Aşılaması Hakkındaki Bilgi, Tutum ve Uygulamalarının Değerlendirilmesi: Sistematik Derleme

ÖZET

Amaç: Bu sistematik derleme, Türkiye'deki aile hekimlerinin (aile hekimliği uzmanları, aile hekimleri, aile hekimliği asistanları) erişkin aşılarına ilişkin bilgi, tutum, düşünce ve davranışlarını araştırmayı amaçlamaktadır.

Yöntem: Bu sistematik derlemede, "PubMed, Google Scholar, Ulusal tez merkezi" veritabanlarında 2013-2023 yılları arasında Türkçe ve İngilizce olarak yayımlanan tanımlayıcı çalışmaların retrospektif bir araştırması yoluyla veri toplanmıştır. Dahil edilen çalışmaların uygunluğunu belirlemek için PICOS yöntemi kullanılmış ve sistematik inceleme içindeki çalışmaların metodolojik kalitesi, The Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols Checklist (PRISMA) kontrol listesi akış diyagramı kullanılarak değerlendirilmiştir.

Bulgular: Başlık olarak seçilen 177 makale, özet analizi için incelendi; bunların arasından 55 makale ve tez, tam metin değerlendirmesi için incelemeye uygun bulundu. Bunların detaylı bir şekilde incelenmesi sonucunda, toplamda 23 makale ve tez çalışmaya dahil edilmek üzere seçildi. Aile hekimlerinin influenza aşısı ve HPV aşısı bilgisi diğer aşılardan daha yüksekti ve bunu hepatit B izledi. COVID-19, hepatit B, tetanoz, influenza aşılarının aile hekimleri tarafından erişkinlere en sık önerilen aşılar olduğu görüldü.

Sonuç: Sonuç olarak, bu sistematik derleme, aile hekimlerinin erişkinler arasında aşılama konusunda önemli bir rol oynadığını vurgulamaktadır. Bu çalışma sonuçlarına göre aile hekimlerinin bilgi eksikliklerini, uygulamalarını ele alarak, sağlık profesyonelleri içinde aşılama kültürünü teşvik edip, aşılanma oranlarını artırabilir ve nihayetinde daha iyi halk sağlığı sonuçlarına katkıda bulunabiliriz.

Anahtar Kelimeler: Aile Hekimi, Aile Hekimliği, Erişkin Bağışıklama, Sistematik Derleme.

INTRODUCTION

In the dynamic field of healthcare, the pivotal role of family physicians in safeguarding public health is indisputable. As gatekeepers of preventive medicine, their understanding, perspectives, and actions significantly influence the landscape of adult vaccination-a cornerstone of proactive healthcare (1,2).

Adult vaccination necessitates a nuanced examination of the factors shaping its implementation within the Turkish healthcare context. The importance of adult immunization has also been emphasized with The Expanded Programme on Immunization (EPI) in Türkiye (3). Also the United States Centers for Disease Control and Prevention (CDC) has established vaccination schedules within their "proposed adult immunization program" each year (4). Family physicians, who are the cornerstone of preventive medicine, are expected to be the leading healthcare professionals in adult immunization. They are expected to have up-to-date knowledge on this subject and to make recommendations regarding adult immunization in practice. Knowing the knowledge, attitudes and behaviors of family physicians on this issue is important in adult immunization strategies. There are many cross-sectional studies internationally and nationally. Systematic reviews have been found that provide an overview of these studies internationally (5-8); however, a systematic review at the national level has not been encountered. By delving into the intricacies of knowledge dissemination, individual attitudes, professional thoughts, and behavioral patterns, we effort to provide a foundation for targeted interventions that can fortify and optimize adult vaccination strategies among family physicians in Türkiye. Through this exploration, we anticipate contributing valuable insights that not only enrich the existing literature but also serve as a catalyst for enhancing preventive healthcare practices within the Turkish medical landscape. This systematic review was conducted to examine the knowledge, attitudes, thoughts and behaviors of family physicians (family medicine specialists, family physicians, family medicine assistants) in Türkiye regarding adult vaccines.

MATERIAL AND METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols Checklist (PRISMA) was used to prepare this systematic review (9). In order to reduce the risk of bias in the study, literature search, article selection, data extraction and quality assessment were performed independently by two researchers, and consensus was reached by discussing any differences of opinion. In addition, before starting the study, a pilot study was conducted in a session attended by both researchers on all stages and a common road map was determined.

Eligibility Criteria: Articles to be included in the study were screened according to the following inclusion criteria/PICOS:

Patient/participants (P): Family Physicians in Türkiye

Intervention (I): Adult vaccinations

Comparison (C): None

Outcomes (O): Knowledge, attitudes, thoughts and behaviors towards adult vaccines

Study Design (S): Descriptive, quantitative studies published in Turkish and English between 2013 and 2023.

The criteria for exclusion in this systematic review included reviews, case reports, experimental studies, letters to the editor and congress proceedings. In addition, studies that were not of a survey nature and included only those using methods, adult vaccine refusal studies were also excluded.

Screening Strategy: The literature screenings were conducted between June 2023 and September 2023. A retrospective review of cross-sectional and qualitative studies published in Turkish and English in "PubMed, Google Scholar, National thesis center" databases between 2013-2023 was performed. The keywords ((family physician) OR (family doctor) OR (general practitioner)) AND ((vaccine*) OR (adult vaccine*)) were searched in accordance with MeSH in Turkish and in English. The references list of the included studies was reviewed to access additional studies.

Selection Criteria for Research: The identification and selection of articles to be included in this systematic review were made independently by the first and second researchers based on the inclusion criteria. Microsoft Excel program was used by the researchers for storing and sorting the articles. After removing the duplicates from the articles included in the systematic review and re-examining the articles according to the title and abstract, respectively, the articles to be included in the study were determined. At any stage of the research, when there was a difference of opinion between the researchers, a consensus was reached by discussing in an online session. The PRISMA flow diagram for the selection process of articles is given in Figure 1.

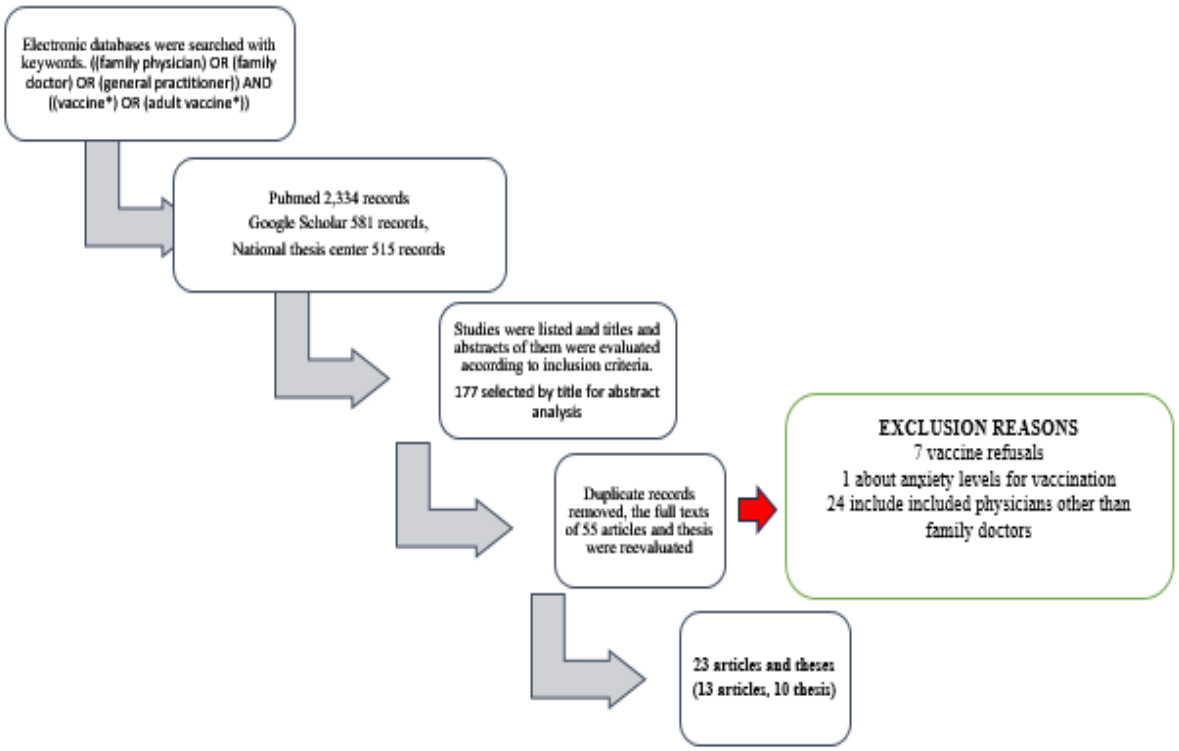

Figure 1. The PRISMA flow diagram for the selection process of articles

Obtaining Data: Studies included in the systematic review; "author and year of publication, objective, pattern/type, sample volume, year, form of publication, data on family physicians' knowledge, attitudes, thoughts and behaviors regarding adult vaccines and quality score" were collected.

RESULTS

Study Selection: As a result of the search, 2,334 records on Pubmed, 515 records on National Thesis Center and 581 records on Google Scholar were identified through data base searching, 177 selected by title for abstract analysis. As a result of the removal of repetitive records and examination according to the abstract, 55 articles and theses were considered to be examined for the full-text review. As a result of the detailed examination of the full text and theses, a total of 23 articles and theses were selected to be included in the study.

Study Characteristics: The total sample size of the articles included in the systematic review was 4996 (family doctors, family medicine specialist or family medicine residents), and it was determined that the number of samples in the studies varied between 48-606. Of the studies; 43.4% (n=10) were thesis, 65.2% (n=15) of them were in Turkish language; 30.4% (n=7) were conducted online survey; 21.7% (n=5) of them were published in SCI-Expanded journal. The type of paper; the type of survey and the language of study were shown in Figure-2 and the descriptive features of the studies were presented at Table 1.

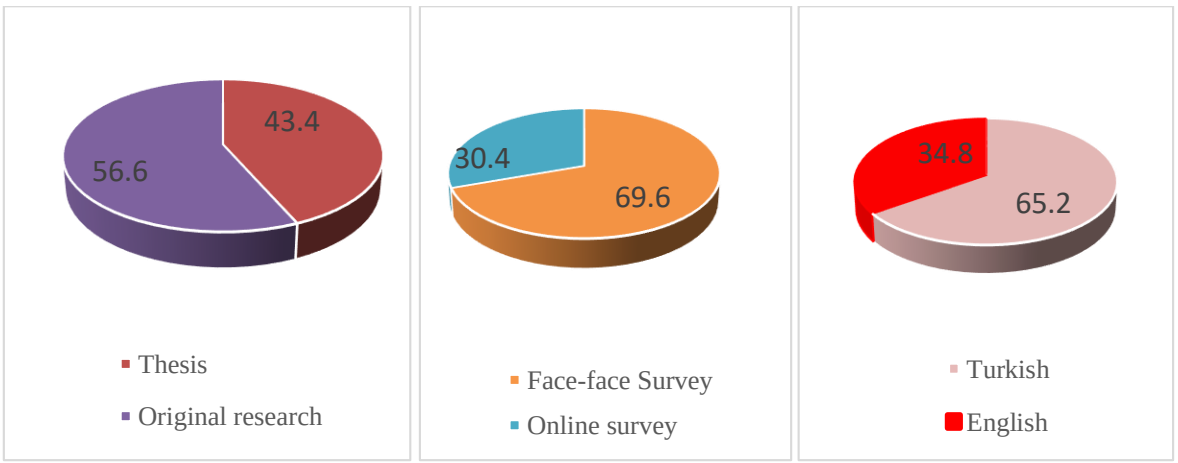

Figure 2. The type of paper; the type of survey and the language of study graphics

Table 1. The descriptive features of the studies (N=23)

Author/Year	Journal İndex	Study type	Sample size	Survey method
Akan 2016 (10)	SCI-E	Cross-sectional	606 FD	E-Survey
Akgül 2021 (11)	Ulakbim	Cross-sectional	48 FD	Survey (self-administered)
Aslan 2016 (12)	Thesis	Cross-sectional	107 FD	Survey (self-administered)
Ateş Bulut 2021 (13)	SCI-E	Cross-sectional	435 Physicians/191 FD	E-Survey
Aydemir 2023 (14)	Thesis	Cross-sectional	136 FD 22 FMS 58 FMS residents	Survey (self-administered)
Aysu Revanlı 2016 (15)	Other index	Cross-sectional	263 FD	Survey (self-administered)
Bulca Acar 2021 (17)	Ulakbim	Cross-sectional	494 FD	E-Survey
Celep 2020 (18)	SCI-E	Cross-sectional	97 FD	Survey (self-administered)
Demir 2021 (19)	Thesis	Cross-sectional	475 HP/108 FD	Survey (self-administered)
Deveci 2020 (20)	Thesis	Cross-sectional	310 FMS residents 208 FMS	Survey (self-administered)
Engin 2021 (21)	Other index	Cross-sectional	259 FD	Survey (self-administered)
Gümüstakim 2019 (22)	Other index	Descriptive	264 FD	E-Survey
Ketenci 2023 (23)	Other index	Cross-sectional	57 FD	Survey (self-administered)
Köksoy 2021 (24)	Thesis	Cross-sectional	159 FD	E-Survey
Köse 2022 (25)	Thesis	Descriptive	101 FD	Survey
Oğuzöncül 2021 (26)	Ulakbim	Descriptive	165 FD	Survey
Özbakır Acar 2019 (27)	Other index	Descriptive	154 FD	Survey
Pekgenç 2017 (28)	Thesis	Descriptive	253 FD	Survey
Us 2020 (29)	Thesis	Cross-sectional	202 FMS	Survey
Yağız 2019 (30)	Thesis	Cross-sectional	137 FD	Survey
Yağmur 2021 (31)	Thesis	Cross-sectional	343 FMS	Survey
Yetik 2023 (32)	SCI-E	Cross-sectional	113 FD	E-Survey
Yılmaz Karadağ 2019 (33)	SCI-E	Cross-sectional	221 FD	E-Survey

SCI-E: Science Citation Index-Expanded; FD: Family Doctor; FMS: Family Medicine Specialist; HP: Health Personnel; E-survey: online survey

In the articles included in our study, the knowledge, attitudes and behaviors of family physicians on influenza vaccination (4 studies), pneumococcal vaccination (1 study), both influenza and pneumococcal vaccination (1 study); human papillomavirus (HPV) vaccination (6 studies), elderly immunization (2 studies), COVID-19 vaccination (3 studies), pregnant vaccination (1 study), health worker vaccination (2 studies) and general adult immunization (5 studies) were evaluated. The objective of studies and adult vaccination types were presented in Table 2.

Seventeen of the studies (70.8%) evaluated the level of knowledge of family physicians. When evaluated according to their own opinions of family physicians, influenza vaccine (61.7%-69.3%) and HPV vaccine (50.5%-89.3%) knowledge were higher and followed by hepatitis B (45.5%), tetanus-diphteria (Td) (41.3%), COVID-19 (29.7%), pneumococcus (19.5%-58.1%) and zona zoster (13%-59.7%). Six of them evaluate attitudes and twenty two of them evaluated behaviors. When the studies were evaluated, the frequency of recommending influenza vaccination were changed between 34.6%-89.8%; pneumococcal vaccination recommendation frequencies were between 14.3%-65.2%; HPV vaccination recommendation frequencies were between 36.2%-83%; COVID-19 vaccine recommendation frequencies were between 98.5%-99.1%; hepatitis B (HBV) vaccination recommendation frequencies were between 19.3%-94.7%; tetanus vaccine recommendation frequencies were between 22.8%-90.9%. Of the family physicians, 18.7%-79.4% had influenza vaccination in the previous year; 19.5% had their children vaccinated against HPV.

Table 2. The objective of studies and adult vaccination types (N=23)

Author/Year	Objective of the study	Type of the adult vaccination
Akan 2016 (10)	To determine the factors that influenced the decisions of family physicians working in primary care health services to receive influenza vaccines	Influenza vaccination
Akgül 2021 (11)	To evaluate the level of knowledge of primary care physicians participating in the symposium on vaccination practices	General adult vaccination
Aslan 2016 (12)	To determine the vaccination rate of family physicians regarding influenza and pneumococcal vaccines, their knowledge, attitudes and behaviors about vaccines	Influenza and pneumococcal vaccination
Ateş Bulut 2021 (13)	To show the knowledge and attitudes of the physicians to older adults' vaccination schemes.	Older adults' vaccination
Aydemir 2023 (14)	To evaluate knowledge, attitudes and behaviors of family physicians about HPV infection and vaccine	HPV vaccination
Aysu Revanlı 2016 (15)	To investigate the level of knowledge and attitudes of family physicians about HPV and zona vaccines	HPV and zona vaccination
Bulca Acar 2021 (17)	To reveal the opinions of family physicians on the COVID-19 vaccine	COVID-19 vaccination
Celep 2020 (18)	To determine the knowledge and attitude of pregnant women and their primary healthcare providers towards immunization during pregnancy	Pregnant vaccination
Demir 2021 (19)	To determine the level of knowledge of health workers (including family doctors) about immunization services for health workers, to evaluate their attitudes and behaviors and raising awareness	Health worker vaccination
Deveci 2020 (20)	To determine the level of knowledge about HPV infections and HPV vaccine in family medicine residents by filling out a questionnaire and to examine the deficiencies	HPV vaccination
Engin 2021 (21)	To determine the knowledge, attitudes and behaviors of family physicians working to provide primary health care services about influenza vaccination	Influenza vaccination
Gümüstakim 2019 (22)	To identify the shortcomings in this area and draw a roadmap for what arrangements should be made in terms of physicians and patients in order to increase adult immunization rates in primary care	General adult vaccination
Ketenci 2023 (23)	To evaluate the knowledge, attitudes and behaviors of family physicians, on the implementation of vaccine pharmacovigilance and post-vaccine adverse effect signaling system in COVID-19 vaccination programs	COVID-19 vaccination
Köksoy 2021 (24)	To investigate the knowledge, attitudes and behaviors of physicians who are receiving specialty training in the field of family medicine about streptococcus pneumonia vaccine	Pneumococcal vaccination
Köse 2022 (25)	To assess knowledge, attitudes and behaviors of physicians working in relevant clinics about HPV vaccines	HPV vaccination
Oğuzöncül 2021 (26)	To investigate the knowledge, attitudes and behaviors of family physicians working in primary care about health worker vaccination	Health worker vaccination
Özbakır Acar 2019 (27)	To assess FDs' and primary health care personnels' (nurses and midwifes) knowledge and attitudes about cervical cancer (risk factors, screening, prevention) and the HPV vaccine	HPV vaccination
Pekgenç 2017 (28)	To reveal the attitudes of physicians (including family physicians) about immunization of the elderly, to raise awareness about immunization of the elderly and to increase vaccination rates which are below the targeted levels	Older adults' vaccination
Us 2020 (29)	To evaluate the knowledge of family medicine residents working in Ankara about upper respiratory tract infections, use of antiviral drugs in upper respiratory tract infections and influenza vaccine	Influenza vaccination
Yağız 2019 (30)	To determine the rate at which physicians administer seasonal influenza vaccine to themselves, to determine which patients they recommend it to, and to identify prejudices of physicians	Influenza vaccination
Yağmur 2021 (31)	To evaluate the knowledge, attitudes and behaviors of family medicine residents about influenza, pneumococcal and COVID-19 vaccines during the COVID-19 pandemic period	COVID-19 vaccination
Yetik 2023 (32)	To evaluate the level of knowledge, compliance with the screening program, and tendency to inform patients of the doctors working in family health centers where HPV testing is performed within the scope of the cervical cancer screening program in our country	HPV vaccination
Yılmaz Karadağ 2019 (33)	To assess the factors influencing primary care physicians' approach to adult vaccination in specific risk groups and evaluate the compliance to adult immunization guidelines	General adult vaccination

FD: Family Doctor; HBV: Hepatitis B; HPV: Human Papillomavirus

Table 3. The Knowledge, Attitude and Behaviours of family physicians in studies (N=23)

Author/Year	Knowledge	Attitude	Behaviour
Akan 2016 (10)		-The factors that led to increased vaccination compliance: working duration, age, chronic disease history and living with a person over 65 years. -Vaccine compliance is associated with higher odds ratio of 10.93 compared to vaccine non-compliance about "flu vaccine should be mandatory for health care workers" comment; 3.06 about "flu vaccine should be mandatory for family physicians" comment.	Vaccine compliancy among the physicians was 27.3%
Akgül 2021 (11)	64.6% of the participants answered 23 or more questions correctly out of 34 questions asked in the knowledge assessment.		81.3% of FD stated that they recommend influenza vaccination.
Aslan 2016 (12)	The average correct answer for 10 information questions about influenza vaccine was 5.9±2.1, and the average correct answer for 9 information questions about pneumococcal vaccine was 4.1±2.1.	23.4% of FD do not believe in the protection of the influenza vaccine.	-18.7% of FD get own regular influenza vaccination every year. -34.6% of FD stated that they recommend influenza vaccination. -20.6% of FD stated that they recommend pneumoccus vaccination.
Ateş Bulut 2021 (13)			-80.1% of FD had questioned the vaccination history of the patients. -Predicting four or five of the suggested vaccinations in older adults was 1,66 fold higher in FD than other specialists.
Aydemir 2023 (14)	50.5% of FD thought that they have knowledge about the HPV vaccine.	87% of FD thought that HPV vaccination should be on the national vaccination calendar.	-6% of FD stated that they had vaccinated against HPV. -19.5% stated that they had their children vaccinated against HPV. -65.7% stated that they recommended HPV vaccination to their patients.
Aysu Revanlı 2016 (15)	-89.3% of FD stated that they had knowledge about HPV vaccine. -59.7% of FD stated that they had knowledge about Herpes Zoster vaccine.	65.7% of FD stated that they were positive about recommending Herpes Zoster vaccine.	59.5% of FD stated that they recommend HPV vaccination to their patients.
Bulca Acar 2021 (17)			-6.3% had no intention of getting vaccinated against the COVID-19. -79.4% of FD get own regular influenza vaccination every year.
Celep 2020 (18)			The rate of Td vaccination was 98% for pregnants, 85.5% of pregnants' source of influenza recommendation was primary health-care services.
Demir 2021 (19)	32.5% of them have 12-13 correct answers, 19.6% have 14-15 correct answers in 15 questions.		40.2% of FD stated that they received regular influenza vaccine, 87.2% stated that they received HBV Vaccine, 39.3% stated that they received Measles, mumps, rubella (MMR) vaccine, 90.9% stated that they received Tetanus Vaccine, and 11.4% stated that they received Chickenpox Vaccine.

Deveci 2020 (20)	The rate of "I don't know" answers to questions containing general information about HPV was between 0.3-5.8%.		67.4% of FD stated that they recommend HPV vaccination.
Engin 2021 (21)			47.6% of FD get own influenza vaccination.
Gümüstakim 2019 (22)	34.4% thought they have enough information about adult vaccination.		82.2% of FD get own vaccination.
Ketenci 2023 (23)	29.7% of FD thought they had sufficient knowledge about the COVID-19 vaccination program.		
Köksoy 2021 (24)	19.5% of FD thought they had sufficient knowledge about pneumococcal vaccine.		-22.6% of FD recommended pneumococcal vaccine to everyone. -78.6% of FD informed their patients with an indication about pneumococcal vaccine.
Köse 2022 (25)	The average number of correct answers of FDs was 12.40±2.95 in 18 questions.		17.1% of FD stated that they vaccinated against HPV, 71% of them recommend it.
Oğuzöncül 2021 (26)	The average number of correct answers of FD was 7.59±2.17 in 13 questions.	-The average attitude score of FD was 10.74±1.54. -The flu vaccine, of which, 15.8% of the participants had the most hesitation in administration.	-43.6% of the study participants had their relatives vaccinated. -33.3% had themselves vaccinated outside the vaccination schedule. -52.6% were administered influenza, 19.3% HBV, 22.8% tetanus, 1.8% MMR, 1.8% meningococcus vaccine. -34.7% were administered influenza, 27.8% rota, 16.7% HBV, 11.7% tetanus, 5.6% pneumococcus, 2.8% MMR and 1.4% meningococcus vaccine to their relatives.
Özbakır Acar 2019 (27)	-56.7% of FD stated that they have knowledge about the HPV vaccine. -18% of the physicians knew that the HPV vaccine is suitable for both girls and boys. -84% of the physicians were aware of the protective role of the HPV vaccine.		-83% of them stated to recommend their patients HPV vaccination. -64.9% of them reported that they suggest HPV vaccination to their own daughters.
Pekgenç 2017 (28)	61.7% stated that they had adequate knowledge about influenza vaccine, 58.1% about pneumococcal vaccine, 41.3% about tetanus, 13% about zona zoster, and 45.5% about HBV vaccine.		40.3% of physicians recommended influenza vaccine, 32% pneumococcal vaccine, 47.8% recommended tetanus vaccine if there was an injury, and 50.2% recommended zona zoster vaccine for patients over 65 years of age.
Us 2020 (29)	"The flu vaccine is recommended only for patients at risk." 59.9% of physicians FD and "Pregnant women can be vaccinated with the flu vaccine." 83.1% of the physicians answered the proposition correctly.		
Yağız 2019 (30)	69.3% of FD reported having sufficient knowledge about influenza vaccine.		48.2% of FD get own regular influenza vaccination every year, 89.8% of them recommend it to all patients.

Yağmur 2021 (31)	The average number of correct answers of FDs was 81.8±12.1 in 7 questions.	While 36.7% of FDs reported that they had the influenza vaccine in the past year, 90.4% reported that they had the COVID-19 vaccine and 14.3% reported that they had the pneumococcal vaccine.
Yetik 2023 (32)		53.1% of FD reported that they recommend HPV vaccination.
Yılmaz Karadağ 2019 (33)		-72.4% of FD reported they follow the Adult Immunization Algorithm. -65.6% of them stated that they recommend tetanus, 71.2% influenza and 62.5% HBV to their over 65 years of aged patients.

FD: Family Doctor; HBV: Hepatitis B; HPV: Human Papillomavirus; MMR: Measles, Mumps, Rubella; Td: Tetanus-Diphteria

DISCUSSION

In recent years, adult immunization has become as important as child immunization worldwide. Family physicians can play a decisive role in promoting adult immunization. As a result of the this systematic review, it was observed that the level of knowledge of family physicians in Türkiye about adult immunization, vaccination and vaccine recommendation rates were generally lower than international studies.

In the international literature, it was observed that no systematic review was conducted on theses and usually they were conducted on original researchs (5-8). When the general contents of systematic reviews were evaluated; in the systematic review by Prieto-Campo et al. on adult immunization related to family physicians, it was seen that all of them were cross-sectional, in English language and a total of 41 studies were evaluated (5). In the systematic review by Pavlovic et al. on adult immunization related to all health workers including family physicians, it was seen that all of them were in English language and there were cross sectional and qualitative type studies a total of 98 studies were evaluated (6). In the systematic review by Collange et al. on adult immunization related to family physicians, it was seen that all of them were cross-sectional, in English language and a total of 11 studies were evaluated (8). Another prominent feature of international studies was the biggest part of them were face-to-face method (6,8).

The systematic review examined a diverse array of articles focusing on the knowledge, attitudes, and behaviors of family physicians regarding various vaccination types. The included studies covered a wide spectrum of vaccination topics, including influenza, pneumococcal, HPV, elderly immunization, COVID-19, pregnant vaccination, health worker vaccination, and general adult immunization (10-33). The distribution of studies across different vaccination types reflects the breadth of interest and concern regarding vaccination practices among family physicians. Notably, the review identified a relatively higher number of studies evaluating HPV vaccination (6 studies) (14,15,20,25,27,32) and general adult immunization (11,1,22,33), indicating a significant research focus on these areas within the context of family physician practices. In the systematic review by Collange et al, all studies included seasonal influenza vaccination, three of them also considered other vaccines (8).

The systematic review findings shed light on the varying levels of knowledge among family physicians regarding different vaccines. Notably, the majority of studies (70.8%) focused on assessing the knowledge levels of family physicians, highlighting the significance of this aspect in vaccine recommendation and administration (11,12,14-16,19,20,22-31). When examining the results in detail, it becomes evident that influenza and HPV vaccines were among the vaccines with the highest knowledge levels, as reported by family physicians themselves (14,15,26,29,30). However, the results also reveal disparities in knowledge levels across different vaccines. While influenza and HPV vaccines demonstrated relatively higher knowledge levels ranging from 61.7% to 89.3%, other vaccines such as HBV, tetanus, COVID-19, pneumococcus, and zona zoster exhibited lower levels of knowledge, with percentages ranging from 13% to 58.1%. This discrepancy underscores the need for targeted educational interventions and training programs to address gaps in knowledge among family physicians, particularly concerning vaccines with lower awareness levels. Accessing data sources grounded in scientific evidence or official resources (such as EMA, CDC, FDA or national sources) is crucial for acquiring accurate knowledge, which correlates with increased personal vaccination and recommendations to patients (3,4).

The systematic review included studies that assessed both attitudes and behaviors, revealing varying frequencies of recommending and receiving vaccinations among family physicians across different vaccine types. Firstly, the review identified disparities in the frequency of recommending various vaccines among family physicians. For instance, while the frequency of recommending the influenza vaccine ranged from 34.6% to 89.8%, suggesting variations in practice among healthcare providers, the recommendation frequencies for other

vaccines such as pneumococcal, HPV, COVID-19, HBV, and tetanus vaccines also exhibited considerable variability. These findings highlight the need for standardized guidelines and continuous education to ensure consistent and evidence-based vaccine recommendations among family physicians. Escriva-Boulley et al. conducted a systematic review about cognitions and behaviours of general practitioners in France regarding HPV vaccination and they mentioned about up to 50% of general practitioners do not recommend HPV vaccination because of concerns, including changes in patients' health behaviours and doubts about safety and/or efficacy (7).

Moreover, the review highlighted variations in the personal vaccination practices of family physicians. The percentage of family physicians who received the influenza vaccine in the previous year ranged from 18.7% to 79.4% (11,12,16-19,21,26,28,30,31,33), indicating differences in adherence to vaccination recommendations within this professional group. Similarly, the percentage of family physicians who had their children vaccinated against HPV was relatively low at 19.5% (14,15,26,29,30), suggesting potential gaps in knowledge or attitudes towards specific vaccines even among healthcare providers. These findings underscore the importance of addressing barriers to vaccination uptake among family physicians, including concerns about vaccine safety and efficacy, lack of awareness or training, and personal beliefs. Strategies aimed at promoting vaccination among healthcare providers should focus on addressing these barriers and providing tailored educational interventions to improve vaccine acceptance and uptake. Furthermore, the high recommendation frequencies for COVID-19 vaccination (ranging from 98.5% to 99.1%) among family physicians reflect the importance of prioritizing vaccination against emerging infectious diseases (17,23,31). The widespread acceptance and recommendation of COVID-19 vaccination among healthcare providers underscore their role as vaccine advocates and influencers in public health efforts.

The systematic review comprehensively examined the knowledge, attitudes, and behaviors of family physicians regarding various vaccination types, including influenza, pneumococcal, HPV, COVID-19, and others. This comprehensive coverage provides a holistic understanding of family physicians' perspectives on adult immunization in national level.

Limitations of study: Our research faces common limitations associated with synthesizing data from retrospective surveys reliant on self-reporting. The review may be subject to publication bias, as it only included published studies and may have missed unpublished or gray literature. This could affect the comprehensiveness and representativeness of the synthesized evidence. The review focused on studies conducted in Türkiye, which may limit the applicability of the findings to other geographical regions with different healthcare systems, cultural contexts, and vaccination policies. The review did not provide detailed information on the quality assessment of the included studies, such as the risk of bias assessment or the use of standardized quality appraisal tools. The included studies varied in terms of study design, methodology, and outcome measures, contributing to heterogeneity across the synthesized evidence. This heterogeneity may limit the comparability and synthesis of findings across studies.

Conclusion

The findings of this systematic review provide valuable insights into the knowledge, attitudes, and behaviors of family physicians regarding vaccination across diverse patient populations and vaccine types. The review identified disparities in the frequency of recommending various vaccines among family physicians, highlighting the need for standardized guidelines and continuous education to ensure consistent and evidence-based vaccine recommendations.

In conclusion, this systematic review emphasizes the critical role of family physicians in promoting vaccination among adult populations. By addressing knowledge gaps, addressing concerns, and promoting a culture of vaccination within the healthcare community, we can enhance vaccine uptake and ultimately contribute to improved public health outcomes and disease prevention efforts.

Declaration of Competing Interest

None to declare.

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Informed Consent Statement

Not applicable.

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REVIEW

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The Beneficial Effect of Exercise and Vitamin D Supplementation on Comorbidities Associated with Systemic Lupus Erythematosus

ABSTRACT

Objective: Systemic lupus erythematosus (SLE) is a multisystem chronic autoimmune disease characterized by recurrent and relapsing attacks that may affect the locomotor system as well as the liver and kidneys. Vitamin D deficiency is thought to play a role in the pathogenesis of SLE. Therefore, the primary aim of this literature review is to determine the role of vitamin D deficiency on SLE symptoms. The secondary aim is to explain the benefits of exercise on SLE-related comorbidities.

Methods: A comprehensive literature search on SLE symptoms, biochemistry, and pathophysiology was conducted via Google Scholar. The impact of exercise on comorbidities associated with SLE was examined.

Results: The precise etiology of the disease remains elusive, although there is mounting evidence that vitamin D deficiency is associated with symptoms of SLE. In addition to pharmacological treatment for the involvement of the locomotor system in SLE patients, physiotherapy applications are also included. This review presents evidence of the positive effects of exercise on pain, fatigue, and sleep problems caused by disease-related or side effects of pharmacological applications used in the treatment of SLE patients.

Conclusions: It is not possible to correct the symptoms of SLE associated with vitamin D deficiency by means of vitamin D supplementation alone. At this juncture, it is hypothesized that exercise may offer potential benefits in correcting vitamin D deficiency. Consequently, exercise exerts a beneficial influence on the comorbidities associated with SLE. Future studies should be planned to establish an appropriate exercise prescription for SLE.

Keywords: Systemic Lupus Erythematosus, Exercise, Fatigue, Pain, Sleep Disorders, Vitamin D

Egzersiz ve D Vitamini Desteğinin Sistemik Lupus Eritematozus ile İlişkili Komorbiditeler Üzerindeki Faydalı Etkisi

ÖZET

Amaç: Sistemik lupus eritematozus (SLE), lokomotor sistemin yanı sıra karaciğer ve böbrekleri de etkileyebilen, tekrarlayan ve nükseden ataklarla karakterize multisistem kronik otoimmün bir hastalıktır. D vitamini eksikliğinin SLE patogenezinde rol oynadığı düşünülmektedir. Bu nedenle, bu literatür taramasının birincil amacı D vitamini eksikliğinin SLE semptomları üzerindeki rolünü belirlemektir. İkincil amaç ise egzersizin SLE ile ilişkili komorbiditeler üzerindeki faydalarını açıklamaktır.

Yöntem: Google Akademik aracılığıyla SLE semptomları, biyokimyası ve patofizyolojisi hakkında kapsamlı bir literatür taraması yapılmıştır. Egzersizin SLE ile ilişkili komorbiditeler üzerindeki etkisi incelenmiştir.

Bulgular: D vitamini eksikliğinin SLE semptomlarıyla ilişkili olduğuna dair kanıtlar artmakla birlikte, hastalığın kesin etiyolojisi halen tam olarak bilinmemektedir. SLE hastalarında lokomotor sistem tutulumuna yönelik farmakolojik tedavinin yanı sıra fizyoterapi uygulamaları da yer almaktadır. Bu derlemede, SLE hastalarının tedavisinde kullanılan farmakolojik uygulamaların yan etkileri veya hastalığa bağlı olarak ortaya çıkan ağrı, yorgunluk ve uyku sorunları üzerinde egzersizin olumlu etkilerine dair kanıtlar sunulmaktadır.

Sonuç: D vitamini eksikliği ile ilişkili SLE semptomlarını sadece D vitamini takviyesi ile düzeltmek mümkün değildir. Bu noktada, egzersizin D vitamini eksikliğini düzeltmede potansiyel faydalar sağlayabileceği varsayılmaktadır. Sonuç olarak, egzersiz SLE ile ilişkili komorbiditeler üzerinde faydalı bir etkiye sahiptir. SLE için uygun bir egzersiz reçetesi oluşturmak üzere gelecekteki çalışmalar planlanmalıdır.

Anahtar Kelimeler: Sistemik Lupus Eritematozus, Egzersiz, Yorgunluk, Ağrı, Uyku Bozuklukları, D Vitamini.

INTRODUCTION

Background

Systemic Lupus Erythematosus (SLE), an autoimmune disease, is characterized by chronic inflammation and multiple organ damage due to the continuous production of autoantibodies (1). As immune cells are stimulated more frequently in SLE, autoantibodies and immunological complexes are produced. Additionally, cytokines including IL-17 and IL-10, chemokines, vasoactive peptides, oxidants, and proteolytic enzymes are released. In response to inflammatory cytokines, the liver secretes hepcidin, which inhibits the release of iron from macrophages and the absorption of iron from the gut, thereby preventing erythropoiesis (2). The accumulation of chronic oxidation products causes chronic inflammation, and irreversible tissue damage to the kidneys, lungs, and other tissues (3).

The cause of the disease is not fully known. Genetic predisposition, gender, and environmental factors are thought to trigger an abnormal immune response leading to the development of systemic lupus erythematosus (4). In addition, vitamin D deficiency is thought to play a role in the pathogenesis of SLE. It has been emphasized that 25-hydroxyvitamin D levels are low in various autoimmune diseases, including rheumatic diseases (5).

Therefore, our primary aim in this literature review is to determine the role of vitamin D deficiency on SLE symptoms. Our secondary aim is to explain the benefits of exercise on SLE-related comorbidities.

Main Text

Vitamin D and Deficiency in SLE: Vitamin D is a pro-hormone that can be consumed by food or produced in the skin's epidermis following exposure to UV rays. It has significant influence on the cardiovascular system, mineral metabolism, and bone health (6, 7). The result of a meta-analysis showed that SLE patients generally exhibited significantly lower serum vitamin D levels compared with healthy controls (7). In vitamin D deficiency, it has been found that there is a deterioration in the cell's ability to respond to pathological and physiological signals (8).

There is an opinion that the decrease in sleep duration and deterioration of sleep quality in SLE patients may be associated with low vitamin D levels (9). In addition, disease duration, anxiety, depression, subjective sleep quality, and sleep disturbances were found to be significantly associated with fatigue (10).

It has been reported that arthritis is improved with vitamin D supplementation in animal models of SLE (11), and disease activity and fatigue symptoms are improved in human models (12). However, the available literature is conflicting regarding the efficacy of vitamin D supplementation on symptoms and recovery in SLE (13-15).

Therefore, it is important to implement therapies aimed at improving the pathogenic mechanism causing vitamin D deficiency. Improving the function of the kidneys and liver, the source of metabolic transformations of vitamin D may have an important role in correcting vitamin D deficiency and alleviating the accompanying symptoms.

Vitamin D and Exercise: Vitamin D deficiency causes muscle pain and muscle weakness due to atrophy of type 2 muscle fibers, hypotonia, peak muscle contraction time, and prolongation of muscle relaxation time (16, 17). It has been observed that vitamin D receptors (VDRs) identified in muscle tissue are increased with vitamin D supplementation (18).

Vitamin D is lipophilic and tends to accumulate in adipose tissue. Vitamin D3 and 25(OH)D accumulation was observed in adipose tissue (19, 20). Exercise, an effective stimulus for lipid mobilization, helps mobilize vitamin D accumulated in adipose tissue (21, 22).

Particularly submaximal endurance training has been shown in the literature to significantly boost fat metabolism (23). Stored vitamin D metabolites are released when lipolytic enzymes release triglycerides from adipocytes. A number of substances, including insulin, beta-adrenergic hormones, atrial natriuretic peptides (ANPs), and brain natriuretic peptides (BNPs), influence lipolysis (24). The release of these hormones, the promotion of lipolytic actions, and the release of vitamin D metabolites from adipose tissue are all possible benefits of endurance exercise (25).

Sleep Problems and the Effect of Exercise in Systemic Lupus Erythematosus: Drugs that are commonly prescribed for the treatment of symptoms of rheumatic diseases and commonly used in SLE (Prednisone) may have adverse effects on sleep (26).

It has been shown in previous studies that vitamin D deficiency, which is very common in SLE patients, affects sleep quality, psychological state, and depression, including in the non-SLE population (27, 28). There is evidence that musculoskeletal pain caused by vitamin D deficiency also affects sleep quality (28). In addition, due to the immune regulatory role of vitamin D, an increase in the production of inflammatory cytokines, which can affect sleep patterns and quality, has been observed in deficiency. This can cause obstructive sleep apnea, airway myopathy, and chronic rhinitis in individuals (29).

Physical activity is considered a non-pharmacological complementary method recommended for treating sleep problems by improving sleep quality (30). In the literature, it is stated that exercise contributes positively to overall sleep quality (31). In a meta-analysis conducted in 2019, it was reported that exercise in the evening contributes to sleep positively (32).

In addition to improving the overall sleep quality of exercise alone, it can be effective for the treatment of sleep disorders due to vitamin D deficiency in SLE by providing vitamin D mobilization, which accumulates in adipose tissue.

Pain and The Effect of Exercise in Systemic Lupus Erythematosus: Lupus nephritis is one of the indicators of poor prognosis in systemic lupus erythematosus. According to the findings of an analysis in the literature comparing children with juvenile idiopathic arthritis (JIA) with active and inactive lupus nephritis and healthy controls, urinary Prostaglandin D synthase (PGDS) levels were reported to be higher in children with active lupus nephritis (LN) than in healthy controls and children with inactive lupus (33). This highlights that the increase in prostaglandins in SLE adversely affects the prognosis. Prostaglandins are mediators synthesized in the cells of the organism, involved in inflammation and pain formation. Vitamin D is involved in inhibiting the synthesis of Prostaglandin E2 (PGE2) in fibroblasts (34). Current studies have shown that vitamin D supplementation reduces musculoskeletal pain and levels of inflammatory cytokines, including prostaglandin E2 (PGE2) (35). In line with this information, the mechanism of action of vitamin D on pain is explained by the reduction of inflammation and the inhibition of PGE2, which affects pain formation.

In addition, exercise increases the secretion of endorphins and serotonin in the body (36). β-endorphins, which are part of the endogenous opioid system, are involved in pain relief. For this reason, by stimulating the body to secrete more endorphins with regular exercise, it is possible to benefit more from the analgesic effect of endorphins.

In a recent review including only RCTs, exercise and psychological interventions have been shown to improve pain, fatigue, depression, and quality of life in individuals with SLE (37). In addition, a recent pilot RCT reported improvement in hand function, pain, activity limitation, and quality of life with upper extremity resistance training in patients with SLE without a negative effect on disease activity (38).

Fatigue and The Effect of Exercise in Systemic Lupus Erythematosus: One of the most common symptoms in patients with SLE is fatigue. Several mechanisms have been described for how vitamin D deficiency can cause fatigue. Reduced exercise capacity (39), decreased strength (40), decreased quality of life (41), and elevated levels of weariness (42) are a few of the processes discovered in people with SLE. Fatigue may result from proximal muscular weakness brought on by a loss in type 2 muscle fibers due to vitamin D insufficiency (43).

In a study in the literature, individuals with chronic fatigue syndrome and controls without chronic fatigue syndrome were compared. Individuals with chronic fatigue have been found to have higher serum TNF-α levels (44). This indicates that TNF-α is elevated in the presence of sleep disorders and chronic fatigue. In a prospective cohort study of SLE patients, elevated serum TNF-α levels were seen (45). In addition, in another study conducted with lupus patients, a significant inverse correlation was found between serum 25(OH)D and TNF-α levels in patients (46). Starkie et al. reported that endurance exercise with 8 healthy male individuals significantly reduced TNF-α production (47).

Balsamo et al. evaluated a total of 50 individuals, including 25 premenopausal SLE patients with low SLE disease activity index and 25 healthy controls. They reported that muscle strength in SLE patients was lower than in the healthy control group. They provided evidence that insufficient muscle strength causes increased fatigue, decreased performance, and quality of life in SLE patients (48).

In the literature, aerobic exercise is widely recommended for individuals with SLE to increase exercise tolerance by increasing cardiovascular fitness. A meta-analysis of studies in individuals with SLE showed a significant increase and improvement in physical fitness and function of the exercise group compared to controls (49). Another study comparing 93 patients with SLE and 41 sedentary controls showed that patients with SLE had lower exercise capacity and muscle strength than sedentary controls, and reported more fatigue than sedentary individuals (40).

In an RCT conducted with children aged 7-15 years with SLE, it was emphasized that 12-week, twice-weekly supervised, moderate-intensity aerobic exercise is a safe and effective method to improve cardiorespiratory capacity (50).

The increase in cardiorespiratory capacity prevents the development of fatigue in individuals and provides an increase in physical functions and quality of life. In this respect, the exercises deemed appropriate by the physiotherapist for SLE patients contribute positively to the quality of life by providing improvement/decrease in the symptoms of the patient.

The Table 1 below provides a summary of the potential mechanisms by which vitamin D deficiency may affect sleep problems, pain, and fatigue in SLE. Furthermore, the table provides an overview of the potential benefits of exercise in this context.

Table 1. The effect of vitamin D deficiency and exercise on comorbidities in SLE.

Comorbidities in SLE	The Effect of Vitamin D Deficiency	The Effect of Exercise
Sleep Problems	Musculoskeletal pain caused by vitamin D deficiency affects sleep quality (28). Due to the immunoregulatory role of vitamin D, an increase in the production of inflammatory cytokines that may affect sleep patterns and quality is observed in vitamin D deficiency.	It is a non-pharmacological method recommended for the treatment of sleep problems (30). It contributes positively to general sleep quality (31). Especially exercise performed in the evening positively affects the transition to sleep (32). It may be effective in treating vitamin D deficiency-related sleep disorders in SLE by mobilizing vitamin D accumulated in adipose tissue (21, 22).
Pain	The mechanism of action of vitamin D on pain is explained by the reduction of inflammation and inhibition of prostaglandin E2, which affects pain formation (34, 35).	Exercise and psychological interventions reduce pain in individuals with SLE (37). Upper extremity resistance exercises reduce pain (38).
Fatigue	Fatigue may result from proximal muscle weakness caused by the loss of type 2 muscle fibres due to vitamin D deficiency (43). TNF-α is increased in the presence of sleep disorders and chronic fatigue. High serum TNF-α levels have been observed in patients with SLE (45). There is a significant inverse correlation between serum 25(OH)D and TNF-α levels (46).	Exercise improves physical fitness and functions (49). Patients with SLE have lower exercise capacity and muscle strength compared to sedentary controls. They report more fatigue than sedentary individuals (40). Supervised, moderate-intensity aerobic exercise twice a week for 12 weeks is a safe and effective method to improve cardiorespiratory capacity in SLE (50). Endurance exercises reduce fatigue by decreasing TNF-α production (47).

CONCLUSION

Prescription of exercises deemed appropriate for SLE patients by the physiotherapist may help to improve/reduce fatigue, sleep problems, and pain symptoms seen in SLE, improve the quality of life of patients, and eliminate vitamin D deficiency due to SLE. In this direction, the importance of physiotherapy applications should be emphasized in addition to medical treatment in SLE patients. Future studies should be planned to create an appropriate exercise prescription for SLE.

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REVIEW

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Rhythm and Conduction Disturbances in patients with COVID-19 and Their Significance in Family Medicine Practice

ABSTRACT

SARS-Cov-2 (Severe acute respiratory syndrome coronavirus 2) belongs to the group of viruses containing ribonucleic acid (RNA). The most common clinical manifestations include fever, upper and or lower respiratory tract involvement of varying severity. As the incidence of the disease increases and information about its course accumulates, it is known that there is an increased mortality from cardiovascular complications, including as a result of arrhythmias. It is assumed that the main mechanisms by which they occur are the entry of the virus into the heart cell through the expression of angiotensin-converting enzyme receptor 2, which leads to increased levels of angiotensin 2 and its many-sided negative effects, the development of a systemic inflammatory over-response (cytokine storm), directly cardiac damage, hypoxia, electrolyte disturbances, water imbalance. The disorders that are registered are tachyarrhythmias and bradyarrhythmias. In the conditions of the emerging COVID-19 (coronavirus disease of 2019) pandemic, general practitioners in Bulgaria played a significant role in diagnosing and treating this disease. Of particular importance is their competence regarding the establishment of possible complications from the cardiovascular system. Knowledge of the most common rhythm and conduction disorders, as well as the mechanisms of their occurrence, are decisive for the correct management and their potential outcome.

Keywords: SARS-Cov-2, COVID-19, Rhythm and Conduction Disturbances

COVİD-19 Hastalarında Ritim ve İleti Anormallikleri ve Bunların Aile Hekimliği Pratiğindeki Önemi

ÖZET

SARS-Cov-2 (Şiddetli akut solunum sendromu koronavirüsü 2) ribonükleik asit (RNA) içeren virüsler grubuna aittir. En yaygın klinik belirtiler arasında, farklı derecede ateş, üst ve/veya alt solunum yolu etkisi vardır. Hastalığın görülme oranı arttıkça ve bu hastalığın ilerlemesi hakkında bilgi biriktirdiğinde, kardiyovasküler komplikasyonlar, aritmi sonuçları da dahil olmak üzere ölüm oranının arttığı biliniyor. Bunların meydana geldiği ana mekanizmalar, angiotensin dönüştüren enzim reseptör 2'nin ifadesi yoluyla kalp hücresine virüsün girmesidir, bu da angiotensin 2 seviyelerinin artmasına ve çok yönlü olumsuz etkileri, sistemik iltihaplı aşırı tepki (sitokin fırtınası), doğrudan kalp hasarı, hipoksiya, elektrolit bozuklukları, su dengesizliği gelişmesine yol açar. Kayıtlı hastalıklar taşiaritmi ve bradiaritmi'dir. Gelişen COVID-19 (Koronavirüs hastalığı 2019) salgını koşullarında, Bulgaristan'daki genel tıp uzmanları bu hastalığın teşhisinde ve tedavisinde önemli bir rol oynadı. Özellikle kardiyovasküler sistemle ilgili olası komplikasyonların tespiti konusunda yetkinlikleri önemlidir. En yaygın ritm ve iletkenlik bozukluklarının yanı sıra bunların ortaya çıkış mekanizmalarının bilinmesi doğru yönetimi ve potansiyel sonuçları için çok önemlidir.

Anahtar Kelimeler: SARS-Cov-2, COVID-19, ritm ve iletkenlik bozuklukları.

INTRODUCTION

SARS-Cov-2 (Severe acute respiratory syndrome coronavirus 2) belongs to the group of viruses containing ribonucleic acid (RNA). It is assumed to have a zoonotic origin, and its transfer to humans occurred via the intermediate natural reservoir, pangolins (placental mammals) (1). The airborne route of spread makes it possible to infect a huge number very quickly and as a result, on March 11, 2020, the World Health Organization declared a pandemic. The first officially recorded case of the disease caused by the "new" coronavirus (COVID-19) was in Wuhan, China. Most often, the disease manifests with fever, and involvement of the upper and or lower respiratory tract varying from bilateral inflammatory changes in the lung parenchyma to severe respiratory distress syndrome with respiratory failure necessitating intensive treatment with oxygen supply or intubation with mechanical ventilation. As the incidence of the disease increases and information about its course accumulates, it is known that there is an increased mortality from cardiovascular complications, including as a result of arrhythmias (2, 3, 4).

The purpose of this article is to present the pathway of cardiac damage, the causes and mechanism of occurrence of rhythm and conduction disorders associated with COVID-19, and their type, as well as their importance for general medical practice.

Penetration of SARS-Cov-2 into the Human Cell: Entry of SARS-Cov-2 into the cell occurs through its binding via spike (S1 and S2) protein to angiotensin-converting enzyme receptor 2 (ACE 2) (5). It is expressed mainly by type 1 and type 2 pneumocytes in the lung, but also in other tissues such as the heart, kidney, and intestine, thereby reaching their damage (6). According to data from an autopsy study, in 24 of 39 patients who died of COVID-19, the virus was identified in heart tissue, suggesting a possible direct mechanism of damage (7). Another study demonstrated increased values of high-sensitivity troponin I in 27.8% of patients hospitalized for COVID-19 (8). Abnormalities have been associated with a higher risk of complications such as acute respiratory distress syndrome, coagulopathy, and malignant arrhythmias, as well as increased mortality, especially in patients with underlying cardiac pathology and advanced age, compared to these normal levels (9).

Causes and Mechanism of Occurrence of Rhythm and Conduction Disturbances in COVID-19

I. Myocarditis: Myocarditis represents the inflammatory damage of the myocardium with or without the occurrence of necrosis. It is assumed that, on the one hand, it occurs as a result of the penetration of the virus into the cell through the ACE receptor with an increase in the levels of angiotensin II, and on the other hand, a negative effect is exerted by the cytokine storm (10). The subsequent results of this are related to:

1) fibrosis and remodeling, which are the substrate for rhythm-conduction disorders

2) increasing the concentration of inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6). IL-6 leads to damage to the cell membrane by displacing plakoglobin (desmosomal protein), subsequent inflammatory edema resulting in electrical conduction disturbances with imbalance and arrhythmias (10).

3) endothelial dysfunction leading to ischemia

4) channelopathies

5) change in calcium levels

II. Pericarditis: The exact pathophysiological mechanism by which inflammatory involvement of the pericardium occurs in COVID-19 is not fully understood. It is assumed that the basis is the systemic inflammatory response due to the viral infection. Another possible pathway is associated with inflammatory-induced endothelial damage. The hyperinflammatory response in SARS-Cov-2 infection is characterized by an increase in the levels of interleukins (IL-1, IL-2, IL-6, IL-7), granulocyte-macrophage colony-stimulating factor, interferon-γ, inducible protein 10, monocyte chemoattractant protein 1, macrophage inflammatory protein 1-α, and tumor necrosis factor (TNF)-α. The resulting cytokine storm and the additional involvement of an imbalance between T1 and T2 helpers is the cause of multi-organ damage in COVID-19, including the heart (11). According to a study of patients with COVID-19, 26% of them had acute electrocardiographic (ECG) changes, including atrial fibrillation, tachy-brady syndrome, ST-T deviations, and deviations typical of pericarditis (12).

III. Hypoxia and Myocardial Ischemia: In patients with severe COVID-19 and low oxygen levels, shifts toward low cellular pH occur as a result of anaerobic respiration, leading to increases in cytosolic calcium and extracellular potassium. This may account for early and late depolarizations and changes in action potential duration. Increasing extracellular potassium levels can lower the action potential threshold resulting in faster conduction between cardiac cells. Under hypoxic conditions, the junctional protein connexin-43 can be dephosphorylated, thereby reducing electrical coupling. Underlying cicatricial changes secondary to myocardial ischemia can also impair conduction and lead to arrhythmias (13).

IV. Systemic Inflammation, Cytokines, and Sympathetic Activity: The systemic inflammatory response to COVID-19 is associated with an increase in TNF-α and IL-6 levels and the occurrence of a "cytokine storm" that might be part of the mechanism of occurrence of induced coagulopathy (14). As a result, other vascular complications

develop, such as pulmonary embolism with an acute right-sided burden with accompanying rhythm-conduction disorders (15). Acute myocardial ischemia, including myocardial infarction, represents other life-threatening conditions arising as a result of a viral-induced prothrombogenic state and hypercoagulation, inflammatory-induced endothelial dysfunction, rupture of an underlying atherosclerotic plaque, and overactivation of the sympathetic nervous system, which are the substrate for rhythm and conduction disturbances. Continued sympathetic activation after myocardial infarction can lead to lysis of surrounding adipose tissue, inducing ventricular tachyarrhythmias (16). Other mechanisms by which increased neurogenic activity leads to the occurrence of atrial tachyarrhythmias include enhanced automaticity, prolonged action potential duration, and delayed repolarization. On the other hand, IL-6, TNF-α, and IL-1 can affect the function of potassium and calcium ion channels in ventricular cardiomyocytes and prolong the duration of the action potential. This may increase the risk of Torsade de Pointes ventricular tachycardia and subsequent ventricular fibrillation.

V. Electrolyte Disorders and Water Imbalance: Patients with COVID-19 may experience diarrhea, dehydration, and kidney failure, leading to electrolyte disturbances and water imbalance. Altered levels of potassium, calcium, and magnesium significantly increase the risk of life-threatening arrhythmias, especially ventricular. Hypocalcemia, hypomagnesemia, and hypokalemia can lead to QT prolongation and subsequent ventricular extrasystole, ventricular tachycardia including Torsades de Pointes type, and ventricular fibrillation (17).

VI. Medicines Used in the Treatment of COVID-19: Medications used in the treatment of COVID-19 may have a proarrhythmic effect. Countries have adopted different treatment protocols worldwide, but the most frequently used therapeutic regimens include hydroxychloroquine, azithromycin, lopinavir, and ritonavir. Since SARS-Cov-2 is an RNA virus similar to HIV, lopinavir, and ritonavir have been proposed to manage COVID-19. Arrhythmias are reported to be associated with QT prolongation and include ventricular ectopies, ventricular tachycardia including Torsades de Pointes type, and ventricular fibrillation (18). Baseline electrocardiogram (ECG) and further monitoring during the drug administration might be considered to detect QT interval deviations.

VII. Underlying Cardiac Pathology: Patients with **congenital long QT interval syndrome** are at increased risk of malignant tachyarrhythmias, especially in septic conditions or administration of medications that further prolong the QT interval, such as hydroxychloroquine or others with a similar effect (19). **Brugada syndrome** increases the risk of ventricular arrhythmias and sudden cardiac death. Elevated body temperature probably further affects the risk of cardiac arrest in these patients, which is why timely administration of antipyretics is necessary for SARS-Cov-2 infection (19). **Congenital heart abnormalities** such as tetralogy of Fallot, Epstein, valvular defects, and septal defects, are also causes of arrhythmias. They arise based on abnormalities in the conduction system, cicatrixes after corrective surgery, hypoxia, remodeling, changes in cardiac volumes and pressures (20). Patients with **severe heart failure** may develop malignant arrhythmias and die of sudden cardiac death in 40% of cases. Underlying changes in cardiac tissue such as cicatrixes, remodeling, as well as increased levels of catecholamines, and electrolyte disturbances, are the main causes of rhythm and conduction disturbances (21).

VIII.Severe Course of COVID-19 Requiring Intensive Care: Arrhythmias occurring in critically ill patients in intensive care units' account for the majority of cases with these disorders. According to data from a study in China, these were observed in 44% of people (22). Another study reported a 10-fold greater likelihood of developing atrial fibrillation, non-sustained ventricular tachycardia, and bradyarrhythmia. The main factor associated with significance was intensive care unit admission, compared with other variables such as age, sex, race, body mass index, presence of cardiovascular disease, and chronic kidney disease (23). In addition, a strong correlation has been found between mechanical ventilation, high troponin levels, and C-reactive protein in the occurrence of ventricular arrhythmias (24). Atrial arrhythmias were recorded in 17.7% of mechanically ventilated patients treated in an intensive care unit in New York (25). In 23 of 54 critically ill patients, the most common rhythm disturbance was sinus tachycardia (26). The incidence of cardiac arrest in this category of patients is 11% is almost always due to asystole and is significantly associated with in-hospital mortality (23).

Rhythm Disturbances in COVID-19: Data from a survey of 1,197 electrophysiologists worldwide indicated **atrial fibrillation** as the most common tachyarrhythmia (n = 179). Next were ventricular extrasystoles and non-sustained ventricular tachycardia (n = 103), paroxysmal supraventricular tachycardias (n = 39), cardiac arrest due to pulseless electrical activity (n = 38), cardiac arrest due to ventricular tachycardia or ventricular fibrillation (n = 33), sustained monomorphic ventricular tachycardia (n = 26), polymorphic ventricular tachycardia and Torsade de Pointes (n = 24), sustained atrial tachycardia (n = 24). The overall proportion of tachyarrhythmias in this study was 34.26% (27).

Conduction Disturbances and Bradyarrhythmias in COVID-19: Data from the same study indicated sinus bradycardia (n = 51) and complete atrioventricular block (n = 51) as the most

common, followed by hip block and delayed intraventricular conduction (n = 26), second-degree atrioventricular block (n = 21) and first-degree atrioventricular block (n = 18). (27).

In a statistical analysis of 38 published cases of hospitalized patients with COVID-19 in whom bradyarrhythmia was recorded, the second and third-degree atrioventricular block was most commonly registered [in 26 (68%) patients], followed by a bundle branch block (46% left bundle branch block, 54% right bundle branch block) [in 11/26 (42 %)]. Sinus arrest or sick sinus syndrome was described in 12/38 (32%) of them, rarely associated with bundle branch block (8%) (28).

CONCLUSION

Infection with SARS-Cov-2 can lead to severe rhythm and conduction disturbances that increase mortality from COVID-19. A wide spectrum of this pathology has been registered, but the exact mechanisms for its occurrence remain not yet fully understood. It is assumed that the basis is the hyperinflammatory response of the human body combined with a direct toxic effect and penetration of the virus into the heart cell. General practitioners are the most numerous group of medical specialists in Bulgaria and work at the entrance of the healthcare system. They serve a diverse group of patients of different ages and with a variety of co-morbidities, while at the same time, they have established lasting relationships and know their medical and family history well, which helps them and significantly improves their work. In the outbreak of the COVID-19 pandemic, family doctors played an essential role in the diagnosis and treatment of the viral infection, with a number of them themselves losing their lives fighting on the front lines. Given the possible complications from the cardiovascular system during COVID-19, some of which are life-threatening, the competence of general practitioners in this aspect is extremely important. Knowing the rhythm and conduction disturbances accompanying the infection with SARS-Cov-2 determines the timely diagnosis, starting the correct treatment at home, or building a correct judgment about the indications for hospitalization. The high level of clinical training of family doctors and their team is of decisive importance for the prognosis and outcome of the disease and can reduce mortality from cardiovascular complications.

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CASE REPORT

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Attention! One of the Causes of Second Degree Mobitz Type 1 AV Block: Pheniramine Maleate

ABSTRACT
Atrioventricular (AV) blockade is the loss of function of the pathways that provide electrical conduction between the sinoatrial (SA) node and the atrioventricular (AV) node. It is rated according to the level of distortion in the transmission.
Myocarditis, inferior myocardial infarction (MI), previous heart operation, and treatment with drugs such as beta-blockers, calcium channel blockers, digoxin, and amiodarone can cause AV blockade.
A patient was referred to the emergency department with swelling of her lips, itching, and rash. There were widespread urticarial rashes on her body. Pheniramine maleate was administered intramuscularly. Ten minutes later, the patient developed bradycardia and hypotension. A 2nd-degree Mobitz type 1 block was detected on the ECG.
Pheniramine maleate is a first-generation, stable, potent sedative and antihistamine from the alkylamine group. It should be kept in mind that pheniramine maleate may cause AV blocks.

Keywords: Arrhythmia, Pheniramin Maleat, Antihistamine

Dikkat! İkinci Derece Mobitz Tip 1 AV Blok Nedenlerinden Biri: Feniramin Maleat

ÖZET
Atrioventriküler (AV) blok, sinoatriyal (SA) düğüm ile atriyoventriküler (AV) düğüm arasındaki elektriksel iletimi sağlayan yolların işlev kaybıdır. İletimdeki bozulma seviyesine göre derecelendirilir.
Miyokardit, inferior miyokard enfarktüsü (MI), geçirilmiş kalp operasyonu, beta-blokörler, kalsiyum kanal blokörleri, digoksin ve amiodaron gibi ilaçlarla tedavi AV bloğuna neden olabilir.
Bu çalışmamızda dudaklarında şişme, kaşıntı ve döküntü şikayetleri ile acil servise getirilen olguyu sunduk. Hastanın vücudunda yaygın ürtikeryal döküntüler vardı. Feniramin maleat intramüsküler olarak uygulanan olguda 10 dakika sonra bradikardi ve hipotansiyon gelişti. Çekilen EKG'de ikinci derece Mobitz tip 1 blok tespit edildi.
Feniramin maleat, alkilamin grubundan birinci nesil, stabil, güçlü bir sedatif ve antihistaminiktir. Bu çalışma ile Feniramin maleatın AV bloklara neden olabileceği konusunda farkındalık oluşturmayı ve literature katkı yapmayı amaçladık

Anahtar Kelimeler: Aritmi, Feniramin Maleat, Antihistamin.

INTRODUCTION

Atrioventricular blocks (AV blocks) are the loss of function of the cardiac electroconductive pathways connecting the sinoatrial node (SA node) and the atrioventricular node (AV node) (1). Depending on the degree and type of conduction block, AV blocks may decrease cardiac output secondary to losing coordination of the atriums and ventricles. Hemodynamic instability may start suddenly and unexpectedly, causing syncope (Stokes–Adams attack) or sudden cardiac death (2). Rhythm problems are less common in the pediatric population than in adults. However, the increase in diagnostic possibilities, the success rate of surgical interventions for congenital heart diseases, and the successes achieved in other treatments have caused pediatric AV blocks to be encountered more frequently (3).

Pheniramine maleate is a first-generation, stable, potent sedative, alkylamine group antihistamine. It binds to H1 receptors reversibly and is a competitive antagonist. It is widely distributed throughout the body, including the central nervous system. It treats urticaria, allergic rhinitis, angioedema, conjunctivitis, and itchy skin disorders (4).

We wanted to contribute to the literature by reporting a patient who was referred to the emergency department due to urticaria and developed a 2nd-degree Mobitz type 1 cardiac block after pheniramine maleate treatment.

Case Report

A 16-year-old female patient was referred to the emergency department with swelling of her lips, itching, and a rash that developed suddenly on her body and spread rapidly. The patient did not have shortness of breath, cough, or difficulty swallowing, did not have a history of drug use or allergies, and did not have a known disease in the family. On physical examination, the patient's fever was 36.7°C, pulse was 65/min, blood pressure was 100/70 mmHg, and femoral pulses were palpable. There were widespread urticarial rashes on her body, puffy from the skin, pale in the middle, and reddened around, with pronounced borders. Uvular edema was not detected. Her respiratory sounds were normal, her cardiac rhythm was regular on heart examination, and there was no murmur. Other system examinations were normal. Blood and urinalysis were performed. Pheniramine maleate was administered intramuscularly.

Ten minutes after the treatment, her rash began to fade, and the swelling on her lip began to regress; however, at that time, she developed weakness, dizziness, and blackout. The patient's heart rate was 47/min, and her blood pressure was 80/40 mmHg. A 2nd-degree Mobitz type 1 block was detected on the ECG (Figure 1). The patient was placed in the Trendelenburg position. 20 ml/kg of isotonic fluid was administered intravenously in 15 minutes. The patient's plasma electrolyte levels were normal. After 1 hour of follow-up, his complaints regressed. On the control ECG, cardiac pulses were in sinus rhythm and regular, and the heart rate was 55/min (Figure 2). The echocardiographic examination was normal. During the 24-hour Holter examination, the rhythm was sinus, with a minimum heart rate of 47/min, a maximum heart rate of 141/min, and a total of 4 VEs and 60 SVEs. No block was detected.

Informed consent was obtained from the parents before this article was written.

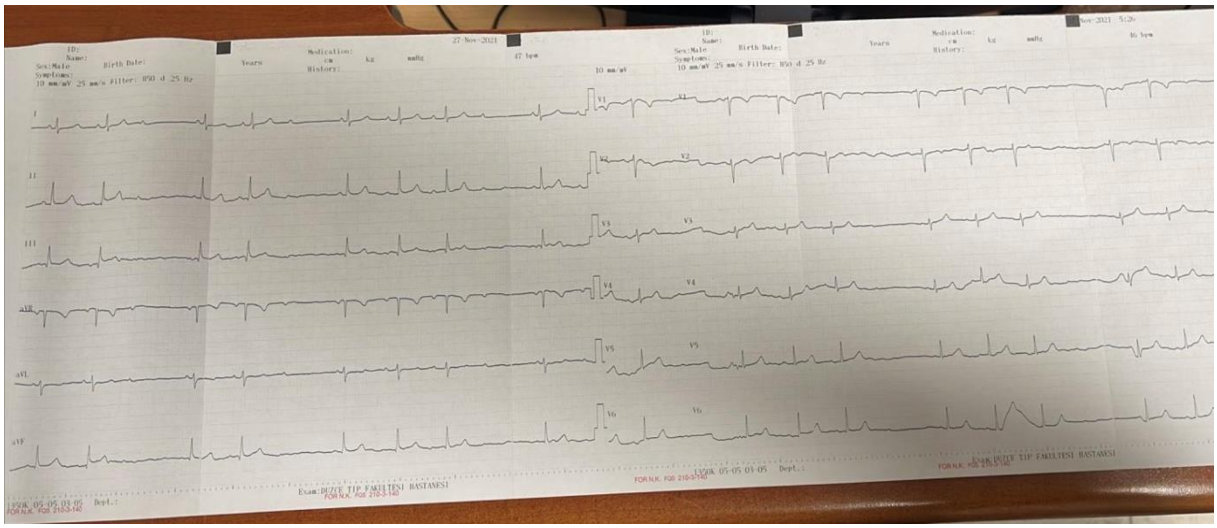

Figure 1. Second-degree Mobitz type 1 block observed on the patient's ECG during the symptomatic period

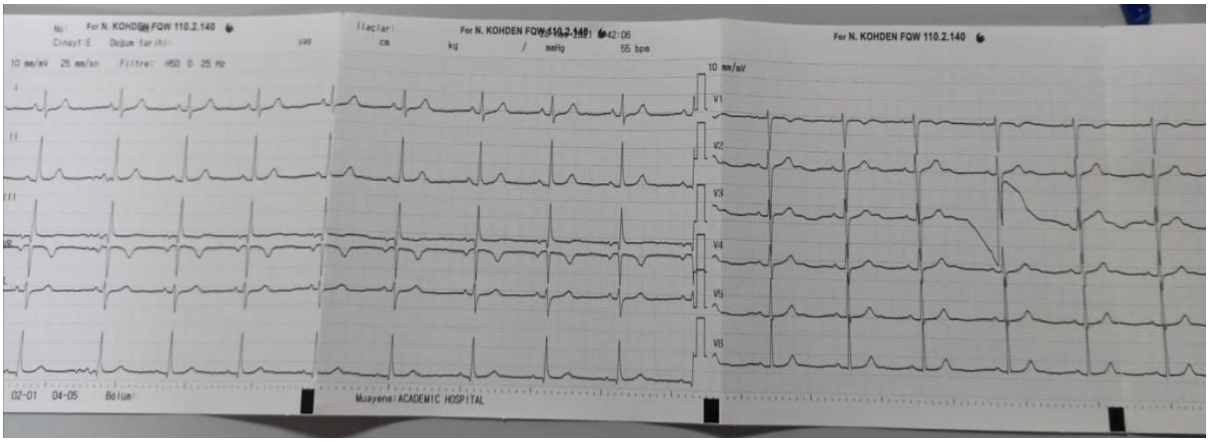

Figure 2. Control ECG, sinus rhythm, and block were not observed

DISCUSSION

The atrioventricular block is the inability to transmit electrical impulses from the atrium to the ventricles healthily. The AV blocks are divided into 3 types: first-degree (1°), second-degree (2°), and third-degree (3°). First-degree AV block is characterized by prolonged AV conduction and prolonging the P-R interval on ECG (5). A second-degree Mobitz type 1 block (Wenckebach) involves slowing AV conduction, resulting in prolonged PR interval and a nontransmitted P wave. Second-degree Mobitz type 2 AV blocks were defined as P waves that were not conducted at regular intervals without prolongation of the PR interval. This is important because of the risk of returning to a third-degree block over time (2).

Second-degree Mobitz type 1 block is observed in healthy individuals during sleep or in young athletes with increased vagal tone. Although it is generally considered a benign condition, a study conducted in Denmark reported that 43% of patients with a 2nd-degree Mobitz type 1 AV block required a pacemaker within 1 year with a higher degree of AV block. A significant relationship was also reported between 2nd-degree Mobitz type 1 AV block and cardiovascular death (6). Drugs such as beta-blockers, calcium channel blockers, digoxin and amiodarone, inferior MI, and myocarditis can cause second-degree Mobitz type 1 block. It can also be observed following cardiac operations (mitral valve repair, tetralogy of Fallot repair) (7,8). If there was no history of congenital heart disease, surgery, or symptoms of heart failure, follow-up was sufficient.

Drugs such as beta-blockers, calcium channel blockers, digoxin, and amiodarone can cause second-degree Mobitz type 1 block, but such transmission problems have not been reported thus far with pheniramine maleate, an antihistamine we used to treat urticaria in our patient.

Pheniramine maleate: This compound is a first-generation, stable, potent sedative antihistamine in the alkylamine group. It binds to H1 receptors reversibly and is a competitive antagonist. It is widely distributed throughout the body, including the central nervous system. It treats urticaria, allergic rhinitis, angioedema, conjunctivitis, and itchy skin disorders (4). The cardiac side effects of pheniramine maleate are tachycardia and arrhythmia. In a study of Levi's animal model, it was reported that antihistamines, including pheniramine maleate, have an antagonistic effect on the negative dromotropic effect of histamine and even have an antiarrhythmic effect by increasing the threshold of the histamine-dependent AV block of the AV node (9). However, a 2nd-degree Mobitz type 1 block developed after antihistamine treatment in our patient.

In this article, we aimed to raise awareness about the side effects of pheniramine maleate and contribute to the literature by presenting a patient who was referred to the emergency department due to urticaria and developed a second-degree Mobitz Type 1 block after pheniramine maleate treatment. To the best of our knowledge, no cases of second-degree Mobitz type 2 block after pheniramine treatment have been reported in the literature.

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LETTER TO EDITOR

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Enhancing Cancer Screening Awareness in Diabetic and Non-Diabetic Populations

ABSTRACT

I would like to share my opinions on the article "Exploring Perspectives on Cancer Screening in People Aged 30-70: A Comparative Study of Those with and Without Type 2 Diabetes," published in the Konuralp Medical Journal (2024;16(1):26-31). First and foremost, I commend the authors for their significant contributions to the field, addressing a topic of critical importance to physicians engaged in cancer research. This study, which investigates attitudes and behaviors towards cancer screening in individuals with and without type 2 diabetes mellitus (T2DM), is particularly notable for its potential public health implications given the increased cancer risk associated with diabetes (1).

Keywords: Cancer Screening, Type 2 Diabetes, Public Health Issue

Diyabetik ve Diyabetik Olmayan Popülasyonlarda Kanser Taraması Farkındalığının Artırılması

ÖZET

Konuralp Tıp Dergisi'nde (2024;16(1): 26-31). Öncelikle, kanser araştırmalarıyla uğraşan hekimler için kritik öneme sahip bir konuyu ele alan yazarları, alana yaptıkları önemli katkılardan dolayı kutluyorum. Tip 2 diyabeti (T2DM) olan ve olmayan bireylerde kanser taramasına yönelik tutum ve davranışları araştıran bu çalışma, diyabetle ilişkili artan kanser riski göz önüne alındığında, özellikle halk sağlığına olası etkileri açısından dikkat çekicidir (1).

Anahtar Kelimeler: Kanser taraması, Tip 2 Diyabet, Halk sağlığı sorunu.

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Dear Editor,

I would like to share my opinions on the article “Exploring Perspectives on Cancer Screening in People Aged 30-70: A Comparative Study of Those with and Without Type 2 Diabetes,” published in the Konuralp Medical Journal (2024;16(1):26-31). First and foremost, I commend the authors for their significant contributions to the field, addressing a topic of critical importance to physicians engaged in cancer research. This study, which investigates attitudes and behaviors towards cancer screening in individuals with and without type 2 diabetes mellitus (T2DM), is particularly notable for its potential public health implications given the increased cancer risk associated with diabetes (1).

The study's prospective case-control design and the use of a validated attitude scale for cancer screening (ASFCS) are methodological strengths that ensure a structured and reliable approach to data collection. The sample size of 197 participants, divided into groups with and without T2DM, provides a valuable comparative perspective. However, the limitation to a single center and the relatively small number of participants may affect the generalizability of the findings. Additionally, excluding individuals with mental or psychological disorders and those with active or past cancer further narrows the scope of the study.

A significant limitation is the study's cross-sectional nature, which prevents the assessment of causality between diabetes and cancer screening attitudes. The reliance on self-reported data could introduce bias due to participants' subjective perceptions and potential inaccuracies in reporting their behaviors and attitudes. The primary finding—the absence of a statistically significant difference in cancer screening attitudes between individuals with and without T2DM—contrasts with existing literature suggesting that diabetic patients generally have lower screening rates and may exhibit less favorable behaviors towards cancer screenings. However, the study does find a weak but significant positive correlation between age and cancer screening attitudes among non-diabetic individuals, indicating that older adults may have more positive attitudes towards cancer screening.

One critical implication of their finding is the need for tailored interventions to promote cancer screening among diabetic patients. Given the higher cancer risk in this population, healthcare providers must prioritize education and awareness initiatives. The lack of a significant difference in attitudes between the groups suggests that factors other than diabetes status, such as access to healthcare, education level, and socioeconomic status, might play more crucial roles in determining screening behaviors. The discussion section effectively situates the findings within the broader context of existing research. It references studies by Öztürk et al. (2019), Sevinç et al. (2019), and Tekpınar et al. (2017), which similarly found a positive correlation between age and attitudes towards cancer screening (2). However, it contrasts these with studies by Onitilo et al. (2009) and McBean et al. (2007), which highlight that younger individuals and those with higher education levels are more likely to undergo screenings (3).

The article also touches on the complex interplay between chronic diseases and preventive healthcare behaviors. References to Bynum et al. (2005) and Zhao et al. (2008) underscore the impact of education on screening rates, though the study’s findings do not align with these observations, possibly due to the homogeneous education level among participants (4,5).

The study concludes with a call for increased awareness and improved cancer screening rates among diabetic patients. I agree with this recommendation, which is well-founded given the documented higher cancer risk in this population. The authors suggest that primary care physicians play a crucial role in educating and guiding diabetic patients about the importance of regular screenings.

I believe, Future research should aim to overcome the limitations of this study by including a larger, more diverse sample from multiple centers. Longitudinal studies could provide more insights into how attitudes and behaviors towards cancer screening evolve over time in individuals with T2DM. Additionally, exploring the psychological barriers and facilitators to screening in this population could offer more targeted intervention strategies. Despite its limitations, this research makes a valuable contribution to our understanding of cancer screening attitudes in diabetic and non-diabetic individuals. It points out the need for heightened awareness and proactive screening measures for diabetic patients. By addressing these needs, healthcare systems can better manage the dual burden of diabetes and cancer, ultimately improving patient outcomes and quality of life.

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