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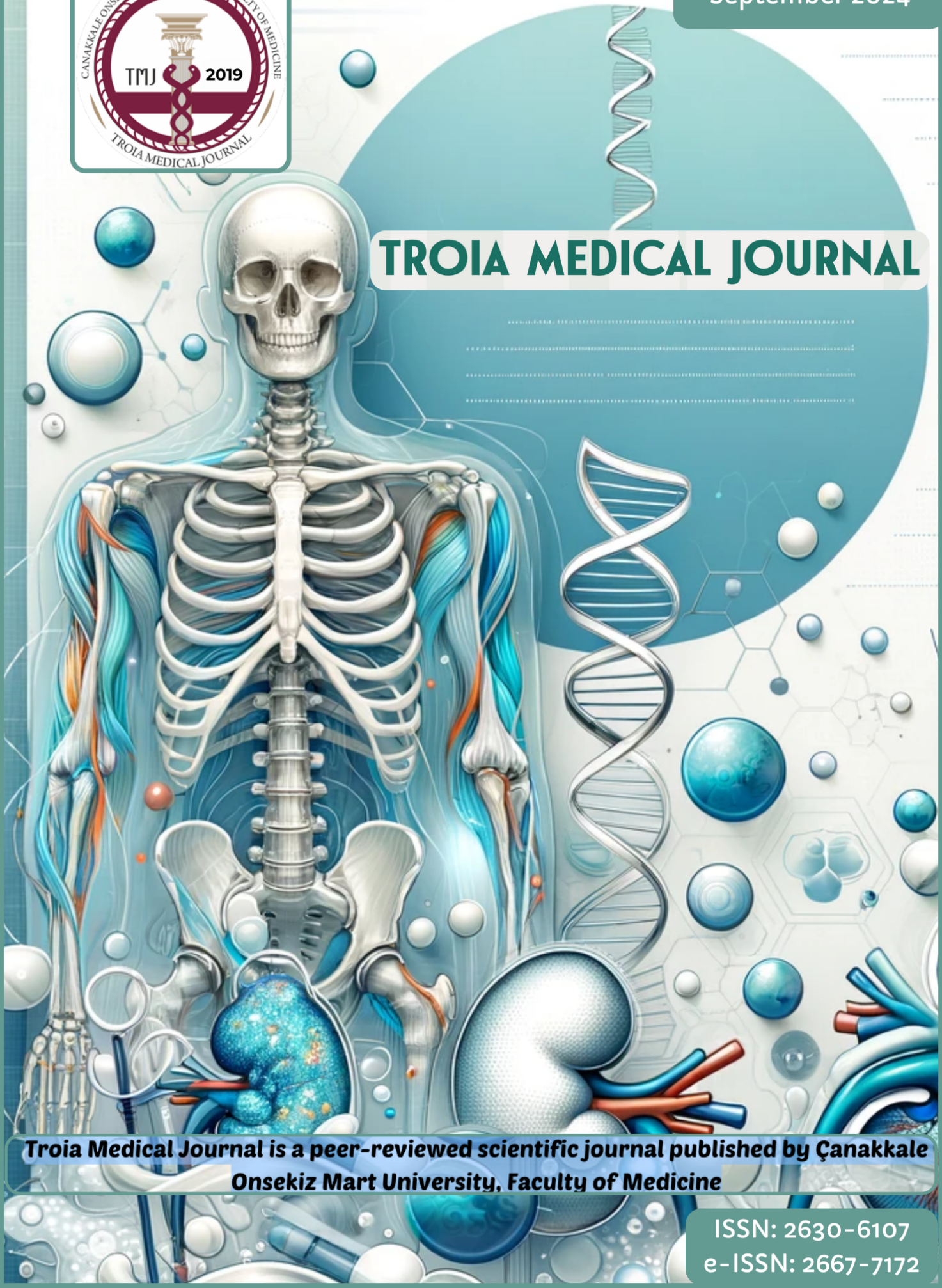

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RESEARCH ARTICLE

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Diagnostic impact of diffusion weighted imaging in acute appendicitis

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ABSTRACT

Objective: This study reveals the impact of using diffusion-weighted imaging (DWI) to accurately diagnose acute appendicitis as an alternative to CT.

Methods: In our study, 41 patients with suspected acute appendicitis, who had undergone magnetic resonance imaging (MRI) following sonographic (US) evaluation, and been referred to the radiology department during a period of 5 months were included. Two radiologists separately evaluated diffusion-weighted images. A five-range scoring system was used in the evaluation of diffusion MRI for each B-value. Any score that is 3 or higher is considered acute appendicitis. Statistical analysis was performed, and ROC curves were used for comparison.

Results: In our study, 41 patients were examined. After the exclusion of 6 patients, out of the 35 patients (13 women, 22 men; mean age: 34, age range: 16 to 80) included in the study, 19 (46%) underwent surgery, and pathology results confirmed acute appendicitis. The results of all operated patients were consistent with the ultrasonography reports. However, ultrasonography had three false-positive results. Of these patients, two were identified by two observers and one by a single observer as not having appendicitis via DWI. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy rate for DWI were measured as 52-89%, 50-87.5%, 59-80%, 68-84%, and 65-80%, respectively.

Conclusion: According to our study, with the advancement of technology, we believe that MRI usage in appendicitis will possibly increase, potentially surpassing CT, especially in selected cases due to the absence of radiation dose concerns.

Keywords: Appendicitis, Acute abdomen, Magnetic Resonance Imaging

ÖZET

Akut appendisitte difüzyon ağırlıklı görüntülemenin tanıdaki etkisi

Amaç: Bu çalışma, akut appendisitin kesin tanısında BT'ye alternatif olarak diffüzyon ağırlıklı görüntüleme (DAG) kullanmanın etkisini ortaya koymaktadır.

Yöntem: 5 aylık bir dönemde, akut appendisit şüphesiyle başvuran ve ultrasonografik (US) değerlendirme ardından magnetik rezonans görüntüleme (MRG) yapılmak üzere radyoloji bölümüne yönlendirilen 41 hasta çalışmamıza dahil edildi. İki radyolog, diffüzyon ağırlıklı görüntüleri bağımsız olarak değerlendirdiler. Diffüzyon MRG değerlendirmesinde her B değeri için beş aralıklı bir puanlama sistemi kullanıldı. Puanlama 3 veya daha yüksekse, bu durum akut appendisit olarak kabul edildi. İstatistiksel analiz yapıldı ve karşılaştırmada ROC analizi kullanıldı.

Bulgular: Çalışmamızda 41 hasta incelendi. 6 hastanın çalışmadan çıkartılmasından sonra, 35 hastanın (13 kadın, 22 erkek; ortalama yaş: 34, yaş aralığı: 16 ila 80) 19'u (%46) ameliyat edildi ve patoloji sonuçları akut apandisiti doğruladı. Ameliyat edilen tüm hastaların sonuçları ultrasonografi raporlarıyla uyumluydu. Ancak ultrasonografinin 3 yanlış pozitif sonucu mevcuttu. Bu hastalardan ikisi, iki gözlemci tarafından, biri ise tek gözlemci tarafından DAG ile appendisit olmadığı şeklinde saptanabildi. DAG için sensitivite, spesifite, pozitif prediktif değer, negatif prediktif değer ve doğruluk oranı sırasıyla %52-89, %50-87.5, %59-80, %68-84 ve %65-80 olarak ölçüldü.

Sonuç: Çalışmamıza göre, teknolojinin ilerlemesiyle appendisit vakalarında MRG kullanımının artabileceğini ve özellikle seçili vakalarda radyasyon dozu endişesi olmaması nedeniyle BT'yi potansiyel olarak geçebilece-ğine inanmaktayız.

Anahtar kelimeler: Appendisit, Akut batın, Manyetik Rezonans Görüntüleme

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INTRODUCTION

The leading reason for acute abdominal pain that requires surgical attention is appendicitis [1]. Imaging is critical when it comes to evaluating patients with suspected acute appendicitis, especially in guiding treatment choices and planning for surgery. Currently, computed tomography (CT) is the preferred modality for imaging evaluation in patients with suspected appendicitis. As a result of its high sensitivity, specificity, and rapid accessibility, CT has been proven to be a useful method for diagnosis [2]. Prior research has also demonstrated that CT greatly lessens the expenses for care as well as negative appendectomy rates [3]. However, downsides of CT do include the use of intravenous contrast agents, the possibility of allergic reactions or contrast-induced acute kidney injury, and exposure to ionizing radiation.

Magnetic resonance imaging (MRI) has garnered recent attention since it does not necessitate using intravenous contrast agents, does not involve ionizing radiation, and effectively identifies inflammation. Furthermore, MRI is less affected by patient-specific factors such as large body habitus or technical proficiency compared to ultrasound (US), which provides a significant advantage[4]. The focus of this study is to highlight the benefits and drawbacks of diffusion sequences in MRI, which are critically important for evaluating ischemia in acute appendicitis assessment. DWI offers insights into the biophysical traits of tissues, an example being microstructure, microcirculation, and cell structure, as well as enabling the characterization of biological tissues through water molecule diffusion characteristics. The diffusion coefficient measures the degree of molecular mobility at a microscopic level.

In our study, we investigated the contribution of diffusion-weighted MRI with low b-values (200-400-600 s/mm2) in identifying acute appendicitis among patients with suspected cases.

MATERIALS and METHODS

Patient Selection: Our study comprised a total of 41 patients who underwent a lower abdominal MRI with a preliminary acute appendicitis diagnosis between January and May 2010. Based on biochemical and physical examination findings, an ultrasound was performed. Due to inconclusive ultrasound results, an MRI was conducted with a preliminary diagnosis of appendicitis (Figure 1). The patients' data were retrospectively reviewed from the database. After obtaining approval from the ethics committee for the study design, written informed consent was obtained from every participating patient.

MRI Technique: A 1.5 Tesla MRI unit (Excite 2.0, GE MEDICAL SYSTEMS) with an 8-channel body coil was used. Sedation and anesthesia were not administered to the patients. Contrast agents were not administered. Routine MRI sequences included T2-.

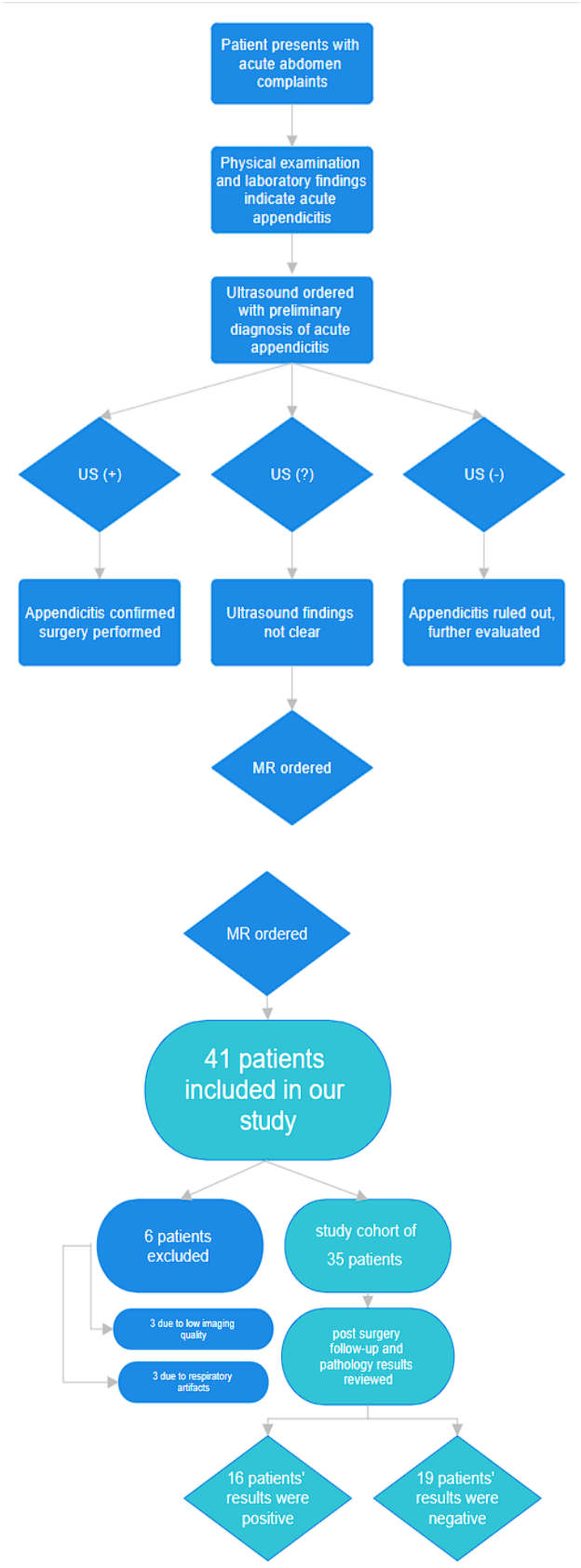

Figure 1: Flowchart presenting the patient selection and processing for our study.

weighted imaging as well as diffusion-weighted imaging (DWI) at B-values of 200, 400, and 600 s/mm². The imaging covered the lower abdominal region. DWI images were acquired without breath-holding. An intensity increase in the restricted diffusion area was expected in images with a higher gradient strength. DWI parameters were set as follows: inversion time (IT) 2200 ms, echo time (TE) minimum, repetition time (TR) 10,000 ms, spacing 1.00, phase 160, field of view (FOV) 44, number of excitations (Nex) 4, slice thickness 10 mm, duration 3 minutes. The total duration of the MRI scan was 14 minutes. No respiratory artifacts were observed in the 35 patients that were selected for the study.

MRI Evaluation: The image processing was performed by workstation, and the reference sequence utilized to confirm the location of appendicitis was T2-weighted imaging. Two different radiologists, who had two and four years of experience and who were blinded to ultrasonography and pathology findings, evaluated the images retrospectively. All patients with a preliminary diagnosis of acute appendicitis completed the procedure. Two radiologists who were blinded to pathology and ultrasonography results evaluated the B200, B400, and B600 images regarding the likelihood of appendicitis using a 5-point Likert scale ranging from 1 to 5 (Table 1).

1	No probability for appendicitis
2	Low probability for appendicitis
3	Intermediate probability for appendicitis
4	High probability for appendicitis
5	Appendicitis

Table 1. Scoring system used for evaluating DWI images in our study.

These were the routine B-values at the hospital where the data was retrieved. The scoring system was a subjective method used by two physicians based on the severity of diffusion restriction of the appendix itself, without considering secondary findings of appendicitis such as peri-appendiceal inflammation or fluid; 1 meaning no diffusion restriction and 5 being the most severe. Scores of three or higher were considered positive for appendicitis on DWI images, and calculations were performed (Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value, Accuracy). Additionally, the patients were then assessed using ROC analysis.

The investigator radiologist gathered clinical data, ultrasonography findings, diffusion-weighted MRI images, surgical-pathology results, and clinical follow-up outcomes of the study patients retrospectively.

RESULTS

Our study comprised 35 patients who underwent diffusion-weighted MRI for suspected acute appendicitis. Out of the participants, 63% (22) were male, and 37% (13) were female. The age of the patients varied from 16 to 80 years, with the mean age being 34. All patients underwent a transabdominal ultrasound (USG) examination for suspected acute appendicitis. Out of the 41 patients initially considered for the study, six were excluded due to low-quality diffusion images and respiratory artifacts. Consequently, the study cohort comprises 35 individuals.

Nineteen patients in our study underwent surgery for appendicitis. Among the remaining 16 patients, clinical symptoms improved during clinical follow-up, and one patient was diagnosed with nephrolithiasis based on laboratory findings.

The sensitivity, specificity, positive predictive value, and negative predictive values for B200, B400, and B600 diffusion-weighted images were calculated for two different evaluating radiologists and are presented (Table 2).

All 19 appendicitis patients in our study were diagnosed as positive on ultrasonography. However, among the three non-appendicitis patients, ultrasonography indicated appendicitis. In contrast, all of these patients were evaluated as non-appendicitis cases by one of our radiologists on diffusion-weighted images, while the other radiologist interpreted only one patient as non-appendicitis.

Sensitivity values for B200, B400, and B600 images were measured as 73.6%, 84%, and 89%, respectively, by the first radiologist, and 57%, 52%, and 63%, respectively, by the second radiologist (Table 2).

Magnetic resonance imaging (MRI) findings for selected patients are illustrated in Figures 1, 2, and 3.

	1st Radiologist B200	2nd Radiologist B200	1st Radiologist B400	2nd Radiologist B400	1st Radiologist B600	2nd Radiologist B600
Specificity	10/16 % 62.5	14/16 % 87,5	12/16 % 75	13/16 % 81,5	8/16 % 50	12/16 % 75
Sensitivity	14/19 % 73,6	11/19 % 57	16/19 % 84	10/19 % 52	17/19 % 89	12/19 % 63
Positive predictive value	10/15 % 66	14/22 % 63	12/15 % 80	13/22 % 59	8/10 % 80	12/19 % 63
Negative predictive value	14/20 % 70	11/13 % 84	16/20 % 80	10/13 % 76	17/25 % 68	12/16 % 75
Accuracy	24/35 % 68	25/35 % 71	28/35 % 80	23/35 % 65	25/35 % 71	24/35 % 68

Table 2. Comparison of sensitivity, specificity, positive and negative predictive value and accuracy values of B200, B400 and B600 DWI in terms of the 1st and 2nd radiologists

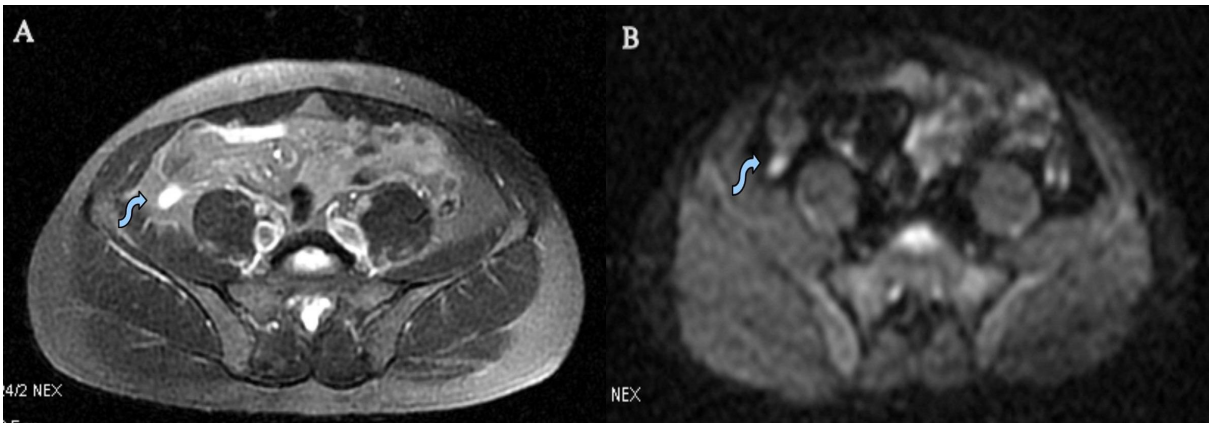

Figure 2: One of our patients, a 16-year-old male who had a pre-diagnosis of acute appendicitis underwent MRI. After surgery, the pathology report confirmed appendicitis. A. T2-weighted image revealing increased wall thickness of the appendix (curved arrow) and peri-appendiceal free fluid. B. Diffusion-weighted image displaying diffusion restriction in the appendix wall (curved arrow).

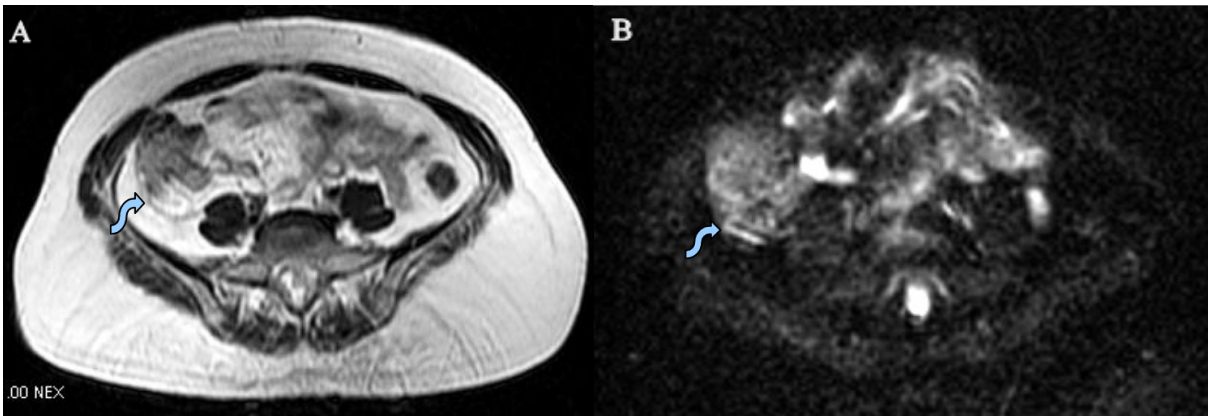

Figure 3: One of our patients, a 41-year-old female patient who had a pre-diagnosis of acute appendicitis underwent MRI. The patient underwent surgery on the same day, and the pathology report confirmed appendicitis. A. In the T2-weighted image, there is an increase in wall thickness of the appendix (curved arrow). B. In the diffusion-weighted image, diffusion restriction is observed in the appendix wall (curved arrow).

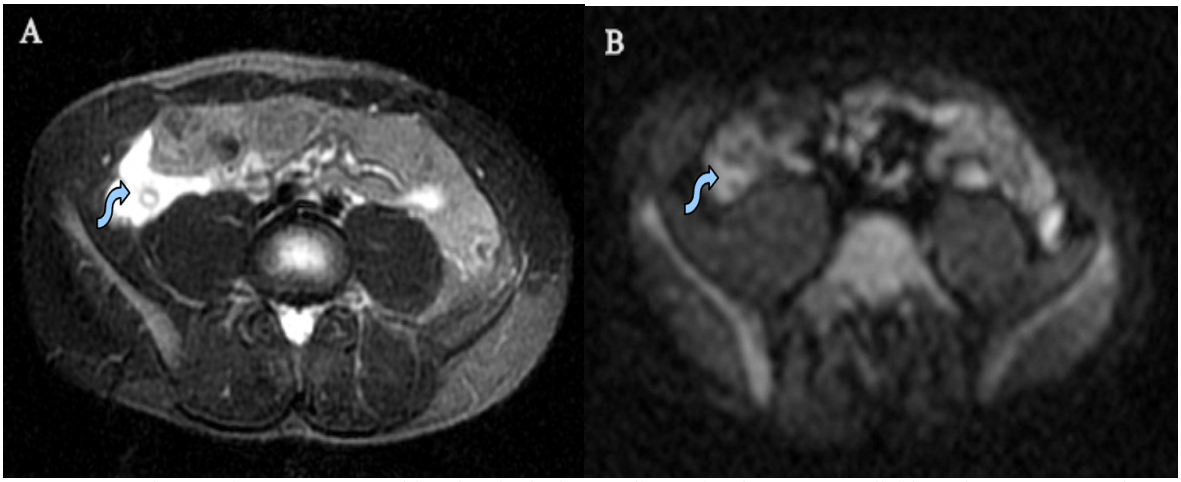

Figure 4: One of our patients, a 32-year-old male who had a pre-diagnosis of acute appendicitis underwent MRI. After surgery, the pathology report confirmed appendicitis. A. In the T2-weighted image, there is increased signal intensity in the appendix and surrounding area (curved arrow). B. In the diffusion-weighted image, there is significant diffusion restriction in the appendix wall (curved arrow)

DISCUSSION

In recent studies, ultrasound has emerged as the favored imaging modality for adult patients undergoing evaluation for suspected appendicitis. CT is suggested for cases where the diagnosis remains uncertain following an ultrasound evaluation[5]. The usage of CT in suspected appendicitis cases, in addition to ultrasound, has significantly reduced the likelihood of negative appendectomy without negatively impacting hospital stay and perforation rates. However, the noteworthy downside of CT is the significant exposure of radiation to the patient, which is particularly concerning for children, young patients, and pregnant individuals[6]. MR imaging has demonstrated favorable outcomes in the detection and exclusion of appendicitis [6-12].

In a recently conducted study, Bijnen et al. emphasized a remarkable association between the extraction of a healthy appendix and increased expenses and complications. To curtail costs, exploring the utilization of supplementary diagnostic tools ought to be taken into account. Diagnostic laparoscopy, an expensive diagnostic method, must preferably be reserved for selected patients to prevent further escalation of costs [13].

MR imaging is not a commonly employed modality when it comes to acute appendicitis diagnosis. It has been reported to be valuable in assessing local inflammation in cases of acute abdomen[14]. MRI features Short Tau Inversion Recovery (STIR) sequences that are particularly sensitive to fluid collections, providing rapid imaging with good resolution at a slice thickness of 2-4 mm[15-17]. Fast T2-weighted and T1-weighted images are useful for tissue visualization. However, findings such as thickened bowel walls, local inflammatory signs, and fluid collections located in the lower right quadrant might indicate conditions other than acute appendicitis. A meta-analysis evaluated a comparison among the diagnostic accuracy of MRI, CT, and US examinations among pediatric patients showing clinical suspicion of acute appendicitis. As a result, MRI showed a slight advantage over US as well as CT, though the difference did not result in being statistically meaningful [17].

In a meta-analysis conducted by Barger et al., MRI was reported to have a sensitivity of 92-99% and a specificity of 94-99%[18]. These rates are almost comparable to those of CT imaging. MRI has been reported as a viable alternative to CT scans for secondary imaging in the diagnosis of acute appendicitis in children[19]. However, interpreting MR images requires experience. The primary reason for the difference in interpretations in our study may be the varying levels of experience with DW-MRI in diagnosing appendicitis. Consequently, the use of MRI for the diagnosis of acute appendicitis appears to be limited to pregnant women and children[20]. With the increased use of DW-MRI in acute appendicitis, the differences in interpretation among doctors may decrease, leading to a broader clinical application.

There are multiple limitations to the use of MR in acute appendicitis. These include high costs and the requirement for a 24-hour operating MRI system. Though there are disadvantages like this, advancements in MRI technology over the recent years, along with an increasing number of MRI devices, are likely to reduce these challenges. Moreover, ensuring patient comfort during MRI examinations can be challenging. In our study, a safe, comfortable, and rapid investigation was provided to patients with pain using an MRI protocol without oral or intravenous contrast administration. None of the patients pre-diagnosed with appendicitis left the procedure incomplete.

One noteworthy limitation of our study is that we chose a reference slice thickness of 10 mm for

diffusion-weighted images. This choice substantially reduced the sensitivity and specificity of diffusion-weighted images. In addition, the B-values that were chosen were routinely used in the hospital where the data was taken. At low b-values, DWI (Diffusion-Weighted Imaging) is more similar to a T2-weighted image. Therefore, the absence of T2 images did not pose a problem in our study. However, we encountered issues due to the low spatial resolution, low signal-to-noise ratio (SNR), and motion-related artifacts (such as respiration, arterial pulsations, and bowel movements) in diffusion images. The scans were generated within a timeframe of 30-60 milliseconds. Consequently, most of the issues related to motion artifacts were eliminated. The low spatial resolution issues of DWI, particularly at high b-values (e.g., 1000 s/mm²), restrict the appearance of anatomical details in most images when SNR decreases. Therefore, we utilized low b-value (200-400-600 s/mm²) images due to the similarity of DWI images to T2 images, which aided in visualizing anatomical details.

Furthermore, one of the most critical issues in appendicitis diagnosis is the presence of various differential diagnoses causing right lower quadrant pain, including diverticulitis, Crohn's disease, and mesenteric lymphadenitis. These conditions can lead to secondary findings of appendicitis, such as peri-appendiceal inflammation and fluid collection. We posit that diffusion MRI's ability to demonstrate ischemia at the cellular level in the appendix will be valuable in differentiating these pathologies. As diffusion MRI is a rapid imaging technique and with further improvement of MRI technology to correct observed artifacts, we anticipate an increase in its utility for excluding other pathologies. We believe that the usage of MRI in appendicitis will increase, potentially surpassing CT, especially in selected cases, due to the absence of radiation dose concerns, with the advancement of MRI technology, reduced artifacts, and improved resolution.

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RESEARCH ARTICLE

Smoking and quitting behavior of hospitalized COVID-19 patients

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ABSTRACT

Objective: The relationship between Covid-19 and smoking is controversial. In this study, our aim was to determine the association between smoking and hospitalization duration and to demonstrate how smoking habits change following COVID-19 disease.

Methods: This prospective cohort study conducted on patients hospitalized at pandemic services of a university hospital between 01.10.2020-30.11.2020. Sociodemographic variables and smoking habits were assessed through a face-to-face interview. Individuals who were still smoking were contacted by phone six months after discharge, and their smoking habits were re-evaluated.

Results: Total of 373 patients were included in the study with average age of 63.0±15.0.and 175 (%46.9) were female. Of the participants, 192 (51.5%) had never smoked, 148 (39.7%) had quit smoking, and 33 (8.8%) were still smokers. Length of hospitalization of smokers, never-smokers and quitters were not statistically different. There was no statistically significant difference in terms of worsening status between smokers, ex-smokers and never smokers. Of the total 33 current smoker, 10 (33.3%) quit smoking and did not start again, 13 (43.3%) quit smoking but started again, and 7 (23.3%) did not quit smoking at the follow up.

Conclusion: In our study, it was observed that smoking did not affect the course of COVID-19 disease and length of stay. Also, history COVID-19 can affect smoking habits and may lead to smoking cessation.

Keywords: COVID-19; Smoking; Smoking Cessation; Length of Stay

ÖZET

Hastaneye yatırılan COVID-19 hastalarının sigara içme ve bırakma davranışları

Amaç: COVID-19 ile sigara içiciliği arasındaki ilişki tartışmalıdır. Biz bu çalışmada sigara ile hastane yatış süresi arasındaki ilişkiyi saptamayı ve COVID-19 hastalığı sonrası sigara içme alışkanlıklarının nasıl değiştiğini göstermeyi amaçladık.

Yöntem: Bu prospektif kohort çalışması, 01.10.2020-30.11.2020 tarihleri arasında bir üniversite hastanesinin pandemi servisinde yatan hastalarda gerçekleştirildi. Sosyodemografik değişkenler ve sigara içme alışkanlıkları yüz yüze görüşmelerle değerlendirildi. Hala sigara içen bireyler, taburculuktan altı ay sonra telefon ile arandı ve sigara içme alışkanlıkları tekrar değerlendirildi.

Bulgular: Çalışmaya ortalama yaşları 63.0±15.0 olan toplam 373 hasta dahil edildi ve bunlardan 175'i (%46,9) kadındı. Katılımcıların 192'si (%51,5) hiç sigara içmemiş, 148'i (%39,7) sigarayı bırakmış ve 33'ü (%8,8) hala sigara içiyordu. Sigara içenlerin, hiç sigara içmeyenlerin ve sigarayı bırakanların hastanede kalma süreleri istatistiksel olarak farklı değildi. Sigara içenler, bırakanlar ve hiç sigara içmeyenler arasında kötüleşme durumu açısından istatistiksel olarak anlamlı bir fark bulunmadı. Toplam 33 mevcut sigara içicisinden 10'u (%33,3) sigarayı bıraktı ve tekrar başlamadı, 13'ü (%43,3) sigarayı bıraktı ancak tekrar başladı ve 7'si (%23,3) takipte sigara içmeyi bırakmadı.

Sonuç: Çalışmamızda, sigaranın COVID-19 hastalığının seyrini ve hastanede kalma süresini etkilemediği gözlemlendi. Ayrıca, COVID-19 geçmişi, sigara içme alışkanlıklarını etkileyebilir ve sigara bırakmaya yol açabilir.

Anahtar kelimeler: COVİD-19; Sigara; Sigara Bıraktırma; Yatış Süresi

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INTRODUCTION

COVID-19 is a broad clinical picture caused by the SARS-Cov-2 virus, which can range from asymptomatic infection, upper respiratory tract infection, viral pneumonia, respiratory failure, acute respiratory distress syndrome and death [1,2]. The first case was reported from Wuhan province of China on December 31, 2019, and the epidemic quickly turned into a pandemic [3]. Although information about the factors determining the prognosis of the disease is limited, it is thought that the use of tobacco and tobacco products negatively affects the course of COVID-19 disease [4]. It is thought to cause this because it has negative effects on lung health and the immune system, is associated with many respiratory diseases, and makes the body more susceptible to infectious diseases. It has been determined that COVID-19 patients who smoke have more severe symptoms and higher rates of intensive care admission than patients who have never smoked [5,6].

Smoking is still one of the leading causes of preventable health problems in Turkey, as in the world. According to 2019 data, 28% of the population in Turkey, 41.3% of men and 14.9% of women use tobacco [7]. Mortality and morbidity caused by smoking increase not only for the user, but also for the passive smoker who is exposed to environmental tobacco smoke even though he does not use it [8]. 70% of tobacco users state that they want to quit, but only one third try to quit. Professional help is often not sought when quitting smoking and relapses are common. Even when help is received, the quit rate may be low, but it is known that professional help increases the success of quitting smoking [9].

In this study, our aim was to determine the association between smoking and hospitalization duration and to demonstrate how smoking habits change following COVID-19 disease.

MATERIALS and METHODS

Study Setting and Sampling

This prospective cohort study conducted at University Hospital. The research population is the patients hospitalized in group 1 and group 2 pandemic wards at the hospital. The sample of the research is individuals aged 18 and over who were hospitalized in Group 1 and Group 2 pandemic services between 01.10.2020-30.11.2020. Group 1 consists of patients with no or less than 50% lung involvement and oxygen saturation above 93% in room air, and group 2 consists of patients with lung involvement greater than 50% and oxygen saturation below 93% in room air. Intensive care patients and patients with diseases or disabilities that would prevent compliance with the study method (such as those with psychiatric diseases that would disrupt the assessment of reality, dementia patients) were excluded. Of the 442 patients hospitalized in these wards between the specified dates, 373 (84.3%) were included in the study, and 69 patients were excluded from the study because they did not meet the specified criteria.

Variables

For non-smokers: Socio demographic variables, duration of hospitalization, transfer status to higher or lower level of care.

For former smoker: Addition to non-smokers; participation history of any smoking cessation program, age of starting to smoke, total cigarette smoking (pack/year).

For current smokers: Addition to former smokers; level of nicotine addiction measured by the Fagerström Test for Nicotine Dependency scale (FTND), level of concern for smoking in relation with COVID-19 (scored from 1 to 10) and smoking status 6 months after discharge [10].

Application

All participants were viewed by face to face in pandemic wards. All preventive measures to prevent contamination had been taken by the researchers. First part of data form was completed at this stage.

Patients who stated that they have been smoking were contacted by phone after 6 months of discharge. Questions were asked about smoking cessation status after discharge, participation in smoking cessation programs, the relationship between the level of anxiety about smoking and COVID-19, and the effect of the pandemic on the amount of smoking.

Statistical Analysis

Descriptive data consisting of frequency and percentage for categorical variables, mean and standard deviation for continuous variables were calculated and presented. The relationships between variables were analyzed with tests selected in accordance with the variable characteristics. In cases where the number of samples is larger than 30, the requirement for normal distribution in parametric tests is ignored based on the central limit theorem [11]. Test constants absolute p values are reported for all analyses. $P<0.05$ was accepted as the general statistical significance limit.

Ethical Approval

Approval was received from Çanakkale Onsekiz Mart University clinical research ethics committee with the decision numbered 12-09 dated 23/09/2020. Approval of Ministry of Health for scientific research studies on COVID-19 was received on 07.08.2020. Patients participating in the study were given verbal and written information about the study and their consent was obtained.

RESULTS

Total of 373 patients were included in the study and 175 (%46.9) were female. The average age was calculated as 63.0±15.0. The sociodemographic data of the participants with details are given in Table 1.

Of the participants, 192 (51.5%) had never smoked, 148 (39.7%) had quit smoking, and 33 (8.8%) were still smokers. There was a significant difference observed between smoking status and the mean age of the participants ($F=5.976$; $p=0.003$). Post-hoc analysis

		Number of case (n)	Percentage (%)
Gender	Female	175	46.9
	Male	198	53.1
Living place	Rural	79	21.2
	Urban	294	78.8
Marital status	Married	286	76.7
	Single	25	6.7
	Widowed	62	16.6
Educational status	Illiterate	37	9.9
	Primary school graduate	190	50.9
	Secondary school graduate	31	8.3
	High school graduate	61	16.4
	College/University	54	14.5
Economic status	Low	104	27.9
	Mediocre	252	67.6
	High	17	4.6

Table 1. Sociodemographic data of the participants

revealed no significant difference in the mean ages between those who had never smoked and those who had quit smoking, but the mean age of these two groups was significantly higher compared to smokers.

The average amount of cigarettes smoked by ex-smokers was calculated as 27.18±21.28 [range 1 - 100] packs/year, and among current smokers was 40.76±31.37 [range 2 - 140]. 5 out of 148 ex-smokers (3.3%) stated that they participated in a smoking cessation program. Of these, 1 received psychological support, 2 received nicotine replacement therapy, and 2 received pharmacological treatment. 5 out of 33 current smokers (15.1%) stated that they participated in a smoking cessation program. Of these, 2 received psychological support, 2 received nicotine replacement therapy, and 1 received pharmacological treatment. A statistically significant difference was observed between ex-smokers and current smokers in terms of participation in the smoking cessation program (X^2=8.205; p=0.042). There was no significant difference in attempting to quit smoking between genders (X^2=0.383; p=0.536).

204 (54.6%) of the patients were hospitalized in group 1 and 169 (45.3%) were in group 2 pandemic wards. The average length of hospitalization was 11.87±10.30 [range 2 - 130] days. Length of hospitalization of smokers, never-smokers and quitters were not different (KW X^2=2.339; p=0.311). A significant positive correlation was detected between length of hospitalization and age (r=0.156; p=0.003). A significant negative correlation was detected between length of hospitalization and education level and economic level (r=-0.153; p=0.003, r=-0.146; p=0.005, respectively). No significant correlation was found between the amount of smoking in packs/year and the length of hospitalization (r=0.028; p=0.706). No significant correlation was found between FTND score and length of hospitalization (r=0.126; p=0.483).

Among the participants, 300 patients (80.4%) were discharged to home from the ward they were hospitalized, 8 patients (2.1%) were transferred from Group 1 to Group 2 wards, 31 patients (8.3%) were transferred to intensive care. 34 patients (9.1%) died. Among the deceased, 16 (47.0%) had never smoked, 16 (47.0%) had quit smoking, and 2 (5.9%) were current smokers. The rate of smokers and ex-smokers was 48.5%, and a worsening clinical course was observed in 20.4% of this group. There was no statistically significant difference in terms of worsening status between smokers, ex-smokers and never smokers (X^2=3.798; p=0.704). Deterioration data according to smoking status are given in Table 2.

	Never smoker	Ex-smoker	Current smoker
No change	156 (%81.3)	118 (%79.7)	26 (%78.8)
Transferred from group 1 to group 2	4 (%2.1)	2 (%1.4)	2 (%6.1)
Transferred to intensive care unit	16 (%8.3)	12 (%8.1)	3 (%9.1)
Deceased	16 (%8.3)	16 (%10.8)	2 (%6.1)

Table 2. Change in hospitalization conditions according to smoking status

There was a smoker at home for 116 (31.0%) participants. Of these 89 (76.7%) smoked outside the house, and 27 (23.3%) smoked inside the house. There was no statistically significant difference in terms of deterioration between those who had a smoker at home and those who did not (X^2=7.286; p=0.063).

After discharge, 1 participant (3.3%) reported receiving psychological support and 29 (96.7%) reported that they did not participate in any program. The average daily amount of cigarettes smoked by current smokers was 19.45±11.90 [range 2 - 50]. The amount of cigarettes smoked by men was significantly higher than by women (t=5.225; p=0.029). 24 (72.7%) of current smokers stated that they had tried to quit smoking before.

Six months after the first interview, 30 of 33 smoker patients were contacted by phone. Of the 3 patients excluded, 2 were died and 1 was still in intensive care unit. According to the statements of interviewed patients, 10 (33.3%) quit smoking and did not start again, 13 (43.3%) quit smoking but started again, and 7 (23.3%) did not quit smoking. When the FTND score averages of these 3 groups were compared, no statistically significant difference was detected (KW X^2=1.364; p=0.506).

Level of concern for smoking in relation with COVID-19 after discharge; The average score of those who quit smoking and did not start again was 8.70±0.65 [range 5 - 10], of those who quit smoking and started again was 4.85±0.45 [range 2 - 7], of those who did not quit smoking was 3.14±0.76 [range 1 - 6] and the difference between them was statistically significant (KW X^2=14.92; p=0.001).

When the change in the number of cigarettes smoked after discharge was questioned, it was found that 17 people (85.0%) decreased the number of cigarettes they smoked and 3 people (15.0%) increased the number of cigarettes they smoked. There was no statistically significant difference between the two groups in terms of FTND score averages (t=0.091; p=0.767). The mean pre-discharge anxiety score of people who stated that they had reduced their smoking use was significantly higher than those who stated that they had increased their smoking (t=4.895; p=0.040). The average post-discharge anxiety score of people who stated that they reduced their smoking was significantly higher than those who stated that they increased their smoking (t=5.709; p=0.028).

DISCUSSION

Smoking is one of the biggest causes of preventable diseases. It is thought that smoking affects the course of lung diseases by triggering local and systemic inflammation, changing the genetic structure of the lung tissue, and disrupting the normal function of the respiratory tract epithelium [5,6] One of the diseases that smoking may negatively affect is COVID-19. The fight against tobacco continues under pandemic conditions. In order to increase the success of quitting smoking, it may be beneficial to investigate the factors affecting patients' attitudes and the effects of smoking on the course of COVID-19 disease.

373 COVID-19 patients over the age of 18 hospitalized in pandemic wards were included in the study. The average hospital stay of the patients was 11.9 days. There was a positive correlation between length of stay and age, and a negative correlation with education level and perception of income level. In a meta-analysis that included a total of 11 590 COVID-19 patients, it was determined that 6.3% of the participants were smokers or had quit smoking, and 29.8% of these patients had a worsening clinical course, significantly more than non-smokers [12]. In this study, the rate of smokers or ex-smokers was 48.5%, and a worsening of the clinical course was observed in 20.4% of this group, but there was no significant difference with the non-smoking group.

In a study conducted in Lebanon on 743 patients hospitalized with COVID-19, the effect of smoking on the course of the disease and mortality was examined. Patients who did not need oxygen were classified as having mild COVID-19 and, unlike this study, they were excluded from the study, oxygen saturation was lower than 93% and/or or patients with a respiratory rate of more than 30 breaths per minute were classified as severe, and patients requiring mechanical ventilation, organ failure, or in shock were classified as critical COVID-19. The average age of the patients was 49.7 years, which was lower than in this study. 62.3% of the patients were male, and according to this study, the proportion of men was higher. The length of stay was similarly 11.3 days. The mortality rate of the patients was 17.4%, which was higher than in this study. The smoking rate of deceased patients was 60.5%, which was significantly higher than the rate in our study. In our study, 47.0% of the deceased patients had quit smoking, 5.9% were smokers, and there was

no significant difference in smoking status between those who died and those who were discharged. In the study, the length of stay of smokers was longer than that of non-smokers, but in our study, there was no significant difference between smoking status and length of stay. Similar to our study, there was no relationship between gender and length of stay and deterioration. The reason why the smoking rate in the study is higher than in our study may be that the smoking rate of the Lebanese population is higher than in Turkey (38%-28%) and the average age in the study is lower, and the reason for the higher death rates compared to our study is that patients in need of intensive care are also included in the study [13].

In a study conducted on 767 people hospitalized in Malatya due to COVID-19, it was found that gender had no effect on the length of stay, but was correlated with age, similar to the results of our study [14]. In a thesis study conducted on 107 patients in Düzce, it was shown that the average length of stay of COVID-19 patients was 7.6 days, the average age was 56.5, and there was no relationship between length of stay and age and gender. The reason why the hospitalization period was shorter than in our study may be that the average age of the patients was younger [15].

51.5% of the participants had never smoked, 39.7% had quit smoking, and 8.8% were smokers. According to 2019 TÜİK data, 28% of the population in Turkey smokes, 14.2% have quit and 54.5% have never smoked [7]. In our study, the average age of participants who quit smoking and never smoked was higher than that of current smokers. It was thought that the significantly low number of smokers, but the high number of quitters might be due to the high average age.

The average amount of smoking in packs/year was calculated as 29.7, and it was higher in current smokers than in those who quit. The average daily amount of cigarettes smoked by current smokers was 40.8 packs/year and 19.5 cigarettes. 72.2% of current smokers stated that they had tried to quit smoking before. 3.3% of ex-smokers and 15.1% of current smokers stated that they had previously received a smoking cessation program (psychological support, NRT, pharmacological treatment), and the difference between them was significant. In a study conducted on 320 patients who applied to the smoking cessation clinic in Ağrı, similar to our study, the average age of starting smoking was 18 and the majority were primary school graduates, but the amount of smoking in packs/year was lower (23 packs/year). 69.3% of the participants had tried to quit smoking before, and this rate was similar to that in our study. Unlike our study, the FTND score of those who quit smoking was lower than those who did not quit [16].

Although there is no study on the relationship between passive smoking and COVID-19 disease, it is thought that cigarette smoke exposure increases the risk of severe COVID-19 by increasing the production of angiotensin-converting enzyme-2 (ACE-2) in the lung tissue. [17]. According to the Global Adult Tobacco Survey 2012 data, exposure to passive smoking at home was determined to be 38.3% in Turkey, while in our study, 31% of the participants had a smoker at home [18]. In our study, no relationship was found between passive smoking, smoking inside or outside the house, proximity of the smoker, length of stay, and worsening of the patient's condition.

In a study conducted in Ankara, smoking cessation status was examined in 111 patients with acute coronary syndrome in the six-month period after discharge [19]. Unlike our study, the average age of the patients was 53, lower than in our study, and 94.6% were male. Similar to our study, most of the patients lived in urban areas, were primary school graduates, and had low-middle income perception, and these factors had no effect on quitting smoking. Those who quit smoking and started smoking again were mostly single or widowed. In our study, there was no relationship between marital status and smoking cessation. In the study, 30.4% of the patients quit smoking in the sixth month after discharge. Similarly, in our study, 33.3% quit smoking and did not start again, and there was no relationship between FTND score and smoking cessation. Again, similar to our study, it was found that passive smoking, smoking inside or outside the house, or the proximity of the smoker did not affect quitting smoking. In a thesis study conducted in Aydın, the smoking cessation success of 126 patients followed in a smoking cessation clinic was examined at the end of six months. Similar to our study, no relationship was found between sociodemographic data and smoking cessation, but differently, it was observed that the quitting rate of those with high addiction levels was lower [20].

It is thought that the COVID-19 pandemic may directly or indirectly affect smoking habits. While the amount of cigarettes used may decrease due to concern about getting sick and complications, the amount used may increase due to factors such as the quarantine period, economic concerns, and increased stress [21]. In a study conducted with 5896 participants from seventeen Middle Eastern and North African countries, it was shown that there was no change in smoking behavior during the pandemic period [22]. In a representative study conducted in the USA, it was observed that 40% of smokers increased their consumption amount during the pandemic period [23]. In our study, in the first interview, 30.3% of the participants stated that they reduced the number of cigarettes they smoked during the pandemic, and 12.1% stated that they increased it. When questioned about the change in the amount of cigarettes smoked after discharge, 85.0% of the participants stated that they reduced the amount of cigarettes they smoked, and 15.0% stated that they increased it. The pre- and post-discharge anxiety scores of people who reported reducing their smoking were higher than those who increased their smoking. The reason for the majority of those who reduced their smoking in our study may

be that the sample was hospitalized patients due to COVID-19. It can be assumed that health anxiety in these patients will be higher than in the general population, and therefore they will be more willing to quit or reduce smoking.

Limitations of our study; The reasons were the low number of active smokers, the exclusion of intensive care patients from the study, and the lack of sufficient studies on the subject. The study can be improved in the next step by determining the parameters that can be used to evaluate disease severity and by studying on a larger sample.

CONCLUSION

In our study, it was observed that smoking or passive smoking did not affect the course of COVID-19 disease and length of stay. There are studies with conflicting results regarding the relationship between smoking, passive smoking and COVID-19. Hospitalization or home isolation during the pandemic should be seen as an opportunity to quit smoking, and all physicians and healthcare professionals should guide patients to quit smoking. For inpatients, it may be effective to first plan short motivational interviews by the physician who follows them in the ward. Informational documents or brochures about the harms of smoking can be prepared and given to inpatients. Especially patients with high addiction levels and withdrawal symptoms can be evaluated for pharmacological treatment. The success of patients in quitting smoking can be increased by referring them to smoking cessation clinics or family physicians in the city after discharge.

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RESEARCH ARTICLE

Effect of vitamin-D and other factors on the presence and severity of urinary incontinence and overactive bladder in elderly individuals

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ABSTRACT

Objective: This study aimed to investigate the effect of serum vitamin D levels on urinary incontinence and overactive bladder in elderly individuals.

Methods: The study included 106 elderly individuals who had their serum vitamin D levels measured in the past year. Sociodemographic characteristics, habits, medical histories, medications used, height, and weight data were collected. The ICIQ-UI short form and Overactive Bladder-V8 form were administered. Participants were grouped based on their vitamin D levels.

Results: Among participants, 17.9% had severe vitamin D deficiency, 28.3% had vitamin D deficiency, 18.9% had vitamin D insufficiency, and 34.9% had normal vitamin D levels. No significant association was found between vitamin D levels and the presence of urinary incontinence and overactive bladder. When participants were grouped by vitamin D levels, there was no significant difference in the presence of urinary incontinence and overactive bladder among the groups. However, a significant difference was found in the severity of overactive bladder. Individuals with normal vitamin D levels had significantly higher rates of urinary incontinence and overactive bladder compared to those with lower levels.

Conclusion: Urinary incontinence increases with age and may be associated with aging-related comorbidities. Although reports in the literature suggest a relationship between vitamin D deficiency and urinary incontinence and overactive bladder, this relationship was not confirmed in our study. This discrepancy may be due to differences in the characteristics of the populations studied in the literature.

Keywords: Vitamin D, urinary incontinence, overactive bladder

ÖZET

Vitamin D ve diğer faktörlerin yaşlı bireylerde üriner inkontinans ve aşırı aktif mesane varlığı ve şiddetine etkisi

Amaç: Bu çalışmada, yaşlı bireylerde serum vitamin D düzeyinin üriner inkontinans (UI) ve aşırı aktif mesane (OAB) üzerindeki etkisi araştırılmıştır.

Yöntem: Çalışmaya, son bir yıl içinde serum vitamin D düzeyi ölçülmüş 106 yaşlı birey dahil edilmiştir. Katılımcıların sosyodemografik özellikleri, alışkanlıkları, tıbbi geçmişleri, kullandıkları ilaçlar, boy ve vücut ağırlığı verileri toplanmış, ICIQ-UI kısa formu ve Aşırı Aktif Mesane - V8 formu uygulanmıştır. Katılımcılar vitamin D düzeylerine göre gruplandırılmıştır.

Bulgular: Katılımcıların %17,9'u ciddi D vitamini eksikliği, %28,3'ü D vitamini eksikliği, %18,9'u D vitamini yetersizliği gösterirken, %34,9'unun vitamin D düzeyi normaldi. Vitamin D düzeyi ile üriner inkontinans ve aşırı aktif mesane varlığı arasında anlamlı bir ilişki bulunmamıştır. Katılımcılar vitamin D düzeylerine göre gruplandırıldığında, gruplar üriner inkontinans ve aşırı aktif mesane varlığı açısından anlamlı bir farklılık göstermedi. Ancak, aşırı aktif mesane şiddeti açısından anlamlı bir farklılık tespit edildi. Vitamin D düzeyi normal olan bireylerde üriner inkontinans ve aşırı aktif mesane görülme oranı, düşük düzeyde olanlara göre anlamlı şekilde yüksekti.

Sonuç: Üriner inkontinans yaşla birlikte artmaktadır ve yaşlanma ile artan komorbid hastalıklarla ilişkilendirilebilir. Vitamin D eksikliği ile üriner inkontinans ve aşırı aktif mesane arasında ilişkiye dair literatürde raporlar bulunmasına rağmen, bu ilişki çalışmamızda doğrulanmamıştır. Bu fark, literatürdeki çalışmalarda incelenen popülasyonların farklı özelliklere sahip olmasından kaynaklanabilir.

Anahtar kelimeler: Vitamin D, üriner inkontinans, aşırı aktif mesane

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INTRODUCTION

Due to the increase in average life expectancy both in Turkey and worldwide, the elderly population is steadily growing. This steady growth has led to an increased prevalence of chronic diseases, including urinary incontinence (UI) and lower urinary tract dysfunctions, which are more commonly observed due to physiological changes associated with aging. UI is not merely a consequence of aging; it is a pathological condition that affects individuals across all age groups[1]. While urinary incontinence may not directly cause mortality, it can lead to decreased quality of life, psychological stress, depression, and social isolation [2].

Urinary incontinence is defined as any involuntary urine leakage regardless of volume, whereas overactive bladder (OAB) is characterized by increased urinary frequency, urgency, and nocturia, with or without UI [3]. OAB and UI can have overlapping symptoms, and while OAB may or may not include UI, it shares similar negative impacts on quality of life. Temporary or permanent UI can develop for various reasons.

In Europe, the prevalence of OAB is observed to be 10.8% in men and 12.8% in women. Interestingly, while there is no significant gender difference in the overall frequency of OAB, urgency incontinence is reported to be more common in women. The prevalence of OAB in women with UI was found to be 6.3%, while in men it was 3.1% [4]. In Turkey, however, the focus has been predominantly on women, with studies reporting UI prevalence as high as 44.8% [5].

Another common condition in the elderly is vitamin D deficiency. This deficiency is particularly concerning given the role of vitamin D in various bodily functions beyond bone health, including muscle function. The reason for the high prevalence of vitamin D deficiency is thought to be the limited number of foods containing vitamin D, with only a small portion (10-20%) being obtainable through diet, and minimal absorption from the gastrointestinal tract. Furthermore, the majority (80-90%) of vitamin D is synthesized in the skin under the influence of UVB radiation [6].

It is estimated that nearly one billion people worldwide have vitamin D deficiency. Vitamin D levels vary widely across different populations and geographical regions. Studies have shown that vitamin D levels vary between different countries and even within the same country. Numerous studies conducted in Turkey have confirmed that vitamin D deficiency is widespread [7].

In addition to its effects on electrolyte balance and skeletal muscles, vitamin D is known to have an effect on smooth muscles [8]. Recent research has also suggested that vitamin D plays a critical role in the function of pelvic floor muscles, which are essential for maintaining urinary continence [9]. The NHANES study showed that individuals with serum 25(OH) Vitamin D levels below 30 ng/ml had more frequent pelvic floor weakness-related conditions [10]. Moreover, the presence of vitamin D receptors in the prostate and bladder further supports the hypothesis that vitamin D may influence lower urinary tract function. Additionally, the presence of Vitamin D receptors in the prostate and bladder is known, and vitamin D receptor agonists are believed to have anti-inflammatory and antiproliferative properties [11].

In light of all this data, the question arises as to whether serum 25(OH) vitamin D deficiency affects UI and OAB. Several studies have suggested a potential link between vitamin D levels and the severity of UI and OAB symptoms [12]. Moreover, some cases have been reported where UI symptoms improved following vitamin D supplementation [13]. It is quite remarkable to see that a condition causing social distress as UI may be associated with a easily treatable condition of Vitamin D deficiency.

This study aimed to investigate the relationship between vitamin D deficiency and UI and OAB. By understanding this relationship, we hope to contribute to the growing body of evidence on the role of vitamin D in managing UI and OAB, particularly in elderly populations.

MATERIALS and METHODS

This observational study included individuals aged 65 years and older. Participants were selected based on their serum 25(OH) Vitamin D levels measured at Çanakkale Onsekiz Mart University Hospital between June 1, 2016, and May 31, 2017. The study was approved by local ethics committee.

Records of Çanakkale Onsekiz Mart University Hospital were scanned, and patients aged 65 and over who had their serum 25(OH) Vitamin D levels measured within the last year were identified. Participants were then contacted via telephone, using the contact information available in the hospital's patient registry. Patients were informed about the study's purpose and methodology. Inclusion criteria were carefully applied, ensuring the selection of a homogenous study group. Participants who met the inclusion criteria and agreed to participate were scheduled for face-to-face interviews at the Family Medicine Polyclinics. Exclusion criteria were strictly enforced to minimize potential confounding factors. Excluded individuals included those on diuretics, those who had undergone significant urological or gynecological surgeries, and those with benign prostatic hyperplasia or significant hearing impairments. A standardized questionnaire was administered, covering sociodemographic information, medical history, and lifestyle factors relevant to the study's objectives.

The initial pool of 1,145 patients was narrowed down due to various reasons, including outdated contact information, failure to reach participants after multiple attempts, and patient refusal to participate. Among the patients who could be reached, 105 individuals refused to participate in the study, 519 individuals were using diuretic drugs, 34 individuals had a known diagnosis of benign prostatic hyperplasia, 14 individuals could not be communicated with directly due to hearing problems, 56 individuals had a history of genitourinary surgery, 43 individuals had a history of dementia or psychiatric illness that could affect their compliance with the study, 17 individuals had deceased, 13 individuals did not attend their appointment, and 1 individual did not speak Turkish, thus they were excluded from the study.

Collected data included comprehensive sociodemographic details, medical histories, and physical measurements such as height and weight. The presence of drugs that could influence UI or OAB (such as ACE inhibitors, antimuscarinics, antipsychotics, calcium channel blockers, cholinesterase inhibitors, estrogen, GABAergic agents, narcotic analgesics, sedative-hypnotics, tricyclic antidepressants, thiazolidinediones, α-adrenergic blockers, α-adrenergic agonists) was particularly noted. The questionnaire's reliability and validity had been previously confirmed in similar population groups.

To assess participants' UI an OAB status, the ICIQ-UI short form and AAM-V8 were used. These validated instruments provided a reliable measure of UI and OAB severity and impact on daily life. **The International Consultation on Incontinence Questionnaire Short Form (ICIQ-UI)** is one of the

scales developed to measure the impact of urinary incontinence symptoms on quality of life and the effectiveness of treatment. The Turkish version of the ICIQ-UI was validated by Çetinel et al. [14]. This short and simple questionnaire facilitates the screening of incontinence for physicians in both primary and secondary healthcare settings, summarizes the level, impact, and perceived cause of symptoms in a short but comprehensive manner. The ICIQ-UI assesses the frequency, severity, and impact of UI, with a scoring system ranging from 0 to 21. Although a score value for diagnosis is not defined, as patients' complaints increase, the obtained score increases.

The Overactive Bladder Questionnaire (OAB-V8) was developed based on the OAB-q (overactive bladder questionnaire) form by Coyne et al. in 2002 for the OAB syndrome [15]. The OAB-V8 includes 8 items scored from 0 ("not bothered at all") to 5 ("bothered a very great deal"), with an additional 2 points for male participants. Individuals scoring ≥8 points are considered to be at risk for OAB. The questionnaire was translated into 14 languages and tested for validity and reliability by Acquadro et al. in 2006 [16]. The validity and reliability study of the questionnaire in Turkish was conducted by Tarcan et al. [17].

Statistical Analysis: Participants were grouped according to their serum 25(OH) Vitamin D levels as follows: sufficient (>30 ng/ml), insufficient (20-30 ng/ml), deficient (<20 ng/ml), and severely deficient (<10 ng/ml) [18]. After the data was transferred to digital format, the conformity of continuous variables to normal distribution was checked by histograms. Appropriate statistical tests were applied to compare groups based on vitamin D levels, UI, and OAB severity Test constants and p-values were reported for all tests. A significance level of $p<0.05$ was accepted. The effect size of the correlation was interpreted based on the magnitude of the correlation coefficient (r) and categorized as follows: A correlation coefficient between 0.10 and 0.29 indicates a small effect, a coefficient between 0.30 and 0.49 indicates a medium effect, and a coefficient of 0.50 or higher indicates a large effect.

RESULTS

The study included 106 participants, comprising 80 (75.5%) females and 26 (24.5%) males. The mean age of the participants was 71.7 ± 5.6 [65-88] years, with no significant difference between genders (U=922.5; p=0.387).

Of the participants, 5 (4.7%) were illiterate, 59 (55.6%) had completed primary school, 9 (8.5%) had completed middle school, 18 (17.0%) had completed high school, and 15 (14.2%) had completed university education. Regarding their current employment status, 54 (50.9%) were housewives, one (0.9%) was a civil servant, one (0.9%) was a laborer, and 50 (47.3%) were retired. Among the participants, 66 (62.3%) were married, 5 (4.7%) were single or divorced, and 35 (33%) were widowed. Twenty-two participants (20.8%) were living alone.

Regarding body weight status, one participant (0.9%) was underweight, 31 (29.2%) had normal weight, 46 (43.5%) were overweight, 27 (25.5%) were obese, and one (0.9%) was morbidly obese.

Among female participants, 8 (10.0%) had never been pregnant, 3 (3.8%) had been pregnant once, and 69 (86.2%) had been pregnant at least twice. Regarding their childbirth history, 8 (10.0%) were nulliparous, 6 (7.5%) were primiparous, and 66 (82.5%) were multiparous. The mean number of pregnancies among female participants was 3.4 ± 1.8 [0-9], and the mean number of childbirths was 2.5 ± 1.3 [0-6]. The mean age of menopause among participants was found to be 46.9 ± 6.6 years. Nine (11.2%) participants reported receiving hormone replacement therapy during the postmenopausal period.

Regarding smoking habits, 75 (70.8%) participants had never smoked, 22 (20.8%) had quit smoking after a period of use, and 9 (8.5%) were still smoking. Alcohol consumption was reported by 14 (13.2%) participants, all of whom consumed alcohol in social settings, and none of the participants reported regular alcohol consumption. The mean daily consumption of tea, and coffee among participants was 2.4 ± 2.5 [0-12] cups, and 0.5 ± 0.8 [0-5] cups respectively.

Ninety-eight participants (92.5%) had a history of various chronic diseases. The most commonly observed comorbidities were hypertension in 56 (52.8%) individuals, musculoskeletal disorders in 50 (47.2%), diabetes mellitus in 26 (24.5%), and hypothyroidism in 25 (23.6%).

Furthermore, 102 participants (96.2%) reported regular medication use. The mean number of medications used among those who reported regular medication use was 3.5 ± 2.1 [1-11]. Among the group using regular medication, it was found that 39 (61.8%) individuals were using medications from categories that might increase the risk of UI.

Participants had a mean serum 25(OH) Vitamin D level of 25.2 ± 15.6 [3-70] ng/ml, with no significant difference between genders (U=925.0; p=0.398). When participants were classified according to their serum 25(OH) Vitamin D levels, 19 (17.9%) had severe deficiency, 30 (28.3%) had deficiency, 20 (18.9%) had insufficiency, and 37 (34.9%) had normal serum 25(OH) vitamin D levels. When the participants' serum 25(OH) vitamin D levels were examined in two subgroups as normal and lower than normal, 37 individuals (34.9%) had normal levels, while 69 individuals (65.1%) had levels lower than normal.

Among the participants, 93 had a mean serum calcium level of 9.6 ± 0.6 [7.7 - 12.7] mg/dl.

According to the ICIQ-UI short form, 57 (53.8%) individuals had no UI. Among the 49 (46.2%) participants with UI, the frequency of enuresis was as follows: 26 (24.5%) experienced once a week or less, 12 (11.3%) 2 or 3 times a week, 4 (3.8%) once a day, and 7 (6.6%) several times a day. Additionally, 37 (34.5%) participants experienced enuresis before reaching the toilet, 21 (19.8%) when coughing or sneezing, 5 (4.7%) while asleep, 11 (10.4%) with movement, 2 (1.9%) after urination, and 5 (4.7%) had unexplained enuresis. No participants reported continuous enuresis.

The rate of UI among females (53.8%) was significantly higher than that among males (23.1%) (X^2=7.427; p=0.006). The distribution of variables among participants with UI is presented in Table 1.

The participants' OAB-V8 total score was calculated as an average of 8.4 ± 4.9 [0 - 25]. According to these scores, 50 (47.2%) individuals had OAB syndrome. The distribution of variables for those with OAB syndrome is presented in Table 2. When evaluating only patients with OAB, the severity score of postmenopausal hormone replacement therapy users (9.4 ± 1.5) was significantly lower than those who did not use it (13.3 ± 4.7) (U=52.0; p=0.032).

Participant characteristics and the severity of UI and OAB scores are presented in Table 3. A significant positive correlation with small effect size was observed between OAB severity and age (tau_b=0.220; p=0.002). A positive correlation with small effect size was also found between OAB severity and the number of childbirths (tau_b=0.176; p=0.041).

Participant Characteristics	Urinary Incontinence Present	No Urinary Incontinence	Statistics
Gender (Female)	43 (87.8%)	37 (64.9%)	**X^2=7.427; p=0.006**
Age	72.5 ± 6.2	71.0 ± 5.1	t=1.322; p=0.189
Smoking	11 (22.4%)	20 (35.1%)	X^2=2.034; p=0.154
Alcohol Use	4 (8.2%)	10 (17.5%)	X^2=2.023; p=0.155
Postmenopausal HRT Use	6 (14.0%)	3 (8.1%)	X^2=0.681; p=0.409
Hypertension	29 (59.2%)	27 (47.4%)	X^2=1.476; p=0.224
Diabetes	12 (24.5%)	14 (24.6%)	X^2<0.001; p=0.993
Hypothyroidism	12 (24.5%)	13 (22.8%)	X^2=0.041; p=0.839
Musculoskeletal Disorders	23 (46.9%)	28 (49.1%)	X^2=0.050; p=0.822
Use of Urinary Incontinence Facilitating Drugs	20 (40.8%)	19 (35.8%)	X^2=0.266; p=0.606

HRT: hormon replacement therapy

Table 1. Presence of Urinary Incontinence According to Participant Characteristics

Urinary incontinence patients' serum 25(OH) Vitamin D levels (28.2±16.6 ng/ml) were not significantly different from those without complaints (22.6±14.4 ng/ml) (t=1.879; p=0.063). Of those with normal serum 25(OH) vitamin D levels, 23 (62.2%) experienced urinary incontinence, while among those with levels lower than normal, 26 (37.7%) experienced it (X^2=5.807; p=0.016).

The serum 25(OH) Vitamin D levels of patients with OAB (28.0±17.2 ng/ml) did not significantly differ from those without OAB (22.7±13.7 ng/ml) (t=1.786; p=0.077). Of those with normal serum 25(OH) vitamin D levels, 22 (59.5%) had an overactive bladder, while among those with levels lower than normal, 28 (40.6%) had it. The difference between the two groups was not significant (X^2=3.445; p=0.063).

Participants' UI and OAB statuses according to Vitamin D level groups are shown in Table 4. There was no significant difference in the rates of urinary incontinence or OAB among the groups when participants were classified based on their serum 25(OH) vitamin D levels (X^2=6.673; p=0.083, X^2=4.585; p=0.205, respectively).

OAB: Overactive Active Bladder	**OAB Present**	**OAB Absent**
Gender (Female)	38, 76.0%	42, 75.0%
Age	73.0±6.0	70.5±5.1
Smoking	17, 34.0%	14, 25.0%
Alcohol Use	7, 14.0%	7, 12.5%
Postmenopausal Hormone Replacement Therapy	7, 18.4%	2, 4.8%
Hypertension	32, 64.0%	24, 42.9%
Diabetes	9, 18.0%	17, 30.4%
Hypothyroidism	8, 16.0%	17, 30.4%
Musculoskeletal Diseases	26, 52.0%	25, 44.6%
Use of Incontinence Facilitating Drugs	23, 46.9%	16, 30.2%

Table 2. Presence of Overactive Active Bladder according to participant characteristics

Participant Characteristic	Urinary Incontinence Severity	OAB Severity
Age	tau_b=0.105; p=0.161	**tau_b=0.220; p=0.002**
BMI	tau_b=0.130; p=0.075	tau_b=0.106; p=0.068
Parity (Number of Pregnancies)	tau_b=0.087; p=0.324	tau_b=0.149; p=0.076
Number of Births	tau_b=0.142; p=0.118	**tau_b=0.176; p=0.041**
Age at Menopause	tau_b=0.043; p=0.609	tau_b=-0.027; p=0.735
Number of Medications	tau_b=0.115; p=0.147	tau_b=0.112; p=0.131
Tea Consumption	tau_b=-0.135; p=0.084	tau_b=-0.066; p=0.363
Coffee Consumption	tau_b=-0.047; p=0.581	tau_b=-0.111; p=0.162
OAB: Overactive Active Bladder		

Table 3. Variation and Relationships of Participant Characteristics with Urinary Incontinence Severity and OAB Severity Scores

Vitamin D Level Group	Total Participants	Participants with Urinary Incontinence	Participants with OAB
Normal	37 (35.0%)	23 (46.9%)	22 (44.0%)
Vitamin D Insufficiency	20 (18.8%)	6 (12.2%)	9 (18.0%)
Vitamin D Deficiency	30 (28.3%)	13 (26.5%)	10 (20.0%)
Severe Vitamin D Deficiency	19 (17.9%)	7 (14.3%)	9 (18.0%)
Total	106 (100.0%)	49 (100.0%)	50 (100.0%)
		X^2=6.673; p=0.083	X^2=4.585; p=0.205

Table 4. Urinary incontinence and Overactive Active Bladder statuses according to Vitamin D level groups

There was no significant correlation between participants' serum 25(OH) Vitamin D levels and UI severity scores (tau_b=0.099; p=0.174). However, there was a significant positive correlation with small effect size between OAB severity and serum 25(OH) Vitamin D levels (tau_b=0.148; p=0.030).

Urinary incontinence patients' calcium levels (9.7±0.8 ng/ml) did not significantly differ from those without UI (9.5±0.5 ng/ml) (t=1.368; p=0.175). Similarly, there was no significant difference in calcium levels between patients with OAB (9.6±0.8 ng/ml) and those without OAB (9.7±0.6 ng/ml) (t=0.736; p=0.463). There was no significant correlation between calcium levels and the severity of UI (tau_b=0.119; p=0.130) or OAB severity (tau_b= -0.065; p=0.373).

DISCUSSION

Urinary incontinence is a significant condition that affects the social life of individuals, particularly in the elderly where functional decline due to various reasons is more prevalent. The increasing prevalence of this condition, which adversely affects individuals physically, psychologically, and socially, necessitates the investigation of possible associated factors and the identification of preventable causes. In the elderly Vitamin D deficiency is commonly observed. Given its effects on the detrusor muscle of the bladder and the prostate gland, it is thought that UI and OAB may be more common in individuals with Vitamin D deficiency.

In our study, which aimed to evaluate the relationship between Vitamin D deficiency and UI in 106 elderly individuals, those with normal serum 25(OH) Vitamin D levels were found to have a significantly higher prevalence of UI compared to those with low levels. While no significant difference in the occurrence of OAB was observed among the participants based on serum 25(OH) Vitamin D level categories, there was a significant positive correlation between serum 25(OH) Vitamin D levels and OAB severity.

With increasing life expectancy and aging population, the prevalence of UI in the elderly is progressively rising due to

the increasing incidence of comorbidities and physiological changes associated with aging, such as pelvic floor muscle dysfunction and urinary system diseases. In our study, the prevalence of UI was found to be 46.2%. An epidemiological review by Hunskaar et al. observed UI prevalence ranging from 6% to 72% [19]. In the study conducted by Kılıç et al., urinary incontinence was detected in 49.7% of women and 28.6% of men [20]. In other studies conducted in Turkey, Çetinel et al. reported a UI prevalence of 35.7%, Koçak et al. reported 23.9%, and Ekin et al. reported 33.7% [21-23].

In a cross-sectional population-based survey by Irwin et al. it was found that 12.8% of women and 10.8% of men had OAB [4]. In our study, the prevalence of OAB was 47.2%, which is higher and predominantly observed in women. Zhu et al. conducted a review of 28 studies and similarly found that OAB is associated with age, consistent with our findings [24].

Tampakoudis et al. examined the urinary incontinence status between two groups of women, smokers and non-smokers, and found a higher incidence of UI in smokers [25]. Hannestead et al. reported a significantly higher prevalence of UI in active smokers and individuals who quit smoking [26]. The lack of association between smoking and UI in our study may be attributed to the inclusion of both genders and the lower prevalence of smoking among women in our country.

In a study by Tamanini et al., the most common comorbid pathologies and their prevalence rates in patients with UI or OAB were found to be similar to our study [27]. Öztürk et al. examined the UI status of women aged 35 and older and, similar to our study, demonstrated no association with diabetes and hypertension [28].

In a study conducted by Kaur et al. in India in 2017 among women aged 65 and older, the participants with UI had a mean vitamin D level of 11.2 ± 6.3 ng/ml, while in the control group it was found to be 14.6 ± 7.3 ng/ml, and a significant difference was observed between the groups [29]. Our study results are consistent with these findings. In our study, the vitamin D levels were determined to have a general average of 25.2 ± 15.6 ng/ml. It is well known that vitamin D is effective on muscle and bone physiology. The relationship between pelvic muscle function and vitamin D, which could affect the development of urinary incontinence, is frequently investigated. In women aged 50 and over, low vitamin D levels were found to be significantly associated with UI and at least one pelvic floor disorder [10].

In a study conducted by Kılıç et al. in 2016, it was found that UI was significantly higher in individuals with low vitamin D levels, diabetes, and high Ca levels, while OAB was significantly higher in individuals with low vitamin D levels and high serum Ca levels [20]. In our study, Ca levels and diabetes were not found to be associated with the presence of UI and OAB. When the participants in our study were classified into groups based on their serum 25(OH) Vitamin D levels as normal and low, it was found that the UI was significantly higher in the group with normal vitamin D levels compared to the group with low levels. Although an OAB was more commonly observed, the difference was not significant.

In a cohort study conducted by Vaughan et al., it was observed that out of 187 participants initially without UI, UI developed in 175 of them during follow-up. After adjusting for age, gender, and ethnic factors, a significant association was found between baseline vitamin D levels and UI [30].

Navaneethan et al. found in their prospective study among postmenopausal women that total pelvic floor dysfunction was significantly associated with Vitamin D levels and being in menopause for more than 5 years [9]. Isolated pelvic organ prolapse was also significantly associated with Vitamin D. Isolated stress UI, however, was found to be associated with obesity, sunlight exposure, and serum 25(OH) Vitamin D levels. In our study, since self-reported data were collected, the categorization of incontinence reported by participants may have been suboptimal, leading to the inability to identify similar relationships.

In a retrospective study conducted by Parker-Autrey et al., the relationship between vitamin D and pelvic floor dysfunction was investigated in women aged 18 and over. It was found that pelvic floor dysfunction was significantly higher in the group with low Vitamin D levels [31]. In a cohort study conducted by Dallosso et al., involving individuals over 40 years old, participants were queried about urinary symptoms and dietary habits annually for one year. It was observed that high Vitamin D intake significantly reduced the incidence of developing OAB [32].

In our study, we did not find a significant relationship between Vitamin D levels and UI measured by the ICIQ-UI short form or the presence of OAB measured by the OAB-V8 scale among participants aged 65 and above who presented to our hospital. However, we did find a significant association between Vitamin D levels and the severity of OAB measured by the OAB-V8 scale, where those with normal Vitamin D levels had significantly higher OAB severity compared to those with low levels.

The reasons for this discrepancy in results could be attributed to several factors. These include differences in the age groups of participants selected in different studies, the specific exclusion criteria applied in our study leading to a more specific group of participants, the use of different cutoff values for serum 25(OH) Vitamin D levels in classifying participants, and methodological differences in the evaluation of UI and OAB presence in studies (such as physical examination, urodynamic tests, different scales, etc.). Further research on this topic is warranted.

The relationship between vitamin D levels and various health outcomes remains controversial. This discrepancy may be due to limitations in study designs, such as inadequate dosing or baseline vitamin D levels [33]. The inconsistency in results may also stem from measuring different forms of vitamin D or using varying assay methods [34]. Despite extensive research, highly convincing evidence for a clear role of vitamin D does not exist for most outcomes [35]. Future studies should consider adjusting for long-term vitamin D supplementation, solar exposure, and other potential confounders.

This study has several limitations. Firstly, serum 25(OH) vitamin D levels were measured only once, without accounting for seasonal variations, duration of sun exposure, and dietary habits. As a result, the measured vitamin D levels may not fully reflect the participants' long-term vitamin D status. Additionally, the cross-sectional design of the study limits our ability to establish causality between vitamin D levels and health outcomes. The observed discrepancies between measured vitamin D levels and various health outcomes may also be attributed to the lack of measurement of different forms of vitamin D or the use of varying assay methods. Furthermore, the sample size in this study was limited, which may affect the generalizability of the findings. Specifically, the small number of male participants limits our ability to assess gender differences ef-

fectively, and this imbalance may have contributed to the lack of significant findings in gender comparisons.

In this study, participants aged 65 and above who had their serum 25(OH) vitamin D levels measured at our hospital in the past year were identified through hospital records and invited to participate. It is possible that those who agreed to participate and attended the interview were in better health, lived closer to the hospital, and were more health-conscious, potentially influencing the study results. Additionally, serum 25(OH) vitamin D measurements were not performed concurrently with the evaluation of UI. The limited number of participants, due to the strict inclusion and exclusion criteria, further restricted recruitment. Moreover, pelvic examination or urodynamic testing was not conducted, and the UI status was entirely based on self-reporting. These factors may have contributed to the possible suboptimal assessment of UI in this study.

There are very few studies in our country that investigate the effects of vitamin D on UI. The exclusion criteria in our study were carefully designed to minimize potential confounding factors. However, the results from studies investigating the relationship between vitamin D and UI, both in our country and internationally, remain contradictory. More controlled, prospective studies are needed to provide a clearer evaluation of this relationship and to confirm the findings.

Conclusion

According to the results of our study, there was no significant relationship between serum 25(OH) Vitamin D levels and the presence of UI and OAB. However, a significant positive correlation was found between the severity of OAB and serum 25(OH) Vitamin D levels. When participants were grouped according to their serum 25(OH) Vitamin D levels, no significant difference was observed in the presence of UI and OAB, but a significant difference was found in terms of the severity of OAB.

When participants were categorized based on their serum 25(OH) Vitamin D levels, it was observed that both UI and OAB were significantly more common in the group with normal Vitamin D levels. These findings suggest that the effects of vitamin D levels on UI and OAB may be complex and require further investigation.

Limitations of our study include the limited number of participants, the lack of simultaneous measurement of serum 25(OH) Vitamin D levels with UI, and the reliance on participant-reported UI status. Considering these limitations, future studies should be more comprehensive. In conclusion, further research is needed to better understand the relationship between Vitamin D deficiency and UI and OAB in the elderly.

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PPD sonrası gelişen atipik büllöz reaksiyon: Tüberküloz lenfadenit olgu sunumu

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ÖZET

Tüberkülozun tanısında en eski ve en sık kullanılan tüberküloz tarama testi, saflaştırılmış bir protein türevinin (pürifiye protein derivesi = PPD) deri içine enjekte edildiği uygulamadır. PPD uygulanan bölgede 48-72 saat içinde sertleşme, gecikmiş tipte aşırı duyarlılık reaksiyonunu ve M. tuberculosis ile enfeksiyonu gösterir. Bu yazıda aynı gün içinde aynı koldan PPD ve COVID-19 Biontech aşılaması yapılan ve PPD enjeksiyon bölgesinde atipik büllöz reaksiyon gelişen bir olgu sunulmuştur. PPD ve COVID-19 aşılamalarının aynı gün aynı kola uygulandığı olgularda benzer klinik bulguların gelişebileceği akılda tutulmalı, bu iki işlemin mümkün olduğunca farklı zamanlarda uygulanmasına dikkat edilmelidir.

Anahtar kelimeler: PPD, atipik büllöz reaksiyon, tüberküloz, COVID-19 aşı

ABSTRACT

Atypical bullous reaction after PPD: A case report of tuberculous lymphadenitis

The oldest and most commonly used tuberculosis screening test in the diagnosis of tuberculosis is the application in which a purified protein derivative (purified protein derivative = PPD) is injected into the skin. Hardening in the PPD treated area within 48-72 hours indicates delayed-type hypersensitivity reaction and infection with M. tuberculosis. In this article, a case who was injected with PPD and COVID-19 Biontech from the same arm on the same day and who developed an atypical bullous reaction at the ppd injection site is presented. It should be kept in mind that similar clinical findings may develop in cases where PPD and COVID-19 vaccinations are applied to the same arm on the same day, and care should be taken to apply these two procedures at different times as much as possible.

Keywords: PPD, atypical bullous reaction, tuberculosıs, COVID-19 Vaccine

GİRİŞ

Tüberkülozun tanısında en eski ve en sık kullanılan tüberküloz tarama testi, saflaştırılmış bir protein türevinin (pürifiye protein derivesi = PPD) deri içine enjekte edildiği uygulamadır [1]. PPD, tüberküloz basil kültürü filtresinden protein presipitasyonu ile izole edilen antijenik öğeleri içerir ve daha önce M. tuberculosis ile karşılaşmış, yani enfeksiyon geçirmiş bir bireyin hücresel immünite cevabını gösterir. Şu anda mevcut olan tüberkülin deri testi antijenleri, *Mycobacterium tuberculosis* enfeksiyonunun tespiti için %100'den daha az duyarlı ve spesifik olsa da, daha iyi tanı yöntemleri yaygın olarak mevcut değildir[2]. PPD uygulanan bölgede 48-72 saat içinde sertleşme, gecikmiş tipte aşırı duyarlılık reaksiyonunu ve M. tuberculosis ile enfeksiyonu gösterir. Endürasyon olmadan eritem varlığı negatif olarak kabul edilir [3-6]. Bağışıklık sistemi yeterli kişilerde 10 mm'lik bir endurasyon pozitif test yanıtı olarak kabul edilirken, HIV enfeksiyonu olan veya bağışıklık sistemini baskılayıcı ilaç tedavisi görenler gibi bağışıklık yetersizliği olan bireylerde 5 mm'lik bir yanıt pozitif kabul edilebilir. Eritem ve sertleşme normal yanıt olsa da, PPD testin den sonra kabarcıklar, granülomlar ve lokal nekroz gibi atipik reaksiyonlar çok nadirdir[7-8]. Abartılı tüberkülin yanıtı, aktif tüberküloz gelişme olasılığının daha yüksek olmasıyla ilişkilidir[9].

Olgumuzda aynı gün içinde aynı koldan arka arkaya PPD ve COVID-19 Biontech aşısı yapılması sonrasında gelişen atipik büllöz reaksiyon sunulmuştur.

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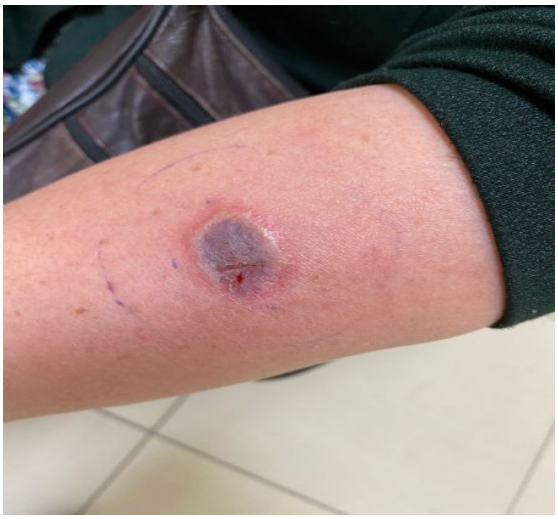
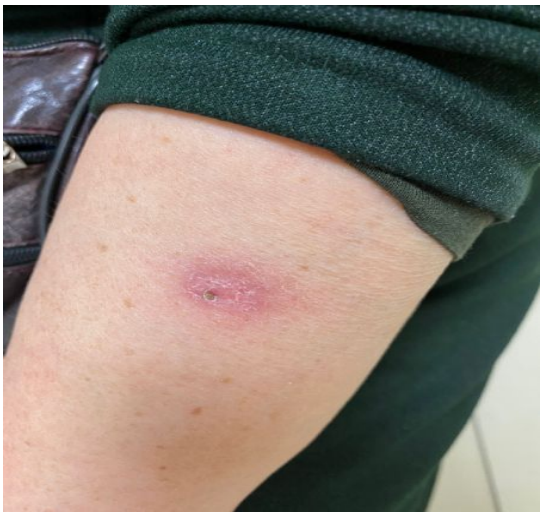
OLGU SUNUMU

63 yaşında Çan'da kırsal bölgede yaşayan kadın hasta sağ submandibular bölgede 1 yıldır devam eden şişlik, halsizlik şikayetleriyle enfeksiyon hastalıkları polikliniğine başvurdu. Fizik muayenesinde sağ submandibular bölgede 2x3 cm yumuşak kıvamlı hareketli hassas lenfadenopatisi olan hastanın dış merkezde yapılan ultrasonunda sağ submandibular bölgede yaklaşık 22x11 mm, oval, kısmi vaskülarize, hipoekojen lezyon (lap?) raporlandı. LAP etiyolojisine yönelik bakılan Toxoplasma, Rubella, Citomegalovirüs, Hepatitler, Brucella, tularemi ve kedi tırmığı elisa ve seroloji testleri negatifti. Akciğer grafisi normaldi. Yapılan sağ submandibular ve sol aksiller lenf nodu tru-cut biyopsisinde kazeifiye granülomatöz lenfadenit saptanması üzerine tüberküloz öyküsü olmayan hastaya PPD yapılması planlandı. Aynı gün içinde sol kola PPD'si ve COVID Biontech aşısı yapılan hastanın 4. gününde sol kol posteriorunda 1x3cm boyutunda anüler, , kenarları büllöz keskin sınırlı ağrılı lezyon izlendi (Resim 1). Endurasyon yoktu. Dermatoloji tarafından değerlendirilen hastada atipik büllöz reaksiyon geliştiği düşünülerek PPD belirsiz olarak yorumlandı. PPD bölgesinden alınan cilt biyopsisi sonucu epidermiste ve dermiste nekroz, abse, kronik inflamatuar hücreler olarak geldi. Tüberküloz lenfadenit ön tanısıyla hastaya anti tüberküloz tedavisi başlandı. Tedavi süresi 6 ay olarak düzenlendi. 10 gün sonra yapılan kontrol muayenesinde büllöz reaksiyonun kaybolduğu görüldü(Resim2).



Resim1.*PPD uygulama sonrası 4. gün*



Resim2. 10 gün sonraki kontrol muayenesi

TARTIŞMA

Canlı zayıflatılmış *Mycobacterium bovis* enjeksiyonuna dayanan ve lokal enfeksiyona neden olabilen BCG aşılamasının aksine, PPD *Mycobacterium tuberculosis*'in 200 den fazla enfektif olmayan saflaştırılmış proteinden oluşur ve lokal enfeksiyona neden olamaz[10].

İlk kez 1890 yılında Koch tarafından kaynatılmış basil kültürlerinin özütü olan "Old Tuberculin" geliştirilerek 1930 yılına kadar sağlıklı bireylerde M.tuberculosis varlığını tespit etmede kullanıldı[11]. Bugün PPD tüberkülin deri testi; Tüberkülozda tanı amacıyla, BCG aşısının etkinliğini belirlemek ve kontrolünü sağlamak için, kemoprofilakside kullanılmaktadır[12].

Literatür tarandığında PPD sonrası gelişen atipik ve çoğunlukla granülomatöz veya büllöz görünümlü deri testi yanıtları veren olgular gösterilmiştir[9,13-17]. Mevcut veriler, pozitif bir tüberkülin reaksiyonunun vakaların yaklaşık %1 ila %2'sinde bir miktar kabarma ile ilişkili olacağını tahmin etmektedir[18]. Ancak PPD'ye karşı nekrotik reaksiyonlar son derece nadirdir.

Olgumuzda literatürle uyumlu olarak PPD sonrası hastamızda atipik büllöz reaksiyon gelişmiştir. Aynı gün ve aynı koldan hastaya Biontech aşısının da yapılmış olmasının mevcut gelişen reaksiyona bir katkısının olup olmadığı tartışmaya açık olup mevcut reaksiyonun aşıyla mı yoksa PPD deri testiyle mi indüklenmiş olduğu bilinmemektedir.

Sonuç olarak, literatürde yer aldığı şekilde çok sık olmamakla birlikte PPD sonrası atipik deri yanıtları gelişebileceği akılda tutulmalı ve aynı koldan aşılama ya da başka bir uygulama yapılmaması önerilmektedir.

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