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Journal article on the Internet

Abood S. Quality improvement initiative in nursing homes: The ANA acts in an advisory role. Am J Nurs [serial on the Internet] 2002 [cited 12 Aug 2002]; 102. Available from: www.nursingworld.org/AJN/2002/june/wawatch.htm

Website

Cancer-pain.org [homepage on the Internet]. New York: Association of Cancer Online Resources [updated 16 May 2002; cited 9 Jul 2002]. Available from: www.cancer-pain.org

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The Intensive Care Society of Australia and New Zealand. Mechanical ventilation strategy in ARDS: Guidelines. Int Care J Aust 1996;164:282-4.

Acknowledgements

The source of financial grants and the contribution of colleagues or institutions should be acknowledged.

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CASE REPORT

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Orjinal Araştırma / Original Article

Interreader Agreement in Multiparametric Prostate Magnetic Resonance Imaging: A Head-to-Head Comparison between PI-RADSv2 and v2.1

Multiparametrik Prostat Manyetik Rezonans Görüntülemede Okuyucular Arası Uyum: PI-RADSv2 ve v2.1'in Bire Bir Karşılaştırılması

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Abstract

Aim: The purpose of this study is to compare PI-RADSv2 with v2.1 in terms of interreader agreement.

Material and Method: Two hundred-two patients who had both multiparametric prostate magnetic resonance imaging (mpMRI) and 12 quadrant systematic biopsies were included in this retrospective study. Acquisition parameters were totally complied with proposal of PI-RADSv2 and 2.1 guidelines. mpMRIs were evaluated by two radiologists independently. Index lesion's score was used to determine diagnostic performance of the systems. Gleason ≥ 3+4 tumors were considered clinically significant prostate cancer (CSCa). Kappa statistic was used to determine interreader agreement on overall PI-RADS scores. Area under the curve (AUC) was calculated in detection of CSCa using receiver operating characteristic curve (ROC).

Result: The numbers of cases with PI-RADSv2 and v2.1 scores from 1 to 5 were 46, 21, 13, 41, 81 and 46, 26, 9, 43, 78, by reader 1 and 51, 10, 18, 43, 80 and 51, 15, 19, 37, 80 by reader 2, respectively. There was "substantial" agreement between two readers for both scoring systems. Kappa values were 0.600 in PI-RADSv2 and 0.624 in PI-RADSv2.1. Ninety-eight (48.5%) patients had CSCa. AUC values of PI-RADSv2 and v2.1 scoring systems were 0.861 and 0.851 for reader 1, 0.873 and 0.883 for reader 2, respectively.

Conclusion: Interreader agreement was "substantial" in mpMRI and slightly improved with PI-RADSv2.1. Diagnostic performance of the two systems were almost equal.

Keywords: Gleason, image-guided biopsy, multiparametric MRI, prostate cancer

Öz

Amaç: Bu yazının amacı, okuyucular arası uyum açısından PI-RADSv2 ile v2.1'in karşılaştırılmasıdır.

Gereç ve Yöntem: Multiparametrik prostat manyetik rezonans görüntüleme (mpMRG) ve 12 kadran sistematik biyopsi yapılan 202 olgu, bu retrospektif çalışmayı oluşturmaktadır. Görüntüleme parametrelerinde PI-RADSv2 ve v2.1'in sunduğu tüm önerilere uyuldu. mpMRG'ler iki radyolog tarafından ayrı ayrı değerlendirildi. Sistemlerin tanısal performansını belirlemede indeks lezyon esas alındı. Gleason ≥ 3+4 tümörler klinik anlamlı prostat kanseri (KAK) kabul edildi. Genel PI-RADS skoru için okuyucular arası uyumun belirlenmesinde kappa istatistiği kullanıldı. KAK tespitinde eğrinin altındaki alan (EAA), alıcı işletim karakteristiği eğrisi kullanılarak hesaplandı.

Bulgular: PI-RADSv2 ve v2.1 için skoru 1'den 5'e olan olgu sayısı okuyucu 1 için sırasıyla 46, 21, 13, 41, 81 ve 46, 26, 9, 43, 78 iken, okuyucu 2 için sırasıyla 46, 21, 13, 41, 81 ve 46, 26, 9, 43, 78 idi. Her iki skorlama sistemi için iki okuyucu arasındaki uyum "iyi" düzeydeydi. Kappa değerleri PI-RADSv2 için 0,600, PI-RADSv2.1 için 0,624 idi. Doksan-sekiz (%48,5) olguda KAK görüldü. PI-RADSv2 ve v2.1 skorlama sistemi için EAA değerleri okuyucu 1 için sırasıyla 0,861 ve 0,851, okuyucu 2 için sırasıyla 0,873 ve 0,883 idi.

Sonuç: Okuyucular arası uyum mpMRG'de "iyi" olup PI-RADSv2.1 ile hafif artmıştır. Her iki sistemin tanısal performansı neredeyse eşittir.

Anahtar Kelimeler: Gleason, görüntüleme eşliğinde biyopsi, multiparametrik MRG, prostat kanseri

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INTRODUCTION

Prostate cancer is the second most common cancer of men in Turkey.[1] The incidence is higher in developed countries, reflecting a greater use of screening and diagnostic tools.[2] Multiparametric prostate magnetic resonance imaging (mpMRI) is popular in diagnosing and local staging.[3] The publication of the prostate imaging-reporting and data system (PI-RADS) guideline introduced a standardization in acquisition and reporting.[4] The guideline was revised in 2019 and the current version 2.1 (v2.1) has been published.[5]

The main problem in the evaluation of mpMRI was inconsistency among readers.[6-9] The reason is subjective signal definitions as "mild, moderate, marked" in PI-RADSv2.[6] These qualitative definitions facilitate use of mpMRI while it causes differences among readers in interpretation.[7,9] The current PI-RADSv2.1 presents minor revisions.[5] For example, the addition of "a more pronounced signal change than any other focus in the same zone" provides a more detailed definition of category 4 in peripheral zone (PZ).[3] These updates in signal description propose to increase the compatibility between readers.[5]

The purpose of this study is to compare PI-RADSv2 with v2.1 in terms of interreader agreement. Additionally, the PI-RADS scores were also compared with each other in the diagnosis of clinically significant prostate cancer (CSCa).

MATERIAL AND METHOD

Patient selection

This retrospective study was approved by the local ethic committee (approval number: 12.05.2020-651). The patients who had mpMRI and 12 quadrant systematic biopsies were included between 2019 and 2020. Informed consent was obtained from all participants. mpMRI indications were elevated prostate-specific antigen (PSA ≥ 4) and/or abnormal digital rectal examination (DRE). Biopsy indications were elevated or rising PSA or suspicion PCa in DRE or abnormal mpMRI (PI-RADS score ≥ 3). PI-RADS scoring is not possible after treatment so the patients treated before mpMRI were excluded. Two patients were also excluded due to severe susceptibility artifact secondary to hip prosthesis.

Technical parameters of the mpMRIs

All mpMRIs were acquired on a 1.5T scanner (Aera, Siemens Healthineers, Erlangen, Germany). The protocol included the following sequences: Turbo spin-echo T2-weighted imaging (T2WI) with axial, sagittal, and coronal orientations (Axial T2WI parameters were as follows: repetition time, 5660 msec; echo time, 99 msec; the field of view, 200×180 mm; acquisition matrix, 320×288; slice thickness, 3 mm with no gap), a diffusion-weighted imaging (DWI) with an axial orientation (repetition time, 4000 msec; echo time, 76 msec; b-values, 0, 200, 600 and 1400 sec/mm2; the field of view, 200×180 mm; acquisition matrix, 100×90; slice thickness, 3 mm with no gap) with apparent diffusion coefficient (ADC) mapping, and dynamic contrast-enhanced (DCE) sequences with an axial orientation (repetition time, 2.48 msec; echo time, 1.52 msec; the field of view, 260×215 mm; acquisition matrix, 160×108; slice thickness 3 mm with 0.3 mm gap; temporal resolution, 7 sec). All parameters were complied with proposal of the PI-RADSv2.1 guideline.[5]

Radiological evaluation

mpMRIs were evaluated by two radiologists individually (reader 1 with 5 years of experience in prostate imaging; reader 2 with 4 years of experience in this field). The radiologists were blinded to any clinical or pathological information. The radiologists scored the lesions two times using PI-RADSv2 and PI-RADSv2.1. Interreader agreement was calculated for PI-RADSv2 and v2.1 respectively. The score of the index lesion was considered in patient-based statistical analysis.

Major scoring revisions in PI-RADSv2.1 were as follows: In PZ, category 2, "linear/wedge shaped" on ADC and high b-value images; category 3, "discrete and different from background" instead of "mild"; category 4, "more pronounced signal change than any other focus in the same zone" instead of "marked". In transition zone (TZ), round, completely encapsulated nodules were clarified as category 1. Atypical nodules were classified as category 2. Overall PI-RADS score upgraded from 2 to 3 for the lesion with T2WI score of 2, and DWI score of 4 or 5.

Pathological assessment

The pathological evaluation was based on the pathology reports. Tumors were graded by the genitourinary pathologists as proposed by the International Society of Urological Pathology (ISUP) in 2014. Accordingly, Gleason 3+3 tumors were categorized as ISUP 1, Gleason 3+4 tumors as ISUP 2, Gleason 4+3 tumors as ISUP 3, Gleason 4+4 tumors as ISUP 4, and Gleason ≥ 4+5 tumors as ISUP 5. ISUP ≥ 2 tumors were considered CSCa as defined in the PI-RADSv2.1.[5] The highest scored biopsy core was considered in patient-based statistical analysis.

Statistical analysis

Statistical analyzes were done using SPSS version 20.0 (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.). Kappa statistic was used to determine interreader agreement on overall PI-RADS scores. Accordingly, it was classified as follows: 0.01–0.20, slight; 0.21–0.40, fair; 0.41–0.60, moderate; 0.61–0.80, substantial, and 0.81–0.99, almost perfect.

The PI-RADSv2 and v2.1 scores of the readers were compared in diagnosing CSCa using patient-based analysis. Area under the curve (AUC) was calculated using receiver operating characteristic curve (ROC).

RESULTS

The median age of 202 patients included in this study was 67 (standard deviation, ±7; range, 46-84). The median PSA level was 7.7 ng/dL (±16.7, 1.21-119).

Reader 1 was assigned no lesion in 46 patients. Reader 1 detected 249 lesions in PZ, 29 lesions in TZ lesions in 156 patients. Reader 2 was assigned no lesion in 51 patients. Reader 2 detected 216 lesions in PZ, 25 lesions in TZ in 151 patients. Forty-eight and thirty-six patients had multifocal lesions by reader 1 and reader 2, respectively (**Table 1**). Median dimension of the lesions 15 mm for both readers.

The numbers of cases with PI-RADSv2 and v2.1 scores from 1 to 5 were 46, 21, 13, 41, 81 and 46, 26, 9, 43, 78 by reader 1, respectively (**Table 2**). The numbers of cases with PI-RADSv2 and v2.1 scores from 1 to 5 were 51, 10, 18, 43, 80 and 51, 15, 19, 37, 80 by reader 2, respectively (**Figure 1 and 2**). There was substantial agreement between two readers for both scoring systems overally. Kappa values were 0.600 in PI-RADSv2 and 0.624 in PI-RADSv2.1.

Table 1. Lesion counts on mpMRIs by two different radiologists

Number of lesions	Reader 1	Reader 2
No lesion	46	51
One lesion	156	151
Two lesions	28	22
Three lesions	14	10
Four lesions	6	4

Table 2. The numbers of cases with PI-RADSv2 and v2.1 by two radiologists

Type of scores	PI-RADSv2, R1 (n)	PI-RADSv2.1, R1 (n)	PI-RADSv2, R2 (n)	PI-RADSv2.1, R2 (n)
Score 1	46	46	51	51
Score 2	21	26	10	15
Score 3	13	9	18	19
Score 4	41	43	43	37
Score 5	81	78	80	80

R, reader; PI-RADS, prostate imaging-reporting and data system; v2, version 2; v2.1, version 2.1; n: number of patients.

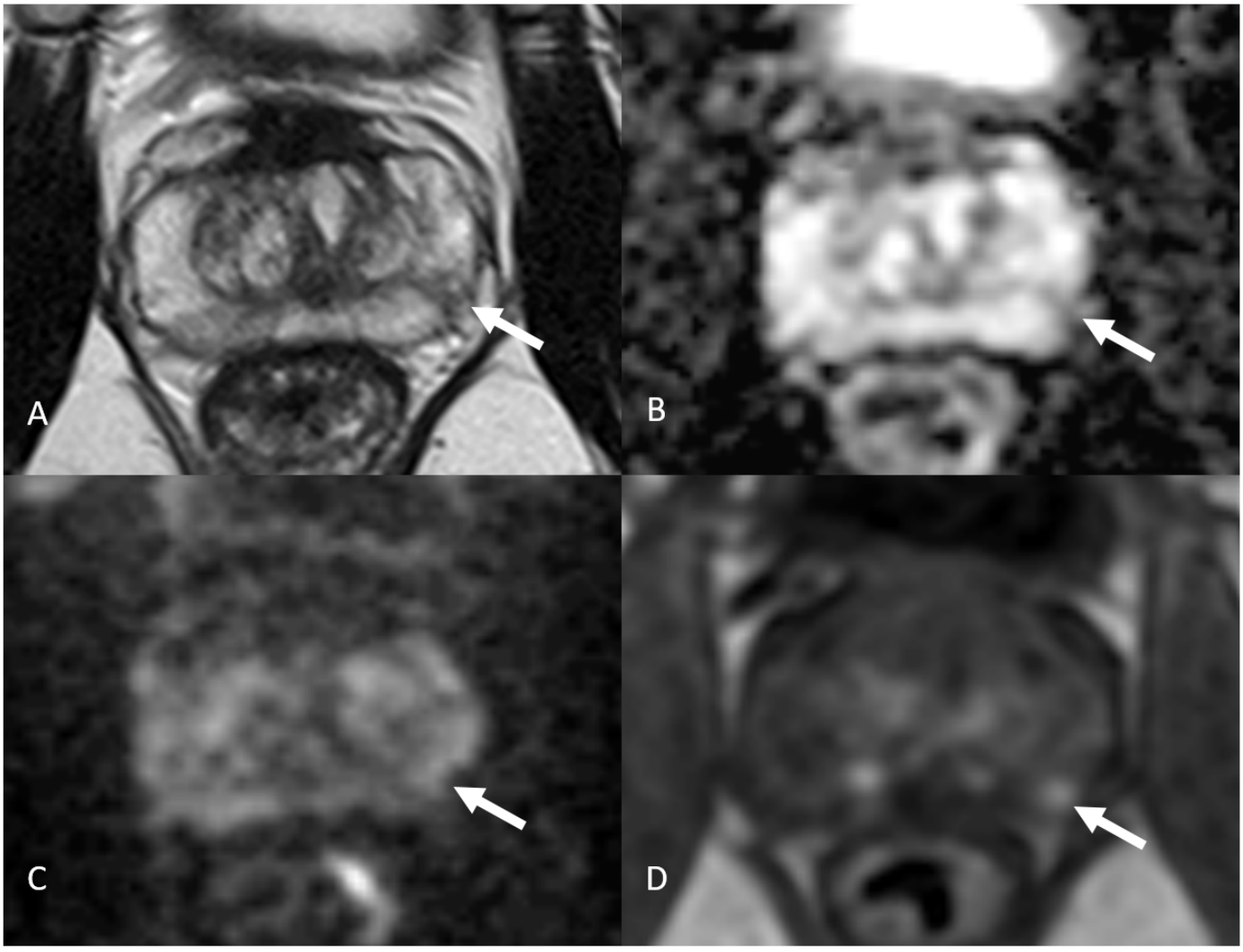

Figure 1. Multiparametric MRI of the 47 year-old man with a PSA of 3.16 ng/dl (a. T2WI, b. ADC map, c. high b-value DWI and d. DCE-MRI). Arrows are showing a left mid PZ lesion. Reader 1 assigned this lesion as category 4 (3+1) for both PI-RADSv2 and v2.1. Reader 2 assigned category 4 (3+1) using PI-RADSv2 but category 2 using PI-RADSv2.1 because of linear-wedge shaped appearance. Systematic biopsy resulted in Gleason 3+3 tumor with 40% involvement on two core from left mid PZ.

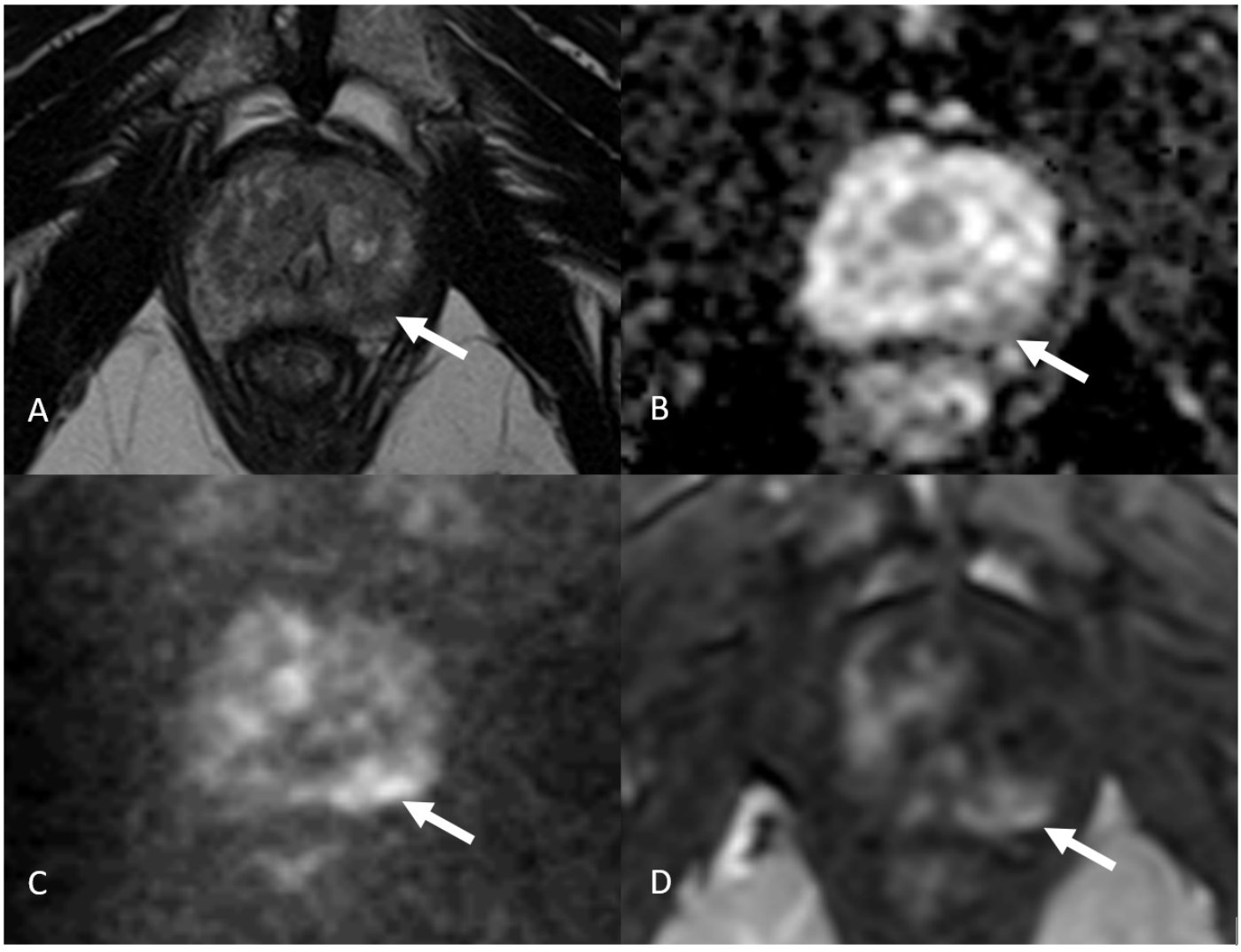

Figure 2. Multiparametric MRI of the 69 year-old man with a PSA of 4.68 ng/dl (a. T2WI, b. ADC map, c. high b-value DWI and d. DCE-MRI). Arrows are showing a left apical PZ lesion with 15mm in diameter. Reader 1 and reader 2 assigned this lesion as category 5 for both PI-RADSv2 and v2.1. Systematic biopsy resulted in Gleason 3+4 tumor with 20% involvement on four cores from left apical and mid PZ.

Pathological outcomes were showed that there was no tumor in 64 (31.7%) patients. The numbers of cases with ISUP scores from 1 to 5 were 40, 44, 28, 13 and 13, respectively. Ninety-eight (48.5%) patients had CSCa. In patient-based analysis, AUC values of PI-RADSv2 and v2.1 scoring systems were 0.861 and 0.851 for reader 1, 0.873 and 0.883 for reader 2, respectively (**Figure 3**).

DISCUSSION

This is one of the earliest studies comparing the PI-RADS guidelines in terms of interreader agreement and diagnosis of CSCa. The results were reflecting minimal progression on interreader reproducibility with PI-RADSv2.1. Detection of CSCa did not improve with current version substantially.

The PI-RADSv2.1 still assigns a score from 1 to 5 to predict likelihood of CSCa. It introduced minor updates for

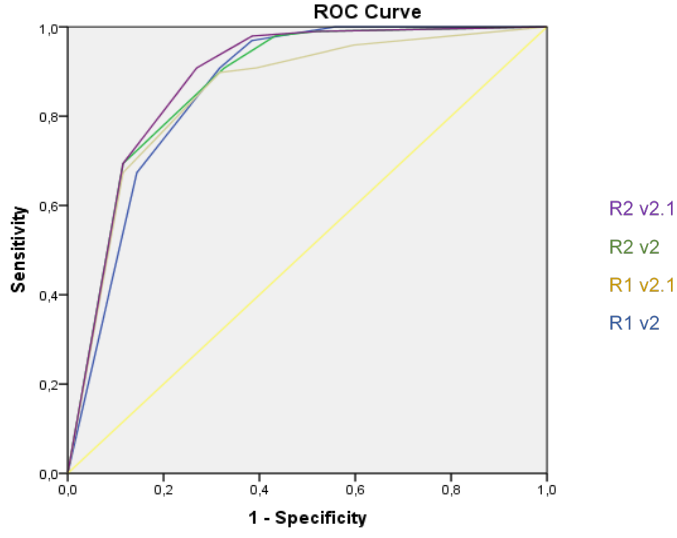

Figure 3. ROC curves of two different scoring systems among two readers in detection of clinically significant prostate cancer

interpretation of mpMRI.[5] DWI category 2 was defined as indistinct hypointense on ADC in PZ. It was upgraded to category 3 when it was defined as mild-moderate hypointense on ADC and isointense-mildly hyperintense on high b-value DWI in the former version.[4] The revised version included morphologic appearance additional to signal descriptive.[3] Category 2 is stated as linear-wedge shaped hypointense on ADC and/or linear-wedge shaped hyperintense on high b-value DWI currently. "Discrete and different from the background" is added to former signal description in clarifying category 3 in PZ.[5] In our study, the numbers of lesions assigned as score 2 were increased using PI-RADSv2.1 by two readers. We observed that some lesions assigned as score 3 in the former version were downgraded to score 2 using PI-RADSv2.1. The term "linear-wedged shaped appearance" was catalyzed downgrading from category 3 into category 2. We did not search for the pathological outcome of those downgraded lesions since the purpose of this work was different. This would be an attractive point for a large-scale study investigating only downgraded lesions.

Round and completely encapsulated nodules are typical benign nodules and evaluated in category 1 now, while they may be scored as category 2 in PI-RADSv2. This revision clarifies the definition of benign typical nodule.[3] In the study of Linhares Moreira et al, the most common score change was observed in TZ with downgrading of typical BPH nodules from category 2 into category 1 with the PI-RADSv2.1.[10] In our study, the number of category 1 lesions did not change for both readers. We had already reported it as "category 1 with typical BPH nodules" in the former version. If we reported all BPH nodules as score 2, we would hardly be able to report as score 1 considering that BPH nodules were quite common.

Interreader agreement was fair to moderate in PI-RADSv2.[8,9,11,12] PI-RADS guidelines were constituted by the experienced radiologists that make uncertain the reproducibility across inexperienced readers. Seven radiologists had a moderate agreement (kappa = 0.591) in detection of index lesion using PI-RADSv2.1.[13] Tamada et al.[14] researched on TZ cancers and reported that interreader agreement was moderate (kappa = 0.580) for PI-RADSv2 and substantial (kappa = 0.645) for PI-RADSv2.1. These findings were replicated in another study comparing the PI-RADSv2 and v2.1 in interpretation of TZ lesion and concluded that PI-RADSv2.1 had higher agreement than PI-RADSv2 (kappa = 0.700 and 0.622, respectively).[15] These findings were also supported for PZ lesions in the study of Bhayana et al.[16] They found that interreader agreement was higher in PI-RADSv2.1 (kappa = 0.64) than PI-RADSv2 (kappa = 0.51). Unlikely, Hötker et al.[17] claimed that interreader agreement was higher in the former version (Kappa = 0.57 for PI-RADSv2 and Kappa = 0.51 for PI-RADSv2.1). But the difference of experience between the readers was higher in this study. Additionally, the potential reason for this decrease may being less familiar with the new version according to the authors. In our study, we directly compared both versions and found that interreader agreement improved slightly with current version (kappa = 0.600 in PI-RADSv2 vs kappa = 0.624 in PI-RADSv2.1). Additional descriptors may enhance the interreader agreement.

There were a few studies searching diagnostic performance of PI-RADSv2.1 which was published recently in September 2019. Wei et al reported that PI-RADSv2.1 had higher diagnostic accuracy with an AUC of 0.929 than PI-RADSv2 with an AUC of 0.899 in diagnosing of CSCa in TZ (15). In another study, both versions had almost identical performance (AUCs of PI-RADSv2 and v2.1 0.874 and 0.879, respectively) in detection of CSCa (17). In our study, PI-RADSv2 and v2.1 scoring systems had parallel performance and AUC values were 0.861 and 0.851 for reader 1, 0.873 and 0.883 for reader 2, respectively.

There were several limitations of this study. Firstly, this was a retrospective study with a small sample size. The results needed to be supported with large-scale prospective study. Secondly, the patients were not sampled with targeted biopsy. Targeted biopsy may enhance the accuracy of mpMRI and provides more accurate radio-pathological concordance. The aim of this work was to compare the two score systems not diagnostic accuracy of mpMRI. Comparison of the systems with each other may trivialize this limitation. Thirdly, index lesion in mpMRI was considered in detection of CSCa. This was problematic in cases with multifocal tumors and prevented lesion-based analysis. So, we introduced patient-based results of CSCa detection. Current findings should also be confirmed by prospective randomized studies.

CONCLUSION

Interreader agreement was substantial and slightly improved with PI-RADSv2.1. Diagnostic performance of PI-RADSv2 and v2.1 were similar in detection of CSCa.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study was approved by institutional Review Board of İzmir Katip Çelebi University (Non-Interventional Clinical Studies, 12.05.2020, 651).

Informed Consent: Due to the retrospective design of the study, informed consent of the patients was not necessary.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflict of interest to declare.

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

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Orjinal Araştırma / Original Article

Effects Of Age, Body Mass Index, Complete Blood Count Parameters, and Biochemical Parameters on Stable COPD Patients

Stabil KOAH Hastalarında Yaş, Vücut Kitle İndeksi, Tam Kan Sayımı ve Biyokimyasal Parametrelerin Etkileri

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Abstract

Aim: Chronic obstructive pulmonary disease (COPD) is worldwide and mainly affects the elderly. It is often impossible to define COPD with specific lines, and it has no complete cure procedure, mostly established by guidelines. The GOLD guideline uses a sectional COPD evaluation approach to group patients by symptoms and former history of exacerbations. The concurrent detection of various biomarkers reflecting different pathobiological pathways might help recognize patients with an increased risk of death. Studies showed that obesity is related to decreased lung function in the general population due to respiratory mechanics, muscular discomfort, and breath control.

Material and Method: Ninety patients with COPD, whose mean age was 62, and 74% were male, were divided into four groups as A, B, C, and D according to the GOLD classification, were included in our study. Analyses were conducted to investigate the association between biochemical parameters, BMI, age, gender, and disease severity, according to GOLD subgroups.

Results: It has been demonstrated that COPD patients are generally over the age of 40 and age correlates with the severity of the disease consistent with previous studies. Our study has shown that COPD usually occurs over the age of 40, and there is a relationship between advanced age and the severity of COPD.

Conclusion: Our results are consistent with previous studies where COPD patients are usually over 40 years old, and age is linked to disease severity. While the BMI values of the patients in group B were higher than those of group A, it was compatible with studies showing the relationship between obesity and severity of COPD; being higher than C and D groups was consistent with the studies revealing the obesity paradox. Crp, Procalcitonin, Sedimentation, Calcium, Magnesium levels, and other complete blood count values showed no significant difference between GOLD groups.

Keywords: Body mass index, complete blood count parameters, COPD

Öz

Amaç: Kronik obstrüktif akciğer hastalığı (KOAH) dünya çapında görülür ve esas olarak yaşlıları etkiler. KOAH'ı belirli çizgilerle tanımlamak genellikle imkansızdır ve çoğunlukla kılavuzlarla belirlenmiş tam bir tedavi prosedürü yoktur. Global Initiative For Chronic Obstructive Lung Disease (GOLD) hastaları semptomlara ve eski alevlenme öyküsüne göre gruplandırmak için bölümsel bir KOAH değerlendirme yaklaşımı kullanır . Farklı patobiyolojik yolları yansıtan çeşitli biyobelirteçlerin eşzamanlı tespiti, artmış ölüm riski olan hastaların tanınmasına yardımcı olabilir. Çalışmalar obezitenin, solunum mekaniği, kas rahatsızlıkları ve akciğer fonksiyonları üzerine olumsuz etkileri olduğunu göstermiştir.

Gereç ve Yöntem: Çalışmamıza ortalama yaşı 62,% 74'ü erkek olan 90 KOAH'lı hasta dahil edildi.Hastalar GOLD sınıflamasına göre A, B, C ve D olmak üzere dört gruba ayrıldı. Biyokimyasal parametreler,Vücut Kitle indeksi (VKİ), yaş, cinsiyet ve hastalık şiddeti arasındaki ilişkiyi GOLD alt gruplarına göre araştırmak için analizler yapıldı.

Bulgular: KOAH Grup B'deki hastaların VKİ değerleri A grubuna göre daha yüksek iken, obezite ile KOAH şiddeti arasında anlamlı ilişki tespit edildi. GOLD C ve D gruplarında VKI değerinin yüksek olması obezite paradoksunu ortaya koyan çalışmalarla uyumluydu. C-reactive protein (CRP), Prokalsitonin, Sedimantasyon, Kalsiyum, Magnezyum seviyeleri ve diğer tam kan sayımı değerleri GOLD grupları arasında anlamlı bir fark göstermedi.

Sonuç: Çalışmamız KOAH'ın genellikle 40 yaşın üzerinde ortaya çıktığını, ileri yaş ile KOAH'ın şiddeti arasında ilişki olduğunu göstermiştir. Grup B'deki hastaların VKİ değerleri A grubuna göre daha yüksek iken, obezite ile KOAH şiddeti arasındaki ilişkiyi gösteren çalışmalarla uyumluydu; C ve D gruplarından yüksek olması obezite paradoksunu ortaya koyan çalışmalarla uyumluydu. Crp, Prokalsitonin, Sedimantasyon, Kalsiyum, Magnezyum seviyeleri ve diğer tam kan sayımı değerleri GOLD grupları arasında anlamlı bir fark göstermedi.

Anahtar Kelimeler: Vücut kitle indeksi, tam kan parametreleri, KOAH

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a commonplace disease worldwide and mainly affects the elderly. Global authorities 2017 report by; COPD, often caused by severe exposure to damaging particles or gases, persevering airflow restriction, and alveolar abnormalities. Chronic airflow restriction, which is characteristic of COPD, is a small airway disease (obstructive bronchiolitis) that varies from person to person. It develops as a result of parenchymal destruction (emphysema). Although these pathologies are not always together, they evolve at different rates over time. Chronic inflammation constricts small airways and destroys the lung parenchyma. Loss of small airways also causes airflow restriction and contributes to mucociliary dysfunction. COPD is a multicomponent and variable disease. Therefore, it is often impossible to define COPD with specific lines, and it has no complete cure procedure, mostly established by guidelines. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) system classifies airflow restriction into stages. The GOLD guideline uses a sectional COPD evaluation approach to group patients by symptoms and former history of exacerbations.[1] Prognosis changes with several factors, including genetic predispositions, environmental factors, comorbidities, and acute attacks. Even though short-term survival is contingent on the overall seriousness of the acute attacks, long-term survival is intent on by the severeness of COPD and the existence of comorbid conditions. Commonly, the prognosis depends on the FEV1 pulmonary function testing. Scientists showed a significant correlation between increased FEV1 and lower risk of COPD aggravation.[2]

Higher levels of multiple biomarkers are related to mortality in stable COPD patients. The concurrent detection of various biomarkers reflecting different pathobiological pathways might help recognize patients with an increased risk of death.[3] Many biomarkers separately associated with increased risk of death, and a few had the more distant supply to mortality prediction with known clinical variables.[4] Although because COPD is a complex and heterogeneous disease with differing phenotypes, the aim of finding a single biomarker of COPD is a dream for now.[5] Besides, biomarkers don't have to come from the lungs to be functional in predict prognosis.[6] A panel of predictive biomarkers is needed to understand ongoing disease.[7] Aggravations in chronic obstructive pulmonary disease (COPD) are significant contributors to worsening lung function, impaired quality of life, emergency healthcare use, and COPD-related mortality. COPD aggravations are heterogeneous in terms of airway inflammation and etiology.

About 60% of COPD patients have blood eosinophil counts of ≥2%, which appears to be associated with an increased risk of aggravations. However, the association between blood eosinophil counts at stable disease and COPD aggravations in the subsequent year are incompletely understood. Even though the eosinophil evaluation is currently in discussion, eosinophil count is important as biomarkers to design the treatment. Specifically, eosinophils help assess which patients may benefit from inhaled corticosteroid therapy, especially concerning aggravation prevention.[8] Additionally, a large epidemiologic study found bilirubin concentrations negatively associated with COPD incidence.[9] C-reactive protein (CRP) binds bacteria, oxidized lipids, and apoptotic cells and enables their destruction via the immune system. Moderately increased serum CRP levels associates with inflammation in atherosclerosis and therefore increased risk of coronary heart disease and myocardial infarction. Supporting proof now suggests that increased serum CRP levels also associate with lung inflammation in stable COPD. Therefore, serum CRP could be a predictor of future COPD outcomes.[10] Procalcitonin (PCT) is more sensitive and specific in differentiating bacterial infection from noninfectious inflammation. PCT is a polypeptide that producing from neuroendocrine cells of the thyroid and lungs. The high level of PCT found in serum during severe sepsis, and septic shock reflects bacterial infections. Recently, PCT guidance provides clinically relevant information and safely reduce antibiotic use in patients with respiratory illness. Delay in diagnosis and treatment of COPD aggravations and its associated comorbidities increases the mortality risk, but timely recognition of these patients and intervention is essential.[11-13]

Obesity, distinguished by extreme body fat accumulation, can be assessed by body mass index (BMI). Obesity is a frequent comorbidity of COPD, with approximately ranges from 6% to 54%. The severity of COPD depends on the degree of airway restriction, which is an indicator of lung dysfunction. Body weight affects lung function independent of tobacco use. Many studies have shown that obesity is related to decreased lung function in the general population due to gas exchange, respiratory mechanics, muscular discomfort, and breath control. Obesity could also strengthen to lessen lung function through chronic low-grade inflammation.[14] The authors proposed that obesity in patients with COPD might advance to worse COPD-related health outcomes such as acute exacerbation of COPD and dyspnea scores.[15] Therefore, it is accepted that obesity in patients with COPD should be treated with weight loss via exercise, which is useful for reformed lung function and diminished complications. Nonetheless, a meta-analysis by Cao et al. demonstrated that overweight and obese patients with COPD had a decreased risk of all-cause mortality.[16] This circumstance is known as the "obesity paradox," which is decribed as an opposite relationship between survival and obesity and has been monitored in numerous chronic diseases, as well as type II diabetes mellitus, stroke, and chronic kidney disease. The connection between obesity and mortality in patients with COPD has been controversial, but evidence has indicated a dose-response relationship between BMI and mortality.[17]

Some studies have determined that younger patients with COPD show more depression and anxiety symptoms and low quality of life than older ones. This information is consistent with research on a diversity of chronic illnesses that specify that young age disease is associated with more psychological distress and lessens life quality. More distant, the influence of age on patient outcomes may vary based on educational and social supplies. The effect of age may be substantial between

individuals with fewer resources. Psychosocial interventions can pick out the most in need if authorities can recognize persons' attributes for whom a young age presents a higher risk for adverse outcomes.[18]

This study investigated whether BMI, age, complete blood count, and various biochemical parameters are associated with disease severity in COPD patients. We used the GOLD index to determine the severity of the disease.

MATERIAL AND METHOD

Ninety patients with COPD, whose mean age was 62, and 74% were male, diagnosed and treated Afyonkarahisar university of health sciences Medical Faculty, Department of Pulmonology, Afyon, Turkey were included in our study. According to the GOLD classification, the patients were divided into four groups as A, B, C, and D. Pulmonary function test data, complete blood count values, Crp, Pct, sedimentation, calcium, and magnesium parameters of the patients were compared according to the groups. Univariable and multivariable analyses were conducted to investigate the association between biochemical parameters, BMI, age, gender, and disease severity, according to GOLD subgroups. Groups were adjusted to describe potential confounding factors: smoking status, pef25-75 value, asthma history, moderate exacerbations, or one or more severe exacerbations during one year. Standard distribution variables calculated using the ANOVA test. We analyzed variables as mean±standard error (SE), mean±standard deviation (SD). P-values below 0.05 were considered significant. Statistical analyses were performed using JASP 0.14 statistical software (JASP team, Amsterdam, Netherlands).

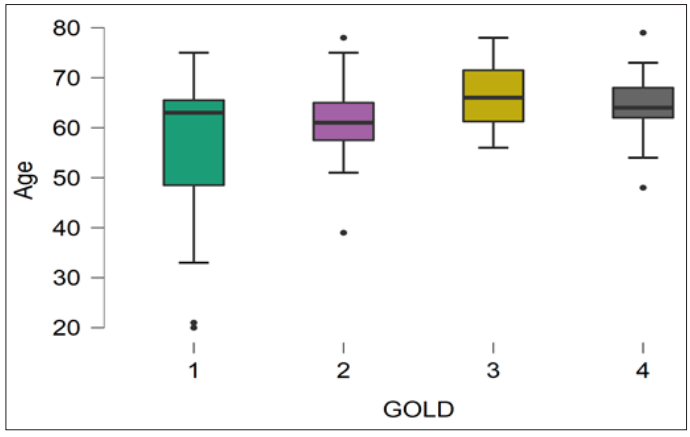

Figure 1. Relationship between age and GOLD groups. A, B, C and D groups are shown as 1, 2, 3 and 4.

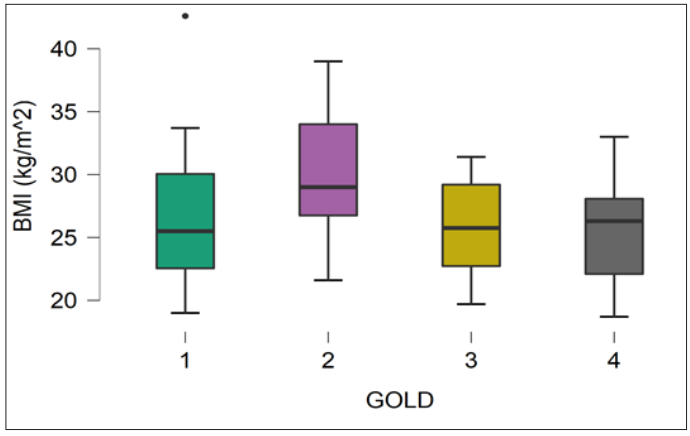

Figure 2. Relationship between BMI and GOLD groups. A, B, C and D groups are shown as 1, 2, 3 and 4.

RESULTS

According to the GOLD classification, a statistically significant difference was found between mean age values of group A and groups C and D (p <0.001, p=0.015), and the statistically insignificant difference between group B (p=0.129) (**Figure 1**). Groups C and D were older than group A. The mean BMI values of group B were significantly higher than groups A, C, and D (p=0.047, p=0.026, p=0.021) shown in **Figure 2**. Neutrophil percentage values were significantly different between the groups (p=0.004), and group C had a significantly higher percentage of neutrophils than group A (p=0.026). Similarly, monocyte percentage values were significantly different between the groups (p=0.048), and group C had a significantly lower percentage of monocytes than group A (p=0.028). However, platelet levels were significantly different between the groups (p=0.004), and group C had significantly lower platelet levels than group A (p=0.006). The groups' eosinophil percentage values were 3.49, 2.41, and 2.35, 3.16, respectively, but no statistical correlation could be established between them. Crp, Procalcitonin, Sedimentation, Calcium, Magnesium levels, and other complete blood count values showed no significant difference between GOLD groups. Descriptive statistics are given in **Table 1**.

Table 1. Mean and SD levels and p-values of evaluated parameters according to GOLD groups.

GOLD	A	B	C	D	p-Value
BMI (kg/m^2)	26.6±5.8	30.1±5.3	26.2±3.7	25.5±4.0	=0.021
Age	54.3±15.7	61.8±9.1	66.3±6.8	64.3±7.9	<0.001
Fev1/Fvc (%)	63.3±5.9	58.4±8.1	57.2±8.0	48.4±10.7	<0.001
Eosinophile(%)	3.32±1.74	2.39±1.44	2.60±1.29	3.05±2.57	=0.004
Crp (mg/L)	2.064±1.32	0.57±0.26	1.86±1.59	2.03±1.97	=0.867
Sedimentation (mm/hour)	36.1±13.2	24.1±13.3	27.5±14.3	26.8±17.4	=0.643
Hct (%ml)	40.2±7.3	44.1±6.2	43.7±7.2	45.1±6.2	=0.941

BMI: Body mass index, Crp: C-reaktif protein Hct: Hematocrit

DISCUSSION

COPD is generally diagnosed after the age of 45 and is mostly acknowledged disease of the elderly. It's thought to be an advancing sickness that takes many years to develop. As stated by the Burden of Obstructive Lung Disease (BOLD) Initiative, the approximate international prevalence of stage II or worse COPD is recently 10.1% in persons aged 40 years and older. However, it should be kept in mind that in some genetic conditions such as alpha-1 anti-trypsin deficiency, COPD can be seen under the age of 40.[19] According to the results we obtained in our study, the mean age was 61+/-10 years, and the average ages, according to the groups, were 55, 61, 64, and 59, respectively. Our results are consistent with previous studies where COPD patients are usually over 40 years old, and age is linked to disease severity. The longer individuals have particular risk factors for COPD; they would more probably develop the disease as an older adult. There is accumulating confirmation that aging characteristics are notable features of COPD. These aging characteristics have been defined in several sub-groups of COPD patients, different lung compartments, and a range of cell types. So, they could commit to different COPD phenotypes. A better considerate of the principal differences and similarities between normal lung aging and the pathology of COPD may develop our comprehension of the mechanisms utilizing COPD pathology, especially in those patients that produce the most vigorous form of COPD at a relatively young age.[20]

While spirometry is used for diagnosis and degree of COPD intensity concerning the GOLD guidelines, classification of overweight and obesity is based on body mass index (BMI) as described by the World Health Organization (WHO). The prevalence of obesity, designated as BMI >30 kg/m^2, has increased during the last decades and alters from 10–20% in most European countries to 32% in the USA. Obesity has a central role in improving metabolic syndrome and has been determined as a significant risk factor for chronic illnesses like type 2 diabetes mellitus and cardiovascular disease.[21-22] Obesity is associated with respiratory conditions such as obstructive sleep apnoea syndrome and obesity hypoventilation syndrome, and gathering proof proposes a relationship between obesity and asthma.[23] A possible connection between obesity and COPD is also progressively realized, although not much is known about this relation's mechanisms.[24] In patients with COPD, obesity is usually correlated with a heightened risk of mortality; on the other hand, surprisingly, several studies have indicated that being overweight or obese may offer a survival advantage over a fatless phenotype.[25] COPD patients with a reduced BMI lean to have an advanced mortality rate than patients of normal BMI. Individuals that were overweight or obese had a lower risk of mortality, which formed the "obesity paradox." BMI is a simple sign of weight for height and cannot diversify between lean muscle mass metabolically and functionally active and fat mass. Consequently, BMI can be a fallacious index of survival or health outcomes in COPD patients.[26] Our study found that the BMI averages of the patients in the GOLD B group were compatible with obesity and were significantly higher than the other groups. While the BMI values of the patients in group B were higher than those of group A, it was compatible with studies showing the relationship between obesity and severity of COPD; being higher than C and D groups was consistent with the studies revealing the obesity paradox. Considering all groups, BMI values were not correlated with COPD severity. At this point, we concluded that BMI values do not correlate with disease severity and prognosis since they do not reflect the amount of muscle mass that is more closely related to the prediction of COPD. Concerning BMI evaluation in COPD, we predict that respiratory muscle amount and activity are more valuable in predicting the disease's clinical course.

Evaluation of COPD is set mainly on clinical presentations, which can be unstable, and due to these, many biomarkers are also appraised.[27] Blood culture has been mostly used as a conventional approach for the detection of any infectious reason. Nonetheless, blood cultures are time-consuming, and it takes days to weeks to specify the microorganism in the blood. Complete blood count analysis like total leukocyte and the neutrophil count is performed in all exacerbation cases and has a restricted significance in the early detection of community-acquired pneumonia.[28] Even though new markers as procalcitonin and pro-adrenomedullin are being interpreted, these markers' quick application is hindered by validation, expenses, and accessibility.[29] Studies indicated the relationship between lymphocyte count, hemoglobin, platelet count, mean platelet volume, platelet distribution width, and reticulocyte distribution width with COPD.[30,31] COPD patients can divide into eosinophilic (peripheral blood eosinophil rate ≥2%) and neutrophilic (peripheral blood eosinophil rate <2%), and further subdivided according to the place of admission (inpatient, outpatient, or intensive care unit [ICU]) as a sign of disease intensity.[32] Eosinophil percentage values were more outstanding than two in our patient groups, which showed us that we have patients with the eosinophilic type that is a valuable indicator for corticosteroid response. Still, the lack of difference between the groups made it impossible for us to differentiate. Group C had a significantly higher percentage of neutrophils, substantially lower percentage of monocytes, and appreciably lower platelet levels than group A. We could not reach differential values in terms of complete blood count parameters in patients. Whole blood parameters, which are stated to be useful in determining the severity of COPD in the literature, and the practice of using them in proportion to each other, were evaluated based on acute exacerbation cases. We studied these parameters in our patients for general evaluation, not acute exacerbation. Therefore, we could not find values that differentiate in the data according to disease severity. Consequently, we do not see it to evaluate according to these parameters in COPD patients, except for acute attacks. Using the same logic, we better understand why Crp, Procalcitonin, Sedimentation, Calcium, and Magnesium levels do not differ significantly between groups. Although there are many studies on acute exacerbation, there are not enough studies to evaluate patients in general and to predict the severity of the disease,

and advanced studies, mainly including control groups, are needed. The essential data we have obtained in our study is that; Age and BMI have a significant effect on disease severity and prognosis in patients with COPD, except for acute attacks.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Academical Ethics Committee of Afyonkarahisar Health Science Üniversity (Permission granted: 11.09.2020, Decision no: 2020/396).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Problems Related to Surgery and Pathology in Lip Cancer Patients and Their Management

Dudak Kanseri Hastalarinda Cerrahi ve Patolojiye İlişkin Sorunlar ve Yönetimi

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Abstract

Purpose: Lip cancers are the second most common cancers of head and neck region. Due to its functional and aesthetic consequences and aggressive course, clinical approach including surgical margins, type of neck dissection and reconstruction techniques are debated topics in lip cancer. We investigated reliability of preoperative evaluations, pathological risk factors for recurrence or metastasis, surgery related morbidities and their management.

Material and Method: The records of patients with basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) were reviewed retrospectively. Demographic data of the patients were evaluated, the reliability of the punch biopsy and radiological imaging was discussed and the effects of pathological features on the risk of recurrence and metastasis was investigated. Surgery related morbidities were revealed. All these problems and their solutions were discussed in the light of literature.

Results: Punch biopsy was found unreliable in this study. Relapses were associated with advanced stage and perineural invasion while cervical metastasis was related with the size of the specimen and surgical margins. Donor site morbidities were higher in local flaps. Recurrence or metastases were not observed in patients who were treated with extensive excision, neck dissection and reconstruction with free flap.

Conclusions: Early diagnosis and functional and aesthetic repair are the most important factors in terms of prognosis in lip cancer. First surgery is very important that determines the prognosis. As the stage progresses, the surgery becomes complex but prognosis can be as good as early stages with good clinical approach.

Keywords: Lip, cancer, prognosis, reconstruction, techniques

Öz

Giriş: Dudak kanserleri baş boyun bölgesinde ikinci sıklıkta görülen kanserlerdir. Fonksiyonel ve estetik sonuçları ve agresif seyri sebebiyle cerrahi eksizyon sınırları, boyun diseksiyonu tipi ve rekonstrüksiyon seçenekleri gibi klinik yaklaşım tipleri dudak kanseri hakkında tartışılan konulardır. Çalışmada cerrahi öncesi yapılan değerlendirmelerin güvenilirliği, rekürrens ve metastaz için risk faktörleri, cerrahiye bağlı morbiditeler ve tedavileri araştırıldı.

Gereç ve Yöntem: Kliniğimizde tedavi edilen bazal hücreli karsinom ve squamoz hücreli karsinom tanılı hastaların verileri retrospektif olarak tarandı. Hastaların demografik verileri değerlendirildi, punch biyopsi ve radyolojik görüntülemelerin güvenilirliği tartışıldı ve patolojik özelliklerin rekürrens ve metastaz risk üzerine etkileri araştırıldı. Cerrahi sonrası morbiditeler değerlendirilerek tüm bu problemler ve çözüm yolları literatür eşliğide tartışıldı.

Sonuç: Bu çalışmada punch biyopsi güvenilir bulunmadı. Rekürrensler ileri evre ve perinöral invazyon ile, servikal metastazlar ise çıkartılan lezyon boyutu ve cerrahi sınır ile ilişkili bulundu. Lokal fleplerde donor alan morbiditeleri daha yüksekti. Geniş eksizyon, boyun diseksiyonu ve serbest flep ile rekonstrüksiyon yapılan hasta grubunda rekürrens veya metastaz gözlenmedi.

Tartışma: Erken tanı ve fonksiyonel-estetik onarım dudak kanseri prognozunda en önemli faktörlerdir. Yapılan ilk cerrahi prognozu belirlediğinden çok önemlidir. Evre ilerledikçe cerrahi kompleksleşir fakat iyi bir klinik yaklaşım ile erken evreler kadar iyi bir prognoz sağlanabilir.

Anahtar Kelimeler: Dudak, kanser, prognoz, rekonstruksiyon

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INTRODUCTION

Lip carcinoma is one of the most common type of malignant tumors of head and neck region, with an incidence of 1.8 per 100,000.[1] While melanoma is very rare, the most common histopathological type in lip cancer is squamous cell carcinoma (SCC) and it is more aggressive when located on lips compared to other cutaneous parts of head and neck region.[2,3] Due to its functional and aesthetic consequences and aggressive course, clinical approach including surgical margins, type of neck dissection and reconstruction techniques are debated topics in lip cancer.

When surgery, radiotherapy, chemotherapy are used together or alone in the treatment, the first and the main treatment method is surgical excision. Radiotherapy can be used to treat small cutaneous lesions at early stages or in patients at high risk for operation or who do not accept the surgery.[4]

First surgery is very important that determines the prognosis; excision with clean surgical margins and neck dissection in the advanced stages are highly important. To remove the tumor safely, it is recommended to plan the tumor-free surgical margins at least 10 mm.[5] On the other hand, Babington et all reported ideal margins as 4-5 mm and offered adjuvan radiotherapy if the goal is not achieved.[6]

Lymph node metastasis rates range from 3 to 29%. While some authors prefer to do elective node dissection for all patients, others choose to do for only clinical node positive patients.[7] Five percent of patients, who have not undergone neck dissection due to negative clinical and imaging findings, present with recurrences in the neck region later.[8] Sentinel node dissection is recommended for node-negative lip SCC as a safe and feasible procedure.[9] It is recommended to do elective node dissection for tumors larger than 3 cm; and selective node dissection in perineural invasion and low differentiation.[10,11] However, there is still no consensus in this topic. Surgeons choose 'overtreatment' or 'wait and see'.

The best reconstruction technique should be selected according to the defect. The main goal in reconstruction is to provide a functional and aesthetic repair. The aim of our study was to evaluate patients who were admitted to our clinic with lip cancer and to obtain demographic properties of the patients, determinate the location, type, differentiation and stage of the tumors, address the reliability of preoperative radiologic images and punch biopsies, asses the regional metastasis and local recurrence rates according to the pathological features, assess local and other morbidities according to surgical procedure including excision, reconstruction techniques and neck dissection, compare all these problems and their managements with literature.

MATERIAL AND METHOD

The records of 66 patients with malign lip tumors were retrospectively reviewed after the approval of local Ethics Committee and in compliance with the Declaration of Helsinki. Malignant melanoma or any other tumors in any part of the body or who receive chemotherapy and/or radiotherapy, also patients with concomitant diseases were excluded to be able to discuss only surgery and pathology related problems. Minimum follow-up time was two years.

Age and sex of the patients were obtained as demographic properties. Location, type, differentiation and stage of the tumors were determined.

The reliability of punch biopsy and preoperative ultrasonographic (USG) results were investigated by comparing with last pathology results.

Pathological features including tumor type, size, distance to surgical margins, presence of perineural invasion, differentiation, and stage were compared with lymph node metastases and recurrence rates.

Microstomies, commissural deterioration, vestibular insufficiency, drooling, donor-side morbidities were evaluated by comparing the types of flaps used for reconstruction according to the defect. Presence of hemorrhage, embolism, or nerve injury, fistula, recurrence rates were evaluated related to neck dissection.

All statistical analyses were performed in two ways using SPSS 15 (IBM Inc, USA) software. Nonparametric assessments were performed by Mann-Whitney U test for numerical data in comparison between independent data groups, and categorical data were compared by Fisher's Chi-square test. Student t test was used to compare survival rates between independent data groups. Two-tailed p values <0.05 were considered significant.

RESULT

41 men and 25 women (mean age: 65.6 years) were included in the study. Regarding the location; 77% of the tumors were in lower lip and 94% of those were SCC. In the upper lip, 87% of the patients had SCC and the remaining 13% had BCC. Lip tumor location was in 29% medial, 26% left lateral and 45% right lateral region.

According to the staging system defined by the 7th edition of the American Joint Committee on Cancer (AJCC), 64% of patients were stage 1, 17% of patients were stage 2, 4% of patients were stage 3, and 11% of patients were stage 4a.[12] When patients pathological results were evaluated in terms of differentiation grade; 63% were well, 34% were moderate, and 3% were less differentiated.

There were three false possitive and one false negative results of preoperative USG investigation about metastatic lenf nodes comparing the last pathology results.

In 55% of 20 patients who underwent punch biopsy of 4 mm in diameter were compatible with the actual pathology; while 45% were incompatible.

There was no significant difference between patients with punch compatible and incompatible results according to the stage ($p=0.722$) and tumor type ($p=0.596$). It was observed

that the patients whose punch biopsy results were not clearly distinguished and/or resulted with benign lesions, returned to the clinic with recurrence within 12 months.

Properties of the patients and risk factors for recurrence, properties of the patients and risk factors for cervical lymph node metastasis were described in **Table 1-4**.

We defined the surgical margins minimum 5 mm for BCC and 10 mm for SCC. In our study, pathological margin was positive in 5 patients (7.57%) who underwent excision with a minimum of 1 cm limit and required re-excision. For this reason, factors such as tumor size, the time passed since the lesion appeared, and the presence of LAP were evaluated from the patients who applied to our clinic, and excision is performed with a 2 cm surgical margin for the patients who were in advanced stages.

Minimum follow-up time was two years in this study. At second year overall survival (OS) rate was 90.9% and disease free survival (DFS) rate was 80.3%, locoregional recurrence-free survival (LRFS) rate was 80.3%. Recurrence was seen in nine patient and locoregional metastasis was seen in 6 patient within the first two years. Recurrence was more frequent in patients with advanced stage (sig.= 0.041<p value=0.05) and perineural invasion (sig.=0.009<p value 0.05) and locoregional metastasis was proportional to the size of the specimen (sig.=0.014<p value=0.05) and proximity to the surgical border (sig.=0.025<p value=0.05).

Table 1. Properties of the patients with recurrence

	Age	Sex	Specimen Size (cm)	Lesion Size	Location	Surgical Margin	Diferenciation	Stage	Perineural İnvasion	Perinodal İnvasion
1	59	M	3.5x3x1,2	1.7x1.2x1	Lateral Inferior	4 mm	Moderate	1	-	-
2	80	M	4x2.5x1.5	1.5x1.2x1.2	Median Inferior	4 mm	Well	4a	+	+
3	45	F	2.5x1x1.5	2.4x0.6x0.5	Median Infeior	2 mm	Well	4a	-	-
4	65	F	4.3x2.4x2.6	2x1x1	Lateral Upper	14 mm	Moderate	2	-	-
5	62	F	3.5x2x1.5	2.8x1x1.8	Lateral Inferior	3 mm	Well	4b	+	-
6	64	M	2.5x2.5x1.5	1.7x1.5x1.1	Lateral Inferior	4 mm	Poor	1	-	-
7	61	M	3.5x2.6x1.7	2x1.6x1.1	Lateral Inferior	4 mm	Well	2	-	-
8	74	F	7x3x2	6.8x3.5x5	Lateral Inferior	0 mm	Moderate	4a	+	+
9	63	M	8.2x7x5.5	6.5x5x5.5	Lateral Inferior	5 mm	Moderate	4a	+	-

Table 2. Risk factors for recurrence

	Recurrence +	Recurrence -	P value
Specimen size	496.240 mm^3 (SD±108.89)	102.260 mm^3 (SD±62.35)	sig.= 0.782>p value=0.05
Lesion size	66.214 mm^3 (SD±35.11)	35.424 mm^3 (SD±11.93)	sig.= 0.333>p value=0.05
Surgical Margin	3 mm (SD±2.646)	5.02 mm (SD±4.102)	sig.= 0.162>p value=0.05
Stage	2.56 (SD±1.424)	1.8 (SD±1.142)	sig.= 0.041<p value=0.05
Location	8 inferior,1 upper	14 upper, 43 infeior	sig.=0.58>p value 0.05
Pathologic type	8 SCC, 1 BCC	15 BCC, 42 SCC	sig.=0.07>p value 0.05
Perineural invasion	4 (+), 5 (-)	5 (+), 52 (-)	sig.=0.009<p value 0.05

Table 3. Properties of the patients with cervical lymph node metastasis

	Age	Sex	Specimen Size (cm)	Lesion Size	Location	Surgical Margin	Diferenciation	Stage	Perineural İnvasion	Perinodal İnvasion
1	78	F	4x3.5x2	3x3x2	Lateral Upper	5 mm	Moderate	2	-	-
2	56	F	7.5x3.5x1,3	5.8x2.9x1.1	Median Inferıor	2 mm	Moderate	4b	-	-
3	69	M	1.3x1.2x0.8	1.1x1x0.7	Median Inferior	1 mm	Well	1	-	-
4	54	M	1.4x0.6x0.5	0.7x0.6x0.5	Median Inferior	0 mm	Well	1	-	-
5	58	F	2x1.8x1.3	0.6x0.5x0.5	Lateral Inferior	5 mm	Well	1	-	-
6	54	M	2.5x1.3x1	2.1x0.7x0.4	Median Inferior	0 mm	Well	2	-	-

Table 4. Risk factors for cervical lymph node metastasis

	Metastasıs +	Metastasıs -	P value
Specimen size	1287.020 mm^3 (SD±493.89)	101.728 mm^3 (SD±46.61)	sig.= 0.014<p value=0.05
Lesion size	44.465 mm^3 (SD±16.99)	8.657 mm^3 (SD±5.59)	sig.= 0.504>p value=0.05
Surgical Margin	2.43 mm (SD±2.225)	5.02 mm (SD±4.058)	sig.= 0.025<p value=0.05
Stage	2.14 (SD±1.345)	1.90 (SD±1.199	sig.= 0.623<p value=0.05
Location	5 inferior,1 upper	14 upper, 46 infeior	sig.=0.95>p value 0.05
Pathologic type	6 SCC	16 BCC, 44SCC	
Perineural invasion	6 (-)	9 (+), 57 (-)	

For reconstruction; primary closure (37.5%), local flaps (33%), regional flaps (12.5%) and free flaps (radial forearm fasciocutaneous, split rectus muscle (**Figure 1**), fibula ossecutaneous, DIEP fasciocutaneous) (16.6%) were used according to the defect size and location. Among the patients who underwent reconstruction with free flaps; one was having stage 1 disease, three were stage 2, three were stage 3, two were 4a, and one was 4b and three of them were with recurrences. No microstomies were observed except one patient who was repaired with a free split rectus muscle flap. There was no drooling in any of the patients whose commissure was preserved and that reconstructed with free radial forearm flap containing palmaris longus. Tendon exposures at radial forearm flap donor area were repaired with ulnar artery based perforator flap in 2 patients. Sensory loss was observed in 2 patients treated with Eslander flap, and drooling was observed in a patient who was treated with Gilles flap. Orocutaneous fistula was determined in 2 patients; one was repaired by classical methods; the other was controlled by early Botulinum toxin injections.

We used tongue flap for one patient with vestibular sulcus insufficiency that was reconstructed with local flap; and applied horizontal incision and vertical suturation for the other. K-M plasty was required in 2 patients complained of microstomies after reconstruction with Gilles and free split rectus muscle flap. Five patients with mandibular invasion were treated with bone graft after segmental mandibulectomy; one patient was treated with reconstruction plate alone, and one patient with free fibula flap.

Neck dissection was performed during the initial surgery in 16 patients with SCC. While there were no recurrences in long-term in the patients who had neck dissection; neck dissection was not present in any of the patients who had metastasis in follow-up. No complications such as intraoperative hemorrhage, embolism, or nerve injury occurred in any of the patients, while there was chylous fistula in 2 patients, and they were spontaneously dropped back with fat free diet.

DISCUSSION

The lip is an important aesthetic unit in the lower 1/3 of the face and an essential structure for many functions such as eating, drinking, speaking and laughing. The most common lip cancer type is SCC, originating from epithelium.[13] Lip cancer requires a good clinical approach due to its aggressive course. Early diagnosis and adequate treatment are the most important factors in terms of prognosis. USG is useful in evaluating the spread to neck soft tissues and lymph nodes. Computed tomography (CT) is more valuable in evaluating invasion into bone structures.[14] Immunological agents can be used in the treatment.[15] However, definitive treatment is provided by surgery.

In literature, 75% of the patients diagnosed with lip cancer are over 50 years old.[16] In our study, the average age of the patients was 65.6 years. Our results were compatible with the previous literature. However, in the literature, male to female ratio was reported as 6-8/1, but in our study 62% of the patients were male which was a highly lower ratio compared with the literature.[17]

Figure 1. Reconstruction of the defect at lower lip with free split rectus abdominis muscle flap, contruction at the flap at long-term follow-up

Salgarelli and colleagues found that 80-95% of the lesions were at lower lip, 2-12% of them were at upper lip, and 1-15% of them were in the commissure in the patients with lip cancer.[18] In our study, 77% of the patients with lip cancer had lower, 23% had upper lip localizations, which was compatible with the literature.

While SCC is most commonly located in lower lip, BCC is seen most frequently in upper lip.[19] In our study, consistent with the literature there were 13% (n=2) SCC and 87% (n=13) BCC in the patients with upper lip tumors. Pathological results were SCC in 94% (n=48) and BCC in 6% (n=3) of patients with lower lip tumors, compatible with the literature.

Effiom et al.[20] detected poor differentiation in 47.6% of 233 patients in their studies in Nijeria. It can be diagnosed earlier in developed countries. In our study, 65% of the patients were at stage 1, 16% were at stage 2, 5% were at stage 3, 10% were at stage 4a and 4% were at stage 4b.

Ultrasonography has been found to be used for the detection of preoperative neck metastases with close sensitivity and specificity compared with computerized tomography and/or magnetic resonance imaging by Yoon et al.[21] Patients were routinely screened with pre-operative neck USG for the detection of lymphadenopathy (LAP) presence in our clinic. When the results of USG examination and pathology were compared in this study, it was seen that there were three false positive and one false negative results and the difference was not statistically significant.

It has been described that 75% of local recurrences and metastases of SCCs is seen within 2 years.[22] Local recurrence rate in the literature is reported as 5- 15%.[23] In our study, recurrence was observed in 13.6% in the first two years, statistically related with advanced stage and perineural invasion.

Lymph node metastasis rates range from 3 to 29% in lip tumor and it is recommended to do elective node dissection for tumors larger than 3 cm; and selective node dissection in perineural invasion and low differenciation.[11,24] In our study, metastasis was observed in 9.09% in the first two years, statistically related with size of the specimen and proximity to the surgical border.

First surgery is very important that determines the prognosis. To remove the tumor safely, it is recommended to plan the surgical margins at least 10 mm.[5] In our study, surgical margin was positive in 5 patients (7.57%) who underwent excision with a minimum of 1 cm limit and required re-excision. For this reason, factors such as tumor size, the time passed after the first appearance of the lesion, and the presence of LAP were evaluated in patients who applied to our clinic, and excision was performed with a 2 cm surgical margin.

The main goal in reconstruction is to provide a functional and aesthetic repair. For this purpose there are many options. While reconstruction like with like and short operation time are advantages of local flaps; microstomy, scar formation in the lip, numbness are disadvantages. In reconstruction with free flaps, the tumor excision is performed more courageously, which provides better prognosis with negative surgical margins but donor site morbidity in any other part of the body is disadvantage. Tendon exposures were occurred in two patients at radial forearm flap donor area repaired with ulnar artery based perforator flap.

During reconstruction with local flaps from the opposite lip, flap width should be planned as half of the defect. While the disadvantage of repairing with Abbe flap is requirement of a two stage operation; commissure may be replaced with Eslander flap and as stated by Kroll, commissuroplasty may be required.[24] Defects up to 80% can be repaired by Gilles flap but microstomy, loss of sensation and oral incubation may take place.[26] Since the neurovascular structures are protected in Karapandzic flap, motor and sensory function is obtained.[27] Sensory loss was observed in 2 patients treated with Eslander flap, and drooling was observed in a patient who was treated with Gilles flap. Orocutaneous fistula was determined in 2 patients; one was repaired by classical methods; the other was controlled by early Botulinum toxin injections. We used tongue flap for one patient with vestibular sulcus insufficiency that was reconstructed with local flap; and applied horizontal incision and vertical suturation for the other. K-M plasty was required in 2 patients complained of microstomies after reconstruction with Gilles and free split rectus muscle flap.

In this study, as the stage progressed, the amount of excision and repair techniques became more complex. Elective or selective neck dissection were applied for all of the patients who were reconstructed with free flap at the same time and no recurrence or metastasis was observed in any of these patients though they were in advanced stages. Through this information, aggressive treatment in lip cancer management could also provide cure in advanced stage.

The disadvantages of repairing with free flaps are the long operation time and insufficient motor and sensory functions after reconstruction. However, radial forearm flap is the most commonly preferred free flap for reconstruction of lip; 2 patients were repaired with free split rectus muscles to obtain motor functions.[28] The disadvantage of this flap is that the duration of the innervation of the muscle is long and some atrophy may occur since the patient's are geriatric. Therefore, flap size should be planned at least 50% larger than the defect.

CONCLUSION

The lip is an important aesthetic unit in the lower 1/3 of the face and a necessary structure for many functions such as eating, drinking, speaking, and laughing. Early diagnosis and adequate treatment are the most important factors in terms of prognosis. In the surgical treatment of lip cancer, the tumor should be removed as widely as possible and reconstructed with sufficient tissue to obtain a functional and aesthetically successful result. We believe that as the stage progress, the surgery becomes complex but prognosis can be as good as early stages with good clinical approach.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Selcuk University Ethic Committee (Permission granted: 07.06.2017, Decision no: 70632468-050.01.04).

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

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Orjinal Araştırma / Original Article

The Effect of Different Monitor Use on Radiography Interpretation in Emergency Medicine

Acil Tıpta Farklı Monitör Kullanımının Radyografi Değerlendirmeye Etkisi

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Abstract

Aim: Although it is recommended to use a medical monitor in radiology guides, it is rare to use a medical monitor in non-radiology departments. In this study, the effect of using LED, tablet and medical monitor in the radiography evaluation of inexperienced physicians in the emergency room was investigated.

Material and Method: Fifty medical intern from the medical school were included in the study. Participants were asked to diagnose pre-prepared radiography sets on LEDs, tablets and medical monitors and to request a radiology consultation for radiographs they could not decide. The diagnoses of medical interns and cases of requesting radiology consultation were recorded.

Results: The median values of the correct diagnosis of the participants according to the monitors; 13.5 on led monitor, 13 on tablet monitor and 16 on medical monitor. The median value of the desired radiology consultation numbers; 6 on led monitor, 7 on tablet monitor and 4 on medical monitor. The medical monitor has statistically significant difference to the other two monitors, in the correct diagnosis and number of consultations desired.

Conclusion: The use of medical monitors by inexperienced physicians in the emergency room where workload is extreme and time is valuable, will increase the diagnosis accuracy and decrease the rate of request for consultation

Keywords: Emergency medicine, radiography, radiologic technology

Öz

Amaç: Radyoloji kılavuzlarında medikal monitör kullanımı önerilmesine rağmen medikal monitörlerin radyoloji dışı bölümlerde kullanımı nadirdir. Bu çalışmada acil serviste tecrübesiz hekimlerin radyografi yorumlanmasına; led, tablet ve medikal monitör kullanımının etkisini araştırdık.

Gereç ve Yöntem: Çalışmaya tıp fakültesinden 50 intörn doktor dahil edildi. Katılımcılardan önceden hazırlanmış radyografi setlerine led, tablet ve medikal monitörlerde tanı koymaları, karar veremedikleri radyografiler için radyoloji konsültasyonu istemeleri istendi. Katılımcıların tanıları ve radyoloji konsültasyonu isteme durumları kaydedildi.

Bulgular: Katılımcıların monitörlere göre doğru tanılarının median değerleri; led monitörde 13.5, tablet monitörde 13 ve medical monitörde 16 olarak bulundu. İstenilen radyoloji konsültasyonu sayılarının medyan değeri; led monitörde 6, tablet monitörde 7 ve medikal monitörde 4 olarak bulundu. Medikal monitör, doğru tanı ve istenilen konsültasyon sayısında diğer iki monitöre göre istatistiksel olarak üstün bulundu.

Sonuç: Tecrübesiz hekimlerin, acil servis gibi iş yükünün fazla ve zamanın değerli olduğu yerlerde medikal monitör kullanmaları tanı doğruluğunu artıracak ve konsültasyon isteme oranını azaltacaktır.

Anahtar Sözcükler: Acil tıp, radyografi, radyolojik teknoloji

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INTRODUCTION

Radiological imaging methods are frequently used examinations in the field of emergency medicine. Conventional radiographs form the basis of radiological imaging and are used in patient management in the emergency service.[1] Rapid and accurate interpretation of radiological images affects patient management positively in emergency departments competing with time.

Led monitors are widely used in non-radiology departments in hospitals. Today, the use of tablets is gradually increasing in medicine as well as in daily life. The use of mobile devices enables the physicians to evaluate the examination at the bedside of the patient and make consultations quickly. In the literature, no significant difference between the led monitor and tablet monitor was found in the studies comparing the two monitors in radiological evaluations.[2,3] Medical monitors become prominent at this point because the brightness level of led screens is not the same in all areas.[4] Although it is recommended to use medical monitors in radiology guidelines, the usage of medical monitors in non-radiology departments is rare.[5-8]

In this study, we investigated the effects of using LEDs, tablets, and medical monitors on radiography interpretation of inexperienced physicians in the emergency service.

MATERIAL AND METHOD

This study was carried out at Balıkesir University between December 2019 and February 2020. 50 medical intern from the medical school who completed their emergency medicine education were included in the study. Participants were asked to diagnose previously prepared radiography sets displayed on different monitors. They were told that they could ask for a radiology consultation for radiographs they could not decide on. Three different sets of radiographs were used in order to prevent the increased experience of medical interns while evaluating the radiographs. Radiography sets were prepared for the study by a radiology team blinded to the study. The sets were created from 20 similar radiographs (10 musculoskeletal, 5 chest, and 5 gastrointestinal) at the same difficulty level, containing the same pathologies. All radiographs were selected from images captured by using the same X-Ray device (XGEO GU60A Samsung, Korea). All participants evaluated the first radiography set on the LED monitor (18.5" VS197D Asus, Taiwan), the second radiography set on the tablet monitor (10.2" iPad 7th generation Apple Inc., Cupertino, CA), and the third radiography set on the medical monitor (21.3" RadiForce GX340 Eizo, Japan); all three sets were displayed over Picture Archival and Communication Systems (PACS). The physical conditions (e.g. light intensity, light angle, etc.) of the place where radiographic images are evaluated are important. Therefore, in our study, physicians utilized the monitors in the same room and under the same physical conditions. The diagnoses of medical interns and the requests of radiology consultation were recorded. The diagnoses given by medical interns to radiographs were evaluated by comparing with the diagnoses specified by the radiology team.

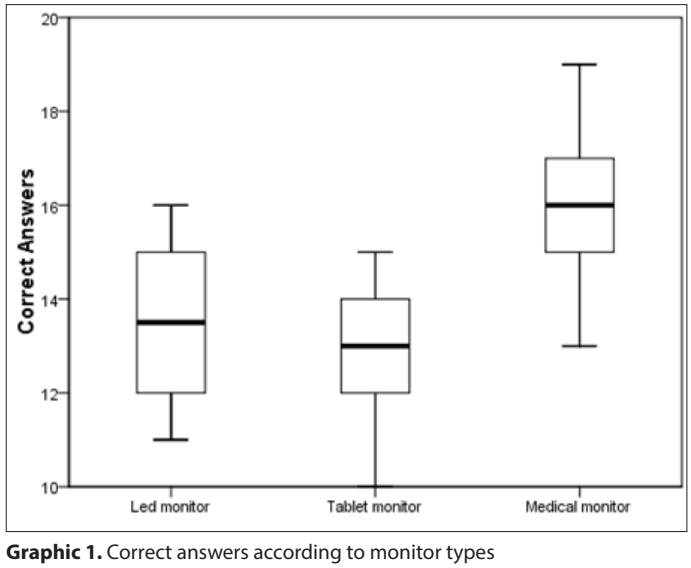
Data analysis

Statistical analyses were done with SPSS 25.0 (IBM Corporation, Armonk, New York, United States) and PAST 3 (Hammer, Ø., Harper, D.A.T., Ryan, P.D. 2001. Paleontological statistics). Mardia's and omnibus tests were performed to check univariate and multivariate normality; whereas, variance homogeneity was tested with the Box-M test. In the comparison of dependent quantitative variables with other measurements, Friedman's two-way test (Monte Carlo) test was utilized. Next, Dunn's test was performed for the post-hoc analysis. Quantitative variables are displayed with minimum and maximum values as well as the median in the tables. Variables were examined at 95% confidence interval and p value was set as less than 0.05 for the significant results.

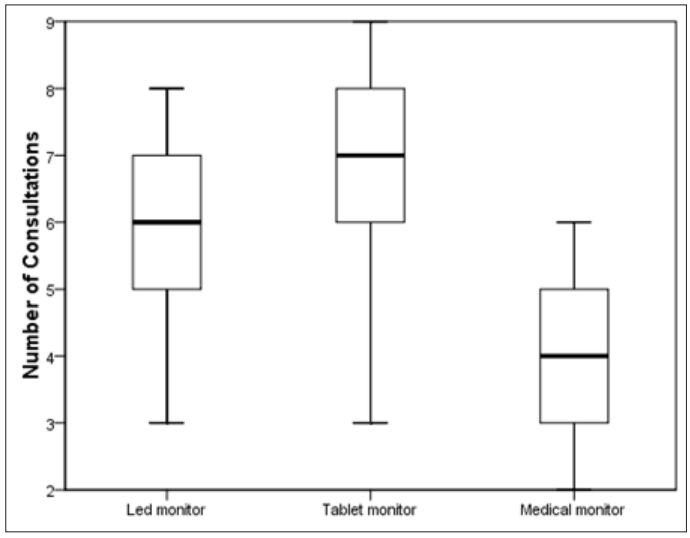
RESULTS

The median values of the correct diagnosis of the participants according to the monitors are as follows: 13.5 on led monitor, 13 on tablet monitor, and 16 on medical monitor. The median value of the number of radiology consultation requests are 6 on led monitor, 7 on tablet monitor, and 4 on medical monitor (**Table 1**).

When the monitors are compared in pairwise; the difference between the led and tablet monitor on the number of correct diagnoses and consultation requests was non-significant. However, the medical monitor was found to be statistically superior to the other two monitors in the correct diagnosis and the number of consultation requests (**Table 1**, **Graphic 1,2**).



Graphic 1. Correct answers according to monitor types



Graphic 2. The number of requested consultations according to monitor types

Table 1: Correct answers and the number of consultation requests on different monitors

		Correct Answers	Number of Consultations
		Median (Min/Max)	Median (Min/Max)
Led Monitor	I	13.5 (11/16)	6 (3/8)
Tablet Monitor	II	13 (10/15)	7 (3/9)
Medical Monitor	III	16 (13/19)	4 (2/6)
P Value		<0.001	<0.001
Pairwise comparison	I→II	0.197	0.531
	I→III	<0.001	<0.001
	II→III	<0.001	<0.001

Friedman Test (Monte Carlo); Post Hoc Test: Dunn's Test

DISCUSSION

In medicine, radiology is prominent among the departments benefiting the most from technological advances. Conventional radiography is one of the most used radiological examinations in the field of emergency medicine where rapid diagnosis and treatment are crucial.[1] Radiographs in emergency departments are generally evaluated on led monitors. With the widespread use of tablet monitors in hospitals in recent years, evaluation of radiological examinations on tablet monitors has increased.[2,9-11] Many studies revealed that tablet monitors can be used to evaluate radiological examinations.[2,12,13] When evaluating radiological examinations, it is extremely important that the screen has resolution, brightness and a wide range of grayscale. Therefore, medical monitors recommended by radiology guidelines are used as the gold standard.[5-8] Studies showed that tablet and led monitor have the same power of performance, and there is not significant difference between LED/LCD monitor and medical monitor.[9-13] There are studies in the literature showing that physician's performance is not affected by monitors.[14,15] However, the level of experience of physicians did not take place in these studies. We think that the physician's experience is important in radiological evaluations. Unlike the literature, in the current study, we compared the effects of three different monitors on conventional radiography evaluation performance of inexperienced physicians who are medical interns. To the authors' knowledge, the effects of these three monitors on radiography evaluation in the emergency service were not investigated yet.

In our study, there was not statistically significant difference between led and tablet monitors. However, the medical monitor provided higher diagnostic accuracy than the other two monitors. In addition, physicians requested fewer consultations while using the medical monitor. According to the results, the medical monitor enabled physicians to make more accurate and precise decisions. In addition to the literature, we think that medical interns benefit more from medical monitor's visual features because they are inexperienced. The effect of the medical monitor on increasing diagnostic accuracy and reducing the number of consultation request was also statistically significant ($p<0.001$).

Although it was recommended in the guidelines that monitor size should be wider than 15" for radiological evaluations, the size of the tablet monitor we used was 10.2".[5,8] However, it can be seen from the results that the tablet monitor has no disadvantages compared to the led monitor. Tablet monitors provide physicians with the advantage of radiographic evaluation at the bedside since they are portable. We think that this advantage is much more important in the fields such as emergency services and critical care areas where workload is high and time is limited.

Limitations

Considering the limitations, different radiography sets were used in our study. The fact that physicians looked at the same radiographs even on different monitors would increase familiarity with the radiographs. To prevent this, different sets of radiographs were prepared. Although the sets were created from similar radiographs containing the same pathologies by the independent radiology team blinded to the procedures, the difference between the sets may have affected the results.

CONCLUSION

The use of medical monitors by inexperienced medical interns in places such as emergency service where workload is high and time is invaluable will increase the accuracy of diagnosis and decrease the rate of requesting consultation. Additionally, there is not significant difference in radiography evaluation between led monitor and tablet monitor which has the advantages of portability.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study was conducted with the Balikesir University Clinical Research Ethic Committee with decision no. 2019/177 and date: 20.11.2019.

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Orjinal Araştırma / Original Article

The Effects of Immunophenotyping with Flow Cytometry on Prognosis in Acute Lymphoblastic Leukemia

Akut Lenfoblastik Lösemide Flow Sitometri ile İmmünofenotiplemenin Prognoz Üzerine Etkileri

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Abstract

Background: The identification of immunophenotype subgroups is very important for the diagnosis and prognosis of acute lymphoblastic leukemia (ALL).

Material and Method: The study is designed as a retrospective cohort study which included 105 children with ALL (65 males, 40 females; mean age 5.9±3.8 years) who were treated TR-ALL 2000 (modified) BFM treatment protocol.

Results: The distributions of EGIL classification were pro-B ALL (n=1), common B ALL (n=46), pre-B ALL (n=40), pre-T ALL (n=8), cortical T ALL (n=6), and mature T ALL (n=4). Leukocyte≥100,000/mm^3, lymphadenopathy≥2 cm, mediastinal involvement were commonly identified in T ALL group. T ALL had a poor response to chemotherapy according to 8th-day peripheral circulation blast counts and 15th-day bone marrow aspiration (BMA) blast counts. The recurrence, mortality, and death rate in the induction period of treatment were frequently detected in T ALL group. The variables that had prognostic potential, as indicated by univariate analyses, were leukocyte count, hepatomegaly, splenomegaly, and lymphadenopathy at the time of diagnosis, 8th-day steroid response, 15th-day BMA response, risk group, recurrence, and immunophenotyping. Multivariate Cox regression analysis demonstrated that only the leukocyte count (HR 2.51, $p < 0.001$) was a predictor of prognosis.

Conclusion: Immunophenotyping may be effective in the diagnosis and prognosis of ALL, identification of risk groups, and in risk-based treatment planning. T ALL had a poor prognosis.

Keywords: Flow cytometry, immunophenotyping, acute lymphoblastic leukemia, children

Öz

Giriş: Akut lenfoblastik löseminin (ALL) tanı ve prognozu için immünofenotip alt gruplarının tanımlanması çok önemlidir.

Gereç ve Yöntem: Çalışma, TR-ALL 2000 (modifiye) BFM tedavi protokolü ile tedavi edilen 105 ALL olgu (65 erkek, 40 kadın; ortalama yaş 5.9 ± 3.8 yıl) içeren retrospektif kohort çalışması olarak tasarlanmıştı.

Bulgular: EGIL sınıflaması dağılımları pro-B ALL (n=1), common B ALL (n=46), pre-B ALL (n=40), pre-T ALL (n=8), kortikal T ALL (n=6) ve matür T ALL (n=4). T ALL grubunda lökosit ≥100.000/mm^3, lenfadenopati ≥2 cm, mediastinal tutulum yaygın olarak tespit edildi. T ALL, 8.gün periferik kan yaymasında blast sayısı ve 15. gün kemik iliği aspirasyonu (KİA)' nundaki blast sayısına göre kemoterapiye kötü yanıt gösterdiği saptandı. Tedavinin indüksiyon döneminde nüks, mortalite ve ölüm oranı T ALL grubunda sık olarak görüldü. Tek değişkenli analizle gösterilen prognostik potansiyele sahip olan değişkenler tanı anında lökosit sayısı, hepatomegali, splenomegali ve lenfadenopati, 8. gün steroid yanıtı, 15. gün KİA yanıtı, risk grubu, nüks ve immünofenotip idi. Çok değişkenli Cox regresyon analizinde ise sadece lökosit sayısının (HR 2.51, $p < 0.001$) prognozu önemli derecede etkilediğini göstermiştir.

Sonuç: İmmünofenotipleme ALL'nin tanı ve prognozunda, risk gruplarının tanımlanmasında ve riske bağlı tedavi planlamasında etkili olabilir. T ALL tanısı alan hastalarda prognozun kötü olacağı gösterildi.

Anahtar Kelimeler: Akım sitometrisi, immünofenotipleme, akut lenfoblastik lösemi, çocuk

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INTRODUCTION

Leukemia comprises nearly 25-30% of childhood malignancies.[1] For acute lymphoblastic leukemia (ALL), previously known as a deadly disease, developments in diagnosis and treatment and advances in support treatments have achieved lengthened disease-free survival in most cases. In fact, 70-80% of cases have the chance of full recovery from the disease (cure).[1,2]

For pediatric ALL patients, for determination of both risk group and prognosis, the following factors are known; age, gender, leukocyte count, hematocrit value, platelet count, hepatomegaly, splenomegaly, lymphadenopathy presence, MSS involvement, testis involvement, mediastinal mass, and other extramedullary involvement, French-American-British (FAB) classification (L1, L2, L3), response to treatment, the molecular genetics such translocations, and the Minimal Residual Disease (MRD) status is defined by qPCR or NGS. Additionally, in recent times immunophenotyping results obtained by investigation of cytogenetic and molecular genetic disorders with flow cytometry have gained importance.[3-6]

The study aims to research the properties and effect on the prognosis of ALL immunophenotype subgroups and the evaluation of correlations between clinical and other laboratory data identified during the diagnosis stage.

MATERIAL AND METHOD

The study included 105 cases with ALL diagnosed in Pediatric Hematology and Oncology Department and treated with TR-ALL 2000 (modified) BFM protocol, followed up between January 2008 to March 2012. The study is designed as retrospective cohort study. The patients' gender, age at diagnosis, leukocyte count, hematocrit value, platelet count, hepatomegaly, splenomegaly, lymphadenomegaly, central nervous system (CNS) involvement, testis involvement, mediastinal mass and other extramedullary involvement, French-American-British (FAB) classification (L1, L2, L3), immunophenotyping with flow cytometric investigation, translocations (t (4;11), t (9;22), t (12,21), t (1;19)), 8th-day prednisone response, and 15th-day and 33th-day bone marrow aspiration (BMA) blast rates, risk groups, surveillance duration, relaps, and mortality were retrospectively obtained from patients' medical records. The study was approved by the local Ethics Committee of Dr. Behçet Uz Children's Hospital in accordance with the Helsinki Declaration (Project Number: 2012/47). Informed consent was obtained from each parent and/or patients.

Mediastinal involvement was assessed by thorax radiography (P/A and lateral). Central nervous system (CNS) involvement was defined as presence of leukemic cells in cerebrospinal fluid (CSF) with lumbar puncture and findings by Magnetic Resonance Imaging (MRI). Abdominal ultrasonography was investigated organomegaly, renal involvement, mass, and lymphadenopathy. Hepatomegaly was defined as ≥2 cm liver palpation at the right mid costal margin, splenomegaly was defined as ≥2 cm enlargement of the spleen in the left upper quadrant on physical examination. Testis involvement was evaluated by testis ultrasonography for all male patients.

Cytogenetic, FISH and molecular investigations examined in aspiration material and t (9;22), t (1;19), t (4;11), and t (12;21) translocations were evaluated at the Gentest Genetic Laboratory in Özel Şifa Hospital.

Prednisone response is explained as the peripheral blast count on day 8 of treatment. Prednisone good response (PGR) was characterized by <1.000/μL, while prednisone poor response (PPR) showed ≥1.000/μL peripheral blast count on 8th-day treatment. Response in BM was evaluated on 15th-day and 33th-day of induction treatment and was classified as M1 (<5%), M2 (5 to <25%), and M3 (≥25% leukemic blasts). Complete remission (CR) was described as M1 BM on day 33 of induction therapy, the absence of leukemic blasts in blood and CSF, and no symptom of local disease. Relapse was characterized by recurrence of 25% lymphoblasts or over in BM or local leukemic involvements at any site.

Risk group stratification is categorized three groups; patients with initial leukocyte count <20.000/mm^3 and age ≥1 and < 6 years, and blast counts <1.000/mm^3 in peripheral blood on 8th-day after 7 day prednisolone and IT MTX treatment, no T cell immunology, t (9;22) (BCR/ABL) and t (4;11) (MLL/AF4) negative and M1 on 33th-day were defined as standard risk group (SRG).

The patients with initial leukocyte count ≥20.000/mm^3 or age <1 or ≥6 years, and blast counts <1.000/mm^3 in peripheral blood on 8th-day after 7 day prednisolone and IT MTX treatment, t (9;22) (BCR/ABL) and t (4;11) (MLL/AF4) negative on 33th-day, were described as moderate risk group (MRG).

The cases with blast counts ≥1000/mm^3 on 8th-day in peripheral blood, t (9;22) (BCR/ABL) and t (4;11) (MLL/AF4) positive, without full remission on 33th-day, with hypodiploidy (chromosome <45) chromosome anomaly, and presence of each criteria alone independent of age and leukocyte count (one criterion is sufficient) were characterized as high risk group (HRG).[6]

Flow cytometry

Immunophenotyping assays were administered by four-color [FITC (Fluorescein Isothiocyanate), PE (Phycoerythrin), PC5 (Phycoerythrin-Cyanine 5) or PC7 (Phycoerythrin-Cyanine 7)] flow cytometry analysis of BM samples. Cytoplasmic and surface cell markers were identified using according to Immunological Characterization of Leukemia (EGIL) classification.[7]

The reactivity with fluorescent-conjugated monoclonal antibodies (Moab) was against T-cell-related antigens (CD1a, CD2, CD3, CD4, CD5, CD7, and CD8), B-cell differentiation markers (CD10, CD19, CD20, CD22, CD79a), myeloid cell antigens (CD11b, CD13, CD14, CD15, CD33, CD117, and Moab anti myeloperoxidase [MPO]), nonlineage restrict molecules (nuclear enzyme TdT, CD45, HLA-Dr, CD34), and also Moab against IgM heavy chains (mü chain) and light chains of immunoglobulins (κ and λ). The B cell ALL group was classified as pro-B cell ALL, common B cell ALL, pre-B cell ALL,

and mature B cell ALL. According to subtypes of B-cell ALL, pro-B cell ALL was defined as positive CD19, CD22, CD34, and negative CD10, cytoplasmic and surficial IgM. Common B ALL was described as positive CD19, CD22, CD10. Pre-B cell ALL group was characterized by positive CD19, CD22, CD10, cyμ, and negative sIgM. Mature B cell ALL was defined as positive CD10, CD19, CD20, CD22, cyμ, and sIgM. In addition, T cell ALL were separated into four subtypes as pro-T cell ALL, pre-T cell ALL, thymic (cortical) T cell ALL, and mature T cell ALL according to EGIL classification. Pro-T cell ALL was defined as positive cytoplasmic CD3, CD7, TdT, and negative CD2, CD1a. Pre-T cell ALL was identified as positive cytoplasmic CD3, CD7, TdT, CD2, and negative CD1a. Cortical T cell ALL was described as positive cytoplasmic CD3, CD5, CD7 and CD1a. Mature T cell ALL group was defined as positive CD5, CD7, and negative CD1a with surface CD3 expression.[7] Immunophenotyping results were assessed as positive when at least 20% of cells were positive for all Moab.[8]

BM samples were studied in EDTA tubes. The white blood cell count was examined and diluted to 10.000-15.000 cells in 1 ml. The dilution process used isotonic fluid. Each tube had antibodies inserted using different pipettes. After adding the antibodies, the bone marrow diluted to 100 microliters was added. After ensuring good mixing of antibody and bone marrow, tubes were incubated at room temperature in a dark place for 20 minutes. After the incubation duration, tubes obtained with the full blood lysis method had 500 microliters of Optilyse-C fluid added and they were mixed for a few seconds. They were left for incubation in the dark at room temperature for 10 minutes. The tubes then had 500 microliters isotonic fluid added and were incubated at room temperature and protected from light.

Statistical analysis: The obtained data were recorded on an assessment form. All statistical analyses were performed with the aid of SPSS 21.0 for Windows program. Descriptive statistics of data used mean, standard deviation, proportion and frequency values. Variables distribution was checked with the Kolmogorov Smirnov test. The quantitative data were analyzed with ANOVA test. For analysis of qualitative data, the chi-square test was used and the Fisher test if chi-square conditions were not provided. Kaplan-Meier and Cox regression analysis were used for survival analysis. P-value <0.05 was considered as significant.

RESULTS

Demographic features

This study included 105 patients (40 female, 65 male) with ALL. The mean age was 5.9±3.8 years. The distribution of demographic characteristics at all patients according to EGIL classification is given in **Table 1**. Only one patient was pro-B cell ALL (4 years old). While the mean age at diagnosis was 5.1±3.5 years, and 5.5±3.6 years in Common-B cell ALL, and pre-B cell ALL, the mean age at diagnosis was 9.1±2.6 years, 7.3±6.0 years, and 10.5±3.1 years in pre-T ALL, cortical T-ALL, and mature T-ALL, respectively. 13 (72.2%) patients with T-cell ALL were diagnosed above 6 years (p=0.001). **Table 2** was showed the distributions of age, and gender in immunophenotypes groups among ALL patients. The mean surveillance duration in T-cell ALL was 25.6±18.8 months and was shorter despite not statistically significant (**Table 2**).

Clinical and Laboratory characteristics

Patients with T cell ALL showed higher levels of leukocyte counts (p=0.001). Especially, leukocyte counts on admission were found above 100.000/mm^3 in patients with T cell ALL (p<0.05) (**Figure 1**).

Lymphadenopathy above 2 cm highly occurred in the T cell ALL groups than common B cell ALL and pre-B cell ALL groups (p<0.001) (**Figure 2**). At admission, extramedullary involvement was identified in 29 patients. Of theme, 11 cases had mediastinal involvement, eight cases had CNS involvement and four cases had testis involvement. Of three patients with CNS involvement were one retinal involvement, and three facial paralysis. T cell ALL group significantly highly suffered from mediastinal involvement (p<0.05). Mediastinal involvement was not identified in pre-B cell ALL cases. There were no significant differences between the immunophenotype subgroups in terms of extramedullary involvement besides mediastinal involvement (**Table 3**).

Table 1. Distribution of demographic characteristics at all patients according to immunophenotype subgroups

	B-ALL		T-ALL		
	Common B-ALL	Pre-B ALL	Pre-T ALL	Cortical T-ALL	Mature T-ALL
Case numbers	46	40	8	6	4
Incidence (%)	44%	38%	7.5%	5.5%	4%
Gender (M/F) (n)	31/16	20/20	6/2	5/1	3/1
Age (year)	5.1±3.5	5.5±3.6	9.1±2.6	7.3±6.0	10.5±3.1

ALL: acute lymphoblastic leukemia

Table 2. Age, gender and surveillance duration in immunophenotype groups

		Total (n=105)	Common B-ALL (n=47)	Pre-B ALL (n=40)	T-ALL (n=18)	p
		N (%)/ Mean ± SD	N (%)/ Mean ± SD	N (%)/ Mean ± SD	N (%)/ Mean ± SD	
Age	1-6 years	70 (66.7%)	35 (74.5%)	30 (75.0%)	5 (27.8%)	0.001
	>6 years	35 (33.3%)	12 (25.5%)	10 (25.0%)	13 (72.2%)	
Gender	male	65 (61.9%)	31(66.0%)	20 (50.0%)	14 (77.8%)	0.098
	female	40 (38.1%)	16 (34.0%)	20 (50.0%)	4 (22.2%)	
Surveillance duration (months)		32.9±18.8	31.9±17.9	36.9±18.9	25.6±18.8	0.097

Chi square test, ALL: acute lymphoblastic leukemia

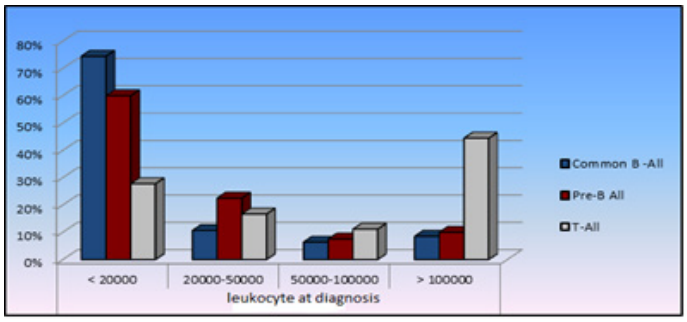

Figure 1. Distribution of leukocyte counts at time of diagnosis in ALL immunophenotype

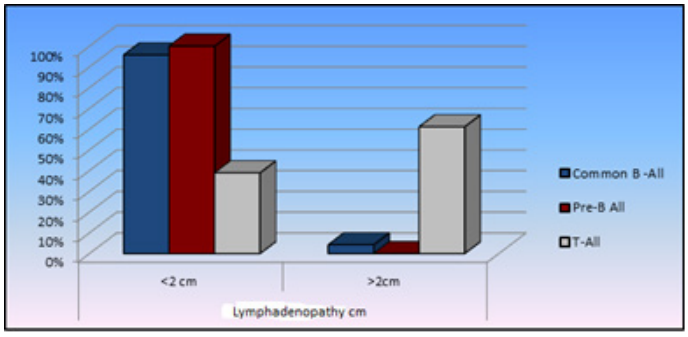

Figure 2. Distribution of lymphadenopathy in ALL immunophenotypes groups

While PPR on 8th-day and M3 on 15th-day BMA more often occurred in T –cell ALL groups, M3 on 33th-day BMA was similar between all immunophenotype subgroups (**Table 4**).

When 91 patients with cytogenetic investigation performed are investigated, 38.5% (35 patients) were identified to have cytogenetic anomalies. When the literature is investigated in terms of cytogenetic anomalies t (12;21) translocation is defined as having good prognosis, while t (1;19), t (4;11) and t (9;22) groups have poor prognosis. As a result, translocation results were evaluated by separated into two groups. Translocation distribution was no significant difference among immunophenotype subgroups (p=0.246).

Of the 105, 11 (10.5%) patients was not follow-up, 16 (17.0%) had mortality. When evaluated according to immunophenotype subgroups, 5 (10.6%) common B cell ALL, 5 (12.5%) pre-B cell ALL, and 6 (33.3%) T cell ALL patients were observed mortality. The mortality rate in the T cell ALL group was significantly higher than in the common B cell ALL and pre-B cell ALL groups (p=0.036) (**Table 5**).

The general relapse rate of all patients was identified as 13.6% (12 cases). When relapse is evaluated among immunophenotype subgroups, the relapse rate was 8.5% in the common B cell ALL group and 7.5% in the pre-B cell ALL group, while it was found to be statistically significantly high at 27.8% in the T cell ALL group (p<0.05). Even though mortality was observed in 41.7% of cases who had a relapse, 2.6% of cases who had not relapse died.

Table 3. Extramedullary involvement in ALL immunophenotypes

		Common B-ALL (n=47)		Pre-B-ALL (n=40)		T-ALL (n=18)		p
		n	%	n	%	n	%	
Mediastinal involvement		2	4.3%	0	0.0%	9	50.0%	<0.05
CNS involvement	CNS1	42	89.4%	37	92.5%	15	83.3%	
	CNS2	2	4.3%	0	0.0%	1	5.6%	>0.05
	CNS3	3	6.4%	3	7.5%	2	11.1%	
Testis involvement		3	9.7%	0	0.0%	1	7.1%	>0.05

Table 4. Treatment response in ALL immunophenotypes

		Common B-All (n=47)		Pre-B-All (n=40)		T-All (n=18)		p
		n	%	n	%	n	%	
8th-day steroid response	Good	46	97.9%	38	95.0%	11	61.1%	<0.05
	Poor	1	2.1%	2	5.0%	7	38.9%	
15th-day BMA response	M1	40	85.1%	34	85.0%	9	50.0%	
	M2	5	10.6%	5	12.5%	1	5.6%	<0.05
	M3	2	4.3%	1	2.5%	8	44.4%	
33th-day BMA response	M1	47	100%	39	97.5%	16	88.9%	
	M2	0	0.0%	1	2.5%	1	5.6%	>0.05
	M3	0	0.0%	0	0.0%	1	5.6%	

BMA: bone marrow aspiration, ALL: acute lymphoblastic leukemia

Table 5. Surveillance outcomes for ALL immunophenotypes

		Common B-ALL (n=47)		Pre-B-ALL (n=40)		T-ALL (n=18)		p
		n	%	n	%	n	%	
Final status	Mortality	5	10.6%	5	12.5%	6	33.3%	0.036
	Survival	35	74.5%	34	85.0%	9	50.0%	
Death in induction	No	44	95.7%	37	94.9%	15	88.2%	>0.05
	Yes	2	4.3%	2	5.1%	2	11.8%	

There was no statistically significant difference between the event free survival (EFS) and the overall survival (OS) rates in the common B ALL, pre-B ALL and T ALL groups (Kaplan Meier log rank p=0.103, p=0.05, respectively). The EFS rates are shown in **Table 6**. But 3 years EFS and 5 years EFS more lowly occurred 55%, 55% in T cell ALL groups, respectively. 3 years OS was found 63% in T cell ALL groups (**Table 7**). When OS analyzed between the common B ALL and T cell ALL groups, and between the pre-B ALL and T cell ALL groups, statistically significant differences were identified (Kaplan Meier log-rank, p=0.03, p=0.038, respectively). There was no statistically significant difference between the OS rates in the common B ALL and pre-B ALL groups (Kaplan Meier log-rank p=0.936) (**Figure 3**).

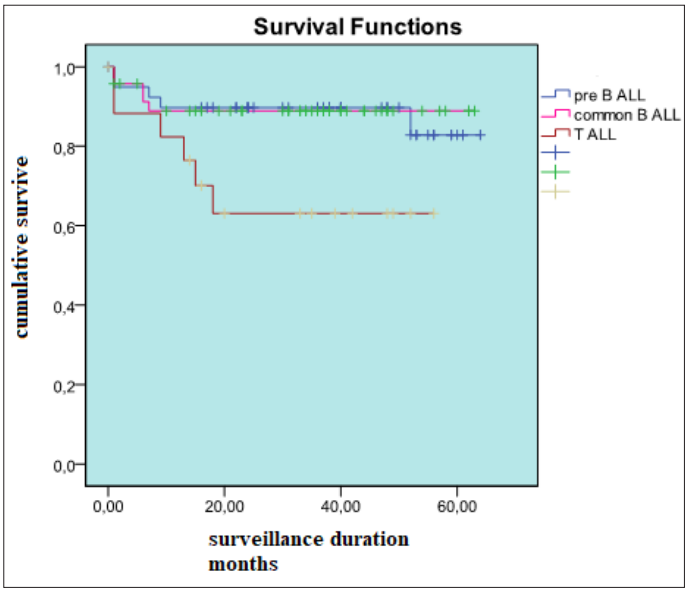

Figure 3. Overall survival rates according to immunophenotype subgroups (Kaplam-Meier curve)

Logistic regression analysis results

A univariate model found the effect of leukocyte count at the time of diagnosis, hepatomegaly, splenomegaly, lymphadenopathy presence, 8th-day steroid response, 15th-day BMA response, risk group, immunophenotyping and recurrence development were significant for the patients' survival ($p<0.05$). The univariate model found no significant effect for age, gender, hematocrit value, platelet value, CNS involvement, cytogenetic anomaly presence, and 33th-day BMA response ($p>0.05$) (**Table 8**).

The multivariate model revealed that only leukocyte value had an effect on survival, while all other variables remained insignificant (**Table 8**).

DISCUSSION

In the early period of development, lymphoid cells differentiate to lymphocytes by migrating from bone marrow to the lymph glands, spleen, and thymus. Thus, leukemia develops as a result of problems occurring for a variety of reasons at any stage of these differentiation steps. At the same time, uncontrolled proliferation of mutant cells forming as a result of some mutations may be responsible for the pathogenesis.[8]

European BFM study group reported that the distribution of immunophenotypes was 86% precursor B-ALL and 14% T-ALL rates.[10] Besides 83% of patients in our study were diagnosed with B cell ALL, 17% of patients were diagnosed with T cell ALL. T cell ALL incidence rate in our study is similar to the 7.3% to 16% rates reported in the literature.[1] Blastic cells are in common B cell phenotype for most of the ALL patients. Moreover, the rate for common B cell ALL observed 51.6% in several studies.[11] Most of our ALL patients (44%) had common B cell ALL phenotype consistent with the literature. In addition, Scrappe et al. showed that immunophenotypes were characterized by 6% pro-B ALL, nearly 75% common B cell ALL, and 19% pre-B cell ALL.[12]

Table 6. Event-free survival (EFS) of cases according to immunophenotype subgroups

		n count	Median event duration	EFS		p
				3 year EFS	5 year EFS	
Immunophenotype	Common B -ALL	47	34 months (1-63 months)	80%	69%	0.103
	Pre-B ALL	40	31.5 months (0-64 months)	77%	77%	
	T-ALL	18	19 months (0-56 months)	55%	55%	

Chi-square test (Fisher test), ALL: acute lymphoblastic leukemia

Table 7. Overall survival (OS) of cases according to immunophenotype subgroups

		n count	Median surveillance duration	Overall survival rate		p
				3 year OS	5 year OS	
Immunophenotype	Common B -ALL	47	35 months (1-63 months)	89%	89%	0.050
	Pre-B ALL	40	39 months (0.5-64 months)	90%	83%	
	T-ALL	18	19 months (0.5-56 months)	63%	-	
	Total	105	36 months (0-64 months)	85%	81%	

Kaplan Meier, ALL: acute lymphoblastic leukemia

Table 8. Evaluation of the effects of all variables on survival

Univariate model	H.R	95% confidence interval		p
		Minimum	Maximum	
Age	1.04	0.91	1.19	0.526
Sex	1.00	0.36	2.74	0.994
Leukocyte count	2.51	1.65	3.81	<0.001
Hematocrit	1.18	0.34	4.15	0.794
Platelets	0.53	0.26	1.10	0.087
Hepatomegaly	1.14	1.01	1.28	0.030
Lymphadenopathy	5.12	1.77	14.80	0.003
Splenomegaly	1.90	1.05	3.44	0.035
CNS Involvement	1.58	0.79	3.19	0.197
Cytogenetics	0.99	0.12	8.48	0.993
8th day steroid response	7.18	2.59	19.88	0.000
15th day BMA response	2.65	1.55	4.52	0.000
33rd day BMA response	2.02	0.70	5.89	0.196
Recurrence	3.31	1.15	9.53	0.027
Risk group (SRG/MRG/HRG)	6.26	0.11	0.58	0.001
Immunophenotyping	5.52	1.7	12.8	0.004
Multivariate reduced model				
Leukocyte count	2.51	1.65	3.81	<0.001

Cox-Regression, CNS: central nervous system, BMA: bone marrow aspiration, SRG: standard risk group, MRG: moderate risk group, HRG: high risk group

While the Turkish BFM study group reported that the male/female (M/F) ratio in TR-ALL BFM 2000 protocol was 1.2 (28), M/F ratio in developed countries was 1/1.2.[13,14] In our study, the M/F ratio was identified 1.6/1 and was observed to be similar to recent studies. A study in Brazil by Rego et al. described that the M/F ratio in T cell ALL cases was 4.2/1 and highly dominated by males.[15] In this study, the M/F ratio in T cell ALL cases was 3.5/1, similarly the literature.

Scrappe et al. showed that the median age of 2178 cases was 4.6 years.[12] In addition, Noronha et al.[11] reported that the median age of T cell ALL cases was 8 years. The mean age of our patients was 5.9±3.8 years, the mean age of T cell ALL cases also was 8.8±4.1 years.

Leukemia in children with T cell ALL usually presents with hyperleukocytosis. 18% of precursor B ALL cases had leukocyte count >50.000/mm^3, while 51.4% of T cell ALL cases had leukocyte count >50.000/mm^3.[16] Noronha et al.[11] reported hyperleukocytosis in 81% of T cell ALL cases. Our study showed 50% (8/16) of our patients had WBC >100000/mm^3 at the time of diagnosis.

Patients with T cell ALL usualy present with hepatosplenomegaly and extramedullary involvement.[17] Physical examination of our patients, 61.1% of T cell ALL group revealed lymphadenopathy above 2 cm. Schrappe et al.[12] reported 8.1% mediastinal involvement at the time of diagnosis, 10.5% of our patients were observed similarly. In addition, most of mediastinal involvement usually present in the T cell ALL patients.[14] In our study, the mediastinal involvement was 50% of T cell ALL despite 4.3% of common B cell ALL cases.

61.1% of T cell ALL cases were PPR, against 97.9% of common B cell ALL, and 95% of pre-B ALL cases were PGR in the 8th-day steroid response.[18] In our study, 38.9 of T cell ALL cases were PPR in the 8th-day steroid response. Our study showed that patients with T cell ALL respond well to chemotherapy in the 8th-day steroid response.

The recently study determined M1 in 61.9% and M3 in 11.6% of precursor B cell, in spite of M1 in 55.1% and M3 in 25.3% in T cell ALL according to immunophenotype subgroup in 15th-day BMA response.[19] Our results showed that M3 had a higher rate in T cell ALL patients in the 15th-day BMA response.

Relapse occurs for almost high rates in patients with T cell ALL. Patients with relapse had a short survival duration.[12] Simultaneously, mortality consisted of T cell phenotype for most of the patients with ALL.[17] Most of our T cell ALL patients had relapse, death during induction treatment, and mortality as consistent with the literature.

Six-year EFS rate was observed 80.2% of precursor B ALL and 74.8% of T cell ALL in a study investigating 2169 pediatric cases received ALL-BFM 95 protocol in Austria.[20] 6-year EFS rates were identified as 77.5% at T cell ALL patients (n=121) treated with BFM protocol from 1989 to 1998.[21] In our study, the 3-year EFS and 5-year EFS was 80%, 69% in the common B cell ALL group, respectively. In the pre-B cell ALL group, both 3-year EFS and 5-year EFS were similarly 77%. Despite the statistically not significant differences between EFS rates in the immunophenotype subgroups, 3-year EFS in T cell ALL group had lower rates (55.0%) compared to the other two groups. In addition, our study reported overall the prognosis of T cell ALL group was poor.

CONCLUSION

T cell ALL is associated with male gender, old age, high leukocyte counts, extramedullary involvement such as mediastinal mass or CNS involvement. Leukocyte counts, hepatomegaly, splenomegaly, lymphadenopathy, 8th-day steroid response, 15th-day BMA response, risk group, immunophenotype, and relapse were significantly related to prognosis. EFS and OS in patients with T cell ALL were lower than B cell ALL. T cell ALL is linked to poor prognosis.

The limitations of our study were a single-center experience, retrospective cohort study, low numbers of T cell ALL patients, short duration of follow up for evaluating EFS and OS and did not include <1-year-old patient.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was approved by the local Ethics Committee of Dr. Behçet Uz Children's Hospital in accordance with the Helsinki Declaration (Project Number: 2012/47).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: Accumulation of data: Sultan Adın Köker, data analysis/interpretation: Yeşim Oymak, Ferah Genel, statistical analysis: Dilek Ince, Yeşim Oymak, supervision or mentorship: Raziye Canan Vergin, Ferah Genel

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Orjinal Araştırma / Original Article

Comparison of Body Compositions Evaluated with Bioelectrical Impedance Analysis (BIA) with Metabolic, Hormonal and Anthropometric Measurements in PCOS Patients

PCOS Hastalarında Biyoelektrik İmpedans Analizi ile Değerlendirilen Vücut Kompozisyonlarının; Metabolik, Hormonal ve Antropometrik Ölçümlerle Karşılaştırılması

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Abstract

Aim: In this study, it was aimed to compare the body composition parameters measured by BIA(Bioelectrical Impedance Analysis) and the metabolic, anthropometric and hormonal parameters of the PCOS patients with the healthy control group and to examine the effect of PCOS on body composition parameters. It is aimed to give a better direction to PCOS follow-up and treatment.

Material and Method: 23 non-obese PCOS patients were involved to this prospective study. PCOS diagnosis was made according to the Rotterdam Consensus. Antropometric, metabolic and hormonal parameters were measured. Body compositions were measured by BIA.

Results: When the relationship between body composition parameters and metabolic and hormonal values were examined, significant correlations were found. There was a negative correlation between AUC-insulin levels and SHBG while a significant positive correlation between free testosterone in hirsute women with PCOS. There was a significant negative correlation between free testosterone level increase and body fat ratio while a significant positive correlation between SHBG and body fat ratio. There was a significant negative correlation between DHEAS and BMI and the hip circumference. When the relationship between body composition and antropometric parameters were examined, a significant positive correlation was found between BMI and body fat ratio, total body water and basal metabolic rate in women with PCOS.

Conclusion: In this study, significant correlations were found between body compositions and hormonal, metabolic and anthropometric parameters in patients with PCOS. Based on these findings, we believe that BIA can play an important role in outpatient follow-up of patients with PCOS.

Keywords: PCOS, Body composition characteristics, BIA, Metabolic, hormonal and antropometric parameters

Öz

Amaç: Bu çalışmada, PCOS'lu ve sağlıklı kontrol grubu hastalarında, vücut kompozisyon parametreleri BIA (Biyoelektrik İmpedans Analizi) ile ölçülerek, metabolik, antropometrik ve hormonal parametrelerle karşılaştırılmıştır. Böylece, PCOS'un vücut kompozisyon parametreleri üzerindeki etkileri incelenerek, PCOS takip ve tedavisine daha iyi yön verebilmek hedeflenmiştir.

Gereç ve Yöntem: Bu prospektif çalışmaya 23 obez olmayan PKOS hastası dahil edildi. PCOS tanısı Rotterdam Konsensus Konferansı'na göre konuldu. Antropometrik, metabolik ve hormonal parametreler ölçüldü. Vücut kompozisyonları BIA ile ölçüldü.

Bulgular: Vücut kompozisyon parametreleri ile metabolik ve hormonal değerler arasındaki ilişki incelendiğinde anlamlı korelasyonlar tespit edildi. PCOS'lu kıllı kadınlarda AUC-insülin seviyeleri ile SHBG arasında negatif bir korelasyon varken serbest testosteron arasında anlamlı bir pozitif korelasyon bulundu. Serbest testosteron seviyesi artışı ile vücut yağ oranı arasında anlamlı negatif korelasyon varken, SHBG ile vücut yağ oranı arasında anlamlı pozitif korelasyon tespit edildi. DHEAS ile vücut kitle indeksi (VKİ) ve kalça çevresi arasında anlamlı negatif korelasyon bulundu. Vücut kompozisyonları ile antropometrik parametreler arasındaki ilişki incelendiğinde ise, PKOS'lu kadınlarda VKİ ile vücut yağ oranı, toplam vücut suyu ve bazal metabolik hız arasında anlamlı pozitif korelasyonlar bulundu.

Sonuç: Bu çalışmada, PKOS' lu hastalarda vücut kompozisyonları ile hormonal, metabolik ve antropometrik parametreler arasında önemli korelasyonlar bulundu. Bu bulgulara dayanarak, basit ve noninvaziv bir yöntem olan BIA'nın PCOS'lu hastaların poliklinik takiplerinde önemli bir yer alabileceği kanaatindeyiz.

Anahtar Kelimeler: PCOS, Vücut kompozisyon karakteristikleri, BIA, Metabolik, hormonal ve antropometrik parametreler

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INTRODUCTON

Polycystic Ovary Syndrome (PCOS) is a common reproductive and endocrine disorder characterized by hyperandrogenism, anovulation and menstrual dysfunction affecting 5-10% of women of childbearing age.[1,2] In PCOS increased incidence of metabolic syndrome components (insulin resistance, impaired glucose tolerance and type 2 diabetes, dyslipidemia, hypertension, and cardiovascular risk profile) have been demonstrated. Obesity is present in 30-75% of women with PCOS and it is an aggravating factor for clinical entities of metabolic syndrome.[3,4]

Currently, there is still no consensus on the etiopathogenesis and diagnostic criteria of PCOS.[5] Since it is a chronic endocrine and metabolic disorder, it is likely that body composition will change over time. In this study, it was aimed to compare the body composition parameters measured by BIA (Bioelectrical Impedance Analysis) and the metabolic anthropometric and hormonal parameters of the PCOS patients with the healthy control group and to examine the effect of PCOS on body composition parameters that might give better direction to follow-up and treatment of PCOS.

MATERIAL AND METHOD

This study was conducted at Endocrinology Outpatient Clinic on 23 patients who were admitted by oligo/amenore, weight gain, increased body hair and infertility complaints and diagnosed to have PCOS according to the Rotterdam criteria 6 and on 20 healthy women of similar age and weight. Diabetic patients, steroid preparation users, oral contraceptive users, patients with any systemic (liver, kidney, heart) disease, patients using medicine that can affect insulin resistance for any reason, and smokers were not included in the study. Before the study, ethics committee approval was obtained from Harran University Faculty of Medicine. The standard form for data including identification information, age, height and weight, medical and gynecological history and physical examination findings has been filled.

Metabolic and Hormonal parameters

The study group received standard 75 g oral glucose tolerans test (OGTT) to assess insulin resistance. Serum glucose (mg/dl) and insulin (uIU/ml) levels were measured in these blood samples. The area under the curve (AUC) for glucose and insulin was calculated from these values by trapezoidal rule. AUC-Glucose and AUC-Insulin were used as mixed variables in data analysis reflecting blood glucose and insulin levels. The insulin sensitivity index (ISI) was calculated using the ISI-Composite formula described by Matsuda and De Fronzo, which is as valuable as the gold standard clamp technique.[7]

Triglyceride, total cholesterol, HDL-cholesterol and LDL-cholesterol values were measured in blood samples taken after at least 10 hours of fasting. Blood samples were taken between days 3 and 8 of the menstrual cycle for hormonal evaluation. TT, fT, Östradiol, PRL, DHEAS, SHBG, Cortisol levels were measured. A 1 mg dexamethasone suppression test was performed to exclude Cushing's disease in all the patients. At 11.00 pm, 1 mg dexamethasone was applied and at 8.00 am patients with venous cortisol level of 3 mcg/dl or less were considered normal.

Antropometric parameters

At the time of initial admission Body mass indexes (BMI) in kg/m^2 were calculated by measuring the height (m) and weight (kg) of the patients and waist circumference, hip circumference, waist/hip circumference ratio were measued.

Body Composition Parameters Measured By Bioelectrical Impedance Analysis

In the morning of the day when anthropometric measurements were made, after at least 8 hours of rest, BIA was performed on the two groups of patients with empty stomach and empty bladder. Biodynamics BIA 450, USA, Bioimpedance Analyzer was used in the procedure. The patients were told to drink 7-8 glasses of water a day before the procedure, and not to drink much tea/coffee and not to smoke many cigarettes. The metal and decorative items on the patient and, if any, large metal clothing items (such as belts) were removed. The individual to be measured was asked to stay in supine position on the examination table with dress but without shoe and socks. For measurement, two electrodes were placed on the dorsal side of the right hand and right wrist and two electrodes were placed on the dorsal side of the right foot and the right ankle (using standard tetrapolar electrodes). Afterwards, the instrument was turned on and the required information was entered and the measurement was performed . Body fat ratio (BFR), fat mass (FM), total body water (TBW), basal metabolic rate (BMR), lean body mass (LBM) were measured by BIA.

Statistical Analysis

Anthropometric parameters, metabolic parameters and body composition parameters measured by BIA were compared between the study group and the control group. SPSS (Statistical Package for Social Sciences) for Windows 11.5 program was used for the statistical analysis. For descriptive statistical methods (Mean, Standard deviation) and for comparison of normally distributed quantitative data.of study and control group Student t test was used. Man Witney U test was used for non-normal distribution parameters . Chi-square test was used for comparison of qualitative data. Pearson correlation test was used for normal distribution parameters and Spearman's correlation test was used for non-normal distribution parameters . The results were evaluated in a 95% confidence interval and a significance level of $p<0.05$.

RESULTS

There were 23 women with PCOS who had a BMI of 18.91-26.93 kg/m^2 between 18 and 32 years (22.0±3.43), and 20 women with a BMI of 18.26-24.97 kg/m^2 between 17 and 33 years (24.0±4.02) were included in the study .

When we compare the hormonal and metabolic parameters, there was a significany in LH, TT, fT, SHBG. As to be aspected, the LH, TT anf fT levels were significantly higher in PCOS group while SHBG level were significantly low. Ferriman Galwey score were also significantly higher in PCOS group (p<0.001). When lipid profiles, metabolic parameters were compared and there was no statistically significant difference (p>0.05) (**Table 1**).

Table 1. Comparison of hormonal and metabolic parameters of study groups

	PCOS Group (n=23)	Control Group (n=20)	P
FSH (mIU/ml)	4.61±1.32	5.33±4.76	>0.05
LH (mIU/ml)	12.79±6.32	6.23±3.12	<0.001
TT (ng/dl)	70.90±26.09	46.8±17.5	p=0.001
fT (pg/ml)	12.22±5.56	6.87±4.46	<0.001
SHBG (nmol/L)	40.37±21.07	75.36±60.60	<0.05
DHEAS(ug/dl)	268.52±117.85	245.34±124.05	>0.05
AUC glucose	199.16±40.96	207.22±42.39	>0.05
AUC insulin	80.67±29.64	88.21±5060	>0.05
ISI	7.06±2.79	6.66±2.64	>0.05
Basal Metabolic Speed (cal)	1264.6±20.1	1078.9±397.7	>0.05
Ferriman-Galwey Score	13.91±4.89	5.80±1.43	<0.001

Mean±SD

Between study groups there was also no statistically significant difference in the anthropometric measurements and in the body composition components (p> 0.05) (**Table 2**).

Table 2. Comparison of anthropometric and body composition values of study groups

	PCOS Group (n=23)	Control Group (n=20)	P
Waist Circumference (cm)	70.56±5.11	68.35±7.07	>0.05
Hip Circumference (cm)	94.21±7.70	92.1±9.84	>0.05
Waist/Hip ratio	0.75±0.04	0.74±069	>0.05
Fat Mass (kg)	14.42±4.04	14.33±2.90	>0.05
Body fat ratio (%)	26.12±5.58	26.26±5.77	>0.05
LBM (%)	40.53±6.44	38.32±5.12	>0.05
TBW (liter)	30.33±3.80	29.03±2.84	>0.05

Mean±SD

However, when correlation of androgenemias and Ferriman-Galwey scores with BMI, body composition values, AUC-insulin AUC-glucose and ISI were examined in patients with PCOS, there was significant negative correlation between insulin sensitivity and total and free testosterone levels in hirsute women with PCOS (r=-0.448, p<0.05, r=-0.538, p<0.01, respectively) (**Table 3**). There was a negative correlation between SHBG and AUC-insulin levels (r=-0.540, p<0.01) and a significant positive correlation between free testosterone increase and AUC-insulin levels (r=0.06, p<0.01).

In hirsute women with PCOS, there was a significant negative correlation (r=-0.544, p<0.01) between free testosterone level increase and body fat ratio and a significant positive correlation (r=0.544, p<0.01) with lean body mass. In women with PCOS, there was a significant positive correlation between SHBG and body fat ratio (r=0.418, p<0.05) and a negative correlation with DHEAS (r=-0.572, p<0.01).There was a significantly positive correlation between lean body mass and DHEAS(r=0.572, p<0.01). There was a significant negative correlation between DHEAS and BMI and the hip circumference (r=-0.584, p<0.01; r=-0.425, p<0.05, respectively). However, there was no significant relationship between free testosterone level and BMI, waist circumference, hip circumference and waist/hip ratio.

When the relationship between body composition and antropometric parameters were examined, a significant positive correlation was found between BMI and body fat ratio, total body water and basal metabolic rate in women with PCOS (r=0.609, p<0.01; r=0.414, p<0.05; r=0.455, p<0.05) while the fat-free body mass showed a significant negative correlation with BMI (r=-0.609, p<0.05).There was a strong positive correlation between total body water and waist circumference (r=0.616, p<0.01) and a positive correlation between total body water and hip circumference (r=0.491, p<0.05).

There was a strong positive correlation between basal metabolic rate (BMR) and waist circumference and hip circumference (r=0.646, p<0.01; r=0.537, p<0.01, respectively (**Table 4**).

When the relationship between body composition values and metabolic parameters is examined, there was a significant negative correlation between insulin sensitivity (ISI) and total body water (r=-0.514, p<0.05), while a significant negative correlation was found between ISI and basal metabolic rate (r=-0.539, p<0.01). Lipid profile values and anthropometric and body composition characteristics were not significantly correlated (**Table 5**).

Table 4. The association of body composition parameters with clinical, metabolic and hormonal values (r)

	BFR (%)	LBM (%)	TBW(%)	BMR(cal)
BMI	0.609[b]	-0.609[b]	0.414[a]	0.455[a]
Waist Circumference	0.315	-0.315	0.616[b]	0.646[b]
Hip Circumference	0.296	-0.296	0.491[a]	0.537[b]
Waist/Hip Ratio	-0.045	0.045	0.098	0.074
LH	-0.160	0.160	0.190	0.186
TT	-0.503[a]	0.503[a]	0.399	0.374
fT	-0.544[b]	0.544[b]	0.289	0.258
SHBG	0.160	-0.160	0.167	0.180
DHEAS	-0.572[b]	0.572[b]	0.067	0.039
AUC-glucose	-0.100	0.100	0.170	0.191
AUC-insulin	-0.254	0.254	0.405	0.405
ISI	0.137	-0.137	-0.514[a]	-0.539[b]

a= p<0.05 b= p<0.01

Table 3. The association of androgenemia and Ferriman - Galwey scores with BMI, body composition values and ISI in patients with PCOS (r) (r)

	LH	TT	fT	SHBG	DHEAS	FGs
BMI	-0.038	-0.20	-0.349	0.346	-0.584[b]	-0.393
Waist Circumference	0.062	0.007	-0.030	0.143	-0.310	-0.436
Hip Circumference	0.163	0.076	-0.074	0.182	-0.425[a]	-0.384
Waist/Hip Ratio	-0.011	-0.202	0.066	-0.132	0.260	0.001
BFR	-0.110	-0.503[a]	-0.544[b]	0.418[a]	-0.572[b]	-0.525[a]
LBM	-0.609	0.503[a]	0.544[b]	-0.018	0.572[b]	0.525[a]
TBW	0.190	0.399	0.239	-0.032	0.067	0.159
AUC- glucose	-0.155	0.259	0.324	-0.154	0.343	0.083
AUC- insulin	0.228	0.369	0.06[b]	-0.540[b]	0.422[a]	0.126
ISI	-0.035	-0.448[a]	-0.538[b]	0.361	-0.282	0.089

a = p<0.05 b = p<0.01

Tablo 5. The association of anthropometric and body composition values with metabolic parameters (r)

	AUC-glucose	AUC-insulin	ISI	Trigliseride	Cholesterol	LDL	HDL
BMI	0.004	-0.086	-0.130	0.015	0.196	0.208	0.016
BFR	-0.100	-0.254	0.137	0.071	0.204	0.152	0.075
LBM	0.100	0.254	-0.137	-0.071	-0.204	-0.152	-0.075
TBW	0.170	0.405	-0.514[a]	-0.60	0.103	0.090	0.096
BMR	0.191	0.405	-0.539[b]	-0.028	0.130	0.122	0.069
Waist C.	-0.038	0.117	-0.267	-0.038	0.140	0.086	0.153
Waist/Hip	-0.155	-0.207	0.067	0.075	-0.083	-0.053	-0.134

a = p< 0.05 b = p< 0.01

DISCUSSION

In this study we found that there was no statistically significant difference in the metabolic parameters, anthropometric measurements and in the body composition components between PCOS and control group. However , when correlation of androgenemias and Ferriman – Galwey scores with BMI, body composition parameters and metabolic parameters were examined significant correlations were found.

Insulin resistance is thought to play an important role in the pathophysiology of PCOS in recent years as it is known that insulin directly affects the production of in vitro ovarian androgen and in many PCOS patients insulin resistance and hyperinsulinemia are present independent of obesity.[7-9] In our study, a negative correlation was found between total and free testosterone levels and insulin sensitivity. In hirsute women with PCOS there was a significant positive correlation between free testosterone increase and AUC-insulin levels. Negative correlation was found between AUC insulin and SHBG levels. This supports the information in the literature about the association of hyperinsulinemia with hyperandrogenic activity.

Georgopoulos et al.[10] reported that in hirsute women with PCOS, BMR evaluated by indirect calorimetry was decreased compared with control subjects, independently of obesity and IR. Adjusted BMR was significantly decreased both in women with PCOS with or without IR and particularly in women with PCOS and IR. In our study, we also found that the BMR decreased as insulin sensitivity increased in patients with PCOS. We additionally found that total body water also decreased as insulin sensitivity increased in PCOS patients compared to control group.

Different publications have been reported in the literature regarding the body composition of PCOS patients. Geronikolou et al. made ECW, TBW, FM, and LBM and ICW measurements in their study with BIA in adolescents with PCOS and found similar results with the control group. The fact that the study was in the adolescent age group and limited sample size may have affected the results.[11] However, the hormonal parameters were not studied in this study. Studies have shown that androgen excess and adipose tissue hypertrophy play a role in the pathophysiology of PCOS.[12] In our study we found some correalations between hormones and body composition parameters in hirsute patients with PCOS. As free testosterone, total testesteron and DHEAS increases, BFR decreases and LBM increases. Additionally there was a positive corrrealation found between SHBG and BFR which means that the increase of SHBG leads to an increased level of BFR.

Churchill et al. reported that after adjusting age and BMI, there was no significant difference in BMR between PCOS women and controls.[13] Although age and body mass index similar groups were selected in our study, it was found that BMR increased statistically significantly as BMI increased in patients with PCOS. In these patients, it was also found that body fat ratio and TBW were statistically significantly higher. In addition, we found that as the waist and hip circumference increased in patients with PCOS, BMR and total body water increased significantly. It was found that waist and hip circumference was significantly higher in PCOS patients with higher TBW and insulin sensitivity was decreased in these patients.

On the other hand, we want to emphysize that various methods of determining body composition have been developed.

With such sophisticated methods, body composition can be determined much closer to real values. However, a significant portion of these methods (such as densitometers, CT, MRI, DEXA) are not used for routine clinical and epidemiological studies because they require expensive equipment and consumables, and are impractical.

The bioelectrical impedance analysis (BIA) method developed in recent years is a method based on determining the permeability of a weak electrical current in the human body. BFM, BFR, LBM, TBW and ratio can be determined by using the related formulas in the obtained permeability data. Studies have shown that the findings obtained with the BIA method are similar to those obtained with complex methods (densitometer, total body water calculation, etc.) so that makes use of the BIA method in policlinic work more common.[14,15]

CONCLUSION

In this study, we found significant correlations between the body compositions measured by the BIA and other hormonal, metabolic and antropometric parameters. In future, we believe that BIA, which is a simple and noninvasive method, can take an important place in the outpatient clinic follow-up of patients with PCOS.

ABBREVIATIONS

AUC: Area under the curve, BFM: Body fat mass, BFR: Body fat ratio, BIA: Bioelectrical impedance analysis, BMI: Body mass index, BMR: Body mass ratio, DHEAS: Dehydroepiandrosterone sulfate, FGs: Ferriman-Galwey score, FSH: Follicle-stimulating hormone, fT: Free testesteron, HDL: high-density lipoprotein, ISI: Insulin sensitivity index, LBM: Lean body mass, LH: Luteinizing hormone, LDL: Low-density lipoprotein, OGTT: Oral glucose tolerance test, PCOS: Polycystic Ovary Syndrome, SHBG: Sex hormone -binding globülin, TBW: Total body water, TT: Total testesteron

ETHICAL DECLARATIONS

Ethics Committee Approval: Ethics committee approval was obtained from Harran University Faculty of Medicine (06/29.03.2007).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Orjinal Araştırma / Original Article

Evaluation of The Total Laboratory Performance of Our Clinical Laboratory with Six-Sigma Method

Klinik Laboratuvarımızın Toplam Kalite Performansının Altı-Sigma Metoduyla Değerlendirilmesi

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Abstract

Aim: In order to evaluate the performance of the clinical laboratories, a quality measurement method, The Six-Sigma Methodology, is used. We aimed to evaluate the analytical performance of our clinical laboratory by using the internal and external quality control data of 28 analytes, and by calculating their process sigma values.

Material and Method: Sigma values of 28 analytes of our laboratory were determined from coefficient of variation (%CV) and bias for 3 subsequent months from November 2018 to January 2019. If the sigma values are >6, between 3 and 6, and <3, they are classified as world-class, good and un-acceptable, respectively.

Results: 6 (%21) analytes; T Protein, Creatinin, Ca, Na, Cl, HbA1c; provided <3 sigma value, 1 (%04) analyte; lipase; provided between 3-6 value and 11 (%39) analytes; amylase, GGT, ALT, LDH, CRP, Lactate, BUN, Direct Bil., T Bil., CK and CK-MB; provided > 6 sigma value for both Internal Quality Control levels (IQC1 and IQC2) for three consecutive months, respectively.

Conclusions: In terms of Six-Sigma Metrics; our results were generally found as world-class or good. An appropriate quality control scheduling should be carried out for each test by using Six-Sigma Methodology in all clinical chemistry laboratories.

Keywords: Internal quality control, external quality control, six sigma, variation coefficient, standard deviation, bias

Öz

Amaç: Klinik laboratuvarların performansını değerlendirmek için bir kalite ölçüm yöntemi olan 'Altı Sigma Metodolojisi' kullanılmaktadır. Bu çalışmada, klinik laboratuvarımızın analitik performansını 28 analitin iç ve dış kalite kontrol verilerini kullanarak ve süreç sigma değerlerini hesaplayarak değerlendirmeyi amaçladık.

Gereç ve Yöntem: 28 analitin Sigma değerleri, Kasım 2018'den Ocak 2019'a kadar birbirini takip eden 3 ay boyunca varyasyon katsayısı (%CV) ve bias kullanılarak belirlendi. Sigma değerleri >6, 3 ila 6 arasındaysa ve <3 ise, sırasıyla; birinci sınıf veya dünya standartlarında, iyi ve kabul edilemez olarak değerlendirildi.

Bulgular: Art arda üç ay boyunca hem IQC1 hem de IQC2 seviyeleri için 6 (%21) analit; T Protein, Kreatinin, Ca, Na, Cl, HbA1c, <3 Sigma değeri sağladı, 1 (%04) analit; lipaz ise 3-6 Sigma değeri ve 11 (%39) analit; amilaz, GGT, ALT, LDH, CRP, Laktat, BUN, Direct Bil., T Bil., CK ve CK-MB ise >6 sigma değeri sağladı.

Sonuç: Sonuçlarımızın Altı-Sigma Metrikleri genel olarak dünya standartlarında veya iyi olarak bulunmuştur. Tüm klinik kimya laboratuvarlarında Altı-Sigma Metodolojisi kullanılarak her test için uygun bir kalite kontrol planlaması yapılmalıdır.

Anahtar Kelimeler: İç kalite kontrol, dış kalite kontrol, altı sigma, varyasyon katsayısı, biyas

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INTRODUCTION

Clinical laboratories target to provide efficient and high quality service from the test request to the conclusion. In order to achieve efficiency and quality, errors occurring in laboratory processes must be determined and reset gradually. Only in this way, standards can be achieved that can be practiced and used medically. Quality levels of laboratory results depend on many factors, such as; the request and result management system used, the skill of the technician, and the analytical system used.

Quality management is defined as compliance with regulatory rules, accreditation rules and international standards.[1] In total quality management, it is aimed to evaluate the process and identify possible error steps. The importance of quality control practices is understood when something goes bad. But they seem like a waste of time when things are going well. The main points of Internal Quality Control's (IQC) success are the ability to provide advanced planning, predict what can go wrong, warn when something goes wrong, ensure that a problem can be answered in a planned way and minimize damage.

In clinical laboratories, the analysis process performance evaluation covers all analytical phases; such as error percentages for pre-analytical phase, precision and reproducibility measurement (Bias, and SD) for the analytical phase, and delayed reports and panic value statements for the post-analytical phase. Analytical process performance evaluation can be accomplished by using the process sigma levels of internal and external quality control results.

Six sigma methodology is a quality management tool based on statistical calculations focused on process variables.[2] Variations during process are thought to be the main source of errors. Process sigma level is the main indicator of this methodology. Poor quality costs determined from process sigma levels and defined as false probability (MFPO) in million opportunities provide an evaluation of process performance. By reducing poor quality costs, a significant improvements in the process can be obtained.[3,4]

In our work, it is targeted to evaluate 28 analytes of our clinical laboratory in terms of six sigma methodology.

MATERIAL AND METHOD

In our study, after taking approval of local ethics committee with the code of 18-KAEK-259, we investigated 28 analytes; glucose (Glu), alkaline phosphatase (ALP), amylase, gamma glutamyl transferase (GGT), alanine amino transferase (ALT), aspartate amino transferase (AST), lactate dehydrogenase (LDH), C-Reactive Protein (CRP), blood urea nitrogen (BUN), creatinine, uric acid, lipase, ammoniac (NH3), lactate, D-Dimer, Total Bilirubin (T.Bil), Direct Bilirubin (D.Bil), creatinine kinase (CK), CK-MB, total protein (T.Prot.), Albumin (Alb), sodium (Na), potassium (K), chlorine (Cl), magnesium (Mg), calcium (Ca), Phosphate (P), hemoglobin A1c (HbA1c) retrospectively for 3 consecutive months between November 2018 - January 2019 concerning six sigma methodology. We analyzed serum immuno assay tests by using the Cobas e 601 auto analyzer of Roche Diagnostics. We analyzed both levels of IQC materials on daily basis. We calibrate the instruments of our clinical laboratory systematically. We took throughput of IQC from laboratory data management system of Enlil LIS of our hospital.

After determining the SD and mean values of analytes, we calculated bias, % CV, and sigma values of them. In **Table 1**, we presented our laboratory mean and SD values of each test and the target means.

Coefficient of variation (CV%), the uncertainty, is calculated from the Standard deviation and IQC data.

CV (%) = (average of SD/IQC data) × 100.

The percentage difference of the average of the obtained results for each analyte of our laboratory from the target values in the annexes provided under the Roche control is termed as Bias.

Bias%=[(our lab IQC data - average of target IQC data)/ average of IQC Data target] × 100

Total permissible error (TEa): TEa targets from a single source are used for Sigma metrics calculation.[8] **Table 2** highlights TEa values of analytes.

Analytical performance characteristic of an analyte is defined as 'Sigma Value'. CV (obtained from IQC data), Bias% and TEa values are considered in Sigma metric calculation.

Sigma metric (s) = (TEa %- Bias %)/CV %

Sigma level <3 is regarded as poor performance. Indicator of a good performance ise ≥3 sigma level. To be mentioned 'a world class performance' it must be more than 6 sigma levels.[3]

RESULTS

Table 1 demonstrates comparison of the choosen analytes of our laboratory for both levels of IQC1 and IQC2.

In our study, CV % values were calculated for consecutive three months as < 5, except Lipase for QC1 and, Lipase and NH3 for QC2. Bias, CV% and TEa values of the two levels of QC for all analytes are shown in **Table 2**.

In **Table 3,** calculated sigma values of all analytes are shown and the maximum value of all was figured out as 54.17.

For both IQC levels, during three months , our 7/8, 11/8, 11/10 parameters provided < 3 sigma metrics, 6/6, 3/3, 5/6 parameters provided between 3-6 sigma metrics and 14/14, 14/14, 12/12 parameters provided > 6 sigma metric values, respectively. **Table 4** shows the sigma levels of analytes.

Table 1. The target mean, laboratory mean and SD values of each test.

Assay Name	IQC1				IQC2			
	Target Mean	November Lab Mean ±SD	December Lab Mean ±SD	January Lab Mean ±SD	Target Mean	November Lab Mean ±SD	December Lab Mean ±SD	January Lab Mean ±SD
Glucose	101	105.76±1.25	104.21±3.12	103.17±2.8	236	237.57±3.66	237.61±6.02	238.03±5.63
ALP	92.1	90.63±2.18	91.7±2.87	92.85±2.56	230	223.31±5.47	221.25±5.32	222.23±6.04
Amylase	80.5	80.97±1.07	80.69±1.15	81.63±1.41	195	189.06±2.21	192.34±2.3	197.28±2.36
GGT	53.05	54.56±1.48	55.05±1.28	55.61±0.97	241	242.97±4.33	247.35±4.96	250.37±3.59
AST	46.1	46.76±1.16	47.01±1.32	46.54±1.22	138.5	137.59±2.89	141.28±3.63	144.84±3.96
ALT	45.3	44.38±1.1	44.56±1.2	45.75±1.47	117.5	111.25±2.01	110.15±2.74	115.59±4.71
LDH	162	164.78±2.62	165±2.28	164.31±2.61	297	292.22±3.92	293.59±4.92	300.34±3.3
Posphate	4.25	4.35±0.08	4.35±0.21	4.42±0.1	7.735	7.58±0.11	7.81±0.13	8.4±0.2
CRP	8.06	7.5±0.11	7.56±0.23	7.55±0.13	39.2	35.05±0.9	35.93±1.3	36.42±0.98
T. Protein	4.71	4.73±0.08	4.78±0.06	4.77±0.07	7.515	7.6±0.13	7.58±0.09	7.6±0.09
Albumin	3.07	2.95±0.08	2.98±0.08	3.06±0.11	4.83	4.77±0.09	4.72±0.08	4.79±0.16
Creatinine	1.07	1.09±0.04	1.1±0.05	1.12±0.04	3.975	4.13±0.14	4.07±0.14	4.01±0.14
Uric Acid	4.7	4.82±0.13	4.68±0.07	4.81±0.13	9.835	9.49±0.18	9.83±0.16	10.58±0.29
Lipase	45.3	45.9±3.96	45.91±3.46	45.88±3.43	100.35	96.52±7.31	100.02±7.44	100.06±6.76
NH3	217	208.95±7.34	209.69±9.81	213.67±6.65	58.5	57.44±5.49	57.4±4.6	60.65±4.74
Lactate	1.66	1.72±0.04	1.72±0.03	1.7±0.02	3.575	3.46±0.07	3.62±0.06	3.83±0.06
BUN	18.2	18.71±0.39	18.38±0.33	18.23±0.39	54.45	55.58±1.13	55.63±1.01	55.84±1.12
D-Dimer	0.815	0.82±0.03	0.81±0.03	0.82±0.06	3.8	3.79±0.05	3.77±0.03	3.84±0.13
Calcium	8.86	9.07±0.13	9.06±0.13	9.1±0.11	13.6	13.88±0.2	13.83±0.17	13.95±0.18
Direct Bil.	1.02	0.95±0.02	0.97±0.03	0.98±0.02	2.6	2.4±0.06	2.49±0.06	2.61±0.04
Total Bil.	0.989	0.97±0.03	0.98±0.03	1±0.03	3.935	3.78±0.09	3.82±0.08	4.03±0.09
Mg	2.09	2.05±0.04	2.05±0.07	2.04±0.06	3.35	3.21±0.05	3.31±0.08	3.43±0.07
CK	161	156.03±1.99	158.75±3.3	159.59±3.25	282	263.86±3.48	274.59±4.13	294.14±5.11
CK-MB	43.6	41.99±0.77	42.25±0.21	42±1.01	94.45	88.78±1.62	89.18±1.44	92.41±1.26
Na	111	112.12±2.31	111.47±1.52	112.2±2.8	136	135.51±3.43	134.81±1.74	138.44±2.26
K	3.77	3.8±0.08	3.76±0.08	3.78±0.08	6.945	6.79±0.15	6.89±0.08	7.21±0.12
Cl	80.6	81.32±2.3	79.83±1.84	81.05±1.57	108	108.5±2.42	106.66±1.81	108.82±1.94
HbA1C	10.4	5.49±0.12	10.49±0.18	10.48±0.16	5.63	10.5±0.12	5.58±0.1	5.55±0.08

DISCUSSION

One of the most important quality control analyzes used in quality and performance evaluation is 'The Six Sigma Method' and is carried out by statistical calculations.[5] The Sigma Metrics provide quantitative comparison of various autoanalyzers, laboratories and methods throughout the world.[6] If six standard deviations between the average of an analyte and its upper and lower margins can be maintained, errors can be reduced in the laboratory.[7]

TEa is the tolerance limits of a clinical laboratory. If the TEa value is less than the difference between the real analytical concentration of the patient samples and the reported concentration, the result is unreliable.[7] The degree of diversity of a test used is termed as TEa and is used in clinical decisions managing further treatment or follow-up.

CV% to determine the diversity of a test; expressed as a percentage of the ratio of change to average. The ≤5% CV value indicates that the analytical method or analyzer has good performance, while the ≥10% CV value shows inadequate performance.[9]

Verma et al.[5] calculated the averages of % CVs of 2nd and 3rd level IQCs for 16 parameters from January 2017 to December 2017. The mean of CVs for level 2 was between 2.12% (albumin) and 5.42% (creatinine), and for level 3, it was between 2% (albumin) and 3.62% (HDL-cholesterol). The CV average of all parameters was below 5%, with very good accuracy.

For level 2 IQC, 11 (68.5 %) out of 16 parameters failed to meet sigma metrics. Five of them failed to meet a minimum of quality performance with less than 3, and the other six parameters barely met minimal performance with 3 to 6. For level 3 IQC, 8 (50%) six-parameter sigma quality performance failed. Three of them had metrics below 3, while 5 had between 3 and 6. The TEAs of all analytes were lower than those of pre-determined TEAs except AST and ALT.

In a study on an architect i2000 SR autoanalizer, carried out by Litten J et al.[6] control CVs of CEA, total PSA, FT3, FT4, TSH, ferritin, FSH and vitamin B12 immune tests ranged between 1.34% and 18.87%, and most of the CV values were below 5%. In this study, pathological and normal IQC levels % CV values for tests including CEA, ferritin, FSH, FT3 were found <5 for

Table 2. TEa, bias and CV values of the two levels of quality control for the assays.

Assay Name	TEa (%)	IQC1						IQC2					
		November		December		January		November		December		January	
		%CV	% Bias	%CV	% Bias	%CV	% Bias	%CV	% Bias	%CV	% Bias	%CV	% Bias
Glucose	6.96	1.18	4.71	2.99	3.18	2.71	2.15	1.54	2.40	2.53	0.68	2.36	-0.82
ALP	12.04	2.41	-1.60	3.13	-0.43	2.76	0.81	2.45	-4.57	2.40	-3.81	2.72	-1.67
Amylase	14.6	1.33	0.58	1.43	0.24	1.73	1.40	1.17	-0.49	1.20	-1.36	1.20	-1.36
GGT	22.11	2.71	1.98	2.33	2.90	1.75	3.94	1.78	0.82	2.01	2.63	1.43	3.89
AST	16.69	2.48	1.42	2.81	1.96	2.62	0.96	2.10	1.17	2.57	2.01	2.73	2.72
ALT	27.48	2.48	-2.04	2.70	-1.64	3.22	1.00	1.81	-2.41	2.49	-6.26	4.08	-4.47
LDH	11.4	1.59	1.72	1.38	1.85	1.59	1.43	1.34	0.07	1.68	-1.15	1.10	-0.55
Posphate	10.11	1.82	2.29	4.92	2.34	2.16	3.95	1.47	2.69	1.68	0.92	2.41	3.80
CRP	66.54	1.43	-6.97	3.03	-6.17	1.75	-6.28	2.56	-8.95	3.62	-8.34	2.70	-8.73
Total Protein	3.63	1.75	0.35	1.22	1.43	1.46	1.32	1.75	0.56	1.14	0.89	1.24	1.78
Albumin	4.07	2.65	-4.01	2.77	-2.84	3.71	-0.45	1.85	-2.72	1.66	-2.23	3.38	0.58
Creatinine	8.87	4.00	1.87	4.47	2.95	3.78	5.12	3.35	0.98	3.39	2.41	3.43	3.99
Uric Acid	11.97	2.71	2.53	1.55	-0.49	2.65	2.41	1.93	2.35	1.64	-0.10	2.78	1.72
Lipase	37.88	8.62	1.32	7.55	1.35	7.47	1.27	7.57	-2.21	7.44	-0.33	6.76	-1.90
NH3	29.6	3.51	-3.71	4.68	-3.37	3.11	-1.08	9.56	-1.82	8.01	-1.88	7.82	3.68
Lactate	30.4	2.36	3.55	1.87	3.33	1.44	2.33	2.08	2.29	1.73	1.35	1.59	1.46
BUN	15.55	2.10	2.80	1.79	0.97	2.12	0.16	2.03	2.36	1.81	2.17	2.00	2.26
D-Dimer	28.04	3.19	2.46	3.36	-0.38	6.69	0.37	1.27	-0.18	0.88	-0.69	3.40	1.00
Calcium	2.55	1.42	2.35	1.40	2.24	1.26	2.75	1.43	2.07	1.22	1.66	1.31	2.58
Direct Bil.	44.5	2.05	-6.86	3.19	-4.90	2.31	-4.13	2.33	-4.54	2.32	-4.17	1.68	-3.13
Total Bil.	26.94	3.40	-2.34	3.31	-1.35	3.00	0.62	2.28	-1.36	2.17	-3.05	2.20	-0.16
Mg	4.8	1.98	-2.09	3.52	-2.15	2.99	-2.55	1.47	-0.55	2.33	-1.28	2.14	-1.08
CK	30.3	1.28	-3.08	2.08	-1.40	2.03	-0.88	1.32	-1.54	1.50	-2.63	1.74	-0.63
CK-MB	24.1	1.84	-3.70	0.50	-3.10	2.40	-3.66	1.82	-5.05	1.62	-5.58	1.36	-3.14
Na	0.73	2.06	1.01	1.36	0.42	2.49	1.08	2.53	0.38	1.29	-0.87	1.63	1.05
K	5.61	2.17	0.71	2.09	-0.36	2.18	0.39	2.19	0.66	1.17	-0.83	1.70	0.91
Cl	1.5	2.82	0.89	2.31	-0.96	1.94	0.55	2.23	0.46	1.69	-1.24	1.78	0.76
HbA1c	3	2.27	-2.51	1.69	0.89	1.56	0.80	1.11	0.93	1.85	-0.98	1.47	-1.38

every three months. CV values of other tests were found as <5 or >5 for 3 months, but did not exceed 10%. Inconsistency of the IQC through calibration preparation, transport or storage, and mistakes during sample use d by laboratory technicians may be the causes of CV% and bias variability.

In our study, average CV% of QC1 excluding Lipase; it was calculated as 2.42% ranging between 0.50% (CK-MB) and 6.69% (D-Dimer). For QC2, the average CV% value excluding Lipase and NH3 was calculated as 1.98% ranging between 0.88% (D-Dimer) and 4.08% (ALT). For both levels, for Lipase, they were calculated as 7.88 and 7.26, respectively, and 8.46 for the second level for NH3.

For Glu, ALP, Amylase, GGT, ALT, AST, LDH, CRP, BUN, Creatinine, Uric Acid, Lactate, D-Dimer, T. Bil, D. Bil, CK, CK-MB, T. Prot, Alb, Na, K, Cl, Mg, Ca, P, HbA1c tests, CV % values of both IQC levels were calculated as <5% for 3 consecutive months. Lipase was determined as >5% of both IQC levels for every three months. For NH3, CV% values of IQC2 levels were found to be >5% for every three months. However, no value was >10%.

Evaluating the analytical stage, optimization of laboratory tests' quality measurements and quality control rules based on sigma values are defined as Six Sigma Methodology. IQC applications must be specific for tests and must be created in a harmony with the sigma values of each test. The analysis of analytical processes before and after analytics should be done to evaluate the overall performance of the laboratory.

Ercan et al.[7] determined sigma values as 4.38/4.01 and 8.12/9.7 for first and second level IQC for vitamin B12 and folate tests in Beckman Coulter UniCel® DxI 800 Immuno assay System autoanalyst, respectively.

In their study, Nanda et al.[8] found sigma metric values for glucose, cholesterol and urea as 3.2, 2.2, 5.2, respectively. Sigma metric values for triglycerides and SGOT were found to be greater than 6.

James O Westgard et al.[9] found that sigma metric values for glucose and total cholesterol were in a range between 2.9 to 3.3, and 2.9 to 3.0, respectively. For ALP, while the value of sigma metrics was greater than 6, it was between 3.1 and 5.9 in a study by Bhawna Singh et al.[10] Sigma metric values for creatinine were found to be 3.1. In a study by Carl Garber[11] , sigma metric values of creatinine were found to be 6.0.

Table 3. The sigma metrics for 3 months and overall sigma metrics for the assays.

Assay Name	November		December		January	
	IQC1 sigma metrics	IQC2 sigma metrics	IQC1 sigma metrics	IQC2 sigma metrics	IQC1 sigma metrics	IQC2 sigma metrics
Glucose	1.90	2.96	1.26	2.48	1.77	3.29
ALP	5.66	6.79	3.99	6.59	4.07	5.04
Amylase	10.56	12.93	10.07	13.35	7.65	13.35
GGT	7.42	11.95	8.26	9.70	10.38	12.71
AST	6.16	7.39	5.24	5.72	6.00	5.11
ALT	11.90	16.53	10.77	13.54	8.23	7.84
LDH	6.08	8.43	6.91	7.49	6.28	10.88
Posphate	4.31	5.05	1.58	5.47	2.86	2.62
CRP	51.51	29.55	23.97	20.67	41.71	27.93
Total Protein	1.87	1.76	1.79	2.41	1.58	1.50
Albumin	3.05	3.66	2.50	3.79	1.22	1.03
Creatinine	1.75	2.35	1.33	1.90	0.99	1.42
Uric Acid	5.00	5.00	8.04	7.36	3.60	3.69
Lipase	4.24	5.30	4.84	5.14	4.90	5.89
NH3	9.48	3.29	7.05	3.93	9.86	3.32
Lactate	11.37	13.52	14.50	16.77	19.50	18.19
BUN	6.08	6.48	8.14	7.38	7.24	6.65
D-Dimer	8.01	22.13	8.46	32.74	4.14	7.94
Calcium	0.14	0.34	0.22	0.73	-0.16	-0.02
Direct Bil.	25.08	21.03	15.47	21.02	21.02	28.29
Total Bil.	8.61	12.39	8.53	13.82	8.76	12.30
Mg	3.47	3.65	1.98	2.60	2.45	2.75
CK	26.16	24.13	15.23	21.89	15.33	17.80
CK-MB	15.07	16.01	54.17	18.33	11.56	20.00
Na	-0.14	0.14	0.23	1.24	-0.14	-0.20
K	2.25	2.26	2.85	5.50	2.40	2.77
Cl	0.22	0.46	1.07	1.62	0.41	0.41
HbA1C	2.43	1.86	1.25	2.15	1.41	2.99

For guiding QC strategy design Sigma values are very useful. For high sigma process, to detect any out-of-control situation that may cause a significant risk for the emergence of unreliable results, designing a QC procedure is relatively easy.[8]

In the study of Nar et al.[12] , the sigma metrics of Folate, LH, PRL, TPSA, TSH and vitamin B12 were above the average of 6.0 for 3 months. Therefore, for these parameters, they did not need any changes in the QC protocol and patient results were released. For parameters such as CA 19-9, CA 15-3, CEA, ferritin, PTH, FT3, cortisol, FSH and testosterone, the sigma metric values were between 3 and 6 on average.

Gulbahar et al.[13] conducted a study on Roche Cobas e 602 autoanalyser and the two level IQC sigma values of TSH, FT3 and FT4 were compared with two immunoassay analyzers. When the sigma values were calculated, it was found as 'World class' and 'unacceptable' for TSH and FT4, respectively. In both analyzers, FT3 was found as 'unacceptable' and 'good' for the two levels IQC of the first analyzer and the second level of the second analyzer, respectively.

Differences in sigma values of the study of Nar et al.[12] with other studies may be due to autoanalysis, quality control materials, or pre-analytical and post-analytical conditions. They conducted that sigma metric values are required to determine the design and implementation of IQC acceptability criteria and rational control design according to sigma values with the help of Westgard Operational Spesifications Chart (OPSpecschart) in the clinical biochemistry laboratory.[8]

The errors during the calibrator preparation can be the IQC malfunction during transportation or storage, and mistakes during sample preperation by laboratory technicians. For better bias and CV%, a protocol should be established for the transportation and division of the IQC and calibrator samples to avoid interventions caused by laboratory technicians through the experiment.

Nanda et al.[15], in their study for routine biochemistry tests found six sigma values; >6 for AST, ALT, ALP, total bilirubin and uric acid tests; in the range of 3-6 for glu, creat, triglyceride tests; <3 for urea, Alb, T.prot., total cholesterol and chlorine tests.

Table 4. The distribution of groups and tests according to sigma values.

Sigma metrics	November		December		January	
	IQC1	IQC2	IQC1	IQC2	IQC1	IQC2
Grup 1 (<3)	Glucose	Glucose	Glucose	Glucose	Glucose	Posphate
	Total Protein	Total Protein	Posphate	Total Protein	Posphate	Total Protein
	Creatinine	Creatinine	Total Protein	Creatinine	Total Protein	Albumin
	Calcium	Calcium	Albumin	Calcium	Albumin	Creatinine
	Na	Na	Creatinine	Mg	Creatinine	Calcium
	Cl	K	Calcium	Na	Calcium	Mg
	HbA1C	Cl	Mg	Cl	Mg	Na
		HbA1C	Na	HbA1C	Na	K
			K		K	Cl
			Cl		Cl	HbA1C
			HbA1C		HbA1C	
Grup 2 (3–6)	ALP	Posphate	ALP	Albumin	ALP	Glucose
	Posphate	Albumin	AST	Lipase	AST	ALP
	Albumin	Uric Acid	Lipase	K	Uric Acid	AST
	Uric Acid	Lipase			Lipase	Uric Acid
	Lipase	NH3			D-Dimer	Lipase
	Mg	Mg				NH3
Grup 3 (>6)	Amylase	ALP	Amylase	ALP	Amylase	Amylase
	GGT	Amylase	GGT	Amylase	GGT	GGT
	AST	GGT	ALT	GGT	ALT	ALT
	ALT	AST	LDH	ALT	LDH	LDH
	LDH	ALT	CRP	LDH	CRP	CRP
	CRP	LDH	Uric Acid	CRP	NH3	Lactate
	NH3	CRP	NH3	Uric Acid	Lactate	BUN
	Lactate	Lactate	Lactate	Lactate	BUN	D-Dimer
	BUN	BUN	BUN	BUN	Direct Bil.	Direct Bil.
	D-Dimer	D-Dimer	D-Dimer	D-Dimer	Total Bil.	Total Bil.
	Direct Bil.	Direct Bil.	Direct Bil.	Direct Bil.	CK	CK
	Total Bil.	Total Bil.	Total Bil.	Total Bil.	CK-MB	CK-MB
	CK	CK	CK	CK		
	CK-MB	CK-MB	CK-MB	CK-MB		

Chaudhary et al.[16] defined sigma values in their study for routine biochemistry tests in a 4-month period; >3 for Glu, ALP, T prot., Triglyceride, HDL-cholesterol, amylase and uric acid; it was found less than <3 for AST, ALT and total cholesterol.

In a study by Adiga et al.[14], sigma values of ALT, direct bilirubin, total bilirubin, calcium, creat, urea (D1) and AST, direct bilirubin, urea (D2) were <3; AST, Glu, cholesterol, uric acid, T prot. (D1) and ALT, calcium, cholesterol, Creat, Glu, total bilirubin (D2) were 3-6; Alb, ALP, triglyceride, HDL (D1) and Alb, ALP, HDL, T. Prot., TG, uric acid (D2) were >6.

In their study, Nar et al.[12] evaluated the laboratory performances of immuno assay tests on the Cobas e 601 analyzer (Roche Diagnostics, Germany) for 3 months from June 2015 to August 2015. TSH was determined to be >6 sigma in both levels of quality control during three month. The sigma value for FT3 was between 3 and 6 for the first level for 3 months, while for the second level that was >6 and between 3 and 6 for three months, respectively. Mean sigma values of TSH, FT4 and FT3 were found to be 13.06/16.13, 3.97/3.69, 3.75/6.57 for both levels, respectively, for the three-months. According to these results, TSH was found as 'World standards' for both levels; FT3 was found as 'good' and 'World standards' for the first and second levels, and FT4 was found as 'good' for both levels. Sigma values for both IQC levels for AFP, cortisol, ferritin and total PSA tests, 6.98/11.17, 4.15/6,33, 6,77/7,35, 13,62/13,42 were found. Vitamin B12 and folate tests were found to be 12.52/10.67, 7.89/9.83 in sigma values for both IQC levels.

Six (21%) parameters; T Protein, Creatinin, Ca, Na, Cl, HbA1c; provided < 3 sigma value, 1 (04%) parameter; lipase; provided between 3-6 value and 11 (39%) parameters; amylase, GGT, ALT, LDH, CRP, Lactate, BUN, Direct Bil., T Bil., CK and CK-MB; provided >6 sigma value for both IQC1 and IQC2 levels for three months, respectively

T. Protein, Ca, Na, Cl, HbA1c produced <3 sigma value for every three months and for both IQC levels. For these parameters

necessity of implementing a very strict internal and external quality control and corrective activities appeared. A 3-6 sigma value was determined for the lipase and QC monitoring was stil acceptable for this parameter, although it was stil within acceptable limits. >6 sigma values were observed for Amylase, GGT, ALT, LDH, CRP, Lactate, BUN, T. Bil, D. Bil., CK, CK-MB. Therefore, for these parameters, we did not need any changes in the QC protocol and patient results were released.

As a result of our study, calibrations of the parameters with low six sigma level are performed more frequently in our laboratories and the number of IQCs per day has been increased.

CONCLUSION

Laboratories need to design their own quality control (QC) protocols to meet the quality wanted. Laboratory errors can be reduced by preserving analyte mean and six Standard deviations between its upper and lower limits.

ETHICAL DECLARATIONS

Ethics Committee Approval: We took approval of Tokat Gaziosmanpasa University, Deanery of Medical Faculty, Clinical Researches Ethics Committee at 20.11.2018 with the code of 18-KAEK-259.

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

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Orjinal Araştırma / Original Article

Relationship of COVID-19 Pandemic with Anxiety, Anger, Sleep and Emotion Regulation in Healthcare Professionals

COVID-19 Pandemisinin Sağlık Çalışanlarında Kaygı, Öfke, Uyku ve Duygu Düzenleme ile İlişkisi

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Abstract

Objective: Epidemic diseases have caused significant mental responses throughout the society and especially healthcare professionals, as well as those who have been infected. Healthcare professionals have a big role in the fight against the new coronavirus infection (COVID-19). When the literature is reviewed in terms of risky professions, as the cases increase, the psychological influence has increased significantly among the healthcare professionals dealing with the care of patients as an occupational group. The aim of this study is to research the effect of pandemic on anxiety, anger, sleep and emotion regulation in healthcare professionals.

Material and Method: The study included 261 doctors and 145 nurses. Data were collected by the Sociodemographic Data Form, State-Trait Anxiety Inventory (STAI), State-Trait Anger Expression Inventory (STAEI), Insomnia Severity Index (ISI) and Difficulties in Emotion Regulation Scale (DERS).

Results: State anxiety levels 50.5%, anger levels 34.8%, insomnia severity levels 35.4% and 36.1% of emotion regulation difficulty levels were detected of healthcare professions. It was determined that the state anxiety level increases the levels of trait anger and insomnia severity, the level of emotion regulation difficulty increases the levels of trait anger and the level of insomnia severity increases the level of trait anger of healthcare professions significantly.

Conclusion: We consider that the study will be guiding in terms of the degree of mental response of the healthcare professionals and the psychological and social support to be given to this group after the pandemic.

Keywords: COVID-19, anxiety, anger, insomnia, emotion regulation, frontline healthcare workers

Öz

Amaç: Salgın hastalıklar tarih boyunca hastalığa yakalananlar kadar tüm toplumda ve özellikle de sağlık çalışanlarında önemli ruhsal etkilenmelere yol açmıştır. Yeni coronavirus enfeksiyonu (COVID-19) ile mücadelede sağlık çalışanlarının rolü büyüktür. Riskli meslekler açısından literatür incelendiğinde; vakalar arttıkça meslek grubu olarak hastaların bakımı ile ilgilenen sağlık personellerinde hastalık ciddi artış göstermiştir. Bu çalışmada amacımız; COVID-19 pandemisinden fiziksel ve ruhsal olarak ciddi biçimde etkilenen sağlık çalışanlarında pandeminin kaygı, öfke, uyku ve duygu düzenleme üzerine etkisini araştırmaktır.

Gereç ve Yöntem: Araştırmaya 406 sağlık çalışanı (261 hekim, 145 hemşire) dahil edilmiştir. Araştırmada Sosyodemografik Veri Formu, Durumluk Kaygı Ölçeği (DKÖ), Sürekli Öfke Ölçeği (SÖÖ), Uykusuzluk Şiddeti Ölçeği (UŞİ) ve Duygu Düzenleme Güçlüğü Ölçeği (DDGÖ) ile veriler toplanmıştır.

Bulgular: Sağlık çalışanlarının durumluk kaygı düzeylerinin %50,5, sürekli öfke düzeylerinin %34,8, uykusuzluk şiddeti düzeylerinin %35,4 ve duygu düzenleme güçlüğü düzeylerinin %36,1 olarak tespit edildi. Sağlık çalışanlarının durumluk kaygı düzeyinin sürekli öfke ve uykusuzluk şiddeti düzeylerini, duygu düzenleme güçlüğü düzeyinin sürekli öfke düzeylerini ve uykusuzluk şiddeti düzeyinin sürekli öfke düzeylerini anlamlı olarak arttırdığı tespit edilmiştir.

Sonuç: Çalışmamızın sağlık çalışanlarının ruhsal açıdan hem pandemiden etkilenme dereceleri açısından hem de pandemi sonrası bu gruba verilecek ruhsal ve sosyal destek açısından yol gösterici olacağı kanaatindeyiz.

Anahtar Kelimeler: COVID-19, kaygı, öfke, uykusuzluk, duygu düzenleme, sağlık çalışanı

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) was declared as an international public health state of emergency and pandemia by the World Health Organization (WHO) with the detection of infection in 34 regions of China on 30 January 2020. The agent that is the cause of pneumonia has been identified as a new coronavirus and is defined as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The source of infection was identified as a bat and with the formation of 15 sets of healthcare professionals all of which were infected by an infected patient, the pathogen showed a rapid pattern of transmission from person to person. In Wuhan, China's Hubei province, where the infection was first identified, the infection grew exponentially and spread rapidly across the World.[1-5]

One of the groups that are seriously affected physically and psychologically by this negative situation is healthcare professionals. Continuously increasing number of cases, increasing workload, constantly updating information about the disease, depletion of personal protection equipment, widespread media exposure, lack of specific medicines, inadequate support, the risk of transmission of the infection and the risk of carrying the disease home increased the mental burden of healthcare professionals.[6-8] According to July 2020 data Ministry of Health of Turkey, a total of 8 thousand 227 healthcare professionals (the ratio of the average number of cases, 7.2%) have been infected.[9]

Healthcare professionals, especially those who care for COVID-19 patients have become more touchy to both high risk of infection and mental influence. A study in China has shown that those who are at the highest risk for mental illness; young people, healthcare professionals and people who spend a lot of time thinking about pandemia.[10]

Disease-induced stigma and feeling of loneliness that is brought by stigmatize can be added to the stress of those struggling with the disease and their relatives. Depression, feeling of loneliness, helplessness, hopelessness, anxiety and panic feeling, intense fears, irritability, intolerance, bursts of anger, unwillingness, difficulty in concentration, excessive mental struggles and thoughts, sleep and appetite problems, physical problems can take part in human lives as mental problems that everyone can experience.[11]

Anxiety can be expressed as a state of fear and tension felt under a threat. State anxiety is the fear that the individual feels due to the stressful situations person in and is an indication of the individual's emotions of tension and uneasiness. Moreover, individuals who experience state anxiety frequently are also at risk of becoming trait anxiety and many other anxiety situations may follow (social, somatic, etc.).[12] The emergence and consequences of COVID-19 caused worldwide fear, concern and anxiety among people. With the determination of high risk of transmission and mortality rates of the infection, people as a matter of course have begun to worry and concern about COVID-19. Anxiety and fear can increase the damage caused by the disease. Individuals may not think clearly and straight when reacting to COVID-19 with high levels of fear and anxiety.[13,14] Differences were determined between medical and non-medical healthcare professionals in terms of symptoms of depression, anxiety, stress and post-traumatic stress disorder. These differences can also be a guide for post-pandemic rehabilitation studies.[15]

Anger is an emotion, thinking that deliberately misdone to one's self, characterized by feeling hostility towards someone or something. The feeling of anger, which plays a very important role in daily life, occurs when the person is faced with obstructiveness. Conditions that cause anger which is one of the universal emotions and the way anger is expressed varies according to several factors such as age, gender, education level, work environment and culture.[16] In infectious disease pandemias, the risk of infection in healthcare professionals, changing working conditions, although protective equipment is sufficient uncertainty how long the situation will last, fear of carrying the disease, disease-induced stigma may cause an increase in anger.[17] Furthermore, increased anxiety, severity of insomnia and emotion regulation difficulties can increase anger.

Light, lifestyle, meal times, physical activity and stress level are important in the sleep wake cycle. In the pandemia situation, the change of overtime period and working order, increased anxiety and depression levels of healthcare professionals not only affect daily life but also sleep.[18] In addition, a study showed that; anxiety, depression and stress levels and physical symptoms increased in healthcare professionals during pandemia.[19]

Emotion regulation often involves changes in emotional response. During emotion regulation, the person can increase, sustain or decrease the intensity of their positive or negative emotions.[20] Emotional regulation and management play a determining role in health protection and mental disorders.[21] Increasing anxiety level in pandemia situation is likely to accompany emotional regulation difficulty, anger and insomnia.

The purpose of this study is to research the effect of pandemia on anxiety, anger, sleep and emotion regulation in healthcare professionals who are severely affected physically and mentally by the COVID-19 pandemia. It is also aimed to examine the effect of these variables on each other. Especially when reviewing the literature on COVID-19, the effects of pandemia on depression, anxiety, post-traumatic stress disorder and sleep in healthcare professionals were searched, and there was no research article on the effect of anger and emotion regulation difficulty.

MATERIAL AND METHOD

Sample

The universe of the research consists of doctors and midwives/nurses in Turkey. According to the data of the Ministry of Health in 2020, the number of doctors and midwives/nurses working in Turkey is approximately 370,332. With the sampling error of 0.05 from the universe, considering the reliability[22] the number

of sub-participation was determined as 384 and 406 doctors and midwives/nurses who work actively were included in the study. Socio-demographic data form and scales containing questionnaire form were prepared by Google Drive program and applied to participants by sharing it via social media groups and e-mail. Repeating access was blocked by the programme for participants to do the tests one more time.

Data Collection Tool

Online survey method was used by using Google Drive program to collect the research data. In the survey; totally 5 sections ranked as sociodemographic data form, State-Trait Anxiety Inventory (STAI), State-Trait Anger Expression Inventory (STAEI), Insomnia Severity Index (ISI) and Difficulties in Emotion Regulation Scale (DERS).

Sociodemographic Data Form: Questions about sociodemographic characteristics such as age and gender etc. of the participants and Covid-19 were prepared and posed by the researcher.

State-Trait Anxiety Inventory (STAI): It is a 40-item self-report scale developed by Spielberger to measure the state and trait anxiety level of the individual.[23] The inventory consists of two different sub-scales: state anxiety and trait anxiety. In this study, state anxiety sub-scale was used. The Turkish validity and reliability study were conducted by Öner et al.[24] provides four-point likert-type measurement.

State-Trait Anger Expression Inventory (STAEI): It was developed by Spielberger et al.[25] and the trait anger subscale of the scale was used in our study. It was adapted to Turkish by Ozer[26] and is a 4-point likert-type scale with 10 items.

Insomnia Severity Index (ISI): It is a measurement tool developed to evaluate the severity of insomnia and has high validity and reliability.[27] Scale items consisting of seven questions are scored between 0-4. The scores that can be obtained from the scale vary between 0-28. Turkish validity and reliability study were made by Boysan et al.[28]

Difficulties in Emotion Regulation Scale (DERS): It is a 5-point likert-type scale consisting of 36 items developed by Gratz and Roemer.[29] High scores from the scale indicate high level of emotion regulation difficulties. Adaptation of the scale to Turkish, validity and reliability studies were conducted by Rugancı and it was reported to be a valid and reliable measurement tool.[30]

Process

Ethics committee approval for the study, numbered 46418926-050.03.04, dated 24.04.2020, was received from Hamidiye Scientific Research Ethics Committee of Health Sciences University. A questionnaire application including sociodemographic data form and scales was applied to 406 doctors and midwives/nurses who work actively in Turkey between the dates of 25-29 April 2020. Those with a history of psychiatric illness and using psychiatric medication were not included in the study.

Data Analysis

In the analysis of the data collected within the scope of the research, quantitative analysis method was employed by using SPSS 24.0 program. Within the scope of quantitative analysis; descriptive statistical methods such as mean, standard deviation, percentage, skewness and kurtosis and simple linear (regression) analysis, with $p<0.05$ significance level and 95% confidence interval were used.

In addition, it was decided whether the data shows normal distribution or not by examining the skewness and kurtosis coefficients. The skewness and kurtosis values in the range of ±1.50 are interpreted as normal distribution.[31] In the study, the skewness and kurtosis coefficients of the state anxiety total score were -0.206 and -0.433, of the trait anger total score 0.675 and 0.425, of the total score of insomnia severity are 0.655 and 0.155,of the emotion regulation difficulty total score included in the regression were found to be 0.376 and -0.112.

RESULTS

A total of 406 doctors and midwives/nurses working in Turkey in April 2020 were included in this study which was conducted to examine the correlation of Covid-19 pandemic with anger, anxiety, sleep and emotion regulation in healthcare professionals. In the study, 236 (58.1%) women and 170 (41.9%) men, 261 (64.3%) doctors, 145 (35.7%) midwives/nurses participated. The average age of healthcare professionals, ranging in age from 21 to 62, is 35.57± 8.66. As a marital status, 262 (64.5%) of the participants are married, 126 (31.1%) are single, 16 (3.9%) are divorced and 2 (0.5%) are widows (spouse passed away). Also, 171 (42.1%) of the participants did not have children, 72 (17.7%) had 1 child, 112 (27.6%) had 2 children, 40 (9.8%) had 3 children, 11 (2.7%) have 4 or more children. The average daily working hours of the participants are 11.94±6.76 and the average number of hospital watches per week is 1.73 ±1.77.

Participants, 262 people (65.4%), work with patients treated for COVID-19 and 141 (34.7%) have a history of contact with COVID-19. The number of participants who received the COVID-19 test was 156 (38.4%) and of those 21 (13.5%) were positive, 135 (86.5%) were negative and 3 (1.9%) participants were hospitalized. Near of kin of 16 (3.9%) participants were diagnosed with COVID-19. On the other hand, the number of those who think that they have sufficient protective equipment while working is 260 (64.0%). Moreover, 363 (89.4%) of the participants are concerned about transmitting COVID-19 to people in their homes and 342 (84.2%) to people outside of hospitals or other health institutions.

Healthcare professionals' included the study the average of state anxiety was 50.30±10.56, the average of trait anger was 20.45±5.52, the average of insomnia was 9.92±5.75 and the emotion regulation difficulties were 87.96±18.01 found to be. Descriptive statistics on the state anxiety, trait anger, insomnia severity and emotion regulation difficulty levels of the healthcare professionals included in the study are given in **Table 1**.

Table 1. Descriptive statistics on state anxiety, trait anger, ınsomnia severity, and emotion regulation difficulty levels of participants

	Min.	Max.	Mean	Sd.	%*
State Anxiety	20.00	75.00	50.30	10.56	50.5
Trait Anger	10.00	40.00	20.45	5.52	34.8
Insomnia Severity	0.00	28.00	9.92	5.75	35.4
Emotion Regulation Difficulty	52.00	143.00	87.96	18.01	36.1

* Rated to the lowest and highest scores that can be obtained from the scales.

It was found that the state anxiety level of women and midwives/nurses was significantly higher than that of men and doctors; trait anger levels of healthcare professionals under the age of 35 are significantly higher than those aged 35 and over; insomnia severity levels of women, midwives/nurses, healthcare professionals under the age of 35, single/widowed/divorced, working 9 hours or more per day and those who have 2 or more hospital watches per week are significantly higher; women's emotion regulation difficulty levels were significantly higher than men ($p<0.05$). Apart from these, no significant difference was found ($p>0.05$).

The findings obtained as a result of comparing the state anxiety, trait anger, insomnia severity, and emotion regulation difficulty according to demographic characteristics are given in **Table 2**.

When the general situation was reviwed, it was found that the state anxiety level of the healthcare professionals showed a positive correlation with the trait anger levels (ß=0.213; $p<0.01$). Accordingly, as the level of anxiety measured in healthcare professionals increases, anger levels may also increase.

The findings obtained as a result of simple linear regression analysis to determine the effect of state anxiety on trait anger are given in **Table 3**.

When the general situation was reviwed, it was found that the state anxiety level of the healthcare professionals showed a positive correlation with the insomnia severity levels (ß=0.392; $p<0.01$). Accordingly, as the level of anxiety measured in healthcare professionals increases, there can be an increase in the level of insomnia severity.

Simple linear regression analysis findings to determine the effect of state anxiety on insomnia severity are given in **Table 4**.

When the general situation was reviwed, it was found that the level of insomnia severity of healthcare professionals was positively correlated with trait anger levels (ß=0.304; $p<0.01$). Accordingly, as the severity of insomnia in healthcare professionals decreases, there can be a significant decrease in anger level.

Simple linear regression analysis findings to determine the effect of insomnia severity on trait anger are given in **Table 5**.

Tablo 3. The Effect of State Anxiety on Trait Anger

Variable	Group	Model	Unstandardized Coefficients		Standardized Coefficients	t	p
			ß	S. Error	ß		
General Situation		Constant	14.861	1.306	0.213	4.375	0.000*
		State Anxiety	0.111	0.025			
Profession	Doctor	Constant	15.182	1.608	0.194	3.184	0.002*
		State Anxiety	0.103	0.032			
	Nurse	Constant	14.446	2.388	0.225	2.763	0.006*
		State Anxiety	0.122	0.044			
Gender	Female	Constant	15.776	1.704	0.180	2.800	0.006*
		State Anxiety	0.089	0.032			
	Male	Constant	12.627	2.160	0.274	3.698	0.000*
		State Anxiety	0.165	0.045			
Result of Covid-19 Test	Pozitive	Constant	10.727	6.518	0.354	1.651	0.115
		State Anxiety	0.202	0.122			
	Negative	Constant	17.016	2.455	0.144	1.677	0.096
		State Anxiety	0.079	0.047			
History of Covid-19 Contact	Yes	Constant	14.965	2.319	0.221	2.668	0.009*
		State Anxiety	0.120	0.045			
	No	Constant	14.868	1.578	0.206	3.420	0.001*
		State Anxiety	0.105	0.031			
Hospitalization	Yes	Constant	9.134	18.852	0.373	0.402	0.757
		State Anxiety	0.165	0.411			
	No	Constant	16.481	2.312	0.166	2.069	0.040*
		State Anxiety	0.091	0.044			

* Dependent Variable: Trait Anger, *p<.05

Table 2. Comparison of state anxiety, trait anger, ınsomnia severity, and emotion regulation difficulty based on demographic characteristics

		n	Mean	Sd.	t	Sd	p
State Anxiety	Female	236	52.43	10.63	4.924	404	0.000*
	Male	170	47.35	9.74			
	Doctor	261	48.66	10.68	-4.289	404	0.000*
	Nurse	145	53.26	9.68			
	Under 35 years old	205	49.99	10.37	-0.602	404	0.547
	35 years old and over	201	50.62	10.76			
	Married	262	50.03	10.50	-0.711	404	0.478
	Single/Widow/Divorced	144	50.81	10.67			
	Daily working 0-8 hours	227	50.22	10.42	-0.187	404	0.852
	Daily working 9+ hours	179	50.41	10.76			
	Weekly hospital watch 0-1	197	50.41	10.07	0.191	404	0.849
	Weekly hospital watch 2+	209	50.21	11.02			
Trait Anger	Female	236	20.45	5.27	0.001	339.8	0.999
	Male	170	20.45	5.87			
	Doctor	261	20.18	5.66	-1.321	404	0.187
	Nurse	145	20.94	5.24			
	Under 35 Years Old	205	21.35	5.96	3.341	391.2	0.001*
	35 years old and over	201	19.54	4.87			
	Married	262	20.38	5.55	-0.371	404	0.711
	Single/Widow/Divorced	144	20.59	5.47			
	Daily working 0-8 hours	227	20.11	5.42	-1.413	404	0.159
	Daily working 9+ hours	179	20.89	5.62			
	Weekly hospital watch 0-1	197	20.58	5.47	0.444	404	0.657
	Weekly hospital watch 2+	209	20.33	5.58			
Insomnia Severity	Female	236	10.45	5.64	2.197	404	0.029*
	Male	170	9.19	5.84			
	Doctor	261	8.96	5.38	-4.655	404	0.000*
	Nurse	145	11.66	5.99			
	Under 35 Years Old	205	10.91	5.96	3.552	400.9	0.000*
	35 years old and over	201	8.92	5.35			
	Married	262	9.41	5.70	-2.450	404	0.015*
	Single/Widow/Divorced	144	10.86	5.73			
	Daily working 0-8 hours	227	9.24	5.72	-2.727	404	0.007*
	Daily working 9+ hours	179	10.79	5.69			
	Weekly hospital watch 0-1	197	9.06	5.70	-2.981	404	0.003*
	Weekly hospital watch 2+	209	10.74	5.69			
Emotion Regulation Difficulty	Female	236	89.73	16.53	2.285	324.3	0.023*
	Male	170	85.50	19.67			
	Doctor	261	87.80	18.90	-0.244	335.1	0.808
	Nurse	145	88.24	16.34			
	Under 35 Years Old	205	89.45	18.61	1.691	404	0.092
	35 years old and over	201	86.44	17.29			
	Married	262	88.05	18.37	0.140	404	0.889
	Single/Widow/Divorced	144	87.79	17.39			
	Daily working 0-8 hours	227	87.68	17.98	-0.350	404	0.727
	Daily working 9+ hours	179	88.31	18.09			
	Weekly hospital watch 0-1	197	88.44	19.18	0.522	404	0.602
	Weekly hospital watch 2+	209	87.51	16.86			

*p < .05

When the general situation was reviwed, it was found that the level of emotional regulation difficulties of healthcare professionals was positively correlated with trait anger levels (ß=0.492; p<0.01). Accordingly, emotion regulation difficulty in healthcare professionals predicts trait anger significantly.

Simple linear regression analysis findings to determine the effect of emotion regulation difficulty on trait anger are given in **Table 6**.

Tablo 4. Effect of State Anxiety on Insomnia Severity

Variable	Group	Model	Unstandardized Coefficients		Standardized Coefficients	t	p
			ß	S. Error	ß		
General Situation		Constant	-0.821	1.281	0.392	8.568	0.000*
		State Anxiety	0.214	0.025			
Profession	Doctor	Constant	0.471	1.464	0.346	5.936	0.000*
		State Anxiety	0.174	0.029			
	Nurse	Constant	-1.396	2.574	0.396	5.155	0.000*
		State Anxiety	0.245	0.048			
Gender	Female	Constant	-0.100	1.716	0.379	6.274	0.000*
		State Anxiety	0.201	0.032			
	Male	Constant	-1.627	2.068	0.381	5.339	0.000*
		State Anxiety	0.228	0.043			
Result of Covid-19 Test	Pozitive	Constant	-7.939	5.582	0.597	3.240	0.004*
		State Anxiety	0.339	0.105			
	Negative	Constant	2.084	2.455	0.289	3.480	0.001*
		State Anxiety	0.164	0.047			
History of Covid-19 Contact	Yes	Constant	-0.391	2.071	0.399	5.132	0.000*
		State Anxiety	0.205	0.040			
	No	Constant	-1.035	1.628	0.389	6.850	0.000*
		State Anxiety	0.218	0.032			
Hospitalization	Yes	Constant	-35.273	20.081	0.905	2.133	0.279
		State Anxiety	0.933	0.437			
	No	Constant	1.136	2.282	0.320	4.155	0.000*
		State Anxiety	0.181	0.044			

* Dependent Variable: Insomnia Severity, *p < .05.

Tablo 5. The Effect of Insomnia Severity on Trait Anger

Variable	Group	Model	Unstandardized Coefficients		Standardized Coefficients	t	p
			ß	S. Error	ß		
General Situation		Constant	17.556	0.521	0.304	60.420	0.000*
		Insomnia Severity	0.292	0.045			
Profession	Doctor	Constant	17.592	0.656	0.275	4.610	0.000*
		Insomnia Severity	0.289	0.063			
	Nurse	Constant	17.469	0.901	0.340	4.326	0.000*
		Insomnia Severity	0.297	0.069			
Gender	Female	Constant	18.429	0.709	0.207	3.242	0.001*
		Insomnia Severity	0.194	0.060			
	Male	Constant	16.526	0.763	0.426	6.095	0.000*
		Insomnia Severity	0.427	0.070			
Result of Covid-19 Test	Pozitive	Constant	18.663	0.527	0.267	1.207	0.242
		Insomnia Severity	0.267	0.222			
	Negative	Constant	18.933	0.983	0.209	2.470	0.015*
		Insomnia Severity	0.203	0.082			
History of Covid-19 Contact	Yes	Constant	18.190	0.976	0.269	3.293	0.001*
		Insomnia Severity	0.283	0.086			
	No	Constant	17.241	0.614	0.323	5.527	0.000*
		Insomnia Severity	0.294	0.053			
Hospitalization	Yes	Constant	16.845	3.755	0.057	0.057	0.964
		Insomnia Severity	-0.024	0.429			
	No	Constant	19.012	0.926	0.212	2.672	0.008*
		Insomnia Severity	0.207	0.077			

* Dependent Variable: Trait Anger, *p < .05.

Tablo 6. The Effect of Emotion Regulation Difficulty on Trait Anger

Variable	Group	Model	Unstandardized Coefficients		Standardized Coefficients	t	p
			ß	S. Error	ß		
General Situation		Constant	7.180	1.191	0.492	110.374	0.000*
		Emotion Regulation Difficulty	0.151	0.013			
Profession	Doctor	Constant	6.510	10.427	0.520	9.803	0.000*
		Emotion Regulation Difficulty	0.156	00.016			
	Nurse	Constant	8.717	20.170	0.432	5.726	0.000*
		Emotion Regulation Difficulty	0.138	00.024			
Gender	Female	Constant	7.275	10.686	0.461	7.946	0.000*
		Emotion Regulation Difficulty	0.147	00.018			
	Male	Constant	6.864	10.708	0.533	8.164	0.000*
		Emotion Regulation Difficulty	0.159	00.019			
Result of Covid-19 Test	Pozitive	Constant	14.879	70.622	0.192	0.853	0.404
		Emotion Regulation Difficulty	0.071	00.084			
	Negative	Constant	6.338	20.043	0.538	7.354	0.000*
		Emotion Regulation Difficulty	0.165	00.022			
History of Covid-19 Contact	Yes	Constant	8.800	20.099	0.450	5.948	0.000*
		Emotion Regulation Difficulty	0.137	00.023			
	No	Constant	6.392	10.448	0.513	9.692	0.000*
		Emotion Regulation Difficulty	0.158	00.016			
Hospitalization	Yes	Constant	4.922	10.826	0.988	6.528	0.097
		Emotion Regulation Difficulty	0.126	00.019			
	No	Constant	7.165	20.016	0.500	7.088	0.000*
		Emotion Regulation Difficulty	0.157	0.022			

* Dependent Variable: Trait Anger, *p < .05.

As a result of the research, it was determined that the state anxiety level of healthcare professionals correlated positively with the level of trait anger and insomnia severity and the level of emotion regulation difficulty with the level of trait anger and the level of insomnia severity with the level of trait anger.

However, whether the COVID-19 test result is positive or negative is not a significant predictor of the effect of state anxiety and emotion regulation difficulty on trait anger. No positive relationship was found between the state anxiety and emotion regulation difficulty level with trait anger level in all healthcare professionals with positive and negative results (p>0.05).

Moreover, COVID-19 test result and hospitalization eliminates the significant effect of state anxiety and insomnia severity on trait anger. The relationship which shows positive correlation between state anxiety on insomnia severity and between emotion regulation difficulty and trait anger disappear in the case of hospitalization.

DISCUSSION

Even if the clear effect of the COVID-19 pandemic on global mental health has not been recorded and measured yet, literature knowledge has shown that healthcare professionals can develop psychiatric disorders after dealing with stressful social occurrences.[32,33] The fact that COVID-19 is transmissible from person to person, associated with high morbidity and potentially being fatal can intensify the perception of the individual's danger. In addition, the insufficiency of materials that may happen due to uncertainty of the process and increase of COVID-19 cases cause the pressure on healthcare professionals and the anxiety.[4,5]

In pandemia, healthcare professionals are exposed to factors such as high risk of infection transmission, change of work routines, disappointment, stigma, isolation, patients who have negative feelings, lack of contact with their families and fatigue. The stressful situation created by the pandemia causes mental health problems such as anxiety, depressive symptoms, insomnia, denial, anger and fear. These mental health problems not only affect the attention, comprehension and decision-making ability of healthcare professionals, but also prevent the fight against COVID-19 and have a lasting impact on general mental health. Checking this situation is important to protect long-term mental health of medical healthcare professionals and to control epidemia.[34,35]

In a survey study conducted with 7236 participants; anxiety levels, depressive symptoms, sleep quality were determined respectively, 35.1%, 20.1%, 18.2% and the public was under a great mental health burden during the COVID-19 pandemic in China, especially young people and healthcare professionals were found to be at risk for mental disorders.[7] In a study comparing 1255 non-medical healthcare professionals and 927 medical healthcare professionals, insomnia, anxiety, depression, somatization and obsessive compulsive symptoms were found significantly higher in medical healthcare professionals.[36] In a cross-sectional study, an online questionnaire was applied

to 2042 healthcare professionals and 257 administrative staff and the levels of fear, anxiety and depression were compared. Healthcare professionals were found to experience 1.4 times more fear, twice as much more depression and anxiety.[37] Only healthcare professionals were included in our study and it is not possible to compare with the general population sample, but increased anxiety, anger, insomnia severity and emotion regulation difficulty are among our findings.

In a multicenter study conducted with 764 nurses and 493 doctors, the participants reported 50.4% of symptoms of depression, 44.6% anxiety, 34% insomnia and 71.5% acute stress. Symptom levels were higher in those working with patients diagnosed with COVID-19, in women, for those working in Wuhan and in nurses.[38] In a study conducted with 230 participants in the pandemic hospital, the frequency of anxiety was 23.04% and the incidence of post-traumatic stress disorder was 27.39%, and the risk was higher in nurses and female staff.[39] According to the data of our study, working with patients diagnosed with COVID-19 does not affect the level of symptoms, but the state anxiety level in women and midwives/nurses; trait anger level in healthcare professionals under the age of 35; emotion regulation difficulty in women were found to be significantly higher.

In a study conducted with 123 participants in Wuhan, 38% of the participants had sleep disorder and a significant correlation was determined between sleep disorder and working with pediatric patients and depression scores.[40] In a study comparing 2110 healthcare professionals and 2158 students via online survey, psychological stress was determined significantly higher in healthcare professionals and insomnia severity was reported to be significantly higher in healthcare professionals in Wuhan.[41] In a study conducted with 180 healthcare professionals working in COVID-19 service in China, social support levels were significantly associated with self-efficacy and sleep quality and negatively correlated to the degree of anxiety and stress. Anxiety levels were significantly associated with stress levels that negatively affect self-efficacy and sleep quality.[19] In our study, the severity of insomnia in healthcare professionals is high and insomnia severity is significantly higher in women, midwives/nurses, healthcare professionals under the age of 35, unmarried ones, those who work over 8 hours a day, those who have hospital watches 2 or more times a week. Moreover, the level of anxiety and insomnia severity and insomnia severity and anger levels were found to be significantly related. While hospitalization eliminates these two significant correlations, negative results of COVID-19 test removes the significant effect of insomnia severity on the level of trait anger. The situation may be about the passing acceptance stage of the disease after hospitalization and relevant with the continuing fears of prognosis for people whose test result is positive.

In an online survey study involving 183 doctors and 811 nurses, symptoms of anxiety, insomnia and acute stress were examined, 36% had sub-threshold symptoms, 34.4% had mild symptoms, 22.4% had moderate symptoms, and 6.2% serious symptoms were detected. Relationship between high symptom cluster and contact history, less access to psychological material and resources via media have been reported.[42] In our study, no correlation was found between the history of contact and symptom level.

In a study with 38 doctors and nurses working in COVID-19 related services and 21 doctors and nurses working in other departments, significant levels of depression and anxiety were found, and no difference was found between those who worked in the service associated with COVID-19 and who did not work.[43] In our study, approximately two-thirds of the healthcare professionals work in services associated with COVID-19, and there was no significant difference between those who worked in the COVID-19 service and those who did not work in terms of symptom of anxiety, anger, insomnia and emotion regulation difficulty.

The most limitation of the study is that the tests were applied online.

CONCLUSION

Health systems around the world are under high pressure and systematic interventions for mental health services are urgently needed for medical staff.[44-46] These actions can show us ways to better control the COVID-19 pandemia, taking into account that the psychological problems of healthcare professionals can affect their attention, comprehension and decision making. Thus, more serious mental disorders can be prevented by early intervention. As a result, more comprehensive studies involving different aspects of being affected are needed to understand the pandemic's psychological effects more clearly. As we have seen in the literature, studies examining the pandemic's psychological effects on healthcare professionals are limited and no study on anger and emotion regulation difficulty. We think that our study will contribute to the literature and psychological rehabilitation studies during and after the pandemia..

ETHICAL DECLARATIONS

Ethics Committee Approval: Ethics committee approval for the study, numbered 46418926-050.03.04, dated 24.04.2020, was received from Hamidiye Scientific Research Ethics Committee of Health Sciences University.

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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

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Orjinal Araştırma / Original Article

Complementary Alternative Medicine Methods Preferred By Women Diagnosed With Urinary Tract Infections

İdrar Yolu Enfeksiyonları Tanısı Alan Kadınların Tercih Ettikleri Tamamlayıcı Alternatif Tedavi Yöntemleri

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Abstract

Introduction: The study was planned to determine the causes of infection in women diagnosed with urinary tract infections and the preferred complementary and alternative treatment methods of the women.

Material and Method: In the study, 180 women diagnosed with urinary tract infection (UTI) were interviewed. The required permissions were received. The data descriptive information form and Complementary and Alternative Medicine (CAM) Scale were used.

Results: The average age of women participating in the study is 40.21±15.42. 73.4% of the participants were diagnosed with more than one UTIs in one year. Almost all of the women who participated in the study stated that they used a complementary and alternative medicine method for UTIs (92.8%) and 97.8% of them expressed that this method was effective.

The use of CAM methods was more common in those with higher education, housewifes or retired, women, those who performed vaginal douching had chronic diseases or incontinence. The use of CAM is less in those who are diagnosed with more than three UTIs in a year.

Conclusion: The most commonly used herbal methods are parsley, rosehip, green tea, nettle, linden, thyme and chamomile; dietary methods are yogurt, milk and dairy products, honey, pomegranate, garlic; religious methods are prayers; the psychological approach is exercise.

Keywords: Urinary tract infection, preference, women, complementary and alternative treatment methods

Öz

Amaç: Çalışma, idrar yolları enfeksiyon tanısı alan kadınlarda enfeksiyon sebepleri ve tercih ettikleri tamamlayıcı ve alternatif tedavi yöntemlerini belirlemek için planlandı.

Gereç ve Yöntem: Çalışmada İdrar yolları enfeksiyonu (İYE) tanısı alan 180 kadınla görüşüldü. Gerekli izinler alındı. Veriler tanımlayıcı bilgi formu ile Tamamlayıcı ve Alternatif Tıp Yaklaşımları Ölçeği kullanıldı.

Bulgular: Çalışmaya katılan kadınların yaş ortalaması 40.21±15.42 dir. Katılımcıların %73.4'ü bir yılda birden fazla İYE tanısı almış. Çalışmada kadınların hemen hemen hepsi İYE için (%92.8) herhangi bir tamamlayıcı ve alternatif tedavi yöntemi kullanmış ve %97.8'i yöntemin etkili olduğunu ifade etmiştir. Eğitim durumu yüksek olanlarda, ev hanımı ya da emekli olanlarda, vajinal duş yapanlarda, kronik bir hastalığı veya inkontinansı olanlarda TAT kullanımı daha yaygındır. Bir yılda üçten fazla sayıda İYE tanısı alanlarda TAT kullanımı daha azdır.

Sonuç: En sık kullanılan bitkisel yöntemler; maydanoz, kuşburnu, yeşil çay, ısırgan, ıhlamur, kekik ve papatyadır. En sık kullanılan besinsel yöntemler; yoğurt, süt ve süt ürünleri, bal, nar, sarımsak, en sık kullanılan dini yöntemler; dua etmek ve namaz, en sık kullanılan ruhsal yaklaşım ise egzersizdir.

Anahtar Kelimeler: İdrar yolu enfeksiyonu, tercih, kadın, tamamlayıcı ve alternatif tedavi yöntemleri

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INTRODUCTION

Urinary tract infections (UTIs) are the microbial infiltration of the sterile urinary tract and are one of the most frequently seen bacterial infections across the world. UTIs covers urethra (urethritis), urinary bladder (cystitis), ureter (urethritis) and kidney (pyelonephritis) infections. It is estimated that annually more than 8 million UTIs people suffer from in the United States and many of them consult a physician. About 1% of patients diagnosed with UTIs receive antibiotic treatment requiring hospitalization.[1]

UTIs are one of the most common bacterial infections affecting women. In particular, they affect 50-60% of young and sexually active women. Approximately one in three women gets antibiotic treatment before the age of 24, the infection is repeated within 6 months and the UTI attack is experienced at least once in one-fourth of women.[2] UTIs in Turkey is one of the most common infections in outpatient services in both in inpatient facilities. According to reports from Turkey, 21-49% of hospital-acquired infections are urinary tract infections.[3] The passage of fecal bacteria in the urinary tract is easier in women than in men because of the shorter urethra, the proximity of the urethral meatus to the anus and the anatomical structure of women. In addition, among other risk factors, the diagnosis of UTIs before the age of 15 years, the history of UTIs in the mother or previous experience with UTIs and the use of spermicides as a method of contraception play a part.[2] The colonization of gastrointestinal pathogens during the coitus, urinary system obstruction, incomplete micturition, abnormal anatomical structure and low vaginal estrogen level are among the causes of UTIs as well.[4]

Recurrent UTIs are the occurrence of three infections in one year or more than two infections in six months. The main symptoms of UTIs are dysuria, frequent urination, cloudy urine and sometimes hematuria.[5] In general, UTIs without complications are limited to the bladder and are healed rapidly after antibiotic treatment. For this reason, they are less serious, but it can causes long-term sequelae. Even if they are not seen as very disturbing, UTIs without complications decreases the quality of life and productivity of the patient. In a study carried out with women studying at the university, among the patients diagnosed with UTIs it was reported that for 2.4 days their activity was limited, for 1.2 days they lost time and for 0.4 days they were confined to bed due to symptoms.[6]

The total cost associated with community-based UTIs including doctor visits, antibiotic prescriptions, hospitalizations and sick leave is reported to be approximately $1.6 billion each year in the United States.[7] For the treatment of UTIs, multiple antibiotic treatments are used in general, and afterward, resistance to the drugs develops. Effective alternative and complementary therapies are important especially for the treatment of recurrent UTIs. Herbal products are widely used although there are not many studies on such products used to relieve urinary symptoms. The leaf extract of Arctostaphylos uva-ursi (uva-ursi or bearberry) has been approved by the German Federal Institute of Drugs and Medical Devices for the use of urinary tract inflammation and is supplied with a prescription in Germany. It is reported that these plants have diuretic, urinary antiseptic and anti-inflammatory properties. Extract components include flavonoids, iridocyte, hydroquinone glycosides (mainly arbutine), tannins and terpenoids.[8] There is evidence that the Uva-Ursi plant is used in the United Kingdom to relieve symptoms of acute UTIs. In a study carried out with 309 women, it was reported that uvacin which contains uva-ursi was reduced the duration of the disease. However, although the numbers that indicate the use of the product are low, the recommended rates are high.[9]

In studies in Turkey it is widely used Complementary and Alternative Medicine (CAM) method. There are many studies especially on cancer, menopausal period, infertility, diabetes, metabolic diseases.[10-12] However, as a result of the literature review, there are insufficient number of studies on CAM methods and effects used for UTI. In fact, there is no study about the methods used CAM to treat UTI in Turkey. The aim of the present study was, to determine the causes of UTIs in women in Turkey, the infection as well as the complementary and alternative treatment methods they prefer to cope with it.

MATERIAL AND METHOD

Sampling Technique, Inclusion Criteria

The study is quantitative, descriptive and cross-sectional. The study was carried out in Gümüşhane, a province of the Eastern Black Sea region. The level of education is below the average in Turkey. The research population was composed of women who applied to a public hospital urology and gynecology polyclinic in Gümüşhane. The sample consists of 180 women who were reached between 20.02.2018-20.06.2018 and have the criteria for inclusion in the study. Women who applied to outpatient clinics, able to communicate in Turkish; were between the ages of 20-65 and diagnosed with UTI in the past year were included in the study. Patients who had a social or psychological status that would prevent them from participating in the study, women who were newly diagnosed and patients who did not wish to participate in the study after being informed of it were excluded.

Data Collection

In order to collect the data comfortably and safely, women were interviewed in a suitable outpatient clinic. The purpose of the study was explained to the participants, verbal consent was obtained from those who wanted to participate in the study and data were collected. A woman was interviewed for about 20 minutes.

Descriptive Information Form, and Complementary and Alternative Medicine Scale (CAMS) were used in the collection of the study data. The Descriptive Information Form consists of two parts. The first part questions the socio-demographic characteristics and the second part questions the risk factors for UTIs and includes questions about perineum hygiene, chronic diseases, family planning methods, sexually transmitted infections and UTIs.

Complementary and Alternative Medicine Scale: The Complementary and Alternative Medicine Scale was improved by Can et al. The scale consists of five subgroups of 55 CAM interventions often used. The five subgroups are as follows: herbal supplement subgroup (29 items), religious practices subgroup (5 items), mind-body practices subgroup (5 items), biological practices subgroup (3 items) and dietary supplement subgroup (14 items). CAMS assesses the use of individual CAM methods by dichotomous responses, where 0 means "no" and 1 means "yes". Sub-dimension scores were estimated by summing up the scores of individual items and the total score of the scale is the sum of individual sub-dimension scores. The Kuder-Richardson 20 (KR20) coefficient for the scale was 0.84.[13]

Ethical considerations

The required permission to conduct the study was obtained from the administration unit of the Health Directorate and from the Scientific Research and Publication Board of XXX University (Number=95674917-604.01.02). Eligible women were informed about the study. Verbal consent was obtained from the women, who accepted to participate in the study. Each woman was interviewed for 15 minutes to fill in the data collection questionnaire.

Data Analysis and Interpretation

The data obtained as a result of the research were evaluated with SPSS-22 program, error checks, tables and statistical analyzes were made. Numbers and percentages are given in statistical evaluations. Before normality analysis, missing data and extreme value extractions were made. Afterwards, histogram drawings were made for compliance with normal distribution, skewness and kurtosis values were examined, and Kolmogorov-Smirnov analyzes were performed. After all the steps, logarithmic transformations were applied to the CAMS, which did not show normal distribution, but it was determined that normal distribution conditions did not occur. Therefore, in order to determine whether independent variables make a difference on CAM, Mann-Whitney U and Kruskal Wallis tests was performed. $p < 0.05$ was accepted as statistical significance level.

RESULTS

Some socio-demographic characteristics of the women are shown in **Table 1**. The mean age of the participants was 40.21±15.42 (min=18, max=65). 45.0% of the participants were primary school graduates, 61.1% were housewives/reired, and the income of 58.3% of the women equaled to their expenses.

The mean Body Mass Index (BMI) of the women was 26.05 ± 5.05 (min=15, max=43) and the mean number of pregnancies was 2.91±2.71 (min=0, max=12). Some characteristics of genital hygiene are shown in **Table 2**.

Table 1. Some socio-demographic characteristics of women

Educational Background	**n**	**%**
Primary school graduate	81	45.0
Secondary/high school graduate	38	21.1
University graduate	61	33.9
Total	180	100.0
Income status	**n**	**%**
Income is less than Expense	66	36.7
Equal Income&Expense	105	58.3
Income is much more than Expense	9	5.0
Total	180	100.0
Employment Status	**n**	**%**
Housewife /Retired	110	61.1
Employed	37	20.6
Student	33	18.3
Total	180	100.0
Abode	**n**	**%**
Married	127	70.6
Single/Separated	52	29.4
Total	179	100.0

Forty-six percent of the women changed their pad every 3-4 hours during menstruation period, 51.1% performed vaginal douching (wash the vagina), 58.9% of them wore cotton underwear and 32.2% of them complained of urinary incontinence. 73.4% of the participants were diagnosed with more than one UTI in one year.

As a result of the evaluation of some variables of the participants diagnosed with a UTI in one year it was found that housewives, those with low education level, who wash their hands only after leaving the toilet, those who washed from the front to the back, the ones who perform vaginal douching, those who do not care to wear cotton underwear were more likely to experience a UTI in a year ($p < 0.05$). There were no statistically significant differences in the prevalence of UTI diagnoses within a year due to income status, smoking, the number of pad changes, the frequency of changing underwear, being sexually active and urinary incontinence ($p > 0.05$).

The number of women diagnosed with UTI in a year; was high in housewifes (X^2=17.884, p=0.007), those with low education levels (X^2=19.124, p=0.004), those who performed vaginal douching (X^2=9.499, p=0.023), those with chronic diseases (X^2=13.012, p=0.0009) and those with urinary incontinence complaints (X^2=12.939, p=0.005).

Almost all of the women who participated in the study stated that they used a CAM method for UTIs (92.8%) and 97.8% of them expressed that the method was effective. CAM methods used by women with UTI diagnosis are shown in **Table 3**.

The use of CAM was common in women diagnosed with UTI (73.3% of them used herbal, 75.6% nutritional, 76.7% religious and 17.8% psychological approaches). The most commonly used herbal methods were parsley, rosehip, green tea, nettle, linden, thyme and chamomile; the dietary methods were yogurt, milk and dairy products, honey, pomegranate, garlic; religious methods were prayers and the psychical approach was exercise.

Table 2. Some characteristics of women concerning genital hygiene

The frequency of changing pad	**n**	**%**
1-2 hours	26	20.6
3-4 hours	58	46.0
5-6 hours	26	20.6
6 hours or more	16	12.8
Total	126	100.0
Cleanliness	**n**	**%**
With water	49	27.2
With toilet paper	12	6.6
With water and toilet paper	118	65.6
With water and soap	1	0.6
Total	180	100.0
Frequency of changing underwear	**n**	**%**
One time per week	11	6.1
Two-three times per week	97	53.9
Daily	60	33.3
2 times a day	12	6.7
Total	180	100.0
Sexual activity	**n**	**%**
Yes	98	54.4
No	82	45.6
Total	180	100.0
How many times a year diagnosed with UTI	**n**	**%**
Once	48	26.6
Two-three times	64	35.6
Four-five times	34	18.9
Six and more times	34	18.9
Total	180	100.0
Birth control (BC) method	**n**	**%**
Yes	70	38.8
No	110	61.2
Total	180	100.0
The vaginal douching	**n**	**%**
Yes	92	51.1
No	88	48.9
Total	180	100.0
Handwashing	**n**	**%**
Before toilet	3	1.7
After toilet	109	60.6
Before and after toilet	66	36.6
Do not care	2	1.1
Total	180	100.0
How the cleanliness provided	**n**	**%**
Front to back	102	56.7
Back to front	64	35.6
Do not care	14	7.8
Total	180	100.0
Underwear feature	**n**	**%**
I wear cotton underwear	106	58.9
I wear synthetic underwear	5	2.8
Do not care	69	38.3
Total	180	100.0
STI experience	**n**	**%**
Yes	18	10.0
No	162	90.0
Total	180	100.0
Urinary incontinence	**n**	**%**
Often	30	16.7
Occasionally	27	15.0
Rarely	1	0.6
Never	122	67.7
Total	180	100.0
Preferred BC methods	**n**	**%**
Contraceptives	8	11.5
Intrauterine device	20	28.5
Condom	11	15.8
Withdrawal method	**28**	**40**
Tubal ligation	3	4.2
Total	70	100.0

UTI: Urinary tract infections, BC: Birth control, STI: Sexually Transmitted Infections

Table 3. Use of CAM Therapies* (n=356)

Herbal supplements	**n**	**%**
VStinging nettle	41	22.8
Rosehip	95	52.8
Linden tea-	43	23.9
Grape seed	4	2.2
Daisy	34	18.9
Green tea	51	28.3
Sage tea	17	9.4
Nigella sativa	19	10.6
Blueberries	3	1.7
Mallow	4	2.2
Ginger	11	6.1
Sweet almond	2	1.1
Curcuma	6	3.3
Flax seed	1	0.6
Vitamin	12	6.7
Centaury	3	1.7
Thyme	28	15.6
Yarrow	2	1.1
Juniper	1	0.6
Omega 3	3	1.7
Other		
Onion juice	38	21.1
Apple cider vinegar	17	9.5
Cherry stalk	6	3.3
Parsley	102	56.7
Mind-body practices	**n**	**%**
Exercise	31	17.2
Meditation	-	-
Yoga	-	-
Acupuncture	1	0.6
Music	-	-
Dietary supplements	**n**	**%**
Yoghurt	101	56.1
Milk and milk products	97	53.9
Honey	62	34.4
Carob syrup	14	7.8
Anzer honey	1	0.6
Mullberry syrup	9	5.6
Chestnut honey	1	0.6
Pomegranate	20	11.1
Grapefruit	6	3.3
Garlic	26	14.4
Carrot	15	8.3
Other fruits and vegetables	25	13.9
Red meat	11	6.1
Fish	9	5.6
Chicken	3	1.7
Bread/pastry	3	1.7
Sweet-tat	3	1.7
Other (kefir)	5	2.8
Religious practices	**n**	**%**
Namaz**	58	32.2
Pray	132	73.3
Carry written amulet	9	5.6
Visit place where holy man is bruied	2	1.1
Biological practices	**-**	**-**

* Some patients used more than one CAM therapy so the percentages of CAM use are given according to the related item.
** Namaz= Prayer performed by Muslims five times a day.

The methods used by the participants for coping with UTIs were drinking plenty of water, particularly making hot application to feet and taking a warm shower. The comparison of sub-dimension and total score averages of CAM scale according to the characteristics of the participants is shown in **Table 4**.

The use of CAM methods was more common in those with higher education, housewifes or retired, women, those who performed vaginal douching had chronic diseases or incontinence. The use of CAM methods was less in patients who suffered from more than three UTIs in a year and there was a significant difference between them.

DISCUSSION

UTIs are very common in the community, can be easily treated and can cause morbidity, and sometimes, although very rarely, cause mortality. UTIs are bacterial infections that are most common among females and reduce the quality of life.[14] Although they require proper antibiotic treatment, 30-50% of women who have UTIs have a recurrent infection in 6-12 months. The chronic recurrent UTIs (more than two in one year) are present in 2-5% of women.[15] It was reported in a study that women had a higher risk of contracting a second UTI after the first one, and 20% of patients had a recurrence within 6 months.[16] In this study, it was observed that the rate of women diagnosed with more than one UTI in a year was 73.4%. The rate of women diagnosed with four or more was 37.8%. The woman diagnosed with UTIs once had a risk for subsequent infections.

Table 4. Comparison of sub-dimension and total score averages of CAM scale according to characteristics of the participants

	Herbal Approaches Median (%95 CI)	Nutritional Approaches Median (%95 CI)	Religious Approaches Median (%95 CI)	Spiritual Approaches Median (%95 CI)	Total Median (%95 CI)
Educational Background					
Primary	2.00 (1.97-2.86)	2.00 (1.77-2.76)	2.00 (1.29-1.74)	0.00 (0.10-0.28)	6.00 (5.44-7.37)
Secondary/high	2.00 (1.78-3.00)	2.00 (2.03-2.65)	2.00 (1.46-2.00)	0.00 (0.11-0.40)	7.00 (5.78-7.69)
University	1.00 (1.09-1.95)	2.00 (1.62-2.73)	2.00 (1.07-1.54)	0.00 (0.02-0.17)	5.00 (4.13-6.09)
Test value	KW=9.193 p=0.010	KW=1.683 p=0.431	KW=4.050 p=0.132	KW=4.717 p=0.095	KW=7.314 p=0.026
Employment Status					
Housewife	2.00 (2.00-2.75)	2.00 (1.89-2.63)	2.00 (1.39-1.75)	0.00 (0.10-0.25)	6.00 (5.64-7.15)
Employed	1.00 (1.25-2.47)	2.00 (1.55-2.55)	2.00 (1.09-1.77)	0.00 (0.05-0.32)	5.00 (4.36-6.71)
Student	1.00 (0.92-2.04)	2.00 (1.55-3.35)	2.00 (0.97-1.62)	0.00 (0.02-0.28)	5.00 (3.92-6.85)
Test value	KW=6.261 p=0.044	KW=0.047 p=0.977	KW=2.034 p=0.362	KW=0.200 p=0.905	KW=2.877 p=0.237
The vaginal douching					
Yes	2.00 (1.85-2.66)	2.00 (1.92-2.70)	2.00 (1.32-1.71)	0.00 (0.14-0.31)	7.00 (5.54-7.10)
No	2.00 (1.55-2.35)	2.00 (1.74-2.64)	2.00 (1.26-1.67)	0.00 (0.05-0.19)	5.00 (4.86-6.61)
Test value	U=3651.000 p=0.247	U=3751.000 p=0.386	U=3958.500 p=0.772	U=3630.000 p=0.071	U=3544.000 p=0.148
Chronic disease condition					
Yes	2.00 (1.69-2.64)	2.00 (1.88-2.88)	2.00 (1.39-1.83)	0.00 (0.06-0.24)	7.00 (5.39-7.25)
No	2.00 (1.72-2.43)	2.00 (1.81-2.54)	2.00 (1.24-1.60)	0.00 (0.11-0.26)	5.00 (5.12-6.62)
Test value	U=3622.500 p=0.727	U=3517.000 p=0.503	U=3367.000 p=0.212	U=3597.500 p=0.529	U=3379.000 p=0.284
Diagnosis of UTI in one year					
Once	2.00 (1.43-2.69)	2.00 (1.76-2.86)	2.00 (1.50-2.04)	0.00 (0.05-0.27)	5.50 (5.10-7.51)
Twice-Thrice	2.00 (1.89-2.82)	3.00 (2.26-3.38)	2.00 (1.35-1.79)	0.00 (0.11-0.32)	7.00 (5.92-8.03)
4-5 times	1.00 (0.96-2.03)	2.00 (1.14-2.02)	1.00 (0.74-1.48)	0.00 (0.02-0.27)	4.00 (3.37-5.33)
6 and more	2.00 (1.65-2.99)	2.00 (1.05-2.47)	2.00 (1.01-1.62)	0.00 (0.02-2.49)	6.00 (4.30-6.81)
Test value	KW=5.666 p=0.129	KW=12.380 p=0.006	KW=11.291 p=0.010	KW=1.208 p=0.751	KW=10.420 p=0.015
Incontinence status					
Yes	2.00 (1.92-2.90)	2.00 (1.59-2.61)	2.00 (1.26-1.76)	0.00 (0.11-0.33)	6.50 (5.34-7.17)
No	2.00 (1.62-2.31)	2.00 (1.96-2.69)	2.00 (1.31-1.65)	0.00 (0.09-0.22)	5.00 (5.18-6.67)
Test value	U=2986.000 p=0.085	U=3336.000 p=0.528	U=3514.500 p=0.935	U=3296.000 p=0.263	U=3209.00 p=0.312

KW= Kruskal Wallis Test, U= Mann Whitney U Test, CAM= Complementary and Alternative Medicine

Sexual contact, no micturition, the use of spermicidal gel, the use of diaphragm, pregnancy, low socioeconomic status, diabetes, sexually transmitted infections, vaginal douching, daily use of pads, hygienic behavior and history of recurrent infection are risk factors for UTIs in women.[16.17] In this study, approximately half of the women diagnosed with UTIs were primary school graduates, 61.1% were housewives and 70.6% were married. When the hygiene behaviors of the participants were examined it was found that only 36.7% of the participants washed their hands before and after going to the toilet, 56.7% cleaning from front to back, 10% had Sexually Transmitted Diseases (STDs), and 51.1% performed vaginal douching. UTI diagnosis was high in housewives, in those with low education level, in those who washed their hands only after leaving the toilet, in those who washed from back to front in those who performed vaginal douching, in those who do not pay attention to the choice of underwear, and in those who have chronic disease and urinary incontinence.

According to the latest studies in UTI management, it has been reported that the use of Chinese herbal medicines alone or with medicines are beneficial. It was also reported that it prevented infections, which were recurrent at least six months later.[18] Almost all of the women participated in the study stated that they used a CAM method for UTI (92.8%) and 97.8% of them expressed that the method was effective. It was determined that women did not only use biological methods. The most commonly used herbal methods were parsley, rosehip, green tea, nettle, linden, thyme and chamomile; dietary methods were yogurt, milk and dairy products, honey, pomegranate, garlic; religious methods were prayers and the psychological approach was exercise. It was determined that they did not prefer only biological methods. In the last review studies, 4 alternative approaches other than drugs were recommended. These were cornelian cherry, prebiotic, Chinese herbal medicine and D-mannose. It has been emphasized that prebiotics are not very effective when mixed with placebo or when used alone. It was also reported that the efficacy was high with medical treatment. [19] Some of the fruit juices used have been reported to be effective. Especially the use of bilberry for a long time was reported to be effective in reducing UTI complaints. The use of cornelian cherry juice for 12 months was reported to reduce the frequency of UTI and to be effective for the regression of symptoms.[20]

It is recommended to use CAM methods especially to prevent recurrent infections, to increase the effectiveness of treatment, to reduce the side effects and the treatment costs. There are many uses of CAM in some countries and the studies about endemic methods continue. For example, traditional methods are commonly used in China to treat various pathologies, including chronic and refractory infectious diseases.[21] 33 women with more than 3 UTIs per year were included in a study. Annual UTI incidence of the women was determined as 6.6 + 2.5. 4 weeks-treatment consisting of 10 plants (Rhizoma Anemarrhenae, Cortex Phellodendri Chinensis, Angelica sinensis, Rehmannia glutinosa, Libosch, Wolfiporiacocos, Salvia miltiorrhiza, Rhubarb, Polygonum aviculare L., Dianthus superbus, and Talcum) was applied to women who were resistant to at least 8 antibiotics. After 2 weeks, 25 patients (73.52%) experienced significant symptomatic relief; in 4 weeks, 30 patients (88.23%) recovered; and 3 patients (7.5%) did not come around. Recurrence was observed in only 4 (11.76%) of the patients recovered after 6 months of follow-up and this rate was indicated to be a much lower than the antibiotic treatment. No adverse effects were reported among these cases.[22] In the study, it was found that almost all of the women used CAM. In particular, various herbal and dietary sources were preferred. The vast majority of women drunk parsley and rosehip juice, and consumed milk, milk products and yoghurt. Staying hydrated and warm applications were also used to cope. In a study, many methods were recommended for UTIs as well as the elimination of many ailments. Staying hydrated, sweet juicy fruit (grape, pear, plum, mango, melon, apple), pumpkin, yellow squash, cucumber, organic food were recommended to be eaten.[23]

In this study, the use of the CAM method was more common in; housewives, those who have a high educational level and perform vaginal douching, those with a chronic disease and incontinence. In addition, the use of the CAM method was less in those who were diagnosed with more than three UTIs in a year.

CONCLUSIONS

As a result of the research; genital hygiene behaviors were determined to affect the frequency of UTI diagnosis. Almost all women with UTIs use a CAM method (%92.8). It was found that the women with UTIs especially preferred; parsley, rosehip, green tea, nettle, linden, thyme and chamomile as herbal methods; yogurt, milk and dairy products, honey, pomegranate, garlic as dietary methods; prayers as religious methods and exercise as psychological approach. Almost all women using the method stated that the method was effective (97.8%).

It is necessary to prevent UTIs to reduce health cost and improve women's quality of life. It is very important to raise awareness for improper practices. Women's CAM methods and their effects on health must be researched. It is recommended to determine the methods varying by countries and regions and to carry out comprehensive researches.

ETHICAL DECLARATIONS

Ethics Comittee Approval: The study was carried out with the permission of the Scientific Research and Publication Board of Gümüşhane University (Number=95674917-604.01.02).

Informed Consent: The study was conducted on a voluntary basis. Verbal consent was obtained from the participants.

Status of Peer-review: Externally peer-reviewed.

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Orjinal Araştırma / Original Article

Evaluation of the Relationship between Internet Addiction and the Thoracal Kyphosis Angle on Medical Faculty Students

Tıp Fakültesi Öğrencilerinde İnternet Bağımlılığının Torakal Kifoz Açısı ile İlişkisinin Değerlendirilmesi

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Abstract

Aim: For the last 20 years, various problems caused by internet has brought attention to researchers. People who actively use the Internet can spend 40 to 80 hours per week on a computer or phone. Their sleep patterns, daily life and exercise habits change over time. These changes bring along some illnesses such as back pain, neck pain and carpal tunnel syndrome. Many of these ailments underlie postural disorders. The most common of these postural disorders is increased thoracic kyphosis. Our aim is to determine the effect of internet usage on thoracic kyphosis angle in healthy individuals.

Material and Method: We conducted our study in 322 (K =152, E =170) students who were educated at Sakarya University Medical Faculty. Internet usage questionnaire was applied to the participants to measure the level and duration of internet usage. Thoracic kyphosis angle measurement was done with Flexicurve device Statistical comparisons were made using SPSS software.

Results: In our study, the kyphosis angles of the participants varied between 21,067 degrees and 49,546 degrees. The average score of the questionnaire on internet usage was 32,508 (slightly dependent), while the average daily internet use was 200 minutes. When the questionnaire scores and kyphosis angle values were compared, the result was statistically significant ($p=0.016$, $p<0.05$).

Conclusion: It is important to identify and evaluate the negative effects of internet use on our posture. People should pay attention to internet usage times and body postures during use in order to protect their postures during internet use. Otherwise, there will be an increase in thoracic kyphosis angle with serious disorders in the posture.

Keywords: Thoracic angle, kyphosis, internet addiction, flexicurve

Öz

Amaç: İnternetin beraberinde getirdiği sorunlar son 20 yıl boyunca araştırmacılar tarafından da ilgi odağı olmuştur. İnterneti aktif olarak kullanan kişiler bilgisayar veya telefon başında haftalık 40 ila 80 saate tekabül eden süreler geçirebilmektedirler. Bu kişilerin zamanla uyku düzenleri, gündelik hayat ve egzersiz alışkanlıkları değişmektedir. Bu değişimler beraberinde sırt ağrısı, boyun ağrısı, karpal tünel sendromu gibi bazı rahatsızlıkları getirmektedirler. Bu rahatsızlıkların birçoğunun temelinde postüral bozukluklar yatmaktadır. Bu postüral bozukluklardan en sık karşılaşanı torakal kifoz artışıdır. Bizim amacımız sağlıklı bireylerde internet kullanımının torakal kifoz açısı üzerindeki etkisini saptamaktır.

Gereç ve Yöntem: Çalışmamızı Sakarya Üniversitesi Tıp Fakültesinde eğitim alan toplam 322 (K=152, E=170) öğrencide gerçekleştirdik. Katılımcılara internet kullanım düzeyi ve süresini ölçmek amacı ile İnternet kullanım anketi uygulandı. Torakal kifoz açısı ölçümü Flexicurve cihazı ile yapıldı. Cihaz C7-T12 omurgaları arasına yerleştirilip daha sonra milimetrik kâğıda geçirildi ve ortaya çıkan şeklin açı değeri özel bir formül ile hesaplandı. İstatistiksel karşılaştırmalar SPSS paket programı kullanılarak yapıldı.

Bulgular: Çalışmamızda katılımcılarının kifoz açıları 21,067 derece ile 49,546 derece arasında değişmekteydi. İnternet kullanımı ile ilgili anketin ortalama puanı 32,508 (az bağımlı) iken günlük internet kullanım ortalaması ise 200 dakikaydı. Anket puanları ile kifoz açısı değerleri karşılaştırıldığında ortaya çıkan sonuç istatiksel olarak anlamlıydı ($p=0,016$, $p<0.05$).

Sonuç: İnternet kullanımının postürümüz üzerindeki negatif etkilerini saptamak ve değerlendirmek önemlidir. Kişilerin internet kullanımları sırasında postürlerini korumak amacıyla internet kullanım sürelerine ve kullanım sırasındaki vücut duruşlarına dikkat etmeleri gerekmektedir. Aksi takdirde postürde ciddi bozukluklar ile birlikte torakal kifoz açısında bir artış ortaya çıkmaktadır.

Anahtar Kelimeler: Torakal açı, kifoz, internet bağımlılığı, flexicurve

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INTRODUCTION

The Internet occupies a large place in our lives in many sectors such as information, communication, and shopping, and is increasing its popularity day by day in whole world. However, it also brings some problems with individuals.[1]

For the last 20 years, various problems caused by internet has brought attention to researchers. Dr. Kimberly Young[3] has defined excessive internet use in individuals as internet addiction and used the Internet Addiction Test created by him to determine this. This test is widely used in research on the subject today.[2] People with high internet usage can spend 40 to 80 hours a week on their computer or phone to use the internet. Their sleep patterns, daily life and exercise habits change over time. These changes bring along some conditions such as back pain, neck pain and carpal tunnel syndrome. Many of these ailments underlie postural disorders.[3]

Posture is that every part of the body is in the position adjacent to the body and the most stable compared to the whole body. It is also described as the combination of positions with joints in every movement we perform with our body.[4] Some factors such as race, gender, daily habits, the conditions that the world has put before us, the occupation and psychology of the person, the exercise factor, and the discomfort that a person experiences in his life affect posture formation. Especially daily life habits are one of the most important factors affecting posture. People who spend a long time at the computer or on the phone begin to acquire a distorted posture, called the forward head posture, in front of the spinal center of gravity.[5] The forward head posture causes a strain on the neck. As a result of stretching, a mechanical stress occurs in the region, which causes an imbalance in the muscles in the region[6] Muscle imbalance; Rolling shoulders reveal a synchronous postural disorder including increased shoulder elevation, increased thoracic kyphosis and forward head posture. In this postural disorder, the Cervical and Thoracic vertebrae are primarily affected.[7] As the vertebrae are affected, an increase in thoracic kyphosis angle is observed. Normal thoracic kyphosis angle value varies between 20° and 40°. This value is called hypokyphosis (flatback) if it is below 20 degrees, and hyper kyphosis if it is above 40 degrees. While the normal kyphosis angle varies between 20-40 degrees in young individuals, this value varies between 20-48 degrees in women and 20-44 degrees in men.[8,9]

The mean kyphosis angle has been defined as 37°±9° and this has been confirmed in many studies. Thoracic hypokyphosis is biomechanically studied in 5 different forms: Scheuermann's disease, Postural Kyphosis, Congenital Kyphosis, Age-related Hyper kyphosis, Neurological Hyper kyphosis. The most common of these is postural kyphosis. Postural kyphosis is a disorder that results from weakening of the muscles and ligaments affecting the spine due to wrong postural habits, without causing any visible damage to the vertebrae.[10,11] In our study, the type of kyphosis that we will associate with the use of the internet is Postural Kyphosis.

There are many publications in the literature regarding internet use and thoracic kyphosis. However, the number of publications that relate the use of the internet to the thoracic kyphosis angle is limited. Therefore, in our study, we aimed to determine the relationship between internet use and thoracic kyphosis angle in Sakarya University medical students.

MATERIAL AND METHOD

We conducted our study in 322 (F=152, M=170) students who were educated at Sakarya University Medical Faculty. Ethics committee approval was obtained before starting our measurements (71522473/050.01.04/452), and a voluntary consent form was obtained from the participants during the application. Our study did not include those with any physical or mental disabilities, those who had undergone surgical operations that could affect the spine indirectly or directly, those with shoulder impingement syndrome, diagnosed disc hernias and duct narrowing. Our experiement (the thoracic kyphosis measurements and internet usage test) was conducted using the flexicurve device on the participants. Before starting the study, the researchers who took the measurement made many trial measurements in order to gain experience and to identify possible unexpected situations and after being completely confident, the measurements were then made on the students. On the measurement basis, a participant was asked to stand straight, looking back and naturally and normally as in his daily life. Afterwards, certain reference points (C7-T12-L4) were determined by palpation method. To determine the T12 point, the crista iliaca section of Os coxae was palpated. Then the right middle of the upper boundaries of the right and left crista iliaca was determined as the processes spinosus of the 4th Lumbar vertebra and palpated upward and marked by the processus spinosus of the 12th thoracic vertebra. The processus spinosus of the 7th cervical vertebra was also determined and marked by palpation method. After these markings were made, the Flexicurve device was placed between C7-T12 and the device was pressed in such a way that it does not disturb the patient's balance in order to take the shape of the person's spine and completely touch the patient's thoracic region (**Figure1**). The resulting shape was immediately transferred to the millimeter graph paper we fixed on the table with a wooden pen. After the figure was created properly, the E, L1, L2 and L values, shown in **Figure 1**, were carefully measured with the normal ruler. After the measurement, the Kyphosis angle was calculated with the mathematical formula (arc tan (E/L1) + arc tan (E/L2)) shown in **Figure 2**.

After the measurement process of the participants was completed, the participants were given a questionnaire called Internet Usage Test and asked to be filled in objectively.

Figure 1. Flexicurve device on the participant use of

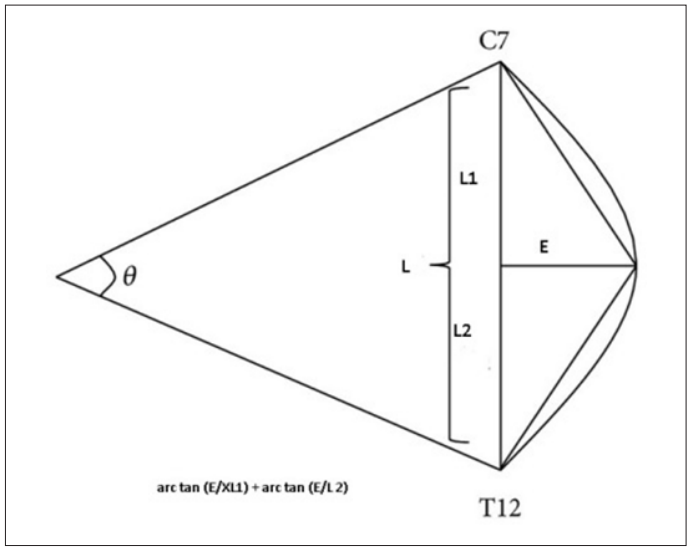

Figure 2. Mathematical formula showing how kyphosis angle is calculated
(C7 represents 7. cervical vertebrae, T12 represents 12. Thoracic vertebrae, Θ represents the thoracic kyphosis angle, A represents the most protruding point (Apex) of the thoracic part of the spine)

Internet Usage Test

Internet usage test It was created by Kimberly Young[3] and is used to detect internet addiction. The test contains 20 questions and the answer range of each question is between 0 and 5 (0 =never; 1 =rarely; 2 =sometimes; 3 =often; 4 =very often, 5 =always). At the end of the test, the score range varies between 0 and 100. In this context, the results from 0 to 19 show that there is no excess in internet use, and results from 20 to 39 indicate low level internet use. Results from 40 to 69 indicate medium level internet usage, while results from 70 to 100 indicate high level internet usage. We determined participant with 0-19 as 1st group, 20-39 as 2nd group, 40-69 as 3rd group, and 70-100 points as 4th group. The results in our study were determined and recorded in this way.

Statistical Analysis

All obtained data were analysed by utilising ''Statistical Packages fort he Soial Science" (SPSS) 21 statistics program on a computer. After administrating descriptive statistical analyses (frequency, percentage distribution, mean±standart deviation), normal distribution of continuous variable was assessed by Shapiro-Wilk and Kolomogrov Smirnov Tests. Chi-square test sor Fisher Exact test were conducted in order to evaluate the group difference in terms of discrete variables, and <0,05 value was accepted statistically significant.

RESULTS

The kyphosis angles of 170 male and 152 female participants in our study ranged from 21,067° to 49,546° (x±s=34,570±5,135) (**Table 1**). The average kyphosis angle in men was found to be 33.825°, whereas the average kyphosis angle in women was 35. 405° (**Table 2**). When we compare it by gender factor, the average kyphosis angle in men is lower than women and this difference is statistically significant (p: 0.006).

Table 1. Display of minimum, maximum values. arithmetic mean and standard deviations of the resulting results

	Min	Max	Mean± std
Kyphosis Angle	21.067°	49.546°	34.570±5.135
Survey Score	0.000	100.000	32.508±15.572
Internet Usage Time	20 min.	600 min.	200.87±47.858
Body Mass Index	16.286	37.040	23.689±14.866

Table 2. Display of average values of kyphosis angle and survey scores according to gender factor

	Man (N:170)	Woman (N:152)	P Value
Kyphosis Angle	33.825°	35.405°	*0.006
Survey Score	33.664	31.215	*0.184

*p<0,005 statistically significant.

Internet usage questionnaire scores of the participants ranged from 0 to 100 points (x±s =32,508±15,572) (**Table 1**). While this average is 33,664 in men, it is 31,215 in women (**Table 2**). When we compare the scores by gender factor, it was seen that the resulting value was statistically insignificant (p: 0.184).

In our study, when the internet usage survey scores and kyphosis angle values were compared, the result was statistically significant (p: 0.016).

When the internet usage levels and kyphosis angle values were compared, the result was not found statistically significant (0.055). **Table 3** shows the Internet usage levels and kyphosis angles average values.

In our study, the internet usage time of the participants varied between 20 minutes and 600 minutes per day and the

average was found as 200.87 minutes/day. While this average is 204.70 min/day for women, it is 197.44 min/day for men. When the internet usage times are compared by gender factor, the result is statistically insignificant (p: 0,507).

In addition, body mass index values ranged between 16,286 and 37,040, and the average value was calculated as 23,689. While the average BMI value of men was found to be 23.709, this value was found to be 21.757 for women.

DISCUSSION

We cannot ignore the fact that the internet occupies a place in our lives in many sectors in today's world and its popularity is increasing day by day. This fact brings us many benefits as well as some problems. It is very important to detect and evaluate the disorders brought by the Internet. Among these disorders, postural disorders caused by internet use are at the top of the list. During the use of the Internet, people cannot maintain their postures properly and after having access to the internet, they have difficulty leaving the environment and returning to normal life. This situation causes serious changes in the posture. One of these postural disorders is increased thoracic kyphosis.

In our study, we found the mean thoracic kyphosis angle as 34,570±5,135 degrees and found that there was a significant relationship between thoracic kyphosis angle and both internet addiction and duration of internet use. The reason for the increase in thoracic kyphosis angle value with the internet usage time is that people cannot maintain their body postures during the internet use. When we look at the literature, there are publications showing the effects of computer, telephone and internet use on posture.[12,13] Büyükturan et al.[14] in their study on 113 female participants using the spinal mouse device, they determined the thoracic kyphosis angle as 51.63±11.42. Büyükturan and her friends attributed the mean kyphosis angle to be higher than the normal values between 20 and 40, similar to our hypothesis, the participants were university students, and the time spent at the desk and the use of smart devices were higher. However, this value is much higher than the values in our study and in many studies in the literature.[8-10]

When we evaluated by gender factor in our study, the mean thoracic kyphosis angle in women was significantly higher than in men. Goh et al.[15] with the study of 220 radiographic images, and Fon. et al.[16] the results of their study using 316 radiographic images are similar to ours. In both studies, the mean kyphosis angle in women was higher than in men, and this difference was emphasized to be statistically significant. This difference is attributed to women living a more inactive life than men. Our observation is similarly that the female participants in our study are more inactive. It has also been emphasized in publications that the force of the back extensors in women is affected by the high release of estrogen hormone, which increases the angle of thoracic kyphosis.[17]

Contrary to many studies in the literature and our study, Kargarfard et al.[18] conducted an analysis of spinal curvatures using the flexicurve device on 1448 participants (730 females and 718 males), with an average kyphosis angle of 28.20±12.78° in women and 31.87±10.70° in men and stressed that this difference was statistically significant.[8]

In fact, in many studies[19-21] on thoracic kyphosis angle, the sample size was kept narrow (**Table 4**). Nadri et al.[19] the study examining the relationship between thoracic kyphosis angle and low back pain among dentists in Iran was carried out with 84 participants. In their study, they found that there was a significant relationship between thoracic kyphosis angle and study experience, and emphasized that this angle was higher in women, similar to our study.

Table 4. Comparison of the sample size in 4 study

	Number of Female	Number of Male	Total
Our Study	152	177	322
Hamed Nahri's Study	35	43	78
Eva Barrett's Study	4	7	11
Daniel M. Grindle's Study	22	18	40

When we look at the studies revealed in the literature, one thing that draws our attention is that the flexicurve device used throughout the study was never changed. [22,23]

While we were carrying out our study, we continued with a new flexicurve device every 50 measurements, considering that the device would lose its ability to take shape over time.

Radiographic measurements are also frequently encountered in publications, and their validity has been validated, but the fact that this measurement technique emits radiation and is more expensive than the flexicurve device cannot be ruled out.[24] It is also emphasized that there is a deviation of±5° even in the cobb angle method, which is described as the gold standard.[25] Carman et al.[26] they revealed that radiographic measurements may also vary depending on the observer performing the measurement. In their study, 5 different observers (4 orthopedists and 1 physiotherapist) made thoracic kyphosis angle measurements on the same radiographic images. For each radiographic measurement, 2 calculations were made and then the calculations were compared. In the calculation of thoracic kyphosis angle, they found the mean absolute value of the difference between the observers to be 3.3 degrees and reported that 95 percent of the differences were 7 degrees (0-30) or less. When we look at all these studies; It is important to identify and evaluate the negative effects of internet use on our posture. People should pay attention to internet usage times and body postures during use in order to protect their postures during internet use, otherwise an increase in thoracic kyphosis angle is observed. In order to prevent thoracic kyphosis increase, individuals can pay attention to internet usage time and body postures as well as strengthening their back muscles and stretching exercises in the pectoral region. When measuring

thoracic kyphosis angle, the flexicurve device we used has revealed results close to the values in the literature and can be used when evaluating the spinal curvatures when ease of use is also considered.

As the limitations of our study; In our study conducted with 322 (170M 152F) participants, when we divided the internet usage survey scores into 4 groups according to the internet usage levels, only 6 participants were included in the 4th group, which caused the statistical results to be meaningless when comparing the internet usage level and thoracic kyphosis angle. In this context, keeping the number of participants at a certain rate can contribute to the creation of more accurate and objective results. It is also a matter of debate how objective the participants are when completing the Internet usage survey. We think that in publications about internet addiction, people tend to hide their internet use from their environment and some participants may not have filled the questionnaires objectively.

CONCLUSION

As a result of our study, when we examined all the findings, we came to the conclusion that internet use has a negative effect on thoracic kyphosis angle and this should be evaluated and determined.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Medical Faculty Ethics Committee of Sakarya University (Permission granted: 2020, Decision no: 71522473/050.01.04/452).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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

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Orjinal Araştırma / Original Article

Investigation of Midwifery Students' Knowledge, Opinions and Religious Attitudes about Breast Milk Banking

Ebelik Bölümü Öğrencilerinin Anne Sütü Bankası Hakkındaki Bilgi, Görüş ve Dini Yönelimleri Arasındaki İlişkinin İncelenmesi

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Abstract

Aim: This study was carried out to investigate the relationship between midwifery students' knowledge, views, and religious attitudes about breast milk banking (BMB).

Material and Method: The population of this cross-sectional and descriptive study consisted of students from the Faculty of Health Sciences Midwifery Department. No sampling procedure was implemented in the study; instead, the entire population was targeted. Accordingly, 230 students who were at the school during the study and agreed to participate were included in the study. The data was collected using a "descriptive information form", which was developed by the researchers and aimed to collect information about participants' socio-demographic characteristics and knowledge and views on breast milk banking, and the "Religious Attitudes Scale" (RAS).

Results: The analysis of the students' responses to the questions checking their knowledge on BMB indicated that 37.0% knew BMB and that some of them had no idea about whether there was a need for BMB in our country (43.0%), whether using milk from a breast milk bank would matter religiously (41.3%), whether donor milk would cause an infection in newborns (48.3%), and whether milk obtained from a milk bank would be reliable (59.6%). The evaluation of students' views showed that 46.1% were not sure about donating their own milk to a breast milk bank, 38.2% would contact a breast milk bank when their baby needed milk, 42.2% thought donating milk was ethical, and that 56.1% said they would recommend this institution to mothers who had insufficient milk. The mean scores of the students from the RAS and the correlation analysis conducted to determine the knowledge and opinions of the students about BMB revealed that as the mean RAS scores increased, using milk from a milk bank would create problems religiously.

Conclusion: In this study, it was found that most of the students had poor knowledge and negative opinions about BMB and that increased religious orientation led to taking a negative view against breast milk banking.

Keywords: Breast milk, milk bank, religious attitude, midwifery

Öz

Amaç: Bu araştırma ebelik bölümü öğrencilerinin anne sütü bankası hakkındaki bilgi, görüş ve dini yönelimleri arasındaki ilişkinin incelenmesi amacıyla yapılmıştır.

Gereç ve Yöntem: Kesitsel ve tanımlayıcı olarak yapılan araştırmanın evrenini Sağlık Bilimleri Fakültesi Ebelik Bölümü öğrencileri oluşturmuştur. Örneklem seçilmemiş evrenin tamamına ulaşılması planlanmış olup araştırma tarihlerinde okulda bulunan ve araştırmaya katılmayı kabul eden 230 öğrenci çalışmaya alınmıştır. Veriler, araştırmacılar tarafından hazırlanan, öğrencilerin bazı sosyo-demografik özelliklerini, anne sütü bankası hakkındaki bilgi ve görüşlerini belirlemeye yönelik " tanıtıcı bilgi formu" ve "Dini Yönelim Ölçeği" (DYÖ) kullanılarak toplanmıştır.

Bulgular: Öğrencilere yöneltilen bilgi soruları değerlendirildiğinde; %37,0'ının anne sütü bankasının ne olduğunu bildiği, %43,0'ının ülkemizde anne sütü bankasına ihtiyaç olup olmadığını, %41,3'ünün anne sütü bankasından süt kullanmanın dini açıdan sorun olup olmayacağını, %48,3'ünün donör sütünün yenidoğanlarda enfeksiyona sebep olup olmayacağını, %59,6'sının süt bankasından alınan sütlerin güvenilirliği konusunda bir fikrinin olmadığını ifade ettikleri belirlenmiştir. Öğrencilerin görüşleri değerlendirildiğinde; %46,1'nin kendi sütünü anne sütü bankasına bağışlama konusunda emin olmadığını, %38,2'sinin bebeği ihtiyaç duyduğunda anne sütü bankasına başvuracağını, %42,2'sinin süt bağışlamanın etik olduğunu ve %56,1'inin ise sütü yetersiz annelere bu kuruluşu önereceklerini ifade ettikleri belirlenmiştir. Öğrencilerin DYÖ'den aldıkları puan ortalaması ile anne sütü bankası hakkındaki bilgi ve görüşlerini belirlemeye yönelik yapılan korelasyon analizinde; DYÖ puan ortalaması arttıkça süt bankasından süt kullanmanın dini açıdan sorun yaratacağı saptanmıştır.

Sonuç: Yapılan bu araştırmada, öğrencilerin çoğunun anne sütü bankası hakkında bilgilerinin zayıf ve görüşlerinin olumsuz olduğu, dini yönelimi artan öğrencilerin anne sütü bankasına karşı dini açıdan görüşlerinin olumsuzlaştığı saptanmıştır.

Anahtar Kelimeler: Anne sütü, süt bankası, dini yönelim, ebelik

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INTRODUCTION

Breastfeeding plays an important role in achieving the growth and development of the newborn, decreasing infant mortality and morbidity, and establishing a mother-baby bond. However, in some cases, it may not be possible for the baby to feed on its own mother's milk. An important source of breast milk is the donor milk in breast milk banks, which provide breast milk for babies who cannot be breastfed for various reasons.[1] The World Health Organization (WHO) and the United Nations International Children's Emergency Fund (UNICEF) (2009) state that in cases where the newborn cannot receive breast milk from its own mother, the best alternative is to obtain milk from a healthy foster-mother or a breast milk bank that meets international standards.[2-5] Therefore, the breast milk bank is an important institution for babies and families who need breast milk. However, mothers who cannot breastfeed prefer the breast milk of a familiar mother or formula over donor milk due to religious beliefs, economic reasons, distrust in screening tests, unfamiliarity with donors, lack of pasteurization, and inadequate knowledge of BMB.[4, 6]

Guidelines on the collection, processing, and distribution of donor milk have been developed in collaboration with representatives from the United States Food and Drug Administration Center for Disease Control and the American Academy of Pediatrics. These guidelines have been updated annually since 1990.[7] Breast milk banks also accept donations from healthy mothers whose babies are older than six months and have started supplementary foods. [8] Donors are questioned for consumption of alcohol and caffeinated beverages, drug use, infectious disease history, diet, age of their current children, place of residence, and the amount of milk to be donated, and necessary laboratory tests are performed.[4] The "voluntary" application of donors is important for the process and motivation. Milk banks provide sterile bottles and milk pumps to eligible donors and collect donated milk frozen. These frozen milk blocks are prepared for pasteurization separately or by mixing. The donor does not earn an income in return for this donated milk.[1,4,7]

BMB is generally not approved in Muslim societies like our country as it causes religious and ethical dilemmas.[1] However, in terms of newborn health, it is very important to provide BMB service supported by health policies within the framework of ethical and legal rules by eliminating the lack of information related to the topic. None of the hospitals in our country with maternal and child health clinics offer BMB services. The main reason for this is that there are no official banks or centers, the donor and the recipient do not know each other, and that the religious and traditional beliefs do not favor it. However, mothers in rural areas of our country who cannot breastfeed their babies usually turn to the nursing-mother practice. However, milk brotherhood is the most important obstacle to this practice.[7] The education of mothers and promoting education in this area can contribute to the removal of all these cultural barriers. There are few studies on this topic in our country, and there are no studies on religious attitudes at all.[1,5,11] If midwives are educated about the importance of milk banks and breast milk for babies during their school years, they can give information about the importance of breast milk and milk banks to every woman they will reach when they have graduated. Therefore, it is necessary to know the opinions and knowledge of midwifery students about breast milk banking. This study was carried out to determine the knowledge, views, and religious attitudes of midwifery students who are also prospective mothers and will provide counseling, training, and support on breastfeeding, and evaluate the relationship between them.

MATERIAL AND METHOD

This study used a cross-sectional and descriptive design and was carried out between February 19, 2018 and March 2, 2018 with a total of 283 students from the Faculty of Health Sciences Midwifery Department of a university in Turkey.

The midwifery students of the mentioned faculty made up the population of the study. A sampling procedure was not performed; instead, a total of 230 students who were at school during the study and who voluntarily agreed to participate were included in the study.

Data Collection Tools

The data was collected using a "Descriptive Information Form" which was developed by the researchers based on the literature.[1,4,5,9] and aimed to collect socio-demographic information about students and their knowledge and views about breast milk banking, and the "Religious Attitude Scale (RAS)".

The Descriptive Information Form: This form contains 21 questions aiming to determine some of the socio-demographic characteristics of the students and their knowledge and views about breast milk banking.

The Religious Attitude Scale: This scale was developed by Onay (2004) and its validity and reliability study was carried out by the same author. It is a measurement tool that aims to determine the extent of religion in people's lives (thoughts, behaviors, and emotions) quantitatively.[9] RAS is a four-point Likert-type psychometric measurement tool with rating options, such as "never, sometimes, often and always". There are a total of 18 items on the scale, 6 of which are reversed. It has three sub-dimensions, namely, thought (items 1, 2, 4, 8, 9, 12, 15, and 17), behavior (items 3, 5, 10, 13, 14, and 18), and emotion (items 6, 7, 11, and 16). The lowest and highest scores that can be obtained from the scale range from 18 to 72. High scores indicate increased levels of religious attitude, while low scores indicate decreased levels of religious attitude. The Cronbach's Alpha and Gutman Split-half value of the scale is 0.95.[4]

Legal and Ethical Situation

At the outset, the permission of the educational institution was obtained. Informed verbal and written consent of the participants of the study group were obtained. Participants were informed about the topic and purpose of the study by the researchers. The forms were distributed to the students, who agreed to participate in the study and delivered informed consent, and they were asked to fill out the forms within 15-20 minutes under the observation of the researchers.

Data Analysis

The data was evaluated by doing the necessary statistical analysis using appropriate software. Frequency distributions and the chi-square test were used for data analysis, and the Bonferroni test was employed to determine the source of differences between groups. Statistical significance was accepted as $p < 0.05$.

RESULTS

The mean age of the students in the study was 20.39±1.50 (min.-max.=18-26) years, 27.0% were first-year students, and 48.3% were found to spend most of their lives in a province (**Table 1**).

The evaluation of the students' responses to the information questions about BMB indicated that 37.0% of the students knew what BMB was and that some of them had no idea about whether the donated milk would cause any problem in newborn health (54.3%), whether BMB was needed in our country (43.0%), whether using milk from a breast milk bank would matter religiously (41.3%), whether donor milk would lead to an infection in newborns (48.3%), and whether milk from a milk bank would be reliable (59.6%). Also, it was determined that 43.9% of the students stated that milk obtained from the milk bank would increase the risk of developing allergic reactions in the newborn and that 53.5% reported the immunological benefit of the milk obtained from a milk bank would be higher than the formula (**Table 1**).

The analysis of the students' opinions about BMB showed that 46.1% were not sure about whether they would donate their own milk to a breast milk bank, 38.2% stated they would contact a breast milk bank when their baby needed it, 42.2% thought donating milk was ethical, and that 56.1% (n=129) stated that they would recommend this institution to mothers with inadequate milk. Also, 35.2% of the students believed that there would be a demand for BMB institutions, 43.9% thought that these institutions should be established in every city, and 49.6% stated they would support the establishment of breast milk banks in Turkey. Moreover, 72.6% of the students stated that milk obtained from a breast milk bank would not replace the baby's own mother's milk, 58.3% stated the donor and the recipient needed to know each other's identities, and 41.7% thought that mothers who would donate milk would not deprive their baby of their milk (**Table 2**).

Table 1. Distribution of the descriptive information about the students according to their knowledge about breast milk banking

Characteristics	n	%
Year		
1st year	62	27.0
2nd year	60	26.1
3rd year	59	25.7
4th year	49	21.2
The longest place of residence		
Province	111	48.3
County	72	31.3
Town/Village	47	20.4
Knowledge of breast milk banking		
Yes	85	37.0
No	74	32.2
Somewhat	71	30.8
Donated milk causes problems in newborn health.		
Yes	48	20.9
No	57	24,8
No idea	125	54.3
There is a need for breast milk banking in our country.		
Yes	95	41.3
No	36	15.7
No idea	99	43.0
Using milk from a milk bank causes problems religiously.		
Yes	65	28.3
No	70	30.4
No idea	95	41.3
Milk from a milk bank can cause an infection in the newborn.		
Yes	86	37.4
No	33	14.3
No idea	111	48.3
Milk from a milk bank is reliable.		
Yes	43	18.7
No	50	21.7
No idea	137	59.6
Milk from a milk bank increases the risk for developing allergic reactions.		
Yes	101	43.9
No	29	12.6
No idea	100	43.5
The immunological benefit of milk from a milk bank is more than formula.		
Yes	123	53.5
No	17	7.4
No idea	90	39.1
Total	**230**	**100**

The comparison of students' knowledge of BMB and their willingness to donate their own milk to a breast milk bank indicated a statistically significant difference ($\chi 2=28.237$, $p=0.000$) ($p<0.05$). The examination of the difference with advanced analyses (Bonferroni test) showed that the student group who had limited knowledge of BMB was not sure whether they wanted to donate their own milk to a breast milk bank, and that this was the source of the difference.

When students' knowledge of BMB and whether they would contact a breast milk bank when their baby needed milk were compared, a statistically significant difference was found ($\chi 2=25.193$, $p=0.001$) ($p<0.05$). When the source of this difference was examined with advanced analyses, it was found to stem from the fact that the student group who had limited knowledge about BMB had no idea about contacting a breast milk bank when their baby needed milk.

A statistically significant difference was found when students' knowledge of BMB and their understanding of the ethical

Table 2. Distribution of students' knowledge and thoughts about breast milk banking

Characteristics	Status of knowledge of breast milk banking				Test value χ^2; p
	Yes (n=85)	No (n=74)	Somewhat (n=71)	Total (n=230)	
Would you donate milk to a breast milk bank?					
Yes	33 (14.3%)	17 (7.4%)	13 (5.7%)	63 (27.4%)	
No	32 (13.9%)	13 (5.7%)	16 (6.9%)	61 (26.5%)	28.237; 0.000
Undecided	20 (8.8%)	44 (19.1%)	42 (18.2%)	106 (46.1%)	
Would you contact a breast milk bank when your baby needed milk?					
Yes	38 (16.5%)	26 (11.3%)	24 (10.4%)	88 (38.2%)	
No	34 (14.8%)	11 (4.8%)	20 (8.7%)	65 (28.3%)	25.193; 0.001
No idea	13 (5.7%)	37 (16.1%)	27 (11.7%)	77 (33.5%)	
Donating milk to a breast milk bank is ethical.					
Yes	49 (21.3%)	31 (13.5%)	17 (7.4%)	97 (42.2%)	
No	19 (8.3%)	11 (4.8%)	9 (3,9%)	39 (17.0%)	30.803; 0.001
No idea	17 (7.4%)	32 (13.9%)	45 (19.5%)	94 (40.8%)	
Would you recommend breast milk banking to mothers with inadequate breast milk?					
Yes	55 (23.9%)	45 (19.6%)	29(12.6%)	129 (56.1%)	
No	16 (6.9%)	8 (3.5%)	8 (3.5%)	32 (13.9%)	19.527; 0.001
No idea	14 (6.2%)	21 (9.1%)	34 (14.8%)	69 (30.0%)	
Do you believe that there will be a demand for breast milk banking in our country?					
Yes	29 (12.6%)	32 (13.9%)	20 (8.7%)	81 (35.2%)	
No	34 (14.8%)	18 (7.8%)	18 (7.8%)	70 (30.4%)	11.345; 0.023
No idea	22 (9.6%)	24 (10.5%)	33 (14.3%)	79 (34.4%)	
There should be a breast milk bank in every city.					
Yes	47 (20.4%)	35 (15.2%)	19 (8.3%)	101 (43.9%)	
No	16 (7.0%)	14 (6.1%)	11 (4.7%)	41 (17.8%)	18.608; 0.001
No idea	22(9.6%)	25 (10.9%)	41 (17.8%)	88 (38.3%)	
Milk from a breast milk bank can replace the infants' own mother's milk.					
Yes	9 (3.9%)	8 (3.5%)	3 (1.3%)	20 (8.7%)	
No	60 (26.1%)	53 (23.0%)	54 (23.5%)	167 (72.6%)	2.627;0.622
No idea	16 (7.0%)	13 (5.7%)	14 (6.0%)	43 (18.7%)	
A mother will deprive her infant of her milk when she donates milk.					
Yes	25 (10.9%)	14 (6.0%)	25 (10.9%)	64 (27.8%)	
No	38 (16.5%)	37 (16.2%)	21 (9.0%)	96 (41.7%)	8.605; 0.072
No idea	22 (9.6%)	23 (10.0%)	25 (10.9%)	70 (30.5%)	
Milk donors and recipients should know each others' identities.					
Yes	55 (23.9%)	42 (18.3%)	37 (16.1%)	134 (58.3%)	
No	21 (9.2%)	25 (10.9%)	22 (9.5%)	68 (29.6%)	4.195;0.380
No idea	9 (3.9%)	7 (3.0%)	12 (5.2%)	28 (12.1%)	
Would you support the establishment of breast milk banks in Turkey?					
Yes	48 (20.9%)	38 (16.5%)	28 (12.2%)	114 (49.6%)	
No	21 (9.1%)	8 (3.5%)	11 (4.8%)	40 (17.4%)	15.764; 0.003
No idea	16 (7.0%)	28 (12.2%)	32 (13.8%)	76 (33.0%)	
Total	**85 (37.0%)**	**74 (32.2%)**	**71 (30.8%)**	**(100.0%)**	

status of donating milk to a breast milk bank were compared (X2=30.803, p=0.001) (p <0.05). Advanced analyses indicated that this difference came from the student group who had limited knowledge about BMB and had no idea about the ethics of donating milk to a breast milk bank.

It was determined that there was a statistically significant difference between students' knowledge of BMB and their status of recommending BMB to mothers with insufficient milk ($\chi2$=19.527; p=0.001) (p<0.05). When the source of the difference was examined with advanced analyses, it was observed to come from the fact that the student group who had limited knowledge about BMB had no idea about recommending BMB to mothers with inadequate milk.

There was a statistically significant difference between students' knowledge of BMB and their belief that there would be a demand for BMB in our country ($\chi2$=11.345, p=0.023) (p<0.05). When the source of the difference was examined with advanced analyses, it was determined to stem from the fact that the student group who had limited knowledge of BMB had no idea about whether there would be a demand for BMB in our country.

The comparison between students' knowledge of BMB and the idea that there should be breast milk banks in every city indicated there was a statistically significant difference between the two ($\chi2$=18.608, p=0.001) (p<0.05). Advanced analyses of the difference showed that it stemmed from the fact that the student group who had limited knowledge of BMB did not have any idea about the need for breast milk banks in every city.

A statistically significant difference was found between students' knowledge of BMB and the status of supporting the establishment of BMB in Turkey ($\chi2$=15,764; p=0,003) (p<0.05). Advanced analyses indicated that this difference came from the fact that the student group who had limited knowledge and those who did not know anything about BMB at all had no idea about the establishment of BMB in Turkey.

A statistically significant difference was not determined between the students' knowledge of BMB and the status of whether the milk taken from a milk bank would replace the baby's own mother's milk, whether a mother donating milk would deprive her baby of her own milk, and whether the milk donor and the recipient needed to know each other's identities ($\chi2=2.627$, $p=0.622$; $\chi2=8.605$, $p=0.072$; $\chi2=4.195$, $p=0.380$, respectively) ($p>0.05$) (**Table 2**).

The mean overall score of the students from the RAS was 57.98±7.77 (min.-max.=21-72). The mean total scores of the students from the thought, behavior, and emotion sub-dimensions were 27.66±3.84 (min.-max.=10-32), 16.92±3.24 (min.-max.=7-24), and 13.40±2.16 (min.-max=4-16), respectively. In the correlation analysis performed to determine the mean RAS scores of the students and their knowledge and opinions about breast milk banking, an insignificant negative correlation was found between the mean RAS score and the status of whether using milk from a milk bank mattered religiously ($r=-0.160$; $p=0.015$). Accordingly, it was determined that as the mean RAS score increased, using milk from a milk bank would cause problems religiously. The analysis indicated that there was an insignificantly low positive correlation between the mean RAS score and the status of whether one should contact a milk bank when the baby needed milk ($r=0.161$; $p=0.015$). Accordingly, as the mean RAS score increased, the status of contacting a breast milk bank when the baby needed milk increased, as well (**Table 3**).

Table 3. Correlation analysis for determining the mean RAS scores of students and their knowledge and opinions about breast milk banking

Knowledge and attitudes about breast milk banking	Mean RAS scores	
	r	p
Using milk from a milk bank causes problems religiously.	-0.160	0.015
Agreeing to donate your own milk to a breast milk bank	0.064	0.334
Contacting a breast milk bank when your baby needs milk	0.161	0.015
Donating milk to a breast milk bank is ethical.	0.062	0.349
Recommending breast milk banking to mothers with inadequate breast milk	0.080	0.226
Believing that there will be a demand for breast milk banking in Turkey	0.080	0.227
Breast milk banks should be available in all cities.	0.071	0.283
Milk from a breast milk bank can replace the infant's own mother's milk.	0.044	0.507
Mothers will deprive their babies of their milk when they donate milk.	-0.117	0.075
Milk donors and recipients should know each others' identities.	-0.077	0.245
Supporting the establishment of breast milk banking in Turkey	0.066	0.323

DISCUSSION

This study was carried out to examine the relationship between midwifery students' knowledge, views and religious attitudes about breast milk banking. All of the midwifery students in the study were female, and 27.0% of them were first-year students. In our study, 37.0% of the students were found to know breast milk banking. The fact that the majority of the students in the study were first-year students and that topics, such as breast milk/breastfeeding, were not included in the first-year curriculum might have been a reason for the low number of students who knew what BMB was. In our study, some of the students had no idea about whether the donated milk would cause a problem in newborn health (54.3%), whether there was a need for BMB in our country (43.0%), whether donor milk would cause an infection in newborns (48.3%), and whether the milk obtained from a milk bank was reliable (59.6%). In their study investigating the knowledge and opinions of healthcare personnel (with 344 midwives, nurses and physicians) on BMB in our country, Şentürk Erenel et al.[5] (2017)found the majority of the healthcare workers knew there were no milk banks in our country but that they confirmed the statements that "babies who are fed with milk obtained from milk banks have a high risk of developing infection" and that "milk obtained from a milk bank is reliable", which indicated they did not have any idea about the topic.

In our study, 41.3% of the students stated that they did not have any idea about whether using milk from a breast milk bank would lead to a problem religiously. In their study conducted with mothers having infants, Ekşioğlu et al.[11] (2015)found that most of the mothers supported milk banking and that they would donate milk. They also determined that the reason why mothers did not want to donate milk was that they thought that it posed a risk of illness and that it was religiously inappropriate. Gürol et al.[12] (2013)reported that some of the mothers perceived religious reasons (36.3%) and social and moral reasons (28.9%) as an obstacle to donating milk. From a religious point of view, it is stated that according to Islamic law, breastfeeding of a baby by a woman other than its biological mother is considered legitimate. According to Islamic understanding, even if they have different fathers, children who are breastfed by the same women become "foster siblings". This kinship, which is established on breastfeeding, is not limited to those who suck and breastfeed, but also creates barriers to marriage between the baby breastfed and other children of the nursing mother.[13] However, religiously illegitimate marriages can be prevented by establishing breast milk banks and centers, especially for premature children, by developing a high-security kinship registry system in which nursing women and the child they breastfeed are identified.[14] In this study, the majority of the students did not express their opinion on the subject and experienced contradictions due to the aforementioned reasons.

In our study, 43.9% of the students stated that milk obtained from a milk bank would increase the risk of developing

allergic reactions in the newborn, and 53.5% reported that the immunological benefit of the milk obtained from a milk bank would be higher than the formula. In the study of Şentürk Erenel et al.[5] (2017), 39.6% of the participants stated that they did not know whether "milk obtained from a milk bank increased the risk of developing allergic reactions in the baby", and 65.6% responded correctly to "the immunological benefit of milk obtained from a milk bank was less than the formula" by stating it was an incorrect statement. Donor breast milk is one of the most ideal alternatives for newborns to ensure the continuation of growth and development in cases where their own mother cannot provide breast milk. It is safer to pasteurize breast milk to reduce some risks.

It is necessary to carry out studies to make BMB a public health policy. Donor milk can be used in hospitals with postpartum and newborn units within the scope of a program based on the principles of medical ethics, such as respect for autonomy, honesty, benefit, giving no harm, reliability, and justice.[7] Milk banks should collect information about donors and recipients, have a document/record system providing information to both parties, and be established as non-profit organizations.[4] In a study conducted in Taipei City Hospital Milk Bank, which was established as a non-profit institution in 2005 in Taipei, the capital city of Taiwan, it was reported that the amount of donor milk of the bank increased 3 times in the last 6 months and that the number of milk donors and recipients increased rapidly each year. It was stated in the study that milk donors were mostly educated, working, primiparous women. It was also reported that important data, such as basic data of the donor, working staff, bacteriological results before and after pasteurization, were recorded on a database for all donations.[3] In our study, 35.2% of the students believed there would be a demand for breast milk banking, 43.9% thought these institutions should be available in every city, and 49,6% stated they would support the establishment of BMB in Turkey. In addition, 46.1% of the students were not sure about donating their own milk to a breast milk bank, 38.2% would contact a breast milk bank when their baby needed milk, 42.2% thought that donating milk was ethical, and 56.1% stated that they would recommend this institution to mothers whose breast milk was inadequate. Midwifery students receive education on breast milk after the first year. However, 72.6% of the students thought milk obtained from a breast milk bank would not replace the baby's own mother milk, 58.3% stated those who donate milk and those who receive it should know each other's identities, 41.7% thought mothers who donated milk would not deprive their baby of their milk. In a study conducted with 695 mothers with children aged below 1 in Brazil, it was reported that 7.3% of the mothers donated their milk. Also, 59.9% of the mothers in the study had knowledge about breast milk banking, 47.1% were encouraged to donate their milk, and that 78.9% did not have any doubts or difficulties in donating their milk.[10] However, it was remarkable that the rate of mothers who donated their milk was 7.3% despite these rates in the study.

There are no official problems in Christianity, Buddhism, and Hinduism regarding the issue of breast milk donation, which causes some religious contradictions. Milk donation in these religions is encouraged. Sharing milk is considered a virtue in Islam. There are several verses in the Quran, the holy book of Islam, stating that a mother's breastfeeding is a virtuous act and encouraging breastfeeding. Despite the importance given to human milk, the establishment of breast milk banks is a complex issue in the Islamic world. This is because a child younger than 2 years old who is breastfed more than 5 times by a donor mother is considered to have sibling relation with the children of the mother donating milk, although they do not have biological ties. This means that they cannot marry as they are considered brothers or sisters.[15] In a study conducted with 948 women who donated their milk in India, 40.9% of the women were Hindu, 41.4% Muslim, 63.8% Catholic, and 22.2% were from other religions, and it was stated that religion did not affect breast milk donation.[16] In a study investigating the knowledge, attitudes, and views of 401 religious leaders on human milk banking and the availability of milk banks in Turkey, 71.3% of the participants indicated that BMB would be acceptable provided that the number of recipients in the milk pool were limited.[17] In another study investigating the perceptions of women about BMB in Turkey, it was found that the participants had a positive attitude towards milk banking but they had some concerns about the religious aspects of the case. Women who thought that milk banking was not suitable for Muslims were uncomfortable with the possibility that future babies might accidentally marry other babies who shared the same milk.[18] In this study, it was determined that 41.3% of the students had no idea about whether using milk from a breast milk bank would cause a problem religiously. It was determined that as the mean RAS scores of the students increased, they thought that using milk from a milk bank would cause problems religiously. Accordingly, the views of the students with increased religious attitude became more negative against BMB religiously. Although students are in a health school, the topic is included in the curriculum, students study a curriculum rich in content related to the importance of breast milk, and they are raised as baby/mother-friendly individuals, they still have concerns and contradictions with the effect of religious attitude. Also, it was found that using milk from a milk bank would cause problems religiously as their mean RAS scores increased; yet, this increase also meant that the status of contacting a milk bank when the baby needed milk increased, as well. This may have been because the benefits of breast milk were not known by all students.

CONCLUSION

In this study, it was found that most of the students had poor knowledge and negative opinions about breast milk banking. Also, as the mean RAS scores of the students increased, they thought that using milk from a milk bank would create problems religiously. Accordingly, the views of the students with an increased religious attitude towards BMB became negative religiously.

ETHICAL DECLARATIONS

Ethics Committee Approval: This research was conducted on midwifery students. For this research ethical commitee approval was not granded but the permission of the educational institution was obtained.

Informed Consent: Informed verbal and written consent of the participants of the study group were obtained.

Referee Evaluation Process: Externally peer-reviewed.

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Orjinal Araştırma / Original Article

The Evaluation of Catheter Infections in Kidney Disease Patients

Böbrek Hastalığı Olan Hastalarda Kateter Enfeksiyonlarının Değerlendirilmesi

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Abstract

Aim: In our study, we aimed to review the factors retrospectively that may be related to catheter infection (CI) in patients who received hemodialysis (HD) treatment in our clinic and followed up due to CI.

Material and Method: The files of 105 patients who were hospitalized in the Nephrology clinic or Intensıve Care Unıt (ICU) and who were diagnosed as CI while on HD treatment were analyzed retrospectively.

Results: Forty-seven (44.8%) of the patients were male, 58 (55.2%) were female and the mean age was 62.3±17.6 (19-90). The average length of hospital stay of the patients was 16 (2-60) days and the infection was mortal in 16 (15.2%) patients. In the cultures taken from the catheters, in 51 (48.6%) patients Gr (+) bacteria, in 24 (22.9%) patients Gr (-) bacteria and in 2 (1.9%) patients fungi were detected. There was no reproduction in 26 (24.8%) catheter cultures. The methicillin resistance (MR) was 87.6% and the highest resistance was detected in Coagulase Negative Staphylococcus (CNS) and *S. aureus* culture samples. 43 (41.0%) of the patients didn't respond to antibiotics during treatment and catheter exchange was required in these patients. Catheter replacement requirement was significantly higher in the Gr (-) bacterial group (14 patients, 58.3%) (p=0.050).

Conclusion: To prevent CI, it is important to reveal the factors related to infection. Microbiological agent distribution and resistance rate of each clinic and HD unit are different. Antibiotherapy should be planned according to this agent distribution to decrease antibiotic resistance.

Keywords: Kidney disease, catheter infections, gram negative bacteria, hemodialysis

Öz

Amaç: Çalışmamızda kliniğimizde hemodiyaliz (HD) tedavisi gören ve kateter enfeksiyonu nedeniyle takip edilen hastalarda, kateter enfeksiyonu ile ilişkili olabilecek faktörleri gözden geçirmeyi amaçladık.

Gereç ve Yöntem: Nefroloji kliniğinde veya Yoğun Bakım Ünitesinde (YBÜ) yatan ve HD tedavisi sırasında kateter enfeksiyonu tanısı alan 105 hastanın dosyası retrospektif olarak incelendi.

Bulgular: Hastaların 48'i (%44,8) erkek, 58'i (%55,2) kadın ve ortalama yaş 62,3±17,6 (19-90) idi. Hastaların ortalama hastanede kalış süresi 16 (2-60) gün ve 16 (%15,2) hastada enfeksiyon mortaldi. Kateterlerden alınan kültürlerde 51 (%48,6) hastada Gr (+) bakteri, 24 (%22,9) hastada Gr (-) bakteri ve 2 (%1,9) hastada mantar tespit edildi. 26 (%24,8) kateter kültüründe üreme olmadı. Metisilin direnci (MR) %87,6 idi ve en yüksek direnç, Koagülaz Negatif Stafilokok (KNS) ve S. aureus kültür örneklerinde saptandı. Hastaların 43'ü (%41,0) tedavi sırasında antibiyotiklere yanıt vermedi ve bu hastalarda kateter değişimi gerekti. Kateter replasman gereksinimi Gr (-) bakteri grubunda anlamlı olarak daha yüksekti (14 hasta, %58,3) (p=0,050).

Sonuç: Kateter enfeksiyonunu önlemek için enfeksiyonla ilişkili faktörleri ortaya koymak önemlidir. Her bir klinik ve HD ünitesinin mikrobiyolojik ajan dağılımı ve direnç oranı farklıdır. Antibiyotik direncini azaltmak için antibiyoterapi bu ajan dağılımına göre planlanmalıdır.

Anahtar Kelimeler: Böbrek hastalığı, kateter enfeksiyonları, gram negatif bakteri, hemodiyaliz

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INTRODUCTION

The best vascular access pathway in HD is arteriovenous fistula (AVF). Other options are arteriovenous graft (AVG) and catheters. Generally for the first HD a catheter is using because of unmaturated AVF. Today, tunnelled catheters with double lumen and a cuff are used to reduce the risk of infection in medium and long term.[1] The most common complications in HD patients are cardiovascular events and infections, these are the most important causes of hospitalizations. Infections related to vascular access routes constitute approximately 28% of infection related hospitalizations in chronic kidney disease (CKD).[2] Infection risk in tunneled catheters is 10 times higher than AVF and AVG.[3] Compared to patients with AVF, catheterized patients had 53% increase in all-cause mortality risk, 2-3 fold increase in risk of fatal and non-fatal infection, and 68% increase in hospitalization risk, respectively.[4]

Frequent occurrence of CI brings with it other problems. Patients whose hospitalizations are frequent and prolonged have additional problems and the rate of resistance to antibiotics increases due to frequent using of antibiotics. Therefore, newer and more expensive treatments are used. [2] For these reasons, more studies are needed to explain the causes of CI, related factors and methods of protection from infections. In this study, we reviewed the factors retrospectively that may be related to CI in patients who received HD treatment in our clinic and followed up due to CI.

MATERIAL AND METHOD

Patient Characteristics and Exclusion Criterias

In this study, the culture results of the blood samples taken from the HD catheter, peripheral vein and catheter tip of 450 patients with kidney disease who were hospitalized in the Nephrology clinic or ICU between July 2016 and February 2020 were analyzed, retrospectively. Ethical approval for the study was obtained. CI was defined as the infection in a patient with concomitant clinical signs of infection and no other source of infection other than catheter and also concomitant growth of the same microorganism from the peripheral vein, catheter or catheter tip culture.[3]

According to culture results, CI were determined in 105 of 450 patients and these patients were included in the study. The remaining 345 patients were excluded from the study for reasons such as infection focus other than catheter, not being able to make a clear diagnosis of CI and the presence of ongoing infection before catheter insertion. Patients' age, gender, cause of CKD, additional diseases, location where the catheter was inserted, temporary or permanent catheter type, application complaint, dialysis duration, catheter culture result, methicillin sensitivity, hospital stay, ICU hospitalization, mortality rates and laboratory data were recorded.

Catheter Insertion

HD catheters were inserted in a sterilized environment by interventional radiology or cardiovascular surgeons. The insertion area of the catheter was sterilized with a mixture of 2% glutaraldehyde and 70% ethyl alcohol. Internal jugular vein, femoral vein and subclavian vein were preferred for catheter insertion. The catheters were closed by dressing with chlorhexidine after each dialysis session.

Obtaining of Cultures

The sowing of the catheter samples was carried out in accordance with the semi-quantitative culture and quantitative culture techniques. The culture plates were evaluated after 48 hours incubation at 37°C and >15 CFU in the semantictative culture. In quantitative culture >1000 CFU/ml growth was considered as significant. Blood cultures from peripheral venous blood and from the catheter were evaluated in the BACTEC FX 9120 (Becton Dickinson, USA) automated blood culture device. Identification of isolated bacteria was carried out using conventional methods and where necessary, fully automated identification systems (VITEC 2 Compact, Biomerieux, France). Antibiotic susceptibility tests were performed using a fully automated system according to the criteria of "European Committee on Antimicrobial Susceptibility Testing (EUCAST)".

Statistical Analysis

SPSS 22.0 version was used for statistical analysis. Results were shown as±standard deviations and frequencies. Variables were evaluated using the Kolmogorov-Smirnov test for normality of distribution. In comparison of categorical variables, Fisher's exact test and Chi-square test were used according to their suitability. In the comparison of the two groups, those with normal distribution were performed with the T-test and those without normal distribution were performed with the Mann Whitney U test. If the p value was less than 0.05, the statistically was considered as significant.

RESULTS

Forty seven (44.8%) of the patients were male, 58 (55.2%) were female, and the mean age was 62.3±17.6 (age range 19-90). The mean dialysis time was 3.14±3.5 (3-19) years and 9 (8.6%) patients due to acute kidney disease (AKD), 96 (91.4%) patients due to CKD were on dialysis treatment. Diabetes mellitus (DM) (35 patients, 33.3%) and hypertension (HT) (23 patients, 21.9%) were the most common etiologies of CKD patients. The most common complaint of patients was chills-tremor (58.1%). Seventy-three (69.5%) patients were hospitalized from nephrology polyclinic, 32 (30.5%) patients developed CI during their hospitalization. The mean hospitalization time of the patients was 16 (2-90) days and the infection was mortal in 16 (15.2%) patients. In 15 (14.3%) patients, there was a history of ICU hospitalization and in 14 of these patients the infection was mortal. CI recurred in 29 (27.6%) of patients after treatment and they hospitalizated again. The demographic data of the patients are given in **Table 1**.

Table 1. Demographic data of patients

	All patients (n=105)	Gr (+) (n=51)	Gr (-) (n=24)	p
Gender (M/F)	47 (44.8%)	25 (49%)	12 (50%)	0.567
Age (years)	62.3±1.6	62.1±18.1	69.1±9.5	0.033
Dialysis time (years)	3.14±3.5	3.2±3.6	3.6±3.8	0.479
Hospital stay days	16 (2-60)	16 (2-60)	16.5 (2-45)	1.0
Mortality (yes)	16 (15.2%)	8 (15.7%)	4 (16.7%)	0.579
Application complaint				0.086
Fever	61 (58.1%)	27 (52.9%)	17 (70.8%)	
Nausea and vomiting	5 (4.8%)	1 (2%)	2 (8.3%)	
Confusion	3 (2.9%)	2 (3.9%)	0 (0%)	
Catheter outlet infection	2 (1.9%)	2 (3.9%)	0 (0%)	
Nonspecific	34 (32.4%)	19 (37.3%)	5 (20.8%)	
Kidney disease				0.369
AKD	9 (8.6%)	5 (9.8%)	1 (4.2%)	
CKD	96 (91.4%)	46 (90.2%)	23 (95.8%)	
CKD etiology				0.478
DM	35 (33.3%)	17 (33.3%)	7 (29.2%)	
HT	23 (21.9%)	9 (17.6%)	9 (37.5%)	
GN	3 (2.9%)	2 (3.9%)	0 (0%)	
PKD	4 (3.8%)	2 (3.9%)	2 (8.3%)	
Amyloidosis	4 (3.8%)	2 (3.9%)	0 (0%)	
Urological	4 (3.8%)	2 (3.9%)	1 (4.2%)	
Other	14 (13.3%)	7 (13.7%)	1 (4.2%)	
Unknown	18 (17.1%)	10 (19.6%)	4 (16.7%)	
DM (yes)	49 (46.7%)	28 (54.9%)	9 (37.5%)	0.123
HT (yes)	63(60%)	33 (64.7%)	16 (66.7%)	0.541
CAD (yes)	43 (41%)	21 (41.2%)	11 (45.8%)	0.447
Diagnosis place				0.143
Polyclinic	73 (69.5%)	35 (68.6%)	20 (83.3%)	
During hospitalization	32 (30.5%)	16 (31.4%)	4 (16.7%)	
Rehospitilization (yes)	29 (27.6%)	17 (33.3%)	7 (29.2%)	0.467
ICU stay (yes)	15 (14.3%)	5 (9.8%)	5 (20.8%)	0.171

DM: Diabetes mellitus, HT: Hypertension, CAD: Coronary artery disease, GN: Glomerulonephritis, PKD: Polycystic kidney disease

The patients were grouped as Gr (+) and Gr (-) bacteria group according to catheter culture results. In the cultures taken from the catheter, in 51 (48.6%) patients Gr (+) bacteria, in 24 (22.9%) patients Gr (-) bacteria and in 2 (1.9%) patients fungi were growth. The status of patients related to CI is indicated in **Table 2**. When the demographic data of the patients are compared between the two groups, the average age was higher in the Gr (-) bacterial group (p=0.033) but in other datas there was no statistically significant differences (**Table 1**).

Gr (+) bacterias (51, 48.6%) were the most frequently detected microorganisms according to culture results and among 35 (33.3%) of them were CNS, 11 (10.5%) were *S. aureus*. In Gr (-) bacteria group (24, 22.9%) *Enterobacter species* (9, 8.9%) was the most common agent. The other encountered Gr (-) bacterias were as follows; *Pseudomonas* (1, 1%), *E. coli* ESBL (+) (3, 2.9%), *E. coli* ESBL (-) (3, 2.9%), *Klebsiella* ESBL (+) (3, 2.9%), *Klebsiella* ESBL (-) (1, 1%), *Acinetobacter* (3, 2.9%), *Stenotrophomonas maltophilia* (1, 1%). Candida was detected in 2 (1.9%) patients. The rate of MR was 87.6%, and the highest resistance was detected in CNS and *S. aureus* species. There was no growth of bacteria in the catheter cultures of remaining 26 (24.8%) patients.

In 43 (41.0%) patients needed catheter replacement during their treatment. When all Gr (-) bacteria group were examined, more than half (14, 58.3%) required catheter replacement during treatment and this rate was significantly higher compared to Gr (+) bacteria group (p=0.05). Catheter exchange was required in all patients with *Pseudomonas*, *Stenotrophomonas maltophilia*, ESBL (+) *E. coli* and *Klebsiella* (**Table 3**).

The Gr (-) bacteria group had lower CRP (p=0.046) and sedimentation (p=0.022) values and higher calcium levels (p=0.044) when compared to the Gr (+) bacteria group. There were no statistically significant difference between the other laboratory values of the two groups (**Table 4**).

Table 2. Status of patients related to CI

	All patients (n=105)	Gr (+) (n=51)	Gr (-) (n=24)	p
Catheter location				0.864
Right jugular vein	82 (78.1%)	41 (80.4%)	19 (79.2%)	
Left jugular vein	12 (12.1%)	6 (11.8%)	4 (16.7%)	
Femoral vein	10 (9.5%)	4 (7.8%)	1 (4.2%)	
Subclavian vein	1 (1%)	0 (0%)	0 (0%)	
Catheter status				0.236
Temporary	26 (24.8%)	14 (27.5%)	4 (16.7%)	
Permanent	79 (75.2%)	37 (72.5%)	20 (83.3%)	
Catheter culture result				
No reproduction	26 (24.8%)			
Contaminated	2 (1.9%)			
Gr (+) bacteria	51 (48.6%)			
Gr (-) bacteria	24 (22.9%)			
Fungi	2 (1.9%)			
Catheter replacement (yes)	43 (41.0%)	18 (35.3%)	14(58.3%)	0.050
Metastatic infection				
Endocarditis	0 (0%)	0 (0%)	0 (0%)	
Septic arthritis	0 (0%)	0 (0%)	0 (0%)	
Osteomyelitis	2 (1.9%)	1 (2%)	0 (0%)	
Brain abscess	0 (0%)	0 (0%)	0 (0%)	
None	103 (98.1%)	50 (98%)	24 (100%)	

Table 3. Microorganisms in blood culture, methicillin sensitivity and need for catheter exchange

	All patients (n=105)	Methicillin resistant	Methicillin sensitive	Catheter replacement (yes)
No reproduction	26 (24.8%)			9 (20.9%)
Contaminated	2 (1.9%)			1 (2.3%)
Staf. Aureus	11 (10.5%)	9 (17.6%)	2 (3.9%)	3 (7.0%)
CNS	35 (33.3%)	34 (66.6%)	1 (1.9%)	15 (34.9%)
Enterococcus	5 (4.7%)	0 (0.0%)	5 (9.6%)	1 (2.3%)
Enterobacter	9 (8.9%)			4 (9.3%)
Pseudomonas	1 (1%)			1 (2.3%)
E. coli ESBL (+)	3 (2.9%)			3 (7.0%)
E. coli ESBL (-)	3 (2.9%)			0 (0.0%)
Klebsiella ESBL (+)	3 (2.9%)			3 (7.0%)
Klebsiella ESBL (-)	1 (1%)			0 (0.0%)
Acinetobacter	3 (2.9%)			1 (2.3%)
Stenot. maltophilia	1 (1%)			1 (2.3%)
Candida	2 (1.9%)			1 (2.3%)

Table 4. Laboratory parameters of patients

	All patients (n=105)	Gr (+) (n=51)	Gr (-) (n=24)	p
Hb	10.0±1.8	10.2±1.9	10.5±1.4	0.547
WBC	10.5±5.4	10.7±6.6	10.4±3.0	0.856
Plt	206.8±104.5	201.4±82.7	175.2±67.8	0.268
CRP	87.28±69.33	95.7±61.9	78.5±84.5	0.046
Procalcitonin	15.31±25.33	16.2±27.3	21.7±29.9	0.078
Sedimantation	54.3±28.1	56.3±28.0	42.2±20.0	0.022
Glucose	133.7±63.2	130.7±66.2	150.6±74.9	0.191
Creatinin	5.1±2.4	5.2±2.7	5.1±2.5	0.298
Na	136.0±4.2	135.4±4.6	136.4±3.3	0.312
K	4.7±0.9	4.7±0.9	5.0±1.0	0.161
Ca	8.9±0.8	8.7±0.8	9.0±0.5	0.044
P	3.9±2.2	3.9±2.2	3.8±2.2	0.532
Albumin	3.1±0.5	3.1±0.4	3.1±0.6	0.914
Üric acid	4.8±2.1	4.9±2.2	4.5±2.0	0.443
Ferritin	881.6±734.6	762.9±516.4	784.7±626.1	0.868
PTH	247.3±317.9	280.5±410.9	169.6±139.2	0.212

DISCUSSION

Vascular access infections are common in HD patients and often require hospitalization. CI rates are a reportable parameter and also are a benchmark and performance indicator for both hospital and dialysis facilities.[5] CI are an important problem for HD patients worldwide, so we evaluated the factors related to CI with this study. In our study, 105 patients who were followed with CI were admitted with the most common chills-tremors complaint and mostly hospitalized from polyclinic. In one third of the patients, CI developed during hospitalization. The development of such a high rate of CI during hospitalization may be due to factors such as frequent hospitalization of patients, prolonged hospitalization, presence of multiple drug resistant (MDR) bacteria in our clinic and ICU hospitalization for a different reason.

DM and HT were the most common etiologies of CKD in our study. Raji et al.[5] found that catheter-related complications were higher in CKD patients due to DM. There was some of our patients whose blood glucose levels could not be regulated. Hyperglycemia in uncontrolled DM increases the risk of infection, thrombosis and catheter failure due to bacterial growth, immunosuppression and increased vascular insufficiency.[6,7] There are studies reporting that infection rate is high especially in patients with multisystemic disease in CKD etiology.[8] Other risk factors related to CI are aging, long-term hospitalization, frequent use of antibiotics, duration of catheter, malnutrition, hypoalbuminemia.[9] The average age of our patients was 62.3±17.6 and the mean age was higher in the group with CI due to Gr (-) bacterias. Our study was retrospective, no clear information about catheter duration, frequency of antibiotic use and nutritional status could be obtained.

In HD patients, Gr (+) bacteria are predominant in CI and the most common bacteria is *S. aureus*. In the HD population, *S. aureus* infection is 100 times more common than the general population.[10] Vascular access infections with *S. aureus* are one of the worst clinical scenarios in HD patients. It is potentially not only mortal but can also cause loss of vascular access despite the timely removal of infected grafts and catheters.[11] At the same time, *S. aureus* infections can cause metastatic infections such as endocarditis, osteomyelitis. In our study, the most common bacteria was CNS, second frequent agent was *S. aureus* and in only one patient osteomyelitis was detected. In our study, MR was 87.6% and this rate was higher compared to other studies. Nyugen et al.[12] Alhazmi et al.[11] reported the resistance of *S. aureus* methicillin as 40% and 50%, respectively. Fram et al.[13] reported that the use of previous antimicrobial drugs caused more and higher resistant infections. Reason of higher MR in our study might be the that our clinic serves as the third step facility so that there might be the presence of MDR microorganisms, frequent and broad spectrum antibiotic use and frequent hospitalization of patients. In a quarter of our patients had no reproduction in their cultures. This can be seen when there is a recent history of antibiotic use, presence of bacteria that can't be produced, and the difficulties associated with delivering the culture to the laboratory.

Although Gr (+) bacteria are predominant in CI, the frequency and dominance of Gr (-) bacteria have increased recently. In a recent study on the relationship between Gr (-) bacteria and CI, Murray et al.[14] reported 95 cases of Gr (-) bacteremia in 84 patients from 1242 HD patients (0.175/1000 HD days). Interestingly, the source of Gr (-) bacteria was found to be associated with vascular access in only 29.5% of patients (16.8% catheter related). While urinary, biliary, intraabdominal and infected foot ulcers were identified as the source in 53.7% of the remaining patients, no source could be found in 16.8%. The most frequent isolated Gr (-) agents were as follows *E. coli* (47.5%), *Enterobacter* (13.1%) and *Klebsiella* (11.1%) respectively. While the first 3-month mortality was 28.6%, the mortality in 3 years was 46.4%.[14] In other studies related to Gr (-) bacteria in ICU patients, mortality was found to be 48% in the first 30 days and 60% in the study duration (0.178/1000 ICU day-1.13/1000 ICU day).[15,16] In our study, Gr (-) bacteria was grown in 22.9% of the patients and *Enterobacter* was most common and *E. coli* was the second common agents. In studies, the dominance of *Enterobacter* was frequently associated with hospitalization or ICU hospitalization.[14] Some studies have associated frequent hospitalization with the risk of *P. aeruginosa*.[17] Our mortality rate due to Gr (-) bacteria was 16.7%. Murray et al.[14] linked the cause of high mortality due to Gr (-) to the late removal of catheters because of vascular access restriction. The early removal of catheters in patients whom with positive control culture results might be the cause of low mortality in our study.

Gr (-) infections have become important with increasing antibiotic resistance in recent years.[18] In most countries, the rate of MRSA decreases while the rate of MDR Gr (-) bacteria increases.[21] MDR Gr (-) bacteria ratio is high in HD patients.[22] The non-fermented Gr (-) bacterias such as Acinetobacter, *Pseudomonas aeruginosa* and *Stenotrophomonas maltophilia* are highly resistant to antibiotics and catheter replacement may be required, as in our study. Pop-vicas et al.[21] reported Gr (-) bacterial colonization in HD patients. Colonization risk factors are common use of antibiotics and frequent hospitalizations. The way to prevent Gr (-) bacteremia is to start with antibiotics which include both Gr (+) and Gr (-) bacteria and rearrange the antibiotic treatment after a definitive microbiological diagnosis.[18] Candida was observed in 2 patients' catheter culture hospitalized in ICU. ICU hospitalization, colonization of the mucous membranes and insertion of permanent intravascular catheters are the main predisposing factors for Candida infections.[22,23]

Laboratory parameters are also important for the identification of CI. Acute phase reactants increase in infectious situations but are insufficient to determine the type of bacteria. CRP concentrations increase in the presence of bacterial infections and are higher in Gr (+) bacteremia than in Gr (-) bacteremia. In the case of Gr (-) bacteremia, procalcitonin levels increase. It was reported in the literatüre that procalcitonin levels and baseline CRP values were unrelated to local infection, systemic infection and mortality but affect the length of hospital stay.[24] CRP, sedimentation and procalcitonin values were above normal in our patients. Sedimentation (p=0.022) and CRP (p=0.046) were higher in CI due to Gr (+) bacterias.

Although the average calcium levels of our patients were normal but calcium levels were lower in the Gr (+) bacterial group (p=0.044). Although our data was different, Zaloga et al. reported that that all patients had normal calcium levels before sepsis, but during Gr (-) bacterial septic attack hypocalcaemia had developed and during Gr (+) bacterial sepsis it had remained in normal ranges. Hypocalcemia might develop as a result of disruption in calcitriol synthesis due to the renal failure that developed during sepsis. In addition, it was determined that hypotensive patients had more severe hypocalcemia and that hypocalcemia was associated with high mortality during sepsis.[25]

CONCLUSIONS

As a result; CI are common in patients on dialysis and are associated with serious mortality and morbidity. To prevent CI, it is important to reveal infection related factors. Microbiological agent distribution and resistance rate of each clinic and HD unit are different. Antibiotherapy should be planned according to this factor distribution to reduce antibiotic resistance. The frequency of Gr (-) infections with high mortality increased nowadays therefore when starting empirical treatment antibiotherapy must be regulated according to this knowledge.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Sağlık Bilimleri University Konya Training and Research Hospital Medical Specialty Education Board (Permission granted: 06.02.2020, Decision no: 35-35).

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

Referee Evaluation Process: Externally peer-reviewed.

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Demographic Characteristics of Patients Admitted to Private Hospital Emergency Service

Özel Hastane Acil Servisine Başvuran Hastaların Demografik Özellikleri

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Abstract

Aim: Increasing the productivity of emergency services is only possible with the documentation and analysis of data on services provided. In this study, we aimed to evaluate demographic characteristics of patients admitted to the emergency unit using a computer-based patient registry system.

Material and Method: 33,886 outpatients admitted to the emergency unit between 01.09.2017 and 31.08.2019 were retrospectively analyzed. Demographic characteristics of the patients, main complaints, time of admission, triage classification, and International Classification of Diseases diagnosis codes were evaluated.

Results: Among outpatients admitted to the emergency unit, 58% were males and 42% were females. A total of 43% outpatients were 0-12 months of age, 21% were 1-5 years of age, 15% were 28-39 years of age, and 9% were 40-64 years of age. In total, 39% outpatients were admitted to the emergency unit due to upper respiratory tract diseases. Of the patients, 95,42% were treated in the outpatient setting. The highest admission rates were in December and January. The highest admission rate was on Sunday, while the least was on Wednesday and Thursday. The highest admission time period was between 20:00–00:00, while the least was between 04:00–08:00.

Conclusion: Our study results show that supportive measures for healthcare professionals including specialists and medical equipment should be provided, in particular between 20:00–00:00, at the weekends, and in winter seasons, when the overall admission rate increases. Based on these results, we suggest that documentation and analysis of demographic data of patients admitted to the emergency unit can contribute to physical and labor force planning of emergency units.

Keywords: Emergency, triage, private hospital

Öz

Amaç: Acil servis hizmetlerinin daha verimli hale getirilebilmesi ancak verilen hizmete ait verilerin dokümantasyonu ve değerlendirilmesi ile mümkün olabilir. Bu çalışmada bilgisayar tabanlı hasta veri kayıt sistemi kullanılarak acil servise başvuran hastalar demografik açıdan değerlendirildi.

Gereç ve Yöntem: 01.09.2017 ila 31.08.2019 tarihleri arasında acil servise ayaktan başvuran 33.886 hasta retrospektif olarak değerlendirildi. Hastaların demografik özellikleri, şikâyetleri, başvuru saati, tiraj sınıflaması ICD tanı kodlama sistemine göre tanıları değerlendirildi.

Bulgular: Acile başvuran hastaların %58 erkek, %42 kadın idi. Hastalarımızın %43'ü 0-12 ay yaş gurubunda, %21'i 1-5 yaş grubunda, %15'i hasta 18-39 yaş grubunda, ve %9'u 40-64 yaş grubunda idi. Hastaların %39'u hasta üst solunum yolu hastalıkları nedeniyle başvurmuştu. Hastaların %95.42'si ayaktan tedavisi yapılmıştır. En fazla başvuru Aralık (%12) ve Ocak (%11) aylarında yapılmıştı. Hastaların en çok başvuru yaptığı gün pazar (%25), en az ise çarşamba ve perşembe (%10) idi. En çok başvuru yapılan saat 20-00 (%30) en az ise 04-08 (%7) idi.

Sonuç: Hasta yoğunluğunu fazla olduğu kış aylarında, hafta sonu ve 20 ila 24 saatleri arasında hekim, sağlık personeli ve araç-gereç takviyesi gerektiği görülmektedir. Acil servise başvuran hastaların demografik verilerinin kaydı ve analizi, acil servislerin fiziki ve işgücü planlaması açısından katkıda bulunabilir.

Anahtar kelimeler: Acil servis, triyaj, özel hastane

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INTRODUCTION

Emergency services are the healthcare units that have to make a rapid and at the same time correct diagnosis due to the organ or life risk of the patient group they serve and provide this service 24 hours a day, seven days a week. Therefore, due to many sociological reasons such as fast and minimum waiting time in emergency services, not requesting co-payments from patients, rapid turnover of examination results, application of non-emergency patients with simple ailments to receive services, the emergency services become crowded.

Overcrowding of the emergency service causes personel and equipment shortages, and this vicious circle leads to patient and employee dissatisfaction. Bringing the emergency department staff and equipment to the most appropriate number and quality will contribute to the satisfaction of the patient/patient relatives and employees. For this reason, both the physical conditions of the emergency services and the competence and number of staff should be at an optimal state. The most ideal number and quality of required emergency service personnel, equipment are tried to be provided by both examining the emergency service applications, and retrospectively investigating the patients.

In this way, the extent which the increase in the number of patients due to seasonally increasing diseases is reflected in the emergency service is determined. It can also contribute to the organization of polyclinics of hospitals.[1-3]

In our country, healthcare service and emergency healthcare, which has an important place in this service, are provided by public hospitals, while a significant portion of this service by private hospitals established by private enterprises. Private hospitals are owned by real or legal persons and provide examination, medical intervention, surgery, medical care and necessary treatments for inpatients or outpatients.[4]

In this study, it was aimed to contribute to the data of our country by determining the demographic and epidemiological characteristics of the patients who applied to the emergency service of a private hospital in Istanbul.

MATERIAL AND METHOD

Necessary permissions were obtained from the hospital administration for this study. The study was a retrospective and file-scanning study and ethics committee approval vas taken from the Clinical Research Ethic Committee of Sultangazi Haseki Research and Education Hospital. The file numbers of the patients who applied to the private hospital emergency service during 24 months between 09.01.2017 and 08.31.2019 were retrieved from the hospital patient information system. Again, the file numbers and patient records were analyzed retrospectively from the hospital information system. Patients whose medical chartscould not be reached and those with missinginformation were excluded from the study. A total of 33,886 patients were included in the study. The demographic characteristics of the patients included in the study were evaluated in terms of the time of their admission, triage classification and diagnoses they received. Admissiontimes were grouped according tothe month (January, February, March, April, May, June, July, August, September, October, November, December), day (Monday, Tuesday, Wednesday, Thursday, Friday, Saturday, Sunday) andhourly shifts in the time periods of the day. (00:00-03:59, 04:00-07:59, 08:00-11:59, 12:00-15:59, 16:00-19:59, 20:00-23:59). Triage classification was made according to Annex-7 mentioned in the section 'Color Coding and Triage Application' in Article 8 of the 'Communiqué on the Application Procedures and Principles of Emergency ServicesProvided inInpatient Health Care Facilities' published by the Ministry of Health in the Official Gazette with the number 27378 on October 16, 2019.[5]

Statistical Analysis:Results of the data analyzedwere evaluated using Microsoft Excel XP and SPSS (version 13.0, SPSS Inc., Chicago, Illinois, USA) programs. Values are given as numbers and percentages.

RESULTS

A total of34,126 patients applied to the private hospital where the study was conducted for two years. Two hundred and fortypatients were excluded from the study, and 33.886 patients were included in the study.

During this period 19,464 (58%) male, and 14,422 (42%) female patients applied to the hospitalAverageages of the male, and female patients were 13.86, and14.95, years respectively. While43% (14.644) of the patients referred to our hospitals were infants (**Table 1**).

Table 1. Distribution of the patients admitted according to age and gender

Age Groups	Male		Female		Total	
	n	%	n	%	n	%
Infancy (0-12 months)	8.514	25	6.130	18	14.644	43
Preschool (1-5 years)	4.153	12	3.147	9	7.300	21
School Age (6-11 years)	1.342	4	949	3	2.291	7
Adolescence (12-17 years)	489	1	348	1	837	2
Youth (18-39 years)	3.131	9	2.175	6	5.306	15
Middle Age (40-64 years)	1.532	5	1.224	4	2.756	9
Aged (≥65 years)	752	2	303	1	449	3
Total	19.464	58	14.422	42	33.886	100

When the types of social security that the patients had were examined, it was seen that 59% (19.786) of them were under the coverage ofSSI (Social Security Institution: SSK) and the majority ofthe SSI members were male. Only 8% (n=2.921) of the refugees who came to our country after fleeing the civil war in Syria had "Temporary Protection" social security. However, 'General Health Insurance'was provided to only 3% ofthe poor citizens of Republic of Turkey who had not any income (**Table 2**).

Table 2. Distribution of the patients according to types of social security coverage

Social Security	Male		Female		Total	
	n	%	n	%	n	%
SSI[1]	12.087	36	7.699	23	19.786	59
BAĞKUR[2]	2.214	7	1.736	5	3.950	12
Retirement Fund	1.712	5	2.140	6	3.852	11
Temporary Protection Insurance	1.785	5	1.136	3	2.921	8
International Insurance	672	2	624	2	1.296	4
Private Insurance	545	2	501	1	1.046	3
General Health Insurance	449	1	586	2	1.035	3
Total	19.464	58	14.422	42	33.886	100

[1]SSI: Social Insurance Institution
[2]BAĞKUR: Social security organization for artisans and the self-employed

When we examine the patients according to triage coding and diseases, it is seen more than half of the patients (56%) who applied received the Green Triage Code. It has been determined that the vast majority (13.070) of the patientswho receivedGreen Triage Code hadupper respiratory tract infections (**Table 3**). It was observed that 95.42% of the patients were discharged after being examined and treated in the emergency service When we examine the patients who applied to the Private Hospital Emergency Department according to the month of their applications; the patients mostly applied in December (12%) followed by January (11%) and August (11%). The least number of applications were seenin July, with a rate of 6 percent (**Figure 1**). The patientsmostly applied on Sunday (25%) followed by Saturday (19 %). It was determined that the least number of applications occurredin the middle of the week (Wednesday and Thursday with 10% each) (**Figure 2**). When the application time is evaluated, it is seen that the highest number of applications (30%) were made during the nightshift between 8:00 PM and midnight which is called the"prime-time". It was determined that the least number of applications (7%) were madefrom 04:00 am to the start of the working hours (**Figure 3**).

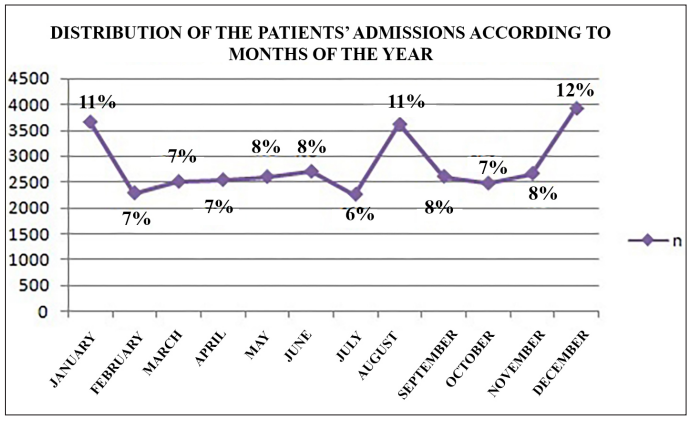

Figure 1. Distribution of the patients' admissions according to months of the year.

Table 3. Number of patients according to triage codes, anddisease groups.

	Male	Female	Total
Red Triage Code			
Allergy, Angioneurotic Edema	2	4	6
Cardiopulmonary Arrest	69	53	122
Pulmonary Infection	116	133	249
Surgical Abdominal Pain	14	12	26
Extremity Embolism	26	14	40
Gastrointestinal Bleeding	8	6	14
İntoxication	94	164	258
Bleeding Diathesis	4	2	6
Heart Diseases	259	199	458
COPD*, Bronchial Asthma	5	3	8
Seizures	161	140	301
Pulmonary Embolism	9	7	16
Central Nervous System Infections	12	14	26
Sepsis	21	30	51
Cerebrovascular Diseases	92	95	187
Trauma	86	45	131
Burns	29	38	67
Total Number of Patients with Red Triage Code	1.007 (%3)	959 (%3)	1.966 (%6)
Yellow Triage Code			
Allergy	248	254	502
Pulmonary Infection	787	802	1.589
Renal Failure, Electrolyte Disorder	51	34	85
Electrocution	32	9	41
Epistaxis	37	31	68
Facial Paralysis	94	74	168
Gastrointestinal Infection	414	516	930
Animal, Insect Bites	39	26	65
Hypo/Hyperglycemia	111	114	225
Heart Diseases	408	510	918
COPD*, Bronchial Asthma	297	161	458
Non-Surgical Abdominal Pain	1.115	770	1.885
Psychiatric Emergencies	335	409	744
Trauma	2.370	664	3.034
Urinary Infection	289	381	670
Urologic Emergencies	306	244	550
Vertigo	231	211	442
Foreign Body in Body Cavities	181	172	353
Burns	66	55	121
Total Number of Patients with Yellow Triage Code	7.411 (%22)	5.437 (%16)	12.848 (%38)
Green Triage Code			
Non-Specific Headache	217	297	514
Skin-Soft Tissue Infection	84	62	146
Dermatitis	136	105	241
Gastrointestinal Infection	1.354	556	1.910
Non-Traumatic Musculoskeletal Pain	387	338	725
Conjunctivitis	109	95	204
Upper Respiratory Tract Infections	7.298	5.772	13.070
Trauma	1.376	720	2.096
Burns	85	81	166
Total Number of Patients with Green Code	11.046 (%33)	8.026 (%23)	19.072 (%56)
Grand Total	19.464 (%58)	14.422 (%42)	33.886 (%100)

* COPDChronic Obstructive Pulmonary Disease

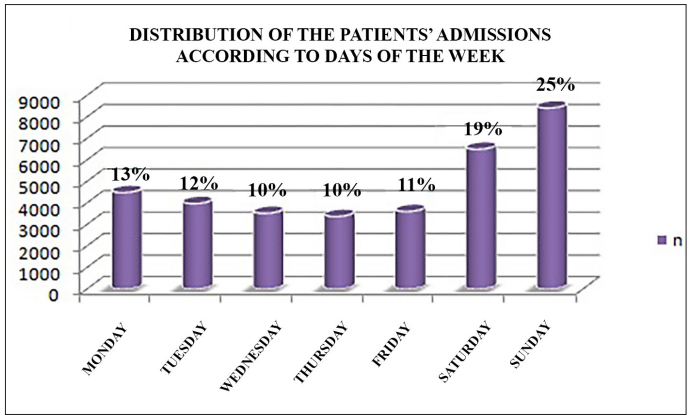

Figure 2. Distribution of the patients' admissions according to days of the week

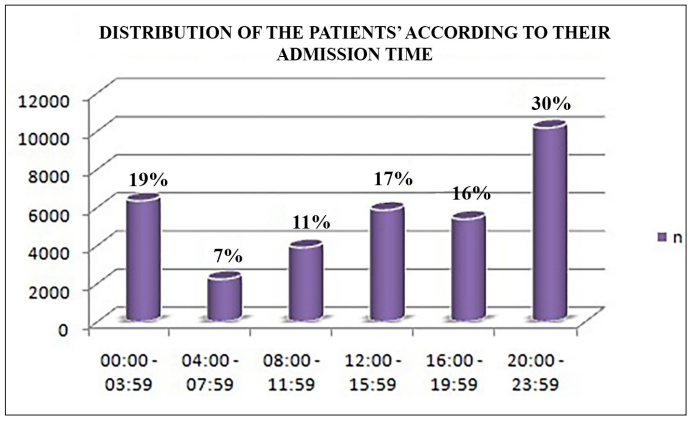

Figure 3. Distribution of the patients according to their admission times

DISCUSSION

Emergency Services are hospital departments that have toadmit everypatient that applied, have to make a fast and correct decision, can be accessibleevery day and every hour of the week, and has a wide range of patients.[2] It has the characteristic of being the showcase of a hospital, as it is frequently said by the administrators, which mostlyencounterpeopledue to the long working time and highernumber of patient applications, and demonstratesthe hospital's service quality and competence, examination and treatment efficiency.

However, emergency rooms (ERs)becomecrowded due tothe increasing number of admissions to ERs in our country which naturally result indissatisfaction of patients and staff.[6] Emergency room patients rightly expect quality and priority health care service.[1,2] Providing fast and accurate service at high quality can be achieved with a good planning of staff and equipment.

Descriptive studies on the demographic characteristics and diagnostic and treatment process of patients admitted to emergency services in our country are mostly carried out in tertiary healthcare institutions. In this study, the patients who applied to a private hospital emergency service, which has been serving for 25 years and operating in the central district namely in the suburbs of our metropolitan citywhere the people with middle and lower socio-economic class live and work, were evaluated in terms of demographic characteristics, admission time and triage codes. This study is the first study conducted in our countryusing a private hospital'semergency service data.

In the study conducted by Çevik et al.[7] in a state hospital, it was determined that 50.86% of the patients admittedto the emergency serviceswere women and 49.14% of them were men. The majority of the admissions (37.89%) consisted of young adults (20-39 years old), and the authorsstated that greaternumber of these patients aged 20-24 and over 65 yearscompared to other age groups. In the study conducted by Kılıçarslan et al.[8] at auniversity hospital, the investigators determined that 52.6% of the patients were male and the majority of the patients (37.89%) were young adults (20-39 years old). Besides, among them more frequentlypatientsaged 20-24 and over 65 years of age were more numerousthan the other age groups.

In the study conducted by Edirne et al.[19] in a university hospital, the authors stated that 43.2% of the patients were male. In the study conducted by Köse et al.[3] in a state hospital, the investigatorsfound that 54.8% of applications were made bymale patients, andthe most (77%) of themaged17-65 years. While Türkdoğan et al.[10] determined that most frequently (55.2%) female patients hadappliedto the emergency services. Aydın et al.[2] observed that the ER applications were more frequently (51.53%) made by male patients In the study conducted by Polat et al.[11] the authors stated that 25% of emergency room admissions in our country consisted of patients in the pediatric age group.

In this study, when the patients who applied to the emergency service were evaluated according to their gender, admissions consisted of 58% male and 42% female patientswithout anysignificant difference between both genders ($p>0.05$) (**Table 1**). When the patients are examined in terms of age periods, it is seen that the least admission is in infancy with 43%. The least number of applicants are adolescents followed by the elderly patient group. As can be seen in the literature, admissions to the emergency department in terms of age and gender vary according to the region where the hospital is located.

Overyears, improvements and reforms have been made in the fields ofhealth and social security in Turkey. The patients who did not have social security coverage and income were provided with social security firstly under the name of 'Green Card' and then the scope of the social security coveragewas expanded under the 'General Health Insurance'.[12] Health insurance has been provided for asylum seekers who came to our country after fleeing from the civil war in Syria, and the "Directive on Principles Regarding Health Services to be Provided to Temporary Protection" was published by the Ministry of Health in 2015. With this directive, a social security umbrella called "Temporary Protection" was created for refugees.[13]

In the study conducted by Çevik et al.[7] in a state hospital, the patients who applied to the emergency services were examined according to their types of social security coverage they received and found that the respective percentages of patients had benefited from the Retirement Fund (42.6%), SSK (38.59%), Bağ-Kur (12.28%), Green Card (1.65%), while 3.12% of the patients were not under any social security coverage. In the study conducted by Köse et al.[3] in a state hospital, 64.4% of the patients who applied to the emergency serviceswere green card holders, and the otherpatients were affiliated to the Social InsuranceInstitution (SSK) (20.5%),to the Social Security Institution (SGK) (4.5%), Bağ-Kur (4.4 %), to the Retirement Fund (2.1%), and others 3.6%.

In the study conducted by Tanrıkulu et al.[1] in a training and research hospital, the authors stated that most (56.2%) of their patients were affiliated to SSK followed by green card holders (25.6%). While 1% patients paid their health expensesby themselves. The patients whose social securitycoverage is defined as "forensic" due to forensic cases such as traffic accidents, assaults, injuries and whose health insurance cannot be determined exactly constituted 3% of the admissions.

In our study most of the patients (59%: n=19.786) were members of SII (SSK)and the majority of the SII members were male. Only 8% (n=2.921)of thepatients had "Temporary Protection" social security, which covers refugees who came to our country after fleeing the civil war in Syria. However, only 3% of the patients who were the citizens of the Republic of Turkey and without any income were provided with 'General Health Insurance' (**Table 2**).

When the literature and our study are examined, it is seen that the rates of social security types differ according to the type of health care institute such asuniversity, educationandresearch hospital, state and private hospital, as well as the socio-economic level of the region where the patient is living.

Although the increasing number of admissionsto emergency services is a worldwide problem, this problem has almost reached the level of disaster in our country. Due to the fact that emergency services are free of charge, examinations are performedrapidly without waiting, admission of non-urgent cases to the emergency services, the growing volume of patients cannot be intervened in time, which results in dissatisfaction with physicians and patients/relatives and consequently violence against health care professionals. In this case, the method to distinguish between emergency and non-emergency patients and how to determine the priority of patients for treatment becomes important. Triage scales are used to distinguish between emergency and non-emergency patients. Using triage methods, the waiting period ofthe patient without treatment is determined, and if the condition of the patient is very urgent, he/sheis immediately intervened, and the patient's loss of life is prevented.

In our country, the 'Communiqué on the Application Procedures and Principles of Emergency Service Services in Inpatient Health Facilities' published in the Official Gazette with the number 27378 on October 16, 2019, published by the Ministry of Health, is included in the Annex-7 mentioned in the 'Color Coding and Triage Application' section in Article 8. Patients were classified inyellow, green, and red areas Thanks to this triage coding, optimization ofthe diagnosis and treatment process of the patients is ensured.[2,14] In the study of Çevik et al. performed in a state hospital, in terms of priority status (triage) of emergency applications; the authors stated that the patients had Stable Conditions (24.34%: green area), Serious Conditions (75.20%: yellow area) and Emergencies requiring Urgent Interventions (0.47%: red area). In addition, when patients who did and did not require emergency medical or surgical intervention werecompared according to their diagnoses; they stated that ENT and eye-related disorders in non-urgent patients, and disorders related to the musculoskeletal system in emergencies were significantly higher, indicating that emergency services were used unnecessarily uınder these circumstances.[7]

In the study conducted by Köse et al.[3] in a state hospital, 88.4% of the patients were discharged from the emergency service on an ambulatory basis, and when the rates of hospitalization, referrals, deaths and outpatient discharges were examined, and theinappropriate applications wereat a higher rate. According to these authors the most important reasons for inappropriately higher admission rates to the ERs includethe socioeconomic and cultural status of the region as well as the low level of education, being able to receive treatment immediately in the ERs without paying contribution fees forexaminations and medicationsreceived, and not benefiting from primary health care centers.

In the study conducted by Türkdoğan et al.[10] in a state hospital, only 5.5% of the study patients were inthe Red Triage category, while 41.4% of them receivedthe Green Triage code. In addition, 95.9% of the patients were discharged after diagnosis and treatment made in the emergency department.

In the study conducted by Kılıçaslanet al. in a university hospital, 10.42% of the patients who applied to the emergency department were in the very urgent patient group called Triage 1, 42.34% were in the Triage 2 (Emergency) group, and nearly half of the patients (47.24%) were in the ' non-emergency' group called Triage 3.

In the study conducted by Edirne et al.[9] in a university hospital, 19.5% of the patients who applied to the Emergency Servicewere treated on an outpatient basis, and in this case, approximately one out of every five patients who applied to the emergency servicedid not meet the emergency patient criteria.

In the study conducted by Tanrıkulu et al.[1] in a training and research hospital, 94.8% of the patients were discharged on an outpatient basis after examination and treatment, and the authors also indicated higher rates of inappropriate use of emergency services.

The ER of the private hospital where this study was conducted provides second-lineemergency care and the triage classification is made by trained nurses, emergency medical technicians. When we examine the patients according to triage coding and diseases, it is seen that more than half of the patients (56%) who were admitted received the Green Triage Code. It has been determined that the vast majority (13.070)of the diseases in the Green Triage Code areas are upper respiratory tract infections (**Table 3**). In addition, 95.42% of the patients were found to be treated in the emergency service and discharged at similar ratesto the emergency service literature data of our country, which demonstrates that improper use of ERsis at a high rate. Whether it is a training and research hospital, a state hospital or a private hospital, unfortunately, patientsapply to the emergency service for social and cultural reasons and refrain fromwaiting in polyclinics, leaving their jobs during polyclinic working hours, and paying contribution fees.

In the study conducted by Kılıçaslan et al.[8] the authors found that the most frequentlyapplications were madeon Monday (15.68%), and the least number of applications occurred on Wednesday (13.53%). When they examined the application hours, they stated that the most applications were made between 07:00 PM and 11:00 PM during night shift, then between 11:00, and12:00 AM during the day shift, and the least number of applications were made between 6:00 and 7:00 AM in the morning. They found that while the number of admissions decreased gradually, especially after midnight, a significant decrease was detected between 01:00 AM and 07:00 AM and patients applying after 02:00 AM were in the very urgent category.

In the study conducted by Türkdoğan et al.[10] the authors found that the most frequently applications to the emergency department were made on Monday and the least on Thursday, and that applications increased in September, November, December and January, and decreased in April, May and June.

In the study conducted by Tanrikulu et al.[1] the researchersstated that the patient admissionrates were 45.1% between 08:00 AM and 05:00 PM, and 44.9% between 05:00 PM and midnight, and the least number of admissions were madebetween midnightand 08:00 AM (10%). They also found that the highest number of applications were madein December, while the minimum number of applications in April, while the number of applications increased as the winter season approached, and decreased in the summer months.

Patients mostly applyto the Private Hospital Emergency Service where this study was conducted in December (12%) followed by January (11%) and August (11%). The least number of admissions were seen in July, with a rate of 6% (**Figure 1**). The patients appliedmostly on Sunday (25%) followed by Saturday (19%). It was determined that the least number of admissions were made in the middle of the week (Wednesday and Thursday with 10% each) (**Figure 2**). When the timeof admissions wasevaluated, it was seen that the highest number of applications (30%) were made in the working shift hoursbetween 08:00 PM and midnight which is called the prime time.

The least number of applications (7%) were made from 04:00 AM to the start of working hours (**Figure 3**). The data of this study are compatible with the data of our country. It is seen that patient applications are increasing in and towards the winter months. We think that this is due to the fact that the people of the region, who went to their hometowns or holiday destinations in the summer, return towards the winter months, and also the epidemic of viral diseases with the cooling of the weather, and the increase in trauma due to rainfall. When the days of the week were examined, the highest number of applications occurred on Sunday followed by Saturdaywhen the polyclinics are closed after noon, because the staff works part time in private hospitals. When the hours of admission are examined, we see that the most applicationsweremade between 08:00 PM and 01:00 AMwhich iscalled the "prime time", in accordance with other studies in our country. We think that this is due to the fact that the local people working during the daytime come to the hospital during their rest periods.

CONCLUSION

The greater number of non-urgent patients in private hospital emergency services as well as in universities, training and research hospitals and state hospitals in our country shows that the problem of inappropriate use of emergency services in our country is increasing in all kinds of hospital emergency services. It is obvious that admission demographic data of the patients applied toemergency services is related to the socio-economic and cultural structure of the people in the region, therefore, emergency room managers and planners should try to get to know and evaluate the local community better.

In the winter months when the patient density is high, it is seen that additional physicians, health personnel, equipment are required at the weekend and between 8:00PM and 12:00 PM. It is necessary to make adjustments to increasethe staff working shifts duringprime-time hours and days when the greater number of patients apply, and to decrease the number of shiftsfrom 00:00 to 08 AM when patient admissions are at the lowest level. With a good staff, physical structure and equipment plan, satisfaction ofboth patient/patient relatives and staff will be provided.

Limitations: Our study is based on limited databecause our study is single-centered and study population is livingin the suburbs of ametropolitan city of our country. We believe that it would be appropriate conduct a study with wider participation of people withdifferent social classes and in different socio-economic regions.

ETHICAL DECLARATIONS

Ethics Committee Approval: Ethics committee approval vas taken from the Clinical Research Ethic Committee of Sultangazi Haseki Research and Education Hospital.

Informed Consent: All patients signed the free and informed consent form.

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Orjinal Araştırma / Original Article

Evaluation of the Hand-To-Face Contact Behaviors of Healthcare Workers and Medical Students in the COVID-19 Pandemic

COVID-19 Pandemisinde Sağlık Çalışanları ve Tıp Fakültesi Öğrencilerinin El-Yüz Temas Davranışlarının Değerlendirilmesi

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Abstract

Background: Respiratory viruses such as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), spread via different transmission routes. While the droplet path plays the most important role in transmission, contamination of the mucous membranes with contaminated hands also plays an important role in the spread. Thus, the aim of the present study was to assess the face-touching behaviors of healthcare workers (HCWs) and intern doctors during the coronavirus diseases 2019 (COVID-19) pandemic.

Material and Method: This study was conducted in July 2020 and in the Selcuk University Faculty of Medicine in Konya, Turkey. While 1-hour COVID-19 training was given to healthcare personnel and interns, participants face-touching behavior was monitored through video recording and was tallied with a scoring sheet.

Results: A total of 141 intern doctors, 46 assistant doctors, 14 nurses, 10 associate doctors, and eight staff members participated in the study. On average, each of the participants touched their face a mean of 17.2 times (median: 16; range: 0–45) per hour. Of all the face touches, 85.2% (3,228/3,787) involved contact with a face mask, whereas 14.7% (559/3,787) involved contact with the eye mucosa. Intern doctors touched their faces significantly less often with a mean of 13.7 times per hour ($p<0.001$), while nurses touched their faces more often with a mean of 28 times per hour ($p<0.001$). Although nurses touched their eye mucosa more often than interns and assistant doctors ($p<0.001$), their contact with the face mask was significantly less frequent than that of the other participants ($p<0.001$).

Conclusions: To date, there are no effective vaccines or antiviral drugs for SARS-CoV-2. For the time being, isolation, social distancing measures, and individuals' protective behaviors are essential for preventing infection. HCWs, medical students, and the broader community should be informed about self-inoculation, which can result from touching one's mucosa or mask with contaminated hands.

Keywords: SARS-CoV-2, face-mask, healthcare workers, medical students

Öz

Amaç: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) gibi solunum yolu virüslerinin farklı bulaşma yolları vardır. Virüsün yayılımında damlacık yolu kadar, ellerle mukozanın kontaminasyonu da önemli rol oynamaktadır. Çalışmamızın amacı, coronavirus disease-19 (COVID-19) salgını sırasında sağlık çalışanları ve intörn doktorların el-yüz temas davranışlarını değerlendirmektir.

Gereç ve Yöntem: Bu çalışma Temmuz 2020'de ve Selçuk Üniversitesi Tıp Fakültesi Konya, Türkiye'de yapılmıştır. Sağlık personeli ve intörn doktorlara 1 saatlik COVID-19 ile ilgili eğitim verilirken, katılımcıların el-yüz temas davranışları video kaydı ile izlenerek puanlama tablosu ile değerlendirildi.

Bulgular: Çalışmaya 141 intörn doktor, 46 asistan doktor, 14 hemşire, 10 öğretim üyesi ve sekiz personel katıldı. Katılımcıların her biri yüzlerine saatte ortalama 17,2 kez (medyan: 16; aralık: 0-45) dokunduğu saptandı. Tüm davranışların % 85,2'si (3,228/3,787) yüz maskesi ile temas,% 14,7'si (559/3,787) göz mukozası ile temastı. İntörn doktorların yüzlerine saatte ortalama 13,7 kez ($P<0,001$), hemşirelerin daha sık; saatte 28 kez dokundukları saptandı ($p<0,001$). Hemşirelerin göz mukozalarına intörn ve asistan doktorlardan daha sık dokunmuş olmalarına rağmen ($p<0,001$), yüz maskesiyle temasları diğer katılımcılara göre anlamlı olarak daha azdı ($p<0,001$).

Sonuçlar: Bugüne kadar SARS-CoV-2 için etkili aşı veya antiviral ilaç bulunamamıştır. Bu nedenle izolasyon, sosyal mesafe önlemleri ve bireysel koruyucu davranışlar enfeksiyonu önlemek için gereklidir. Sağlık çalışanları, tıp fakültesi öğrencileri ve toplumdaki bireylere; kontamine ellerle mukoza veya maskeye temas sonrasında oluşabilecek virüsle kendini enfekte etme durumu anlatılmalıdır.

Anahtar Kelimeler: SARS-CoV-2, yüz maskesi, sağlık çalışanları, tıp öğrencileri

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INTRODUCTION

Nosocomial infections with respiratory tract viruses account for the majority of serious nosocomial viral diseases. Effective preventive strategies are based upon early diagnosis and understanding of the mechanisms of transmission.[1] Respiratory viruses spread via different transmission routes, including contact with droplets or droplet nuclei. Hands contaminated with secretions is the most common route of transmission of respiratory infections in health care settings.[2] Infectious disease can result from virus particles being inhaled or coming into contact with the mucosal surface of the nose or eyes.[3,4] A less well known but common step in the transmission of many respiratory pathogens is self-inoculation.[5] Self-inoculation is a type of contact transmission and acquisition of infection after touching the mucous membranes of the nose, eye, and mouth.[6]

Coronavirus disease 2019 (COVID-19) is primarily a respiratory disease caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) and can be transmitted via respiratory droplets, droplet nuclei, and close contact.[7] The incidence of nosocomial infection is expected to be high.[8] Droplet transmission occurs when close personal contact results in the inoculation of the mouth, nose, or conjunctivae. Transmission also occurs via contact with infected surfaces and objects, with the contaminated substance then being mediated through the respiratory mucosa.[9] SARS-CoV-2 may survive for several hours on inanimate surfaces. One of the predominant mechanisms for COVID-19 to be contagious is self-inoculation from contaminated object.[10] Because of the current lack of effective treatment of COVID-19, it is important to obey infection prevention rules for global health.[11]

Literature on the frequency of the hand-to-face contact habits of healthcare workers (HCWs) and medical students is limited. Thus, the aim of the present study was to assess the face-touching behaviors of HCWs and intern doctors during the COVID-19 pandemic.

MATERIAL AND METHOD

In July 2020, HCWs of the Selçuk University of pediatrics department (consisting of associate doctor, assistant doctor, nurses, and staff) who had completed infection control education in the early stages of the pandemic were invited to a lecture for one hour. Intern doctors who had not received prior professional training were also included in the study. During a one-hour lecture, participants face-touching behavior was monitored through video recording and was tailed with a scoring sheet. The participants attended one hour lecture on five separate occasions by profession groups. Initially, they were informed that they would be recorded on video during the training. To eliminate bias, participants were blinded from the aim of the study. The video recording was viewed multiple times by the investigators to note how many times the participants touched their masks and eye mucosa. A standardized scoring sheet was used to count the frequency of face-touching behaviors.

The study was carried out with the permission of Local Ethics Committee of Selçuk University (Permission granted: 2020-12, Decision no: 2020/293).

RESULTS

A total of 141 intern doctors, 46 assistant doctors, 14 nurses, 10 associate doctors, and eight staff members participated in the study. A total of 219 participants were observed, and 3,787 touches to the face were noted over 60 minutes. On average, each of the participants touched their face a mean of 17.2 times in one hour (median: 16; range: 0–45 times). All participants had face masks. Of all face touches, 85.3 % (3,228/3,787) involved contact with a face mask, whereas 14.7 % (559/3,787) involved contact with the eye mucosa.

Intern doctors touched their faces significantly less often than other participants at a mean of 13.7 times per hour (median: 14; range: 0–21; $p<0.001$). They also touched their face masks less often than assistant doctors ($p<0.001$) and staff members ($p<0.038$). Associate doctors touched their faces a mean of 19 times in one hour (median: 22.5; range: 0–27). Their face mask contact frequency was higher than the frequency of their contact with the eye mucosa ($p<0.001$). Assistant doctors touched their faces a mean of 22.8 times in one hour (median: 24; range: 0–39), whereas staff members touched their faces a mean of 26.7 times in one hour (median: 25; range: 4–41).

Nurses touched their faces more often than the other participants at a mean of 28 times per hour (median: 29; range: 8–44; $p<0.001$). Although nurses touched their eye mucosa more often than interns and assistant doctors ($p<0.001$), their contact with the face masks was significantly less frequent than that of the other participants ($p<0.001$). Other participants' face mask contact frequencies were higher than the frequencies of contacting the eye mucosa ($p<0.001$).

The frequencies of the face-touching behaviors of the participants are shown in **Table 1**.

DISCUSSION

COVID-19 is a new disease, so there is no existing immunity, which has caused it to spread widely and quickly. Hands are considered to be an important source of the spread of infection. Personal protective behaviors and isolation measures are primary and inexpensive methods to prevent the transmission of infection. Therefore, human behavior is central to the transmission of the virus.[2,12] Infection prevention implications include hand hygiene, protection against the inoculation of mucosal surfaces, and disinfection of all frequently touched surfaces.[7]

Touching the face is an involuntary behavior for most people. In a healthcare setting, frequent face touching has the theoretical potential to be a mechanism of acquisition and transmission of infection, particularly during a pandemic. Effective interventions are therefore essential to increase adherence to behaviors.[13,14]

Table 1. Frequency of hand- to- face contact behaviour of healthcare workers and students

	Associate Doctor	Assistant Doctor	Intern Doctor	Nurses	Staff
Number of member (N)	10	46	141	14	8
Male	7	16	54		1
Female	3	30	87	14	7
Touches to the Face	190	1049	1941	393	214
Mean:	19	22.8	13.7	28	26.7
Median-Range:	22.5 (0-27)	24 (0-39)	14 (0-21)	29 (8-44)	25 (4-41)
Touches to Mask	146	923	1635	347	177
Mean:	14.6	20	11.5	3.2	22.1
Median-Range:	17 (0-24)	20 (0-37)	12(0-20)	3 (0-7)	21.5(4-41)
Touches to Eye Mucosa	44	126	306	46	37
Mean:	4.4	2.7	2.1	24.7	4.6
Median-Range:	4.5 (0-10)	3 (0-9)	2 (0-9)	25.5 (8-42)	4 (0-10)

HCWs wear face masks to protect themselves from patients with respiratory infections. In the community, the wearing of masks by infected individuals is important for reducing contagion. Face masks are commonly used as a nonpharmaceutical intervention to control virus transmission during an influenza pandemic. Specifically, several studies concluded that household use might reduce the transmission of influenza during pandemic.[15,16] Also, face masks are the most cost-effective way to slow viral spread and protect risk groups from infections during the COVID-19 pandemic. Eye, nose, and mouth protection may also provide additional benefits.[2] As a disadvantage, masking may lead to more hand-to-face contact, potentially facilitating self-inoculation. The manipulation of masks has been found to create higher risks of contamination and self-contamination.[12,17]

Studies on face touching are limited, as are the rates among HCWs and medical students. In a 2008 study, 10 subjects were each video recorded while performing office-type work, and it was found that they touched their faces an average of 16 times per hour.[18] In another study at the University of Australia, on average, the students touched their faces 23 times each hour. Of all the face touches, 44% involved contact with a mucous membrane (mouth, nose, or eyes).[2] During the influenza A (H1N1) pandemic, face-touching behavior in the community was observed on average 3.3 times per hour.[19]

In our study, on average, each of the participants touched their face a mean of 17.2 times in one hour (median: 16; range: 0–45 times). The frequency was higher than we expected, and most of these cases involved touching the face mask.

During the COVID-19 pandemic, HCWs (including nurses, staff members, assistant doctors, and associate doctors) were trained on infection prevention measures. The intern doctors had returned to the hospital after a long break and had not received professional training about COVID-19 thus far. Even so, intern doctors touched their faces significantly less often than the other participants.

In this study, nurses touched their eye mucosa more often than other participants. Other participants touched their face masks more often than their eye mucosa ($p<0.001$). Of all the face touches, 85.2% involved contact with a face mask. It must be considered that wearing a surgical mask may offer an exaggerated, false sense of security and an overvaluing of the protection.

Associate doctors touched their faces a mean of 19 times in one hour, and it was expected that this frequency would be low. Touching the face is a habitual behavior for most people and, as such, it often goes unnoticed, regardless of education level. Habits can be difficult to change even with theoretical knowledge. One study has shown that facial self-touch movements are frequently performed with no awareness and primarily in stressful situations.[20] Although the knowledge level of HCWs is high about infection precautions, the frequency of face contact habits can be associated with stress about COVID-19.

To our knowledge, this is the first study documenting the frequency of face-touching behaviors among HCWs during the COVID-19 pandemic. Our study shows that HCWs touched their faces quite often. Contamination of frequent touch surfaces in healthcare settings can be a potential source of infection transmission. Members of pediatric clinics who are heavily exposed to respiratory viruses may be at increased risk of acquiring an infection. Standard, droplet, and respiratory precautions along with isolation and social distancing measures should be reviewed frequently during a pandemic. In particular, HCWs and medical student awareness must be increased about that fact that face-touching behavior can result in self-inoculation. Public health campaigns and HCWs education should also focus on correcting these unconscious behaviors.

There are several limitations to the present study. First, participants were recruited from only one department, and the number of participants in each profession was not equal. While we did not inform participants that we were observing their face-touching behaviors, they were informed that the training meeting was being video recorded. Thus, this may have changed their behaviors. An observation study conducted with participants during the performance of their duties could provide more accurate results. Therefore, further studies are necessary.

CONCLUSION

Currently, there are no effective medications or vaccines available for the treatment or prevention of COVID-19. For this reason, following precautions such as isolation and physical distancing is the best way to protect oneself from the infection. HCWs and the broader community must be educated about COVID-19, including how it is transmitted, and how they can protect themselves. Changing behavior is crucial to prevent transmission in the absence of treatment options.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Local Ethics Committee of Selçuk University (Permission granted: 2020-12, Decision no: 2020/293).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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

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Orjinal Araştırma / Original Article

The Relation of Regional and General Anesthesia Applied in Cesarean Patients with Postpartum Depression

Sezaryen Hastalarında Uygulanan Bölgesel ve Genel Anestezinin Doğum Sonrası Depresyon İle İlişkisi

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Abstract

Aim: The purpose of the study is to investigate the relationship between the frequency of depression and the type of anesthesia given to the women that deliver by cesarean section.

Material and Method: The study was carried out prospectively on cesarean patients. The study included 58 patients with general anesthesia (GA) and 61 patients with spinal anesthesia (SA). Right before the surgery the patients filled State Trait Anxiety Inventory-1(STAI-1), a form surveying the anesthesia concerns. Edinburg Postpartum Depression Scale was filled six weeks after the delivery. The data were analyzed by IBM SPSS 20 statistical analysis program.

Results: The difference between the GA and SA groups were insignificant in terms of age, education, socio-economic level and number of pregnancy ($p<0.05$). Both groups had high STAI-1 mean values but the difference between them were insignificant ($p>0.05$). Edinburg Postpartum Depression Scale indicated that depression points were high in 15.5% of the GA group and 8.1% of the SA group. This was statistically significant ($p< 0.01$).

Conclusion: This study showed that postpartum depression rate was higher in patients that had GA compared to the patients with SA. Thus, it is crucial to select the type of anesthesia after careful examination of the patient.

Keywords: Pre-anesthetic anxiety, anesthesia, cesarean, postpartum depression

Öz

Amaç: Çalışmanın amacı sezaryen ile doğum yapan kadınlara verilen anestezi tipi ile doğum sonrası depresyon sıklığı arasındaki ilişkiyi araştırmaktır.

Gereç ve Yöntem: Çalışma prospektif olarak sezaryen hastalarında yapıldı. Çalışmaya 58 genel anestezi (GA) hastası ve 61 spinal anestezi (SA) hastası dahil edildi. Ameliyattan hemen önce hastalardan anestezi endişelerini araştıran bir form olan Durumluk-Sürekli Kaygı Envanteri-1'i (STAI-1) doldurmaları istendi. Edinburg Doğum Sonrası Depresyon Ölçeği, doğumdan altı hafta sonra dolduruldu. Veriler IBM SPSS 20 istatistiksel analiz programı ile analiz edildi.

Bulgular: GA ve SA grupları arasında yaş, eğitim, sosyoekonomik düzey ve gebelik sayısı açısından fark yoktu ($p <0.05$). Her iki grupta da yüksek STAI-1 ortalama değerleri vardı ancak aralarındaki fark önemsizdi ($p> 0.05$). Edinburg Doğum Sonrası Depresyon Ölçeği, GA grubunun% 15.5'inde ve SA grubunun% 8.1'inde depresyon düzeylerinin yüksek olduğunu göstermiştir. Bu fark istatistiksel olarak anlamlı olarak bulunmuştur ($p <0.01$).

Sonuç: Bu çalışma, GA uygulanan hastalarda, doğum sonu depresyon oranının SA uygulanan hastalara göre daha yüksek olduğunu göstermiştir. Bu nedenle, hastanın dikkatle incelenmesinden sonra anestezi tipinin seçilmesi çok önemlidir.

Anahtar Kelimeler: Anestezi öncesi anksiyete, anestezi, sezaryen, doğum sonrası depresyon

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INTRODUCTION

Cesarean was a lifesaving operation for the mothers and the babies, today the rate of elective cesarean has increased.[1,2] During pregnancy, the mother goes through psychosocial and physiological changes. In order to end the pregnancy successfully, mother and the health providers cooperates. Most of the times, type of the delivery and the type of anesthesia in case of cesarean are determined beforehand. Of course, in emergency situations this decision is made by doctors considering all risks. An anesthetist should know the obstetric information and the physical properties of the mother very well; should be able to foresee impacts of anesthetic agents on the mother and the fetus, and therefore, should guide the mother accordingly. Although there is sufficient time for all these procedures in a scenario of an elective cesarean section, in an emergency there is a race against the time. In addition to the patient's anxiety regarding her health, baby's health, delivery, pain, being away from daily routine and unpredictability during the prenatal period, the sensitivity of the mother increases once she faces with an emergency operation.[3] Whereas some mothers prefer participating actively despite the fact that they are going through cesarean, some mothers do not want to see the operation at all and have high level of preoperative anxiety.[4] Such high level of anxiety may cause postpartum depression.[5] Several clinical phenomena for the postpartum period were described in the literature, including maternity blues and postpartum depression.[6] The maternity blues or postnatal blues usually characterizes the first week after giving birth, and it is defined as a sad disposition that could be accompanied by affective lability, soft crying, confusion, fatigue, anxiety, insomnia, lost appetite and irritability and these symptoms had a maximum duration of 10 days and spontaneously and totally regressed.[7-10] Postpartum depression (PPD) is a mental disorder usually occurring within 12 months after birth, which can causes serious harm to both the mothers and families.[11]

The term "depression, in addition to "mood", is used to define one of the most common psychological disorders. In depression the patient feels deep sadness, slowing down of speaking, acts, thinking and all physiological functions. Weakness, vanity, aversion, and pessimism dominate the mood.[12] Postpartum depression is considered as depressive episode that is formed within a year after delivery.[13] After delivery, most of the mothers have temporary and self-restricting mood changes that last up to 2 weeks. Thus, presence of postpartum depression can be indicated 2 weeks after the delivery.[14] Early diagnosis is crucial for treatment. Some studies indicated that the cesarean birth procedure could be considered as a more controlled and safe way of giving birth.[15] Others indicated that the type of birth did not impact the affective disorders during the postpartum period.[16,17] On the other hand some studies indicated that cesarean section is associated with increased risk for postpartum depression.[18]

Aim

The aim of the study is to investigate the relationship between the frequency of depression and the type of anesthesia given to the women that delivers by cesarean section.

MATERIAL AND METHOD

This single-centered prospective study was carried out in a maternity hospital between October 2018 - March 2019 on emergency cesarean section patients that satisfied the study criteria and volunteered to participate in the study. The study included 130 patients of which 65 had general anesthesia (GA) and 65 had spinal anesthesia (SA). The patients who had stillbirths and the ones who did not continue the study after delivery were excluded. The study was finalized with 58 GA and 61 SA cases. Patients that were under 18, the ones that had communication problems and known psychiatric illnesses, and the ones that could not cooperate due to emergency were excluded from the study.

In order to determine the current anxiety of the patients before the cesarean section, "State" part of the State Trait Anxiety Inventory (STAI) was used. Two forms that were prepared in accordance with the literature was filled: A questionnaire form inquiring descriptive properties, socio-demographic properties, obstetric histories and chronic illness of the patients as well as a form consisting of 10 questions that inquire anxiety of patients regarding anesthesia.[19] Postpartum depression clinically is observed two weeks after the delivery at the earliest. Therefore, in this study Edinburg Postpartum Depression Scale was filled six weeks after the delivery. The patients that scored 13 and above were considered as depressive.

STAI-state scale is a self-evaluation inventory consisting of 20 questions that is sensitive to physiological and cognitive phases such as anxiety, uneasiness, nervousness, and worry and it measures subjective fear.[20] The patients are asked to choose one of the options "none, little, a lot, and completely" according to intensity of their feelings, thoughts and behaviors. There are straight and reverse expressions. The reverse expressions correspond to positive feelings; thus, the ones scoring 1 are converted to 4 and vice versa. This scale contains 10 reverse expressions. Oner and Le Compte measured the validity and reliability of this inventory. The alpha reliability of the scale is 0.83-0.87 and the retest reliability is 0.71-0.86. They reported that the item reliability may fluctuate between 0.34 and 0.72. Low scores indicate a low level of anxiety and high scores indicate a high level of anxiety They reported the average score to be between 36 and 41.

Edinburg Postpartum Depression Scale, one of the self-evaluation scales, consisting of 10 questions was developed to indicate postpartum depression.[21] Each question has a score 0-3. Questions 1, 2 and 4 are numbered as 0-1-2-3; the others are numbered as 3-2-1-0. The scores are added. Maximum score is 30 and the breakpoint is calculated as 13.

The data were analyzed by IBM SPSS 20 statistical analysis program. Mean, median, standard deviation, minimum, maximum, percentage, and numbers were used to present the data. If the sample size was <50 Shapiro Wilk-W test and if the sample size was ≥50 Kolmogorov Smirnov test were used to examine the normal distribution of continuous variables.

While comparing the two independent groups, if the normal distribution condition was satisfied, the Independent Samples t-test was used and if the normal distribution condition was not satisfied, the Mann Whitney u-test was used.

When the expected count is >5, Pearson Chi-square test; when the expected count is between 3-5, the chi-square test, and when the expected count is <3 Fisher's Exact test were used for 2x2 comparisons between categorical variables. The statistical significance level was $p<0.05$.

G*Power 3.1.9.2 software was used for power analysis. The power of this data was 1-β=0.99 with GA group=55, SA group=55, α=0.05 and an effect size of d=1.0.

Permission of the University of Health Sciences, Erzurum Regional Training and Research Hospital Ethics Committee was obtained for the study (document no: 3773258-514.10-2018/10-65).

RESULTS

The GA group had 58 and the SA group had 61 patients. Their mean ages were 28.6 ± 6.2 and 28.3 ± 5.3, respectively. With regards to education, number of elementary school graduates was the most in both groups (43.1%, 44.2%). The second ranking group was high school graduates (43.1%, 42.6%). The GA patients who had problems during pregnancy was 22.4% whereas this rate was 47.5% for the SA patients (p=0.04). The rate of family depression history was 5.2% in GA group and 18% in SA group (p=0.01). Both were statistically significant (**Table 1**).

Table 1. Descriptive and obstetric properties

	General anesthesia				Spinal anesthesia				Chi-Square test
	n	%	mean	SD	n	%	mean	SD	
Age	58		28.6	6.2	61		28.3	5.3	
Weight	58		70.3	10.5	61		74.5	12.1	
Education									
Illiterate	10	17.0			4	6.6			$X^2 = 4.1$ P>0.05
Elementary	25	43.1			27	44.2			
High School	18	31.1			26	42.6			
University	5	8.6			4	6.6			
Socio-economic level									
Bad	16	27.6			27	44.3			X^2 =4.8 p>0.05
Average	30	51.7			28	45.9			
Good	12	20.7			6.0	9.8			
Smoking									
Yes	1	1.7			3	4.9			X^2 =0.9 p>0.05
No	57	98.3			58	95.1			
Weeks of pregnancy	58		37.8	1.9	61		38.2	1.8	
Number of pregnancy	58		3.2	1.9	61		3.4	1.4	
Number of deliveries	58		2.6	1.6	61		2.6	1.2	
Alive children	58		2.5	1.4	61		2.5	1.3	
Problems during pregnancy									
Yes	13	22.4			29	47.5			X^2 =8.2 P=0.04
No	45	77.6			32	52.5			
Weight of the baby	58		2817	635	61		3101	574	
General situation of the baby									
Bad	3	5.2			0	0			$X^2 = 3.2$ p>0.05
Average	3	5.2			4	6.6			
Good	52	89.7			57	93.4			
Number of Cesarean									
1	38	65.5			32	52.5			
2	15	25.9			10	16.4			
3 and more	5	8.6			19	31.1			
Chronic illnesses									
Yes	9	15.5			12	19.7			$X^2 = 0.3$ p>0.05
No	49	84.5			49	80.3			
Family's depression history									
Yes	3	5.2			11	18.0			$X^2 = 4.73$ P= 0.03
No	55	94.8			50	82.0			

When the patients were asked about their concerns regarding the anesthesia, 74.1% of the GA patients indicated that they were scared of postoperative pain and 62.1% was scared of needles; whereas 67.2% of the SA patients were afraid of harm that might be given to the baby and 65.6% of them were afraid of postoperative pain. The fear of postoperative paralysis and the needle phobia in the GA group were significantly higher compared to the SA group (p=0.03, p=0.00).

The STAI-State scale indicated that both groups had high levels of anxiety. The mean of the GA group was 42.93±5.45 (58.6 % was above average); the mean of the SA group was 41.85±5.92 (69.1% was above average). There were not statistically significant differences between two groups.

According to evaluation under Edinburg postpartum depression scale, 9 of 58 GA patients (15.5%), 5 of 61 SA patients (8.1%) scored above 13. This was statistically significant (p<0.01) (**Table 2**).

Table 2. Mean of STAI-State and Edinburg Depression Scale of the Cases

	General anesthesia (n=58)		Spinal anesthesia (n=61)	
	Mean	SD	Mean	SD
STAI-1	42.93	5.45	41.85	5.92
Edinburg	9.05	5.25	6.78	4.51

DISCUSSION

This study investigated the impact of anxiety related to anesthesia on postpartum depression in addition to high level of anxiety that is already present in cesarean section patients. Age, weight, socio-economic and education levels of the patients were similar in both groups. Both groups had high levels of postoperative anxiety and the difference between two groups was insignificant. In a study on elective cesarean section patients by Maheshwari et al.[5] preoperative anxiety levels of the GA patients were significantly higher than the SA patients, and the anxious patients preferred GA over SA. This was mainly because the conscious patients were unable to cope with the difficulties that may realize. In a cohort study, postpartum depression level was higher in a cesarean section patients compared to vaginal delivery patients. The idea of going through an operation increases the anxiety level.[22] There is sufficient time to inform the patient that will have elective cesarean section. In a study by Fernandes et al.[4] postpartum anxiety levels increased in patients that had epidural anesthesia. Generally, the patients that will have an operation get concerned about anesthesia and they would like to have some information beforehand.[23] Almost half of the patients in both groups expressed that they were not given enough information about the anesthesia (**Table 3**). This can be listed as one of the factors increasing the anxiety.

There are different perspectives on education and anxiety level. The study of Caumo et al.[16] stated that patients with higher education had more awareness on anesthesia and surgery, and since they were able to reach information on possible complications more easily they had greater level of anxiety. The study of Buonanno et al.[24] reported that the anxiety level was dependent on the previous positive or negative experiences with operation.

In our study, 65.5% of the GA patients and 52.5% of the SA patients had their first cesarean. It was observed that patients that had cesarean section before had lower level of anxiety. With this respect, anxiety levels between two groups were statistically significant. During the study, the concerns of the patients on anesthesia were questioned. The most common fears in GA were the fear of postoperative pain and the needle phobia. It is concluded that the patients opt for GA most probably because the SA requires use of needles. On the other hand, the most common fears in the SA group were the fear of any harm that might be given to the baby and the fear of postoperative pain. As the anxiety regarding the baby is high, mother's willingness to see the baby healthy plays an important role in her decision to choose SA. The fear of paralysis was significantly high in the GA group; these patients did not want to have SA. In a study by Jlala et al.[23] it was reported that informing patients, who will go through elective cesarean under regional anesthesia, by multimedia reduced their anxiety level. However, since there is no time to inform emergency patients this way, they are given brief information and asked to fill out a consent form.

Table 3. Concerns regarding anesthesia

Questions	General anesthesia (n=58)				Spinal anesthesia (n=61)				Chisquare
	Yes	%	No	%	Yes	%	No	%	
1. Information provided by anesthetist was insufficient	28	48.3	30	51.7	25	41.0	36	59.0	X^2 =0.6, p>0.05
2. Anesthetist was inexperienced	13	22.4	45	77.6	18	29.5	43	70.5	X^2 =0.7, p>0.05
3. Unable to wake up after surgery	27	46.6	31	53.4	22	36.1	39	63.9	X^2=1.3, p>0.05
4. Postoperative pain	43	74.1	15	25.9	40	65.6	21	34.4	X^2=1, p>0.05
5. Postoperative stroke	17	29.3	41	70.7	8	13.1	53	86.9	X^2=4.6, p=0.030
6. Needle phobia	36	62.1	22	37.9	18	29.5	43	70.5	X^2=12.7, p= 0.00
7. Staying in intensive care unit	20	34.5	38	65.5	31	50.8	30	49.2	X^2=2.9, p>0.08
8. Harm to baby	35	60.3	23	39.7	41	67.2	20	32.8	X^2=0.6, p>0.05
9. Attitude of the anesthetist	23	39.7	35	60.3	23	37.7	38	62.3	X^2=0.04, p>0.05
10. Problems with the personnel	22	37.9	36	62.1	22	36.1	39	63.9	X^2=0.04, p>0.05

For this study, the STAI-state inventory was filled before the operation but due to the lack of time STAI-trait inventory was not used. In both groups, state anxiety levels were high. Although the anxiety level above the mean was higher in the GA group compared to the SA group, the difference between them was not statistically significant. In a questionnaire by Burkle et al.[25] the most significant reason for the anxiety was reported as fear of death. In our study, 46.6% of the GA patients and 36.1% of the SA patients had the fear of not being able to wake up after the operation.

The patients try to cope with several challenges such as their own health, baby's health, anesthesia concerns, operation fears, and urgency of the situation. The rush before the operation may cause anxiety. The attitude and the support of the professional health staff helps patients to go through a comfortable operation and prevents postoperative depression. In this study, the postpartum depression rate of the GA patients was 15.5% and postpartum depression rate of the SA patients was 8.1%. These were statistically significant, which could be due to higher level of fear and anxiety experienced by the GA patients. The study by Ross et al.[26] on 150 patients reported that perinatal anxiety had closely connected to postpartum depression.

CONCLUSION

In cases of cesarean, preoperative anxiety is high since the patient is unprepared and not provided sufficient information, and the mother is seriously concerned about her and her baby's health. This high level of anxiety triggers depression. In this study, postpartum depression rate was higher in GA patients compared to SA patients. Thus, it is crucial to select the type of anesthesia after careful examination of the patient. Identifying risk factors for mental disorders that may affect pregnancy is an important prerequisite in developing interventions to lower adverse maternal and neonatal outcomes.

ETHICAL DECLARATIONS

Ethic Committee Approval: Permission of the University of Health Sciences, Erzurum Regional Training and Research Hospital Ethics Committee was obtained for the study (document no: 3773258-514.10-2018/10-65).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed

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

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Orjinal Araştırma / Original Article

Investigation of the Sensitivity of *Mycobacterium tuberculosis* Strains Isolated from Various Clinical Samples in Eastern Turkey to Major Anti-tuberculosis Drugs

Türkiyenin Doğusunda Çeşitli Klinik Örneklerden İzole Edilen *Mycobacterium tuberculosis* Suşlarinin Major Anti-Tüberküloz İlaçlara Duyarlılıklarının Araştırılması

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Abstract

Objective: In the study, 419 *Mycobacterium tuberculosis* complex strains, which were isolated from samples sent to the Regional Tuberculosis Laboratory in our city between 2015 and 2019 with suspected tuberculosis from Erzurum and surrounding cities were investigated.

Material and Method: Our research is a retrospective cross-sectional study and clinical samples sent to the Regional Public Health Laboratory with suspicion of Tuberculosis within a five-year period from January 2015 to December 2019 were first evaluated by using Ehrlich-Ziehl-Neelsen staining technique. The samples were then simultaneously inoculated into the automated culture system (BACTEC MGIT 960) with Löwenstein-Jensen medium. Sensitivity research was conducted for isoniazide (INH), rifampicin (RIF), streptomycin (STM) and ethambutol (ETM) antibiotics with BACTEC MGIT 960 system to samples defined by *M. tuberculosis* complex strains identification test (TBc ID) from reproduction positive tubes.

Results: In our study, 337 (80.4%) of the 419 *M. tuberculosis* complex strains investigated in our study were susceptible to all major anti-TB drugs, while 82 (19.6%) were found to be resistant to at least one major anti-TB drug. The distribution of resistance ratios was INH (11.9%), STM (11.7%), RIF (4.1%), ETM (3.6%). Multi-drug resistant (MDR)–TB ratio (IZN+ RIF) was found to be (3.6%).

Conclusions: In our study, in the strains in which resistance to anti-TB drugs was investigated, the highest drug resistance was determined for IZN. The lowest drug resistance was determined for ETM.

Keywords: *Mycobacterium tuberculosis*, drug resistance, multiple drug resistant (MDR) tuberculosis, anti-tuberculosis drugs

Öz

Amaç: Çalışmada ilimizde bulunan Bölge Tüberküloz Laboratuvarı'na 2015-2019 yılları arasında Erzurum ve çevre illerden tüberküloz şüphesi ile gönderilen örneklerden izole edilmiş olan 419 ***Mycobacterium tuberculosis*** kompleks suşun, major anti-tüberküloz ilaçlara karşı direnç durumu araştırıldı.

Gereç ve Yöntem: Araştırmamız retrospektif kesitsel bir çalışma olup, Ocak 2015-Aralık 2019 tarihleri arası beş yıllık sürede Bölge Halk Sağlığı Laboratuvarına Tüberküloz şüphesiyle gönderilen klinik örnekler, ilk önce Ehrlich-Ziehl-Neelsen boyama yöntemi kullanılarak değerlendirildi. Daha sonra örnekler eş zamanlı olarak Löwenstein-Jensen besiyeri ile otomatize kültür sistemine (BACTEC MGIT 960) ekimleri yapıldı. Üremesi pozitif tüplerden identifikasyon testi (TBc ID) ile ***M. tuberculosis*** kompleks suşu tanımlaması yapılan örneklere BACTEC MGIT 960 sistemi ile izoniazid (INH), rifampisin (RIF), streptomisin (STM) ve etambutol (ETM) antibiyotikleri için duyarlılık araştırması yapıldı.

Bulgular: Çalışmamızda ilaç duyarlılığı araştırılan 419 ***M. tuberculosis*** kompleks suş'un 337'si (%80,4) majör anti-TB ilaçların tümüne duyarlı iken 82'si (%19,6) en az bir majör anti-TB ilaca dirençli bulundu. Direnç oranlarının dağılımı IZN (%11,9), STM (%11,7), RIF (%4,1), ETM (%3,6) idi. Çoklu ilaca dirençli (ÇİD)–TB oranı (INH +RIF) (%3,6) olarak bulundu.

Sonuç: Çalışmamızda majör anti-TB ilaçlara karşı direnç araştırılan suşlarda en yüksek ilaç direnci IZN için belirlendi. En düşük ilaç direnci ETM için saptandı.

Anahtar Kelimeler: *Mycobacterium tuberculosis*, ilaç direnci, çoklu ilaç dirençli (ÇİD) tüberküloz, anti-tüberküloz ilaçlar

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INTRODUCTION

Tuberculosis (TB) caused by *M. tuberculosis* is a disease that causes the deaths of more than 1 million people each year in mostly low-income and middle-income countries.[1,2] TB remains one of the top 10 causes of deaths worldwide. Millions of people continue to fall ill from TB every year. [3] There has been a significant decrease in the registered incidence of tuberculosis in Turkey in recent years. As such, while in 2005 the incidence ratio was 29.4 per hundred thousand in 20,535 registered patients, it decreased to 14.6 per hundred thousand in 2017.[4] In our country, out of the 12,046 total number of patients diagnosed with TB in 2017, 92.2% were new cases; 7.8% were previously treated cases; 42.3% were female; 57.7% were male; 66.1% were patients with pulmonary involvement; 33.9% were patients with extrapulmonary involvement.[4]

The treatment of tuberculosis with drugs began towards the end of the 1940s and over time resistance developed against the drugs used in this treatment. Resistance to anti-TB drugs is an important problem.[5] The drug-resistant TB (DR-TB) problem which has attracted attention especially since the early 1990s, has reached a global dimension today. The increase, especially in multi-drug resistant (MDR) TB cases, is the most important problem that threatens the success of TB control programs.[6] While drug resistance can develop spontaneously in a drug-sensitive strain before treatment, MDR-TB could also develop despite the fact that the primary treatment is completed.[7,8] MDR-TB is defined as TB resistant to caused by *M. tuberculosis* complex isolates resistant to INH and RIF which are among the primary (first-line) anti-TB drugs.[9,10] In our country, the number of MDR-TB in 2017 patients was 191. In 2015, the treatment success for MDR-TB patients at the 24th month 2015 was 67.8%.[4] The American Thoracic Society and the Center for Disease Control and Prevention (CDC) recommend susceptibility tests for at least first step anti-TB drugs in all older and new TB cases to ensure that patients with TB can be treated correctly and prevent the development of resistance to anti-TB drugs.[6]

In this study, resistance to INH, RIF, STM and ETM of 419 *M. tuberculosis* isolates isolated from different clinical specimens with suspected tuberculosis from 11 provinces in Erzurum and its surrounding were investigated.

MATERIAL AND METHOD

In our research, sensitivity results for STM, INH, ETM, RIF against major drugs used in TB treatment in 419 *Mycobacterium tuberculosis* complex strains isolated from patient clinical samples sent to the Regional Public Health Laboratory with pre-TB diagnosis between 2015 and 2019 from 13 cities, mainly from cities in eastern Anatolia region were investigated. All operations in the laboratory were performed in Class II biosafety cabins using the necessary protective personal equipment such as gloves, glasses and protective clothing. If different clinical samples had been sent for a patient, only one strain isolated from among these samples was included in the study. Multiple antibiotic sensitivity tests were performed for a patient in one year and if the MDR- *M. tuberculosis* complex strain was not defined in subsequent clinical samples, the first result was included in the study. Whether the patients who participated in the study had previously used anti-TB drugs, could not be definitively revealed because of the changes in our hospital automation systems at different times and the shortcomings in patient records.

Pleural fluid and Cerebrospinal fluid (CSF) samples coming to the laboratory which were thought to have been obtained in aseptic conditions, were processed directly without being decontaminated; while clinical samples such as sputum, abscess, bronchial lavage were processed after homogenization and decontamination using N-acetyl-L-cysteine and sodium hydroxide (NALC and NaOH). Then the pH of the clinical sample was adjusted, and it was centrifuged and intensified. The resulting sediment was simultaneously inoculated in 0.5 ml MGIT tubes (Becton Dickinson Diagnostics, USA), which contain Middlebrook 7H9 liquid medium used simultaneously in both the Löwenstein-Jensen classical culture medium and BACTEC MGİT 960 full automatic systems. 0.8 ml PANTA (polymyxin B, amphotericin B, nalidixic acid, trimethoprim, azlocillin) was added to MGIT tubes before inoculation.

All samples where inoculation was done were left for incubation for 42 days. Acid resistant staining was made in samples that gave positive results. BD MGIT-TBC Identification Test (TBc ID) (Becton Dickinson Diagnostics, USA) detecting MPT64 antigen was administered in accordance with the recommendations of the manufacturer. Sensitivity/resistance to major anti-TB drugs of the strains evaluated as *M. tuberculosis* complex strain was investigated in accordance with the manufacturer's operating procedure using BACTEC MGIT 960 system to be the final concentration of the drug being ETM (5.0 µg/ml), INH (0.1 µg/ml), RIF (1.0 µg/ml), and STM (1.0 µg/ml).

In addition to using H37Rv reference strain (ATCC 35838) during the laboratory internal quality control process where the research was carried out, our laboratory is also included in the external quality program of the Turkish Public Health Laboratory of the Ministry of Health. This research was approved by the "Atatürk University Faculty of Medicine Ethics Board of Clinical Research of " by decree no. 19 on 13.02.2019.

Statistical Analysis

In the analysis of the data used in the study the 22.0 IBM SPSS package program was used. The frequency and percentages of the data was calculated. When evaluating the results of categorical data in our research, A p- value equal or less than 0.05 (≤0.05) is considered statistically significant.

RESULT

A total of 419 strains isolated from Erzurum, Ağrı, Erzincan, Kars, Batman, Mardin, Siirt, Rize, Ardahan, Giresun, Bayburt and Iğdır cities were included in the study between January 2015 and December 2019. The strains were isolated from various clinical materials in the tuberculosis unit of Erzurum Regional Public Health Laboratory. The distribution of clinical samples included in this study are also shown in **Table 1**. It was observed that 259 (61.8%) of patients from whom *M. tuberculosis* complex strain was isolated were male and 160 (38.2%) were female. The distribution of strains taken by year consisted of 61 strains in 2015, 62 in 2016, 106 in 2017, 113 in 2018 and 77 in 2019.

Resistance ratios of strains isolated using BACTEC MGIT 960 method against anti-tuberculosis (anti-TB) drugs are shown in **Table 2** according to gender. 337 (80.4%) of the strains were susceptible to all major anti-TB drugs, while 82 (19.6%) were found to be resistant to at least one major anti-TB drug. The highest resistance ratio was found to be 11.9% against INH, while the lowest resistance ratio was determined to be 3.6% against ETM antibiotics (**Figure 1**). Resistance to STM was 11.7%, resistance to RIF was 4.1% (Figure 1). In our study, while there was single resistance in 51 (12.2%) of the isolates, in 31 (7.4%) of the isolates there was resistance to two or more of the tested drugs (**Table 3**). MDR-TB ratio (IZN+RIF) has been determined 15 (3.6%) isolates. In this study 6 (1.4%) isolates resistant to all four of the antibiotics (IZN+RIF+ETM+STM) were identified. *M. tuberculosis* isolate were found in 200 (47.7%) of all 419 specimens submitted for microscopy.

Table 1. Samples from which *Mycobacterium tuberculosis* complex strain was isolated

Patient sample	Number (n)	Percentage (%)
Sputum	352	84
Broncho alveolar lavage	37	8.8
Aspiration material	15	3.6
Pleural Fluid	11	2.6
Biopsy	3	0.7
Peritoneal fluid	1	0.2
Total	419	100

Table 2. State of resistance to antibiotics depending on gender status

Characteristic	Antibiotic Resistance Positive		P value
	Number (n)	Percentage (%)	
Gender			
Male (n=259)	56	21.6	0.206
Female (n=160)	26	16.3	
Total	82	19.6	

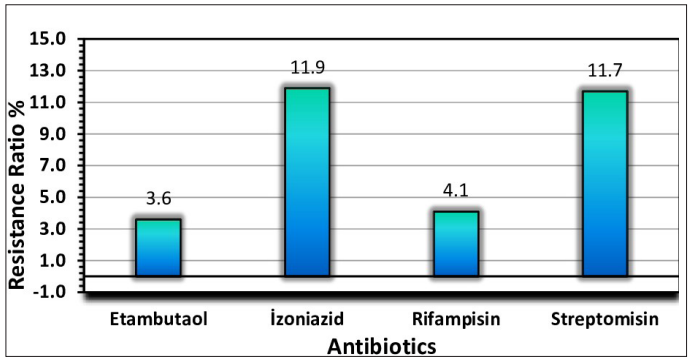

Figure 1. Resistance ratios against major anti-tuberculosis drugs

Table 3. The state of resistance of examined *Mycobacterium tuberculosis* complex strains against major anti-tuberculosis drugs according to years

Characteristic	2015	2016	2017	2018	2019	Toplam
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Tested isolate	61 (100)	62 (100)	106 (100)	113 (100)	77 (100)	419 (100)
Sensitive to anti-TB drugs	50 (82.0)	56 (90.3)	86 (81.1)	83 (73.5)	62 (80.5)	337 (80.4)
Resistance to any drug	11 (18.0)	6 (9.7)	20 (18.9)	30 (26.5)	15 (19.5)	82 (19.6)
STM	4 (6.6)	5 (8.1)	10 (9.4)	23 (20.4)	7 (9.1)	49 (11.7)
INH	11 (18.0)	3 (4.8)	13 (12.3)	14 (12.4)	9 (11.7)	50 (11.9)
RIF	5 (8.2)	1 (1.6)	4 (3.8)	4 (3.5)	3 (3.9)	17 (4.1)
EMB	1 (1.6)	1 (1.6)	5 (4.7)	5 (4.4)	3 (3.9)	15 (3.6)
Resistance to single drug	4 (6.6)	4 (6.5)	12 (11.3)	19 (16.8)	12 (15.6)	51 (12.2)
STM	0 (0)	3 (4.8)	3 (2.8)	15 (13.3)	4 (5.2)	25 (6.0)
INH	4 (6.6)	1 (1.6)	6 (5.7)	4 (3.5)	6 (7.8)	21 (5.0)
RIF	0 (0)	0 (0)	1 (0.9)	0 (0)	0 (0)	1 (0.2)
EMB	0 (0)	0 (0)	2 (1.9)	0 (0)	2 (2.6)	4 (1.0)
Resistant to multiple drugs (MDR)	5 (8.2)	1 (1.6)	3 (2.8)	3 (2.7)	3 (3.9)	15 (3.6)
INH+RIF	3	0 (0)	0 (0)	0 (0)	1 (1.3)	4 (1.0)
INH+RIF+EMB	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
INH+RIF+SM	1 (1.6)	0 (0)	1 (0.9)	2 (1.8)	1 (1.3)	5 (1.2)
INH+RIF+EMB+SM	1 (1.6)	1 (1.6)	2 (1.9)	1 (0.9)	1 (1.3)	6 (1.4)
Other resistance patterns	2 (3.3)	1 (1.6)	4 (3.8)	8 (7.1)	1 (1.3)	16 (3.8)

INH: Isoniazide, RİF: Rifampicin, EMB: Ethambutol, STM: Streptomycin

DISCUSSION

Epidemiological data and lab data are important in terms of evaluating achievements in the fight against tuberculosis, obtaining healthy data and determining real resistance ratios. The data obtained in our study is important for regional evaluation as it includes Erzurum city and surrounding cities. When we look at the resistance ratios of at least one anti-TB drug in some studies conducted in Turkey and around the world; Esenkaya Taşbent et al.[11] found resistance to at least one major drug in 16.9% of patients. In the study by Burak Selek et al.[12] 27.8% of the isolates obtained from patients were found to be resistant to at least one antibiotic. In their study, Artan et al.[9] reported that, 25.5% of the strains isolated from older and new TB patients were resistant to at least one of the anti-TB drugs. In Ethiopia, Adene et al.[13] found 20.2% resistance to any primary anti-TB drug. In Korea, 19.4% of isolates taken from patients in Lee et al.[14] study group. Were shown to be resistant to any one of the anti-TB drugs. In He et al.[15] study in China, the resistance rate against at least the first step drug was 21.2%. According to the results of our study, the resistance rate against any major anti-TB drug was 19.6%.

In the "Tuberculosis War in Turkey 2018 Report" published by the Ministry of Health in Turkey, resistance ratios against major anti-TB drugs in 2009-2016 were reported to be 11.9-15.4% for INH; 4.2-6.8% for RIF; 3.7% to 5.4% for EMB; 8.5%-11.3% for STM. The first option with the highest resistance ratio in this data is the anti-TB drug INH.[16] In a study conducted by Maurya et al. in India, anti-TB resistance ratios were reported as 27.6% for INH, 14.6% for RIF, %14.6 for ETM, 13,8 for SM; In China, Chang et al.[18] reported resistance ratios of 11.7% for INH, 2.8% for RIF, 2.5% for ETM, 11.1% for STM; in Korea Lee et al.[14] found total resistance ratios of 15.5% for INH, 9.3% for RIF, 6.7% for ETM, 5.4% for STM in old and new cases. Previously in Erzurum, Aktaş et al.[19] found resistance ratios of 16.7% for INH, 10% for RIF, 11.7% for STM, 8.3% for EMB against primary anti-TB drugs in their study which investigated the profile of resistance to drugs in two different ways using the by MGIT method. In our study, the average resistance ratios for five years in isolated strains were determined as 11.9% for INH, 4.1% for RIF, 11.7% for STM and 3.6% for EMB. MDR-TB rate was found to be 3.6%. In our study, the highest resistance among major anti-TB drugs was determined for INH, the second highest resistance was found for SM, and the lowest resistance rate was found for EMB antibiotics. The results we obtain are compatible with the Turkish data. According to the previous study of Aktaş et al.[19] there has been a decrease in resistance ratios against other antibiotics, excluding resistance to STM.

In many studies conducted around the world outside Turkey, it also was observed that the most common resistance in *M. tuberculosis* complex strain was against INH. Such high resistance to INH and STM is due to the widespread use of this drug in prophylaxis and treatment. It is also assessed that the widespread use of streptomycin for non-TB reasons may be one of the reasons for the high resistance ratio against this drug.[15] We see some differences in the results of the studies carried out in Turkey and in different parts of the world. We think these differences stem from the characteristics of the patient population, their adaptation to treatment and regional differences. However, although there is no homogeneous distribution of resistance ratios between countries or in different parts of the same country, we can say that we are facing a serious resistance problem for tuberculosis.

In the "Tuberculosis War in Turkey 2018 Report ", the MDR TB rate was reported as 3.3-5.4% in 2009-2016.[16] In the studies on MDR tuberculosis worldwide, quite different MDR-*Mycobacterium tuberculosis* complex strain resistance ratios have been reported. In Japan Hattori et al.[20] reported a very low ratio of 0.2% in their study; in Indonesia, Lisdawati et al.[21] reported MDR- *M. tuberculosis* complex strain rate as 5.4%, in their study; in Ethiopia, Solomon et al.[22] reported a MDR rate of 2.27% in society, while the MDR rate for inmates living in prison was 15.89%; in China, He et al.[15] reported a MDR- *M. tuberculosis* complex strain ratio of 6.2%. In a well-attended study; while in Pakistan Akhtar et al.[23] reported a quite high resistance ratio of 69% in their study.

In our study, the resistance against MDR- *M. tuberculosis* complex strain was 3.6%, and our results were within the Turkish average. However, an increase in MDR drug resistance rates was observed in Erzurum compared to the results of the previous study by Ozmen et al.[24] MDR-TB cases in TB treatment prolong the duration of treatment and reduce the success of treatment. Therefore, the detection of MDR-TB cases in a short time and treating them with appropriate drugs will contribute to the control of TB disease by breaking the chain of transmission. The development of resistance to RIF alone in patients is rarely seen.[6] In our study, RIF resistance alone was detected in only one patient (0.2%) over a five-year period. In addition, resistance to all major anti-TB drugs was observed in 6 strains.

There were some limitations to this study. The laboratory we first studied started to serve in 2014 and the study was done on clinical samples sent from hospitals in different cities. For this reason, limited data about patients was reached. Since the patient's past data could not be reached, no assessment could be made about whether the cases were new or old and the where the location of the disease involvement was.

CONCLUSION

In our study the data presented do not seem to suggest that is any increase or decrease in drug resistance over time. In our study, resistance to major anti-TB drugs was determined for INH, which was the highest drug resistance in the strains investigated. The lowest drug resistance was detected for EM. The results are compatible with previous studies in Turkey. We believe that it would be useful to take into account these resistance ratios against anti-TB drugs when planning the treatment of Tuberculosis in patients in our region.

ETHICAL DECLARATIONS

Ethic Committee Approval: This research was approved by the "Atatürk University Faculty of Medicine Ethics Board of Clinical Research of " by decree no. 19 on 13.02.2019.

Informed Consent: Informed Consent not needed

Referee Evaluation Process: Externally peer-reviewed

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

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

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Orjinal Araştırma / Original Article

Percutaneous Transhepatic Cholangiography, Percutaneous Biliary Drainage and Metallic Endoprotesis Applications in Malign Biliary Obstructions

İnoperabl Malign Biliyer Obstrüksiyonlarda Perkütan Transhepatik Kolanjiyografi, Perkütan Biliyer Drenaj ve Metalik Endoprotez Uygulamaları

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Abstract

Objective: We aimed to present the effectiveness of percutaneous transhepatic cholangiography, percutaneous biliary drainage and metallic endoprotesis applications in patients with inoperable biliary obstructions.

Material and Method: Percutaneous transhepatic cholangiographies (PTC) and percutaneous biliary drainages (PBD) were performed in 44 patients with inoperable malignant obstructive jaundice who had been hospitalized in the radiology department of our hospital over a three years period. Six patients (13.6%) underwent external biliary drainage(EBD), 27 patients (61.4%) underwent internal-external biliary drainage(I-EBD) and metallic stents were placed in 11 patients (25%) on average 6 days (1-34 days) after I-EBD. The mean total bilirubin(TB), ALP, ALT, AST, GGT values taken before and after drainage in all patients were compared.

Results: Biliary drainage was technically successful in all patients. In the first two weeks after biliary drainage, 38 cases (86%) had a general condition improvement, weakness and itching decreased. The mean TB;19.41±9.09; 9.39±15.34, ALP; 701.27±352.53; 357.48±268.70, ALT; 122.45±75.42; 62.91±61.90, AST; 129.14±84.31; 94.93±118.79, GGT; 684.48±428.83; 322.39±253.26 values taken before and after drainage in all patients were compared and a significant decrease was found in the post-procedure values ($p<0.050$). In the follow-up, minor complications were observed in 10 patients (22.7%).

Conclusion: It is necessary to prevent inoperable patients from entering hepato-renal failure in order to prolong life time as much as possible. PBD and stent applications significantly improves impaired liver function, allowing the patients general condition improvement. Low complication rates and quickly improving general condition of patients without need for another surgery gradually increase the value of this radiological intervention.

Keywords: Endoprotesis, malign obstruction, percutaneous biliary drainage

Öz

Amaç: İnoperabl malign bilier obstrüksiyonlu hastalarda, perkütan transhepatik kolanjiyografi (PTK) sonrasında uygulanan perkütan bilier drenaj (PBD) ve metalik endoprotez uygulamalarının etkinliğini sunmayı amaçladık.

Gereç ve Yöntem: Girişimsel radyoloji ünitemize 3 yıllık süre içerisinde refere edilen, malign tıkanma sarılığı olan inopere 44 hastaya, PTK sonrası PBD uygulandı. Altı olguya (%13,6) sadece eksternal bilier drenaj (EBD), 27 olguya (%61,4) sadece internal-eksternal bilier drenaj (İEBD), 11 olguya (%25) ise ortalama 6 gün (1-34 gün) sonra İEBD sonrası metalik stent uygulandı. Drenaj öncesi ve sonrası alınan ortalama total bilirubin (TB), ALP, ALT, AST, GGT değerleri karşılaştırıldı.

Bulgular: Hastaların tümünde safra drenajı sağlanarak işlem başarıyla sonlandırıldı. PBD sonrası ilk 2 haftada 38 olgunun (%86) genel durumunda iyileşme, halsizlik ve kaşıntı gibi şikayetlerde azalma saptandı. Tüm hastalarda drenaj öncesi ve sonrası ortalama total bilirubin (TB); 19,41±9,09; 9,39±15,34, ALP; 701,27±352,53; 357,48±268,70, ALT; 122,45±75,42; 62,91±61,90, AST; 129,14±84,31; 94,93±118,79, GGT; 684,48±428,83; 322,39±253,26 olarak hesaplandı ve işlem sonrası değerlerde anlamlı düşüş saptandı ($p<0,050$). Takipte toplam 10 hastada (%22,7) minör komplikasyonlar izlendi.

Sonuç: İnoperabl malign tıkanma sarılıklı hastalarda yaşamı mümkün olduğunca uzatabilmek için hastanın hepato-renal yetmezliğe girmesini önlemek gereklidir. Perkütan biliyer drenaj ve biliyer endoprotez uygulamaları, bozulmuş olan hepatik fonksiyonları büyük ölçüde düzelterek hastanın genel durumunun iyileşmesine olanak sağlamaktadır. Bir başka cerrahi müdahale gerekmeden hızlı bir şekilde hastanın genel durumunu iyileştirmesi ve düşük komplikasyon oranları bu radyolojik girişimin değerini giderek artırmaktadır.

Anahtar Kelimeler: Malign obstrüksiyon, perkütan biliyer drenaj, stent

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INTRODUCTION

Obstructive jaundice develops as a result of obstruction of the bile ducts by stones, benign strictures or tumours. The morbidity and mortality of obstructive jaundice is quite high. Stone is the most common cause in adults and the second most common cause is malignancy. Definitive treatment of malignant obstruction is surgery. However, approximately 90% of patients admitted to the hospital with malignant obstruction are inoperable.[1] In this case, the aim is to minimize the symptoms by ensuring the passage of bile into the duodenum. Percutaneous biliary drainage (PBD) applied by Molnar and Stockum[2] in the palliative treatment of obstructive jaundice in 1974 was followed by biliary endoprosthesis implantation by Burchardt and Pereiras et al.[3] percutaneous transhepatic intervention in 1978. With today's technological developments, PBD has gained a solid place in the diagnosis and palliative treatment of obstructive jaundice.

Today, this radiological diagnostic and therapeutic approach, which uses ultrasound (US) and fluoroscopy, has been compared with surgical series, and the preference of percutaneous intervention has increased in the face of high morbidity and mortality rates of surgical treatment. Percutaneous transhepatic biliary drainage has been widely accepted for palliative treatment in patients with advanced stage malignant obstruction jaundice who have lost the chance of operation.[4-8] Due to the long-term complications of PBD and the discomfort that patients feel owing to carrying catheters continuously, endoprostheses of various shapes and sizes, previously made of plastic, have been used in order to provide bile drainage. Because of the complications of plastic endoprostheses such as high occlusion rates and migration, metal endoprostheses that can create larger lumen when released, have been used in recent years. The purpose of all these methods is to reduce jaundice and drain bile into the intestine.

In our study, the efficacy of PBD and metallic endoprosthesis implantation in inoperable malignant biliary obstruction, short and long term follow-up results, the life span of patients and their contribution to quality of life were evaluated.

MATERIAL AND METHOD

PBD was performed after percutaneous transhepatic cholangiography (PTC) in 44 inoperable patients with malignant obstructive jaundice who were referred to our interventional radiology unit over a period of 3 years. The ages of the patients to whom we applied PBD ranged between 37 and 80 (mean 63) and 29 were male (65.9%) and 15 were female (34.1%). The hilar observation grading of all patients was done according to the Bismuth typing. Accordingly, 4 of the patients were type I (9%), 4 were type II (9%), 11 were type IIIa (25%), 17 were type IIIb (39%), 8 were type IV (%). 18). 29 of the patients (65.9%) had previously been operated before due to their primaries.

Six cases (13.6%) underwent only external biliary drainage (EBD), 27 cases (61.4%) underwent only internal-external biliary drainage (IEBD), and 11 cases (25%) underwent metallic stent after IEBD. PTC and EBD were applied to one of the patients first from the left, and in the next session, IEBD was applied from the right. IABD catheters were placed in both right and left intrahepatic bile ducts in two patients. Biliary drainage was applied to all other patients (93.2%) by entering from the right. Spontaneously expandable metallic stent was placed in 11 (25%) of the patients underwent IEBD, after 1-34 days (average 6 days). The distribution of the diagnoses of the patients according to the procedure is summarized in **Table 1**.

Table 1. Distribution of patients according to the diagnosis and the procedure

DIAGNOSIS	EBD	IEBD	IEBD	TOTAL
		Stent (-)	Stent (+)	Number of patients
Biliary system malignancy	2	11	3	16 (36.4%)
Periampullary tumor	-	6	1	7 (15.9%)
Metastasis	4	9	7	20 (45.5%)
Primary liver cancer	-	1	-	1 (2.3%)
TOTAL (Number of patients)	6	27	11	44 (100%)

EBD: External Biliary Drainage, IEBD Internal-External Biliary Drainage

Techniques

Written consent was obtained from all patients before the procedure. Before PBD, it was paid attention that the platelet count of all patients was at least 70,000/mm3 and the INR value was below 1.4. Antibiotic prophylaxis (IV ceftriaxone, 1 g) and IV sedation (IV midazolam, 2.5 mg and IV fentanyl, 0.1 mg) were administered to all patients 30 minutes before the procedure.

All patients were treated with US (GE Logic 200 Pro Series) and fluoroscopy (Axiom, Siemens Iconos R 200). After the patients were placed in the supine position, skin cleansing was performed with a baticon. Right side was closed in a sterile manner, keeping the 8-11 intercostal spaces level open. The appropriate intervention location and angle were determined by US, considering the mid axillary line. Local anaesthesia was applied at the site of the intervention with lidocaine. A small incision of approximately 0.5 cm was opened on the skin, and the skin-subcutaneous tissues were gently dissected with a clamp. With real-time US, the patient was kept holding breath, and the dilated intrahepatic bile ducts were entered with a 21G Chiba needle. It was confirmed that the needle was in the bile duct with bile aspiration from the needle. The bile ducts were visualized with fluoroscopy by administering contrast material diluted in half with physiological saline through the connecting piece 'Connecting tube'. PTC procedure was performed by taking cholangiographies of the dilated bile ducts, which were visualized to the level of obstruction.

A 0.018'' nitinol tipped guide wire was advanced into the biliary tract through the needle. The access set (Accustick II Introducer System; Boston Scientific) which was advanced over

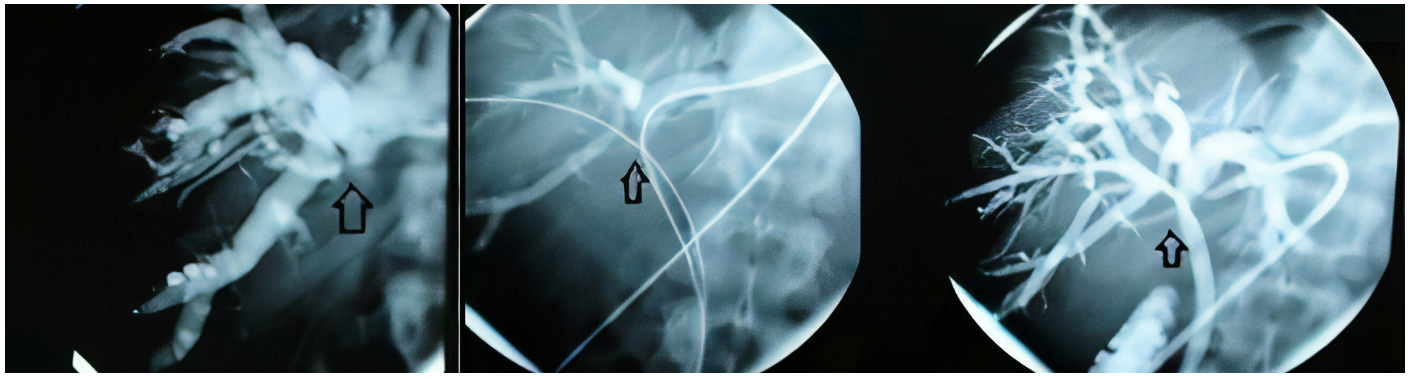

Figure 1. A 37-year-old male patient with Klatskin tumor has a stenosis in the bifurcation in the percutaneous cholangiography image. Bilateral extrenal biliary drainage and internal-external biliary drainage were applied.

the guidewire, was placed in the biliary tract. It was attempted to pass to the distal of the narrow segment with 0.035'' hydrophilic guide wire (Terumo; Terumo Corporation). After the stenosis was passed, the hydrophilic wire was replaced with a 0.035'' rigid guide wire (Amplatz Super Stiff, Boston Scientific). Afterwards, 10 F external-internal drainage catheter (Flexima, Boston Scientific) was placed (**Figure 1**).

In patients in whom stents were planned, a 0.035'' rigid body guide wire was advanced through the external-internal biliary drainage catheter up to the duodenum and the catheter was retrieved. The stent lumen was washed with saline solution by using a syringe. The prepared stent was advanced over the guide wire. It was brought to the appropriate location by using two radiopaque markers indicating the proximal and distal ends on the catheter. Contrast material was given from the 'introducer sheath' and the position was confirmed. The stent was placed by using the trigger mechanism. The carrier was withdrawn at a constant speed and the stent was released in a controlled manner. The used stents were placed on a 7-10F carrier catheter, 10 cm long and their fully opened diameters were 10 mm. A 10 cmx10 mm self-expandable Luminexx wallstent (Bard; Angiomed, Karlsruhe, Germany) was used in all patients. After the stent was opened successfully, an internal-external drainage catheter was placed in the biliary tract to be kept for 1 or 2 days. One day after the procedure, contrast material was administered through the drainage catheter, and stent position, expansion and drainage were observed. The catheter was removed after 2-10 days following the control of the passage.

Monthly checkups of the patients were planned. All radiological findings, biochemistry values, interventional radiological technique, complications of the patients, clinical and laboratory course before and after the procedure were recorded in the observation form prepared previously. Patients' most recent total bilirubin (TB), alkaline phosphatase (ALP), alanine amino transferase (ALT), aspartate amino transferase (AST), gamma glutamyl transferase (GGT) values before drainage, in the first week after drainage and in the late period after drainage were recorded. The patients were divided into two groups as those who underwent only EBD and those who underwent IEBD +/- stent. Primary patency time was defined as the time from the implantation of the stent to the reappearance of obstruction symptoms. If the patient died due to occlusion symptoms, patency time was matched with the patient's life span.

Pre-procedure, post-procedure early and late blood values were compared according to the significance test of the difference between the two pairs (Paired Samples T-Test). Total patient survival and stent patency time were calculated according to the Kaplan-Meier method. Statistical power analysis (power analysis) with the possibility of rejecting the false null hypothesis was used to determine the sample size in the study.

RESULTS

The procedure was successfully completed by providing biliary drainage in all 44 patients who underwent biliary drainage (technical success 100%). The patients were followed for the shortest 2 days and the longest 670 days (median 23 days). In the first 2 weeks after PBD, improvement in the general condition and a decrease in complaints such as weakness and itching of 38 patients (86%) were found.

In 6 patients (13.6%) whose distal stenosis could not be passed in the first session, because their relatives did not want a second procedure, the catheter was left to external drainage only and it was followed. External and internal drainage was performed in the same session in 30 (80%) of 38 patients who underwent IEBD. In 8 of the patients (20%), since the distal of the stenosis could not be passed, an 8 F external drainage catheter was placed first, it was waited for the duration varying between 4-55 days to resolve the edema in the stenosis localization. After the regression of the edema, internal drainage was started.

The catheters of two of the patients in our follow-up; were replaced on day 124 of one patient, the other on day 259 of another, with a new one. The catheters of two patients were dislocated within the first day after the procedure and were corrected with a guide wire.

Stents were implanted in the right lobe using the right transhepatic approach in all patients and in all patients without periampullary tumor, the distal end of the stents was left at the

suprapapillary level in order to minimize the risk of possible ascending cholangitis (**Figures 2a, 2b**).[9] In one patient with a periampullary tumor in which the stent was placed, the stent was left before the papillae when the stenosis could not be overcome. Balloon dilatation was performed in 2 patients, one of which was a periampullary tumor, because the stent width did not reach a sufficient diameter (diameter <8 mm). ERCP-guided stent was placed in 3 patients with IEBD at an external center.

Complications were observed in 10 patients (22.7%) during follow-up. Fever was observed in 6 patients (13.7%) the day after the procedure in the early period and resolved within 24 hours following antibiotic treatment. It was observed that the liver enzymes of the patients did not increase compared to the pre-procedure values and the image was not interpreted as cholangitis. Abscess occurred within the first week after the procedure in 2 patients (4.5%) who also had an operation history, and it was recorded as a procedure complication. None

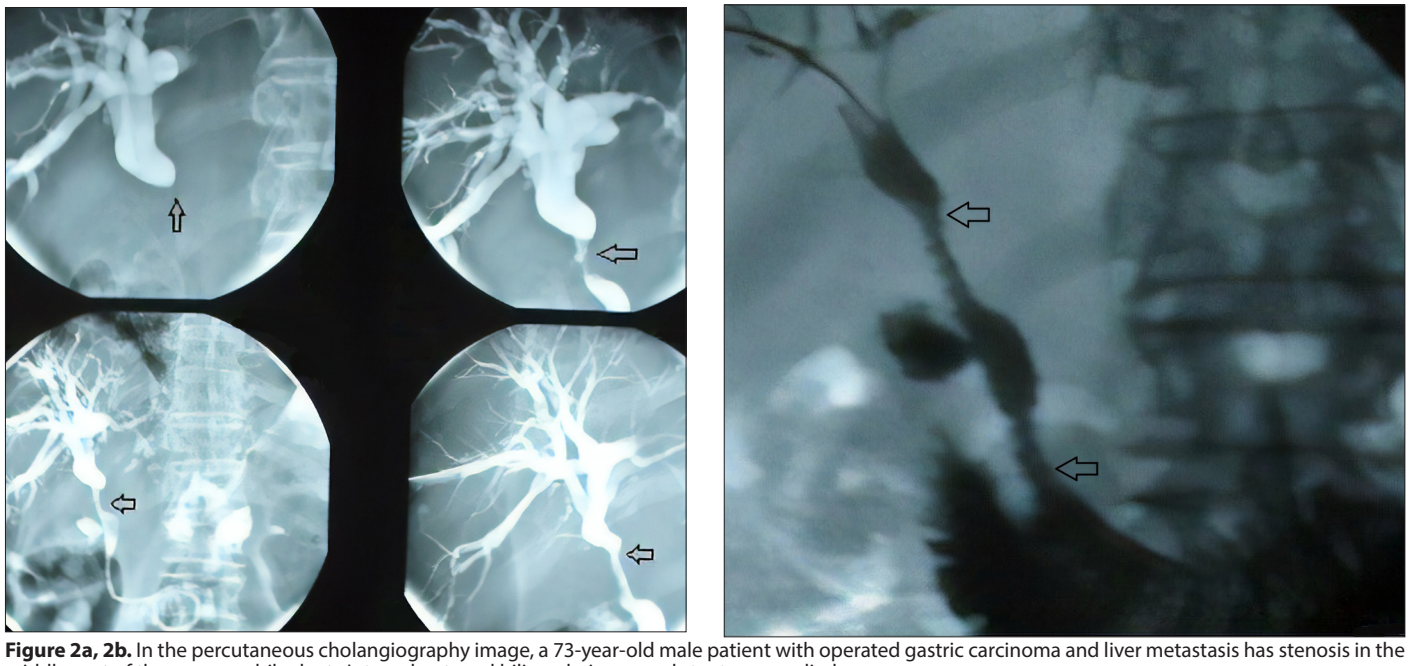

Figure 2a, 2b. In the percutaneous cholangiography image, a 73-year-old male patient with operated gastric carcinoma and liver metastasis has stenosis in the middle part of the common bile duct. Internal-external biliary drainage and stent was applied.

Table 2. Paired Samples T-Test analysis results before and late period after the procedure in patients with drainage

Parameter (Before and after the procedure)	Average	Standard deviation	95% Confidence Interval Lower limit	95% Confidence Interval Upper limit	t-value	Degree of Freedom	Significance Level
TB	10.02	13.04	6.06	13.99	5.09	43	0.000
ALT	59.54	75.26	36.66	82.42	5.24	43	0.000
AST	34.20	103.45	2.75	65.65	2.19	43	0.034
ALP	343.79	270.32	261.61	425.98	8.43	43	0.000
GGT	362.09	363.57	251.55	472.62	6.60	43	0.000

TB: Total bilirubin, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, ALP: alkaline phosphatase, GGT: gamma-glutamyl transferase

Table 3. Paired Samples T-Test analysis results before and early/late period after the procedure in patients with external biliary drainage

Parameter (Before and after the procedure)	Average	Standard deviation	95% Confidence Interval Lower limit	95% Confidence Interval Upper limit	t-value	Degree of Freedom	Significance Level
Early phase TB	7.91	6.36	5.65	10.16	7.14	32	0.000
Late phase TB	9.23	14.59	4.05	14.40	3.63	32	0.001

TB: Total bilirubin

Table 4. Paired Samples T-Test analysis results before and early/late period after the procedure in patients with stent

Parameter (Before and after the procedure)	Average	Standard deviation	95% Confidence Interval Lower limit	95% Confidence Interval Upper limit	t-value	Degree of Freedom	Significance Level
Early phase TB	9.93	6.63	5.47	14.38	4.96	10	0.001
Late phase TB	12.40	6.44	8.07	16.73	6.37	10	0.000

TB: Total bilirubin

of the patients had hematoma, major bleeding, hematobilia, hepatic arteriovenous fistula, hemothorax, sepsis, peritonitis after bile leakage, contrast allergy, or procedural death, which were reported as complications of PBD procedure in the literature. In the long term, obstruction developed in the stent of 2 patients (18.2%). While external drainage was provided again in one of the patients, the other died due to the deterioration of his general condition.

The mean TB, ALP, ALT, AST, GGT values obtained before and after drainage in all patients were compared with the significance test of the difference between the two partners, and a significant decrease was found in the post-procedure values (Paired Samples T Test, p<0.050) (**Table 2**). While no significant TB decrease was detected in the first week in patients who were applied only EBD, the decrease in TB detected in the late period was significant (p=0.006) (**Table 3**). In patients who underwent IEBD +/- stent, a significant decrease in TB was found both in the early (p=0.000) and late periods (p=0.005) (**Table 4**).

During the follow-up, 35 (79.5%) of the patients died due to terminal malignant diseases. Seven patients (15.9%) are still living with their catheters or stents, and 2 patients (4.5%) are out of follow-up. Average lifetimes according to the type of performed transaction were found to be 218 (SE, 52) days in cases with EBD, 192 (SE, 41) days in cases with IEBD alone, and 182 (SE, 103) days in cases with stent implantation. When compared according to the Log-Rang test, no significant difference was found between the groups (p>0.05).

According to the statistical power analysis, 44 observations, 0.05 significance level and Cohen d value as 0.7, test strength for two identical duplex tests was calculated as 0.90008.

DISCUSSION

The prognosis of patients with malignant biliary obstruction is generally poor. The majority of patients with pancreatic cancer, which is the most common cause of malignant obstructive jaundice, are inoperable when diagnosed.[1] Resectability rate in patients with cholangiocarcinoma varies between 10-20% depending on the location of the carcinoma. Therefore, palliative treatment is an appropriate and necessary form of treatment in the majority of patients.[10,11] In appropriate palliative treatment, morbidity and mortality should be low and complications should be less. In the surgical palliative treatment of pancreatic carcinoma, the mortality rate was found to be 15-25%, and the operative morbidity rate as 30%.[12] These rates are far from expected results for successful surgical palliative treatment. The results are related to the natural history of the underlying disease as well as the intraoperative morbidity and mortality. When the causes of mortality and morbidity in these patients are evaluated; It has been reported that carcinomatosis is the main factor and surgical by-pass mortality is close to zero in the absence of metastases and/or infiltrations of the primary disease.[13]

With the rapidly developing PBD applications, a more selective approach has been taken for bilioenteric by-pass, as a result, the operative mortality has decreased to 0-6%. For these reasons, surgical by-pass applications can be recommended in patients with low risk in the palliative treatment of patients with malignant biliary obstruction such as pancreatic carcinoma.[14] PBD is a useful and effective palliative treatment option in patients considered inoperable.[8] However, the effect of routine preoperative decompression on decreasing morbidity and mortality in cases dependent on different etiologies, or who have not lost the chance of operability or benign and uncomplicated, is controversial.[9,14] Various studies have been conducted to evaluate the morbidity and mortality of surgical decompression of the biliary system due to malignant obstruction. Feduska et al.[15] reported the curative and palliative operative mortality of pancreatic adenocarcinoma as 44% and 33%, respectively. They also stated that when serum bilirubin level is between 10 and 30 mg/dL, renal failure occurs in 8% of the patients, hemorrhage in 15%, and operative mortality in 17%. Allison et al.[16] reported the frequency of postoperative renal failure as 17% and operative mortality as 25% in patients with obstructive jaundice, and showed that glomerular filtration rates decreased in patients with jaundice. Dixon et al.[17] reported that serum bilirubin level being 6 mg/dL and alkaline phosphatase level being 600 IU/L increased the risk of operative morbidity and mortality. Nakayama et al.[18] found in a study of 105 patients that operative mortality as 6% in patients with PBD and 28% in patients without it. The mortality rate in cases with pancreaticoduodenectomy with serum bilirubin levels more than 20 mg/dL was found to be 2 times higher than in cases with less jaundice.[19,20]

Since PBD is more prolonged in malignant cases, occlusion, migration of the catheter and other mentioned complications related to the catheter are more common. In addition, since the average age of the patients in the malignant group is generally higher, complications are more common when the general condition is added to this.[13,21] On the other hand, as the immune system of malignant patients is suppressed due to the underlying pathology or the used antineoplastics, the tendency to infections has increased. In various series, major complications (cholangitis, sepsis, pleural effusion, biliary peritonitis, major hemorrhage) have been reported between 4.6% and 25% and procedural death rates between 0% and 5.6% for PBD.[22,23] The most common complication in patients undergoing PBD is reported as cholangitis.[24]

In our study, hematoma, major bleeding, hematobilia, hepatic arteriovenous fistula, hemothorax, sepsis, post-bile leakage peritonitis, contrast allergy, and procedural death did not occur in none of the patients who underwent PTC with a 21G Chiba needle, then to whom it was placed a 10 Fr PBD catheter and for whom it was switched to biliary endoprosthesis. It is also very pleasing that cholangitis, which was reported as the most common complication in long-term biliary drainage patients in the literature, was not observed in any of our patients. In accordance with the literature, we also think that leaving the

distal end of the stent in the suprapapillary region in order to protect the papilla may be quite effective in reducing the possibility of cholangitis, especially in patients with stent implantation.[25] We attribute the fact that we did not encounter early and late complications related to the procedure, which are quite common in the literature, in any of our patients, to the fact that we use a thin (21G Chiba) needle for PTC, after it, that we use a single puncture technique in the drainage phase. On the other hand, we think that close control of patients during PBD plays an important role in minimizing complications such as catheter migration and occlusion.

The complications we observed in a total of 10 patients during follow-up are well below the rates reported in the literature. Cholangitis, which is accepted as a condition that increases mortality considerably in the literature and which has been reported with rates varying between 3.4% and 4.8%, is one of the most troublesome complications of the procedure and its treatment is difficult under these conditions. Cholangitis table was not observed in the patients in our study. High fever was evaluated depending on the acute stress response secondary to the procedure. Although the high success rates of biliary drainage performed by endoscopic way are known, the necessity of passing the papillae during the procedure increases the possibility of cholangitis.[26] One of the important advantages of the percutaneous approach is the preservation of the papilla by US-guided access to the desired bile duct. The rate of patients with abscess (4.5%) is similar to the literature.[23,24,27]

Due to the late complications of PBD and the psychological trauma and physical difficulties caused by continuous catheter carrying, it has revealed the necessity to use permanent catheter parts that are long enough to include only the obstruction level, for the purpose of providing drainage and that are not related to the outside of the body. With the advancing technology, we applied these permanent stents, which are made of plastic and metallic material and called endoprosthesis, to our 11 patients that we applied PBD as long as the clinical condition and social conditions of our patients allow. Our patients are still under follow-up and express their satisfaction with the endoprostheses due to the comfort of being free from the physical and mental discomfort of their catheters.

In our study, there was no difference in life expectancy between patient groups underwent EBD, IEBD, and stent according to the procedure. However, we think that the validity of this result will only be possible with extended studies with a large number of patients.

It has been reported in many studies in the literature that PBD generally decreases the level of TB and does not change other liver enzymes.[5,7,28] In our study, a significant decrease in TB, ALT, AST, ALP, GGT was found after drainage. In addition, the results we found in our study showed that; while only late period TB decrease is significant in patients who undergo EBD, significant TB decrease is found in both early and late periods in patients who undergo IEBD. We believe that this result emphasizes the value of IEBD application.

In the study conducted by Kozlov et al.[24]; PBD was applied on a group of patients guided with US, to the other group guided with fluoroscopy and it has been shown that US guidance significantly reduces the complication and mortality rate, enables 3 times reduction in taken radiation dose, and 2 times reduction in needle punctures. Obviously, the use of US during puncture in addition to scopic imaging, which is indispensable during manipulation of the wire and catheter, significantly reduces the complication and mortality rates.

CONCLUSION

In patients with inoperable malignant obstructive jaundice, it is necessary to prevent the patient from entering hepato-renal failure in order to prolong life as much as possible. Percutaneous biliary drainage and biliary endoprosthesis applications improve the general condition of the patient by substantially correcting impaired hepatic functions.[29] Considering the patient's primary, clinical condition, inoperability, previous operation history, its rapid improvement on the general condition of the patient without the need for another surgical intervention and its low complication rates gradually increase the value of this radiological intervention.

ETHICAL DECLARATIONS

Ethical Situation: It was produced from Gülşah Bayram Ilıkan's thesis titled "Percutaneous Transhepatic Cholangiography, Percutaneous Biliary Drainage and Metallic Endoprosthesis Applications in Inoperable Malign Biliary Obstructions". The defense was made in Ankara Numune Training and Research Hospital in 2007 under the consultancy of İlkay Akmangit, and the thesis was published in 2008.

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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

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

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Orjinal Araştırma / Original Article

Health Beliefs of Women Attending Mammography Unit and Related Factors

Mamografi Ünitesine Gelen Kadinlarin Sağlik İnançlari ve İlişkili Faktörler

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Abstract

Aim: This study was done to evaluate the perceptions of health beliefs and related factors of women attending a mammography unit for mammograms.

Material and Method: The descriptive study was performed with 181 women applying to the mammography unit of a university hospital in Konya, Turkey between 15 March and 20 June 2013. Data were collected with the "Individual Information Form" and "Health Belief Model Scale for Breast Cancer". The data were collected via face-to-face interviews and summarized as number, percentage, mean and standard deviation. To compare the data, independent sample t test, one-way ANOVA, Kruskal-Wallis test, and Mann-Whitney U test were used. In order to conduct the study, permission from the ethics committee, institutional permission and verbal permissions from the participants were obtained.

Results: The average age of the participants was 34.78±8.37. Of women, 68.5% were primary school graduates, and 64.6% were found out to perform breast self-examination (BSE). In the study, the mean scores of the Health Belief Model Scale for Breast Cancer sub-dimensions were compared with some characteristics of the participants (education level, using birth control pill, BSE practicing status, and presence of breast cancer in the family). According to, there was founded a statistically significant difference between women's education level (health motivation, BSE benefits and barriers), using birth control pills (sensitivity), BSE practicing status (health motivation, BSE barriers and self-efficacy, mammography benefits and barriers), and presence of breast cancer in their families (sensitivity, health motivation, BSE benefits) with the scale sub-dimensions ($p<0.05$).

Conclusion: According to these results, it may be suggested to increase awareness training in order to spread the screenings for early diagnosis of breast cancer, taking into account the individual characteristics of women.

Keywords: Breast cancer, mammography, perception of health belief, Health Belief Model

Öz

Amaç: Bu çalışma mamografi ünitesine mamografi çektirmek için gelen kadınların sağlık inanç algılarını ve ilişkili faktörleri değerlendirmek amacıyla yapıldı.

Gereç ve Yöntem: Tanımlayıcı tipteki bu çalışma, 15 Mart-20 Haziran 2013 tarihleri arasında Konya'da bir üniversite hastanesinin mamografi ünitesine başvuran 181 kadın ile gerçekleştirildi. Veriler, "Birey bilgi Formu" ve "Meme Kanseri Sağlık İnanç Modeli Ölçeği" kullanılarak toplandı. Veriler yüz yüze görüşmelerle toplandı ve sayı, yüzde, ortalama ve standart sapma olarak özetlendi. Verileri karşılaştırmak için t, F, Mann Whitney U ve Kruskal Wallis testleri kullanıldı. Çalışmanın yapılabilmesi için etik kurul izni, kurum izni ve katılımcılardan sözel izinleri alındı.

Bulgular: Katılımcıların yaş ortalaması 34,78±8,37 idi. Kadınların % 68,5'i ilkokul mezunuydu ve % 64,6'sının kendi kendine meme muayenesi (KKMM) yaptığı belirlendi. Çalışmada katılımcıların bazı özelliklerine (eğitim düzeyi, doğum kontrol hapı kullanma, KKMM yapma durumu ve ailede meme kanseri varlığı) ile Meme Kanseri Sağlık İnanç Modeli Ölçeğinin alt boyutlarının puan ortalamaları karşılaştırıldı. Buna göre kadınların eğitim düzeyi (sağlık motivasyonu, Kendi Kendine Meme Muayenesi (KKMM) yararları ve engelleri), doğum kontrol hapı kullanma durumları (duyarlılık), KKMM uygulama durumları (sağlık motivasyonu, KKMM engelleri ve öz-yeterlik, mamografi yararları ve engelleri) ve ailelerinde meme kanseri varlığı (duyarlılık, sağlık motivasyonu, KKMM faydaları) ile ölçek alt boyutları arasında istatistiksel olarak anlamlı fark bulundu ($p<0.05$).

Sonuç: Bu sonuçlara göre, kadınların bireysel özellikleri dikkate alınarak meme kanserini erken tanılamaya yönelik taramaların yaygınlaştırılması için bilinçlendirme eğitiminin artırılması önerilebilir.

Anahtar Kelimeler: Meme kanseri, mamografi, sağlık inanç algısı, Sağlık İnanç Modeli

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INTRODUCTION

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death among females worldwide, with an estimated 1.7 million cases and 521.900 deaths in 2012.[1] The American Cancer Society (ACS) reported that 266,120 women will be diagnosed with breast cancer in 2018 and approximately 40,920 women will lose their lives due to breast cancer.[2] In a study evaluating of 195 countries, age-standardized incidence rate of breast cancer has been identified as 45.6/100,000 and the age-standardized death rate was 14.6/100000.[3] According to GLOBOCAN 2018 data of the International Cancer Research Agency, it is estimated that in both sexes in worldwide breast cancer will be ranked second (11.6%, 2,089 million) in the newly diagnosed cancer cases and fifth (6.6%, 27.000) in cancer-related deaths.[4] In the data from Turkey Cancer Statistics for the year 2015 breast cancer takes first place (43.8 per hundred thousand) in the standardized prevalence calculation according to age.[5] According to Turkish Statistical Institute 2017 statistics, deaths due to breast cancer constitute 2.12% (N = 4043) among all cause-related deaths (N= 190.657) and breast cancer is the first among well-and-malignant tumor-related deaths.[6]

In the community, breast cancer awareness and screening programs are of great importance since breast cancer is the most common cancer type in women, and also due to its increasing frequency[7] and due to the fact that it is one of those cancers that can be early detected through screening. Breast cancer typically produces no symptoms when the tumor is small and most easily treated, which is why screening is important for early detection.[2] The most effective way to extend life and reduce the mortality rate in breast cancer is early diagnosis. Breast Self-Examination (BSE), Clinical Breast Examination (CBE) and mammography are the methods used in the early diagnosis of breast cancer. There are different opinions and practices about the application age of early diagnosis methods for breast cancer and which method to apply in each age group. While the ACS proposes mammography each year after the age of 40 years[8], the Canadian Cancer Society (CCS) notes that the risks and benefits of mammography for women aged between 40–49 years should be discussed and recommends a mammogram every two years for women aged between 50–69 years.[9] In Turkey, the Ministry of Health's National Cancer Program proposes a mammogram every two years for women aged between 50–69 years.[10]

The frequency of application of early detection methods for breast cancer varies depending on many factors. These factors may be socio-demographic characteristics, culture, and variables associated with breast cancer and health beliefs.[11] The Health Belief Model (HBM) is a psychosocial model used to describe health behavior. The model was developed in the 1950s in order to explain the need of medical screening programs presented by the US Public Health Service. The primary four concepts in the HBM effecting on preventive health behaviors are (1) perceived susceptibility (perceived vulnerability to a disease or the risks of contracting it), (2) seriousness (perceived severity of the consequences of contracting a disease), (3) benefits (positive results of steps taken to avoid contracting the condition), and (4) barriers (perceived negative aspects of undertaking health behaviors). In 1988, Becker and Rosentock added the concept of health motivation (a general concern for maintaining health) and self-efficacy (the confidence in one's ability to take action) to the model.[12,13]

Although breast cancer is still one of the important public health problems today, it can be identified early with an early screening program. Determining the health beliefs of women in the high risk group for breast cancer can increase their participation in early screening programs.

MATERIAL AND METHOD

This study was conducted to determine the factors affecting the health beliefs of women admitted to the mammography unit. This descriptive study was carried out with women admitted to a mammography unit of a university hospital between 15 March and 20 June 2013 in Konya, Turkey. The population of the study is formed by women admitted to the mammography unit of the radiology department of a university hospital to have a mammogram. The analysis suggested for relational research was used to identify the determining factors used in the calculation of the sample size. The sample number was found as 173 by considering the number of independent variables (n=10), and by using the parameters of .05 significance value, 95% power and .15 effect size. A greater number of individuals have been reached by considering that data loss can be occur and the research was carried out with 181 participants. The women, who were graduated at least from elementary school, underwent mammography for the first time, were not diagnosed with breast cancer and agreed to participate in the study, and were included in the research sample.

A questionnaire and the Champion's Health Belief Model Scale (CHBMS) were used as the data collection instruments for this study. The questionnaire obtained information about the participant's socio-demographic characteristics, and other factors. Socio-demographic variables included age, education status, marital status, and having children. The other factors included menarche age, menstrual irregularity, using birth control pills, menopause status, BSE practicing status, presence of breast cancer in the family and friends. Champion's Health Belief Model Scale was developed in 1984 by Champion based on the HBM and revised in 1993, 1997 and 1999. The original scale consists of a total of 58 questions and eight subscales.[11,13-15] The beliefs of women regarding breast cancer, BSE and mammography are evaluated in the context of the HBM with this scale.[12] In this study, the Turkish version of the scale whose validity and reliability were performed by Gozum and Aydin[16] was used. The Turkish version of the Health Belief Model Scale is a five-point Likert-type scale and consists of six subscales and 52 items including perceived susceptibility (three items), perceived seriousness (six items), health motivation (five items), perceived self-efficacy of BSE (ten items), perceived benefits

of BSE (four items), perceived barriers to BSE (eight items), perceived benefits of mammography (five items) and perceived barriers to mammography (eleven items). Scoring is ranked from 'strongly disagree' 1 point, to 'strongly agree' 5 points. The rise of the points indicates that perceived susceptibility and/or perceived seriousness increased, benefits for the perceived benefits, barriers for the perceived barriers were perceived higher. In the same study, Cronbach's alpha coefficient of the subscales was found to be between .69 and .83.[16] The Cronbach alpha coefficient obtained in this study was .85 for perceived susceptibility, .87 for perceived seriousness, .93 for health motivation, .91 for perceived self-efficacy of BSE, .89 for perceived benefits of BSE, .83 for perceived barriers to BSE, perceived benefits of mammography .86 and .89 for perceived barriers to mammogr mammography.

SPSS package program was used in the analysis of the data. Data are summarised using the number, percentage, mean and standard deviation. Independent sample t test, one-way ANOVA, Kruskal-Wallis test, and Mann-Whitney U test were used for comparison of variables. p-value less than 0.05 was considered significant.

Ethical consideration

Before collection of study data, written permission from the related hospital and the hospital ethics committee (date/number: 2013/313) and verbal permission of the women participating in the study by explaining the purpose of the research were obtained.

RESULTS

The average age of the women in the study was 34.78±8.37 years, 68.5% of them graduated from primary school, 84.5% of them were married and 84.5% of them had children (**Table 1**). The average age of menarche of women was 13.30±1.44 years, it has been determined that 28.2% of them used birth control pills, 8.8% of them entered menopause, 64.6% of them performed BSE and breast cancer occurred in the families of 16.6% and in the friend's circle of 29.8% of participants (**Table 2**).

Table 1. Socio-demographics characteristics of participants (n=181)

	Mean±SD	min-max
Mean age (year)	34.78±8.37	19–59
	n	**%**
Education status		
Primary school	124	68.5
High school	25	13.8
University	32	17.7
Marital status		
Married	153	84.5
Other (single, widowed, divorced)	28	15.5
Having children		
Present	153	84.5
Absent	28	15.5

Some characteristics of the participants in the study (level of education, using birth control pill, BSE practicing status, and presence of breast cancer in their family) and the mean score of the Health Belief Model Scale for Breast Cancer were compared. A significant difference was determined between the level of education and subscales of health motivations, perceived self-efficacy of BSE, and perceived benefits of BSE. It was determined that there was a statistically significant difference between the use of birth control pills and the subscales of perceived susceptibility, with the susceptibility of women who were using birth control pills being higher than others. A statistically significant difference was determined between BSE practicing status and subscales of health motivations, perceived self-efficacy of BSE, perceived benefits of BSE, perceived barriers to BSE, perceived benefits of mammography, and perceived barriers to mammography. A statistically significant difference was determined between presence of breast cancer in their families and the mean scores of the subscales of perceived susceptibility, health motivations, and perceived benefits of BSE (p <.05) (**Table 3**).

Table 2. Health and other characteristics of women (n=181)

	Mean±SD	min-max
Mean menarche age (Year)	13.30±1.44	9–19
	n	**%**
Menstrual irregularity		
Yes	68	37.6
No	113	62.4
Birth control pills use		
Yes	51	28.2
No	130	71.8
Menopause status		
Yes	16	8.8
No	165	91.2
BSE practice		
Performs BSE	117	64.6
Does not perform BSE	64	35.4
Breast cancer in family		
Yes	30	16.6
No	151	83.4
Breast cancer in friends		
Yes	54	29.8
No	127	70.2

BSE=Breast Self-Examination

DISCUSSION

Breast cancer is the most common cancer among women in Turkey as well as all over the world. Delays in diagnosis and treatment reduce the survival rate. BSE and mammography applications of individuals are expressed as early diagnostic or screening behaviours. In this study, the health beliefs and related factors of the women admitted to the mammography unit of a university hospital in Konya city centre were evaluated.

Table 3. Comparison of some characteristics of women with the subscales scores of CHBMS (n=181).

	Perceived susceptibility	Perceived seriousness	Health motivation	Perceived benefits of BSE	Perceived barriers to BSE	Perceived self-efficacy of BSE	Perceived benefits of mammography	Perceived barriers to mammography
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
Education status								
Primary school[a]	7.56±2.93	18.12±5.91	17.44±6.15	13.39±4.44	21.24±6.51	31.00±8.23	16.81±5.13	28.79±8.68
High school[b]	8.52±2.77	17.92±6.93	18.96±6.13	15.44±4.23	22.60±7.84	33.28±7.35	17.44±4.07	29.84±11.86
University[c]	7.28±3.32	21.03±6.51	21.16±4.13	15.50±4.19	17.41±4.59	31.78±9.13	17.63±4.54	25.86±8.41
Test value	KW:3.462	F: 3.018	KW:11.972	KW:10.143	F: 5.742	KW:2.951	KW:.376	KW:2.576
p	.177	.051	.003	.006	.004	.229	.829	.276
Significant difference			a<c	a<b,c	c<a,b			
Birth control pills use								
Yes	8.41±2.98	19.00±6.67	19.16±5.69	14.16±4.25	20.57±6.93	32.09±8.41	17.19±4.92	29.71±9.61
No	7.34±2.95	18.45±6.07	17.98±6.09	14.00±4.54	20.82±6.47	31.20±8.24	16.02±4.69	27.92±8.97
Test value	U:2644.50	t:.529	U:2927.00	U:3335.00	t:-.233	U:3125.50	U:3386.00	U:2923.50
p	,033	,597	,218	,949	,816	,549	,822	,216
BSE practice								
Performs BSE	7.66±2.91	19.02±6.19	19.06±5.76	14.42±4.55	20.01±6.49	32.95±7.88	17.59±4.92	27.18±9.38
Does not perform BSE	7.63±3.15	17.86±6.29	16.94±6.19	13.36±4.23	22.11±6.60	28.72±8.34	16.02±4.69	30.69±8.35
Test value	U:3609.50	t:1.197	U: 2838.00	U:3103.50	t:-2.070	U:2491.50	U:3031.00	U:4689.50
p	.687	.233	.007	.055	.040	.000	.034	.005
Breast cancer in family								
Yes	8.87±3.41	20.03±6.68	19.97±5.85	14.65±4.83	21.90±7.57	31.20±8.57	18.33±4.89	26.40±10.77
No	7.40±2.85	18.32±6.12	17.98±5.98	13.79±4.28	20.52±6.38	31.50±8.25	16.78±4.86	28.82±8.79
Test value	U:1700.00	t:1.376	U:1748.50	U:1711.50	t:1.046	U:2294.00	U:1901.50	U:2685.00
p	.030	.171	.047	.033	.297	.912	.164	.108

t= Independent Sample T-Test, F= One-Way Analysis of Variance (ANOVA), KW= Kruskall Wallis Analysis, U= Mann Whitney U Analysis

Socio-demographic and health characteristics may affect the attitudes of individuals directly and the behavior related to health indirectly. In the study, the health motivation scores of women who were university graduates, were higher than women who were primary school graduates; perceived barriers to BSE scores were lower than women who were both primary and high school graduates. However, perceived benefits of BSE scores of women who were primary school graduates, were lower than women who were both high school and university graduates (**Table 3**). It has been determined in a study conducted by Tastan et al.[17] that health motivation, perceived self-efficacy of BSE, and perceived benefits of BSE scores of women who were university graduates were higher and the perceived barriers to BSE score was lower. It has been determined in another study that there was a statistically significant difference between the educational status and the scores of subscales of benefits, self-efficacy and health motivation. [18] However, it has been determined in an another study that there was not a statistically significant difference between the educational status and the scores of CHBMS.[19] Level of education plays an important role in the prevention, and treatment of breast cancer.[20,21] In addition, the increase in the level of education contributes to the individuals to be more sensitive and aware about health-related issues. It can be said that women need health education in order to enable them to take responsibility for BSE and their bodies, especially to protect their health.

The mean score of perceived susceptibility in women using birth control pill was higher than the other groups, and the difference was significant (p<.05) (**Table 3**). Giving BSE training to women using birth control pill during counseling performed in terms of breast cancer risk for women using birth control pill in this group.

In the study, the mean scores of subscales of health motivation, perceived self-efficacy of BSE, and perceived benefits of mammography of women performing BSE were higher, the mean scores of subscales of the perceived barriers to BSE, and perceived barriers to mammography were lower (Table 3). In analogy with the findings of this study, it has been found in some studies that health motivation[18,19], and perceived self-efficacy of BSE [16-18,22] scores were higher; perceived barriers to BSE[16,17,22] were lower in women performing BSE. In different studies, a positive correlation was found between the performance status of BSE in the past year and subscales of perceived susceptibility[23], seriousness, health motivation, benefits to BSE [25], and self-efficacy[23,25]; a negative correlation was found between status of BSE in the past year and the barriers subscale.[23,25] In one study, CHBMS scores of women according to whether they apply BSE or not, the difference between the average sub-dimension scores of benefit, barriers, health motivation, and self-confidence was found statistically significant.[26] In contrast with this study, it was determined in some studies that the scores of perceived susceptibility[20] and perceived benefits of BSE[16-18,22] were higher in women

performing BSE. However, it has been determined in another study that there was not a statistically significant difference between BSE practicing status and the scores of CHBMS.[17]. In this study, while the difference between BSE practicing status and the subscales of health motivation, perceived self-efficacy of BSE, perceived barriers to BSE, perceived benefits of mammography, and perceived barriers to mammography are compatible with the structure of the Health Belief Model Scale, no difference between BSE performance status and the subscales of perceived susceptibility, perceived seriousness, and perceived benefits of BSE are incompatible with the structure of the scale. According to the theory of the scale, high points in perceived susceptibility, perceived seriousness, health motivation, perceived self-efficacy of BSE, perceived benefits of BSE, and perceived benefits of mammography; and low points in perceived barriers to BSE and perceived barriers to mammography are expected results for women performing BSE.

It has been determined in women with a family history of breast cancer that the mean scores of subscales of perceived susceptibility, health motivation, and perceived benefits of BSE were higher and that there was no relationship with the other subscales (Table 2). It has been determined in the studies conducted in Turkey that, the sores of perceived susceptibility, perceived self-efficacy of BSE and perceived benefits of BSE[17,18] and health motivation[18] were higher and perceived barriers to BSE [18] subscales scores were lower in women with a family history of breast cancer. In one study, the knowledge of breast cancer and awareness about the screening tests for women with a positive family history in terms of breast cancer was found to be higher.[27] Familial risk factor is an important factor for breast cancer. In addition, it is thought that the presence of cancer in the family is a situation that contributes to an increase in the susceptibility and motivation of awareness for early screening methods for breast cancer of individuals.

CONCLUSIONS

In line with the findings of this study, it has been determined that some characteristics of participants (educational status, using birth control pill, BSE practicing status, presence of breast cancer in their family) affected one or several subscales of the Health Belief Model Scale for Breast Cancer. Based on these results, enhancing breast cancer awareness and education for early detection methods, identification of risks for breast cancer and dissemination of screening programs can be recommended. Healthcare professionals can play a crucial role in this matter. Across all healthcare services, especially primary care health services, women could be trained on early detection by video, orally, or the use of leaflets which could suggest to the appropriate demographic that they regularly undergo medical screening for breast cancer. This training is likely to increase individuals' self-effectiveness, susceptibility, seriousness and motivation regarding their health. By raising awareness through planned training, barrier perceptions about early screening methods for breast cancer can be overcome.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was approved by Ethics Committee at Necmettin Erbakan University Meram Medical Faculty Non-Interventional Clinical Research Ethic Committee (date/number: 2013/313).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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

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Orjinal Araştırma / Original Article

Turkey Urticaria Diagnosis and Treatment Guide based; Distribution of Chronic Urticaria Patients Treated in Our Clinic According to Step Therapy

Türkiye Ürtiker Tanı ve Tedavi Kılavuzu Baz Alınarak Kliniğimizde Tedavi Edilen Kronik Ürtikerli Hastaların Basamak Tedavisine Göre Dağılımı

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Abstract

Aim: Chronic urticaria is a condition that requires long-term treatment. In recent years, many countries have created their own guides to evaluate urticaria diagnosis and treatment approaches in an algorithm. In this study, we aimed to evaluate the distribution of patients with chronic urticaria treated in our clinic according to the treatment algorithm the "Turkey Urticaria Diagnosis and Treatment Guide"

Material and Method: The files of the patients who applied to the dermatology clinic of our hospital and were followed up and treated with a diagnosis of chronic urticaria were investigated.

Results: A total of 102 patients with chronic urticaria were included in the study. According to this guide, 17.6% of patients responded with standard dose antihistamine therapy, while the antihistamine dose given in 15.7% of patients was increased. The antihistamine treatment of 5.7% of patients was replaced by a different group of antihistamines at the same dose as the previous one. 52% of patients responded to omalizumab 300 mg/subcutaneous treatment every 28 days. However, 7.8% of the patients received omalizumab treatment every 14 days or cyclosporine treatment was required to be added to omalizumab treatment. Response to other treatments other than standard treatments was received in 1% of patients.

Conclusion: We believe that our study will facilitate predicting the treatment responses of patients in clinical practice by shedding light on the distribution of chronic urticaria patients according to the treatment algorithm.

Keywords: Cyclosporine, omelizumab, treatment, urticaria

Öz

Amaç: Kronik ürtiker, uzun süreli tedavi gerektiren bir durumdur. Son yıllarda birçok ülke ürtiker tanı ve tedavi yaklaşımlarını bir algoritmada değerlendirmek için kendi kılavuzlarını oluşturmuştur. Bu çalışmada, kliniğimizde tedavi gören kronik ürtikerli hastaların "Türkiye Ürtiker Tanı ve Tedavi Rehberi" tedavi algoritmasına göre dağılımını değerlendirmeyi amaçladık.

Gereç ve Yöntem: Hastanemiz dermatoloji kliniğine başvuran ve kronik ürtiker tanısıyla takip ve tedavi edilen hastaların dosyaları incelendi.

Bulgular: Çalışmaya toplam 102 kronik ürtikerli hasta dahil edildi. Bu kılavuza göre hastaların% 17,6'sı standart doz antihistaminik tedavisine yanıt verirken, hastaların% 15,7'sinde verilen antihistaminik dozu artırıldı. Hastaların% 5.7'sinin antihistaminik tedavisi, önceki ile aynı dozda farklı bir antihistaminik grubu ile değiştirildi. Hastaların% 52'si 28 günde bir 300 mg/subkutan omalizumab tedavisine yanıt verdi. Ancak hastaların% 7,8'i 14 günde bir omalizumab tedavisi almış veya omalizumab tedavisine siklosporin tedavisi eklenmesi gerekmiştir. Standart tedaviler dışındaki diğer tedavilere yanıt hastaların% 1'inde alınmıştır.

Sonuç: Çalışmamızın, kronik ürtiker hastalarının tedavi algoritmasına göre dağılımına ışık tutarak klinik pratikte hastaların tedavi yanıtlarını tahmin etmeyi kolaylaştıracağına inanıyoruz.

Anahtar Kelimeler: Siklosporin, omalizumab, tedavi, ürtiker

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INTRODUCTION

Urticaria is a skin disease that is frequently seen in all communities, characterized by itchy and edematous plaques that appear suddenly and disappear spontaneously within 24 hours. The clinical picture lasting less than 6 weeks is defined as acute urticaria, and urticaria that occurs continuously or at intervals for at least 6 weeks is also defined as chronic urticaria.[1,2] The prevalence of chronic urticaria in the general population is between 0.5% and 5%. The most important cell in the pathogenesis of chronic urticaria is mast cells in the skin, and its dominant mediator is histamine.[2] In its treatment, agents that target these factors, which play a major role in pathogenesis, are used. "Turkey is the Urticaria Diagnosis and Treatment Guide" by management of chronic urticaria; it is based on avoiding trigger factors and symptomatic treatment. The gold standard of symptomatic first-line therapy; the second generation is the standard dose use of H1 antihistamines. If symptoms cannot be controlled within 1-2 weeks, in the second step, the current antihistamine dose is increased up to four times.[3] If it is still unresponsive, switch to another antihistamine at the last used dose or add leukotriene receptor antagonists. Biological agents are involved in tertiary therapy, now the only treatment approved for antihistamine-resistant chronic urticaria is omalizumab. If the response to 24-week omalizumab treatment cannot be obtained, the dose of omalizumab is increased or cyclosporine may be given instead. Or cyclosporine can be added to the current omelizumab treatment. Despite all these, if the symptoms cannot be controlled, other treatments (methotrexate, phototherapy, dapson IVIG, etc.) can be tried.[3-5]

Our aim in this study, "Turkey Urticaria Diagnosis and Treatment Guide" is based on; the evaluation of the distribution of patients with chronic urticaria treated in our clinic according to the step treatment in the guide.

MATERIAL AND METHOD

The study was approved by the Local Ethics Committee of Selcuk University Faculty of Medicine (approval number: 2020/192). The files of 102 patients who were admitted to the Department of Dermatology of Selçuk University, followed up and treated with the diagnosis of chronic urticaria without angioedema were scanned from the hospital registry system and evaluated retrospectively. Patients' age, gender, disease duration, etiological factors, comorbidities, urticaria severity, and response treatment steps were recorded. Data Frequency (n) and percentage (%) for categorical data, minimum, maximum, mean ± standard deviation and median descriptive statistics were made for continuous data. The Chi-Square test was used to test whether there is a relationship between the severity of the disease and gender. The chi-square test was evaluated at 5% significance level (95% confidence level).

RESULTS

A total of 102 patients with chronic urticaria, 33 male and 69 female, without angioedema, were included in the study. 67.6% of all patients were female and mean age was 43±16. 32.4% of the patients were male and mean age was 42±18. When the etiological factors of patients with chronic urticaria are evaluated; while 42.2% had stress factor alone, 36.3% were idiopathic and 21.5% were multifactorial (combination of drug use, emotional stress and other factors). Disease severities were evaluated in routine clinical practice, 24.5% of patients had mild, 50% moderate and 25.5% severe disease. The average disease duration was 64 months. The distribution of patients was evaluated according to the treatment steps in "Turkey Urticaria Diagnosis and Treatment Guide". According to this guide, 17.6% of patients responded with standard dose antihistamine therapy, while the antihistamine dose given in 15.7% of patients was increased. Antihistamine treatment of 5.7% of patients was switched by a different group of antihistamines at the same dose as before. 52% of patients responded to omalizumab 300 mg/subcutaneous treatment every 28 days. However, in 7.8% of patients, the use of omalizumab therapy every 14 days or additional cyclosporin treatment was required. 1% of all patients did not benefit from standard treatments, these patients responded to other treatments (IVIG, Dapson, Methotrexate). Short-course corticosteroid therapy was used in cases when the disease exacerbated.

DISCUSSION

In our study, it was found that more than half of the chronic urticaria patients who were followed and treated in our clinic according to "Turkey Urticaria Diagnosis and Treatment Guide" benefit from omalizumab treatment. We attribute this rate, which we found higher than previous literature, to being a tertiary health institution and to follow up resistant patient groups in our clinic.[6,7] The gender distribution of our patients was found 2 times more often in women than in men, similar to the literatüre.[6,8] The mean age and gender of our patients were similar to other literature data.[9] In our study, the average disease duration was observed longer than the literature. [10] According to the reference guideline, while the etiology of the majority of patients was idiopathic, chronic urticaria triggered by emotional stress was found more frequently in our study.[3] When the male and female genders were evaluated separately, there was no significant difference in terms of disease severity. 17.6% of patients responded well to standard dose antihistamine therapy. This rate is similar to the literature data. 39.2% of the patients responded well to high dose antihistamine/high dose different group antihistamine use. This rate is less than the literature. 37.5% of patients with antihistamine dose increase were using montelukast. 39.6% of patients receiving omalizumab gave adequate clinical response to omalizumab treatment alone without the need for antihistamine or montelukast treatment, this rate was similar to the literature.[6]

We believe that our study will facilitate predicting the treatment responses of patients in clinical practice by shedding light on the distribution of chronic urticaria patients according to the treatment steps. The limitations of our study are as follows; urticaria activity score was not used in the evaluation of the treatment response, a subjective evaluation was made, the response to the treatment was based on clinical observational data and foods that played an important role in the etiological factors were not evaluated.

Table 1. Demographic and clinical characteristics of patients

Gender	**n (%)**
Male	33 (32.4)
Female	69 (67.6)
Age mean±sd; median(min-max)	42±16; 42 (1-84)
Disease duration (month) mean±sd; median (min-max)	64±84; 24 (2-360)
Etiological factors	**n (%)**
Emotional stress	43 (42.2)
Idiopathic	37 (36.3)
Infection	5 (4.9)
Drug	2 (2.0)
Other*	8 (7.9)
Multifactorial	7 (6.7)
Disease severties	**n (%)**
Mild	25 (24.5)
Moderate	51 (50.0)
Severe	26 (25.5)

*Thyroid disease, asthma, allergic rhinitis, bee sting, tooth decay history, surgery history, collagen tissue disease
n:number, Sd:standard deviation, min-max: minimum-maximum

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was approved by the Local Ethics Committee of Selcuk University Faculty of Medicine (approval number: 2020/192).

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

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Effects of Career Management Applications on Nursing Students' Career Decisions, Academic Motivation and Career Decision Regrets

Kariyer Yönetimi Uygulamalarının Hemşirelik Öğrencilerinin Kariyer Kararları, Akademik Motivasyon ve Kariyer Karar Pişmanlıkları Üzerine Etkileri

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Abstract

Aim: The aim of this study was to determine the effects of career management applications on career decisions, academic motivation, vocational outcome expectations and career decision regrets in nursing students.

Material and Method: This study is in an experimental research design with pre-application and post-application control groups. The study data was collected from the application and control group by face-to-face interview technique. Before and after the application, the scales and Personal Data Sheet were applied to both groups for the content of the research. The data was evaluated in the SPSS 21 package program.

Results: The data obtained before and after application were interpreted at the level of significance. There was a significant difference between career decision, career decision regret, career outcome expectation and academic motivation scores ($p<0.05$).

Conclusion: Career management applications are effective in increasing the career decisions, academic motivation, vocational outcome expectations and in decreasing the career decision regrets.

Keywords: Nursing, career, decision, motivation, expectation, regret

Öz

Amaç: Bu çalışmanın amacı, hemşirelik öğrencilerinde kariyer yönetimi uygulamalarının kariyer kararları, akademik motivasyon, mesleki sonuç beklentileri ve kariyer karar pişmanlıkları üzerine etkilerini belirlemek amacıyla gerçekleştirilmiştir.

Gereç ve Yöntem: Bu çalışma uygulama öncesi ve uygulama sonrası kontrol grupları ile deneysel bir araştırma tasarımındadır. Çalışma verileri uygulama ve kontrol grubundan yüz yüze görüşme tekniği ile toplanmıştır. Her iki gruba da başvuru öncesi ve sonrasında Kişisel Bilgi Formu ve araştırma içeriğine yönelik ölçekler uygulanmıştır. Veriler SPSS 21 paket programında değerlendirilmiştir.

Bulgular: Uygulama öncesi ve uygulama sonrası elde edilen veriler anlamlılık düzeyinde yorumlanmıştır. Kariyer yönetimi uygulama sonrası öğrencilerde kariyer kararı, kariyer karar pişmanlığı, mesleki sonuç beklentisi ve akademik motivasyon puanları arasında anlamlı bir fark olduğu belirlenmiştir ($p<0,05$).

Sonuç: Kariyer yönetimi uygulamaları, kariyer kararları, akademik motivasyon, mesleki sonuç beklentilerinin artırılmasında ve kariyer karar pişmanlıklarının azaltılmasında etkilidir.

Anahtar Kelimeler: Hemşirelik, kariyer, karar, motivasyon, beklenti, pişmanlık

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INTRODUCTION

Career is an important auxiliary element in the formation of an individual's identity, individual and social status. The individual wants to meet students' needs from the first day in students' work life to satisfy expectations and desires, to make plans for the future, to rise in the hierarchical system at work and to be successful.[1] Career is the means of finding answers to these desires of the individual and achieving a better standard of life both in psychological and social terms.[2] It means proceeding on a chosen line of work and as a result of this, gaining status, having responsibility and achieving respectability.[3] As a result, the fact emerges that the individual who has a successful career looks more positively into the future and is happier because students' achieve the designed targets.[2]

A successful career is only possible through a career management. With the simplest sense, career management means planning made by people about their work lives.[4] Career management applications are important for students in terms of many aspects. The activities carried out in this study help students move to healthy career development and help career planning, responsibility and knowledge about their profession, self-interest, talent, value and personality characteristics. It also develops the ability to recognize and solve any possible problems.

Career management is a process that is focused both on the organization and the individual.[5] Individual career management is the individual efforts towards one's career targets. One's efforts are important in individual career management.[6] Organizational career management, on the other hand, is planned and managed by the organization. In other words, plans and strategies are developed and applied by the organization in organizational career management and data are provided to provide continuous career management.[7]

Career management consists of two components, which are "career planning" and "career development".[8] Career planning is the process of defining the qualifications and objectives of an individual correctly, recognizing the working environment and the career opportunities outside it.[9] Career development is the "lifelong process of managing learning, work, leisure and transitions in order to moved towards a personally determined and evolving future".[10] An individual's self-recognition, harmony with career goals, and development of knowledge and skills through the process of vocational education and training occurs during one's career.[11] Career planning and career development constitutes an uninterrupted process that must be considered together. Supporting the individual in terms of career planning and career development brings benefits both for the individual and the organization, which contributes to the high performance of individuals.[12]

Career decision means that an individual chooses a career field, career program, or a career opportunity, which suits them among various options[13] which have important long-term contributions to the public life by individuals and a sense of personal productivity as well as way of life, emotional welfare, economic and social status.[14] For this reason, it is natural for individuals to become engaged in career decisions at certain times in their lives. Career decisions are complicated behaviors. This complexity of career decisions is affected by the multitude of the factors that affect this process at a significant level.[15] Previous studies showed that the career decision-making process affects many variables like socio-economic and cultural factors, academic achievement, value and positive opinions about the profession.[16]

Psychological factors like the needs, values, interests, general and special abilities and personality traits of the individual, environmental factors like family, characteristics of the region, job opportunities, supply and demand status in the market affect career decision.[15]

Academic motivation is the production of the necessary energy for academic works.[17] Academic motivation expresses the desire, persistence, effort and excitement of the students to learn academic subjects.[18] Academically motivated students become ready for lessons, they are interested in these lessons, they do not become tired of studying immediately and make more learning efforts. For this reason, academic motivation plays a key role throughout academic life.[17]

Vocational outcome expectation means the expectation of individuals for the results of a profession.[19] It is also defined as the decision-making behavior or the beliefs in long-term results acquired as a result of a particular education.[20]

Career decision regret is the awareness that individuals would be better than the current career situation if they did things differently, or the cognitive-based negative emotion they face as a result of this thought.[21] It is the result of a decision that does not give what is desirable and which is disappointing about their career.[22] But career is the most important life role of every individual.[23]

In the literature review, it was determined that there are no applicable studies targeting to determine the effect of career management applications in nursing students on career decisions, academic motivation, expectations of vocational outcome and career decision regrets. It is considered that the present study is the first and important in terms of discussing these topics together in the literature and it will contribute to future studies.

In this study, answers to the following questions were sought:

- "Do career management applications effect nursing students' career decisions?"
- "Do career management applications effect nursing students' academic motivations?"
- "Do career management applications effect nursing students' vocational outcome expectations?"
- "Do career management applications effect nursing students' career decision regrets?"

MATERIAL AND METHOD

Objective and Design

To determine the effect of career management applications in nursing students on career decisions, academic motivation, expectations of vocational outcome and career decision regrets with pre-test & post-test control group study design.

Participants

The universe of study consisted of the students of the Nursing Department of the Faculty of Health Sciences; and the sampling consisted of 40 students who studied at the 3rd grade in the Nursing Department with an average grade of 2.00 or higher who agreed to participate in the study. 20 of the students were included in the application group with simple randomization method and the remaining 20 were included in the control group. In order to calculate the sample size, the data obtained from the sample was used. During the research, power analysis was conducted in accordance with the data of the sample group, in the power analysis using the G Power program, the effect size was determined as 1.23 and the power of the research was 95%.24 And the research was completed with a total of 40 students, 20 in the application group and 20 in the control group. On the basis of the difference between the groups before and after the implementation of the Career Decision Scale scores, the power analysis using the G Power program was found to have a confidence interval of 95%, an effect size of 0.88, and a power of research of 85%.

Instruments

The data of the study were collected with the forms given below:

Personal Information Form: It was prepared by the researchers in line with the literature. The departments, ages, genders, general average grades, classes, places of residence, sources of income and parental education status of the participants were questioned. The questions were prepared in open- ended and multiple-choice design.

Career Decision Scale: A 30-point "Career Decision Scale" that was developed by Yusupu25 was used to measure the career decision levels of the university students. The scoring of the scale is based on 5-Point Likert style (1= This does not fit me, 5= This fits me completely). The lowest score is 30 and the highest score is 150 in the scale. High points mean indecision and low points mean determination. The Cronbach Alpha value of the original scale was 0.91. It was found 0.87 in this study.

Academic Motivation Scale (AMS): This scale was developed by Bozanoglu[17] to determine the differences in the successand motivation levels of students at schools. The Cronbach Alpha was 0.87. It was 0.80 for this study. The scale consists of 20 items. It is scored in the 5-Point Likert style (1= This is absolutely not suitable, 5= This is absolutely suitable). The 19 items in the scale are positively scored except for one item, one item (Item 4) is reversed in scoring. The lowest possible score is 20 and the highest score is 100 in the scale. High scores show that the academic motivation is high.

Vocational Outcome Expectation Scale (VOES): This is a 6-point scale that was developed to measure the beliefs of people in long-term consequences of success as a result of certain educational or career decision-making behaviors. It was developed by Fouad and Smith26 and was adapted into Turkish by Isik.[27] Cronbach Alpha was 0.88. The scoring of the scale is made in the form of a 4-Point Likert style (1= I do not agree at all, 4= I totally agree). The lowest score is 12, the highest score is 48 in the scale. High scores show that the expectation of a vocational outcome is high. Cronbach Alpha was found 0.85 for this study.

Career Decision Regret Scale: The scale was created by Brehaut et al.22 and consists of 5 items and one dimension. The Turkish form of the scale was edited according to 5-Point Likert style (0= I do not agree at all, 4 = I totally agree). Items 1, 3 and 5 are reversely encoded. In the scoring, after the three item points are reversed, the points are added, the total points are obtained. The result is multiplied by 5, value between 0 and 100 is obtained. An increase between 0 and 100 in the score shows that decision regret is increased. If the score received from the scale is between 0 and 24, it is possible to argue that "there are no regrets about the decision"; if it is between 25 and 49, "there is a little regret about the decision"; if it is between 50 and 74, "regrets the decision", if it is between 75 and 100, "regretting the decision very much".[23] Cronbach Alpha was 0.91. In this study, it was 0.87

Data Collection

The study data were collected with face-to-face interview technique from the application and control group. The application was conducted by researchers in the form of training modules and 24/7 mobile consulting every week from 15.00 to 17.00 on Friday. In the first 4 modules, basic trainings were completed on nursing profession and values, training and development of nurses, career management and determination of nursing career paths[28] at the university classrooms. In the next 4 modules, personal SWOT analysis was carried out for each student in the classroom environment, student-specific career paths were determined after the analysis, the questions and answers were evaluated, interviews were made with 3 guests who were experts in thefields of Nursing of Surgery, Internal Medicine and Mental Health. The modules were completed in eight sessions. Mobile support was also provided to the students at the counseling step. For this purpose, the "Osmaniye Korkut Ata University Nursing Career Management" WhatsApp Group was created. The questions of the students were answered at any time. No interventions were made to the control group. The Personal Information Form, Career Decision Scale, Academic Motivation Scale, Vocational Outcome Expectation Scale and Career Decision Regret Scale were applied before and after the applications in the application and control group.

Statistical Analysis

The SPSS Statistics 21 program was used for statistical analyses. The Dependent Sample t-test, Independent Sample t-test, Mann Whitney U-test, Wilcoxon Signed Ranks test and Chi-Square Analysis Methods were used in the analyses of the data obtained in the study.

Ethical Consideration

In the progression of the study, scientific principles as well as the ethical principles of the Helsinki Declaration were held. In this context, the principles of informed consent, autonomy, secrecy and the protection of secrecy, fairness and no harm were taken into consideration. The study was conducted under the supervision and approval of Osmaniye Korkut Ata University Scientific Research and Publication Ethics Board of a public university (2019/4/6) and the Department of Nursing. The selection of the students in the study was based on being volunteers.

Limitations

The study is conducted with 3rd grade the sampling that consisted of the students whose marks were at and above 2.00 at the Nursing Department of a public university in Turkey. The findings of the study were limited with the items of the scales used.

RESULTS

The Socio-demographical characteristics of the application and control group students are given in **Table 1**. It was determined that 90% of the students in the application group were women, 45% stayed with their friends, 45% received scholarship, 40% of the mothers and 60% of the fathers were secondary school graduates. The mean age was 21.30 (SD=0.80), the academic average was 2.97(SD=0.35). It was also determined that 50% of the students in the control group were women, 65% stayed in dormitories, 40% received scholarship, 65% of the mothers and 75% of the fathers were secondary school graduates. The mean age was 21.65 (SD=1.38), the academic average was 2.82 (SD=0.62). It was determined that the students in the application and control group were similar in terms of demographical characteristics, that there were no statistically significant differences between the groups (p>0.05).

The scores before and after the application received by the application and control group were compared (**Table 2**). Before the career management applications, no significant differences were detected between the application and control group in career decision and career decision regret score averages (p>0.05). A significant difference was detected between academic motivation and vocational outcome expectation score averages (respectively p<0.001; p<0.05)

After the career management applications, a significant difference was detected between career decision, academic motivation, vocational outcome expectation and career decision regret score averages in the application and control group (respectively p<0.05; p<0.001; p<0.05; p<0.05).

Table 1. Socio-demographical characteristics of the groups

	Application Group (n=20)		Control Group (n=20)		p
	n	%	n	%	
Gender					
Female	18	90	10	50	0.337*
Male	2	10	10	50	
Residence					
Dormitory	8	40	13	65	
Family	3	15	4	20	0.223*
Friends	9	45	3	15	
Source of Income					
Family	7	35	6	30	
Scholarship	9	45	8	40	0.765*
Credit	4	20	6	30	
Mother's Education					
Illiterate	5	25	5	25	
Secondary School	8	40	13	65	0.070*
High School	7	35	2	10	
Father's Education					
Illiterate	2	10	2	10	
Secondary School	12	60	15	75	0.327*
High School	6	30	3	15	
Mean Age (Mean±Sd)	21.30±0.80		21.65±1.38		0.335**
Academic Average (Mean±Sd)	2.97±0.35		2.82±0.62		0.369**

*x2 test was applied **Thet-Test in Independent Samples was applied.

The average scores of the students at the application and control group are given in **Table 2.**

In the application group students, the score averages before and after the applications for career decision, academic motivation, vocational outcome expectation and career decision regret were compared (**Table 2**). There was a significant difference between the before-the-application and after-the-application score averages of career decision, vocational outcome expectation, academic motivation and career decision regret scores (respectively p<0.001; p:0.001; p<0.001; p<0.05).

In the control group, the scores of the career management applications of the students were compared as before and after the application score averages for career decision, academic motivation, vocational outcome expectation and career decision regret (**Table 2**). No significant differences were determined in terms of the score averages in career decision, academic motivation, vocational outcome expectation, career decision regret before the application and after the application (p>0.05).

Table 2. Average scores of the students at the groups (N=40)

Scales	Scale Averages				Application and Control Group	
	Application group		Control Group		Before the application	After the application
	Before the application Mean±Sd	After the application Mean±Sd	Before the application Mean±Sd	After the application Mean±Sd	p*	p*
Career Decision Scale	95.00±10.33	101.45±9.31	91.75±11.34	95.65±7.52	0.350	0.010
p**	<0.001		0.087			
Academic Motivation Scale (AMS)	76.25±7.25	82.20±11.85	66.80±8.77	68.20±7.83	0.001	0.000
p**	<0.001		0.503			
Vocational Outcome Expectation Scale (VOES)	16.70±1.97	21.65±6.00	14.95±2.28	15.65±2.32	0.013	0.000
p**	<0.001		0.260			
Career Decision Regret Scale	14.75±2.04	19.90±5.24	15.00±2.63	14.75±2.65	0.740	0.000
p**	<0.001		0.811			

p*: The difference between the application and control group (The t-test in Independent Samples and Mann Whitney U-test were applied)
p**: The difference between the scale average scores before the application and after the application (Dependent Paired Samples t-test and Wilcoxon Signed Ranks test were applied).

DISCUSSION

This study was conducted to determine the effect of career management applications, which were prepared in line with the literature, on the career decisions, academic motivation, vocational outcome expectations and career decision regrets of 40 third grade nursing students who studied at a public university with the pre-test & post-test control group research design.

As a result of the analyses of the pre-test & post-test difference scores, it was determined that the career decision, academic motivation, vocational outcome expectation scores of the application group increased, career decision regret scores decreased. These results show that career management applications have a positive effect on increasing the career decisions, academic motivation, vocational outcome expectations and on decreasing the career decision regrets of students. The results of this study were supported by experimental studies in the literature.[29,30]

In the study conducted by McWhirter, Rasheed and Crothers[19] they concluded that a 9-week career course was effective on social cognitive concepts like career decision-making and career skills competency expectations, perceived educational barriers, outcome expectations, career plans and career expectations. In the scope of career course, activities were applied about students' interests, values and skills, how to use career resources, how to collect information about different careers, how to prepare CVs and what training they can receive for potential career options. It was observed that the application had effects on career decisions and career skills competency expectations, outcome expectations and career plans of the students in the application group.

In their study on university students, Reese and Miller[31] compared students who received career development courses and those who did not receive it. In this study, it was determined that the career decision levels of the students who received the course increased at a significant level. Marko and Savickas[32] conducted a study on 25 university students and used applications to increase the career planning and career development of individuals for the future and as a result of the measurements, they determined that there were statistically significant increases in students' future focus and career planning in their career lives between the application group and control group.

In the study conducted by Turner and Lapan[33] it was determined that a computer-aided career intervention program was effective for both individual and group applications in secondary school students to increase their interest in non-traditional professions and their expectations of career competence. In the study of Koen et al.[29] conducted on a group of post-graduate students, it was determined that there was a positive increase in career adjustment skills based on measurements conducted immediately after and six-month program. Foltz and Luzzo[34] conducted a study on university students over the age of 25 and reported that there was significant increases in the career decision-making competencies after they compared the application and control groups.

In their studies, Diegelman and Subich.[35]; Fouad et al.[36]; McWhirter et al.[19]; reported that the career management applications increased the expectation of vocational outcome in students at a significant level, which is similar to the results of the present study. Guillen, on the other hand, concluded that a program that was developed to increase the outcome expectations had no significant effects on improving the expectations and vocational outcome of university students.[37]

It was determined that career management applications increased academic motivation, there was a significant difference between the pre-test and post-test scores, the test scores of the students after career management applications were higher at a significant level. In the literature reviews, there were no studies conducted to determine the effect of career management applications on academic motivation.

The study that was conducted by Saracaloglu[38] on post-graduate students determined that there was a positive and significant relation between research proficiency, attitude towards research and academic motivation and there was a significant and negative relation between research anxiety and academic motivation. Another important result of the study was that it was determined that academic motivation affected research competence. In addition, when the literature was examined, it was determined that the academic motivation concept is one of the factors that affect the success of students.[39]

It was determined that career management applications have a negative effect on career decision regret scores. It is possible to argue that career management applications increase, the career decision regret scores decrease. No studies were detected in the literature conducted to determine the effect of career management applications on decision regret scores. it is possible to argue that only the average scores were compatible with the study.[23]

In the control group, no significant differences were detected between all the scale scores in the time spent when the application was made in the application group.

When the application and control group were compared in terms of application times, it was determined that there was a significant difference between the two groups only in the academic motivation and vocational outcome expectations before the application. The average scores of the application group were high. After the application, significant differences were detected in career decision, academic motivation, vocational outcome expectation and career decision regret scores between the two groups. When the two groups were compared, it was determined that the career decision, academic motivation, vocational outcome expectation scores of the application group were high, career decision regret scores were low. When the after-the-application scores were evaluated, a significant difference was detected in career decision, academic motivation, vocational outcome expectation and career decision regret scores. The career decision, academic motivation, vocational outcome expectation scores of the application group increased and the career decision regret scores decreased.

CONCLUSION

The study findings showed that career management applications are effective in increasing career decision, academic motivation, vocational outcome expectation scores and in decreasing career decision regrets.

Similar studies can be conducted for career planning of students who study at different faculties. Career management applications can also be developed for individuals who work in different branches. It may be recommended that the scope of similar applications are expanded and implemented to different groups in different ages. It is considered that there are no experimental studies on this topic in nursing field in Turkey. It will contribute to the planning and implementation of similar studies.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was conducted under the supervision and approval of Osmaniye Korkut Ata University Scientific Research and Publication Ethics Board of a public university (2019/4/6) and the Department of Nursing.

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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

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Case Report/Olgu sunumu

Histopathological Classification of Neonatal Sacrococcygeal Teratomas: Case Report

Neonatal Sakrokoksigeal Teratomların Histopatolojik Sınıflaması: Olgu Sunumu

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Abstract

Sacrococcygeal teratomas are tumours that arise from the sacrococcygeal region containing tissue from all three germ layers. Sacrococcygeal teratoma (SCT) is a relatively rare tumour affecting new-borns, infants and children with an incidence of one per 40,000 live births with malignant transformation with increasing age. It is four times more common in women than men. With this case study, it was aimed to evaluate the histopathological evaluation and grading of SCT. Examination of pathological specimens including immature and malignant transformation should be done carefully.

Keywords: Sacrococcygeal teratoma, congenital, histopatology, mature, immature

Öz

Sakrokoksigeal teratomlar, her üç germ tabakasından doku içeren sakrokoksigeal bölgeden ortaya çıkan tümörlerdir. Sakrokoksigeal teratom (SKT), artan yaşla birlikte malign transformasyonu olan 40.000 canlı doğumda bir insidansı olan yenidoğanları, bebekleri ve çocukları etkileyen nispeten nadir bir tümördür. Kadınlarda erkeklerden dört kat daha sık görülür. Bu olgu çalışması ile birlikte SKT histopatolojik değerlendirme ve derecelenmesi değerlendirmek amaçlanmıştır. İmmatür ve malign transformasyon içeren patolojik spesmen incelemeleri dikkatlice yapılmalıdır.

Anahtar Kelimeler: Sakrokoksigeal teratom, konjenital, histopatoloji, mature, immature

INTRODUCTION

Teratoma consists of the embryological origin of germ cell tumours. Its name is derived from the Greek word "teratos", which literally means "monsters". The "oma" added to the end is a neoplasm marker.[1] Sacrococcygeal teratoma (SCT) is the most common solid tumour in the neonatal period and its incidence has been reported as one in 35,000-40,000 live births.[2] The first description of teratoma cases was BC. The first description of teratoma cases was BC. It dates back to 2000 BC.[3] Teratomas are germ cell tumours that consist of tissue elements foreign to the organ or anatomic region.[4] In 1863, the word Teratoma was used by Virchow.[5] The most appropriate and new definition for SCT isan encapsulated tumour with tissue or organ components in which three primordial germ layers ofectoderm, mesoderm and endodermcan be traced.[4] Teratomas are mostly seen in the sacrococcygeal, mediastinal, retroperitoneal and gonads in the childhood age group. SKTs are divided into three classes as mature, immature and malignant. In studies, the frequency of mature teratoma is around 80%. Mature teratomas mainly consist of different tissues. With this case report, it is aimed to discuss the histopathological evaluation and classification of SCT accompanied by the rare SCT case in a patient who underwent surgical treatment in the neonatal period.

CASE

The patient was delivered by caesarean at the age of 40 weeks as a third living from the 4th pregnancy of a 36-year-old mother with a weight of 3800 g. No problem of the mother was detected during pregnancy follow-up in our hospital.

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No sacral mass was detected in the detailed ultrasonography examination performed on the 21st week of pregnancy and the ultrasound controls performed during pregnancy. When our patient was born, the head circumference was measured to be 35 cm (50-75 percentile), height 51 cm (50-75 percentile) and 3800 g (50-75 percentile). The first minute apgar score after birth was evaluated as 9, and the 5th minute apgar score as 10. The baby, who was found to have swelling in the sacral area during a postpartum physical examination, was consulted to the Paediatric Surgery Clinic (**Figure 1**). In the first physical examination, a 5x5 cm soft mass with a palpable bone and cystic tissue was palpated, starting from the right gluteal region to the sacral region. Superficial tissue ultrasonography was performed for differential diagnosis of the mass detected in the patient. Superficial tissue ultrasonography performed on the patient was reported as "fluid collection with as size of 19x7 mm having homogeneous structure, dense in content, smooth contoured starting from the level of the coccyx and extending under the skin was observed, a second area with a size of approximately 22x8 mm having similar characteristics was observed in the right paravertebral area" Tumour markers (AFP, B-HCG, LDH) were requested from the patient for the differential diagnosis of the mass. Considering that the patient's sacro-gluteal mass might be SCT, a computed tomography examination was requested to evaluate the intraabdominal extension. Computed tomography report was reported as "Cystic image of 29 mm width was observed in the distal of the right gluteal shadow" (**Figure 2**). AFP value of tumour markers examined in the patient preoperatively were measured as 44756 ng/ml, B-HCG 6.5 mIU/ml, and LDH 726 U/L. As sacrococcygeal teratoma was considered in the patient, it was decided to remove the mass completely. A 7x6 cm diameter cystic mass and coccyx were totally removed by making a chavron incision made around the gluteal mass. The patient was followed up in the neonatal intensive care unit after surgery. Oral feeding was started on the first postoperative day. The patient was discharged on the 7th postoperative day with the recommendation for the control of the paediatric surgery outpatient clinic with stable vital signs, full oral nutrition, stool discharge, clean incision and no problem. The AFP control result obtained on the postoperative 6th day of the patient was 15611 ng/ml. Pathology result was reported as "Sacrococcygeal teratoma with immature neuronal component in microcopic foci showinghigh proliferative activity with 67 in teratoma, accompanied by coccyx containing cartilage and bone marrow" (**Figure 3**, **Figure 4a-f**). The postoperative follow-up and treatment of the patient is maintained with paediatric oncology.

Figure 1. Neonatal Sacrococcygeal teratoma Gluteal Mass Image

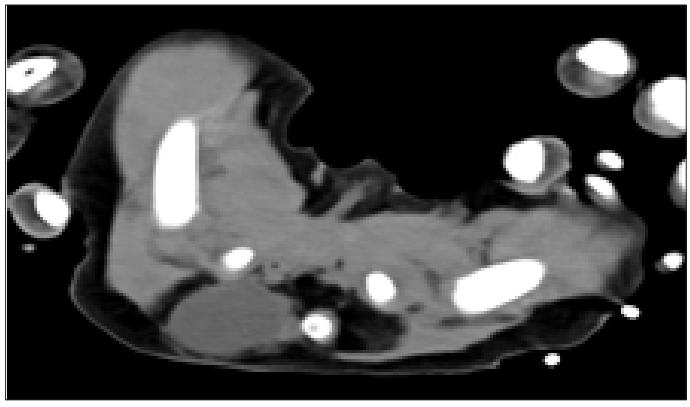

Figure 2. Sacrococcygeal teratoma Computed Tomography Image

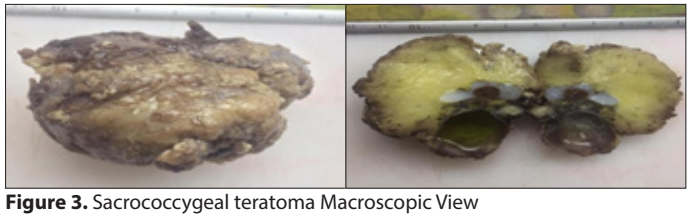

Figure 3. Sacrococcygeal teratoma Macroscopic View

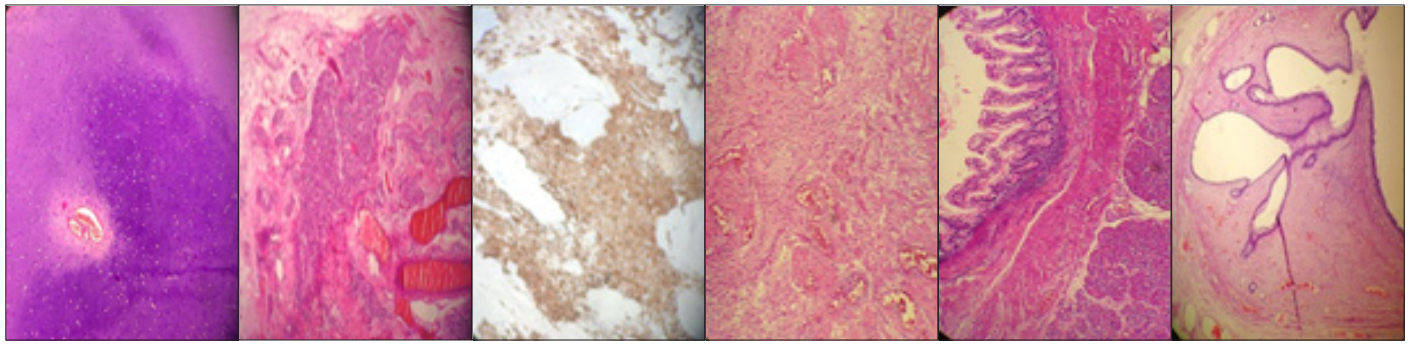

Figure 4. Sacrococcygeal teratoma Histopathological evaluation findings. 4a: Cartilage Tissue, 4b: Peripheral nerve tissue, 4c: Neuronal Component Glial Tissue, 4d: Gastrointestinal mucosa Epithelium, 4e: Glial Tissue Ki-67, 4f: Squamous epithelium tissue

DISCUSSION

Sacrococcygeal teratoma is a relatively rare tumour in the neonatal period. When SCT is present at birth, excisional surgery should be performed as early as possible to prevent malignant transformation that may occur at later ages.[12] The surgical approach in SCTs is total removal of the tumour with the coccyx by using a sacral or sacro-abdominal approach.[13] Most of the SCTs appear at birth as a mass in the sacral region. While most new-borns do not have any other accompanying symptoms, some new-borns may need intensive care due to premature birth, high heart failure and tumour rupture or bleeding within the tumour. Infants with mass lesions in the pelvis may have difficulty in urinating, constipation and signs of an abdominal mass.[14] Although SCTs contain tissues of ectoderm, endoderm and mesoderm origin, their embryological origin is still unclear.[6,7] It is believed that the totipotent cells of the Hensen's node or the remnants of the primitive streak in the coccygeal region emerge in early pregnancy.[15-17] This primitive streak appears as a linear thickening of the ectoderm on the caudal edge of the bilaminar embryonic disc, and subsequently disappears with degenerative changes.[6,7] As the mesoderm reproduces rapidly, the primitive line extends more caudally. The remains of the Hensen's node descend to the coccyx end or anterior surface.[15,17] The growth of these primitive pluripotential cells escapes from the control of embryonic inducers and organizers and results in teratoma as a result of transformation of foreign cells in the anatomical region.[18] Therefore, SCT often occurs near the coccyx, where the highest concentration of primitive cells is present for a longer period of time.[17] SCT consists of multiple neoplastic tissues that are foreign to the sacrococcygeal region and do not contain a specific tissue derived from multiple germ layers.[17] SCT is more common in girls and infants under 3 months.[8-11] According to the Altmann classification, Type 1 and Type 2 SCT (87%) are the most common. Type 3 and Type 4 are extremely rare (**Table 1**). Type 4 SCTs are generally diagnosed at advanced ages.[8] While mixed type (80%) with predominant cystic areas is seen in SCTs, immature solid type can be seen in 20%.[11] Histologically, 80% of SCTs are mature while 20% are immature (**Table 2**). In our case, there are the dominant components of the mature teratoma of ectodermal and endodermal origin, followed by mesodermal, neuroectodermal and organoid endodermal elements. While the ectodermal component usually contains skin and hair follicles and their derivatives, gastrointestinal epithelium, urothelium, and respectively respiratory epithelium are seen most frequently as the endodermal component. The mesodermal component consists of fat, connective tissue, cartilage, bone and muscle tissue with lymphoid tissue. The organoid endodermal component, on the other hand, forms mainly parotid and saliva and pancreatic tissue. Neuroepithelium is seen in all mature teratomas. Immature non-malignant neuroepithelium is seen in immature teratomas. In immature teratomas, rosette formations of primitive tissue are seen. Differential diagnosis of SCTs includes coccygeal meningocele in fetus, myelomeningocele and fetus in fetus.[12,18]

Tablo 1. SCT Altman Classification

Altman classification		Frequency of prevalence
I	The mass is completely outside the pelvis	57.6%
II	Part of the mass is inside the pelvis, most of it outside the pelvis	38.6%
III	Most of the mass is inside the pelvis, some outside the pelvis	3.8%
IV	The mass is completely in the pelvis	Rare

Table 2. Histological diagnosis and tumor grade classification in Sacrococcygeal teratoma

SCT Tumor Maturation	SCT Tumor Grade
Mature Teratoma	Grade 0: Tumor consists only of mature mature tissue
Immature Teratoma	Grade 1: There is a rare immature area in the tumor Grade 2: There are immature areas in the tumor Grade 3: Most of the tumor consists of immature areas

CONCLUSION

Sacrococcygeal teratoma is a relatively rare tumour in the neonatal period. When SCT is detected during delivery, total surgical excision is required as soon as possible to prevent malignant transformation. Histological evaluation is the gold standard in the differential diagnosis of mature or immature SCT.

ETHICAL DECLARATIONS

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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

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

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