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Mehmet Muhurdaroglu[1*]
Ezgi Agadayi[2]
Arzu Kosem[3]

[1]Ankara Sereflikochisar State Hospital Department of Neurology Ankara/Turkey
[2]Sivas Cumhuriyet University, Faculty of Medicine, Department of Medical Education, Sivas, Turkey
[3]Health Sciences University, Ankara City Hospital, Medical Biochemistry Clinic, Ankara, Turkey

Corresponding Author:
Mehmet Muhurdaroglu
Ankara Sereflikochisar State Hospital Department of Neurology Ankara, Turkey
Phone: +90 535 379 2925
mail: m.muhurdaroglu@hotmail.com

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Low Magnesium Levels May Arise as a Risk Factor for the Development of Polyneuropathy in Patients with Type 2 Diabetes

ABSTRACT

Objective: Changes in magnesium metabolism have a different effect on the metabolic and signaling pathways in the development and progression of diabetes. This study aimed to determine the relationship between the serum magnesium level and polyneuropathy in patients with type 2 diabetes mellitus (DM).

Methods: The study included type 2 DM patients who presented to the neurology outpatient clinic of Ankara City Hospital with the complaint of pain and burning sensation in the hands and feet and received a pre-diagnosis of polyneuropathy based on electroneuromyography. Biochemistry and hormone parameters of patients were scanned retrospectively.

Results: A total of 116 patients, 49 (42.2%) female and 67 (57.8%) male, were included in the study. The frequency of polyneuropathy was significantly higher in the group with high HbA1C (>10.1%) compared to the group with low HbA1C (<7.1%) (P=0.004). Mg levels were significantly lower in patients with polyneuropathy (1.8±0.2 mg/dl) compared to those without polyneuropathy (2.0±0.4 mg/dl) (P=0.013). Patients with additional complications other than polyneuropathy had significantly lower magnesium levels than those without such complications(P=0.021). The mean Mg level was 1.82±0.50 mg/dl for the patients with complications while it was 1.88±0.18 mg/dl for those without complications.

Conclusions: This study showed that the magnesium levels were significantly associated with the development of polyneuropathy in patients with type 2 DM. It was concluded that an adequate magnesium level in patients with glycemic control can prevent the development of diabetic polyneuropathy.

Keywords: Diabetes mellitus, Type 2, Diabetic Polyneuropathy, Serum Albumin, Magnesium.

Düşük Magnezyum Seviyeleri Tip 2 Diyabetli Hastalarda Polinöropati Gelişimi İçin Bir Risk Faktörü Olarak Ortaya Çıkabilir

ÖZET

Amaç: Magnezyum metabolizmasındaki değişiklik, diyabetin gelişimi ve ilerlemesi üzerine metabolik ve sinyal yollarında farklı bir etkiye sahiptir. Bu çalışmanın amacı tip 2 Diabetes Mellitusu (DM) olan hastalarda serum magnezyum düzeyinin polinöropati üzerine ilişkisini belirlemektir.

Gereç ve Yöntem: Bu çalışmaya Ankara Şehir Hastanesi nöroloji polikliniğine el ve ayaklarda ağrı ve yanma şikayeti ile başvurup polinöropati ön tanısıyla elektronöromiyografisi yapılan Tip 2 DM tanılı hastalar dahil edildi. Hastaların biyokimya ve hormon parametreleri retrospektif olarak tarandı.

Bulgular: Çalışmaya 49 (%42,2)'u kadın, 67 (%57,8)'i erkek toplam 116 hasta dahil edildi. HbA1C değeri yüksek grupta (>%10,1) polinöropati görülme sıklığı HbA1C düşük gruba (<%7,1) göre anlamlı olarak daha fazlaydı (P=0,004). Mg seviyesi polinöropatisi olan hastalarda (1.8±0.2), Polinöropati saptanmayanlara (2.0±0.4) göre anlamlı derecede düşüktü(P=0,013). Polinöropati dışında ek komplikasyonu olan hastaların magnezyum seviyeleri olmayanlara göre anlamlı derecede daha düşüktü (P=0,021). Ortalama Mg düzeyi komplikasyonlu hastalarda 1,82±0,50 mg/dl iken komplikasyonsuzlarda 1,88±0,18 mg/dl'ydi.

Sonuç: Bu çalışmada Tip 2 DM tanılı hastalarında polinöropati gelişimiyle magnezyum düzeylerinin anlamlı derecede ilişkili olduğunu göstermiştir. Glisemik kontrolü sağlanan hastalarda yeteli magnezyum seviyesinin diyabetik polinöropati gelişimini önleyebileceği sonucuna ulaşılmıştır.

Anahtar Kelimeler: Diabetes mellitus, Tip 2, Diyabetik Polinöropati, Serum Albümini, Magnezyum.

INTRODUCTION

Diabetic polyneuropathy is the most common neurological complication of diabetes and an important cause of morbidity. Diabetic polyneuropathy begins distally and symmetrically in the feet, leading to a gradual loss of integrity of long nerve fibers. In addition to the risks of sensory loss, foot ulcer, and amputation involved in polyneuropathy, approximately 15-20% of patients experience painful symptoms, which are signs of small myelinated fiber involvement that can limit functionality and reduce quality of life (1,2). In nearly half of the cases, pain can be self-limited and resolve spontaneously within a year, while other patients may have permanent symptoms related to pain and loss of functionality (3).

Microelements play a great role in the improving and complications of diabetes (4). An important cation Magnesium (Mg), takes part in cellular mechanisms. These mechanisms are protein synthesis, energy homeostasis, and DNA stability. Hypomagnesemia is the most common micronutrient deficiency detected in diabetic patients. Among type 2 Diabetes mellitus (DM) patients, the prevalence of hypomagnesemia varies between 14 and 48% (5). The main factors under this condition are thought to be inadequate dietary intake, changed insulin metabolism, increased renal excretion, and gastrointestinal malabsorption (6). Serum Mg levels have been found to be associated with diabetic complications. These complications are coronary artery diseases, diabetic retinopathy, nephropathy and polyneuropathy (7-11). In the literature, there are data showing a negative correlation between serum Mg levels and fasting plasma glucose and glycated hemoglobin (HbA_{1C}) levels, as well as a significant decrease in the Mg values of patients with macrovascular complications (8).

It is known that serum albumin has powerful antioxidant properties that prevent the production of free hydroxyl radicals and can scavenge peroxy radicals (9, 10). It has also been suggested that albumin is the main ingredient in extracellular fluids with an antioxidant role (11). Many studies have shown that the excessive production of reactive oxygen species that cause oxidative and nitrosative stress plays a determinant role in the inflammatory pathogenesis and autoimmune diseases of the nervous system, such as neuromyelitisoptica (12), multiple sclerosis (13), and myasthenia gravis (14). Accordingly, a low albumin level can cause polyneuropathy by contributing to inflammation, as in Guillain-Barré syndrome (GBS) (15).

This study aimed to determine the relation of the serum Mg with polyneuropathy in type 2 DM patients with neuropathic pain complaints and to determine the relationship of polyneuropathy with the levels of serum albumin, HbA_{1C}, uric acid, calcium (Ca), sodium, potassium, phosphorus, vitamin B12, vitamin D, thyroid-stimulating hormone (TSH), folate, hemoglobin, ferritin, low-density lipoprotein (LDL), high density lipoprotein (HDL), and triglyceride (TG) in these patients.

MATERIAL AND METHODS

Study Design: This study had a retrospective descriptive design.

Study Population and Design: Type 2 DM patients, presented to the neurology outpatient clinic of Ankara City Hospital between March 1, 2019 and October 1, 2019 with the complaint of pain and burning sensation in the hands and feet and received a pre-diagnosis of polyneuropathy based on electroneuromyography (ENMG) were included in the study. The information of the patients was retrospectively analyzed from their files. The recorded data on HbA_{1C}, uric acid, albumin, urine albumin to creatinine ratio, Mg, blood urea nitrogen (BUN), creatinine, glomerular filtration rate (GFR), alanine transaminase, aspartate transaminase, Ca, sodium, potassium, phosphorus, lipid profile tests (LDL, HDL, TG), TSH, vitamin B12, vitamin D, folate, hemoglobin and ferritin levels and ENMG reports, which had been originally obtained due to medical necessity or for routine control purposes, were screened from the hospital information system. In addition, the patients' files were reviewed to record age, gender, medications used, comorbidities, and DM-related complications. The type 2 DM diagnoses of the patients were not made by our clinic and they were based on the information included in the hospital system. Patients using any medication that could affect the electrolyte balance, such as diuretics and Ca, Mg, vitamin B12 and vitamin D supplements, those with advanced heart failure, liver cirrhosis, active malignancy, or thyroid dysfunction, and those with type 1 DM were excluded from the study. The GFR values of the patients were calculated using the simplified formula of Modification of Diet in Renal Disease (MDRD) (16), and those with a GFR below 60 mL/min were also excluded from the study. In repeated presentations, the initial reference values were taken into consideration. Normal Mg values in our laboratory are between 1.3 - 2.7 mg/dl.

ENMG tests were performed in the neurology clinic of Ankara City Hospital using the Nihon Kohden Neuropack S1 MEB-9400K device. During the test, the skin temperature of the patients was kept at 32-33 °C. Conduction velocity, compound muscle action potential amplitude, and distal latencies were measured as part of motor nerve studies on the median and tibial nerves. In sensory nerve studies, the action potential amplitude and conduction velocities of the medial, ulnar and sural sensory nerves were measured. A diagnosis of sensory polyneuropathy was made only in those with impaired sensory nerve conduction while those accompanied by motor

nerve conduction damage were grouped as sensorimotor polyneuropathy.

Statistical Analysis: The data were analyzed using a statistical package program (Statistical Package for the Social Sciences-SPSS for Windows, Version 25). The normality analysis of numerical values was performed using the Shapiro-Wilk test. Descriptive statistics were obtained. The frequencies of the data were expressed as percentage (%) and n values. The Mann-Whitney U test was used to compare numerical data that did not show normal distribution between two independent groups, and the Kruskal-Wallis H test was used for the comparison of more than two independent groups. The chi-square test was conducted to investigate the statistical difference between two variables with nominal dichotomous distribution. The results were evaluated at the 95% confidence interval and a. significance level of $P<0.05$

Ethical Approval: Prior to the commencement of the study, approval was obtained from the ethics committee of Ankara City Hospital (date and number: 30.01.2020-E1-19-228).

RESULTS

A total of 116 patients were included in the study. Patients' 49 (42.2%) were female and 67 (57.8%) were male. The mean age of the patients was 60.6 ± 10.4 (min: 31-max: 94) years.

According to the tertiles of HbA_{1C}, the patients were divided into three groups (<33 percentile, 33-67 percentile, and >67 percentile). The patients with high mean HbA_{1C} (>10.1%) values had a statistically significantly higher rate of polyneuropathy compared to the group with a low HbA_{1C} (<7.1%) value (P = 0.004). Various parameters compared between the groups are shown in Table 1.

Table 1. Comparison of various parameters between the groups according to the tertiles of HbA_{1C}

	HbA_{1C} (%)			
	Tertile 1 (n=34) <7.1	Tertile2 (n=44) 7.1-10.2	Tertile3 (n=30) >10.2	*P*
Polyneuropathy				
Present	22 (28.9%)	27 (35.5%)	27 (35.5%)	0.004*
Absent	12 (40%)	16 (53.3%)	2 (6.7%)	
Type of polyneuropathy				
Neural	12 (60%)	5 (25%)	3 (15%)	0.001*
Sensorimotor	10 (17.9%)	22 (39.3%)	24 (42.9%)	
Complications				
Present	7 (19.4%)	14 (38.9%)	15 (41.7%)	0.010*
Absent	27 (39.1%)	28 (40.6%)	14 (20.3%)	
Albumin (g/L)	45.9 ± 2.5	44.3 ± 2.2	43.8 ± 4.4	0.155
Magnesium(mg/dl)	1.8 ± 0.2	1.9 ± 0.4	1.8 ± 0.2	0.745
Calcium (mg/dl)	9.5 ± 0.3	9.3 ± 0.4	9.5 ± 0.5	0.439
LDL (mg/dl)	103.5 ± 33.4	115.0 ± 38.9	122.0 ± 44.3	0.183
HDL (mg/dl)	47.3 ± 13.5	43.2 ± 12.5	44.2 ± 9.5	0.347
TG (mg/dl)	153.4 ± 79.4	184.4 ± 75.0	194.6 ± 96.9	0.081
GFR (mg/dl)	92.1 ± 13.1	90.5 ± 14.3	85.1 ± 13.3	0.131

HDL; high-density lipoprotein, LDL; low-density lipoprotein, TG; triglyceride
GFR; glomerular filtration rate, *$P<0.005$

Thirty-three percent (n = 37) of the patients had complications associated with type 2 DM. Patients' 22.4% (n = 26) had coronary artery disease, 8.6% (n = 10) had retinopathy, 6.9% (n = 8) had nephropathy and 0.9% (n = 1) had peripheral artery disease. Of the evaluated ENMG reports, 28.9% (n=33) were normal while 17.5 (n=20) were consistent with sensory polyneuropathy and 53.5% (n = 61) with sensorimotor polyneuropathy. There was no significant difference between the genders in terms of the presence of polyneuropathy (P = 0.291). The mean age of the patients with polyneuropathy was 63.1 ± 9.7 years, while that of the patients without polyneuropathy was 54.9 ± 9.8 years, indicating a significant difference (P < 0.001). However, there was no significant relationship between the type of polyneuropathy detected (sensory/sensorimotor) and gender (P = 0.576). The comparison of various parameters according to the presence of polyneuropathy is presented in Table 2.

When the Mg levels were compared between the patients with different polyneuropathy types, there was no significant difference between those with sensory polyneuropathy and those with sensorimotor polyneuropathy (P = 1.000). The mean Mg level was 1.8 ± 0.2 mg/dl in both the sensory polyneuropathy group and the sensorimotor polyneuropathy group.

Of the patients detected to have polyneuropathy, 36.3% (n = 29) had an additionally diagnosed complication associated with type 2 DM.

According to these results, 27.2% (n = 22) of the patients with polyneuropathy had coronary artery disease, 11.1% (n = 9) had retinopathy, and 6.2% (n = 5) had nephropathy. There was a statistically significant difference between the Mg levels of patients with and without complications (*P*=0.021). The mean Mg level was 1.82 ± 0.50 mg/dl for the patients with complications while it was 1.88 ± 0.18 mg/dl for those without complications. However, no significant difference was observed in the albumin and phosphor levels according to the presence or absence of complications (*P*=0.227 and *P*=0.993, respectively).

Table 2. Comparison of the various parameters of the patients according to the presence of polyneuropathy

	Total (n =116)	Polyneuropathy+ (n=81)	Polyneuropathy- (n=33)	*P*
HbA_{1C} (%)	8.9 ± 2.3	9.2 ± 2.5	8.0 ± 1.6	0.052
BUN (mg/dl)	36.0 ± 12.8	37.0 ± 13.4	32.6 ± 9.9	0.094
Creatinine(mg/dl)	0.8 ± 0.3	0.8 ± 0.1	0.9 ± 0.6	0.529
Uric acid(mg/dl)	5.1 ± 1.4	5.0 ± 1.5	5.3 ± 1.2	0.205
Albumin (g/L)	44.7 ± 3.4	44.0 ± 3.4	46.5 ± 2.4	0.001*
Magnesium(mg/dl)	1.8 ± 0.3	1.8 ± 0.2	2.0 ± 0.4	0.013*
GFR (mL/min)	88.9 ± 13.9	86.6 ± 13.7	94.1 ± 13.1	0.011*
Calcium(mg/dl)	9.4 ± 0.4	9.4 ± 0.4	9.4 ± 0.5	0.733
Sodium(mg/dl)	139.8 ± 2.9	139.5 ± 3.2	140.6 ± 2.1	0.162
Potassium(mg/dl)	4.5 ± 0.4	4.5 ± 0.4	4.6 ± 0.3	0.764
LDL (mg/dl)	112.6 ± 38.3	111.6 ± 38.1	112.3 ± 37.9	0.983
HDL (mg/dl)	44.6 ± 12.2	44.5 ± 11	44.7 ± 15.1	0.605
TG (mg/dl)	176.2 ± 82.7	176.2 ± 81.5	164.3 ± 69.0	0.648
TSH (mU/ml)	1.9 ± 1.6	1.9 ± 1.6	2.1 ± 1.7	0.687
Vitamin B12 (pg/ml)	382.9 ± 191.8	397.8 ± 209	334.6 ± 123.5	0.183
Folic acid (ng/ml)	9.2 ± 3.3	9.2 ± 3.6	9.4 ± 2.4	0.719
Hemoglobin (g/dl)	13.6 ± 1.7	13.7 ± 1.8	13.5 ± 1.6	0.825
Vitamin D (ng/ml)	23.3 ± 13.4	23.7 ± 14.1	21.9 ± 11.3	0.655
Phosphor (mg/dl)	3.6 ± 0.6	3.6 ± 0.4	3.7 ± 0.9	0.839
Ferritin (µg/l)	72.7 ± 77.6	76.6 ± 79.7	60.9 ± 72.0	0.446
UACR (mg/g)	37.0 ± 70.1	42.2 ± 79.1	23.6 ± 36.5	0.575

BUN; blood urea nitrogen, LDL; low-density lipoprotein, HDL; high-density lipoprotein, TG; triglyceride, TSH; thyroid-stimulating hormone,GFR; glomerular filtration rate, UACR; Urine albumin to creatinine ratio *P<0.005

DISCUSSION

The severity and length of hyperglycemia are risk factors for the improving of diabetic polyneuropathy in patients with DM (17, 18). In our study, as the mean HbA_{1C}value increased, the frequency of complications and polyneuropathy, as well as the severity of the latter increased.

Electrolyte disorders are common in diabetic patients and closely associated with increased morbidity and mortality. These disorders are more common in diabetics with poor blood glucose regulation and those with impaired renal function. Hyperglycemia, insulin resistance, or impairment in glucose metabolism might induce glomerular hyperfiltration and increased tubular flow, resulting in decreased tubular reabsorption (6). Complex treatment regimens used by patients with diabetes also stimulate the development of electrolyte disorders in these patients (19). Hypomagnesemia is a common electrolyte disorder among diabetics (20). Diabetic polyneuropathy may present as mixed demyelinating, axonal degeneration or segmental demyelinating. ENMG is a very useful method to detect these disorders (21). In our study, the serum Mg level was found to be statistically lower in patients with diabetic polyneuropathy based on ENMG compared to those without polyneuropathy. In a study conducted with 256 patients with type 2 DM, Zhang et al. performed nerve conduction studies and found that the Mg and phosphate levels were lower in patients with peripheral polyneuropathy (22). In another study for which 978 patients with type 2 DM were recruited, a decrease in Mg was found in proportion to the decrease in the Z score in amplitudes according to the nerve conduction examinations, and it was concluded that Mg could cause peripheral nerve dysfunction through axonal degeneration (23).

Mg is an important element play an important regulator of energy metabolism. It triggers the formation of mitochondrial adenosine triphosphate by preserving transmembrane ion gradients in the inner mitochondrial membrane (24). Mg supplementation has a beneficial effect on glucose control, oxidative stress, and prevention of inflammation (25). In a recent randomized controlled study, it was determined that 12 weeks of Mg supplementation among people with diabetic

foot ulcers regulated ulcer size, glucose metabolism, and serum levels of high-sensitivity C-reactive protein (26). An animal study also showed that Mg acetyltaurate had a preventive effect toward axonal degeneration by reducing oxidative stress through caspase-3 inactivation (27).

Corsonello et al. stated that diabetic patients with microalbuminuria or proteinuria had lower serum ionized magnesium concentration compared to patients with normal albumin in urine (28). Wang et al. found a negative correlation between serum Mg levels and diabetes in terms of macrovascular complications (29). In other studies, hypomagnesemia was found to be associated with diabetic retinopathy in patients with diabetes (30, 31).

Another mechanism for the improvement of diabetic complications changes in metabolic pathways. In these pathways, low Mg levels can modify normal functioning. Sorbitol, a mechanism in the polyol pathway, inhibits inositol transport and results in the inhibition of sodium-potassium adenosine triphosphatase (Na+/K+/ATPase) activity, in diabetes. Intracellular Mg is required for the normal activity of membrane-bound Na+/K+/ATPase, especially in cardiac muscle and neural tissues. Low Mg decrease Na+/K+/ATPase activity, leading to the improving of diabetic polyneuropathy and macro-vascular events (32, 33). In our study, consistent with the literature, the serum Mg level was determined to be lower among the diabetic patients with complications.

Several studies have proven that serum albumin has powerful antioxidant properties that inhibit the production of free hydroxyl radicals and can scavenge peroxy radicals (9, 24). In a study comparing 88 patients diagnosed with GBS presenting with peripheral polyneuropathy and 153 healthy controls, the serum albumin levels were shown to be significantly lower in the former (15). In another study investigating the relationship between microvascular complications and serum albumin, the serum albumin levels were found to be significantly lower in patients with nerve conduction damage observed on ENMG (34). Similarly, in our study, the serum albumin levels of the diabetic patients with polyneuropathy were found to be lower compared to those without polyneuropathy.

Limitation

Our study has certain limitations. First, our sample size was too little to confirm the protective effects of serum electrolytes in diabetic polyneuropathy; therefore, there is a need for prospective studies with larger study populations. However, our study shows that Mg levels are significantly associated with the development of polyneuropathy in diabetic patients. This study can provide a new direction for understanding the possible risk factors and mechanism of polyneuropathy in patients with diabetes.

Conflict of interests: No authors have any conflicts of interest.

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RESEARCH ARTICLE

Abdullah Durhan[1*]
Marlen Suleyman[1]
Koray Kosmaz[1]
Abdullah Senlikci[1]
Ender Erguder[1]
Umit Mercan[2]
Mevlut Recep Pekcici[1]

[1]Ankara Training and Research Hospital, Department of General Surgery, Ankara, Turkey
[2]Şanlıurfa Mehmet Akif Inan Training and Research Hospital, Department of General Surgery, Sanlıurfa, Turkey

Corresponding Author:
Abdullah Durhan
Ankara Training and Research Hospital, Department of General Surgery Ankara, Turkey
Phone: +90 555 698 4527
mail:durhanabdullah@gmail.com

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www.konuralptipdergi.duzce.edu.tr

Does the Albumin to Globulin Ratio Predict Short-term Complications in Gastric Cancer Patients?

ABSTRACT

Objective: Gastric cancer (GC) is a cancer with poor prognosis despite advances in diagnosis and treatment methods, and postoperative morbidity and mortality rates are high. The aim of this study was to evaluate the predictive and early prognostic effect of the pre-treatment albumin to globulin ratio (AGR) in patients with gastric adenocarcinoma (GAC).

Methods: The study included male and female patients who were operated on with the diagnosis of GAC in our general surgery clinic between January 2016 and November 2020. The demographic and postoperative histopathological findings, postoperative complications and in-hospital mortality findings of the patients were evaluated retrospectively from the hospital data.

Results: Evaluation was made of a total of 70 patients operated on with the diagnosis of GAC. In the ROC curve analysis applied to the AGR ratio, the optimum cut-off value was 1.54. A statistically significant difference was found between the high (≥1.54) and low (<1.54) AGR groups in terms of intensive care unit (ICU) length of stay, serious postoperative complications, anastomotic leakage, and in-hospital mortality ($p = 0.050$, $p = 0.016$, $p = 0.011$; $p = 0.005$). In univariate analysis with postoperative serious complications, statistically significant results were found with age> 65 years, high American Society of Anesthesiologist (ASA) score and low AGR ($p = 0.035$, $p <0.001$, $p = 0.016$), whereas in multivariate analysis, only high ASA score was found to be an independent risk factor ($p = 0.031$).

Conclusions: The results of this study demonstrated the relationship between low AGR and serious postoperative complications, anastomotic leakage and early mortality risk in GAC. The AGR ratio, which can be calculated from the albumin and globulin values used in routine clinical practice, can be used as a suitable prognostic factor in this patient group to enable the clinician to take the necessary preoperative precautions.

Keywords: Gastric adenocarcinoma, albumin / globulin ratio, postoperative complication

Albümin-Globulin Oranı Mide Kanseri Hastalarında Kısa Dönem Komplikasyonları Öngörür mü?

ÖZET

Amaç: Gastrik kanser (GK), tanı ve tedavi metodlarındaki gelişmelere rağmen kötü prognozlu bir kanser olup, postoperatif morbidite ve mortalite oranları yüksek seyretmektedir. Bu çalışmada tedavi öncesi bakılan albümin-globülin oranı (AGO)' nun gastrik adeno kanser (GAK) hastalarındaki prediktif ve erken dönem prognostik etkisini değerlendirmeyi amaçladık.

Gereç ve Yöntem: Ocak 2016 ile kasım 2020 arasında, genel cerrahi kliniğimizde GAK tanısı ile opere edilen kadın ve erkek hastalar çalışmaya dahil edildi. Hastaların demografik ve postoperatif histopatolojik bulguları, postoperatif komplikasyonları ve hastane içi mortalite bulguları hastane veri datasından retrospektif olarak değerlendirildi.

Bulgular: GAK tanısı ile ameliyat edilen toplam 70 hastanın değerlendirmesi yapıldı. AGO oranına uygulanan ROC eğri analizinde en uygun kesme değeri 1.54 idi. Yüksek (≥1.54) ve düşük (<1.54) AGO grupları arasında yoğun bakım ünitesi (YBÜ) kalış süresi, postoperatif ciddi komplikasyon, anastomoz kaçağı ve hastane içi mortalite gelişimi için istatisksel anlamlı fark tespit edildi ($p=0.050$, $p=0.016$, $p=0.011$; $p=0.005$). Postoperatif ciddi komplikasyon ile univarite analizde >65 yaş, yüksek American Society of Anesthesiologist (ASA) skoru ve düşük AGO ile istatsisksel anlamlı sonuç bulunurken ($p=0.035$, $p<0.001$, $p=0.016$), multivarite analizde ise sadece yüksek ASA skoru, bağımsız risk faktörü olarak bulundu ($p=0.031$).

Sonuç: AGO ile GAK' da postoperatif ciddi komplikasyon, anastomoz kaçağı ve erken mortalite riski arasındaki ilişki çalışmamızda ortaya konmuş , bu hasta grubunda rutin klinik pratikle ölçülebilen düşük maliyetli AGO oranı preoperatif dönemde klinisyeni gerekli önlemleri alması için uyaran uygun bir prognostik araç olarak kullanılabilir.

Anahtar Kelimeler: Gastrik adenokanser, albümin/globülin oranı, postoperatif komplikasyon

INTRODUCTION

Gastric cancer (GC) is a cancer with poor prognosis despite advances in diagnosis and treatment methods, and postoperative morbidity and mortality rates are high. Although gastric cancer (GC) incidence and mortality rates have decreased in recent years, it still ranks as the third most common cause of cancer-related death (1).

The most widely used current classification system for GC in preoperative staging and predicting prognosis is the tumor, node, metastasis (TNM) staging system defined by the American Joint Committee on Cancer (AJCC) (2). Even in patients with the same TNM staging, early morbidity and survival may differ after curative surgical resection and / or systemic treatment. This has attracted the attention of researchers, and various studies have been conducted to show that there may be different immune mechanisms that affect the development and spread of cancer. It has been discussed in various studies that each patient may have different immune system responses to the development of cancer and that the morbidity and prognosis will be different because the ratio of protective immune system cells secreted against cancer cells and the cytokines secreted are different in each patient (3-6).

Globulin, which constitutes two main components of serum proteins and contains albumin and inflammatory cytokines, which are generally indicators of nutritional status, plays an important role in cancer immunity and prognosis (7). Studies have been conducted on the albumin to globulin ratio (AGR), some of which have included only albumin to predict survival in various types of cancer and others which more recently have evaluated albumin and globulin together (8-10). There are only a few studies in the literature that have examined the relationship between AGR rate and GAC, in terms of severe postoperative complications, early mortality and TNM staging.

Serum markers are easy to measure, reproducible and inexpensive tests, which may be useful in predicting the morbidity and mortality rates of GAC patients during postoperative follow-up, and for closer follow-up of high-risk patients. The aim of this study was to evaluate the predictive and prognostic effect of pre-treatment AGR in GAC patients.

MATERIAL AND METHODS

Approval for the study was granted by the Clinical Research Ethic Committee (decision no:2021/21:545, dated:15.01.2021). Informed consent was not required due to the retrospective nature of the study.

The study included male and female patients who were operated on with the diagnosis of gastric adenocarcinoma (GAC) in our general surgery clinic between January 2016 and November 2020. Patients were excluded from the study if they had chronic liver disease or hematological disease, had undergone surgery for a diagnosis of gastric malignancy other than GAC, had a diagnosis of synchronous or metachronous malignancy, had recurrent disease, had received preoperative chemotherapy and / or radiotherapy, who were operated on under emergency conditions due to obstruction, bleeding or perforation, or if the data were not available.

For retrospective evaluation of the patients, data were retrieved from the hospital database related to age, gender, ASA score, T stage, lymph node, metastasis status, TNM stage, postoperative complications of Clavien-Dindo grade ≥3, anastomotic leaks, albumin, total protein, globulin (total protein-albumin) values, length of stay in hospital and in intensive care unit (ICU), and early mortality (within the first postoperative month). The AGR value was calculated using the formula: AGR = serum albumin / total protein-serum albumin).

Tumor staging was applied according to the AJCC 8th edition TNM staging system published in 2017 (2). Postoperative complications were defined as those that developed in the hospital or within 1 month after surgery. Complication staging was determined according to the Modified Clavien Dindo Classification and severe complications were accepted as those of grade 3 or higher (11). The relationships between AGR and severe postoperative complications, TNM staging and early mortality were analyzed.

Statistical Analysis: Data obtained in the study were analyzed statistically using IBM ® SPSS vn. 23.0 software. Numerical data were expressed as mean ± standard deviation (SD), median (inquartile range) values or as percentages. The normal distribution of the data was determined by histogram graphics and the Kolmogrov Smirnov Test. The optimal cut-off level of AGR was determined using ROC curve analysis. In the comparison of demographic and clinicopathological features and postoperative outcomes between patients with low and high AGR, the Chi -square test or Fisher Exact Test were applied to categorical variables and the Student's t-test or Mann Whitney U-test to numerical variables. Binary logistic regression analysis was used to determine the factors affecting serious postoperative complications. A value of $p<0.05$ was considered statistically significant.

RESULTS

Evaluation was made of a total of 70 patients operated on with the diagnosis of GAC. The patients comprised 48 (68.6%) males and 22 (31.4%) females with a mean age of 64.24 ± 1.50 years. As a result of ROC curve analysis, the optimal cut-off level of AGR for serious postoperative complications was determined as 1.54 (AUC: 0.648 95% CI: 0.579-0.697 p = 0.001; 78% specificity and 72% sensitivity). According to the

optimal cut-off level of 1.54, there were 38 (54.2%) patients in the low AGR (<1.54) group and 32 (45.8%) patients in the high AGR (≥1.54) group. There was no significant difference between the groups in terms of age, gender, TNM stage and operation type. In the low AGR group, patients were determined to have significantly more comorbid diseases compared to the patients in the high AGR group (p = 0.021). The comparisons of demographic and clinicopathological features between the groups of low and high AGR are summarized in Table 1.

Table 1. Comparison of demographic and clinicopathological features between the groups of low and high AGR.

Variables	Total n=70	Low AGR (<1.54) n=38	High AGR (≥1.54) n=32	p value
Age (years)	64.24±13.50	65.84±12.03	62.34±15.03	0.283
Gender (male)	48(68.6)	28(73.7)	20(62.5)	0.315
ASA score				**0.021**
I	18(25.7)	7(18.4)	11(34.4)	
II	37(52.9)	18(47.4)	19(59.4)	
III	14(20)	12(31.6)	2(6.3)	
Operation				0.519
TG	37(52.9)	23(60.5)	14(43.8)	
SG	26(37.1)	12(31.6)	14(43.8)	
GE	2(2.9)	1(2.6)	1(3.1)	
LTG	1(1.4)	0(0)	1(3.1)	
LSG	4(5.7)	2(5.3)	2(6.3)	
TNM stage				0.320
1a	7(10)	2(5.3)	5(15.6)	
1b	11(15.7)	8(21.1)	3(9.4)	
2a	10(14.3)	3(7.9)	7(21.9)	
2b	14(20)	8(21.1)	6(18.8)	
3a	5(7.1)	4(10.5)	1(3.1)	
3b	15(21.4)	8(21.1)	7(21.9)	
3c	4(5.7)	2(5.3)	2(6.3)	
4	4(5.7)	3(7.9)	1(3.1)	
Albumin (g/dl)	38.72±5.19	37.06±4.34	40.70±5.49	**0.003**

Numerical values are given as mean±standard deviation or percentages. AGR: Albumin to Globulin Ratio, ASA: American Society of Anesthesiologists, TG: Total Gastrectomy, SG: Subtotal Gastrectomy, GE: Gastroenterostomy, LTG: Laparoscopic Total Gastrectomy, LSG: Laparoscopic Subtotal Gastrectomy, TNM:Tumor-Node-Metastasis.

Comparisons of postoperative outcomes between the groups of low and high AGR are summarized in Table 2. The length of hospital stay was similar between the groups, and length of ICU stay was significantly longer in patients with low AGR (p=0.050). Significantly more serious postoperative complications were determined in patients with low AGR (42.1% vs 15.6% p=0.016). No anastomotic leakage or in-hospital mortality were observed in patients with high AGR, and these complications were observed at a significant level in the low AGR group (p=0.011; p=0.005 respectively).

Table 2. Comparison of postoperative outcomes between the groups of low and high AGR.

Variables	Total n=70	Low AGR (<1.54) n=38	High AGR (≥1.54) n=32	p value
Hospital Stay (days)	9(7-12)	10(7-12)	9(7.25-11.75)	0.986
ICU Stay (days)	1(0-3)	1.5(0.75-4.25)	1(0-2)	**0.050**
CD ≥3 complications (n%)	21(30)	16(42.1)	5(15.6)	**0.016**
Anastomotic Leakage (n%)	5(7.1)	5(15.6)	0(0)	**0.011**
In-hospital mortality (n%)	6(8.6)	6(15.8)	0(0)	**0.005**

Numerical values are given as median(IQR) or percentage. AGR: Albumin to Globulin Ratio, ICU: Intensive Care Unit, CD: Clavien-Dindo.

In univariate analysis, advanced age (OR: 3.33 95% CI: 1.05-10.52 p=0.035), high ASA score (OR: 8.00 95% CI: 2.26-28.21 p<0.001) and low AGR (OR: 0.25 95% CI: 0.08-0.80 p=0.016) were found to be risk factors associated with serious postoperative complications (CD≥3). In multivariate analysis, high ASA score (OR: 0.22 95% CI: 0.56-0.87 p=0.031) was found to be an independent predictor of serious postoperative complications (Table 3).

Table 3. Univariate and Multivariate analysis of risk factors associated with serious postoperative complications.

Variable	Univariate Analysis			Multivariate Analysis		
	OR	**95% CI**	**p value**	**OR**	**95% CI**	**p value**
Age (>65 years)	3.33	1.05-10.52	**0.035**	-	-	-
High ASA score	8.00	2.26-28.21	**<0.001**	0.22	0.56-0.87	**0.031**
Low AGR (<1.54)	0.25	0.08-0.80	**0.016**	-	-	-

OR: Odds Ratio, CI: Confidence Interval, ASA: American Society of Anesthesiologists, AGR: Albumin to Globulin Ratio.

DISCUSSION

Although the rate of early diagnosis has increased due to widespread screening methods in the East Asian countries, GC is mostly diagnosed at the local advanced or late stage in western countries (1, 12). GC patients lose weight due to malnutrition in the advanced stage of the disease and their immune system is weakened. The close relationship between inflammation and cancer development has recently attracted the attention of researchers (5, 6).

Many recent studies have shown that the albumin protein synthesized by liver cells may be a prognostic marker for survival in various types of cancer (13-15). Serum albumin level is generally accepted to reflect the nutritional status of the body. Recent studies have also shown that the serum albumin level can also reflect the inflammatory state of the body (16). The main task of albumin is to maintain oncotic pressure in plasma and to carry various agents in serum. It has an antioxidant function against carcinogenesis with functions such as albumin, steroid hormone and calcium homeostasis, and the protection of DNA stabilization (17). The cause of hypoalbunemia in patients with GC is due to malnutrition, especially in advanced stages (18). More important than nutrition, proinflammatory cytokines (interleukin-6, interleukin-1 and tumor necrosis factor-alpha) secreted due to inflammation suppress albumin synthesis in the liver and increase vascular permeability, which causes albumin to pass into the interstitial space and consequently a decreased serum albumin level (19).

Serum globulin level has complex components such as acute phase proteins, immunoglobulins and interleukins and is closely related to the immune and inflammatory status of the body. It has been shown that high serum globulin levels caused by the accumulation of acute phase proteins and immunoglobulins generally reflect a persistent inflammatory response (20). Chronic inflammation markers play an important role in the metastasis, development, progression, and proliferation of tumor cells (21). High serum globulin has been reported to be associated with poor outcomes in prostate (22) and ovarian (23) cancers. However, many studies have found no relationship for the prognosis of gastric cancer (17, 24).

Serum albumin and globulin are the two main components of total protein in serum. While inflammation and changes in nutritional status in cancer patients cause different changes in albumin and globulin levels, both proteins are easily affected by dehydration and edema. AGR, however, takes serum albumin and globulin levels into account simultaneously, and can more precisely reflect the nutritional and inflammatory states of the body. Today, there are many studies in literature that have been conducted to predict survival for AGR in various cancer diseases. Guo et al stated that low AGR is associated with poor survival in digestive cancers (9). In a metanalysis of 15,356 patients with various types of cancer, Lv et al reported that low AGR before treatment was associated with poor survival (8).

There are also many studies of AGR predicting survival in GC patients. Low AGR was reported to be associated with poor survival in GC patients who underwent curative treatment (stage 1-3) by Liu et al (25), and in metastatic GC patients by Bozkaya et al. (7). In contrast, Xiao at al. (17) found that albumin was more valuable than AGR for the prediction of survival in a study in which, unlike other studies, albumin and AGR were compared with survival in GC patients.

Studies of albumin and AGR in GC patients are mostly related to survival, and there are few studies which have examined the relationships of albumin and AGR with the risk of postoperative complications. Ai et al. (10) stated that the rate of decrease in albumin values on the first day after surgery in GC patients may be a predictive factor for the risk of postoperative complications. In the current study, a statistically significant relationship

was found between low AGR and length of stay in ICU, serious postoperative complications, anastomotic leakage, and in-hospital mortality. In univariate analysis with serious postoperative complications, advanced age, high ASA score and low AGR were found to be statistically significant, while in multivariate analysis only a high ASA score was found to be an independent risk factor. This study is one of the few studies in literature to have evaluated the predictive value of AGR for the risk of serious postoperative complications, anastomotic leakage and early mortality.

Limitations

This study had some limitations, primarily that it was a single-center retrospective study with a small sample size of 70 patients. Second, due to insufficient data, it was not possible to evaluate medical conditions that could affect the patient's immune system. Third, there was no standard cut-off value for AGR. Until now, no combined method has been used to determine the AGR cut-off value, and various methods have been used to determine the best cut-off value. Different statistical methods can give different cut-off values and therefore a more accurate and predictive measurement can be made by determining a definitive cut-off value with a standardized statistical method.

Conclusion

The results of this study demonstrated the relationship between AGR and serious postoperative complications, anastomotic leakage and the risk of early mortality in gastric cancer patients. The AGR rate can be measured in routine clinical practice at no extra cost and can be used as an appropriate prognostic factor enabling the clinician to take the necessary preoperative precautions. Nevertheless, there is a need for further, multicenter, prospective randomized studies with larger samples to confirm these results.

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RESEARCH ARTICLE

Sahin Cepni[1]
Ahmet Firat[1]

[1] Department of Orthopaedics, Ankara Bilkent City Hospital, Ankara, Turkey

Corresponding Author:
Sahin Cepni
Department of Orthopaedics, Ankara Bilkent City Hospital, Ankara, Turkey
mail: ortdrsahin@yahoo.com

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The Short-Term Results of Unicondylar Knee Prosthesis in Patients with Body Mass Index Over 35

ABSTRACT

Objective: To evaluate the short-term results and complications of unicondylar knee prosthesis in obese patients with medial compartment arthrosis.

Methods: Unicondylar knee prosthesis was applied to 41 patients (36 females, 5 males; average age 56 years) with BMI >35 for the treatment of medial compartment arthrosis. Cementless Oxford phase 3 prosthesis was applied to all patients. Joint range of motion before and after surgery, VAS, OKS, and the KSS part 1 and part 2 scores of the patients were examined.

Results: Flexion was measured as mean 115° (90°- 135°) preoperatively, and 120° (90° - 130°) postoperatively, extension as mean 0° (-10°- 0°) preoperatively and 0° (-15° - 0°) postoperatively, with no significant difference determined. The KSS Part 1 score was mean 58 (range, 36-82) preoperatively, and 85 (range, 57 - 96) postoperatively (p <0.001). The KSS part 2 score was 50 (range, 35- 80) preoperatively and 90 (range, 51 -100) postoperatively (p <0.001). The Oxford score was mean 16 (range, 9 - 30) preoperatively, and 38 (range, 20 - 44) postoperatively (p <0.001). The differences between these scores were determined to be statistically significant. Complications developed in a total of 3 (%7,3) patients as periprosthetic joint infection in 1 patient (2.4%) and insert dislocation in 2 patients (4.9%).

Conclusions: The study findings demonstrated that the application of unicondylar knee prosthesis is effective and successful in obese patients treated for medial gonarthrosis. There is a need for further long-term studies to confirm these results.

Keywords: Unicondylar Knee Prosthesis, Medial Gonarthrosis, Obesity

Beden Kitle İndeksi 35 Üstü Olan Hastalarda Unikondiler Diz Protezi Kısa Dönem Sonuçlarımız

ÖZET

Amaç: Bu çalışmada medial kompartman artrozlu obez hastalarda unikondiler diz protezinin kısa dönem sonuçlarınının ve komplikasyonlarının değerlendirilmesi amaçlandı.

Gereç ve Yöntem: Medial kompartman artrozu tanısıyla BKİ >35 olan 41 hastaya (36 kadın 5 erkek;ort.yaş 56) unikondiler diz protezi uygulandı.Tüm hastalara Oxford faz 3 çimentosuz protez kullanıldı.Hastalar ameliyat öncesi ve sonrası eklem hareket açıklığı, VAS, OKS, KSS part 1 ve KSS part 2 skorlamasına göre değerlendirildi.

Bulgular: Hastaların preop fleksiyonları ortalama 115 (90; 135) derece postop fleksiyonları ortalama 120 (90; 130) derece, preop ekstansiyonları ortalama -5 (-10; 0) derece postop ekstansiyonları ortalama -5 (-15; 0) derece olup anlamlı fark saptanmamıştır.Hastaların preop KSS Part 1 58 (36; 82) postop 85 (57; 96)(p <0.001), preop KSS Part 2 50 (35; 80) postop 90 (51; 100) (p <0.001), preop Oxford skoru 16 (9; 30) postop 38 (20; 44) (p <0.001) olup istatistiksel olarak anlamlı bulunmuştur.1 hastada (%2.4) periprostatik eklem enfeksiyonu ,2 hastada (%4.9) insert çıkığı olmak üzere toplamda 3 hastada(%7,3) komplikasyon saptandı.

Sonuç: Bulgularımız,obez hastalarda unikondiler diz protezi uygulamasanın medial gonartroz tedavisinde kısa dönemde etkili ve başarılı olduğunu göstermektedir.Uzun dönem sonuçlar için daha uzun takip süreli çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Unikondiler Diz Protezi, Medial Gonartroz, Obezite

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konuralptipdergi@duzce.edu.tr
konuralptipdergisi@gmail.com
www.konuralptipdergi.duzce.edu.tr

INTRODUCTION

Knee osteoarthritis is one of the most common joint problems (1). Prolonged life expectancy, an increase in obesity rates and more frequent sedentary lifestyles have caused an increase in knee osteoarthritis (2). Generally, knee osteoarthritis starts in the medial compartment, and unicondylar knee prosthesis (UKP) is an effective treatment method for unicompartmental arthrosis (3, 4).

Patient selection plays an important role in the success of UKP. Despite the view in literature that obesity decreases functional results and implant survival in UKP (5.6), recent studies have shown successful results for obese patients (7, 8). The effect of body mass index (BMI) on functional results and complications after UKP remains controversial.

The aim of the our study was to evaluate the short-term results of patients with BMI >35 who were applied with UKP for a diagnosis of medial compartment arthrosis.

MATERIAL AND METHODS

Approval for the study was granted by the local Ethics Committee (Ankara City Hospital Ethics Committee,ethics committee number-72300690-799) and informed consent was obtained from all patients. A retrospective examination was made of the prospectively collected data of 153 patients applied with UKP between October 2015 and January 2019.

The patients included in the study were with medial compartment arthrosis; <10° varus deformity, < 15° flexion contracture, intact anterior cruciate ligament, and deformity which could be corrected as determined with stress tests. Patients were excluded from the study if they had a history of surgery on the ipsilateral knee, if arthrosis in the affected knee had developed asssociated with post-traumatic deformity or septic sequelae, if they had an inflammatory disease, or could not be contacted during the follow-up period. A total of 41 patients who met these criteria and who had a body mass index above 35 who participated in a final follow-up examination for clinical and radiological evaluation were included in the study.

Preoperatively, all patients were evaluated with orthoroentgenogram, standing anterior-posterior and lateral radiographs and to determine that any varus deformity could be corrected and that there was sufficient lateral cartilage thickness, anterio-posterior radiographs were taken. Postoperatively, the patients were evaluated radiologically with orthoroentgenogram and standing anterior-posterior and lateral radiographs. At the final follow-up examination, patients were evaluated functionally with joint range of motion (ROM), visual analog scale (VAS), the Oxford Knee Score (OKS) and the Knee Society Score (KSS) part 1 and part 2. The VAS is the most widely used tool for estimating both severities of pain and to judge the extent of pain relief (7). The VAS pain scale is an 11-point scale ranging from 0 to 10 with the “worst possible pain” being labeled with a 10 and a “sad face” and “no pain” labeled as a 0 and a “happy face.” The OKS is a 12-item questionnaire specifically designed and developed to assess function and pain after knee arthroplasty (9). The KSS consists of two parts: a knee score, which rates the knee in terms of pain, range of movement, and stability, and a function score, which rates the ability of the patient to walk, the use of ambulatory aids and the ability to climb stairs (10). The KSS, the subjective component of the Knee Society Score, is common in usage and has been validated in numerous studies as a reliable way to evaluate post-operative outcomes after knee arthroplasty.

Surgical Technique: All the patients were administered 2 gr cefazolin prophylaxis 30 mins before the operation. The knee to be operated on was prepared with a knee holder on a standard table so that the knee was in at least 120° flexion. A minimally invasive technique under tourniquet was applied to all patients. A longitudinal incision of 8-10 cm was made, starting from 2 cm above the superior edge of the medial patella and extending to the medial tibial tubercle. The joint was entered with a medial parapatellar arthrotomy, then when it was checked that the anterior cruciate ligament was intact and functional, it was decided to continue with the medial UKP operation. Osteophytes were removed from the intercondylar notch and medial, then the tibial and femoral cuts were made.

After equalisation of the flexion and extension gaps, the components were placed cementless. A mobile polyethylene insert of appropriate thickness was placed, the layers were closed in sequence and the operation was terminated. An Oxford Phase 3 type medial unicondylar prosthesis with a mobile insert was used in all patients (Oxford Knee, Biomet, Swindon, UK). On postoperative day 1, active knee movements were applied and the patients were mobilised with support.

Statistical Analysis: Data obtained in the study were analysed statistically using Statistical Package for the Social Sciences (SPSS) Statistics for Windows, vn 22.0 (IBM, Armonk, NY, USA) and MS-Excel 2016 software.

Conformity of continuous variables to normal distribution was assessed with the Shapiro Wilk test and graphic methods. Data that did not meet parametric assumptions were stated as median (minimum-maximum) values. In the comparisons of two dependent variables, as the distribution of differences was examined and parametric assumptions were not met, the Wilcoxon test was applied. A value of $p<0.05$ was accepted as statistically significant.

RESULTS

The median age of the patients was 56 years (47-75) and median BMI was calculated as 38.2 (35-45).

The mean follow-up period was 23 months (12-38). The demographic data of the patients are shown in Table 1.

Table 1. Demographic Data of the Patients

	Median (minimum; maximum)
Age (years)	56 (47;55)
Follow-up period (months)	23 (12;38)
BMI	38.2(35;45)
Affected side	
Right	20 (58.8%)
Left	21 (51.2%)
Gender	
Female	36 (87.8%)
Male	5 (12.2%)
COMPLICATIONS	
None	38 (92.7%)
Infection	1 (2.4%)
Insert displacement	2 (4.9%)

Shapiro Wilk test results; BMI: body mass index

Flexion was measured as mean 115° (90°-135°) preoperatively, and 120° (90°-130°) postoperatively (p=0.176), extension as mean -5° (-10°-0°) preoperatively and -5° (-15°-0°) postoperatively(p=0.886), with no significant difference determined (Table 2).

Table 2. Comparison of preoperative and postoperative evaluation criteria

	Preoperative	**Postoperative**	**Test**	**Statistic**
	Median (min; max)	**Median (min; max)**	**Z**	**p**
Flexion (degrees)	115 (90; 135)	120 (90; 130)	1.354	0.176
Extension (degrees)	-5 (-10; 0)	-5 (-15; 0)	0.144	0.886
KSS Part 1	58 (36; 82)	85 (57; 96)	4.976	**<0.001**
KSS Part 2	50 (35; 80)	90 (51; 100)	5.578	**<0.001**
Oxford Knee Score	16 (9; 30)	38 (20; 44)	5.580	**<0.001**
VAS Score	7 (4; 9)	2 (0; 4)	5.552	**<0.001**

Z= Wilcoxon test results KSS: knee society score,VAS: visual analogue scale

The VAS scores of the patients decreased by mean 5 points postoperatively and the difference from the preoperative values was determined to be statistically significant (p<0.001) (Table 2). The KSS Part 1 score was mean 58 (36-82) preoperatively, and 85 (57 - 96) postoperatively **(p<0.001)**. The KSS part 2 score was 50 (35- 80) preoperatively, and 90 (51 -100) postoperatively **(p <0.001).**

The Oxford score was mean 16 (9 - 30) preoperatively, and 38 (20 - 44) postoperatively **(p <0.001)**. The differences between these scores were determined to be statistically significant (Table 2). Complications developed in a total of 3 patients as periprosthetic joint infection in 1 patient (2.4%), and insert dislocation in 2 patients (4.9%). In 1 of these cases, a thicker insert was applied, and in the other, semi-restricted revision knee prosthesis was applied because of the development of internal lateral ligament failure.

DISCUSSION

The results of this study showed that a significant improvement was obtained postoperatively in the knee scores of obese patients applied with the Oxford phase 3 UKP. Postoperative complications developed in 3 (7.3%) patients. Plate et al reported mean OKS of 34 at 6 months after UKP operation and stated that it was not related to BMI (11). Woo et al also reported that obesity had no effect on UKP results (12). In a study of 254 patients with a minimum follow-up period of 7 years, Cavaignac et al reported that there was no correlation between obesity and KSS part 1 and KSS part 2 (13). In our study, the mean OKS of 38 was consistent with previous findings in literature.

There are several studies in literature showing the effect of BMI on UKP survival. It has been reported that a high BMI reduces implant survival in fixed implant prostheses (14, 15). In contrast, it has been suggested that because of the mobile insert in Oxford UKP, obesity does not affect the short and mid-term results of prosthesis survival (16,17).

Although Deshmukh and Scott reported patient weight of >90 kg to be a contra-indication (18). Murray et al reported that even high BMI values of 45-50 were not a reason to restrict UKP used with a mobile insert (16). Many studies have claimed that excessive weight leads to early implant loss by increasing the stress in the implant interface (5, 6,19), but there are also studies stating the opposite (20-22). In a 5-year study of patients with BMI >30, Kuipers et al reported a survival rate of 84.7% for the Oxford UKP (22). In another study by Seth A et al, the Oxford UKP survival rate in patients with BMI >40 was reported as 91.7% at the end of 2 years, and 86.3% at the end of 5 years (23). In a mean 5.6 year follow-up of 1000 cases applied with Oxford UKP, Pandit H et al reported a prosthesis survival rate of 96% (17). In a large-scale study of 25,334 UKP and 75, 996 total knee prosthesis (TKP) patients, TKP survival was reported to be 94.6%, and UKP 87%. The most common reason for revision in UKP cases is aseptic loosening (24). In our study, the mean prosthesis survival rate at the end of 2 years was found to be 92.7%. The long-term success of UKP can be maintained with knee kinematics similar to those of a healthy knee. Several clinical and biomechanical studies have shown that with careful patient selection and appropriate surgical technique, ROM was better following UKP than TKP. There are studies that have reported that UKP in the correct placement is 40% more resistant to knee loading than normal knees (25). Woo et al reported that all periprosthetic fractures associated with UKP included the tibial plateau, and these fractures were seen 3-fold more in patients with BMI >35 compared to normal weight positions (12). In our study, no periprosthetic fractures occurred in any patient.

Previous studies have reported higher infection rates in obese patients than in normal weight patients following joint replacement (25). Similarly, morbidly obese patients have been stated to be at higher risk of medical complicatios than normal weight patients (5). In our study, prosthesis infection was seen in 1 (2.4%) patient .No systemic complications developed postoperatively in any of the current series, who comprised 8 cases of ASA 1, 20 of ASA 2, and 13 of ASA 3.

In conclusion, the results of the current study demonstrated that BMI was not a contra-indication for UKP, and did not increase the complication rate compared to that of a normal weight patient population. Nevertheless, there is a need for further long-term follow-up studies with a greater number of cases to provide long-term results.

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RESEARCH ARTICLE

Munise Daye[1*]
Inci Mevlitoglu[2]
Mine Sahingoz[3]
Tahir Kemal Sahin[4]

[1]Necmettin Erbakan University, Meram Medicine Faculty, Department of Dermatology, Konya, Turkey
[2]Kadikoy Medicana Hospital, Department of Dermatology, Istanbul, Turkey
[3]Necmettin Erbakan University Meram Medicine Faculty, Department of Psychiatry, Konya, Turkey
[4]Necmettin Erbakan University, Meram Medicine Faculty, Department of Public Health, Konya, Turkey

Corresponding Author:
Munise Daye
Necmettin Erbakan University, Meram Medicine Faculty, Department of Dermatology, Konya, Turkey
Phone: +90 3322237912
mail: dr_munise@yahoo.com

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konuralptipdergisi@gmail.com
www.konuralptipdergi.duzce.edu.tr

Alexithymia and Behçet's Disease

ABSTRACT

Objective: Behçet's Disease (BD) is an immunoinflammatory systemic disease. In young adults it seen as genital ulceration, uveitis and oral aphthae. In some patients, BD may affect the central nervous system and some psyschiatric symptoms may accompany this disease. There are few studies in the literature evaluating the relationship between BD and alexithymia. In this study, the relationship between BD and alexithymia is evaluated.

Methods: Fifty patients diagnosed according to the International Study Group for Behçet's Disease diagnostic criteria and fifty age and gender-matched healthy individuals were included in the study. Turkish versions of Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI) and Toronto Alexithymia Scale (TAS-20) were applied to the patients and controls.

Results: According to TAS-20 scale, alexithymia was classified as: non-alexithymia, moderate and severe alexithymia. In the classification of TAS, there was a significant difference between the cases and the control group (p = 0.019).In patients with BD, alexithymia was 6 times higher than control group (OR = 6.139)(95% CI = 1,657-23.913).

Conclusions: Behçet's disease is strongly associated with alexithymia. Recognizing of these psychiatric symptoms is important for management of BD patients. Psychotherapeutic interventions should planned by dermatologist.

Keywords: Behçet's Disease, Alexithymia, Toronto Alexithymia Scale

Aleksitimi ve Behçet Hastalığı

ÖZET

Amaç: Behçet Hastalığı (BH) immunoinflamatuar sistemik bir hastalıktır. Genç erişkinlerde sıklıkla genital ülserasyon, üveit ve oral aft ile seyretmektedir. Bazı hastalarda BH santral sinir sistemini etkileyebilmektedir ve bazen psikiyatrik semptomlar hastalığa eşlik edebilmektedir.Literatürde BH'nın aleksitimi ile ilişkisini değerlendiren az sayıda çalışma bulunmaktadır. Bu çalışmada BH ve aleksitimi arasındaki ilişki değerlendirilmektedir.

Gereç ve Yöntem: İnternasyonal Çalışma Grubu Behçet hastalığı tanı kriterlerine göre tanı almış 50 olgu çalışmaya dahil edildi. Olgulara, yaş cinsiyet eşlemeli 50 kişilik kontrol grubu oluşturuldu. Beck Depresyon Envanteri (BDE), Beck Anksiyete Envanteri (BAE) ve Toronto Aleksitimi s kalasının (TAS) Türkçe versiyonu olgulara ve kontrollere uygulandı.

Bulgular: TAS skalasının aleksitimi: yok, orta ve şiddetli aleksitimik olarak sınıflandırıldı. TAS sınıflandırılmasında olgu ve kontrol grubu arasında anlamlı fark saptandı (p = 0.019). Behçet hastalığı olan olgularda aleksitimi kontrole göre 6 kat daha fazlaydı (OR = 6.139) (95% CI = 1,657-23.913).

Sonuç: Behçet hastalığı aleksitimi ile kuvvetle ilişkilidir. Bu psikiyatrik semptomları farketmek Behçet olgularını tedavi etmek açısından önemlidir. Dermatologların olgularında psikoterapotik değerlendirmeleri unutmaması gerektiğini düşünmekteyiz.

Anahtar Kelimeler: Behçet Hastalığı, Aleksitimi, Toronto Aleksitimi Skalası

INTRODUCTION

Turkish physician Prof. Hulusi BEHÇET defined Behçet's disease (BD) in 1937. It is an immunoinflammatory system disease and widely seen in in young adults as genital ulceration, uveitis and oral aphthae. Moreover, it can be characterized by vasculitis of veins and arteries. The exact etiopathogenesis of Behçet's disease has not been clarified (1).

In some patients, BD may affect the central nervous system and some psychiatric symptoms may accompany this disease. These symptoms can be caused by central nervous system involvement in BD patients. It has been reported that the incidence of psychiatric symptoms is about 85% after the first symptoms of BD. Although the etiology of these symptoms is not clear, the progression of BD, involvement of central nervous system, using steroid for treatment in some patients and functional deterioration are thought to be related with the psychiatric symptoms (2,3,4). Alexithymia is a personality disorder of cognitive function and emotional disturbance and described as the state of being alienated at the level of which one cannot express himself or herself. It causes a reduced symbolic thinking and limited ability to verbally express emotions which cannot be differentiated and identified well. Some studies reported that the prevalence of alexithymia is approximately 7–9% and it is a post-traumatic disorder seen generally in schizoid structure (5,6). The word "alexithymia" emerged with the integration of the words a- (not), lexis (words, speech) and thymos (anger, nervousness, emotion) in Greek, introduced firstly by Sifneos in 1973. Its definition as "no speech for emotions" has been changed and refined since its first introduction and actual definition can be considered as the following factors: (i) difficulty in describing feelings to other people;(ii) difficulty in distinguishing between feelings and the bodily emotions (iii) constricted imaginative processes; and (iv) an externally oriented stimulated sensation (7). Other pathologies can be accompanied in alexithymia such as somatoform disorders, alcoholism, drug addiction, posttraumatic stress, asthma, depression, eating disorders (EDs) and so on (8). Furthermore, people with alexithymia have difficulty in distinguishing and appreciating the emotions to regulate in the neuroendocrine and, also, autonomic system which causes some somatic diseases. In the etiology of alexithymia, many factors such as neurobiological deficits, variations in brain neuronal system or genetic influences can play a role. Numerous physiological causes of alexithymia are reported. However, inconsistencies exist between the information given about the pathways. It is known that alexithymia is associated with depression, psychoticism and anxiety. Neuroticism and introversion are also known to have a positive correlation with alexithymia. On the other hand, it is a fact that extraversion and sociability are in a negative relationship with alexithymia (9).

Taylor et al created Toronto Alexithymia Scale (TAS). This is the most reliable measure to evaluate alexithymia (10). Therefore, it is observed that individuals who have difficulty in expressing emotions are at risk for some specific dermatological diseases. Although previous studies have shown conflicting results, it is seen that acne, psoriasis or alopecia areata diseases are accompanied by alexithymia (11,12,13).

There were studies about the association of BD with depression and anxiety but not enough about the relationship between alexithymia and BD. In out patient practice, we observed that the patients with BD have decreased symbolic thinking, and restricted ability to identify, differentiate and verbally express emotions. The aim of this study was to establish whether presence of alexithymia in Behçet patients.

MATERIAL AND METHODS

Study Design: This study was approved by the institutional ethics committee. All patients were recruited from Dermatology outpatient clinic. After explaining purpose of the study to the patients, those who were willing to participate were enrolled to study.

A total of 50 patients (25 men, 25 women) diagnosed with BD according to the criteria of the International Study Group for Behçet's Disease (14) and 50 age-, sex-, economic status- and education status matched healthy control volunteers (24 men, 26 women) were included.

Exclusion criteria for the patient group were as follows: cognitive impairment,having a psychiatric disease, neurologic involvement and using systemic steroids, having any skin diseases such as psoriasis, vitiligo, alopecia areata related with alexithymia. Exclusion criteria for the control group were as follows: cognitive impairment,having a psychiatric disease, neurologic involvement, having any skin diseases such as psoriasis, vitiligo, alopecia areata related with alexithymia. Patients and healthy controls were evaluated with Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI) and Turkish version of TAS-20.

BDI is a self-rating 5 point-Likert-type scale consisting of 21 items which evaluates the level of depression (15).The Turkish version of the scale was reliable and valid and used for the study. The test was scored as 0-9= Minimal, 10-16= Mild, 17-29= Moderate, 30-63= Severe depression (16).

BAI is a self-rating 5 point-Likert-type scale composed of 21 items of anxiety (17). Each question is rated from zero to three points. The Turkish version of the scale was reliable and valid and used for the study. The total score shows the level of anxiety (18).

Taylor et al created Toronto Alexithymia Scale (TAS). This is the most reliable measure to evaluate alexithymia (10). The first form has changed and has reached its current state (TAS-20) of 20 items (19). TAS-20 is a self-report scale consisting of 20-items structured by three factors. First factor describes the difficulty in identifying feelings (DIF=TAS-A), second factor is related with the difficulty in describing feelings (DDF=TAS-B), and third one measures the externally oriented thinking (EOT-TAS-C). All items are rated on a 5-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree), with five items negatively keyed. The range of TAS-20 is between 20 to 100, and the score above 61 is defined as alexithymia, whereas below 51 as non-alexithymia. If the score is between 52 and 60, then it can be suggested as intermediate alexithymia. It was shown that Turkish adaptation of the scale is valid and reliable (20).

Statistical Analyses: The analyses were performed by SPSS 11.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were calculated and presented as mean ± SD for continuous variables / Median (IQR) for discrete variables, frequency and percentages for categorical variables. Continuous variables were detected by Kolmogrov–Smirnov test whether they are distributed normally. In comparison of two independent groups . Student t-test and Mann-Whitney U test as a non-parametric test were used and Kruskal-Wallis test was used to compare multiple groups. Chi-square test was used to determine the relation between categorical variables. The relationship between depression, anxiety and alexithymia was analyzed by Spearman's Rho correlation test. In all analyses, $p<0.05$ was considered as statistically significant for 5% type-I error.

RESULTS

Patients with BD were evaluated in terms of gender and alexithymia, and it was found that 32% of female and 20% of males had alexithymia, 28% of female, 24% of males had moderate alexithymia. In patients with BD there was no significant difference between alexithymia and gender (*p=0.488*). There was no significant difference between median values of the disease duration in terms of alexithymia status of patients with BD (*p=0.588*). Other sociodemographic features of patients were shown on Table 1.

Table 1 The comparison of sociodemographic features of patients with BD and controls in terms of control variables

	BD patients	**Control**	*p*
Age (Mean±SD)	37.7±11.8	36.4±11.4	*0.566*
	n (%)	**n (%)**	
Sex			
Female	25 (50)	26 (52)	*0.841*
Male	25 (50)	24 (48)	
Education			
Primary school	22 (44)	18 (36)	
Secondaryschool	9 (18)	9 (18)	
High school	15 (30)	17 (34)	*0.819*
University	4 (8)	6 (12)	
EconomicStatus(TL)			
≤500	3 (6)	5 (10)	
500-1500	40 (80)	41 (82)	*0.514*
≥1500	7 (14)	4 (8)	

BD:Behçet Disease

TAS is the important classification method for alexithymia patients and significant difference was found between control and patient groups in terms of TAS-20 scores which is higher in patients' group (*p=0.003*).The comparison of BD patients and controls in terms of TAS, BDI, BAI were in Table 2.

Table 2. The comparison of patients with BD between controls in terms of TAS-20, BDI, BAI

	Patients with BD	**Controls**	
	Mean±SD	Mean ±SD	*p*
TAS-20	50.76±12.69	42.96±12.87	*0.003**
TAS-A	14.50±5.50	12.26±4.58	*0.029**
TAS-B	12.70±3.55	10.68±3.79	*0.007**
TAS-C	23.36±6.49	19.82±7.28	*0.012**
BDI	10.5 (9.00)	7.5 (7.50)	*0.100*
BAI	8.00 (3.00-18.25)	8.00 (3.75-11.00)	*0.374*

**: Significant according to p<0.05 level*

BD:Behçet Disease, SD: standard deviation, TAS-20, TAS-A,TAS-B,TAS-C: Toronto Alexithymia Scale 20, A,B,C, BDI:Beck Depression Inventory, BAI: Beck Anxiety Inventory

The risk of having severe alexithymia in patients was about 6 times more than patients who had no alexithymia(OR = 6.14 (95% CI = 1.58 - 23.91); *p=0.002*),and the ratio was significant. The relationship between patients with BD and controls in terms of alexithymia are shown in Table 3. There was no statistically significant difference between median scores of BDI (*p=0.100*) and BAI (*p=0.374*) between patient and control groups.

Table 3. The relationship between patient with BD and controls in terms of subtypes of alexithymia

Alexithymia	**Behçet Disease Patients (n)**	**Controls (n)**	**OR (95% CI)**	***p***
None	24	34	1	- - -
Moderate	13	13	1.42 (0.56-3.59)	*0.108*
Severe	13	3	6.14 (1.58-23.91)	*0.002**

*OR: Odds ratio, CI: Confidence Interval, *: Significant according to p<0.05 level*

However, in patient group, BAI scores were significantly higher in severe alexithymia patients than other subgroups of alexithymia (*p=0.019*) whereas BDI scores were similar in subgroups and with control group (*p=0.238*).

Moreover, we have calculated the correlation coefficients between depression, anxiety and alexithymia scores in BD patients. We found that there was a moderate positive correlation between Behçet's disease and anxiety (r=0.69, *p<0.001*), weak correlation between depression and alexithymia (r=0.33, *p=0.020*), weak association between anxiety and alexithymia (r=0.30, *p=0.037*).

DISCUSSION

Recurrent oral ulcers, ocular involvement, genital ulcers, and skin lesions are main symptoms of BD, and Behçet disease is chronic, multisystemic inflammatory disorder. Arthritis, gastrointestinal lesions, vasculitis, epididymitis, and central nervous system lesions are the other manifestations of BD patients (21). Studies reporting the relationship between BD and anxiety, depression are available in literature (22). Alexithymia is a personality disorder of cognitive function and emotional disturbance and described as the state of being alienated at the level of which one cannot express himself or herself. There are a few studies in the literature evaluating the relationship between BD and alexithymia. We found that BD is strongly associated with alexithymia. In our study; the risk of having severe alexithymia in BD patients was about 6 times more than patients who had no alexithymia and this ratio was significant. In a study; investigators applied TAS-26 scale to 34 BD patients and they found the scores significantly different between patients with BD and controls, also Hamilton depression scale (HAM-D) and BAI scores were significantly different. The stress–immune system axis is important for BD. The remission and relapse period of the disease results damage in the functions of various systems of BD patients. In the progressive course from stress to illness, life events can be a stimulatory factor in promoting the disease by impairing homeostasis. So, because of these patients need to adapt themselves secondarily to situation. In this time coping mechanisms are important (23). Stress is the main cause of anxiety and depression (24). Berthozet al. showed a positive and significant correlation between the level of alexithymia and the state anxiety in their study among 144 university students. It has been argued that reduction in anxiety may cause a reduction in alexithymia and alexithymia has developed a protective defensive mechanism against pain and disturbing feelings (25). Karukiviet al. found a correlation between alexithymia and anxiety, and the patients with anxiety disorders tend to become alexithymic to prevent disturbing bodily sensations (26). Our study showed no difference between patients and controls for anxiety and depression but BAI scores were significantly higher in severe alexithyhimic patients than other subgroups of alexythimia. So; we evaluated if there were linear association with Behçet's disease patients' depression, anxiety, alexithymia parameters or not. We found that there was a moderate linear association with BD and anxiety, mild association between depression and alexithymia, mild association between anxiety and alexithymia. This may be similar to the literature but our patient group sample size was smaller. If we had studied this topic in a larger group, we could find the same association as the literature. So; we thought alexiyhmia is more related with anxiety than depression in Behçet disease. And treatment of anxiety will help to reduce alexithymia in BD patients.

Alexithymic people are not successful to regulate distressing emotions, and hence, this case causes irritated responses in the neuroendocrine and autonomic system due to some somatic diseases. Many researchers working on this issue tried to determine the physiological pathways of alexithymia, but consistent results have not been achieved (27). However, it is clear that alexithymia patients having difficulty to overcome the stress are at risk of the emerging dermatologic diseases. We found that there was no significant difference in median values of the disease duration and alexithymia status of patients with BD. Therefore, we think that the duration of the disease isn't playing a role in alexithymia process but stress of being BD or severity of disease may play a role in alexithymic people.

Talamonti et al; evaluated the relationship between psoriasis and alexithymia in 250 psoriasis patient and 215 healthy individuals with TAS-20 scale. According to this study psoriasis patients had significant alexithymia features (32.4 vs. 9.3%), and there wasno significant differences between alexithymia and patients with severe and mild psoriasis (13).Korkoliakou et al. evaluated 108 psoriasis patients with TAS- 20 and reported that there is a relationship between psychopathology and alexithymia. They found that female patients with psoriasis had higher somatization, depression, anxiety, phobic anxiety, and psychoticism scores compared to male patients. The significance of alexithymia understood because of alexithymia patient's presentation. They have higher somatization, interpersonal sensitivity, anxiety, and phobic anxiety levels than non-alexithymia patients (29). Sellami et. al. found no significant differences between alopecia areata (AA) and alexithymia prevalence and the control group, but overall alexithymia prevalence was high. They reported that this study had no clear results about a possible relationship between alexithymia and AA and they suggested that this topic required more studies to clarify this association between two disease (14).Vitiligo is another dermatologic disease that

was evaluated for alexithymia. A study, performed by Picardi et al. on vitiligo patients, showed that TAS-20 scores of patients were significantly higher than control cohort and the number of alexithymia patients in severe and moderate classifications are higher almost twice than in vitiligo patients (30). Bozkurt et al. found a significantly greater rate of alexithymia in patients with seborrheic dermatitis compared with controls according to TAS-20 (31). In contrast to these results; Sunay et al. evaluated association acne vulgaris with alexithymia and they reported that there was no relationship between acne vulgaris and alexithymia (12). Cömert et al. didn't find any statistically significant difference in the average of alexithymia scores between the seborrheic patient and control groups. However, patients with high anxiety scores were found to be more alexithymic in this study (32). Moreover, our results showed patients with BD had severe or moderate alexithymia six times higher than controls according to TAS-20 scores. According to literature review, this is the first study evaluating the relationship between BD and alexithymia with TAS-20.

We found significant difference between patients with BD and controls regarding alexithymia TAS-20 scores and subgroups of TAS-A, TAS-B, TAS-C. Patients with BD significantly had higher scores than controls on TAS-20, and odd's ratio of severe alexithymia patients had nearly six times higher than the patients in reference category.

CONCLUSION

We found that Behçet's disease is strongly associated with alexithymia. Because of this BD patients require a more detailed examination for psychiatric status, and further studies are required to find possible association of alexithymia and Behçet disease. Alexithymia is an antecedent thing or a consequence thing in the development of Behçet disease. The results show that a psychiatric evaluation and the treatment of alexithymia is important in early follow-up of BD patients. The treatment of psychiatric disorders may also affect the tolerance of stress in these patients to reduce relapses. We think that psychiatric symptoms can accompany BD because of its long term clinical course. These patients must take appropriate psychotherapeutic interventions

Limitations: If we enrolled two- or three-fold higher BD patient and control group there may be a difference of anxiety and depression scores. In this study, we didn't calculate the disease activity index. Severity of disease may play a role in being alexithymic individual..

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RESEARCH ARTICLE

Bora Tetik[1]
Hasan Ucuzal[2]
Seyma Yasar[2]
Cemil Colak[2]

[1]Department of Neurosurgery, Faculty of Medicine, Inonu University, Malatya, Turkey
[2]Department of Biostatistics and Medical Informatics Faculty of Medicine, Inonu University, Malatya, Turkey

Corresponding Author:
Seyma Yasar
Department of Biostatistics and Medical Informatics Faculty of Medicine, Inonu University, Malatya, Turkey
Phone: +90 507 639 7121
*mail:*seyma.yasar@inonu.edu.tr

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Automated Classification of Brain Tumors by Deep Learning-Based Models on Magnetic Resonance Images Using a Developed Web-Based Interface

ABSTRACT

Objective: Primary central nervous system tumors (PCNSTs) compose nearly 3% of newly diagnosed cancers worldwide and are more common in men. The incidence of brain tumors and PCNSTs-related deaths are gradually increasing all over the world. Recently, many studies have focused on automated machine learning (AutoML) algorithms which are developed using deep learning algorithms on medical imaging applications. The main purposes of this study are -to demonstrate the use of artificial intelligence-based techniques to predict medical images of different brain tumors (glioma, meningioma, pituitary adenoma) to provide techicalsupport to radiologists and -to develop a user-friendly and free web-based software to classify brain tumors for making quick and accurate clinical decisions.

Methods: Open-sourced T1-weighted magnetic resonance brain tumor images were achieved from Nanfang Hospital, Guangzhou, China, and General Hospital, Tianjin Medical University, To construct the proposed system which web-based interface and the deep learning-based models, the Keras/Auto-Keras library, which is employed in Python's programming language, is used. Accuracy, sensitivity, specificity, G-mean, F-score, and Matthews correlation coefficient metrics were used for performance evaluations.

Results: While 80% (2599 instances) of the dataset was used in the training phase, 20% (465 instances) was employed in the testing phase. All the performance metrics were higher than 98% for the classification of brain tumors on the training data set. Similarly, all the evaluation metrics were higher than 91% except for sensitivity and MCC for meningioma on the testing dataset.

Conclusions: The results from the experiment reveal that the proposed software can be used to detect and diagnose three types of brain tumors. This developed web-based software can be accessed freely in both English and Turkish at http://biostatapps.inonu.edu.tr/BTSY/.

Keywords: Brain Tumors, Deep-Learning Strategy, Keras/Auto-Keras, T1-Weighted Magnetic Resonance Imaging.

Geliştirilmiş Bir Web Tabanlı Arayüz Kullanarak Beyin Tümörlerinin Manyetik Rezonans Görüntülerinde Derin Öğrenme Tabanlı Modellerle Otomatik Sınıflandırılması

ÖZET

Amaç: Primer santral sinir sistemi tümörleri (PSSST), dünyada yeni teşhis edilen kanserlerin yaklaşık %3'ünü oluşturmaktadır ve erkeklerde sıklığı daha yüksektir. Beyin tümörlerinin ve PSSST'lere bağlı ölümlerin görülme sıklığı tüm dünyada giderek artmaktadır. Son zamanlarda birçok çalışma, tıbbi görüntüleme uygulamalarında derin öğrenme algoritmaları kullanılarak geliştirilen otomatik makine öğrenimi (AutoML) algoritmalarına odaklanmıştır. Bu çalışmanın temel amacı, radyologlara destek sağlamak için beyin tümörlerinin (glioma, menenjiom hipofiz adenomları) tıbbi görüntülerinin analizinde yapay zeka tabanlı tekniklerin kullanımını göstermek, hızlı ve doğru tanı konulması için beyin tümörlerini sınıflandıran kullanıcı dostu ve 'ücretsiz web tabanli bir yazılım geliştirmektir.

Gereç ve Yöntem: Açık kaynaklı T1 ağırlıklı manyetik rezonans beyin tümörü görüntüleri Nanfang Hastanesi, Guangzhou, Çin ve Genel Hastane, Tianjin Tıp Üniversitesinden elde edildi. Önerilen web tabanlı arayüzün ve derin öğrenme tabanlı modellerin oluşturulması için Python'un programlama dilinde kullanılan Keras / Auto-Keras kütüphanesi kullanıldı. Performans değerlendirmelerinde doğruluk, duyarlılık, özgüllük, G-ortalama, F-skor ve Matthews korelasyon katsayısı ölçümleri kullanıldı.

Bulgular: Eğitim aşamasında veri kümesinin %80'i (2599 örnek) kullanılırken, %20'si (465 örnek) test aşamasında kullanıldı. Eğitim veri setinde beyin tümörlerinin sınıflandırılmasında tüm performans ölçütleri %98'in üzerinde sonuçlanmıştır. Benzer şekilde, test veri setinde menenjiom için duyarlılık ve MCC dışındaki tüm değerlendirme ölçütleri % 91'den yüksektir.

Sonuç: Deneysel sonuçlar, önerilen yazılımın üç tip beyin tümörünü tespit etmek ve tanı koymak için kullanılabileceğini ortaya koymaktadır. Geliştirilen bu web tabanlı yazılıma hem İngilizce hem de Türkçe olarak http://biostatapps.inonu.edu.tr/BTSY/ adresinden ücretsiz olarak erişilebilir.

Anahtar Kelimeler: Beyin Tümörleri, Derin Öğrenme Yaklaşımları, Keras / Auto-Keras, T1 Ağırlıklı Manyetik Rezonans Görüntüleme

INTRODUCTION

Primary central nervous system tumors (PCNSTs) are a group of heterogeneous diseases containing more than 100 histological types which are classified according to their morphological and etiological properties, clinical behavior, localization, and molecular structures at the 2016 World Health Organization (WHO) Classification of Tumors of the Central Nervous System (1, 2). PCNSTs are consisting nearly 3% of newly diagnosed cancers worldwide and are more common in men than in women (3). Technological effect due to the increase in the use of assistive tools in diagnosing MRI, the incidence of brain tumors and PCNSTs-related deaths are gradually increasing all over the world. The incidence of PCNSTs ranges from 17.6 / 100000 to 22.0/100000 in Europe and the United States, respectively (4, 5). The incidence of glial tumors in Turkey is 3.3/100000. Although the average 5-year survival for PCNSTs is 33.4%, this period varies according to specific tumor subgroups; such as 100% for pilocytic astrocytoma, 58% for low-grade astrocytoma, 11% for anaplastic astrocytoma, and 1.2% for glioblastoma (6, 7).

The central nervous system tumors can be classified as benign and malignant according to their behaviour. According to WHO, Grade I and II tumors are considered as low grade and benign, while grade III and IV tumors are evaluated as high grade or malignant (1). Approximately two-thirds of central nervous system tumors are benign. Almost 80% of malignant primary central nervous system tumors are gliomas, which make up about one-third of brain tumors. More than half of the diagnosed gliomas are glioblastoma or WHO grade IV tumors (8). Although the incidence of glial tumors exhibits regional changes, the global incidence of all glial tumors is generally 2.98/100000 (9). Although computed tomography is used as the first imaging method in the identification of central nervous system tumors, conventional MR imaging is the basis for the imaging of the central nervous system gliomas In general, while low-grade gliomas emerge hypointense on T1-weighted imaging, hyperintense, and minimal mass effect on T2-weighted imaging. As the tumor stage progresses, irregular bordres with poorly defined mass effect and peripheral edema effect become more heterogeneous (10).

Meningiomas, which form more than a third of all primary central nervous system tumors, are the most common primary intracranial tumors in adults. Its annual incidence is 8.3/100000, and it is more common in women than in men (11). Meningiomas are tumors arising from the arachnoid valve cells (1). According to WHO 2016 classification, meningiomas are examined in three grades as grade I (bening meningioma) 81%, grade II (atypical meningioma) 17%, grade III (malignant meningioma) 2% (11). Computed tomography can be used to identify the lesion and for initial imaging. MR imaging is the most commonly used method for the diagnosis of additional lesions and tumor contours with higher resolution images of intracranial soft tissue. Classically, meningiomas are seen in T1 weighted images and T2 weighted images hyperintense compared to parenchyma, and significant peripheral edema area can be observed in subtypes such as secretory meningiomas (12). The second most common intracranial masses after meningiomas are pituitary adenomas (pituitary tumor) (13). It is a heterogeneous group of lesions that are generally benign in the central nervous system (14). The estimated prevalence in the general population is 16.7% (13).Pituitary adenomas can develop a broad clinical presentation. Many pituitary adenomas do not show symptoms, and while detected incidental, some pituitary adenomas may demonstrate slow-developing nonspecific symptoms and thus may cause delays in the diagnosis and treatment (14). Functional pituitary adenomas can occur with specific symptoms such as hormonal disorders, pressure on the optic nerve, visual field disorders, and organomegaly, with Cushing syndrome, acromegaly/gigantism, hyperthyroidism, or hypogonadism due to hyperprolactinemia (15). MR imaging is used to identify lesions in the pituitary gland and the parasellar region. The standard anterior pituitary gland appears in T1 and T2-weighted images as isointense against gray matter, while the posterior pituitary gland appears in T1-weighted imaging rather than hyperintense and T2-weighted imaging (13, 14). If the patient has symptoms and signs suggesting a brain tumor, radiological imaging should be performed to prove or rule out the presence of the lesion. In a patient with suspected primary central nervous system tumor, the most important imaging method that can provide the necessary information in diagnosis, treatment, and follow-up is MR imaging.

Artificial Intelligence (AI) methods show promise to assist in detecting and assessing image-based tasks, depending on the curing of high-quality training sets. AI technology today provides numerous invaluable tools for intelligent data analysis to solve various medical problems, particularly diagnostic tasks. AI, with its powerful capabilities, seems to be a possible candidate for that role. On the other hand, AI applications ultimately need the radiomics in medical image analysis because the metrics used to train and develop the AI models are provided via radiomics approaches, specifically feature extraction/engineering methods. Examining, interpreting, and reporting MR images can lead to loss of time and/or rarely misinterpretation during the diagnosis phase of the patient. Computer-aided automatic detection and diagnosis systems based on deep learning and image processing algorithms

have been used recently to minimize both the interpretation time of the MR images and the margin of error in the interpretation (16, 17). Deep learning is an artificial intelligence method that uses multi-layered neural networks in object recognition and image classification and is one of the types of machine learning. Instead of learning with encoded rules that differ from the classic machine learning methods, deep learning can automatically learn from the icons of data such as pictures, videos, audio, text, etc. (6).

The main purpose of this study is to demonstrate the use of artificial intelligence-based techniques to predict medical images of different brain tumors to provide clinical support to radiologists. The secondary aim is to develop a user-friendly, free web-based software that can classify brain tumors (glioma, meningioma, pituitary adenomas) and enable specialists to make quick and accurate clinical decisions.

MATERIAL AND METHODS

Dataset: The proposed technique in this study depends on 2D slices. Since typically just a specific number of brain contrast-enhanced MRI with a considerable slice gap are achieved and accessible, the improvement of a 2D picture-based classification for medical applications may be increasingly functional. In the present study, the open-sourced brain tumor images were achieved from Nanfang Hospital, Guangzhou, China, and General Hospital, Tianjin Medical University, China (18). The dataset contained 3064 T1-weighted contrast-enhanced magnetic resonance (MR) images from 233 patients, which included 708 meningiomas, 1426 gliomas, and 930 pituitary tumors. The brain tumor images have an in-plane resolution of 512×512 with a pixel size of 0.49×0.49 mm^2. The thickness and gap of the slice are 6 mm and 1 mm, respectively. The tumor boundary was manually outlined by experienced radiologists (19, 20).

The Proposed Auto-Keras System Based on Deep Learning: Machine learning is a system making forward predictions with a computational model created through sample data and experiences, or making statistical inferences about the structure and distribution of existing data (21). Deep learning, a machine learning sub-branch, is an algorithm that tries to model high-level abstractions of data. In other words, deep learning is an area that develops in the field of machine learning, with very complex layers for processing information nonlinearly. This technique takes its deep name from its deep layers and hierarchical structure (22). Many deep learning techniques have a deeper structure than artificial neural networks. Convolutional Neural Network (CNN), one of these techniques, works forward-looking like artificial neural networks. However, this technique has a feature extraction layer that is not found in artificial neural networks. The main components of CNN are convolution layer, pooling layer, activation functions, fully connected layer, loss layer, regularization, and optimization (23).

Automated machine learning (AutoML) is a fully automated process that starts with the preprocessing of the machine learning (ML) algorithms and ends with the model processing to achieve the best results on a data set (24).It is aimed to minimize human errors in the classical machine learning process with AutoML, which has been used frequently recently. One of the fundamental problems of ML is hyperparameter optimization. While this process in the ML is carried out depending on the experience of the individual, it is performed automatically in the AutoML (25, 26).

Auto-Keras, an AutoML tool, is an open-source Python library created using the Keras deep learning architecture(s). Using the Bayesian optimization method, one of the AutoML approaches, Auto-Keras creates multiple models with ~~a~~ different number of layers and determines the model with the best performance among these models (27). The detailed description of the Auto-Keras system is given in Figure 1.

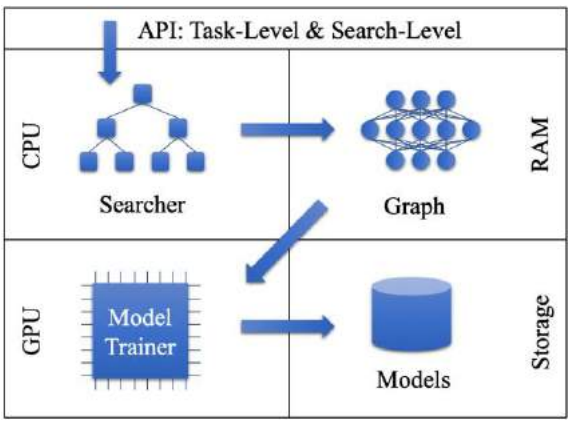


Figure 1. The detailed description of Auto-Keras system (27)

Image preprocessing techniques can improve the classification performance of MR images. In the current study, image rotation, changing width and length, truncating images, rescaling, noise removal approaches, inhomogeneity correction, etc. procedures were applied to the studied MR images for image pre-processing. The dataset used in the development of the deep learning model consists of 3064 T1-weighted MR images of glioma, meningioma, pituitary tumors. To examine the validity and performance of the deep learning model, while 80% (2599 instances) of the whole dataset is used in the training phase, 20% (465 instances) of the whole dataset are employed in the testing phase. H5py (28), random, MatPlotLib, NumPy, and OpenCV libraries for Python programming language are used in the image preprocessing operations described earlier.

Development of The Web-Based Software resting On the Proposed Model: The developed

web-based software can classify glioma, meningioma, and pituitary tumors over T1-weighted MR images. The open-sourced web software developed by using TensorFlow, Keras, Scikit-learn, OpenCV, Pandas, NumPy, MatPlotLib, and Flask libraries of Python programming language is available in Turkish and English at http://biostatapps.inonu.edu.tr/BTSY/. The screenshot of the developed web-based software is given in Figure 2.

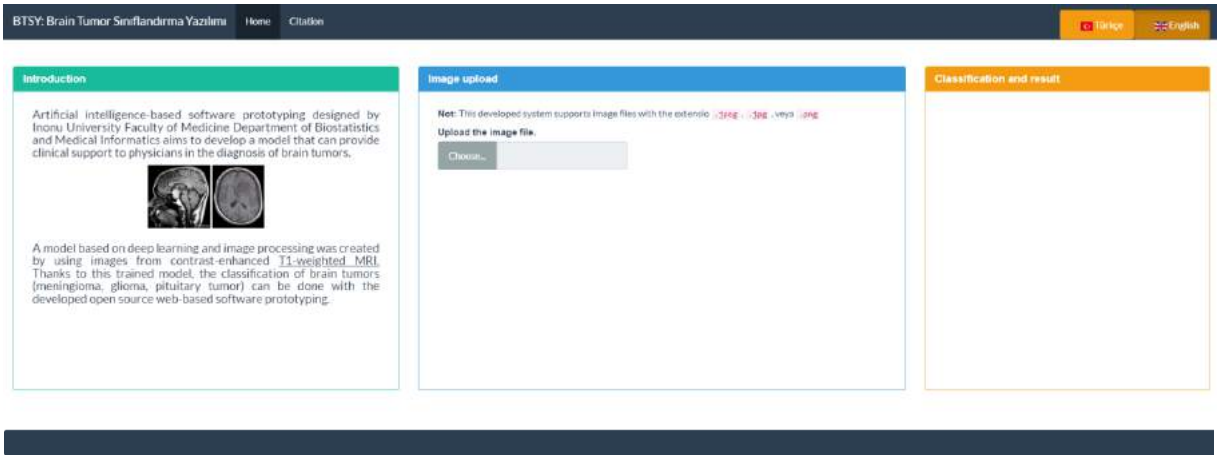


Figure 2. Screenshot of the English web page

The "Home" menu, the first main menu of the developed web-based software, consists ~~of~~ 3 sub-sections: "Introduction", "Image Upload", and "Classification and Result". The "Introduction" sub-section contains information about the operating principle of the software. The T1-weighted MR image of the brain tumor to be analyzed is loaded in the "Image Upload" sub-section. Finally, the type of brain tumor loaded into the system is estimated in the "Classification and Result" sub-section. Since the developed software supports image files with ".jpeg", ".jpg" and ".png" extensions, if a file extension other than these three file extensions is uploaded to the system, the warning in Figure 3 will be displayed in the "Classification and Result" sub-section.

For the filter created to identify the images of irrelevance loaded into the software, at the first stage, all components of the "mxn" pixel matrix calculated for each image are summed with the help of the following formula, and the min-max range is determined for these values.

Figure 3. Unsupported file extension type error

$$A_F = \sum_{i=1}^{m}\sum_{j=1}^{n} a_{ij}$$

Then, images other than these values are defined as irrelevant images. The pseudo-code for this filter is as follows.

PSEUDO-CODE I. MIN-MAX FILTERING

A, B, and C are matrices of each RGB channel of uploaded images.

```
if (A, B and C are not all equal){
  return ("Irrelevant image")
} else {
  if (A_F not in range [192249, 293860]) {
    return ("Irrelevant image")
  }
  else {
    return ("Relevant image")
  }
}
```

Performance evaluation

Performance assessment of the proposed model(s) is performed using evaluation metrics like accuracy, sensitivity, specificity, G-mean, F-score, and Matthews correlation coefficient (MCC). Abbreviations used in these formulas represent TP: true positive number, TN: true negative number, FP: false positive number, and FN: false negative number, respectively (29).

Accuracy = (TP + TN) / (TP + TN + FP + FN)
Sensitivity = TP / (FN + TP)
Specificity = TN / (FP+TN)
G-mean=(Sensitivity*Specificity)$^{1/2}$
F-score= 2TP/(2TP+FP+FN)
MCC=(TP*TN-FP*FN)/
((TP+FP)*(TP+FN)*(TN+FP)*(TN+FN))$^{1/2}$

RESULTS

The performance metrics on the training and testing datasets of the developed deep learning model and the 95% confidence intervals for these metrics are given in Table 1.

When the performance metrics are taken into account, the performance of the developed model to classify brain tumors (Glioma/Meningioma/Pitutiary adenomas) is quite successful in both the training dataset and the testing dataset. The detailed summary information of the proposed Auto-Keras model based on deep learning is given in Table 2.

Table 1. The performance metrics and 95% confidence intervals for the training and testing datasets

	Training Value (%) (95% CI)			Testing Value (%) (95% CI)		
Metrics	**Meningioma**	**Glioma**	**Pitutiary adenomas**	**Meningioma**	**Glioma**	**Pituitary adenomas**
Accuracy	99.81 (99.64-99.98)	99.77 (99.58-99.95)	99.65 (99.43-99.88)	96.29 (94.57-98.01)	96.08 (94.31-97.84)	97.14 (95.62-98.65)
Precision	99.84 (99.68-99.99)	99.92 (99.81-99.99)	98.98 (98.60-99.37)	94.51 (92.43-96.58)	96.97 (95.41-98.53)	91.61 (89.09-94.13)
Sensitivity	99.35 (99.05-99.66)	99.58 (99.34-99.83)	99.87 (99.73-99.99)	87.76 (84.78-90.73)	95.32 (93.40-97.24)	99.24 (98.45-99.99)
Specificity	99.95 (99.86-99.99)	99.93 (99.83-99.99)	99.56 (99.31-99.81)	98.61 (97.55-99.67)	96.88 (95.29-98.46)	96.27 (94.55-97.99)
F-Score	99.60 (99.35-99.84)	99.75 (99.56-99.94)	99.43 (99.14-99.72)	91.01 (88.40-93.61)	96.14 (94.39-97.89)	95.27 (93.34-97.20)
MCC	99.47 (99.19-99.75)	99.54 (99.27-99.80)	99.17 (98.83-99.52)	88.77 (85.90-91.64)	92.17 (89.73-94.61)	93.38 (91.12-95.64)
G-Mean	99.65 (99.43-99.87)	99.75 (99.56-99.94)	99.71 (99.51-99.92)	93.02 (90.71-95.34)	96.09 (94.33-97.85)	97.75 (96.40-99.10)

Table 2. Detailed information about the proposed Auto-Keras model (trimmed table)

Layer number	Layer (type)	Output Shape	Param #	Connected to	Config
1	Input_1 (Inputlayer)	(None, 30, 35, 3)	0		
2	conv2d_1 (Conv2D)	(None, 30, 35, 64)	1792	input_1[0][0]	activation: linear, filters: 64, kernel_size: (3,3), strides: (1,1)
3	batch_normalization_1 (BatchNor)	(None, 30, 35, 64)	256	conv2d_1[0][0]	momentum: 0.99, epsilon: 0.001
4	activation_26 (Activation)	(None, 30, 35, 64)	0	batch_normalization_1[0][0]	activation: relu
5	batch_normalization_2 (BatchNor)	(None, 30, 35, 64)	256	activation_26[0][0]	momentum: 0.99, epsilon: 0.001
6	activation_1 (Activation)	(None, 30, 35, 64)	0	batch_normalization_2[0][0]	activation: relu
7	conv2d_2 (Conv2D)	(None, 30, 35, 64)	36928	activation_1[0][0]	activation: linear, filters: 64, kernel_size: (3,3), strides: (1,1)
8	batch_normalization_3 (BatchNor)	(None, 30, 35, 64)	256	conv2d_2[0][0]	momentum: 0.99, epsilon: 0.001
9	activation_2 (Activation)	(None, 30, 35, 64)	0	batch_normalization_3[0][0]	activation: relu
10	activation_3 (Activation)	(None, 30, 35, 64)	0	activation_1[0][0]	activation: relu
11	conv2d_3 (Conv2D)	(None, 30, 35, 64)	36928	activation_2[0][0]	activation: linear, filters: 64, kernel_size: (3,3), strides: (1,1)
12	conv2d_4 (Conv2D)	(None, 30, 35, 64)	4160	activation_3[0][0]	activation: linear, filters: 64, kernel_size: (1,1), strides: (1,1)
.	.	.	.	.	.
.	.	.	.	.	.
.	.	.	.	.	.
73	batch_normalization_16 (BatchNo)	(None, 30, 35, 512)	2048	add_7[0][0]	momentum: 0.99, epsilon: 0.001
74	activation_22 (Activation)	(None, 30, 35, 512)	0	batch_normalization_16[0][0]	activation: relu
75	conv2d_23 (Conv2D)	(None, 30, 35, 512)	2359808	activation_22[0][0]	activation: linear, filters: 512, kernel_size: (3,3), strides: (1,1)
76	batch_normalization_17 (BatchNo)	(None, 30, 35, 512)	2048	conv2d_23[0][0]	momentum: 0.99, epsilon: 0.001
77	activation_23 (Activation)	(None, 30, 35, 512)	0	batch_normalization_17[0][0]	activation: relu
78	activation_24 (Activation)	(None, 30, 35, 512)	0	activation_22[0][0]	activation: relu
79	conv2d_24 (Conv2D)	(None, 30, 35, 512)	2359808	activation_23[0][0]	activation: linear, filters: 512, kernel_size: (3,3), strides: (1,1)
80	conv2d_25 (Conv2D)	(None, 30, 35, 512)	262656	activation_24[0][0]	activation: linear, filters: 512, kernel_size: (1,1), strides: (1,1)
81	add_8 (Add)	(None, 30, 35, 512)	0	conv2d_24[0][0] conv2d_25[0][0]	
82	global_average_pooling2d_1 (Glo)	(None, 512)	0	add_8[0][0]	
83	dense_1 (Dense)	(None, 3)	1539	global_average_pooling2d_1[0][0]	activation: linear, units: 3

DISCUSSION

Neuroimaging plays a vital role in the diagnosis, treatment, and follow-up of brain tumors. An imaging method that can provide the necessary information in a patient with a suspected brain tumor is MRI among the radiological imaging techniques. MRI is performed to show the lesion or to rule out the presence of the lesion in the patient with suspected signs and symptoms. When assessing the precise location and localization of a tumor in a patient using MR imaging, essential information such as the type of tumor, the tumor's individual characteristics, and its effects on normal brain tissue is collected for treatment and prognosis. Similarly, it gives crucial information in tumor follow-up~~s~~ such as reactive changes of a recurrent tumor and repetitive tumor separation (30).

The main basis for MR imaging of brain tumors is the mass effect and signal changes. In many brain tumors, T1 and T2 relaxation times are prolonged, and therefore the tumors are observed to be hyperintense compared to normal brain tissue in T2 images and hypointense in T1 images. MRI for brain tumor diagnosis should include at least a rapid dual-echo sequence and T1-weighted imaging before and after the application of the paramagnetic agent (30, 33).

MRI is a diagnostic method that displays the organs and structures of the body in a very safe way with high resolution without radiation. While the most essential disadvantage of this method is to cause the malfunction of the devices with magnetic effects towards the patients carrying devices such as pacemakers and infusion pumps, it has the advantage that it does not contain radiation, can be applied in children, pregnant women, cancer patients and can be repeated more than once in one patient (34). Despite its limited disadvantage, the information provided in diagnosis and follow-up by high-resolution examination of the human body causes a significant increase in the number of MRI shots today, leading to delays or misevaluations in the examination of MRI.

The goal of this study is to create a web-based program that can identify brain tumors (glioma, meningioma, pituitary adenomas) using a convolutional neural network of deep learning algorithms based on T1-weighted contrast-enhanced magnetic resonance images. It is believed that medical professionals and other health care professionals can classify brain tumors faster and more accurately, thanks to the free web-based software developed. For this, the program can be used in the detection and classification of brain tumor (i.e., glioma, meningioma, pituitary adenomas) as a clinical decision support tool. Based on the experimental results, all the calculated performance metrics are higher than 98% for the classification of brain tumor types on the training data set. Similarly, all the evaluation metrics are higher than 91% except for sensitivity and MCC for ~~a~~ meningioma on the testing dataset. The proposed model is effectively capable of classifying brain tumor while considering the measured output metrics from the CNN model on the training and testing stages.

A recent research used public data sets to create a CNN-based deep learning method for the classification of brain tumors, with 233 and 73 patients on T1-weighted contrast-enhanced magnetic resonance images totaling 3064 and 516 images, respectively. The system developed in the study performs significantly with the best total accuracy rates of 96.13 percent and 98.7 percent respectively for the two datasets, and can successfully classify multi-classification tasks for a brain tumor (31). In another article, a new deep learning algorithm was built on the CNN deep learning algorithm to classify brain tumors into grade I, grade II, grade III, and grade IV. This algorithm consists of three stages: tumor segmentation, data increase, and the extraction/classification of in-depth features. Experimental results in the studied paper indicate that when applied to the augmented and original datasets, the proposed algorithm has a better performance than the present methods (32). In the previous studies, machine learning and deep learning algorithms were reported to perform well in classifying and predicting T1-weighted contrast-enhanced magnetic resonance images of brain tumors. However, the selection and development of these algorithms require a lot of time and experience when considering the machine learning/data mining applications of the recorded studies over the last years. Thus, in recent years, automatic machine learning and various modelling systems have been commonly developed (24). Authors focused on creating a content-based image retrieval method for the retrieval of brain tumors in T1-weighted contrast-enhanced MR images in another study utilizing the same brain tumor image datasets used in this study (20). Extensive studies of the described research were carried out on a broad dataset of 3604 images of three types of brain tumors, including meningiomas, gliomas, and pituitary tumors, and the mean average precision (MAP) was as high as 94.68%. In the relevant study, while the only MAP was used, the generally recommended other evaluation metrics (accuracy, sensitivity, specificity, MCC, F score, etc.) for supplementary assessment (17) in the classification of brain tumors were not reported (20). Another study using the same image sets in the current research focused on classifying three types of brain tumors in T1-weighted contrast-enhanced MR images (i.e., meningioma, glioma, and pituitary tumor), and compared three methods of classification (support vector machine (SVM), k nearest neighbors (k-NN), sparse representation-based classification (SRC)) (19). The accuracy of

the proposed model in this study outperformed SVM representing the best performance (19).

The number of MRI examinations in Organisation for Economic Co-operation and Development (OECD) countries in 2010 was the lowest (3.6 per million people) among all OECD countries in New Zealand, compared to 59.6 per million people in Turkey. In the United States, 97.6 per million people were monitored at the highest rate among all OECD countries. In 2013, in New Zealand, which had the lowest rate among OECD countries in the past three years, this rate increased to 4.3 per million people and rose to 106.9 per million people in the United States, and in Turkey, it was the highest rate (119.2 per million people) among all OECD countries (35).

Turkey ranked first among all OECD countries with a rate of 157 viewings per 1.000 people, according to the Health Statistics Yearbook 2016 of Turkey's Health Ministry. Besides, in other imaging methods interpreted by radiology experts in inpatient treatment institutions in Turkey, this rate was 188 views per 1000 people in computed tomography, 62.3 per 1000 people in ultrasonography, and 30.3 per 1000 people in doppler ultrasonography In Turkey, on the other hand, there are just 5 radiology specialists per 100,000 people. Furthermore, international standards indicate that if a patient is not allocated for at least 15 minutes in the examination of radiology, serious problems may arise in the correct diagnosis of the patient (36).

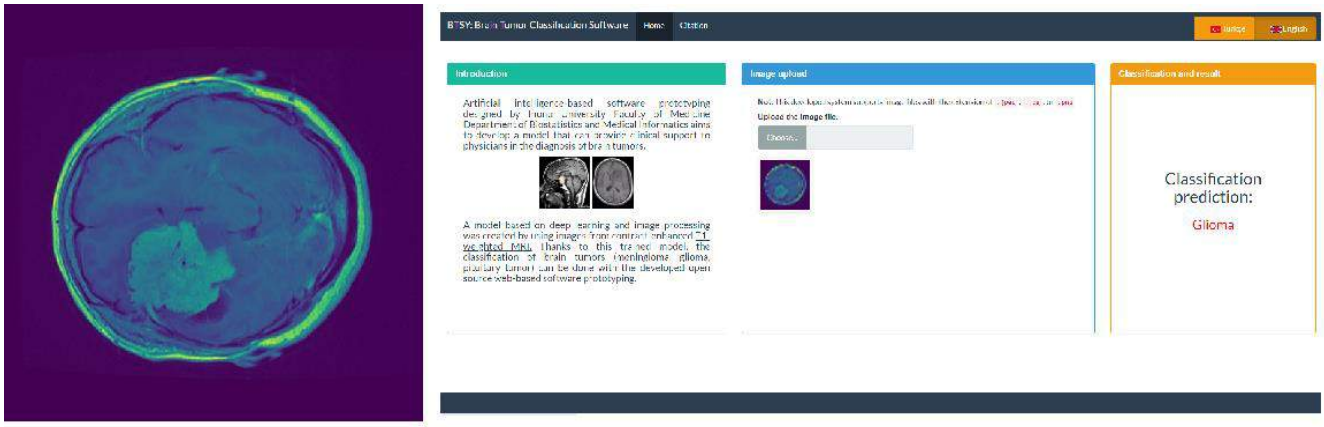
Demanding excessive workload in a short time for radiological evaluations brings physical, spiritual, and mental burnout (37). More than half of physicians in the USA stated that they experienced one or more signs of burnout (38). One or more symptoms of burnout syndrome were observed in 79% of academic radiologists, and excessive workload and work-personal life imbalance were identified as the two factors causing the most stress (39). Also, the burnout of doctors causes a severe cost in the countries. The secondary cost for burnout in the USA was reported to be approximate $ 4.6 billion (40).

A similar workload and burnout table to radiologists can be seen in neurosurgery specialists, another speciality that interprets brain MRI. According to the Global Neurosurgical Workforce Map 2016 data on the website of the World Federation of Neurosurgical Societies (WFNS), while Japan had the highest rate in the world with 5.89 neurosurgeons per 100000 people, the reported rates were 1.6 per 100000 for the USA, 1.5 per 100000 for Germany, 1.26 per 100000 for Turkey, and 0.34 per 100000 for England, respectively. This rate was 0.44 per 100000 in Egypt, which has a third of the neurosurgeons available across the entire African continent, 0.061 per 100000 people in South Africa, 0.049 per 100000 in Kenya, 0.025 per 100000 in Ethiopia and 0.015 per 100000 in Tanzania, while South Sudan, Liberia, and Sierra Leone still have no neurosurgeons (41).

The necessary information about the tumor can be obtained with a brain MRI interpreted correctly by experts. However, the number of radiologists and neurosurgery specialists is not sufficient. In contrast, the number of views made every year has almost doubled every decade, with a rapid increase in the last two decades (42). Also, advanced computer-aided systems based on artificial intelligence can be used in the diagnostic and decision-making process for radiological imaging made at times outside of active working hours. Thus, burnout between radiologists can be reduced by interpreting the image in 3-4 seconds (43).

There are several limitations to our research. Our study included only T1-weighted brain MR images. Other sequences, such as contrast enhanced T1-weighted brain MRI images, would be excluded, lowering precision, sensitivity, and accuracy. Moreover this study not including histopathological confirmation. However, the experimental results obtained from the proposed system are quite successful based on the performance metrics.

In brief, the current research introduces a new public web-based program for classifying brain tumor types based on T1-weighted MR image scans by CNN deep learning algorithm. Figure 4-a and Figure 4-b respectively show the T1-weighted contrast-enhanced MR image of the Glioma tumor and the estimation results of the developed web-based software for this image.



(a) (b)

Figure 4. (a) T1-weighted contrast-enhanced MR image of the Glioma tumor, **(b)** The estimation results of the developed web-based software for Glioma

In the following steps, in addition to medical images of the brain tumors of patients studied in this study, it is envisaged to build a program that can identify data sets that include brain images of healthy individuals.

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RESEARCH ARTICLE

Harun Erdal[1]
Yusuf Serdar Sakin[2]
Mehmet Fuat Cetin[3]
Bulent Celik[4]
Attila Onmez[5]
Ahmet Uygun[2]
Mustafa Gulsen[2]

[1]University of Health Sciences, Gulhane Training and Research Hospital, Deparment of Gastroenterology, Ankara, Turkey
[2]University of Health Sciences, Gulhane Faculty of Medicine, Department of Gastroenterology, Ankara, Turkey
[3]Duzce University, Faculty of Medicine, Department of General Surgery, Duzce, Turkey
[4]Gazi University, Faculty of Science, Departmant of Statistics, Ankara, Turkey
[5]Duzce University, Faculty of Medicine, Department of Internal Medicine, Duzce, Turkey

Corresponding Author:
Harun Erdal
University of Health Sciences, Gulhane Training and Research Hospital, Deparment of Gastroenterology, Ankara, Turkey
Phone: +90 533 639 59 17
mail: drharunerdal@gmail.com

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konuralptipdergisi@gmail.com
www.konuralptipdergi.duzce.edu.tr

The Relationship Between Hyperplastic Gastric Polyps And Helicobacter Pylori

ABSTRACT

Objective: Helicobacter pylori (H. pylori) is a gram-negative bacterium. It is urease positive, mobile, microaerophilic, and spiral-shaped, and it settles in the stomach and the proximal duodenum. It is associated with chronic gastritis, stomach ulcers, duodenal ulcers, stomach cancer, and MALT lymphoma. It can also cause premalignant lesions, such as metaplasia and gastric atrophy. Although several studies are investigating the correlation between H. pylori and hyperplastic polyps (HPs) of the stomach, uncertainty in this regard continues.

Methods: Data from 5378 patients who underwent esophagogastroduodenoscopy at the Department of Gastroenterology, Gülhane Training and Research Hospital,
University Of Health Sciences between October 2016 and March 2019 were retrospectively analyzed, and patients with gastric polyps were evaluated for polyp pathologies and normal mucosa biopsies.

Results: Sixty-one stomach polyps were detected in 49 patients after the retrospective analysis of the data between October 2016 and March 2019. Of the polyps found, 36 were hyperplastic (73%). There was no statistically significant difference between HPs and the presence of H. pylori, age, gender, anatomical location of polyps in the stomach, size, number, presence of metaplasia, or atrophy. The mean age was statistically lower in H. pylori-positive cases.

Conclusions: No correlation was observed between HPs and the presence of H. pylori. There is a need for more extensive, multi-centered, and prospective studies evaluating the relationship between HPs and H. pylori.

Keywords: Helicobacter Pylori, Hyperplastic, Stomach, Polyp.

Hiperplastik Mide Polipleri İle Helikobakter Pilori Arasındaki İlişki

ÖZET

Amaç: Helikobakter pilori (H. pilori), gram-negatif bakteridir. Üreaz pozitif, hareketli, mikroaerofilik, spiral şekilli olup mide ve proksimal duodenuma yerleşmektedir. Kronik gastrit, mide ülseri, duodenum ülseri, mide kanseri ve MALT Lenfoma gibi hastalıklarla ilişkilidir. Ayrıca metaplazi, gastrik atrofi gibi premalign lezyonlara neden olabilir. H. pilori ile midenin hiperplastik polipleri (HP) arasındaki ilişkiyi araştıran çalışmalar olmasına rağmen bu konudaki belirsizlik sürmektedir.

Gereç ve Yöntem: Sağlık Bilimleri Üniversitesi Gülhane Eğitim ve Araştırma Hastanesi Gastroenteroloji Kliniği Endoskopi Ünitesinde Ekim 2016 - Mart 2019 tarihleri arasında özofagogastroduodenoskopi yapılan 5378 hastanın verileri retrospektif olarak analiz edildi ve mide polibi saptanan olguların polip patolojileri ve normal mukoza biyopsileri değerlendirildi.

Bulgular: Ekim 2016 - Mart 2019 arasında verilerin retrospektif taramasında 49 hastada 61 adet mide polibi saptandı. Poliplerin 36'sı (%73) hiperplastik polipti. HP ile H. pilori varlığı, yaş, cinsiyet, polibin midedeki anatomik lokalizasyonu, boyutu, sayısı, metaplazi ve atrofi varlığı açısından istatistiksel olarak anlamlı fark gözlenmedi. H. pilori pozitif olgularda ortalama yaş ise istatistiksel olarak anlamlı şekilde daha düşük bulundu.

Sonuç: Sonuç olarak; hiperplastik polipler ile H. pilori varlığı arasında korelasyon gözlenmedi. HP ile H. pilori arasındaki ilişkiyi değerlendiren daha büyük sayıda, çok merkezli, prospektif çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Helikobakter Pilori, Hiperplastik, Mide, Polip

INTRODUCTION

Marshall and Warren discovered the Helicobacter pylori (H. pylori) bacterium in 1983 (1). It is a gram-negative and urease positive, microaerophilic, spiral-shaped, and motile bacterium localized in the stomach and proximal duodenum (1-3).

The prevalence and incidence of H. pylori vary depending on age and the socioeconomic levels of countries. In developing countries, the frequency varies according to age, with 5% of patients between the ages of 0–5, 25% in their 30s, and around 50% aged 60 and over. The prevalence, which varies between 60–85% in developing countries, has declined to 10–30% in developed countries (4). The frequency of H. pylori is around 80% in Turkey (5).

H. pylori have been found to cause various diseases, such as chronic gastritis, peptic ulcers, peptic ulcer-related complications (gastrointestinal bleeding, perforation, gastric outlet obstruction), gastric cancer, and MALT lymphoma (6–10). It also causes precancerous cellular changes, such as metaplasia and atrophy in the gastric mucosa (11, 12). H. pylori's relationship and coexistence with hyperplastic polyp (HP) formation, which is the most common gastric polyp and considered one of the premalignant lesions of the stomach despite its low probability, is not fully known.

We believe this study will help answer whether the polyps can regress with eradication treatment in the presence of the HP and H. pylori relationship or whether there will be recurrence after a polypectomy.

MATERIAL AND METHODS

Study Design: This is a retrospective study evaluating data collected from patients who underwent esophagogastroduodenoscopy. The data were kept in the electronic database of the endoscopy unit and hospital information system at the University of Health Sciences Gulhane Training and Research Hospital Gastroenterology Clinic from October 2016–March 2019. An Olympus video gastroscope (Olympus GIF-Q150, Olympus Corporation; Tokyo, Japan) was used for all procedures.

The pathology of the polyp and the presence of H. pylori, metaplasia, and atrophy in the biopsies obtained from normal mucosa were recorded in the data form. Also, the patients' ages and genders and the anatomical locations, sizes, and number of polyps were recorded. After the esophagogastroduodenoscopy procedure reports issued between October 2016 and March 2019 were reviewed, the data was recorded in the follow-up form, and the relationships between them were evaluated.

This study was approved by the local ethics committee (Ethics Committee Decision Number: 2019/19/122).

Statistical Analysis: Statistical Package for Social Sciences version 22 was used to evaluate the data obtained from the study. Continuous variables (quantitative variables) obtained by measurement were presented as a mean and standard deviation, and median and interquartile width, where necessary. Categorical variables (qualitative variables) were presented as frequency and percentage values. The Chi-square test and Fisher's exact test were used for statistical evaluation of the categorical variables. The quantitative variables used in the study were analyzed in terms of their conformity to a normal distribution using the Kolmogorov–Smirnov or Shapiro–Wilk test. In the statistical evaluation of intergroup differences in terms of the variable/variables of interest, one-way analysis of variance, and Tukey multiple comparison tests were used for normally distributed variables.

In contrast, the Kruskal–Wallis variance analysis and Bonferroni-corrected Mann–Whitney U tests were used for non-normally distributed variables. Correlations between normally distributed continuous variables were analyzed using the Pearson correlation analysis, while non-normally distributed variables were analyzed using the Spearman correlation analysis. The level of significance was set at $p < 0.05$ in all statistical analyses.

RESULTS

In the retrospective analysis, 61 gastric polyps were detected in 49 patients. Among these polyps, HPs were the most frequent, with 36 cases (73%). H. pylori's positivity rate is 30.6% in all patients. In cases with a polyp size >8 mm, H. pylori's positivity was significantly higher ($p = 0.034$). H. pylori's positivity was not correlated with age, gender, location, size, number of polyps, or the presence of metaplasia and atrophy (Tables 1 and 2). In the HP subgroup, H. pylori's positivity rate is 30.6%. H. pylori's positivity was not correlated with gender, location, size, or number of polyps in the stomach, nor the presence of metaplasia and atrophy. However, the mean age was statistically significantly lower in cases positive for H. pylori ($p = 0.032$) (Tables 3 and 4).

Table 1. Correlation between gastric polyp and H. pylori (gender, location, size, number, pathology, the presence of atrophy and metaplasia) (n:49)

Variables		H. pylori positive (n:13)		H. pylori negative (n:36)		P value
		N	(%)	n	(%)	
Gender	Female	8	(21.1)	30	(78.9)	0.106
	Male	5	(45.5)	6	(54.5)	
Location	Corpus	7	(35.0)	13	(65.0)	-
	Cardia	-	-	2	(100.0)	
	Fundus	1	(25.0)	3	(75.0)	
	Antrum	5	(21.7)	18	(78.3)	
Size	>8 mm	7	(46.7)	8	(53.3)	0.034
	1-8 mm	6	(17.6)	28	(82.4)	
Number	Multiple	4	(36.4)	7	(63.6)	0.402
	Single	9	(23.7)	29	(76.3)	
Pathology	Hyperplastic	11	(30.6)	25	(69.4)	0.288
	Other	2	(15.4)	11	(84.6)	
Atrophy	Yes	3	(27.3)	8	(72.7)	0.950
	No	10	(26.3)	28	(73.7)	
Metaplasia	Yes	4	(23.5)	13	(76.5)	0.729
	No	9	(28.1)	23	(71.9)	

Table 2. Correlation between gastric polyp and H. pylori (age and size) (n: 49)

Variables	H. pylori positive (n:13)		H. pylori negative (n:36)		P value
	Mean	SD	Mean	SD	
Age (years)	57.2	7.2	61.1	13.9	0.344
Size (mm)	11.1	7.3	6.3	3.6	0.009

SD, standard deviation

Table 3. Correlation between hyperplastic gastric polyp and H. pylori (gender, location, size, number, the presence of atrophy and metaplasia) (n:36)

Variables		H. pylori positive (n:11)		H. pylori negative (n:25)		P value
		N	(%)	N	(%)	
Gender	Female	7	(25.9)	20	(74.1)	0.409
	Male	4	(44.4)	5	(55.6)	
Location	Corpus	6	(50.0)	6	(50.0)	-
	Antrum	5	(22.7)	17	(77.3)	
	Cardia	-	-	1	(100.0)	
	Fundus	-	-	1	(100.0)	
Size	>8 mm	6	(50.0)	6	(50.0)	0.124
	1-8 mm	5	(20.8)	19	(79.2)	
Number	Multiple	3	(60.0)	2	(40.0)	0.154
	Single	8	(25.8)	23	(74.2)	
Atrophy	Yes	3	(37.5)	5	(62.5)	0.678
	No	8	(28.6)	20	(71.4)	
Metaplasia	Yes	4	(40.0)	6	(60.0)	0.454
	No	7	(26.9)	19	(73.1)	

Table 4. Correlation between hyperplastic gastric polyp and H. pylori (age and size) (n: 36)

Variables	H. pylori positive (n:11)		H. pylori negative (n:25)		P value
	Mean	SD	Mean	SD	
Age (years)	58.6	6.9	63.9	12.9	0.032
Size (mm)	11.4	7.9	7.0	3.9	0.061

SD, standard deviation

DISCUSSION

In the HP subgroup, the positivity of H. pylori was not correlated with gender, location, size, or the number of polyps in the stomach, nor the presence of metaplasia and atrophy; however, the positivity of H. pylori was significantly higher in cases with a polyp size >8 mm.

The incidence of polyps, one of the stomach's premalignant lesions, ranges from 0.6 to 6% (13, 14). Fundic gland polyps are more common in areas where the prevalence of H. pylori is low. In contrast, HPs are more prevalent in areas where the infection of H. pylori is more common (14, 15). However, the role of H. pylori in the formation of HPs is not fully known.

This study detected 49 cases of gastric polyps. Considering the correlation of H. pylori with parameters such as age, gender, location, size, number, pathology of the polyp, and the presence of metaplasia and atrophy, no difference was found in terms of age and gender. No difference was found in the non-polypoid gastric mucosa in terms of precancerous lesions, such as metaplasia and atrophy, in which H. pylori demonstrated a role in the etiology. A positive correlation was observed between the size of polyps and H. pylori. The positivity of H. pylori was significantly higher in the cases with polyp sizes greater than 8 mm. Although there is no correlation between the presence of polyp and H. pylori positivity, according to this result, it can be concluded that H. pylori play a role in the growth of polyps. Gao et al found that H. pylori's positivity rate is 31.7% in the patients with gastric polyps (16). In the recent studies, H. pylori's positivity rates in the HPs are similar with the present study. Yu et al. and Hu et al. found that H. pylori's positivity rates are 22.7% and 36.4%, respectively (17,18). Also, the study of Nam et al. showed that H. pylori's eradication caused regression in HPs (19).

Considering the correlation of H. pylori with parameters such as age, gender, location, size, the number of polyps in the stomach, and the presence of metaplasia and atrophy in the HPs, the positivity of H. pylori was not correlated with the location, size, and the number of HPs or the presence of metaplasia and atrophy. The mean age was found lower only in cases positive for H. pylori, statistically. Rather than associating this result with HPs, the opinion of the researcher is that H. pylori are related to age distribution. In the literature, the findings on this subject are contradictory. The study by Horward and Pai (20) found no correlation between H. pylori and the location, number, size of HPs, and the presence of intestinal metaplasia; however, studies are reporting a correlation between HPs and H. pylori (21-23).

Our study has some limitations. This is a retrospective study with a small sample size. Furthermore, there is no long-term follow-up of the polyps. There is a need for more extensive, multi-centered, and prospective studies evaluating the correlation between HPs and the positivity of H. pylori, as well as the long-term response of polyps to the eradication therapy.

In conclusion, no correlation was found between the HPs and the positivity of H. pylori.

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RESEARCH ARTICLE

Fatih Alper Akcan[1]
Abdullah Belada[1]

[1]Duzce University Faculty of Medicine, Department of Otorhinolaryngology, Duzce, Turkey

Corresponding Author:
Fatih Alper Akcan
Duzce University Faculty of Medicine, Department of Otorhinolaryngology, Duzce, Turkey
Phone: +90 505 7671113
mail: f.akcan@yahoo.com

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konuralptipdergi@duzce.edu.tr
konuralptipdergisi@gmail.com
www.konuralptipdergi.duzce.edu.tr

Investigation of Risk Factors for Otitis Media With Effusion in Patients with Adenotonsillar Hypertrophy (Risk Assessment in Otitis Media with Effusion)

ABSTRACT

Objective: Sleep Disordered Breathing (USB) is one of the most common childhood disorders ranging from simple snoring to obstructive sleep apnea (OSA), and most common cause of it is the adenotonsillar hypertrophy (ATH). Otitis Media with Effusion (OME) is another important problem in children with USB due to ATH. The aim of this study was to evaluate the possible risk factors for the development of EOM in children with USB due to ATH.

Methods: 171 pediatric patients with ATH-related snoring and sleep apnea complaints were included in the study. The patients were divided into two groups. Group 1: patients with ATH + OME and Group 2: patients with ATH alone. A pre-operative standard questionnaire was used to assess USB severity. Twenty-one different parameters were evaluated for both groups.

Results: Age, sex, exposure to tobacco smoke, cow milk exposure before 12 months, breast milk only for at least 6 months, duration of symptoms, USB symptom scores, history of recurrent tonsillitis, adenoid / nasopharynx (AN) ratio, tonsil size, body mass index (BMI), hemoglobin (Hb) level, hematocrit (Hct) ratio, mean platelet volume (MPV), eosinophil ratio, neutrophil-lymphocyte ratio (NLR), thyroid function tests (TSH, fT4), folate and vitamin B12 levels were evaluated. There was no statistically significant difference between these parameters except BMI. BMI values were 16.08 ± 1.96 in Group 1 and 17.11 ± 2.81 in Group 2, respectively (p: 0.006).

Conclusions: Many different parameters were evaluated for EOM, a multifactorial disease. Among the groups, only BMI was different. Further study is required to identify risk factors for the development of EOM in patients with ATH.

Keywords: Sleep Disordered Breathing, Snoring, Otitis Media With Effusion, Adenotonsillar Hypertrophy, Pediatric.

Adenotonsiller Hipertrofili Hastalarda Efüzyonlu Otitis Media İçin Risk Faktörlerinin Araştırılması (Efüzyonlu Otitis Media'da Risk Değerlendirmesi)

ÖZET

Amaç: Uykuda Solunum Bozukluğu (USB), basit horlamadan obstrüktif uyku apnesine (OSA) kadar uzanan en yaygın çocukluk çağı bozukluklarından biridir ve bunun da en önemli sebepleri arasında ilk sırada adenotonsiller hipertrofi (ATH) gelmektedir. ATH'ye bağlı USB'li çocuklarda karşılaşılan bir diğer önemli sorun ise Efüzyonlu Otitis Media'dır (EOM). Bu çalışmanın amacı, ATH nedeniyle USB olan çocuklarda EOM'nin gelişimindeki olası risk faktörlerini değerlendirmektir.

Gereç ve Yöntem: ATH'ye bağlı horlama ve uyku apnesi şikayetleri olan 171 pediatrik hasta çalışmaya dahil edildi. Hastalar iki gruba ayrıldı. Grup 1: tek başına ATH olanlar ve Grup 2: ATH + EOM olan hastalar. USB şiddetini değerlendirmek için pre-operatif olarak standart bir anket kullanıldı. Her iki grup için yirmi bir farklı parametre değerlendirildi.

Bulgular: Yaş, cinsiyet, tütün dumanına maruz kalma, 12 aydan önce inek sütü maruziyeti, en az 6 ay sadece anne sütü, semptomların süresi, USB semptom skorları, tekrarlayan tonsillit öyküsü, adenoid/nazofarenks (AN) oranı, tonsil büyüklüğü, vücut kitle indeksi (VKİ), hemoglobin (Hb) düzeyi, hematokrit (Hct) oranı, ortalama trombosit hacmi (MPV), eozinofil oranı, nötrofil-lenfosit oranı (NLO), tiroid fonksiyon testleri (TSH, fT4), folat ve B12 vitamini düzeyleri değerlendirildi. VKİ dışında bu parametreler arasında istatistiksel olarak fark yoktu. VKİ değerleri Grup 1'de 16.08 ± 1.96 ve Grup 2'de sırasıyla 17.11 ± 2.81 idi (p: 0.006).

Sonuç: Multifaktöriyel bir hastalık olan EOM için pek çok farklı parametre değerlendirildi. Gruplar arasında sadece VKI farklı olarak tespit edildi. ATH hastalarında EOM gelişimi açısından risk faktörlerini tanımlamak için daha fazla çalışma gereklidir.

Anahtar Kelimeler: Uykuda Solunum Bozukluğu, Horlama, Efüzyonlu Otitis Media, Adenotonsiller Hipertrofi, Pediatrik.

INTRODUCTION

Sleep-disordered breathing (SDB) is one of the most common childhood disorders, from simple snoring to obstructive sleep apnea (OSA) (1). Approximately 2-3% of children are affected by SDB, which can lead to behavioral, cognitive, and growth abnormalities (1,2). The most common cause of SDB in childhood is upper respiratory tract obstruction due to adeno-tonsillar hypertrophy (ATH).

Another important problem encountered in children with ATH-related USB is otitis media with effusion (OME). OME is an inflammatory condition in the middle ear with no signs and symptoms of acute infection (3). It has been reported that this condition affects 90% of children up to the age of 4 years (3,4). The etiology of EMO is multi-factorial, but the main cause is Eustachian tube dysfunction (ED) (5). Inflammatory processes such as atopy and especially upper respiratory tract infections (URIs) can cause ED. The prevalence of EOM was 5.3% to 9% in different countries (6,7).

Several risk factors have been identified in patients with OME, including daily care, allergic rhinitis, and tobacco smoke exposure (8).

The aim of this study is to evaluate the risk factors in the development of EMO in children with SDB due to ATH.

MATERIAL AND METHODS

This study was conducted in Düzce Faculty of Medicine, Department of Otorhinolaryngology between February 2017 and August 2018. The study was conducted in accordance with the Helsinki Declaration Principles and informed consent was obtained from all cases included in the study together with the ethics committee approval (2018-158). One hundred and seventy three pediatric patients included in the study had snoring and sleep apnea complaints due to ATH. The patients with ATH with nasopharyngeal and oropharyngeal obstruction were evaluated by flexible fiber optic endoscopy and direct observation. Patients were determined to have additional systemic diseases like asthma,, allergic rhinitis, chronic rhinosinusitis, etc or not. Adenoid size was graded as grade 1–4 by flexible fiber optic endoscopy (Carl Storz, 2.4 mm) according to the adenoid / nasopharyngeal ratio (9). The tonsil grading scale was graded as: Grade 1, tonsils are only visible in the tonsillarfossa; Grade 2, tonsils can be seen out of the tonsillar fossa; Grade 3, tonsils elongating three-quarters of the midline; and Grade 4, tonsils greater than grade 3 according to the size of the tonsils for (10).

A standard questionnaire was used pre-operatively for SDB; Mouth breathing during sleep, daytime mouth breathing, apnea, snoring, cough, runny nose and restless sleep. Scoring, for each of the above; 0: never, 1: in the meantime, 2: often, and 3: always (11,12). The patients were divided into 3 subgroups according to this questionnaire score; mild: 1-7, moderate: 8-14 and severe: 15-21.

The patients were divided into two groups: those with ATH + OME (Group 1) and those with only ATH (Group 2). All patients underwent adenoidectomy / adenotonsillectomy under general anesthesia for SDB. A ventilation tube was also applied to patients who had OME before the operation. Twenty-one different parameters (laboratory and physical findings) were evaluated for both groups. Age, gender, tobacco smoke exposure, cow milk exposure before 12 months, exclusive breast milk for at least 6 months, duration of symptoms, SDB symptom scores, recurrent tonsillitis history, adenoid / nasopharynx (A / N) ratio, tonsil grade, body mass index (BMI), hemoglobin (Hb) level, hematocrit (Hct) ratio, mean platelet volume (MPV), eosinophil ratio, neutrophil-lymphocyte ratio (NLR), thyroid function tests (TSH, fT4), folate and vitamin B12 levels were evaluated.

The patients with additional systemic diseases like cranio-facial malformation, asthma, allergic rhinitis, chronic rhino-sinusitis etc. and those who had undergone previous adenotonsil surgery and a history of ventilation tube were excluded from the study.

Independent variables were made with the t test or the Mann-Whitney U test. Individual variables were analyzed using the Pearson chi-square test. The statistical analyzes were made with SPSS v.22 package program and the level of significance was set at 0.05.

RESULTS

During the study, a total of 171 patients were evaluated. There were 62 patients in Group 1 and 109 patients in Group 2. The mean age of the groups was 5.00 ± 2.22 and 5.71 ± 2.83, respectively, and there was no significant difference ($p = 0.093$). There was no significant difference between the groups in terms of gender, exposure to tobacco smoke, cow milk exposure before 12 months, only breast milk for at least 6 months, duration of symptoms, SD symptom scores, and recurrent tonsillitis history. The demographic distributions of the groups are summarized in Table 1. AN ratio, tonsil size, BMI, Hb level, Hct ratio, MPV, eosinophil ratio, NLR, thyroid function tests (TSH, fT4), folate and vitamin B12 levels were evaluated. There was no statistically significant difference between these parameters except BMI. BMI values were 16.08 ± 1.96 in Group 1 and 17.11 ± 2.81 in Group 1, respectively (p: 0.006). Physical examination and laboratory parameters are summarized in Table 2.

Table 1. Features of demographic of groups of study and control. İstatistical level of meaningfullness is accepted value of p= 0.05

Variables	Group 1 n=62	Group 2 n=109	*P* value
Age	5.00±2.22	5.71±2.83	0.093
Median value (min-max)	2 (0-4)	2 (1-4)	0.641
Sex			
Man	29 (%46.8)	56 (%51.4)	0.563
Woman	33 (%53.2)	53 (%48.6)	
Exposed of cigarette smoke			
Yes	24 (%38.7)	47 (%43.1)	0.574
No	38 (%61.3)	62 (%56.9)	
Use of cow milk before 1 age	19 (%30.6)	41 (%37.6)	0.359
Breastfeed just first 6 month	35 (%56.5)	72 (%66.1)	0.212
Time of mean symptom (month)	12 (1-60)	24 (2-84)	0.111
Score of symptom:			
• 1-7	1 (%1.6)	6 (%5.5)	0.234
• 8-14	27 (%43.5)	56 (%51.4)	
• 15-21	34 (%54.8)	47 (%43.1)	
Frequency of recurrence tonsillit	7 (%11.3)	13 (%11.9)	0.901

Table 2. Finding of laboratory and physical of groups of study and control.

Variable	Group 1 n=62	Group 2 n=109	*P* value
A/N ratio			
0-25%	0 (%0.0)	4 (%3.7)	
25-50%	1 (%1.6)	5 (%4.6)	0.229
50-75%	22 (%35.5)	45 (%41.3)	
75-100%	39 (%62.9)	55 (%50.5)	
Degree of tonsil			
1	27 (%43.5)	43 (%39.4)	
2	28 (%45.2)	45 (%41.3)	0.561
3	7 (%11.3)	19 (%17.4)	
4	0 (%0.0)	2 (%1.8)	
BMI	16.08±1.96	17.11 ± 2.81	***0.006***
Hemoglobin g/dL	12.64±1.56	12.99±1.01	0.069
Hct %	37.20±3.82	37.98±2.75	0.125
MPV	7.31±0.82	7.50±0.67	0.102
N/L ratio	51.52±13.38	49.90±11.99	0.417
Median ratio of Eosinofil (min-max)	1.65 (0-10.9)	1.90 (0-9.7)	0.336
TSH	2.66±1.45	2.79±1.80	0.624
$_{f}$T4 median (min-max)	1.06 (1-14)	1.05 (1-11)	0.936
Folate	12.58±4.51	12.94±4.42	0.613
Vitamin B_{12}	416.06±165.10	381.67±171.47	0.203

A / N ratio: Adenoid / Nazofarenks ratio. BMI: Body Max İndex. Hct: Hematokrit. MPV: Mean Platelet Volume Hacmi. N / L: Nötrofil / Lenfosit ratio. TSH: Tiroid stimulation hormon. fT4: Free T4. İstatistical level of meaningfullness is accepted value of p= 0.05.

DISCUSSION

OME is an important health problem affecting the quality of life of children. Although it varies according to the method applied and the regions reported, it is generally seen in young age groups (13). OME prevalence of primary school children was 7.6% in a study conducted in Turkey (14). Recent studies have shown that ATH is an important risk factor for OME. However, since not every child with ATH has OEM, the results are discussed below in the context of our findings,

along with previous studies examining additional risk factors.

Age is suggested to be one of the most important factors in the development of OME. Zielhuis et al. (15) suggested that the disease peaked at the age of 2 and 5 years. In our study, it was observed that there was no significant difference between the groups and the average age was around 5 in both groups.

In terms of gender; the majority of patients in both the ATH and ATH + OME groups were male In other studies (4,16). However, studies are available showing that otitis media predominantly affects females (17). In our study, although the rate of women in the OME group was high, the difference was not significant.

Feeding with breast milk is considered to protect newborns from various diseases such as lower respiratory tract infections, nonspecific gastroenteritis, acute otitis media, atopic dermatitis, asthma (young children), obesity, type 1 and 2 diabetes, childhood leukemias, sudden infant death syndrome and necrotizing enterocolitis (18). Although some studies (16,18) found that longer breastfeeding was associated with a lower risk of OME, in our study and others (13,19–21) there was no association between breastfeeding and OME. However, Ip et al. (18) showed that there is a significant difference in the development of OME depending on the duration of breastfeeding.

Some studies have found a relationship between home smoking, particularly parental smoking, and OME (16,22). In our study, no relationship was shown between exposure to tobacco smoke and OME.

When data were evaluated with regard to the size of the adenoid and tonsil; Eliçora et al. (23) showed that there was no difference in OME between patient populations with adenoid size of 75% (Stage 3) and 100% (Stage 4). In our study, all stages were evaluated, but it was observed that there was no difference between the groups in terms of OME. Again, when evaluated according to the size of the tonsil and the history of recurrent tonsillitis, no association was found with OME.

Neutrophil / lymphocyte ratio is the inflammatory parameter that has been defined in recent years and can be easily calculated from peripheral blood analysis. High NLR correlates with the severity of inflammation. Studies have found higher NLR in OME patients compared to the control group (24,25). However, in our study, no significant difference was observed between the groups.

Mean platelet volume (MPV) acts as an indicator of platelet activation. Large platelets with denser granules are more enzymatically and metabolically active. Increased platelet activation plays an important role in the development of inflammation, and platelets have been found to significantly contribute to chronic inflammation and MPV can be used as a marker of inflammatory disease (26,27). Although Somuk et al. (28) found the MPV value in OME patients to be borderline higher than the control group in their study, the results were statistically insignificant. In our study, MPV values were similar in the study and control groups.

Studies have been investigating the relationship between obesity and EOM in recent years [30-33]. Although it was stated in these studies that childhood obesity may be associated with the presence or development of otitis media with effusion, in contrast to these, BMI was found to be lower in the study group in our study ($p = 0.006$).Although our study is the first study evaluating thyroid function tests, vitamin B12 and folate levels with regard to the relationship with OME, no significant difference was found between the groups in terms of these parameters.

CONCLUSION

Epidemiologic, familial, and environmental factors all appear to play a role in the pathogenesis of OME to some extent, and few can be significantly changed to prevent or cure the disease. In our study, only the BMI was found to be different among groups. More studies are needed to identify the risk factors for developing OME in patients with sleep-disordered breathing due to ATH.

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RESEARCH ARTICLE

Birgul Onec[1]
Kursad Onec[2]
Ali Umit Esbah[3]
Onur Esbah[4]

[1]Department of Hematology, Duzce School of Medicine, Duzce, Turkey
[2] Department of Nephrology, Duzce School of Medicine, Duzce, Turkey
[3] Department of Anesthesiology and Intensive Care, Duzce School of Medicine, Duzce, Turkey
[4] Department of Oncology, Duzce School of Medicine, Duzce, Turkey

Corresponding Author:
Onur Esbah
Department of Oncology, Duzce University Faculty of Medicine, 81000, Konuralp Duzce, Turkey
Phone: +90 380 542 13 90
mail:onurilyasoglu131202@tyahoo.com

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www.konuralptipdergi.duzce.edu.tr

Type and Level of Anxiety Affects the Perception of Pain During Bone Marrow Biopsy

ABSTRACT

Objective: Bone marrow aspiration and biopsy (BMAB) is an essential tool for diagnosis of hematological disorders. The most frequent complaint after BMAB is pain but the severity of this pain is described very different among patients. We investigated factors predicting this pain focusing on the role of state and trait anxiety.

Methods: One hundred and ten adult patients undergoing BMAB, were informed adequately and assessed with "The State-Trait Anxiety Inventory" (STAI) before the procedure. In this Likert-type inventory, State Anxiety Scale evaluates the current state of anxiety, asking how respondents feel "at that moment". The Trait Anxiety Scale evaluates relatively stable aspects of "anxiety proneness," including general states of confidence, calmness, and security. After the biopsy, pain was measured with visual analog scale.

Results: Most of the patients (71.8%) described mild pain but moderate to severe pain were significantly more frequent in both high state and trait anxiety groups. Pain severity had a positive but weak correlation with trait anxiety but not with state anxiety. The described pain level was associated with older age but was not with indication of biopsy, performance status, comorbidities or previous BMAB experiences.

Conclusions: Results of our study made us thought that a good communication with the patient and talking about possible outcomes days before procedure might play a role reducing his or her anxiety but because age and trait anxiety cannot be changed by using fast acting anxiolytic drugs, advantage of premedication with anxiolytics in order of reducing pain, would be limited.

Keywords: Biopsy, Pain, Anxiety.

Anksiyetenin Türü ve Düzeyi, Kemik İliği Biyopsisi Sırasında Ağrı Algısını Etkiler

ÖZET

Amaç: Kemik iliği aspirasyon ve biyopsisi (KİAB) hematolojik hastalıkların tanısında kullanılan önemli bir yöntemdir. İşlem sonrası en sık bildirilen yakınma ağrı olmakla birlikte; bu ağrı hastalar tarafından çok farklı düzeylerde tariflenmektedir. Çalışmamızda özellikle durumluk ve süreklilik anksiyetesini merkeze alarak, bu ağrıyı etkileyen faktörleri araştırmak istedik.

Gereç ve Yöntem: Merkezimizde KİAB planlamış 110 hasta, uygun şekilde bilgilendirilerek işlemden hemen önce Durumluk ve Süreklilik Anksiyete Ölçeği (State Trait Anxiety Inventory, STAI) ile değerlendirildi. Bu Likert tipi ölçekde "Durumluk Kaygı Ölçeği", katılımcıların "o anda" nasıl hissettiklerini sorarak mevcut kaygı durumunu değerlendirir. "Süreklilik Kaygı Ölçeği" ise genel güven, sakinlik ve güvenlik durumları dahil olmak üzere "kaygı eğiliminin" nispeten istikrarlı yönlerini değerlendirir. Biyopsi işlemi tamamlandıktan hemen sonra da hastaların ağrı düzeyleri "vizüel analog skala" ile değerlendirildi.

Bulgular: Hastaların çoğu (% 71,8) hafif ağrı tarifledi ancak orta ve şiddetli ağrı; hem yüksek "Durumluk kaygı" hem de yüksek "sürekli kaygı" gruplarında anlamlı olarak daha sıktı. Ağrı şiddeti ile sürekli kaygı arasında pozitif ancak zayıf bir korelasyon olmakla birlikte, durum kaygısı ile ilişkili bulunmadı. Hastaların bildirdiği ağrı düzeyleri ileri yaşla ilişkiliydi ancak biyopsi endikasyonu, hastanın performans durumu, komorbiditeleri veya önceki KİAB deneyimleri ile ilişkili değildi.

Sonuç: Çalışmamızın sonuçları, hastayla iyi bir iletişim kurmanın ve işlemden günler önce olası sonuçlar hakkında konuşmanın kaygısını azaltmada rol oynayabileceğini ancak yaş ve "sürekli kaygı" hızlı etkili anksiyolitik ilaçlar kullanılarak değiştirilemeyeceği için; anksiyolitiklerle premedikasyonun ağrı azaltmada avantajının sınırlı olacağını düşündürmüştür.

Anahtar Kelimeler: Biyopsi, Ağrı, Anksiyete.

INTRODUCTION

Bone marrow aspiration and biopsy (BMAB) is an essential tool for diagnosis and monetarization of hematological disorders. Serious adverse events were reported in less than 0.05% of procedures, so it could be named as a safe procedure (1). The most frequent complaint after this procedure is pain but the severity of this pain is described very different among patients. A prospective study emphasized that pain was a frequent complication; with a bearable pain about 60% and unbearable pain in 3.7% cases (2). Despite the progress in medicine, there was not much focus on studies considering this pain for many years. As medicine becomes more patient-oriented and more emphasis is being placed on patient well-being, we try to decrease the pain associated with medical procedures. The prevalence, predicting factors, and prevention of pain associated with BMAB has recently been investigated in different studies (2-10). Despite more information has been recognized, there are no clear data on pain-causing factors and how to use them in lessening this pain. In our study, we planned to determine the intensity of pain that our patients felt during BMAB procedure, in which we use only local prilocaine and "Adequate information before BMAB". We also investigated factors predicting this pain focusing on the role of state and trait anxiety.

MATERIAL AND METHODS

The study was approved by the ethics committee of the Duzce University School of Medicine with number of 2016-09 at 08.02.2016. All patients were properly informed and gave their written consent to participate in the study. The study was done prospectively in Department of Hematology, from March 2016 to October 2016. One hundred and ten adult patients, for whom bone marrow biopsy was planned for any reason and gave written consent were included. Exclusion criteria was pregnancy, disorders of consciousness, psychiatric disorders, neurologic disorders like Alzheimer or dementia and serious pain related to primary disease.

Clinical Data: Data on baseline characteristics and medical history were obtained from both patient records and interviews. For each subject; age, gender, indications for biopsy, ECOG performance status, duration of total hematologic investigations until BMAP and previous diagnoses are recorded. The information about procedure was given to patient in outpatient clinic, by experienced clinical hematologist and procedure was dated in a few days, in order to answer patient's further questions. Turkish version of "The State-Trait Anxiety Inventory" (STAI) which is a self-assessment inventory, is given to the patients to be answered 15-30 minutes before the biopsy procedure. After normal skin preparation and five minutes after instillation of 10 ml 2% prilocaine to the skin and deeper tissues, BMAB from the posterior iliac spine was carried out by one experienced author. The visual analogue scale (VAS) is used for quantifying pain and discomfort 15 minutes after the procedure. The pathological diagnosis of samples were added at the end of the study.

Measuring Anxiety: STAI is used to measure the presence and severity of current symptoms of anxiety and a generalized propensity to be anxious. This Likert-type inventory was developed by Spielberg et al. and translated into Turkish (STAI-TX) by Öner and Le Compte in 1985 (11). The reliability and validity studies of Turkish version revealed an internal consistency of 0.88- 0.87 and test-retest correlation of 0.71-0.86. (11,12). STAI-TX is a self-report questionnaire that can be administered in an individual format. There are 2 subscales within this inventory. The first part, the State Anxiety Scale (S-Anxiety) evaluates the current state of anxiety, asking how respondents feel "at that moment". The second part, the Trait Anxiety Scale (T-Anxiety) evaluates relatively stable aspects of "anxiety proneness," including general states of confidence, calmness, and security (13). Total scores for both state and trait (S-Anxiety and T-Anxiety scores) are calculated separately, ranging from 20 – 80 for each with the higher score indicating greater anxiety. The patients were grouped through median levels and compared with subscales as "low vs high S-Anxiety groups" and "low vs high T-Anxiety groups"

Measuring Pain: The visual analogue scale (VAS) for pain is a continuous scale comprised of a horizontal line, usually 10 centimeters in length, marked by 2 verbal descriptors, at the each end-points (14). For pain intensity, the scale is anchored by "no pain" (score of 0) and "worst imaginable pain" (score of 100 =100-mm scale) in Turkish. (15). The measures were recorded as mm and grouped 0-39 mm as mild pain, 40-69 as moderate pain and 70-100 mm as severe pain (16). Due to the small sample size in last two groups, these two groups merged into moderate-severe (40-100 mm) group.

Statistical Analysis: Retrospective studies and procedure count performed the year before, were evaluated to calculate the sample size and it was calculated at least 84 subjects with 80% power and 5% Type 1 error. Statistical analysis was performed using the SPSS (version 16.0, SPSS Inc., Chicago, IL, USA) software package. Distribution of numeric variables was tested by using both visual and analytical methods (Kolmogorov–Smirnov and Shapiro-Wilk tests). Descriptive analyses were presented using means ±standard deviations for normally distributed variables or median and interquartile range (IQR) for nonparametric continuous variables. Categorical variables were presented as numbers and percentages and compared using chi-square test.

One-way ANOVA was used to compare normally distributed parameters among groups. Comparisons of non-normally distributed parameters were performed by Kruskal–Wallis test. Comparisons between the two groups were performed with Student t-test for parametric data and Mann–Whitney U-test for nonparametric data. Spearman rank correlation test was performed to determine the relationships between continuous variables. All probability values were calculated by assuming a two-sided p-value of ≤0.05 with confidence intervals (CIs) at the 95% level.

RESULTS

Baseline clinical characteristics, diagnosis' and VAS-pain measurements of the patients are shown in Table 1. The median age was 64 (55-76) in whole group of 110 patients, including 51 males (46.7%) and 59 (53.6%) females. Median age was similar in both genders (63 at woman vs 64 at men) but significantly different in mild vs moderate/severe pain describing groups (62 vs 71 respectively, p=0.004).

Table 1. Baseline clinical characteristics of the patients

	Total n=110	Mild Pain (VAS<40) n=81	Moderate- Severe Pain (VAS≥40) n=29	P value
Age (years)	64 (55-76)	62(53-70)	71 (60-78)	**0.004***
Gender (male, N, %)	51 (46.7%)	39(48.1)	12 (41.4)	0.53
VAS score (mm)	20 (0.95-4.5)	11 (0-39)	55(41-100)	-
State Anxiety score (STAI-TX1)	40 (32-47)	37(31-47)	42(35-48)	0.057
Trait Anxiety score (STAI-TX2)	44.5 (40.75-50)	44 (40-49)	48(44-51)	**0.008***
Previous BMAB				0.977
No	95 (86.4%)	70 (86.4%)	25 (88.2%)	
Yes	15 (13.6%)	11 (13.6%)	4 (13.8%)	
Indication of BMAB				0.441
Anemia	26 (24.5%)	16 (61.5%)	10(38.5%)	
Thrombocytopenia	16 (15.1%)	11 (68.8%)	5(31.2%)	
Leukopenia	3 (2.8%)	3 (100%)	0	
Pancytopenia	9 (8.5%)	8 (88.9%)	1(11.1%)	
Monoclonal Gmp.	12 (11.3%)	10 (83.2%)	2(16.7)	
Polycythemia	2 (1.9%)	2 (100%)	0	
Thrombocytosis	17 (16%)	13 (76.5%)	4(23.5%)	
Leukocytosis	5 (4.7%)	2 (40%)	3 (60%)	
Staging	8(7.5%)	5 (62%)	3 (37.5%)	
LAP/HSM	3 (2.8%)	3 (100%)	0	
Response evaluation	5 (4.7%)	4 (80%)	1(20%)	
ECOG	1 (0-2)	1 (0-2)	1 (0-3)	0.804
Inter-trabecular Area	8(6-10)	8(6-10)	8(6-10)	0.982
Duration of evaluation (months)	2(1-4.75)	2 (1-5)	1.75 (0.625-3.375)	0.435
Comorbidities				0.099
None	26(34.2%)	23(88.5%)	3(11.5%)	
Solid malignancy	6(7.9%)	5(83.3%)	1(16.7%)	
Hypertension	15(19.7%)	12(80%)	3(20%)	
Diabetes	3(3.9%)	2(66.7%)	1(33.3%)	
Ch. renal disease	2(2.6%)	2(100%)	0	
Comorbidities >2	24(31.6%)	13(54.2%)	11(45.8%)	
Diagnosis				0.803
Non-diagnostic	17 (16%)	12(70.6%)	5(29.4%)	
Benign disorders	12(11.3%)	9(75%)	3(25%)	
MDS	32 (30.2%)	25(78.1%)	7(21.9%)	
MM	11(10.4%)	8(72.7%)	3(27.3%)	
MPN	22(20.8%)	16(72.7%)	6(27.3%)	
Leukemia	9(8.5%)	5(55.6%)	4(44.4%)	
Ca./Lymphoma	3(2.8%)	3(100%)	0(0%)	

VAS: visual analog scale, STAI-TX1: State Anxiety Scale,(= S-Anxiety), STAI-TX2: Trait Anxiety Scale (=T-Anxiety), BMAB: Bone marrow aspiration and biopsy, Monoclonal Gmp: Monoclonal Gammopathy, LAP/HSM: Lymphadenopathy or hepatosplenomegaly, ECOG: Eastern Cooperative Oncology Group Performance Status, Ch. renal disease: Chronic renal disease, MDS: Myelodysplastic Syndrome, MM: Multiple myeloma, MPN: myeloproliferative neoplasms, Ca:Carcinoma

Notes: Continuous variables are shown as mean ± SD if normally distributed and as median (IQR, interquartile range) if nonnormally distributed. Categorical variables are shown as frequency and percentages.* :p<0.05

The mean S-Anxiety and T-Anxiety scores were 40 (32-47) and 44.5(40.75-50), respectively in whole sample. Women had significantly have higher S-anxiety (41.9±10.1 vs 38±10.5, p: 0.028) and T-anxiety (47 vs 43.2, p: 0.006) scores compared to men. Median S-Anxiety score was slightly higher in patients describing the procedure more painful (median S-Anxiety score 37 (31-47) in mild vs 42 (35-48) in moderate/severe pain group) but it was not statistically significant (p=0.057). On the other hand, 69% of the moderate/high pain describing patients (VAS >40) had high trait anxiety (69% vs 31%, p: 0.017). Associated with it, median T-Anxiety score was significantly high (T-Anxiety scores 44 (40-49) vs 48(44-51), respectively in mild vs moderate/severe pain groups, p=0.03). Because the median values were also suggested to be clinically significant for symptoms [13], we used them as cut off points. The patients were grouped through median levels and compared in subscales as "low S-Anxiety" vs "high S-Anxiety" groups and "low T-Anxiety" vs "high T-Anxiety" groups.

Pain was measured with horizontal VAS and median VAS score was 20 (IQR 9.5-45 mm) in whole sample. VAS measurements were categorized mild pain as below 40 mm, moderate pain as 40-69 mm and severe pain higher than 70 mm, as described before. Majority (n:79, 71.8%) of patients who experienced BMAB marked it as a mild pain. It was defined as moderate by 19 (17.3 %) of patients and severe by only 12 (10.9%) patients. Because of the small sample size in moderate and severe pain groups, these two groups combined as "moderate to severe pain" with VAS ≥40 mm. When the two (mild vs moderate-severe pain) groups were investigated in terms of S-anxiety and T-anxiety levels, it is demonstrated that high S-anxiety was significantly more common in patients who described moderate-severe pain (p: 0.017).

According to S-Anxiety assessment, a total number 59 (53.6%) of patients had low S-Anxiety scores while were 51 (46.4%) of them had high S-Anxiety scores in whole sample. In low S-Anxiety group, 49 (83.1%) patients marked their pain as mild and 10 (16.9%) patients marked as moderate-severe. In high S-Anxiety group, same frequencies were 32(62.7%) and 19 (37.3%), making moderate-severe pain significantly more frequent in highly anxious subjects (37.3% vs 16.9%, p: 0.016, Figure 1).

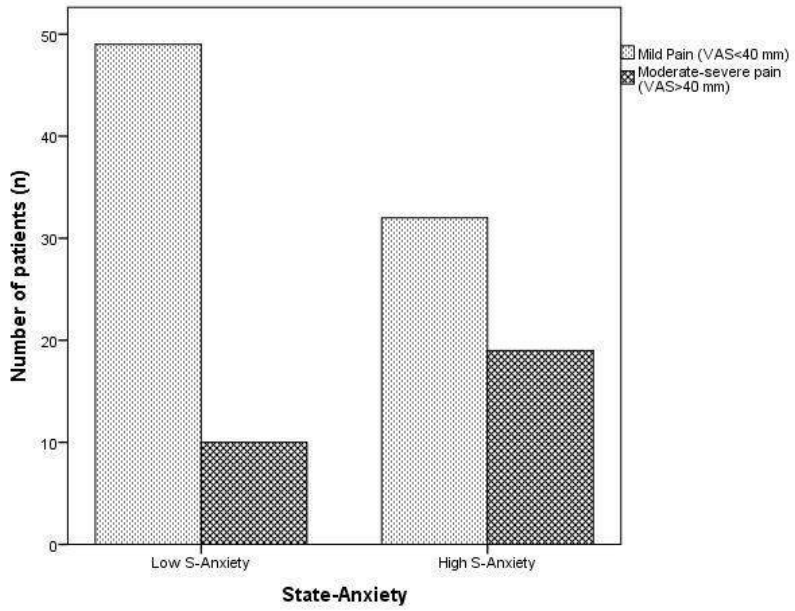

Fig. 1 Pain levels in different State-Anxiety (S-Anxiety) scales. In low S-Anxiety group, 49 (83.1%) patients marked their pain as mild and 10 (16.9%) patients marked as moderate-severe. In high S-Anxiety group, same frequencies were 32(62.7%) and 19 (37.3%), making moderate-severe pain significantly more frequent in highly anxious subjects (p: 0.016)

When patients' T-Anxiety scales were investigated, it was demonstrated that 55 (50%) patients had low and the other half had high T-Anxiety scores. In low T-Anxiety group, 46 (83.6%) patients marked their pain as mild and 9 (16.4%) patients marked as moderate-severe. In high T-Anxiety group, 35 (63.6%) patients were describing their pain as mild and 20 (36.4%) patients were describing as moderate-severe by using VAS. Like S-Anxiety group, there was a significantly high frequency of moderate-severe pain perception in highly anxious patients (36.4% vs 16.4%, p: 0.017, Figure 2). Actually, most of the patients who declared moderate-severe pain, were found highly anxious with both State and Trait antiety scales (Figure 3) Further analyzes revealed a weak but statistically significant positive correlation between the severity of pain and trait

anxiety levels (rs: 0.206, p: 0.03) but correlation between state anxiety and pain scores did not reach statistical significance (p: 0.13). Pain was not associated with indication of biopsy, ECOG, comorbidities, experiance of a previous BMAB, duration of evaluation (from the first application till BMAB), size of the biopsy as inter-trabecular area or final diagnosis (for all p>0.05, Table 1).

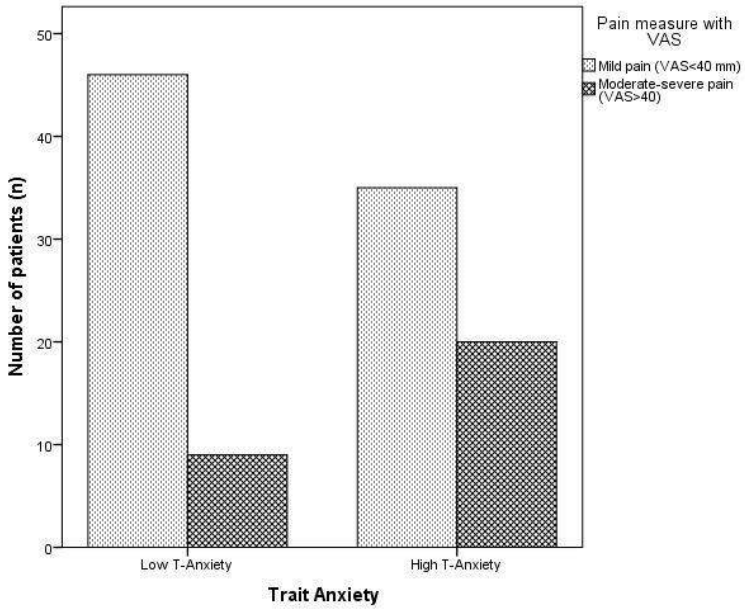

Fig. 2 Pain levels in different Trait-Anxiety (T-Anxiety) scales. In low T-Anxiety group, 46 (83.6%) patients marked their pain as mild and 9 (16.4%) patients marked as moderate-severe. In high T-Anxiety group, 35 (63.6%) patients were describing their pain as mild and 20 (36.4%) patients were describing as moderate-severe (p: 0.017)

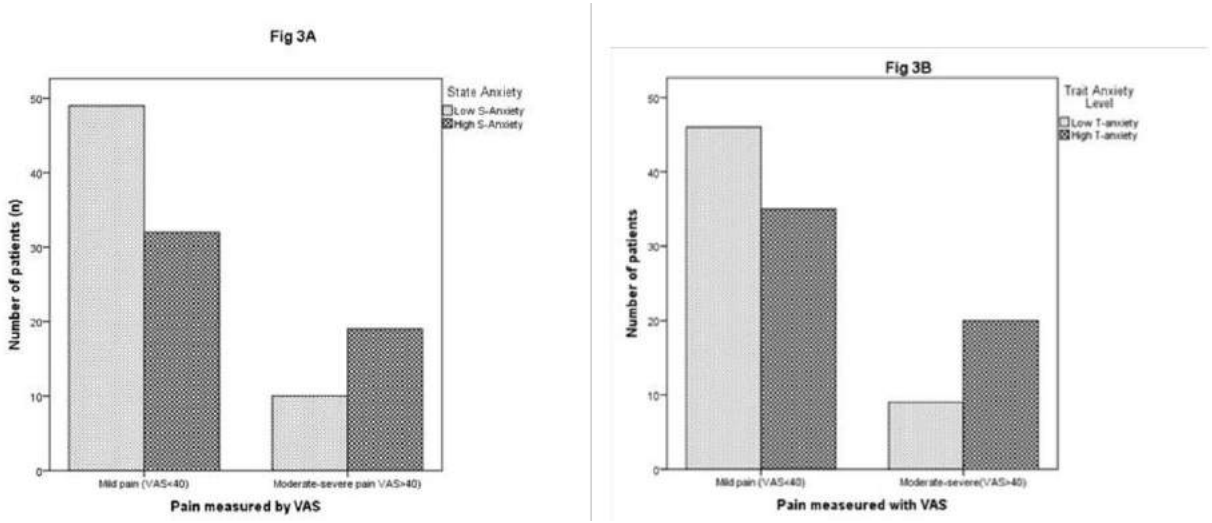

Fig. 3 Most of the patients who declared moderate-severe pain, were found highly anxious with both State and Trait antiety scales. Twenty nine patients declared moderate-severe pain of which, 19 (65.5%) had high State anxiety (S-anxiety, 3A) and 20 (69%) had high Trait anxiety (T-anxiety, 3B)

DISCUSSION

Examination of the bone marrow has a very important role in the diagnosis of hematological disorders, some of which are also periodically monitored with BMABs. After the routine core biopsy was added to the aspiration procedure, the discomfort began to be noticed (17). Inconstancy of this pain level could clearly be seen in studies at this area. The variety of methods of measuring pain may contribute this conflicting data. Never less, the BMAB is described as a painful procedure by most of the patients (ranging 63% to 86%) in all studies with different percent of patients describing it as "severe pain" (ranging 3.7% to 47%)(2,3,6,18,19). VAS is reported to be more sensitive and reliable in measuring pain intensity than other one-

dimensional scales (20,21), therefore, we used VAS to measure pain during BMAB.

In our study, majority (n:79, 71.8%) of patients who experienced BMAB, marked it as a "mild" pain, while it was defined as "moderate" by 19 (17.3 %) and as "severe" (VAS≥70) by only 12 (10.9%) of the patients. This percentage was consistent with Liden's study, in which, only local anesthesia was used like in ours (19). Less pain was reported in studies which BMAB was performed after premedication, but it has potential adverse effects (2,3,6). The need of trained nurse and area for observation, are other handicaps making this premedication difficult to use as routine practice in smaller clinics, like ours.

The studies focusing on factors predicting pain during BMAB reported different factors. In our study group, age and especially trait anxiety were the most relevant factors. Liden et al investigated pain predicting factors in patients who had hematological malignancies and described independent risk factors as pre-existing pain, anxiety about the diagnosis or needle-insertion, and low employment status (19). Age of the patient and duration of the procedure were reported as key factors associated with more severe pain adult patients undergoing BMAB (6). Gronkjaer et al. agreed that age is a key factor and also suggested that aspiration technique (22). According to one of the most recent studies, severe pain is significantly associated only with prior painful BMAB experience and lack of adequate information before procedure (2). This study showed the big influence of good information given by the physician to reduce pain during BMAB and brought to mind the question of whether it is related to anxiety.

In our study, we tried to uncover the role of anxiety on the level of pain felt during BMAB. Anxiety is described as a normal response to threats or challenges, especially those that are perceived to be uncontrollable. State anxiety is a temporary condition experienced in specific situations. It refers to transitory unpleasant feelings of apprehension, tension, nervousness or worry, often accompanied by activation of the autonomic nervous system. It reflects whether a person perceives the specific situation as threatening or not. Trait anxiety is a personality disposition that describes a person's tendency to perceive situations as threatening, and hence to experience state anxiety in stressful situations. Trait anxiety is not observed directly, but is expressed as state anxiety when stress is experienced. (23).

In our study, the pain was mostly associated with patients' age and trait anxiety which is a part of their personality and ordinary life. The age was found associated with pain two previous studies (6,22). To our knowledge, type and level of anxiety was investigated only in one study. Although they used a numerical anxiety scale, Brunetti et al had reported the pain was associated with anxiety (3), like in our study. We demostrated that trait anxiety was positively correlated with the intensity of pain and because trait anxiety is defined as "a personality disposition", medications may not effect this condition. Other factors we investigated like gender, previous BMAB experience, indication of BMAB, ECOG, quality of the specimen, duration of evaluation, comorbidities and diagnosis was not associated with pain.

The first studies in adult patients reporting different levels of pain, mostly focused anxiolytic/amnestic medications to reduce the recall of this pain but using lorazepam premedication results with disphoria and sedation which can cause problems in outpatient setting (17). Following studies using different premedications reported pain in reaching 63.3% and premedication-related complications at 20% - 32.7% of the patients (2,24). So, it is difficult to use these premedications at routine practice for most of the clinics which have to do BMAB as an outpatient procedure.

CONCLUSION

We demonstrated that majority (71.8 %) of patients' experienced mild pain during BMAB with a median VAS score of 20 mm in our population. Age and median T-Anxiety scores of the group describing moderate/high pain, were significantly higher. Significantly high frequency of moderate-severe pain perception was seen in highly anxious patients both in terms of state and trait anxiety but pain was only correlated with the trait anxiety levels.

Results of our study made us thought that a good communication with the patient and talking about possible outcomes days before procedure might play a role reducing his or her anxiety. Because age and trait anxiety cannot be changed by using fast acting anxiolytic drugs, advantage of anxiolytic premedication in order to reduce pain, would be limited.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

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

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RESEARCH ARTICLE

Duygu Ayhan Baser[1]
Mustafa Cankurtaran[2]

[1]Hacettepe University Faculty of Medicine, Department of Family Medicine, Ankara, Turkey
[2]Hacettepe University Faculty of Medicine, Department of Internal Medicine, Division of Geriatrics, Ankara, Turkey

Corresponding Author:
Duygu Ayhan Baser
Hacettepe University Faculty of Medicine, Department of Family Medicine, Ankara, Turkey
Phone: +90 505 664 5210
Mail:duyguayhan@outlook.com

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konuralptipdergi@duzce.edu.tr
konuralptipdergisi@gmail.com
www.konuralptipdergi.duzce.edu.tr

The Assessment of the Orthorexia Nervosa Tendencies among Postpartum Women

ABSTRACT

Objective: Orthorexia Nervosa is a new eating disorder and is known as an excessive control of quality of the eaten foods. During postpartum period, related to the physiological and medical changes, it was stated that most of the women have concerns about their body image and therefore they have tendency to change their lifestyle, and it can lead mothers to Orthorexia Nervosa. The aim of this study was to assess the Orthorexia Nervosa tendencies of postpartum women and investigate the related factors.

Methods: This descriptive study was carried out among postpartum women between 1st December 2018-1st February 2019. We contacted with the women via e-mails through a social media group special for postpartum women which had 10.350 members at the time of study. The minimum sample size for universe was estimated as 370 women, assuming 95% confidence interval and 5% sampling error. The questionnaire consists of two parts: the general features of participants and the ORTO-11 questionnaire.

Results: The mean ORTO-11 scale score of all participants (N=511) was 22.68±4.09 (min=12; max=35) and had statistically significant relationship with age, working status, vocation, family style, the understanding of being healthy, physical activity, diet status and the order of nutrition status. According to cut-off point, 87.7 % (n=426) of the participants were found to be at risk of developing Orthorexia Nervosa.

Conclusions: The tendency toward Orthorexia Nervosa was greater among mothers in postpartum period. Also the mothers who change their eating habits and change the physical activity status after delivery had higher ON tendency than others. So the postpartum period is very important to follow up the mothers about ON and such eating disorders because of the changing lifestyle habits. Family physicians have a critical role in this regard with their preventive medicine qualifications.

Keywords: Eating Disorders, Orthorexia Nervosa, Postpartum Period.

Doğum Sonrası Kadınlarda Ortoreksiya Nervoza Eğilimlerinin Değerlendirilmesi

ÖZET

Amaç: Ortoreksiya Nervosa yeni bir yeme bozukluğudur ve yenen yiyeceklerin kalitesinin aşırı kontrolü olarak bilinir. Doğum sonrası dönemde fizyolojik ve tıbbi değişikliklere bağlı olarak kadınların çoğunun beden imajıyla ilgili endişeleri olduğu ve bu nedenle yaşam tarzlarını değiştirme eğiliminde oldukları ve anneleri Ortoreksiya Nervozaya yönlendirebileceği belirtildi. Bu çalışmanın amacı, postpartum kadınların Ortoreksiya Nervosa eğilimlerini değerlendirmek ve ilgili faktörleri araştırmaktır.

Gereç ve Yöntem: Bu tanımlayıcı araştırma, 1 Aralık 2018-1 Şubat 2019 tarihleri arasında postpartum kadınlarda gerçekleştirildi. Çalışma zamanında 10.350 üyesi olan doğum sonrası kadınlara özel bir sosyal medya grubu aracılığıyla kadınlarla e-posta yoluyla iletişime geçtik. Evren için minimum örneklem büyüklüğü, %95 güven aralığı ve % 5 örnekleme hatası varsayılarak 370 kadın olarak tahmin edilmiştir. Anket iki bölümden oluşmaktadır: katılımcıların genel özellikleri ve ORTO-11 anketi.

Bulgular: Tüm katılımcıların (N=511) ortalama ORTO-11 ölçek puanı 22.68 ± 4.09 (min=12; maks= 35) olup; yaş, çalışma durumu, meslek, aile tipi, sağlıklı olma anlayışı, fiziksel aktivite, diyet durumu ve beslenme sıklığı ile istatistiksel olarak anlamlı ilişki bulundu. Kesim noktasına göre, katılımcıların % 87.7'sinin (n = 426) Orthorexia Nervosa gelişme riski taşıdığı görüldü.

Sonuç: Doğum sonrası dönemde annelerde ON eğilimi yüksek olarak bulundu. Ayrıca doğumdan sonra beslenme alışkanlıklarını ve fiziksel aktivite durumunu değiştiren annelerin ON eğiliminin diğerlerine göre daha yüksek olduğu görüldü. Bu nedenle doğum sonrası dönem, değişen yaşam tarzı alışkanlıkları nedeniyle annelerin ON ve benzeri yeme bozukluklarının yakın takibi açısından çok önemlidir. Aile hekimleri koruyucu hekimlik vasfı ile bu konuda çok kritik bir role sahiptirler.

Anahtar Kelimeler: Yeme Bozuklukları, Ortoreksiya Nervoza, Postpartum Dönem.

INTRODUCTION

In recent years there has been a growing concern in the world about Orthorexia Nervosa (ON). A lot of clinicians have started to interest with ON as a research subject all over the world. ON is a possible new eating disorder and is known as an excessive control of quality of the eaten foods (1) or pathological obsession with eating healthy (2). Several scales/measures for the assessment of Orthorexia Nervosa have been developed and the most widely used questionnaire to detect Orthorexia Nervosa tendency is the ORTO-15, developed by Donini et al. (3). In Turkish version, ORTO-15 scale was adapted to ORTO-11 (4). The prevalence rates of ON are reported from 6% to nearly 90% according to a measurement to identify orthorexia with ORTO-15 or ORTO-11 (3-9).

Pregnancy is a very complex period for women and during this special period and postpartum period there is an increased risk of the onset or worsening of psychiatric disorders, including postpartum depression and anxiety, obsessive–compulsive disorder, post-traumatic stress disorder and eating disorders (10). During postpartum period, related to the physiological and medical changes, it was stated that most of the women have concerns about their body image and therefore they have tendency to change their lifestyle, especially about nutrition and therefore, and it can lead mothers to Orthorexia Nervosa (11). In this period when baby nutrition is also very important, women have concerns about breastfeeding and nutrition of baby and again they may make various changes in their lifestyle (12). This might bring mothers to a pathological point about the consumption of healthy food and lead to healthy diet obsession (ON).

Although there are studies related to eating disorders of women in this special period, there are very few studies on ON tendency of postpartum mothers in literature (12). The aim of this study was to assess the Orthorexia Nervosa tendencies of postpartum women and investigate the related factors.

MATERIAL AND METHODS

This study had a descriptive design. The local ethics committee at XXX University approved the study (number: GO 18/1126-14); informed consent was obtained from all the participants. The study was conducted in two months starting at 1st December, 2018. The universe of the study was composed of mothers who have a child under the age of two in 2018 at the time of study who were members of an online social group called "2017-2018 mothers". We contacted with the women via e-mails through a social media group special for postpartum women which had 10.350 members at the time of study. The minimum sample size for universe was estimated as 370 women, assuming 95% confidence interval and 5% sampling error. All mothers could not be recommended by their group team to join this study, only we could reach the ones who saw the questionnaire during the sharing. A total of 511 participants responded and were included in the study. The mothers who had twins (or more multiple births) were excluded. Mothers who had more than one child were instructed to answer the questions based on their experiences with the youngest child.

Our survey consists of two parts: The questionnaire and the ORTO-11 questionnaire. The questionnaire assessed sociodemographic and anthropometric characteristics (educational status, working status, vocation, family style, weight, height), health status (diagnosed disease, the idea of being healthy, tobacco use, alcohol use, physical activity, diet, vitamin supplementation), delivery and baby feeding features of mothers (type of delivery, desired baby condition, breastfeeding status, difficulty in breastfeeding, concern about the amount of milk, change in nutrition during breastfeeding) and information about their lifestyle changes.

ORTO-11 Questionnaire: Two instruments have been developed to assess ON. The Bratman test is based mostly on clinical experience, and its validity has not been investigated by the author himself or by others (18). In 2005, Donini and colleagues developed the ORTO-15 based on Bratman's test (3). The translation into Turkish was made by Arusoğlu in 2006 and adapted to Turkish as ORTO-11 (4). In the evaluation of the scale, the increase in score shows that the risk of orthorexia nervosa is reduced. The cut-off point used for the evaluation of the ORTO-11 scale in our study was determined by using the cut-off point in Arusoğlu's Turkish adaptation study (4). Individuals who participated in the study were divided into quarterly according to ORTO-11 scores. The cut-off point of the study was determined as 27 points in 25%, and under this value was evaluated as orthorexic tendencies. Cronbach's Alpha of the scale was informed as 0.62.

The data obtained from the study were evaluated with SPSS (Statistical Package for Social Sciences) 23.0 l package programme. Qualitative variables are given as number (S) and percentage (%). Continuous variables obtained by measurement (quantitative variables); arithmetic mean, standard deviation, minimum, maximum values are given. Descriptive statistics were calculated to determine the status of ON among mothers. Each of the scores obtained from the ORTO-11 scale was compared according to sociodemographic and anthropometric characteristics, delivery and breastfeeding features of mothers and physical activity, nutrition and diet status of mothers after delivery by using t test, Mann Whitney U test and ANOVA (F-test). Chi-square and Fisher's exact tests were used to assess

qualitative data. Pearson test was used for the normal distribution and the correlation coefficients and statistical significance were calculated by using the Spearman test. P <0.05 was considered to be significant in all statistical analyzes.

RESULTS

The study population consisted of 511 mothers who volunteered to participate in the study. The mean age of the participants was 31.92±4.44 (min=20; max=46). Mean BMI of the participants was 24.86±11.00 kg/m2 (min=10.52; max=43.43) and according to the WHO classification of nutritional status, 276 (64.3%) of them had normal weight. The mean number of children of mothers was 1.45±0.62 (min=1; max=5). The mean age of children was 15.99±9.03 months (min=1; max= 24).

The mean ORTO-11 scale score of all participants was 22.68±4.09 (min=12; max=35) points. The distribution of ORTO-11 scores based on characteristics of the participants can be seen in Table I. ORTO-11 scores of mothers had statistically significant relationship with age, working status, vocation, and family style. The ORTO-11 scores were higher in mothers older than 40 years, working mothers, health worker mothers, mothers who live at core family and they show less propensity to ON than others. However, teachers and officers had high ortorectic tendency than other mothers. ORTO-11 scores had statistically significant relationship with the idea of being healthy, physical activity status and diet status after delivery. According to the idea of being healthy status; the mothers who think they were healthy had lower ORTO-11 scores and also had ortorectic tendencies. The mothers who doing regular physical activity and those who had regular diet had lower ORTO-11 scores and had high ortorectic tendencies than others.

35.2% (n=180) of the mothers noted that they change all eating habits as regularly (both order and frequency of nutrition) after birth. Those mothers' ORTO 11 score mean was 22.15+3.645 (min=12; max=30) and 91.3% of these mothers had high ortorectic tendencies. 66.7% of them said they had no diet before birth and 88% of them noted that they change their eating habits because of breastfeeding. The distribution of ORTO-11 scores based on birth, breastfeeding status and associated nutritional status of the participants can be seen in Table II. Higher rates of orthorexia tendencies were observed in mothers who changed their eating patterns as regularly after birth.

According to cut-off point, 87.7 % (n=426) of the participants were found to be at the risk of developing ON. The comparison of ON tendency status according to ORTO-11 cut-off points and characteristics, health status and breastfeeding status of participants can be seen in Table III. Among the mothers, there is a significant statistical difference between the ON tendencies of mothers as to BMI, diet status, changing in order and frequency of nutrition's. Overweights, the participants who do occasionally diet, who fed more regular and more often after delivery had higher ON tendency.

DISCUSSION

This study was conducted to examine the maternal nutrition changes after delivery and ON tendencies of those mothers and to investigate the relationship between them. The results were discussed as the following;

The limited literature regarding ON is dominated by studies reporting point prevalence using the ORTO-15/11 or one of their adaptations (3-9). Generally, the biggest part of the studies were performed on the medical faculty students, doctors, dietitians, performance artists, who were defined as risk groups for orthorexia nervosa, and the common feature of these groups is that they are aware of the importance of healthy nutrition and body image (3-9). We planned our study as a hypothesis that mothers after delivery may be in the risk group due to the same features (aware of the importance of healthy nutrition and body image). There is no study on ON tendency of postpartum mothers in literature. This is the first study on this subject.

The mothers' pathological attitudes towards eating, body shape and weight, could have a direct effect on the child and in the way she feeds him/her, hereby the eating disorders such as ON is very important to detect. Mothers can also take care of better quality nutrition to increase the quality and quantity of breast milk during the breastfeeding period and that condition may increase the possibility of ON tendency of mothers. In our study, according to cut-off point of ORTO-11 scale, 87.7 % of the participants were found to be at the risk of developing ON and the mean ORTO-11 scale (22.68±4.09) also supports that result. In literature, the prevalence of ON varies widely from 6% in an Italian sample to 88.7% in a sample comprised entirely of female nutritionists. Bosi et al. have reported that the prevalence rate of 318 resident physicians was 45.5% (7). Fidan et al. determined 43.6% of 878 Turkish medical students have tendency to ON (19). Orthorexia prevalence was identified as 6.9% in the research done by Donini et al (3). Ramacciotti et al. were aimed to determine ON in the "general population" and they found the prevalence rate as 57.6% (5).

Table 1. Distribution of ORTO-11 scores according to some features of participants (N:511)

	Number (n)	Percentage (%)	ORTO-11 score *M± SD*	p
Age**				
30>	143	29.5	22.07±3.96	
30-34	218	45	22.77±4.21	**0.004**
35-39	99	20.5	22.65±4.80	
40≤	24	5.0	25.33±3.70	
Child number*				
1	311	61.6	22.58±4.258	0.514
2≤	194	38.4	22.84±3.814	
Child age**				
6 months≥	66	14.2	22.83±3.913	
7-12 months	67	14.4	23.29±4.057	0.288
13-18 months	187	40.2	22.20±4.154	
19 months≤	145	31.2	22.84±4.351	
Educational Status**				
Primary Education	18	3.6	22.88±3.35	
High School	57	11.6	31.44±4.15	0.140
University	432	84.8	22.83±4.10	
Working status*				
Working	175	34.5	22.33±1.15	**0.001**
Not working	332	65.5	21.66±4.04	
Vocation**				
Physician	268	52.9	23.70±3.85	
Nurse	10	2	21.10±4.01	
Dietician	1	0.2	23.72±4.03	
Other Health workers	9	1.8	23.63±4.40	
Teacher	64	12.6	20.59±3.62	**0.001**
Engineer / Architect	8	1.6	21.43±3.95	
Officer	13	2.6	20.67±3.02	
Worker	3	0.6	22.67±6.35	
Private sector	31	6.1	21.66±4.25	
Other	87	17.2	21.86±4.24	
Family style*				
Core family	453	89.3	22.81±4.06	**0.021**
Large family	54	10.7	21.56±3.96	
BMI**				
Underweight	18	4.2	23.56±4.79	
Normal	276	64.3	22.90±4.22	0.677
Overweight	104	24.2	22.45±3.65	
Obese	32	7.4	22.52±3.97	
Diagnosed Disease *				
Yes	362	71.4	22.79±4.15	0.621
No	145	28.6	22.39±3.93	
The idea of being healthy*				
Yes	427	84.2	21.68±3.79	**0.020**
No	80	15.8	22.87±4.12	
Tobacco use**				
Current smoker	63	12.4	22.01±4.53	
Non smoker	73.2	73.2	22.91±4.01	0.108
Left	12.4	14.0	22.03±4.04	
Alcohol use**				
Yes	52	10.3	23.22±3.69	
No	364	71.8	22.73±4.19	0.390
Left	89	17.6	22.18±3.86	
Physical activity *				
Yes	64	87.2	21.15±4.56	**0.002**
No	442	12.6	22.91±3.97	
Diet**				
Regularly	17	64.7	19.56±3.84	**0.0001**
Occasionally	161	31.8	21.90±4.13	
Never	328	3.4	23.22±3.96	
Vitamin supplementation**				
Yes	59	11.6	23.22±3.69	0.846
Sometimes	165	32.5	22.84±3.97	
No	281	55.4	21.49±4.31	

Mean = M, SD= Standard deviation, BMI: Body mass index

** Independent Sample T test was used for statistical analysis*

*** One-way ANOVA was used for statistical analysis*

P<0.05 was accepted as statistacally significant

Table 2. Distribution of ORTO-11 scores according to factors related to participants' babies (N:511)

	Number (n)	Percentage (%)	ORTO-11 score *M± SD*	p
Type of delivery*				
Vaginal	131	25.8	22.54±4.11	0.466
Cesarean	376	75.2	22.72±4.08	
Desired baby condition*				
Yes	467	92.1	22.75±4.07	0.242
No	40	7.9	21.92±4.22	
Breastfeeding status**				
Yes	403	79.5	22.68±3.92	
No	3	0.6	21.50±2.12	0.866
Left	101	19.9	22.73±4.79	
Difficulty in breastfeeding*				
Yes	195	38.5	22.32±3.97	0.118
No	312	61.5	22.91±4.14	
Concerned about the amount of milk *				
Yes	312	61.7	22.76±4.11	0.666
No	194	38.3	22.58±4.03	
Change in nutrition during breastfeeding*				
Yes	333	65.7	22.69±4.02	0.763
No	174	34.3	22.66±4.22	
Change in eating patterns (order of nutrition)**				
No change	176	34.7	23.69±4.55	
It was irregular	78	15.4	22.00±3.43	**0.001**
It was regularly	249	49.1	22.18±3.79	
Change in frequency of nutrition**				
No change	165	32.5	23.36±4.47	0.104
Yes,more offen	51	10.1	22.56±4.82	
Yes,less than older	286	56.4	22.36±3.68	
Mean = M, SD= Standard deviation				

** Independent Sample T test was used for statistical analysis*
*** One-way ANOVA was used for statistical analysis*
P<0.05 was accepted as statistacally significant

Missbatch et al. administered the translated instrument to 1029 people recruited through social media and found almost 70% of their sample showed "orthorectic" tendencies (20). In this study, the prevalence of orthorexia was also high (87.7%). The fact that the study population is composed of women suggests that the prevalence may be high. And also this special period (breastfeeding, postpartum stress, pregnancy related body shape changes) may affect the results. This condition made us to think about the postpartum anxiety of mothers about weight, body shape and feeding their baby may affect the nutrition status and may cause the ON tendency of them. When we evaluated the ortorectic tendencies of the mothers who change all eating habits as regularly (both order and frequency of nutrition) after birth; their tendency to ON was also higher than other mothers. These result supports our idea. However, it is recommended that this finding to be strengthened by an analytical study with a control group.

Although Arusoğlu and his colleagues indicated that age is not effective on orthorectic tendency (4); it is reported that increasing age can be effective on increasing the orthorexic tendency in the other studies (3,7,19). But in our study we found that lower ages had high ortorectic tendency. The stress of being a mother at a young age may be the reason why our study group came out in this way.

The relationship between the orthorexic tendency and the educational status of individuals was contradictory, and Donini et al. indicated that the orthorectic tendency is high in those with low levels of education (3) and generally, doctors, dietitians defined as in the risk groups for orthorexia nervosa because of their job. Unlike that results we found high ON tendency in officers and teachers and low ON tendency in health workers. We believe that this result may have been affected by some factors (breastfeeding break times, etc) and there will be a need for more extensive research and analysis.

Studies in the literature found a significant relationship between the risk of eating disorder and trying to lose weight, exercise for weight loss, prolonged fasting and vomiting (19,21). Like these studies we found lower scores and also higher ON tendency on the mothers who did regularly physical exercise and diet.

In our study we found that the participants who think they are heathy had higher ortorectic tendencies. When we look to meaning of ON; excessive control of quality of the eaten foods is emphasized. Also the control of quality of the eaten foods is a healthy behavior; however if it is

Table 3. Comparison of ORTO-11 cut-off points according to some features of participants (N:511)

	ON tendency (+)		ON tendency (-)		p
	n	%	n	%	
Age					
30>	122	90.4	13	9.6	
30-34	180	85.7	30	14.3	0.576
35-39	86	89.6	10	10.4	
40≤	21	87.5	3	12.5	
Educational Status					
Primary Education	16	94.1	1	5.9	
High School	47	90.4	5	9.6	0.690
University	361	87	54	13	
Working status					
Working	152	92.7	12	7.3	0.085
Not working	270	84.9	48	15.1	
Family style					
Core family	379	87.3	55	12.7	0.527
Large family	47	90.4	5	9.6	
BMI					
Underweight	13	72.2	5	27.8	
Normal	225	85.6	38	14.4	**0.033**
Overweight	95	94.1	6	5.9	
Obese	26	89.7	3	10.3	
Diagnosed Disease					
Yes	126	86.2	12	13.8	0.121
No	299	91.3	48	8.7	
The idea of being healthy					
Yes	352	93.7	55	6.3	0.076
No	74	86.5	5	13.5	
Tobacco use					
Smoker	54	86.6	6	13.4	0.494
Non smoker	309	91	48	9	
Left	61	90	6	10	
Alcohol use					
Yes	41	87	9	13	0.130
No	301	93.2	45	6.8	
Left	82	82	6	18	
Physical activity					
Yes	56	87.2	6	12.8	0.490
No	369	90.3	54	0.7	
Diet					
Regularly	16	100	0	0	**0.022**
Occasionally	142	92.2	12	7.8	
Never	267	84.8	48	15.2	
Vitamin supplementation					
Yes	52	87.7	5	12.3	0.597
Sometimes	136	86.1	22	13.9	
No	236	91.2	33	8.8	
Type of delivery					
Vaginal	106	86.2	17	13.8	0.565
Cesarean	320	88.2	43	11.8	
Desired baby condition					
Yes	381	89.2	33	10.8	0.761
No	56	80.5	4	19.5	
Breastfeeding status					
Yes	344	82.3	43	17.7	0.185
No	2	100	0	0	
Left	79	88.9	17	11.1	
Difficulty in breastfeeding					
Yes	166	89.7	19	10.3	0.270
No	259	86.3	41	13.7	
Concerned about the amount of milk					
Yes	261	87.7	37	12.3	0.970
No	161	87.6	23	12.4	
Change in nutrition during breastfeeding					
Yes	282	87.1	142	12.9	0.817
No	142	87.9	21	12.1	
Change in order of nutrition					
No change	132	78.1	37	21.9	**<0.001**
It was irregular	70	94.6	4	5.4	
It was regularly	222	92.1	19	7.9	
Change in frequency of nutrition					
No change	125	80.1	31	19.9	**0.001**
Yes,more offen	256	85.4	22	14.6	
Yes,less than older	41	92.1	7	17.9	

Ki square test was used for statistical analysis
P<0.05 was accepted as statistacally significant

excessive; then it can become a disease state (ON). Studies also emphasized that ON is a disease caused by the excess of the idea of being healthy (19,21,23).

Another important result of our study was that mothers who fed more regular and more often compared with before pregnancy, their ON tendency rates were high. This result confirms our hypothesis again. In postpartum period, for various reasons that mothers can change their diet and this change may take an obsessive dimension and as a result ON may occur. The topic of healthy nutrition has been currently and extensively covered in the Turkish media for the past 10–15 years, also there is a lot of social media and television messages especially about mother-infant nutrition. It is thought that the frequent messages have had a cautionary effect.

In our study the ON tendency was found to be higher in mothers who started physical activity after birth. Also the physical activity is an indicative of a healthy living trend. According to the results of a study, it was observed that people who are in the group of sport exhibited more impaired eating attitudes and showed higher orthorectic tendency than those who did not (24).

In some studies, it was stated that body mass index may be an indicator for predicting orthorexic behaviors (19,21,22). Particularly high BMI values are reported to be associated with low ORTO-15 scores (19,21,23). In our study we did not find a relationship between BMI and ORTO scores, but when we used cut off point to describe the ON tendency; we found a relationship between ON tendency and BMI, and it was observed that the overweights had a greater predisposition toward ON. Social interactions and with the media promoting a thin body, and therefore concerns about body weight and body image are increasing. Eating disorders are the group of diseases in which the effort on the body is the one which is observed most clearly.

The study has some strengths and limitations. A vast amount of data was collected from a specific group of people who were postpartum women from different cities, which strengthens the results. However, this is a cross-sectional study, the results cannot be generalized. In addition, as the surveys were sent over the Internet, participant characteristics may not be representative of the whole postpartum women.

CONCLUSION

As a summary, in our study, the tendency toward ON was high among mothers in postpartum period. Also the mothers who change their eating habits and change the physical activity status after delivery had higher ON tendency than others. So the postpartum period is very important to detect the mothers about ON and such eating disorders because of the changing lifestyle habits. Because of the biggest part of our sample breastfeed their baby, the effect of breastfeeding on ON cannot be assessed. The obsession of healthy eating can adversely affect body perception in the course of the process and may pave the way for health problems such as the desire to improve external image, energy and nutrient deficiencies and malnutrition. After delivery the nutrition of baby is important and also regular and healthy nutrition of mother is very important. Because of the frequent visits of primary care due to baby, mothers might want to help from primary care professionals about true and regular nutrition in this period.

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RESEARCH ARTICLE

Sinem Kantarcioglu Coskun[1]
Hulya Ozturk Nazlioglu[2]
Çagatay Buyukuysal[3]

[1]Duzce University, School of Medicine, Department of Pathology, Konuralp, Düzce, Turkey
[2] Bursa Uludag University, School of Medicine, Department,of Pathology, Görükle, Bursa, Turkey
[3] Zonguldak Bulent Ecevit University, School of Medicine, Department of Biostatistics, Zonguldak, Turkey

Corresponding Author:
Sinem Kantarcioglu Coskun
Duzce University, School of Medicine, Department of Pathology, Konuralp, Düzce, Turkey
Phone: +90 507 921 61 97
mail: sinemcoskun@duzce.edu.tr

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www.konuralptipdergi.duzce.edu.tr

Clinicopathological Features of Extranodal Lymphomas: 15 Years' Experience of a Single Center

ABSTRACT

Objective: In this study, we aimed to evaluate the localization and histopathological diagnosis, and clinicopathologic characteristics of primary extranodal lymphomas.

Methods: The pathology reports between 2001 and 2015 in the archives of Uludag University Faculty of Medicine Pathology Department were reviewed and all cases with an extranodal lymphoma diagnosis were analyzed. The information about the diagnosis, tumor localization, symptoms at presentation, presence of B symptoms, lymphocytosis and anemia, chronic infection and chronic disease and concomitant secondary malignancy, tumor diameter, the involvement of another extranodal organ, lymph node, bone marrow, spleen, liver, stage of the disease, serum B2 microglobulin, LDH, albumin levels, sedimentation rate were documented. The localization, histopathological types, age groups, male/female ratios in cases of primary extranodal lymphoma were evaluated.

Results: Total sum of 1743 patients were diagnosed with lymphoma. 480 (%27,53) of these cases were extranodal lymphomas. The most commonly encountered locations of extranodal lymphomas were the skin and the gastrointestinal system. There were 226 primary extranodal skin, 90 gastrointestinal system, 44 central nervous system, 8 genitourinary system, 50 head and neck, 18 musculoskeletal system and soft tissue, 9 mediastinum, 3 bronchus, 10 orbital, 2 liver, 6 pancreas, 4 omentum, 8 endocrine system, and 2 breast located cases. 237 of the primary extranodal lymphomas from our work were mature T/NK celled neoplasias. There were 250 patients with mature B cell lymphoma, 5 cases of Hodgkin lymphoma, and 5 cases of precursor lymphoid neoplasia.

Conclusions: The data from our series were coherent with the literature. Due to the small number of cases with some localization and some histopathological diagnosis, no significant results could be reached about these entities.

Keywords: Extranodal Lymphoma, Skin, Gastrointestinal System, Central Nervous System, Diffuse Large B Cell Lymphoma.

Ekstranodal Lenfomaların Klinikopatolojik Özellikleri: 15 Yıllık Tek Merkez Deneyimi

ÖZET

Amaç: Bu çalışmada 2001-2015 yılları arasında tanı alan primer ekstranodal lenfomaların lokalizasyonlarının ve histopatolojik olarak dağılımının, klinikopatolojik özelliklerinin değerlendirilmesi amaçlandı.

Gereç ve Yöntem: Uludağ Üniversitesi Tıp Fakültesi Patoloji Anabilim Dalı arşivindeki 1 Ocak 2001 ile 31 Aralık 2015 arasındaki patoloji raporları gözden geçirildi, lenfoma tanılı bütün olgular incelendi. Hasta dosyaları incelenerek primer olarak ekstranodal bölgeden kaynaklanan olguların tanısı, hastaneye başvuru semptomları, B semptomu varlığı/yokluğu, tümör çapı, başka ekstranodal organ, lenf nodu, kemik iliği, dalak, karaciğer tutulumu olup olmadığı, kronik enfeksiyon ve kronik hastalık varlığı, hastalığın evresi (Ann Arbor sınıflamasına göre), eşlik eden sekonder malignite varlığı, anemi, lenfositoz varlığı, serum B2 mikroglobulin, LDH, albumin değerleri, sedimentasyon hızı bilgileri dökümante edildi. Primer ekstranodal lenfomalı vakalarda belirlenen histopatolojik tanıların dağılımı, tipleri, yaş grupları, kadın/erkek oranları literatür bilgileri ışığında gözden geçirildi.

Bulgular: 2001 – 2015 yılları arasında Uludağ Üniversitesi Tıp Fakültesi Tıbbi Patoloji Anabilim Dalı'nda toplam 1743 hastaya lenfoma tanısı verilmişti. Bu olguların 480 (%27,53) tanesi ekstranodal kaynaklıydı. Genel olarak en sık görülen ekstranodal lokasyon deri ve gastrointestinal sistemdi. Primer ekstranodal 226 deri, 90 gastrointestinal sistem, 44 santral sinir sistemi, 8 genitoüriner sistem, 50 baş-boyun, 18 kas-iskelet-yumuşak doku, 9 mediasten, 3 bronş, 10 orbita, 2 karaciğer, 6 pankreas, 4 omentum, 8 endokrin sistem, 2 meme yerleşimli olgu mevcuttu. Çalışmamızdaki primer ekstranodal lenfomaların 237'sini matür T/NK hücreli neoplaziler oluşturuyordu. Matür B hücreli lenfomalı 250 hasta mevcuttu. Hodgkin lenfoma tanılı 5, prekürsör lenfoid neoplazi tanılı 5 olgu mevcuttu.

Sonuç: Sonuç olarak çalışmamızdaki veriler literatürle uyumludur. Bazı lokalizasyondaki ve bazı histopatolojik tanılı olguların sayıca azlığı sebebiyle bu antiteler hakkında anlamlı sonuçlara ulaşılamamıştır.

Anahtar Kelimeler: Ekstranodal Lenfoma, Deri, Gastrointestinal Sistem, Santral Sinir Sistemi, Diffüz Büyük B Hücreli Lenfoma.

INTRODUCTION

Lymphoma is the clonal malignancy of the immune system and lymphocytes as a general term that describes a heterogeneous group of diseases (1). Non-Hodgkin lymphomas (NHL) represent about 90% of all malignant lymphomas, while Hodgkin lymphomas (HL) consist of the remaining 10% (2). About a third of NHLs develop from tissues other than the lymph node, and these cases are called extranodal lymphomas (ENL) (3). The definition of ENL is still a confusing problem, especially in the presence of both nodal and extranodal disease. Dawson criteria have been determined for the definition of primary ENL. These criteria are based on the absence of palpable superficial lymph node in the first physical examination, absence of mediastinal lymphadenopathy in the chest X-ray, presence of the dominant lesion in the extranodal region, if there is lymph node involvement, the presence of the white blood cell count in complete blood count should be within normal limits (4). The definition of primary ENL is still controversial in the literature; therefore, the percentages in the studies show more variability than nodal lymphomas. Primary extranodal presentation of stage III and IV lymphomas is questionable, because the secondary extranodal spread may also be present in primary nodal disseminated diseases (5). Krol et al. showed that the rate of ENL can vary between 20% and 34% (6). Recently, the cases have a clinically dominant extranodal component with non-nodal component or minor involvement are accepted as extranodal (5). In this study, we aimed to evaluate the distribution and clinicopathologic characteristics of primary ENLs.

MATERIAL AND METHODS

Pathology reports diagnosed with lymphoma between 2001 and 2015 in the archives of Uludağ University, Faculty of Medicine, Pathology Department were reviewed. The cases which have clinically dominant extranodal component, with non-nodal component or minor involvement were included in the study. Patient files were analyzed. The information about the diagnosis, tumor localization, symptoms at presentation, presence of B symptoms, lymphocytosis and anemia, chronic infection and chronic disease and concomitant secondary malignancy, tumor diameter, the involvement of another extranodal organ, lymph node, bone marrow, spleen, liver, stage of the disease (by the Ann Arbor classification), serum B2 microglobulin, LDH, albumin levels, sedimentation rate were documented. The localization, histopathological types, age groups, male/female ratios in cases of primary ENL were evaluated with the literature information and classification of the World Health Organisation (WHO) Classification of Tumours of Haematopoietic and Lymphoid Tissues (2008,2017) (7,8). Patients with stage III and IV were not included in the study to exclude the possibility of secondary extranodal involvement of a primary nodal onset lymphoma. Cases of acute lymphoblastic leukemia, chronic lymphocytic leukemia, plasma cell myeloma were not included in the study. The study was performed according to the tenets of the Helsinki Declaration and according to approval by the local Ethics Committee of the Uludag University Medical School (prot . No 2016-2/15/EC of 02 February 2016).

Statistical Analysis: Statistical analysis of the study was done in SPSS 22.0 package program. Descriptive statistics of categorical variables in the study are shown with frequency and percentage. Whether there is any change in the diagnosis of the diagnosis by years has been examined by chi-square trend analysis. In the statistical comparisons in the study, if the p-value is below 0.05, it was considered statistically significant.

RESULTS

Between the years 2001 and 2015, 1743 patients were diagnosed as lymphoma in the Pathology Department. The 480 (27.53%) of these cases were from the extranodal origin. The most common extranodal location was the skin and gastrointestinal tract. There were 226 skin, 90 gastrointestinal system, 44 central nervous system, 8 genitourinary system, 50 head and neck region, 18 musculoskeletal-soft tissue, 9 mediastinum, 3 bronchi, 10 orbital, 2 liver, 6 pancreas, 4 omentum, 8 endocrine system and 2 breast located extranodal lymphomas respectively. Mature T / NK cell neoplasms accounted for 237 of the primary extranodal lymphomas in our study. There were 250 patients with mature B cell lymphoma. There were 5 cases with HL and 5 cases with precursor lymphoid neoplasia. Relevant clinicopathological and demographic data are shown in Tables 1,2 and 3, Figure 1.

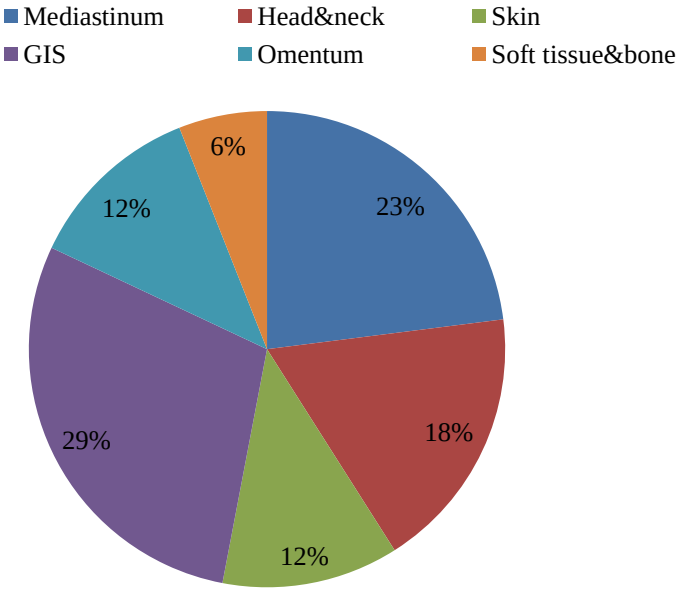

Fig 1. Distribution of tumor locations in pediatric cases

Table 1. Distrubition of extranodal lymphomas

Localisation	Number of cases	(%)
Skin	226	47,1
Gastrointestinal system	90	18.8
Stomach	50	10.4
Small bowel	28	5.8
Colorectal	11	2.3
Eosophagus	1	0.3
Head and neck	50	10.4
Tonsil	28	5.8
Nasal mucosa	6	1.3
Nasapharinx	4	0.8
Oral cavity	3	0.6
Salivary glands	3	0.6
Tongue-basis of tongue	3	0.6
Sinuses	2	0.4
Gum	1	0.3
Central nervous system	44	9.2
Muscles-Skeleton-Soft	18	3.8
tissue	9	1.9
Paravertebral	5	0.7
Bone	1	0.3
Knee	1	0.3
Soft tissue	1	0.3
Muscle	1	0.3
Extremity		
Orbita	10	2.1
Eyelid	3	0.6
Conjunctiva	2	0.4
Lacrimal gland	1	0.3
Eye	1	0.3
Not specified	3	0.6
Mediastinum	9	1.9
Endocrine System	8	1.7
Thyroid gland	5	1.0
Adrenal gland	3	0.7
Urogenital System	8	1.7
Testicle	4	0.8
Kidney	3	0.6
Bladder	1	0.3
Pancreas	6	1.3
Omentum	4	0.8
Bronchus	3	0.6
Liver	2	0.4
Breast	2	0.4
TOTAL	**480**	**100**

Table 2. Histopathological subtypes in pediatric patients

Histopathological diagnosis	Number of cases	(%)
Precursor lymphoid neoplasia	5	29.4
Precursor T cell	5	29.4
Mature B cell neoplasia	10	58.8
Burkitt lymphoma	7	41.2
DBLCL	3	17.6
Mature T cell neoplasia	2	11.8
MF	2	11.8
Total	**17**	**100**

Table 3. Clinical features of extranodal lymphomas in pediatric and adult age groups

CLINICAL FEATURES	ADULT	PEDİATRIC
Number of cases	463	17
Gender		
Male	274	15
Female	189	2
Age groups		
0-5		4
6-9		7
10-19		6
20-29	28	
30-39	59	
40-49	64	
50-59	126	
60+	186	
Nodal involvement	40(8.6%)	1(5.9%)
LDH		
High	61	6
Normal	151	1
Unknown	251	10
B symptoms		
Yes	20	0
No	305	12
Unknown	138	5
Anemia		
Yes	57	3
No	264	7
Unknown	142	7
Lymphocytosis		
Yes	49	1
No	272	9
Unknown	142	7
Albumin		
Low	61	2
Normal	135	6
Unknown	267	9

DISCUSSION

Gastrointestinal System Lymphomas: The gastrointestinal tract is the most common location for extranodal NHL. It constitutes 4-20% of all NHLs and 30-40% of all ENLs (9). There were 90 primary gastrointestinal ENLs in our series. It consists 18.8% of all ENLs. According to the review of Peng et al, the most common location of primary gastrointestinal system lymphomas is the stomach (60-70%), followed by the small intestine, ileocecal region, and colon (10). Primary gastric lymphomas (PGL) in our series constituted 10.41% of extranodal lymphomas and 55.6% of gastrointestinal canal lymphomas.

PGLs are most common in 5 to 6th decades. Men are more affected than women. It is more common in the white race (10). The patient ages in our series were between 27 and 82. The mean age was 58.31. The male to female ratio was 1.63 / 1.

Almost all PGLs are B-cell lymphomas, T cell neoplasms of the stomach and primary gastric HL are extremely rare (11-12). In our series, there were 2 (4%) primary gastric HL cases. There are many studies in the literature reporting that almost

half of B cell PGLs are MALT lymphoma. Diffuse large B cell lymphomas (DLBCL) is the second most common in the stomach, but follicular and mantle cell lymphomas are also common. DLBCL were predominantly observed in the distribution of patients (68%). MALT lymphoma is the second most common lymphoma in the stomach, and represent 7 (14%) of the cases. Mantle cell and Burkitt's lymphoma were equal in number and seen in one case each.

Primary tumors of the small intestine are very rare, representing less than 2% of all gastrointestinal tract malignancies (13). There are 28 cases of small bowel origin in our series, constitute 5.83% of all ENLs and 31.1% of primary gastrointestinal system lymphomas. The ileum is the most common location for primary small bowel lymphomas (PSBL) (60-65%). This is followed by jejunum, duodenum, and other regions (14). Two of the cases in our series were located in the ileocecal region.

PSBLs are more heterogeneous than stomach lymphomas. MALT lymphoma, DLBCL, EATL, mantle cell lymphoma, and immunproliferative small bowel disease (IPSID) are seen in small bowels (15). Twenty four (85.8%) of the cases in our series were mature B cell neoplasia and 2 (7.1%) were T cell neoplasia. DLBCLs accounted for 18 (57.2%) of B cell neoplasms. Burkitt lymphoma was observed in 6 (28.6%) cases. One of two T cell lymphomas was EATL and the other was peripheral T cell lymphoma.

Primary colorectal lymphomas are extremely rare, accounting for only 0.2% of all colorectal tumors. About 6-12% of primary gastrointestinal lymphomas originate from the colorectal region (13). Primary colon lymphomas in our series constituted 2.3% of all ENLs and 12.22% of gastrointestinal system lymphomas.

DLBCL is the most common histological subtype in colon and rectum lymphomas. MALT lymphoma is also commonly seen. Although T cell lymphomas are rare in western countries, their number is increasing in Asian countries (13). Ten (91%) of the cases in our series were of B cell origin. The 7 (63.8%) of them were DLBCL, 2 (18.2%) were mantle cells, 1 (9%) were Burkitt lymphoma. There was 1 (9%) patient with peripheral T cell lymphoma.

Central Nervous System Lymphomas: Primary central nervous system lymphomas (PCNSL) constitute 0.5-1.2% of all intracranial neoplasms and less than 1% of extranodal NHLs (16). There are 44 cases in our series, consist of 9.2% of all ENLs. The incidence of PCNSL has increased in both immunosuppressed and normal individuals in the last three decades (17). There was no significant change in the frequency of PCNSL cases in our series by years ($p = 0.579$). PCNSLs occur at a younger age with immunosuppressed patients. The patients' ages in our series were between 20 and 81, and the mean age was 59.30. The male to female ratio was 1.44 / 1. All of the cases in our series consisted of mature B cell lymphomas.

Skin Lymphomas: Primary cutaneous lymphomas (PCL) are skin-originated non-Hodgkin lymphomas that occur in individuals without evidence of another extracutaneous lymphomatous disease at the time of diagnosis (18). PCLs can develop from both T and B cells. More than 75% of primary skin lymphomas are T cell originated (19). A total of 226 primary cutaneous lymphoma patients diagnosed in our clinic, 223 (98.7%) were mature T cell lymphomas and 3 (1.3%) were mature B cell lymphomas. Mycosis fungoides (MF) is the most common form of cutaneous T cell lymphomas, and it occurs in men two times frequently than women. Most of the cases are 5-6. decades. It rarely affects children and adolescents (20). Patients diagnosed with MF in our series consist of 94.7% all cutaneous lymphomas. There were 124 male and 90 female patients with MF. The male / female ratio was 1.37 / 1. Patient ages ranged from 16 to 89, with a median age of 53.5.

Head&Neck Lymphomas: Lymphomas are the most common neoplasms in the head and neck region after squamous cell carcinomas (21). Malignant lymphomas constitute 5% of all malignancies in the head and neck localization (22). ENLs with head and neck localization was in the 3rd rank after the skin and gastrointestinal tract in our series.

The most common area of head and neck lymphoma is tonsil (56%), followed by the nasopharynx, oral cavity, salivary glands, paranasal sinuses, and tongue root (23). In our series, tonsil was the most frequent site for primary ENLs in the head&neck region. Nasal mucosa (12%), nasopharynx (8%), oral cavity (6%), salivary gland (6%), tongue-base of the tongue (6%), paranasal sinuses (4%) and gingiva (2%), were following frequent localisations respectively.

Some NHL types are particularly common in the head and neck region. The most common B cell neoplasms are precursor B lymphocytic leukemia/lymphoma, MALT lymphoma, follicular lymphoma, mantle cell lymphoma, DLBCL, and Burkitt lymphoma. The most common T and NK cell lymphomas are nasal type extranodal NK / T cell lymphomas (24). B-cell neoplasms constituted 43 (86%) of head and neck lymphomas in our series. The 26 were DLBCL, 5 were Burkitt lymphoma, 5 were follicular lymphoma, 4 were mantle cell lymphoma. Only 6 (12%) of the cases had T cell histology. One case was lymphocyte rich HL.

Muscle-Skeleton-Soft Tissue Lymphomas: Lymphoma can occur anywhere in the musculoskeletal system. Although the secondary involvement of the musculoskeletal system is

common, the primary occurrence is rare (25). Primary musculoskeletal system lymphomas consist of 3.8% ENLs in our series.

According to Bhagavathi's review, primary bone lymphoma is a rare entity; it constitutes 4-5% of ENLs and 3% of all bone malignancies (26). The 27.8% of musculoskeletal lymphomas in our series primarily occurred in the bone. Primary bone lymphomas are seen between the ages of 20-50. There is a male predominance, the male to female ratio is 3: 2 (27). The ages of the patients in our series were between 26 and 80, and the median age was 65. The male to female ratio was 1.5 / 1. Most primary bone lymphomas are DLBCL (26). All of the cases in our series were DLBCL.

Primary skeletal muscle lymphomas cover approximately 0.5% of all ENLs (28). The only case of musculoskeletal lymphoma in our series constituted 0.3% of ENLs.

Mediastinal Lymphomas: Primary mediastinal lymphoma (PML) is rare, constitutes 10% of lymphomas in the mediastinum (29). Nine PML patients in our series accounted for 1.9% of all ENLs. The age range was between 4-57, with a median age of 32. The male to female ratio was 3.5 / 1.

Lymphoblastic lymphoma and DLBCL are the most common subtypes in the mediastinum (29). In our series, 5 (55.5%) of the 9 cases were T lymphoblastic lymphoma and 4 (44.5%) were DLBCL.

Endocrine System Lymphomas: Primary endocrine system lymphomas account for 3% of ENLs (28). In our series, lymphomas originating primarily from the endocrine system constituted 1.7% of all ENLs.

The majority of thyroid lymphomas are B originated. The most common histological subtypes are DLBCL and MALT lymphoma; follicular lymphoma, small lymphocytic lymphoma, and Burkitt lymphoma may also occur (30). More than 90% of reported cases have chronic lymphocytic thyroiditis or Hashimoto's disease (31). Hashimoto's thyroiditis was detected in 40% of the cases in our series. All 5 patients with primary thyroid lymphoma diagnosed in our clinic were all B-cell lymphomas, 2 cases were diagnosed as MALT lymphoma, and 1 case was diagnosed as DLBCL. Two cases were reported as B cell lymphoma, not otherwise specified.

Primary adrenal lymphoma (PAL) is extremely rare. Less than 200 patients with PAL have been reported in the literature. Patients with PAL diagnosed in our clinic accounted for 0.7% of ENLs. Male to female ratio reported in the literature is 2/1 and the average age is 65 (32). In our series, the male to female ratio was 2/1 and the patient ages were between 45-81. All three cases were DLBCL.

Orbital Lymphomas: Primary orbital lymphomas (POL); originates from the conjunctival, lacrimal gland, soft tissues of the eyelid or extraocular muscles constitute 5-15% of all ENLs (33-34). Ten patients with POL in our series accounted for 2.1% of ENLs.

POLs can be seen at any age, but are most frequently diagnosed in the seventh decade. The ages of patients in our series were between 24-92 years and the median age was 64 years. The male to female ratio was 1.5 / 1.

The most common histological subtype is MALT lymphoma in orbit. Other common histological types are lymphoplasmacytic and follicular lymphomas (34). In our series, MALT lymphoma was observed at 60% and DLBCL at 40%, respectively.

Urogenital Tract Lymphomas: Genitourinary lymphomas account for less than 5% of all extranodal NHLs (9). In our study, kidney, bladder, and testicular lymphomas constituted 1.7% of ENLs.

Primary testicular NHLs make up 2% of ENLs (35). Patients diagnosed with primary testicular lymphoma (PTL) in our hospital accounted for 0.8% of all ENLs. PTLs are the most common testicular malignancy between the ages of 60 and 80 (35). The ages of the cases in our series ranged from 58 to 77, the median age was 64.50. The typical presentation is a hard, painless testicular mass with an average diameter of 6 cm. Bilateral involvement occurs in 6-10% of cases (36). All of our cases were unilateral. All of the patients with PTL in our series applied to the clinic with the complaint of swelling in the testicle. The majority (80-98%) of PTLs are DLBCL. All of our patients were DLBCL.

Primary renal lymphomas (PRL) account for 0.7% of all ENLs (37). Patients with PRL in our study accounted for 0.6% of ENLs. Most patients are in the sixth decade, with a mild male predominance (38). The cases in our series were between the ages of 60 and 70, the median age was 65. The female to male ratio was 2/1. B cell lymphomas are the most common type of renal lymphomas (38). All of the cases in our series were DLBCL.

Lymphomas account for approximately 0.2% of bladder-derived primary neoplastic lesions. The only case in our series was a 76-year-old woman who was diagnosed with DLBCL.

Pancreatic Lymphomas: Primary pancreatic lymphoma (PPL) is a rare disease. It constitutes less than 0.5% of all pancreatic masses and less than 2% of all ENLs (39). PPL in our series represents 1.3% of ENLs.

The incidence of PPL increases with age and more common in men (40). The ages of the cases in our series ranged between 33 and 76, and the average age was 52.33. The male to female ratio was 5/1. The most common histological subtype is DLBCL (41). All of our cases were DLBCL.

Breast Lymphomas: Primary breast lymphoma (PBL) is a very rare disease. Only a few hundred cases have been reported in the literature; the majority of these are small retrospective series (42). It constitutes 1.7-2.2% of all ENLs (43). Patients with PBL constitute 0.4% of ENLs in our study. The average age at the time of diagnosis is 60-65. Almost all of the patients are women (43). Two cases with PBL in our series were female patients, one was 43 and the other was 80 years old. The most common histological diagnosis in PBL is DLBCL, both of our cases were DLBCL. Bilateral breast lymphomas are very rare (44). Both cases in our series were unilateral.

Hepatic Lymphomas: Although secondary liver involvement is common in the later stages of lymphoma, primary hepatic lymphoma (PHL) is rare. PHL is liver-derived ENL without other organ involvement. PHL constitutes 0.4% of ENLs (45). A total of 2 cases were diagnosed as PHL in our institute. These cases accounted for 0.4% of ENLs. PHL most often occurs around the age of 55 (45). The male to female ratio is 2.3 / 1 (46). The two cases in our series were females, and their ages were 27 and 66. The majority of PHL is DLBCL. One of the cases in our series is Burkitt's lymphoma; the other has been reported as B cell lymphoma, not otherwise specified.

Pulmonary Lymphomas: Primary pulmonary lymphoma (PPL) is defined as clonal lymphoid proliferation without extrapulmonary involvement at the time of diagnosis (or within 3 months thereafter), affecting the bronchi or parenchyma of one or both lungs. PPLs are very rare. Low-grade B cell forms are most common. High-grade B cell NHLs constitute 11 to 19% of PPL cases. The average age of patients with high-grade PPL is 60 (47). The only case with bronchial DLBCL in our series was a 70-year-old female patient.

The true incidence of non-B cell PPLs is unknown. Tamura et al. reported only one case with T cell lymphoma in a series consisting of 24 PPL cases (48). One patient with T cell PPL in our series was a 61-year-old male.

CONCLUSION

As a result, the data collected from an institution of the Southern Marmara region of Turkey is generally compatible with the literature. The minority in the number of cases with some localisations prevented statistically significant results. There is limited data about ENLs in different regions, further studies with larger series are required to define the most common ENL types in Turkey.

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RESEARCH ARTICLE

Nur Simsek Yurt[1]
Mahcube Cubukcu[1]

[1]Department of Family Medicine, Health Sciences University Samsun Training and Research Hospital, Samsun, Turkey

Corresponding Author:
Nur Simsek Yurt
Department of Family Medicine, Health Sciences University Samsun Training and Research Hospital, Samsun, Turkey
Phone: +90 3623111500
Mail: nursimsekyurt@gmail.com

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konuralptipdergi@duzce.edu.tr
konuralptipdergisi@gmail.com
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Quality of Sleep and Related Factors on Elderly Residents of the Nursing Homes

ABSTRACT

Objective: Our study aims to determine the rate of sleep disorders in elderly people aged 65 and older, living in nursing homes in Samsun, and also to investigate the factors affecting sleep quality through a comprehensive geriatric assessment.

Methods: Our study was performed in the two largest nursing homes in Samsun province between March 1st and April 30th 2018. The sleep quality of the participating individuals was assessed by the Richard's Campbell Sleep Questionnaire (RCSQ) and the Epworth Sleepiness Scale (ESS). This individuals in our study were assessed using Geriatric Depression Scale (GDS), Mini-Mental State Examination (MMSE), Short Form 36 Health Survey (SF-36), Charlson Comorbidity Index (CCI). The obtained data were analyzed with SPSS 23.0 and $p<0.05$ was considered as significant.

Results: A total of 84 people were included in the study and the mean age was 77.06±7.97 years. It was determined that 23.8% of the individuals had poor sleep quality at night according to RCSQ and 42.9% of the individuals had increased daytime sleepiness according to ESS. A significant statistical difference was found between the GDS scores with the RCSQ and ESS scores ($p<0.001$, $p=0.001$, respectively). The presence of depressive symptoms was associated with sleep quality at night and daytime sleepiness. A statistically significant difference was found between the MMSE and RCSQ scores ($p=0.014$). The presence of dementia was associated with sleep quality at night.

Conclusions: The presence of depressive symptoms was found to cause poor sleep quality at night and increased daytime sleepiness. People with dementia had low sleep quality at night. The low life quality was found to associate poor sleep quality at night and increased daytime sleepiness.

Keywords: Aged, Sleep, Depression.

Huzurevinde Yaşayan Yaşlı Bireylerin Uyku Kalitesi ve Etkileyen Faktörler

ÖZET

Amaç: Çalışmamızın amacı, Samsun ilinde huzurevlerinde yaşayan 65 yaş ve üzeri yaşlı bireylerde uyku bozukluğu oranını belirlemek ve kapsamlı geriatrik değerlendirme ile uyku kalitesini etkileyen faktörleri incelemektir.

Gereç ve Yöntem: Çalışmamız 01 Mart-30 Nisan 2018 tarihleri arasında Samsun ilinin en büyük iki huzurevinde yapıldı. Katılımcı bireylerin uyku kalitesi Richard's Campbell Uyku Ölçeği (RCSQ) ve Epworth Uykululuk Ölçeği (ESS) ile değerlendirildi. Çalışmamızdaki bu bireyler Geriatrik Depresyon Ölçeği (GDS), Mini Mental Durum Testi (MMSE), Kısa Form 36 Yaşam Kalitesi Ölçeği (SF-36), Charlson Komorbidite İndeksi (CCI) kullanılarak değerlendirildi. Elde edilen veriler SPSS 23.0 ile analiz edildi ve $p<0.05$ anlamlı kabul edildi.

Bulgular: Çalışmaya toplam 84 kişi dahil edildi ve ortalama yaş 77,06 ± 7,97 yıldı. Çalışmaya katılan bireylerin %23,8'i RCSQ değerlendirmesine göre geceleri kötü uyku kalitesine ve %42,9'u ESS'ye göre artmış gündüz uykululuk durumuna sahipti. GDS skorları ile RCSQ ve ESS skorları arasında istatistiksel olarak anlamlı fark vardı (sırasıyla; $p<0,001$, $p=0,001$). Depresif semptomların varlığı gece uyku kalitesi ve gündüz uykululuk durumu ile ilişkiliydi. MMSE ve RCSQ skorları arasında istatistiksel olarak anlamlı bir fark bulundu ($p=0,014$). Demans varlığı, gece uyku kalitesiyle ilişkiliydi.

Sonuç: Depresif semptomların varlığının gece kötü uyku kalitesine ve gündüz uykululuğunun artmasına neden olduğu saptanmıştır. Demansı olan kişiler, geceleri kötü uyku kalitesine sahipti. Yaşam kalitesinin düşük olmasının gece kötü uyku kalitesi ve gündüz uykululuğunun artması ile ilişkili olduğu tespit edilmiştir.

Anahtar Kelimeler: Yaşlı, Uyku, Depresyon.

INTRODUCTION

Aging is the sum of the events occurring with a genetic program and leads to structural and functional changes on the organism with the effect of environmental factors. World Health Organization (WHO) defines old age as "decreased ability to adapt to environmental factors" (1). Aging is a process that affects both sleep quality and amount of sleep. Sleep disorders are a common complaint among patients of all ages, but research suggests that elderly adults are particularly vulnerable (2). Studies suggest that the frequency of sleep disorders in the elderly compared to the adult population increases and this rate reaches 50% (3). It is reported that sleep disorders are observed in 65% of the elderly who stay in long-term care facilities such as nursing homes (4).

The most frequent sleep problems in old age are reported as having trouble in falling asleep, waking up frequently, waking up very early, need to sleep constantly, and not feeling rested when awakened. Impairment of sleep quality causes sleepiness, fatigue, depression, irritability, pain, muscle tremors, decreased mental functions, and also general health and functional condition in the elderly (5). The studies have shown lower glucose tolerance, elevated blood pressure and increased incidence of stroke and psychiatric illness in older adults suffering from sleep disturbances compared to those who have good-quality sleep (6, 7). Also, sleep disorders in elderly people are associated with an increased risk of falls, substance abuse, negative self-health assessment, and low quality of life (8).

Several changes occur with age that lead to increased risk for sleep disorders, including increased prevalence of medical conditions and medication use, age-related changes in various circadian rhythms, and environmental and lifestyle changes, and all of these have a significant impact on sleep quality (9). Disruptions in daily routines due to retirement along with low levels of physical activity and reduced sunlight exposure may contribute to changes in circadian sleep rhythm (9, 10).

In older adults, sleep disorders are influenced by several factors, including primary sleep disturbances (such as sleep apnea, periodic sleep movements, and restless legs syndrome) or secondary to physical illness, psychiatric conditions, pharmacological interactions or psychosocial factors (11, 12). There is a shift in sleep rhythm in older persons. They usually tend to fall asleep and wake up earlier than younger adults (13). The time to fall asleep is prolonged. Sleep latency does not increase in parallel with age. It starts after the age of 30 and then it plateaus, the second phase of sleep latency increase occurs after the age of 50. Even if the reduction in the amount of sleep is not detected, it is determined that the sleep pattern changes and the quality of sleep decreases (14). Aging-related sleep pattern changes lead to an overall decrease in sleep efficiency with less total sleep time, the reduced time spent in deeper non-rapid eye movement (NREM) sleep stages, and also in rapid eye movement (REM) sleep. Furthermore, higher number of night awakenings result in increased sleep interruption (12, 15)

Given that sleep disorders may increase the risk for various medical illnesses and psychiatric conditions, it is important to identify behavioral and environmental factors. Strategies based on modifying such factors can be adopted to improve sleep quality in the elderly. Our study aims to provide statistics about the rate of sleep disorder among elderly individuals living in a nursing home and investigate the factors that cause impaired sleep quality.

MATERIAL AND METHODS

This cross-sectional, descriptive study research was carried out in Samsun Metropolitan Municipality Nursing Home and Samsun Nursing Home Care and Rehabilitation Center with 84 people between March 1st 2018 and April 30st 2018. Ethics committee approval was obtained with the Ethics Committee Decision dated January 23st 2018 and No. 2 of the Health Sciences University Samsun Training and Research Hospital Ethics Committee.

Each person was first informed about the content of the study and their consent was obtained that they voluntarily participated in the study. The criteria to participate in the study are age of 65 and over, being conscious and not having communication problems, being literate.

The socio-demographic characteristics, diseases, and medications used and the duration of stay in the nursing home were evaluated. In our study, Richard-Campbell Sleep Questionnaire (RCSQ) was used. In addition, Epworth Sleepiness Scale (ESS) was used to assess daytime sleepiness. For comprehensive geriatric evaluation, Short Form 36 Health Survey (SF-36), Mini-Mental State Examination (MMSE), Geriatric Depression Scale (GDS), Charlson Comorbidity Index (CCI) were used.

RCSQ, which is used for the evaluation of night sleep quality, was developed by Richards in 1987 and is a 6-item scale that evaluates the depth of night sleep, falling asleep, frequency of awakening, the awake time when awakened, the quality of sleep and the noise level in the environment. A score between 0 and 25 obtained from the scale indicates very poor sleep, while a score between 76 and 100 indicates very good sleep (16). Adaptation of the RCSQ to Turkish, its validity and reliability studies were carried out by Ozlu in 2010 (17).

ESS is a test used to show daytime sleepiness. In this survey, the possibility of falling asleep in certain situations is questioned on a

normal day when the patient is not overly tired. If the total score is 10 or above, it indicates the presence of excessive daytime sleepiness. Turkish validation study of ESS was performed and the Turkish version was reported to be effective in showing daytime sleepiness (18).

Statistical Analysis: The data were analyzed with SPSS 23.00. Compatibility with normal distribution was examined with Shapiro Wilk. Independent samples Student t-test was used to compare normally distributed data. Mann Whitney-U test and Kruskal Wallis-H test were used in the use of non-normally distributed data. Categorical data were examined by Chi-square test and the relationship between variables was examined by Spearman rank correlation. The results of the analysis are presented as mean ± standard deviation for quantitative and normally distributed data, and as median (min-max) for non-normally distributed data. Categorical data are expressed as frequency (percent). Statistical significance was accepted at $p < 0.05$.

RESULTS

The total number of persons participating in the study was 84 and 26.2% (n=22) were women. In terms of age groups, 50% (n=42) were in the advanced elderly (75-84) category.

The average age of the participants was 77.06 years. The duration of the individuals staying at the nursing home, their average weight and height, their BMI and their comorbidity status are shown in Table 1.

According to the RCSQ scores of the participants, very poor sleep quality was found in 23.8% (n = 20). In the daytime sleepiness analysis, it was observed that 42.9% (n = 36) show increased daytime sleepiness. It was determined that 20.2% (n=17) of the individuals participating in the study had moderate depression and 9.5% (n=8) had severe depression (Table 1).

GDS scores show significant differences between male and female participants (p=0.015). While 51.6% (n = 32) of men had no depression, 40.9% (n = 9) of women had moderate depression. The median value of the GDS varies based on the gender (p=0.036). The median values were 4 and 7 for men and women, respectively (Table 2).

A positive and weak level correlation was found between ESS and age range and BMI (rho=0.223, p=0.034, rho=0.220, p=0.044, respectively).

A statistically significant correlation was detected between ESS and physical function, physical role difficulty, general health status, energy vitality, and mental health scores, which were among the SF 36 scale sub-dimensions (rho=-0.343, p= 0.001, rho=-0.308, p=0.004, rho=-0.258, p=0.018, rho=0.226, p=0.038, rho=-0.233, p=0.033) (Table 3).

The median value of ESS does not differ statistically between the groups of comorbid diseases. The median value of ESS differs between the categories of depression (p=0.001) (Table 4).

The GDS and MMSE median values show a statistically significant difference between RCSQ scores (p<0.001, p=0.014, respectively) (Table 5). The presence of depressive symptoms and dementia was found to be associated with poor sleep quality at night.

A statistically significant difference was found between the RCSQ scores and all subgroups of the SF-36 quality of life scale (Table 5). The low quality of life was found to cause poor sleep quality at night.

DISCUSSION

It is known that with the aging process, some changes occur in the normal sleep pattern, more specifically, the quality of sleep decreases and the complaints of sleeplessness increase (19). It has been determined that sleep disorders affect elderly individuals biologically, socially and psychologically. These changes can affect daily life and even cause life-threatening accidents.

In our study, it was determined that 23.8% of elderly individuals had poor sleep quality and 42.9% of them had increased daytime sleepiness. Siddiqui et al. reports that 51.6% of the participants in their study had poor sleep quality at night and 26.5% of them increased daytime sleepiness (2). In the study of Silva et al. in Portugal, individuals staying in nursing homes had poor sleep quality compared to individuals outside of the institution. It was found that individuals staying in the nursing home had more daytime sleepiness as evaluated using ESS (12). As a result of the study carried out on more than 9,000 people aged 65 and over by the National Aging Institute, it was found that 28% of the elderly individuals had problems in falling asleep and 48% had difficulty in falling asleep and maintaining sleep (5). In a study conducted in nursing homes in Turkey by Eser et al., 60.9% of the elderly reported having low sleep quality (20). Compared to the results of these studies, the rate of elderly individuals with poor sleep quality in our study was found to be lower. The Pittsburgh Sleep Quality Index was used in the evaluation of sleep quality at night in most of these studies. However, sleep quality questionnaires except for the RCSQ have some disadvantages: They have a large number of items (15–27) therefore, it is not easy for older adults to answer them (21). On the other hand, a simple five-item questionnaire (RCSQ) has been used in our study. Since mental, psychological, comorbidity status and quality of life assessments are also taken into account, it was easier to answer the questions for older people staying in the nursing home.

Table 1. Descriptive characteristics of elderly people (n=84)

Variables	Frequency (n)	Percent (%)
Age		
Young old	30	35.7
Advanced elderly	42	50.0
Very old elderly	12	14.3
Gender		
Male	62	73.8
Female	22	26.2
Marital status		
The Married	4	4.8
Single	6	7.1
Divorced	7	8,3
Widow	67	79.8
Educational status		
Literate	26	31.0
Primary high school	46	54.8
High school	8	9.5
University	4	4.8
Use of auxiliary tools		
Not	29	34.5
Walking stick	11	13.1
Crutches	3	3.6
Well chair	10	11.9
Glasses	31	36.9
Drug use status		
No Drugs	7	8.3
Use medication from time to time	9	10.7
Use regular medication <4	34	40.5
Do not use regular medication >4	34	40.5
Comorbidity		
<3	71	84.5
>3	13	15.5
Hypertension		
Yes	43	51.2
No	41	48.8
Coronary artery disease		
Yes	8	9.5
No	76	90.5
Heart failure		
Yes	22	26.2
No	62	73.8
Diabetes Mellitus		
Yes	32	38.1
No	52	61.9
Cerebrovascular disease		
Yes	3	3.6
No	81	96.4
Parkinson disease		
Yes	1	1.2
No	83	98.8
Chronic obstructive pulmonary disease (COPD)		
Yes	8	9.5
No	76	90.5
Cancer		
Yes	2	2.4
No	82	97.6
Musculoskeletal diseases		
Yes	5	6.0
No	79	94.0
Richard Campbell Sleep Questionnaire		
Very bad sleep	20	23.8
Normal sleep	26	31.0
Very good sleep	38	45.2
Epworth Sleepiness Scale		
Normal	31	36.0
Normal but increased daytime sleepiness	17	20.2
Increased but moderate daytime sleepiness	10	11.9
Increased moderate daytime sleepiness	14	16.7
Increased severe daytime sleepiness	12	14.3
Geriatric Depression Scale		
No depression	37	44.0
Mild depression	22	26.2
Moderate depression	17	20.2
Severe depression	8	9.5
Mini-Mental State Examination		
Serious cognitive impairment	30	35.7
Moderate cognitive impairment	25	29.8
No cognitive impairment	29	34.5

Table 2. Comparison of scales stated based on gender

	Male	Female	Test statistics*	p
Richard Campbell Sleep Questionnaire	71(10-96)	60(10-94)	U=575.0	0.276
Epworth Sleepiness Scale	9(0-21)	7.5(0-19)	U=631.5	0.606
Geriatric Depression Scale	4(0-14)	7(0-13)	U=887.5	**0.036**
Mini-Mental State Examination	22(5-29)	17(8-27)	U=493.5	0.055

*Mann–Whitney U test

Table 3. Correlation analysis of Epworth Sleepiness Scale with the specified variables and SF-36 subscales

		Epworth Sleepiness Scale
Age	r	**0.231**
	p	**0.034**
Gender	r	-0.057
	p	0.609
Duration of stay in the nursing home	r	0.062
	p	0,577
Body Mass Index	r	**0.220**
	p	**0.044**
Mini-Mental State Examination	r	-0.210
	p	0.055
Physical function	r	**-0.343**
	p	**0.001**
Physical role difficulty	r	**-0.308**
	p	**0.004**
Emotional role difficulty	r	-0.121
	p	0.271
Energy vitality	r	**-0.226**
	p	**0.038**
Mental health	r	**-0.233**
	p	**0.033**
Social functionality	r	-0.195
	p	0,075
Pain	r	-0.175
	p	0.112
General health perception	r	**-0.258**
	p	**0.018**

r: Spearman rank correlation coefficient

Table 4. Correlation analysis of Epworth Sleepiness Scale with specified scale scores

	Median (min-max)	Test Statistics	P
Geriatric Depression Scale			
No depression	4(0 -21)	χ^2=16.740	**0.001**
Mild depression	14.5(3 -17)		
Moderate depression	9(0 -19)		
Severe depression	12(0 -18)		
Mini-Mental State Examination			
Serious cognitive impairment	12(0 -21)	χ^2=4.769	0.092
Moderate cognitive impairment	6(0 -15)		
No cognitive impairment	9(0 -17)		
Drug use status			
No Drugs	6(0 -11)	χ^2=3.205	0.361
Use medication from time to time	6(0 -16)		
Use regular medication <4	8(0 -19)		
Do not use regular medication >4	10(0 -21)		
Comorbidity			
<3	13(0 -17)	U*=375.0	0.283
>3	8(0 -21)		

χ^2 : Kruskal- Wallis test; *Mann–Whitney U test

Table 5. Correlation analysis of Richard Campbell Sleep Scale with specified scale and SF-36 subscales

	Very bad sleep	Normal sleep	Very good sleep	Test Statistics	p
Duration of stay in the nursing home	48(1 -144)	48(2 -108)	48(6 -132)	χ^2=0.424	0.809
Geriatric Depression Scale	10.5(7 -14)	4(0 -11)	3(0 -12)	χ^2=35.188	**<0.001**
Mini-Mental State Examination	18.5(7 - 24)	23.5(5 - 27)	21.5(7-29)	χ^2=8.473	**0.014**
Physical function	15(0 - 65)	50(0 - 100)	60 (0 - 100)	χ^2=12.594	**0.002**
Physical role difficulty	0(0 - 100)	50(0 - 100)	50 (0 - 100)	χ^2=12.011	**0.002**
Emotional role difficulty	0(0 - 100)	66(0 - 100)	83 (0 - 100)	χ^2=14.438	**0.001**
Energy vitality	12.5(0 - 45)	47.5(4 - 95)	45 (0 - 85)	χ^2=24.756	**<0.001**
Mental health	34(4 - 44)	62(12 - 92)	56 (24 - 84)	χ^2=27.994	**<0.001**
Social functionality	50(0 - 100)	81(12 - 100)	75(25 -100)	χ^2= 16.917	**<0.001**
Pain	32(10 - 100)	90(22 - 100)	85(10 -100)	χ^2= 16.036	**<0.001**
General health perception	27.5(10 - 85)	60(20 - 95)	70(15 - 90)	χ^2=17.013	**<0.001**

χ^2: Kruskal- Wallis test

In our study, a significant statistical correlation was not found between gender, marital status, educational status, length of stay in the nursing home and sleep quality of the elderly. Only a positive weak significant correlation was found between daytime sleepiness and the age range (p=0.034). The lack of correlations can be attributed to the limited data space and therefore more detailed analysis can be made with more participants. In the study conducted by Rocha et al., the prevalence of sleeplessness was higher for women than men of all age groups (22). A possible explanation for female preponderance in this age group is physiological and psychological changes which are coupled with menopause. A study conducted to explore this association found that perimenopausal and post-menopausal women have frequent sleep disorders (23). A study in Finland found that symptoms of insomnia increase with age. However, it has been suggested that this situation is not due to the aging process, but rather due to the comorbidity that increases with age (24). One of our hypotheses in our study is that comorbidity and sleep quality may be related. Analysis was made between comorbidity scoring and RCSQ and ESS mean median and it was not found statistically significant. A wide-scale study with larger number of participants than ours is needed. Comorbid diseases (Hypertension, Coronary Artery Disease, Congestive Heart Failure, Diabetes Mellitus, Cerebrovascular disease, Parkinson's disease, COPD, Cancer) were compared with individual sleep scale scores in our study. No statistical relation was found using both scale scores. Neubauer et al. reported that comorbid diseases such as cardiovascular diseases, diabetes, obesity, dementia, depression, Parkinson's disease, arthritis and lung diseases cause poor sleep quality (25). In a study conducted in Pakistan, the prevalence of sleep disorders was found to be higher in people with coronary artery diseases (2). A study of frequent sleep disorders among the elderly with heart disease and coroner artery disease further augmented the result of a trial that found sleep disorders to be a risk factor for coronary artery calcification, especially when coupled with obstructive sleep apnea (26). In a study conducted by Cuellar et al., it has been stated that the medications started for the treatment of comorbid conditions may cause daytime sleepiness as well as further deterioration of night sleep (27). In our study, significant effect was not observed by polypharmacy. Although there was no significant effect of BMIs on night sleep quality, a positive weak significant correlation was observed between BMIs and daytime sleepiness rates. In the study conducted by Goktaş et al., it was reported that as the BMI increases, sleep quality deteriorates, and obese individuals have a bad sleep quality with a rate of 61.2% (28). Obesity is associated with an increase in neck circumference, and fat accumulation narrows the upper airway, which is responsible for the higher incidence of airway collapsibility in obese patients compared to normal-weight individuals. The studies have proven that weight loss is effective in reducing the severity of sleep apnea; 10-15% reduction in body weight reduces sleep apnea by up to 50% (29).

Individuals with and without risk of depression were classified with the GDS. Analysis was made by using RCSQ and ESS median. A significant statistical difference was found in the median of both scales in the presence of depression risks. Psychiatric disorders such as major depression, panic disorder, and generalized anxiety disorder are strongly linked to sleep disorders (2). A positive correlation was found between ESS and GDS scores in the study of Silva et al. (12). Studies show that daytime sleepiness and depressive symptoms are strongly associated (30, 31). Individuals diagnosed with depression are more likely to experience fatigue and daily sleepiness (30). In a comprehensive study conducted by Gindin et al. in 8 countries, sleep disorders in elderly individuals were found to be highly

correlated with depression (p<0.001) (32). In our study, poor sleep quality was found to be associated with depressive symptoms in accordance with the studies in the literature. Depression and sleep quality have a two-way relationship. While one area of symptoms in depressive disorders is related to sleep changes (insomnia / hypersomnia) with increased risk of developing sleep disorders, poor sleep quality strongly contributes to the onset of depression in the elderly (33).

Another hypothesis of our study is that dementia may be associated with sleep disorders. In our study, MMSE was applied to the participants, and the median value showed a statistically significant difference according to the RCSQ scores (p=0.014). In the study conducted by Criocco et al, it was observed that the rate of dementia increased in elderly individuals with sleeplessness (34). In the study of Siddiqui et al., higher ESS scores were found in patients with dementia (2). The relationship between dementia and aging-related sleep disorders is thought-provoking. The cause of sleep disturbance in elderly people suffering from dementia is a change in circadian rhythm. Melatonin treatments have proven beneficial in treating both dementia and sleep disorders (35).

In our study, the relationship between elderly people's quality of life and sleep disorder was also evaluated. The data obtained using both sleep scales in our study shows that the low quality of life of elderly persons living in the nursing home negatively affects sleep quality and daytime sleepiness. In a study conducted by Schubert et al. with 2800 participants, a statistically significant linear relationship was found between the poor sleep quality and all sub-dimensions of the quality-of-life scale (36). In a study conducted by Hayashino et al. with the participation of 3403 people in Japan, it was found that poor sleep quality and quality of life scale of the individuals were associated with the mental health subgroup (p<0,001) (37). Poor sleep quality in the elderly contributes to increased daytime drowsiness and decreased daytime functioning, resulting in reduced participation of the elderly in daytime occupational activities and diminished levels of physical activity (38).

As seen in our study and other studies, sleep quality and daytime sleepiness were found to be directly related to the quality of life. In order to correct the sleep disorders of the elderly, it is necessary to find solutions that will improve their quality of life. Furthermore, in order to increase the social interaction between elderly people in nursing homes, social activities such as introductory meetings should be organized, and healthy communication between residents should be supported. It is recommended that older individuals are psychologically supported and regularly interviewed by institutional psychologists. If necessary, referring to psychiatry and getting necessary treatment can help improving sleep quality. It is important to prevent the elderly from feeling isolated and lonely through organizing various social activities. Persons with pain should be supported by medical or psychological treatment. Elderly people in the nursing home should be provided proper nutrition and informative trainings (39).

CONCLUSION

In summary, in our study, sleep disorders of elderly people living in nursing homes were evaluated, poor sleep quality at night and daytime sleepiness were found to be an important problem. The presence of depressive symptoms was found to cause poor sleep quality at night and increased daytime sleepiness. People with dementia have low sleep quality at night. The low quality of life was found to cause poor sleep quality at night and increased daytime sleepiness. Elderly people should be supported without delay about their mental, psychological, and medical diseases. It is envisaged that increasing the quality of life, ensuring a positive mood, early diagnosis, and treatment of medical diseases can improve the sleep quality of elderly people.

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RESEARCH ARTICLE

Serdar Aslan[1]
Kemal Peker[2]
Mehmet Ilhan Yildirgan[3]

[1]Bahçelievler Memorial Hospital Department of General Surgery, Turkey
[2]Düzce University, Department of General Surgery, Duzce, Turkey
[3]Atatürk University, Department of General Surgery, Erzurum, Turkey

Corresponding Author:
Kemal Peker
Düzce University, Department of General Surgery, Duzce, Turkey
Phone: +90 5359368528
mail: k.peker@yahoo.com.tr

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konuralptipdergisi@gmail.com
www.konuralptipdergi.duzce.edu.tr

The Role of Early Period ERCP in Acute Biliary Pancreatitis?

ABSTRACT

Objective: Acute pancreatitis;It can be defined as a clinical picture that occurs as a result of non_bacterial inflammation of the pancreas and may progress with pathological findings. For years, various studies have been conducted on the use of Endoscopic Retrograde Cholangiopancreotography and Endoscopic Sphincterotomy for therapeutic purpose in Acute Pancreatitis. For years, various studies have been conducted on the use of Endoscopic Retrograde Cholangiopancreotography and Endoscopic Sphincterotomy for therapeutic purpose in Acute Pancreatitis.
In our study, we aimed to examine either the effectiveness of Endoscopic Retrograde Cholangiopancreotography and Endoscopic Sphincterotomy in patients with mild severity, and how the endoscopic procedure affects the course of the disease.

Methods: In this study, patients with mild pancreatitis were selected among the patients who applied to the Department of General Surgery, of Atatürk University Faculty of Medicine and diagnosed with acute biliary pancreatitis (ABP).
After the patients were separated according to the mild pancreatitis, early (within 72 hours) and late period, they were randomly selected to be performed Endoscopic Retrograde Cholangiopancreotography and Endoscopic Sphincterotomy. 59 patients were detected in this way.

Results: Twelve (20.3%) of the patients included in our study were male, and 47 (79.7%) were female, and their ages were between 25-75 years (mean 64.3 years). Two groups were created in order to perform ERCP/ES in the early and late periods. All patients had acute onset abdominal pain and serum amylase levels have been ranging between (1012-7660 UI/L).

Conclusions: In patients with mild acute biliary pancreatitis, there is no significant difference in the early (first 72 hours) ERCP/ES results compared to the results of patients with ERCP/ES in the late period.

Keywords: Acute Pancreatitis, ERCP, Sphincterotomy.

Akut Bilier Pankreatitte Erken Dönem ERCP'nin Rolü?

ÖZET

Amaç: Akut pankreatit; Pankreasın bakteriyel olmayan enflamasyonu sonucu patolojik bulgularla seyredebilen klinik bir tablo olarak tanımlanabilir. Yıllardan beri Endoskopik Retrograd Kolanjiopankreatikografi ve Endoskopik Sfinkterotomi'nin Akut Pankreatit'de terapötik maksatlı olarak kullanımı ile ilgili çeşitli çalışmalar yapılmaktadır. Bu çalışmalara göre özellikle hafif şiddetli Akut Pankreatit'de erken Endoskopik Retrograd Kolanjiopankreatikografi ve Endoskopik Sfinkterotomi tartışmalı olmaya devam etmektedir.
Biz çalışmamızda hafif şiddetteki Akut Pankreatit'li hastalarında, Endoskopik Retrograd Kolanjiopankreatikografi ve Endoskopik Sfinkterotomi'nin tedavideki etkinliğini, aynı zamanda yapılan endoskopik işlemin hastalığın seyrini nasıl etkilediğini araştırmayı amaçladık.

Gereç ve Yöntem: Bu çalışmada, Atatürk Üniversitesi Tıp Fakültesi Genel Cerrahi Anabilim Dalına, akut bilier pankreatit (ABP) tanısı ile müracaat eden hastalar arasından, Ranson kriterleri ve hastaların klinik durumlarına göre hafif şiddetteki pankreatitli hastalar belirlendi. Hastalar hafif pankreatit tablosuna göre ayrıldıktan sonra erken (72 saat içinde) ve geç dönemde, Endoskopik Retrograd Cholangiopancreotography ve Endoskopik Sfinkterotomi yapılmak üzere randomize bir şekilde seçildi. Bu şekilde 59 hasta tespit edildi.

Bulgular: Çalışmamıza dahil edilen hastaların 12'si (%20,3) erkek, 47'si (%79,7) kadın olup, yaşları 25–75 yıl (ortalama 64,3 yıl) idi. Hastalara erken ve geç dönemde ERCP/ES yapılmak üzere 2 grup oluşturuldu. Hastaların 24(%40,6)'üne erken 35(%59,4)'ine geç dönemde ERCP/ES yapıldı. Tüm hastalarda akut başlayan karın ağrısı vardı ve serum amilaz seviyeleri (1012-7660 Ü/L) arasında değişmekte idi.

Sonuç: Hafif şiddetteki akut bilier pankreatitli hastalarda erken (ilk 72 saat) ERCP/ES sonuçlarının geç dönemde ERCP/ES yapılan hastaların sonuçları ile karşılaştırıldığında anlamlı bir fark yoktur. Bu nedenle hafif şiddetteki akut bilier pankreatitli hastalara erken dönemde ERCP/ES yapılabileceği kanaatindeyiz.

Anahtar Kelimeler: Akut Pankreatit, ERCP, Sfinkterotomi.

INTRODUCTION

Acute pancreatitis is a condition in which pancreatic enzymes increase in blood and urine with abdominal pain, which can proceed by a non-bacterial inflammation of the pancreas with pathological findings ranging from edema to necrosis, it can be defined as a clinical picture characterized by fibrosis and consequently irreversible endocrine and exocrine dysfunction. Although it is known that proteolytic enzymes of the pancreas play a role in the formation of pancreatic inflammation, the mechanisms by which these enzymes in inactive form are activated in pancreatic tissue are still controversial. The transformation of the inactive trypsinogen, which is located in the acinar cells of the pancreas, into the active form of trypsin by various mechanisms, activates other proteolytic enzymes (proelastase, chymotrypsinogen and phospholipase), kinin-kallikrein, complement and fibrinolysis, resulting in the local and systemic findings. Activation and retention of digestive enzymes in the acinar cell causes local destruction (auto-digestion) in the pancreas. This process leads to an increase in vascular permeability, causing edema in the pancreas and increased pancreatic injury by causing ischemia. As a result of that, a chemical inflammation in the retroperitoneal region and a systemic toxicity table accompanying this situation emerge. If microcirculation does not deteriorate in this event, the event is called acute interstitial pancreatitis. In cases where microcirculation is affected and circulation is impaired, necrotizing pancreatitis occurs. Although most of the attacks proceeds benignly, in severe attacks shock, kidney failure and respiratory failure may develop. With the elimination of the primary cause, the morphological changes in the pancreas return to normal completely. As a result of recurrent AP attacks, the development of a failure table in the endocrine and exocrine functions of the pancreas is common (1,2).

As acute pancreatitis causes significant morbidity and mortality, mortality decreases as a result of correct treatment and intensive care, by determining the severity in advance. While 80-85% of AP attacks caused by acinar cell damage are mild and recovered by simple supportive therapy, in 15-20% of cases (3) serious local and systemic complications develop.

Endoscopic Retrograde Cholangiopancreatography (ERCP) and endoscopic sphincterotomy (ES) have an important role in the treatment of AP. In the studies performed, in 45-70% of the patients who had acute biliary pancreatitis (ABP) in the early evaluation and in 15-30% of the evaluation after the symptoms were resolved permanent gallstones were detected. This situation supports the idea that emergency efforts to remove gallstones from bile ducts or ampulla of vater will affect the course of the disease (4). Since the late 1980s, various studies have been conducted on the use of ERCP and ES as a therapeutic purpose in AP. According to these studies, early ERCP and ES continue to be controversial, especially in mild severe AP (5,6).

In this study, we aimed to evaluate the clinical, laboratory and radiological findings of patients with mild AP accompanied by ERCP and ES, and to examine the effectiveness of ERCP and ES in the treatment of patients with AP and how it affects the course of the disease.

MATERIAL AND METHODS

In this study, patients with mild pancreatitis were determined among the patients who applied to the Department of General Surgery, Atatürk University Faculty of Medicine, with the diagnosis of acute biliary pancreatitis (ABP). The following criteria were considered for acute biliary pancreatitis.

After the patients were separated according to the mild pancreatitis table, they were randomly selected to perform Endoscopic Retrograde Cholangiopancreotography (ERCP) and Endoscopic Sphincterotomy (ES) in the early (late 72 hours) and late period. In this way, 59 patients were detected. Twelve (20.3%) of the patients were male, and 47 (79.7%) were female, and their ages were 25-75 years (mean 64.3 years).

Of these patients who had mild acute biliary pancreatitis with the above-mentioned criteria, two groups were put together: those who were ERCP/ES performed in the early period (first 72 hours) and those who were ERCP/ES performed in the late period. The early group consisted of 24 (40.6%) and the late group 35 (59.4%) patients. Patients' records were examined prospectively. In our study, the tomographic appearance of pancreatic tissue to be normal (+1), inflammation was limited only in the peripancreatic area and minimal edema in pancreatic tissue, acute mild pancreatitis (++ 2), inflammation was advanced in the mesenteric area and retroperitoneal area, and the edema in the pancreas was more prominent, acute severe pancreatitis (+++ 3), and additional necrosis in the pancreas were evaluated as necrotizing pancreatitis (++++ 4). The absence of fever was accepted as (0) its presence as (1).

In both groups, the following parameters were examined before and 24 hours after the procedure, considering the study by Alfred D. Roston et al. (7). The same parameters were reworked before and after ERCP/ES in patients, and the results were compared statistically between the groups.

Statistical Analysis: SPSS package program was used in the analysis of the data. In statistical analysis, in order to compare the groups, the pairing t-test was applied to the measurements made before and after, and then the group comparison t-test was applied to the measurements made after. Early and

late ERCP/ES groups were randomly created, and it was understood that in the groups created only GGT was nonhomogeneous in twelve parameters. Eleven other parameters are homogeneous for both groups (early and late ERCP/ES patients). Therefore, both groups were considered statistically homogeneous.

RESULTS

Twelve (20.3%) of the patients included in our study were male, and 47 (79.7%) were female, and their ages were ranging between 25-75 years (mean 64.3 years). Two groups were formed to perform ERCP/ES in the early and late periods. ERCP/ES was performed in 24 (40.6%) of the patients in the early period in 35 (% 59,4) of the patients in the late period. All patients had acute onset abdominal pain and serum amylase levels ranged between (1012-7660 UI/L). In 50 (84.7%) patients, stones in the biliary tract were detected by using ultrasonography (USG) No stones were detected in the biliary tract in ultrasonography (USG) in nine (15.3%) patients. However, in six patients no Stones were detected choledochal pathology (stone, bile mud, large choledochal, ascaris and purulent fluid) was detected during the ERCP procedure. Bilirubin levels and liver enzymes were elevated in eight of nine patients without stones. The remaining one patient's bilirubin and liver enzymes were normal. However, as ascaris was detected during the ERCP procedure, he/she was included in the study. In 33 (55.9%) of 59 patients, one or more of the choledochal pathologies were detected in ERCP, while 26 (44.1%) of the patients were not detected in ERCP proceedings.

In 23 of these 26 patients, stones were found in the biliary tract in USG. The other 3 patients had higher bilirubin levels and liver enzymes. CT was performed before and after the procedure on all patients we included in the study. Pathology was detected in 34 patients (57.6%) in terms of pancreatitis. It was succeeded in the ERCP/ES procedure in all patients included in the study. No complications ever developed in any of our patients. The mean duration of hospital stay of patients who underwent ERCP/ES was 9 ± 2 days in the early period, whereas the average length of hospital stay of patients with ERCP/ES in the late period was 16 ± 2 days. Treatment costs have also decreased since the hospitalization period of the patients who have undergone ERCP/ES procedure in the early period has shortened.

In the study, we observed that local and systemic complications decreased significantly as a result of early ERCP and ES to patients with mild biliary pancreatitis, and the length of hospital stay was significantly shorter compared to the group which undergone ERCP and ES in the late period No significant difference was detected between the results of patients with acute biliary pancreatitis who underwent ERCP and ES in the first 72 hours compared to the parameters we specified in patients with acute biliary pancreatitis in the late 72 hours. In addition, in the group with late ERCP and ES, compared to the group with early ERCP and ES, the results were found to be importantly significant when the GGT, creatinine and glucose values studied before and after the procedure were compared. This situation was interpreted as it was due to the medical treatment given in the past period for late ERCP and ES procedures. When the post-procedure values of both groups were compared, ALT and AST values were found to be significantly different, whereas GGT values were found to be more significantly different. This was attributed to the expected time for medical treatment and procedure for ALT and AST and for non-homogeneousness of GGT values when randomly selecting patients for GGT.

Study results are given in Table (1-3).

Table 1 indicates the comparison of the values studied before and after the procedure in the group with early ERCP / ES.

It was observed that the values studied before Leukocyte, CRP, BUN, ALT, AST, ALP, LDH, CT and Fever parameters compared with the values studied before the procedure decreased and it was statistically significant. Changes in GGT values were found to be statistically significant. Changes in creatine and glucose levels were statistically insignificant.

Table 1 indicates the comparison of the values studied before and after the procedure in the group with early ERCP/ES.

		Before	After		
	N	**X± Standart Deviation**	**X±Standart Deviation**	**t**	**Statistical Situation (P)**
Leukocyte	24	13029.1±4852.1	9745.8±4046.7	5.7	0.000 **
CRP	24	6.4±6.3	3.0±3.7	3.9	0.001**
BUN	24	18.0±8.9	11.2±5.5	3.2	0.004**
Creatine	24	0.8±0.3	0.7±0.1	1.1	0.279 ns
Glucose	24	130.2±57.9	120.9±57.8	0.6	0.552 ns
ALT	24	320.4±282.9	95.1±72.5	4.1	0.000**
AST	24	394.1±402.9	189.6±235.3	3.9	0.001**
ALP	24	469.8±277.0	363.0±268.7	3.5	0.002**
GGT	24	376.7±250.8	295.1±260.6	2.4	0.21*
LDH	24	744.1±414.0	519.2±293.8	3.8	0.001**
CT	24	1.5±0.5	1.0±0.2	4.4	0.000**
Fever	24	0.7±0.4	0.0±0.0	7.4	0.000**

X: is the average value; **: P<0.01 *: P< 0.05 ns: Insignificant

Table 2 indicates the comparison of the values studied before and after the procedure in the group with late ERCP / ES.

Leukocyte, CRP, BUN, Creatine, The values studied before the procedure in terms of glucose, ALT, AST, ALP, GGT, LDH, CT and Fever were compared with the values studied after the procedure and the values were found to be statistically significant.

In the group with late ERCP and ES, as different in the group with early ERCP and ES, the results were found to be highly significant when the GGT, Creatine and glucose values studied before and after the procedure were compared.

Table 2 indicates the comparison of the values studied before and after the procedure in the group with late ERCP/ES.

		Before	After		
	N	**X±Standard Deviation**	**X±Standard Deviation**	**t**	**Statistical Situation (P)**
Leukocyte	35	14348.5±4901.7	8514.2±2636.6	6.9	0.000 **
CRP	35	7.4±6.2	1.9±1.7	6.1	0.000**
BUN	35	18.9±10.4	10.5±4.9	5.6	0.000**
Creatine	35	1.0±0.5	0.8±0.2	2.8	0.007**
Glucose	35	134.5±46.5	103.3±31.1	3.5	0.001 **
ALT	35	216.3±163.3	55.4±59.0	5.7	0.000**
AST	35	222.1±196.9	79.1±121.2	4.4	0.000**
ALP	35	426.8±336.4	250.4±236.8	6.5	0.000**
GGT	35	192.3±138.1	68.6±51.5	6.4	0.000**
LDH	35	669.4±259.8	403.3±201.9	8.0	0.000**
CT	35	1.7±0.5	1.2±0.5	4.6	0.000**
Fever	35	0.7±0.4	0.0±0.2	7.6	0.000**

X: is the average value; **: P<0.01 *: P< 0.05 ns: Insignificant

Table 3 shows the comparison of the studied values of both groups after the procedure. When the post-procedure values of both groups were compared, ALT and AST values were found to be highly significantly different, whereas GGT values were found to be significantly different. The difference between the post-processing values of other parameters other than these parameters was statistically insignificant.

Table 3 shows the comparison of the studied values of both groups after the procedure.

	Early ERCP/ES	**Late ERCP/ES**		
	X± Standard Deviation	**X± Standard Deviation**	**t**	**Statistical Deviation(P)**
Leukocyte	9745.8±4046.7	8514.2±2636.6	1.3	0.198ns
CRP	3.0±3.7	1.9±1.7	1.3	0.190ns
BUN	11.2±5.5	10.5±4.9	0.5	0.604ns
Creatine	0.7±0.1	0.8±0.2	0.7	0.472ns
Glucose	120.9±57.8	103.3±31.1	1.5	0.121ns
ALT	95.1±72.5	55.4±59.0	2.3	0.025*
AST	189.6±235.3	79.1±121.2	2.1	0.042*
ALP	363.0±268.7	250.4±236.8	1.6	0.97ns
GGT	295.1±260.6	68.6±51.5	4.2	0.000**
LDH	519.2±293.8	403.3±201.9	1.6	0.10ns
CT	1.0±0.2	1.2±0.5	1.8	0.72ns
Fever	0.0±0.0	0.0±0.2	1.4	0.160ns

X: is the average value; **: P<0.01 *: P< 0.05 ns: Insignificant

DISCUSSION

The most common disease of the pancreas is acute pancreatitis. Acute pancreatitis is an acute inflammatory process of the pancreas. Its incidence is around 1-5/10,000 (8). Acute pancreatitis displays a wide clinical picture, ranging from mild interstitial edema to severe hemorrhagic gangrene and necrosis. In addition to clinically spontaneous improvement, a severe picture can be seen resulting in abdominal pain or hypotension, fluid sequestration, metabolic disorders, sepsis and death (2). The clinic of acute pancreatitis is variable and covers a spectrum ranging from mild abdominal pain to multiple organ failures and death. The most common symptoms are abdominal pain, nausea and vomiting (7-10). Increasing levels of pancreatic enzymes in the blood is extremely important in diagnosis (11). The mild clinical picture occurs in 90% of patients. The remaining 10% of patients experience severe pancreatitis (8,10,12). Besides clinical findings, laboratory data are also important in the diagnosis of acute pancreatitis. Serum amylase, lipase level, C-reactive protein, leukocyte, blood sugar, BUN, creatine and radiological examinations are helpful for diagnosis (13-15). In addition, elevation in polymorphonuclear elastase, phospholipase A, interleukin 6, α2-macroglobulin values are important hematological and serological blood tests showing the severity of acute pancreatitis and pancreatic necrosis (7). Ultrasonography (USG), Computed tomographic (CT), magnetic resonance imaging (MRI) and ERCP can provide valuable information in

determining morphology and complications in patients with acute pancreatitis (8,13,14). Life threatening serious complications can emerge especially in approximately 20% of cases with necrotizing pancreatitis. The most common complication is infection. Abscess, pancreatic and gastrointestinal haemorrhage, shock, lung and kidney failure are the most common serious complications (8,13).

Ultrasonography offers very useful information in diagnosis. Imaging methods not only provide us with an understanding of the severity of the table, but also provide important information in determining complications and treatment modalities (8). In addition to the diagnosis of the disease, CT is also used for grading the severity of the disease (14).

Discussions about the treatment of acute pancreatitis continue since the day Senn and Fitz made clinical and pathological definitions of the disease in the late 1800s (15,16). The use of prophylactic antibiotics came to light after clarifying the etiopathogenesis of the disease and standardizing certain terms, and after Berger reported that bacterial infection following pancreatic necrosis was progressing with high mortality and morbidity (15,17,18). Although the infection is seen at the rate of 8-10% in patients with acute pancreatitis, it is responsible for 80% of deaths. Since gram negative bacteria are responsible for most of the infections (15,19), the prophylactic antibiotic to be selected must be effective against these micro-organisms. Apart from antibiotic therapy, aprotinin was widely used in medical treatment for protease inhibition. However, after determination of inadequate penetration of pancreatic acinar cells due to its high molecular weight, aprotinin was replaced by gabexate mesylate, a low molecular weight protease inhibitor, but studies with this agent also did not yield any positive result (20). Whereas, it has been reported that it decreases the rate of ERCP-related pancreatitis (20,21). Inhibition of exocrine the pancreatic secretion with octreotide which is somatostatin or its synthetic analogue, has been extensively studied. Although many studies have reported the effect of exocrine secretion inhibition on the course of the disease (11,22,23), it has also been reported that it reduces complications in elective surgery (24) and positively affects (25). In consequence, the place of medical treatment in acute pancreatitis treatment is very limited. Infected necrosis, pancreatic abscess, sterile necrosis leading to multiple organ failures not responding to 72-hour treatment, massive intra-abdominal bleeding, ongoing ileus, intestinal perforation, portal vein thrombosis are conditions that require surgery (26). While pseudocysts developed due to acute pancreatitis have been treated surgically before, today only symptomatic and large cysts are treated and endoscopic and percutaneous drainage is an alternative to surgery (27).

Endoscopic Retrograde Cholangiopancreotography (ERCP) application is gradually increasing. The Baby Scope, which has been on the agenda in recent years, as it can pass through the working channel of the doudenoscope and so provides direct visualization of the pancreas and biliary tract, as well as it offers an opportunity to interfere through a separate working channel. The success of ERCP application has reached 90-95% in accomplished centers. The most frequent causes among the factors that prevent success in ERCP are; the lack of selective cannulation, oddi fibrosis, periampullary diverticulum and malignancies (28-30). The most common indication for ERCP is the presence of stones in the bile duct. Emergency ERCP and ES are the most important treatment options in acute suppurative obstructive cholangitis due to stone (31).

Complications are observed in ERCP, especially in approximately 7-10% of those who underwent ES. While life-threatening conditions such as bleeding, cholangitis, pancreatitis, duodenal perforation gram-negative sepsis are 2-3%, mortality is between 0.1-1.5% (32-35). A small amount of spontaneous bleeding usually occurs shortly after sphincterotomy. However, hemorrhage to the extent required transfusion occurs in 2-3% of patients (36-38) and mortality has been reported as 0.3% (32). The surgical requirement in these patients is 1%.

Ascending cholangitis after bacterial infection of the obstructed biliary tract, usually gram-negative microorganisms occur especially by (Pseudomonas and Enterobacteriaceae) and result in bacteremia. While some authors recommend prophylactic antibiotic treatment before the ERCP (39,40), some authors report that there is no need to that treatment (38,41). The most commonly recommended agents for prophylactic antibiotics are ceftriaxone and cefotaxime, rate of excretion from the bile ducts of which is 45%, and are effective against gram-negative microorganisms. Since anaerobes are also effective at the rate of 9% in bile in obstructive jaundice, it is recommended to add an agent including these microorganisms to the treatment. In order to prevent infection, all the tools that will be used in the process must be well cleaned, sterilized, stored in an aseptic environment and utmost care must be taken during the procedures. Another way to prevent infection is to avoid the injection of pressurized and excessive contrast material into the bile ducts which completely or almost completely blocked (42-44).

An asymptomatic amylase usually develops after the ERCP procedure. Clinical pancreatitis develops 2-3% approximately like bleeding. There are studies indicating that it is beneficial to use a protease inhibitor Gabexate mesylate to prevent

pancreatitis developing after ERCP (43). The discussion on the use of somatostatin prophylactically to prevent pancreatitis after ERCP is also pending. While some authors support this treatment protocol (44,45), some authors do not find it economic (43-45).

In the discussions on the use of octreotide, which is a somatostatin analog, while some authors prophylactically recommend the use of octreotide (44-47), some others do not find it necessary (32,48).

Perforation is one of the most feared complications of each endoscopic intervention. Perforation due to sphincterotomy is less than 1% and the vast majority thereof are retroperitoneal (32,37). The most important reason of the perforation is the uncontrolled incision and the incision of most of the sphincterotomy wire in the papilla. The mistake is caused by the incision length not being proportioned to the width of the choledochus. This complication can be prevented by keeping more than half of the sphincterotomy wire visibly outside the papilla and performing a controlled incision using the coater at short intervals. In addition, it is very important for a safe incision to set the angle well before the incision and the guidewire that passes through the sphincterotomy in the choledochus (32).

Late complications of ERCP include 5-10% restenosis and cholecystitis after 5 years. Papillary stenosis after a sufficient sphincterotomy is a clinically rare condition (49,50). Restenosis usually occurs in the first year. No restenosis is expected after a complete sphincterotomy. Recurrent cholangitis is another late complication that can develop due to forgotten stone or papillary stenosis. The approach to these patients should again be with ERCP. The mentioned late complications have not yet developed in our patients.

The relation between acute pancreatitis and gallstones has been described. If cholecystectomy is not performed, recurrences are frequent. But if biliary tract pathology is corrected, recurrences are rare. The effects of gallstones as a cause of pancreatitis are not fully understood, but they are thought to emerge depending on obstruction of the major pancreatic duct (51,52). To differentiation of the causes of pancreatitis is important. Serum amylase levels are high in non-alcoholics. This is due to the reduction of intracellular amylase levels of the pancreas damaged by chronic alcohol intake. The height of liver enzymes although not very specific, shows that increased bilirubin, ALP, GGT, ALT, AST are possibly of biliary origin (51,53).

The most common imaging method for gallstones is USG (32,54). Although there are different specificity and sensitivity descriptors for acute biliary pancreatitis, the following conditions are an expression of pancreatitis originating in biliary origin. Jaundice, cholangitis, serum amylase to be above 800IU/L, the increase in the level of serum transaminases three times and gallstones and dilatation in bile ducts in USG (50,55). However, it has been stated in a study that the sensitivity, specificity and diagnostic value are not high for each of the three parameters consisting of serum bilirubin, serum ALP and USG. None of these tests is sufficient alone for the detection of choledocholithiasis. However, when these three tests are combined, an important result emerges. If the three parameters specified are normal, the incidence of stone in choledocus is 4.8%. If one of these parameters is abnormal, the presence of stone in the choledocus is 59.3%. This rate is significantly high. Therefore, routine ERCP is not recommended for patients who are normal in biochemical and ultrasonographic terms (14).

In a study performed without considering the severity of pancreatitis, ES or conservative treatment was initiated with ERCP randomly in the first 24 hours in 195 patients. After the acute pancreatitis clinic improved in the conservatively treated group, ERCP was applied electively, and in the same group, ERCP was applied to the patients whose clinic deteriorated during the follow-up. In 127 (65%) of 195 patients, stones were identified as the cause of acute pancreatitis. It was determined that local and systemic complications developed in both groups. However, in the conservatively treated group, severe pancreatitis was found to be higher (30%) and biliary sepsis developed more frequently. In the emergency sickle treated group, complications were found to develop less (18%) compared to the conservatively treated group (51). In another study, 280 patients with acute biliary pancreatitis performed ERCP in the first 24 hours. Stone was removed by performing ERCP and ES to seventy-five patients. Other patients received ERCP and conservative treatment randomly. There was a significant decrease in complications and mortality after treatment in the group ERCP and ES were performed. While the decrease in complications decreased from 36% to 17%, mortality decreased from 13% to 1% (51). In a similar study conducted multicentric, 238 patients with acute biliary pancreatitis who had no icterus were applied emergency ERCP or conventional therapy in 72 hours. 126 of these patients were performed ERCP and in 121 patients successes was achieved. Stone was detected in 58 of these patients. 20 of 112 patients undergoing conservative treatment had ERCP under more elective conditions and 13 of these patients had stones. As a result of the study, it was reported that early ERCP/ES is not beneficial, on the contrary severe complications such as respiratory failure develop (51,56-58).

CONCLUSION

In the light of these informations, in conclusion, ERCP and ES procedures should be performed within 24-48 hours for patients with mechanical icterus, cholangitis or co-canal dilatation, and in the first 24 hours for patients with

severe pancreatitis. Together with the current indications for ERCP, ES should be performed in the following cases. ES should be performed together with ERCP in acute biliary pancreatitis, which is accompanied by stones in the common bile duct during ERCP, in pancreatitis cases that are thought to be biliary origin although there is no stone in the common bile duct in ERCP, recurrent acute pancreatitis with mud and/or microlithiasis in the biliary duct with post-cholecystectomy or developing during pregnancy. In patients with acute biliary pancreatitis, possibly patients requiring stent and patients with pancreatic duct damage during the course of pancreatitis,

In patients with mild acute biliary pancreatitis, there is no significant difference in the early (first 72 hours) ERCP/ES results compared to the results of patients who underwent ERCP/ES in the late period. For this reason, we are of the opinion that ERCP/ES can be performed early in patients with mild acute biliary pancreatitis. In addition, early ERCP/ES procedures will shorten the patient's length of hospital stay and so reduce the treatment costs.

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RESEARCH ARTICLE

Fatma Nihal Ozmen[1]
Hasan Sultanoglu[2]
Umut Yucel Cavus[3]
Alpaslan Ozturk[4]

[1]Iğdır State Hospital, Department of Emergency Medicine, Iğdır, Turkey
[2] Department of Emergency Medicine, School of Medicine, Düzce University, Düzce, Turkey
[3] Department of Emergency Medicine, Ankara Dışkapı Education and Research Hospital, Ankara, Turkey
[4] Tokat Erbaa State Hospital, Department of Biochemistry, Tokat, Turkey

Corresponding Author:
Hasan Sultanoglu
Department of Emergency Medicine, School of Medicine, Düzce University, Düzce, Turkey
Phone: +90 05446368416
mail: drsultanoglu@hotmail.com

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Diagnostic Comparison Of Troponin and Scube 1 Levels In Patients Diagnosed with Stemi and Nstemi In The Emergency Department

ABSTRACT

Objective: In the present study we aimed to compare the levels of troponin and SCUBE 1 markers to determine the diagnostic role of SCUBE 1 in patients with STEMI-NSTEMI.

Methods: This study was prospectively conducted with 119 patients diagnosed with acute myocardial infarction at the emergency department of DışkapıYıldırımBeyazıt Training and Research Hospital and 30 control subjects between 01.10.2016 and 01.02.2017. The relationship between age, sex, acute myocardial infarction (AMI) type, white blood cell (WBC), lymphocyte, neutrophil, neutrophil/lymphocyte ratio, red cell distribution width (RDW), thrombocyte count, aspartate aminotransferase (AST), alanine aminotransferase (ALT), CK, CK-MB, troponin, and SCUBE 1 level was examined. Age, sex, and SCUBE 1 level were compared between the patient and control groups.

Results: The patients had a mean age of 61.5±14.5 years, and 68.9% of them were male. The patients had a SCUBE 1 level of 79.7 ng/mL and the control group 53.2 ng/ml. SCUBE 1 level was comparable between the patients with acute myocardial infarction and the control group ($p>0.05$). A correlation was found between SCUBE 1 level and age ($p>0.05$).Women in the patient group had a significantly higher SCUBE 1 level ($p<0.05$). There was a positive correlation between the WBC, CKMB, and troponin levels, and SCUBE 1 level in the patient group.cor No correlation was found between SCUBE 1 level and neutrophil, lymphocyte, neutrophil/lymphocyte ratio, RDW, platelet, AST, ALT, and CK levels ($p>0.05$). There was no significant correlation between infarction type and SCUBE 1 level ($p>0.05$).

Conclusions: SCUBE 1 level did not significantly rise in patients with acute myocardial infarction. As the test had lower sensitivity and specificity compared to the other markers, we believe that it is not suitable for practical use.

Keywords: SCUBE 1, Acute Myocardial Infarction, Troponin.

Acil Serviste Tanı Alan Stmı ve Nstmı Hastalarda Troponin Değerleri ve Scube 1 Değerlerinin Tanısal Karşılaştırılması

ÖZET

Amaç: Bu çalışmada ST elevasyonlu miyokard ifarktüsü (STEMI) ve ST elevasyonu olmayan miyokard ifarktüsü (NSTEMI) hastalarında troponin ve serum signal peptide-CUB-EGF domain-containing protein 1 (SCUBE 1) markerlarını karşılaştırıp erken tanıdaki SCUBE 1 değerinin tanısal önemini saptamayı amaçladık.

Gereç ve Yöntem: Çalışma 01.10.2016 ve 01.02.2017 tarihleri arasında Dışkapı Yıldırım Beyazıt Eğitim ve Araştırma Hastanesi acil servisinde, akut miyokard infaktüsü tanısı konan 119 hasta ve 30 kontrol grubu ile prospektif olarak gerçekleştirildi. Hastaların yaş, cinsiyet, white blood cell (WBC), nötrofil, lenfosit, nötrofil/lenfosit, red cell distribution width (RDW), trombosit, aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatine kinase (CK) , CK-MB, troponin ve AMİ alt tipinin SCUBE 1 düzeyleri olan ilişkisi incelendi. Veriler SPSS Windows 22 versiyonunda analiz edildi.

Bulgular: Hastaların yaş ortalaması 61,5±14,5 yıl olup, %68,9'u erkekti. Hastaların SCUBE 1 düzeyi 79,7ng/mL, kontrol grubunun SCUBE 1 düzeyi 63,2 ng/ml olarak saptandı. AMI'li hastalar ve kontrol grubu arasında SCUBE 1 düzeyi benzerdi ($p>0,05$). SCUBE 1 düzeyi ve yaş arasında korelasyon saptanmadı ($p>0,05$). Hasta gruptaki kadınlarda SCUBE 1 düzeyi anlamlı olarak yüksekti ($p<0,05$).Hastalarda WBC, CK-MB ve troponin düzeyleri SCUBE 1 arasında pozitif yönlü korelasyon saptandı. Nötrofil, lenfosit, nötrofil/lenfosit oranı RDW, platelet, AST, ALT ve CK düzeylerinin SCUBE 1 ile arasında korelasyon saptanmadı ($p>0,05$). İnfaktüs tipi ve SCUBE 1 düzeyi arasında ilişki saptanmadı ($p>0,05$).

Sonuç: AMI'li hastalarda SCUBE 1 düzeyindeki artış anlamlı değildi. Testin spesifitesi ve sensitivitesinin diğer markerlara göre düşük olması sebebiyle, pratik kullanım için yetersiz olduğu kanısı doğmaktadır.

Anahtar Kelimeler: SCUBE 1, Akut Miyokard İnfaktüsü, Troponin

INTRODUCTION

Cardiovascular diseases (CVD) are the leading cause of death worldwide (1). The term acute coronary syndrome (ACS) is applied to patients in whom there is a suspicion or confirmation of acute myocardial ischemia or infarction (AMI) (2). AMI is diagnosed on the basis of patient history, physical examination, electrocardiogram (ECG), and biochemical markers (3). As cardiac troponins are more sensitive and specific for myocardial injury, they are preferred over conventional markers including creatine kinase (CK), its isoenzyme CK-MB, and myoglobin. A rise in cardiac troponins indicates an irreversible myocardial injury, with elevated troponins in the presence of myocardial ischemia (chest pain, ST-segment changes) being indicative of myocardial infarction (MI) (4).

Fexex SCUBE 1 is a cell surface molecule deposited in the alpha granules of inactive thrombocytes, which is activated by thrombin and translocated to the thrombocyte surface. These molecules, which are released in the form of small and soluble particles, are incorporated into thrombus structure. SCUBE 1 deposition has been immunohistochemically detected in the subendothelial matrix of advanced atherosclerotic lesions in humans (5). Prior studies have reported that, albeit insensitive, SCUBE 1 protein is detectable within 6 hours of the onset of ischemic symptoms and may be a good marker for acute thrombotic diseases (5, 6).

Herein, we aimed to compare troponin and SCUBE 1 to determine the diagnostic role of the latter in patients with STEMI-NSTEMI.

MATERIAL AND METHODS

Our study was performed as a prospective, single-center study after its approval by Dışkapı Yıldırım Beyazıt Training and Research Hospital local ethics committee (No:34/22; Date:16.01.2017). It was conducted in compliance with the Helsinki Declaration and the guidelines for good clinical practice. It enrolled 119 patients who were diagnosed with AMI at the Emergency Department Clinic between 01.10.2016 and 01.02.2017, and 30 healthy controls. In order to reduce the effects of age and sex on the SCUBE 1 level, the control subjects were selected in an age- and sex-matched fashion. Aimed at determining the diagnostic role of SCUBE 1 protein in patients with chest pain, the present study enrolled volunteering patients with AMI aged 18 years or older, who were free of any other disease potentially elevating SCUBE 1 levels. Patients with history of end-stage renal failure, liver failure, decompensated heart failure, known or suspected inflammatory or neoplastic diseases, major surgical intervention or major trauma within last 3 months, cerebral ischemia, acute mesenteric ischemia, peripheral vascular disease, hypertension, pregnancy predisposing to thrombosis, pulmonary embolism history were excluded.

The relationships between SCUBE 1 levels and age, sex, acute myocardial infarction (AMI) type, white blood cell (WBC), lymphocyte, neutrophil, neutrophil/lymphocyte ratio, red cell distribution width (RDW), thrombocyte count, aspartate aminotransferase (AST), alanine aminotransferase (ALT), CK, CK-MB, and troponin were examined. Age, sex, and SCUBE 1 level were compared between the patient and control groups.

SCUBE-1 was studied at 0 h in STMI patients and at 6 h in NSTEMI patients. Patients with STEMI on ECG and 6th hour troponin elevation in STEMI were included in this study. SCUBE1 patients were compared with the patients with definite diagnosis. In order to measure SCUBE 1 level, a 2-cc blood sample was taken from each subject and put into tubes containing standard gel but no anticoagulant. The samples were then centrifuged at 4000 rpm at +4 degrees for 15 minutes. A 1-cc sample was drawn from each subject's serum, put into an Eppendorf tube, and stored at -80 degrees Celsius until the day of biochemical analysis. Twenty-four hours before SCUBE 1 analysis, the Eppendorf tubes were transferred to +4 degrees Celsius, and then slowly thawed to room temperature in a period of 24 hours for the analysis of SCUBE 1 level.

Statistical Analysis: Study data were analyzed with Statistical Package for the Social Sciences (SPSS) 22.0 software package. The normality of data distribution was tested with the Kolmogorov-Smirnov test. Sensitivity and specificity assessed by ROC analysis. Parametric quantitative data were expressed as mean, standard deviation (SD); nonparametric data as the median and interquartile range (IQR); and qualitative data as the number(n) and percentage (%) of the cases. Parametric data were analyzed by Student t-test; non-parametric data by Mann Whitney U test; qualitative data by Pearson Chi-square test; correlation of qualitative data by Spearman's correlation test. A P value of less 0.05 was considered statistically significant.

RESULTS

It enrolled 119 patients who were diagnosed with AMI at the Emergency Department and 30 healthy controls. The mean age of the AMI patients and the control group were 61.5±14.5 years and 62.0±14.1 years, respectively. No significant difference was found between the two groups with respect to mean age ($p>0.05$).

Eighty-two (68.9%) AMI patients were men and 37 (31.1%) were women; 18 (60.0%) control subjects were men and 12 (40.0%) were women. The two groups did not differ significantly with respect to sex distribution (p>0.05).

The mean complete blood count, cardiac enzymes and other laboratory parameters of the patients are given in the table (Table 1).

The median SCUBE 1 level of the patient and control groups were 79.7ng/mL (IQR:40.8) and 63.2 ng/mL (IQR:75.4), respectively. The SCUBE 1 levels of both groups were comparable (p>0.05) (Figure 1).

Table 1. Complete blood count results of the patients

Parameters	Median (IQR)	Minimum maximum
WBC (103/mm3)	10.5 (4.6)	5.1-27.7
Neutrophil (%)	7.1 (4.6)	2.8-87.5
Lymphocyte (%)	2.4 (2.0)	0.3-28.4
Neutrophil /lymphocyte	2.5 (4.1)	0.3-52.9
RDW (%)	13.8 (2.1)	1.9- 22.0
Thrombocyte (103/mm3)	253 (84)	111-617
AST (U/L)	26 (17)	11-349
ALT (U/L)	24 (20)	4-128
CK (ng/mL)	137 (157)	17-3284
CKMB (ng/ml)	19 (20)	5-533
TROPONIn (ng/ml)	0.15 (0.82)	0-99.4

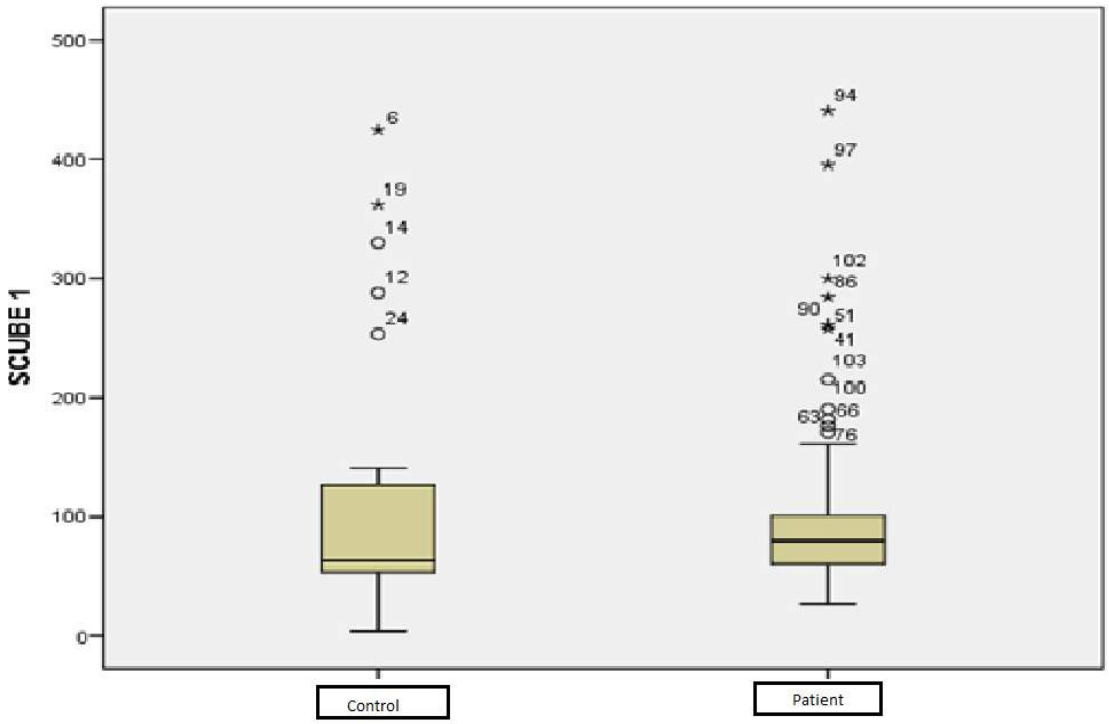

Figure 1. Graphical representation of the comparison between the SCUBE 1 levels of the study groups

In the patients included in the study, the area under the curve was 0.552, the appropriate cut-off value was 64.4 ng / ml, and the sensitivity was 69.7% and the specificity was 46.7% at this cut-off value.

There was a positive correlation between the SCUBE 1 level and WBC in AMI patients (p<0.05). There was not any significant correlation between SCUBE 1 level and lymphocyte, neutrophil, and thrombocyte counts, and neutrophil/lymphocyte ratio, and RDW level in AMI patients (p>0.05)(Table 2).

No significant correlation was found between SCUBE 1 level and AST, ALT, and CK levels in AMI patients (p>0.05). A positive correlation was present between CK-MB, troponin levels, and SCUBE-1 level in AMI patients (Table 2).

Table 2. Correlation between complete blood count parameters and scube 1 level

Parameters	r	p
WBC (103/mm3)	0.233	**0.011**
Neutrophil (%)	-0056	0.549
Lymphocyte (%)	-0.153	0.099
Neutrophil /lymphocyte	0.103	0.268
RDW (%)	0.150	0.109
Thrombocyte (103/mm3)	-0.007	0.939
AST (U/L)	-0.069	0.454
ALT (U/L)	-0.133	0.148
CK (ng/mL)	0.119	0.199
CKMB (ng/ml)	0.218	**0.017**
TROPONIn (ng/ml)	0.306	**0.001**

Spearman's correlation analysis

There was no correlation between age and SCUBE 1 level in AMI patients (p>0.05). The median SCUBE 1 level in men and women was 72.3ng/mL (IQR:40.5) and 92.0 ng/mL (IQR:40.3), respectively. Women had a significantly higher median SCUBE 1 level than men (p<0.05) (Table 3).

Table 3. Comparison of SCUBE 1 level by sex

	Men (n:82) Median (IQR)	Women (n:37) Median (IQR)	p
SCUBE 1	72.3 (40.5)	92(40.3)	**0.028**

Mann Whitney-U test

The median SCUBE 1 levels of the NSTEMU and STEMI patients were 89.2 ng/ml (IQR:39.4) and 72.2 ng/ml (IQR:46.4), respectively. There was not a statistically significant difference between the two groups' SCUBE 1 levels (p>0.05)(Table 4).

Table 4. Comparison of the SCUBE 1 levels of the AMI subtypes

	NSTEMI (n:69) Median (IQR)	STEMI (n:50) Median (IQR)	p
SCUBE 1	89.2 (39.4)	72.2 (46.4)	0.064

Mann Whitney-U test

DISCUSSION

The number of deaths due to coronary artery disease rank first across the globe (3). As AMI has high mortality and morbidity, it is essential to make its diagnosis and to begin its treatment as soon as possible. In practice, however, this is not always the case due to factors related to both patients and physicians (7). Tanrıkulu et al. detected that 23.7% of all patients presenting to the emergency department had cardiovascular disorders (8). Novel diagnostic methods and markers are constantly developed in an attempt to facilitate early diagnosis of ACS.

It is recognized that interactions between thrombocytes, monocytes, and endothelial cells play a role in the pathogenesis of thrombotic events leading to myocardial ischemia (9-11).

According to an experimental study by Türkmen et al., a significant rise in SCUBE 1 level is associated with thrombocyte adhesion; SCUBE 1 level significantly rises within the first two hours in pulmonary thromboembolism (PTE), and the test offers promise in PTE (12). Dai et al. reported that SCUBE 1 level significantly rose in patients with acute ischemic stroke whereas it remained normal in patients with chronic coronary artery disease, with the maximum level being attained at 6th hour. They attributed a stable SCUBE 1 level in chronic arterial diseases to a more stable plaque structure, less severe inflammation, a lesser rate of plaque rupture, and plaque coverage by thick fibrous caps (5). Although SCUBE 1 level was higher in the patient group, it showed no significant difference from that of the control group. We believe that low median CKMB and troponin levels simultaneously studied with SCUBE 1 indicate that blood samples were taken at the early hours of AMI. Therefore, we believe that blood samples may have been taken before the SCUBE 1 level started to rise. SCUBE 1 level may have started to rise due to increased thrombocyte activity during plaque rupture, the release of SCUBE 1 containing granules within thrombocytes, and incorporation of SCUBE 1 into the thrombus structure. Former studies have reported that AMI typically affects individuals aged 55-75 years, and there is a negative, albeit statistically non-significant, the correlation between SCUBE 1 level and age (5,13-15). Ulusoy et al. did not detect any significant correlation between SCUBE 1 level and age among hemodialysis patients (16). It has been reported that SCUBE 1 level is significantly affected by various physiological factors such as increased oxidant levels, exercise, and hydration (6). In agreement with the current literature, our study did not show any significant correlation between age and SCUBE 1 level in AMI patients. We believe that the incidence of AMI increases in advanced age due to a shift of physiological processes from an anabolic state to a catabolic state, increased prevalence of atherosclerosis, and impaired vascular anatomic structures. We also of the opinion that, apart from age, the SCUBE 1 response to AMI is proportional to the affected myocardial area, the extent of necrosis, and the amount of reactive oxygen radicals.

Prior studies have shown that AMI is more common in women (13-15). Ulusoy et al. detected lower SCUBE 1 levels in female patients in a hemodialysis population and attributed that finding to an increased risk for cardiovascular disorders in men (16). Our study was in agreement with the literature data because 68.8.% of its population were male, and SCUBE 1 was significantly higher in women. We are of the opinion that women had a higher SCUBE 1 level owing to having AMI later in life, and atherosclerosis and ischemic events being more prevalent at an advanced age in women.

WBC and its subtypes are known as the classical markers of inflammation in cardiovascular disease (17). Neutrophil/lymphocyte ratio is more valuable than neutrophil, and lymphocyte counts alone and has been shown to be potentially useful for long-term mortality prediction among patients with STEMI undergoing PCI (percutaneous coronary intervention (18,19). Leukocytosis is usually associated with necrosis size in STEMI, glucocorticoid level, and coronary arterial inflammation (18,19). Although RDW is usually used for the differential diagnosis of anemia, it has been recently found to correlate to increased risk of mortality and adverse cardiovascular events among individuals with heart failure, stable coronary artery disease, ACS, AMI, and cardiovascular disease (14,20). Our study detected a positive correlation between WBC and SCUBE 1 level whereas no

significant correlation was found between SCUBE 1 level and neutrophil, lymphocyte, neutrophil/lymphocyte ratio, and RDW. We believe that extensive necrosis increases WBC count and the amount of oxygen radicals, causing a rise in SCUBE 1 level simultaneously with WBC; we also believe that other parameters would have risen in blood samples obtained at more appropriate time intervals.

Dai et al. reported that soluble plasma SCUBE 1 is obtained from activated platelets and may play a pathological role by facilitating platelet adhesion/agglutination and later thrombus formation (5). Ulusoy et al., in a study on patients undergoing dialysis, reported no relationship between SCUBE 1 level and the thrombocyte count (16). Günaydın et al. stated that they found no significant correlation between thrombocyte count and SCUBE 1 level (21). Our study detected a negative but statistically non-significant correlation between SCUBE 1 level and thrombocyte count. This might be explained by SCUBE 1 release into the bloodstream as a result of thrombocyte chemotaxis to rupture area and disruption after plaque rupture.

Our study failed to show any relationship between liver transaminases and angiographically determined cardiovascular diseases (22). Baahrs et al. reported a correlation between stenosis severity and AST, troponin level but not ALT level in AMI (23). So far, the relationship between cardiac troponin concentrations and microvascular obstruction has been reported by many studies (15,24,25). Other studies have failed to show any significant correlation between troponin and SCUBE 1 levels in patients with ischemia (5,21). No study in the literature has yet shown any correlation between SCUBE 1 level and liver enzymes, CK-MB, and CK. Our study showed that AST, ALT, and CK levels showed no correlation with SCUBE 1 level while CK-MB and troponin levels showed a positive correlation with SCUBE 1 level. Considering the pathophysiology of AMI, we believe that SCUBE 1, which takes part in thrombocyte aggregation, is released following plaque rupture, but that event rather locally affects the lesion area. Thus, we think that, although AST, ALT, and CK did not rise, SCUBE 1 level rose in proportion to thrombus aggregation and necrosis size. Additionally, the simultaneous rise of CK-MB, troponin, and SCUBE 1 over time may have caused a joint increase in those markers. The low number of patients in this study and the fact that the SCUBE 1 parameter studied is not in routine use creates potential limitations.

CONCLUSION

SCUBE 1 is not a promising cardiac marker early in the ACS process. Its lower sensitivity and specificity limit its use. Although there was no significant correlation between age and SCUBE 1 level, women had a significantly higher SCUBE 1 level. Our study demonstrated a positive correlation between SCUBE 1 level and WBC, CKMB, and troponin levels but not neutrophil, lymphocyte, neutrophil /lymphocyte ratio, RDW, platelet, AST, ALT, or CK. This may have been related to necrosis size and blood sampling time. No correlation was found between the infarction type and SCUBE 1 level.

In conclusion, no significant rise in SCUBE 1 level could be shown in patients with AMI. As the test had lower sensitivity and specificity than the other markers, we are of the opinion that it is not suitable for practical use, and multi-center studies with a larger population size about this test should be conducted.

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RESEARCH ARTICLE

Gamze Gursul Zagil[1]
Cihan Fidan[1]
Ergun Oksuz[1]
Altug Kut[1]

[1] Baskent University, Faculty of Medicine, Department of Family Medicine, Ankara, Turkey

Corresponding Author:
Ergun Oksuz
Baskent University, Faculty of Medicine, Department of Family Medicine, Ankara, Turkey
mail: eoksuz@baskent.edu.tr

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konuralptipdergisi@gmail.com
www.konuralptipdergi.duzce.edu.tr

Self-Medication Patterns among Turkish University Students

ABSTRACT

Objective: This study aims to determine the prevalence of self-medication practice among university students in Turkey and the effective factors and self-medication practices.

Methods: To conduct a descriptive cross-sectional study, this study was conducted with 494 undergraduate students selected through a stratified random weight-proportional sample. The students were asked to fill in a self-report questionnaire form including introductory characteristics and self-medication practices. Analyses were carried out using descriptive statistics and binary logistic regression.

Results: The prevalence of self-medication at any time was determined to be 81.6% (n=403). The prevalence of self-medication was 84.9% in females and 75.6% in males (OR 2.0, 95% CI 1.2-3.3, p=0.005). Of the participants, 27.5% (n=111) bought the medication by their own preferences and experiences. The most common self-medication symptoms of the participants were headache (90.8%). Self-medication drug groups were in the form of analgesics in 95.9% (n=259) of females and 93.2% (n=123) of males. The prevalence of antibiotic self-medication was 9.5% in the self-medication group and 7.7% for all participants. Due to self-medication, 8.2% (n=33) of the students experienced an adverse effect at any time. The students in the self-medication group believed that there would not be serious adverse effects caused by the OTC drugs even if they caused adverse effects (30.5%) or that they would not cause any adverse effects (3.8%).

Conclusions: Self-medication is a common behavior among university students, with higher rates in females. Students practice this largely by relying on their previous experiences. They mostly prefer medicines previously given by their physicians for similar conditions.

Keywords: Self-Medication, Over-the-Counter Drugs, Youth, Self-Care.

Üniversite Öğrencilerinde Kendi Kendine İlaç Kullanımı

ÖZET

Amaç: Bu çalışmada Türkiye'de üniversite öğrencilerinde sıklığının ve etkili olan faktörlerin belirlenmesi amaçlanmıştır.

Gereç ve Yöntem: Kesitsel tanımlayıcı çalışma için tabakalı rastlantısal ağırlık orantılı örneklem ile seçilen 494 lisans öğrencisinin katılımıyla çalışma yürütülmüştür. Öğrencilere kendi-kendine cevaplayacakları tanıtıcı özellikler ve kendi-kendine tedavi uygulamalarını kapsayan bir soru formu uygulanmıştır. Tanımlayıcı istatistikler ve ikili lojistik regresyon kullanılarak analizler yapılmıştır.

Bulgular: Herhangi bir zamanda kendi-kendine tedavi sıklığı %81,6 (n=403) olarak tespit edilmiştir. Kendi-kendine tedavi sıklığı kadınlarda %84,9 ve erkeklerde %75,6 (OR 2,0, %95 GA 1,2-3,3, p=0,005) olarak bulunmuştur. Katılımcıların %27,5'i (n=111) kendi tercih ve tecrübeleri ile ilaçları satın almıştır. Katılımcıların ilaç aldıkları semptomları en sık baş ağrısı (%90,8) olmuştur. Kendi-kendine tedavi ilaç grupları kadınların %95,9'unda (n=259), erkeklerin %93,2'sinde (n=123) analjezikler şeklinde olmuştur. Antibiyotik kullanımı; kendi-kendine tedavi grubunda %9,5 ve tüm katılımcılar için %7,7 olarak bulunmuştur. Kendi-kendine tedavi nedeniyle %8,2 (n=33) öğrenci herhangi bir zamanda bir yan etki tecrübe etmiştir. Kendi-kendine tedavi grubundaki öğrenciler tezgâh üstü ilaç grubu (OTC) ile yan etki olsa da ciddi yan etkiler olmayacağını (%30,5) veya herhangi bir yan etki olmayacağını (%3,8) düşünmektedir.

Sonuç: Üniversite öğrencileri arasında kendi-kendine tedavi kadınlarda daha yüksek olmak üzere yaygın bir davranıştır. Öğrenciler, büyük ölçüde daha önceki kendi tecrübelerine güvenerek bu uygulamayı yapmaktadır. Ağırlıklı olarak daha önce benzer durumlar için hekimleri tarafından verilmiş ilaçları tercih etmektedirler.

Anahtar Kelimeler: Kendi-Kendine Tedavi, Tezgah Üstü İlaçlar, Gençlik, Özbakım.

INTRODUCTION

The World Health Organization (WHO) defines self-medication as the selection and use of drugs by individuals themselves to treat diseases or symptoms known to them (1, 2). Self-medication is a part of self-care and is a practice where patients take a pro-active role in their health-related decisions (1-5). Purchasing drugs without a prescription, sharing drugs with the members of a social circle, or using leftover drugs at home are all considered self-medication. Individuals knowing their responsibilities for their own health and being aware that professional health care is often unnecessary for simple diseases have contributed to the concept of self-medication (6, 7).

It is believed that self-medication reduces the burden of health services, saves the time spent waiting for a doctor's examination and provides significant cost savings in the use of health resources (2, 4). Although self-medication is an ordinary but important part of the patient behavior in coping with the disease, it may also lead to inappropriate results in some cases (3, 8-13). Safe self-medication refers to as appropriate and conscious use of drugs that are required in some limited situations, such as non-prescription/over-the-counter (OTC) drugs (4, 5, 9, 11, 14). Safe self-medication requires a certain level of knowledge of the drug, in addition to being aware of self-care (9, 11, 15).

An appropriate and responsible self-medication can be economical for both the individual and the healthcare system. College youth, who are in the group that will be affected by the changes in drug use in the medium and long-term, can be considered to have a relatively higher level of education compared to other segments of the society. With these qualities, it is important to understand the views and practices of the university youth on the subject.

This study aims to determine the prevalence of self-medication practice among university students in Turkey, along with the effective factors and self-medication practices.

MATERIAL AND METHODS

For the descriptive cross-sectional study, a biostatistical power analysis was performed for the universe, which included undergraduate students (n=10,009) in a university in Ankara. The minimum sample size was calculated using the equation of $n=[Z2\times P(1-P)]/d2$. Where n is sample size (370), Z is Z statistic for a level of confidence (1.96), P is expected prevalence or proportion (0.5), and d is precision (0.05). With an addition of 10% for non-response, it was decided to recruit a minimum of 426 participants from university (16). The study was conducted with the participation of 494 undergraduate students selected with stratified random weight-proportional sample. A participation approval was obtained from the students with an informed consent form.

In the study, a questionnaire form consisting of four sections was used to evaluate the sociodemographic characteristics of the participants, their current health status and harmful habits, the behaviors they exhibit when they get ill, and their attitudes and experiences about using an OTC.

The study data were entered to the digital environment and analyzed using the SPSS (Statistical Package for Social Sciences) for Windows 17.0 (SPSS Inc. Chicago, IL) software. The descriptive statistics were presented as mean (±) standard deviation (SD), and percentage. In addition to descriptive statistics, the Pearson/Fisher exact Chi-square tests were also performed. The conformity of the variables to normal distribution was tested using the visual (histograms and probability graphs) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). Effective factors were investigated using a binary logistic regression analysis. Odds ratio (OR) values and 95% confidence intervals (95% CI) were calculated.

This study project was approved by the Ethics Committee of Baskent University Faculty of Medicine before starting the study (Project number KA17/123).

RESULTS

The study was completed in the 2017-18 academic year. The study included 494 undergraduate students from 11 faculties. Of the participants, 64.4% (n=318) were female and 35.6% (n=176) were male. The mean age was 20.9 ± 2.0 (18-29) years. Of the participants, 21.0% (n=108) were receiving undergraduate education in a healthcare-related faculty. Of the students, 61.5% (n=304) lived in urban and 38.5% (n = 190) in rural. The family income levels were distributed as 36.8% (n=182) ≤TRY3,500/month and as 63.2% (n=312) >TRY 3,500/month. A large proportion of the participants lived with their parents (67.8%, n=335). Of the students, 37.9% (n=187) were smoker while 39.9% (n=197) consumed alcohol. Of the students, 30.8% (n=152) had a chronic clinical and/or surgical disease diagnosed by a physician to this date. It was determined that 15.8% (n=78) of the participants were using a prescription drug continuously due to a chronic disease (Table 1).

Of the participants, 403 (81.6%) used self-medication at any time. The prevalence of self-medication was 84.9% in females and 75.6% in males (OR 2.0, 95% CI 1.2-3.3, p = 0.005). The mean age was 21.0 ± 2.1 years in the self-medication group and 20.6 ± 2.0 years in the non-self-medication group (OR 1.1, 95% CI 0.9-1.3, p = 0.097). A self-medication prevalence of 82.9% was found in the participants living in urban and 79.5% in those living the rural (OR 0.7, 95% CI 0.4-1.2, p = 0.198). Although a higher prevalence of self-medication was reported in those with a high-

income level (83.0%) and in those who lived alone/with friends (84.9%), it was not significant (p> 0.05). In terms of health-related determinants, a prevalence of 86.2% was determined in those with a chronic disease and of 79.5% in those without any diseases (OR 1.4, 95% CI 0.8-2.3, p = 0.278). Although the prevalence of self-medication was higher in the students who smoke (83.4%) and consume alcohol (84.3%), there was no significant difference (Table 1).

Table 1. Distribution of self-medication by demographic factors

	Self-medication		OR (CI 95%)	p-value
	Yes	No		
Age (mean)	21.0 (2.1)	20.6 (2.0)	1.109 (0.982-1.252)	0.097
Sex				
Male (n=176)	133 (75.6)	43 (24.4)	2.019 (1.233-3.305)	0.005
Female (n=318)	270 (84.9)	48 (15.1)		
Socio-economic status				
Municipality				
Rural	151 (79.5)	39 (20.5)	0.720 (0.437-1.187)	0.198
Urban	252 (82.9)	52 (17.1)		
Income level (TRY/month)				
<3,500	144 (79.1)	38 (20.9)	1.278 (0.784-2.083)	0.326
>3500	259 (83.0)	53 (17.0)		
Living setting				
With parents	268 (80.0)	67 (20.0)	1.429 (0.826-2.473)	0.202
Alone/with friends	135 (84.9)	24 (15.1)		
Health determinants				
Non-smoking	247 (80.5)	60 (19.5)	1.132 (0.647-1.979)	0.665
Smoking	156 (83.4)	31 (16.6)		
Non-Alcohol	237 (79.8)	60 (20.2)	1.209 (0.685-2.134)	0.512
Alcohol	166 (84.3)	31 (15.7)		
Non-illness	272 (79.5)	70 (20.5)	1.356 (0.782-2.349)	0.278
Chronic illness	131 (86.2)	91 (18.4)		

As a source of self-medication, 75.4% (n=304) of the students stated that the OTC drugs they used were previously prescribed by a physician. Secondly, 27.5% (n=111) of the participants stated that they purchased the drugs by their own preferences and experiences. This rate was 25.6% in females (n=69) and 31.6% in males (n=42) (p = 0.203). While 11.2% (n=45) of the students stated that they purchased the drug upon an advice from a pharmacist, 10.7% (n=43) stated that they took the drug from a relative. The rate of taking medication from a relative is 8.1% in females (n=22) and 15.8% in males (n=21) (p = 0.019).

In the gender-based distribution of the self-medication symptoms of the participants, it was determined that the most common cases of taking drugs without consulting any doctor were headache (90.8%) and common cold (59.8%). The prevalence of self-medication due to dysmenorrhea in females was found to be 64.4% (n=174). This was followed by the major symptoms of muscle and/or joint pain (40.0%), abdominal pain (except for dysmenorrhea) (31.3%), dyspeptic complaints (21.3%), nausea/vomiting (17.4%), diarrhea/constipation (14.4%), as per the order of prevalence. While the prevalence of self-medication for abdominal pain (except for dysmenorrhea) was 38.5% in females, this prevalence was found to be significantly lower in males (16.5%) (p=0.000). In general, these health conditions were distributed under three titles, which are pain, cold symptoms, and dyspeptic symptoms (Table 2).

When the self-medication drug groups of the participants were examined, it was found that 95.9% of females (n=259) and 93.2% of males (n=123) used analgesics. Of the students, 58.2% (n=234) stated that they used cold drugs, while 47.5% used myorelaxants, and 41.8% used drugs with vitamin or minerals ingredients. Of the participants, 11.7% (n=47) used anti-acids for self-medication. The prevalence of antibiotic self-medication was found as 9.5% for the university students using self-medication, and as 7.7% for all participants. This rate was 10.0% (n=27) in females and 8.3% in males (n=11) (Table 2).

In the distribution of the reasons of the participants for preferring self-medication, the most common reason is the thought of mild disease with 77.6% (n = 312). Other reasons were determined as school or work intensity with 14.2% (n=57), long waiting times at health institutions with 5.7% (n=23), and other reasons with 2.5% (n = 10), such as the thought that the quality of the services provided by the health-care institution is low, or that an examination by a physician is costly, or that having access to health-care institution is challenging. There was no significant difference in the distribution of the reasons for self-medication preference by gender (p = 0.063).

Table 2. Characteristics of self-medication among participants

	Female (n=270) n (%)	Male (n=133) n (%)	Total (n=403) n (%)	p-value
Symptoms for which drugs were self-medicated				
Headache	248 (91.9)	118 (88.7)	366 (90.8)	0.306
Cold symptoms (Cough, fever etc)	161 (59.6)	80 (60.2)	241 (59.8)	0.920
Dysmenorrhea	174 (64.4)		174 (43.2)	N/A
Muscle and/or joint pain	110 (40.7)	51 (38.3)	161 (40.0)	0.644
Abdominal pain	104 (38.5)	22 816.5)	126 (31.3)	0.000
Dyspepsia	62 (23.0)	24 (18.0)	86 (21.3)	0.257
Nausea/vomiting	50 (18.5)	20 (15.0)	70 (17.4)	0.386
Diarrhea/constipation	38 (14.1)	20 (15.0)	58 (14.4)	0.796
Other	18 (6.7)	9 86.8)	27 (6.7)	0.970
Drug groups for self-medicated				
Analgesics	259 (95.9)	123 (93.2)	382 (95.0)	0.143
Cold medicines	157 (58.1)	77 (58.3)	234 (58.2)	0.961
Myorelaxants	128 (47.4)	63 (47.7)	191 (47.5)	0.994
Vitamins	106 (39.3)	62 (47.0)	168 (41.8)	0.159
Gastrointestinal drugs	27 (10.0)	20 (15.2)	47 (11.7)	0.138
Antibiotics	27 (10.0)	11 (8.3)	38 (9.5)	0.576
Others	2 (0.7)	8 (6.1)	10 (2.5)	0.007*

* Fisher-exact test, N/A: Not available

Upon the investigation of the initial behaviors exhibited by the participants whey they get ill, it was determined that 56.9% of them visited a doctor's office, and that 21.9% of them waited for a while and did not take any drug. It was observed that the behavior of waiting for a while without taking any drug was lower in the self-medication group compared to the other group, but it was not significant (25.3% vs. 21.1%, p = 0.383). The prevalence of resorting to natural supplements or traditional non-medication methods as the initial behavior when they get ill was found to be higher in the non-self-medication group (9.2% vs. 15.2%, p = 0.079). Consulting a relative in the self-medication group was significantly higher compared to the other group (2.2% vs. 9.9%, p = 0.012). Consulting a pharmacist (0.0% vs. 3.0%) was higher compared the non-self-medication group (Table 3).

Table 3. The behaviors of the participants when they get sick according to the self-medication status

Behaviors when they get sick	Self-medication		Total n (%)	p-value
	Yes n (%)	No n (%)		
I go to the physician' examination	229 (56.8)	52 (57.1)	281 (56.9)	0.956
I wait for a while without taking any medication	85 (21.1)	23 (25.3)	108 (21.9)	0.383
I try natural supplements or traditional non-drug methods	37 (9.2)	14 (15.4)	51 (10.3)	0.079
I consult a relative	40 (9.9)	2 (2.2)	42 (8.5)	0.012*
I consult a pharmacist	12 (3.0)	0 (0.0)	12 (2.4)	0.135*

* Fisher-exact test

Some practices that could show the responsibilities of young people were investigated in the self-medication group. Among those, the prevalence of patient information leaflet (PIL) reading behavior was 82.2% in total, distributed as always with 48.4% and sometimes with 33.8% (n=326). Of the young people reading PIL, 2.2% (n=7) reported that they did not understand what they were reading. Although the prevalence of reading PIL was higher in females and not understanding was higher in males, they were insignificant. Of the young people in the self-medication group, 95% (n=383) checked the information on drug boxes such as expiration date. The rate of recommending drugs to others was determined as 38.5% for the self-medication group (Table 4). In the self-medication group, any adverse effect was experienced due to OTC drugs at any time with 8.2% (n=33). Of the self-medication group, 65.7% believe that OTC drugs that are commonly used for self-medication may cause adverse effects, while 30.5% believe that the adverse effects of OTC drugs would not be serious at all even if they develop. Of the young people, 3.8% think that OTC drugs had no adverse effects (Table 4).

Table 4. Characteristics of self-medication practices by gender

	Female n (%)	Male n (%)	Total n(%)	p-value
Read patient information leaflet				
Always	134 (50.0)	58 (45.0)	192 (48.4)	0.480
Sometimes	90 (33.6)	44 (34.1)	134 (33.8)	
Never	44 (16.4)	27 (20.9)	71 (17.9)	
Understand patient information leaflet				
Yes	132 (58.9)	65 (63.7)	197 (60.4)	0.473*
Sometimes	88 (39.3)	34 (33.3)	122 (37.4)	
No	4 (1.8)	3 (3.0)	7 (2.2)	
Non-prescription drugs have adverse effects?				
Yes	176 (65.9)	85 (65.4)	261 (65.7)	0.207
Yes, but not seriously	84 (31.5)	37 (28.5)	121 (30.5)	
No	7 (2.6)	8 (6.2)	15 (3.8)	
Does check the drug expiration date				
Always	149 (55.2)	74 (55.6)	223 (55.3)	0.856
Sometimes	107 (39.6)	53 (39.9)	160 (39.7)	
Never	14 (5.2)	6 (4.5)	20 (5.0)	
Has he/she suggested a non-prescription drug to any relatives				
Yes	103 (38.1)	52 (39.1)	155 (38.5)	0.913
No	167 (61.9)	81 (60.9)	248 (61.5)	
Did he/she have any adverse effects with self-medication				
Yes	20 (7.4)	13 (9.8)	33 (8.2)	0.442
No	250 (92.6)	120 (90.2)	370 (91.8)	

*Fisher-exact test

DISCUSSION

Among university youth in different parts of the world, the prevalence of self-medication has been reported to be in a wide range from 30% to 95% (6, 7, 9, 11-15, 17-20). In our study, we determined the prevalence of self-medication in the university youth in Turkey as 81.6%. The prevalence was significantly higher in females (75.6% vs. 84.9%, OR 2.0, 95% CI 1.2-3.3, p = 0.005). In the literature, self-medication has been found to be more prevalent in females than in males (7, 21). The prevalence of self-medication is generally reported to be higher among females, who are at younger ages, who live alone, who have a low socioeconomic status, who have a chronic disease, and who have psychiatric problems (7, 13). In our study, the prevalence of antibiotic self-medication was found as 10.0% in females and as 8.3% in males, with a total prevalence of practice of 7.7%. In other studies conducted on university students in Turkey, the prevalence of antibiotic self-medication was reported to be 44.0% in 2005 and 36.0% in 2017 (22, 23). In Turkey, the prevalence of antibiotic self-medication in the general population was 19% in 2009 (24). In a 2006 multi-national study conducted in European countries, the prevalence of anti-microbial drug self-medication was reported to be ranging from 7% to 45% by countries for the last year (25).

The reasons for self-medication may vary depending on sociocultural characteristics. Factors such as a high level of education, the presence of leftover drugs from previous treatments, chronic diseases, minor health problems, long waiting times for examinations, high costs of medical examinations by a physician, low numbers of reimbursed drugs, presence of OTC drugs, information on pharmaceutical products in the media, possibility to buy drugs online can be included in the reasons for self-medication (25). In a study conducted in Brazil, more self-medication practices were determined in those with children, in those with home medicine cabinet, and in students with adequate knowledge of drugs (17). In our study, the prevalence of using drugs that were previously prescribed by a physician for self-medication was found to be above 75%. This indicates that self-medication drugs are obtained from leftover drugs from previous treatments. The prevalence of those who supplied drugs by their own preferences or from a relative was 27.5%. The prevalence of purchasing drugs upon a pharmacist's recommendation was found to be lower (10.7%) than the rates previously reported in Turkey (26). In a study conducted in India, when the students were analyzed in terms of their behaviors of taking drugs without consulting a doctor, 31.3% of students studying in a health-related faculty stated that they used medicines previously prescribed by a doctor, while this rate was 24.6% in students who studied in non-health-related faculties (27). In a study conducted in Turkey, it was determined that 71.5% of self-medication drugs were the drugs already available at home (20).

In our study, the participants reported that headache was the most common reason for self-medication with 90.8%. This rate was found as

59.8% for cold symptoms such as cough and fever, and as 40.0% for muscle/joint pain symptoms. The rate of taking drugs due to dysmenorrhea without consulting a doctor was found as 64.4% among the female students who participated in the study. In two separate yet similar studies conducted on university students in Turkey and Brazil, the same ranking of symptom prevalence was found for self-medication (17, 19). In studies conducted in Pakistan and Iran, a similar ranking was reported (7, 28). Symptom rankings for self-medication have been reported as common cold, fever and headache among medical students (27). Self-limiting conditions such as cold and diarrhea are known to constitute the majority of conditions where antibiotics are improperly consumed with self-medication (24, 29, 30).

In 2018, the use of OTC drugs had a prevalence of 81.0% as the primary treatment of simple diseases among the adults living the USA (31). According to the American College of Preventive Medicine (ACPM) data from the year 2009, the most commonly sold OTC drugs in the USA are common cold drugs, painkillers, antacids, and laxative medicines (3, 32). Of the general population in the USA, 92%'siused an OTC drug in the last year, while 55% sed OTCs several times (3). According to the Turkish Pharmaceutical Market Survey Report published by the Turkish Medicines and Medical Devices Agency (TMMDA) in Turkey, analgesics and cold medicines are at the top three in the list of most common over-the-counter drugs sold across the country based on the sales volume in 2015-2016 (33).

Considering studies conducted on university students in Turkey, it was determined that a 2010 study reported the prevalence of non-prescription analgesics as 61.5% and the prevalence of antibiotics as 39.5% (19). Analgesics and antipyretics are the most common drugs taken by medical students in India without consulting a doctor (18). In a recent study conducted on university students in Turkey, it was reported that 86% of female students and 64% of male students took analgesics without consulting a physician. In the same study, 2.8% of females and 4.8% of males stated that they took antibiotics without consulting a physician (34). In our study, 95% of the participants stated that analgesics was the most common self-medication drug they took. Half of the students used cold drugs, while nearly half of them used myorelaxants. The prevalence of antibiotic use without consulting a physician was found as 7.7% among the students in our study. In a study conducted in Izmir in 2005, the prevalence of antibiotic use as a form of self-medication was reported as 45% among university students studying in faculties not related to healthcare (22). This rate is quite high compared to the rates obtained from the studies conducted today. The decline in this rate might be attributed to the recent limitations implemented in Turkey for the sale of antibiotics in pharmacies.

Most of the students who participated in the study stated their reasons for self-medication as the thought of having mild disease. In a similar study conducted on university students in Turkey, 64% of the students reported that they took self-medication drugs that were previously used by them (22). In our study, this prevalence was found to be 75% in the form of taking a previously prescribed drug. In a study conducted on university students in Egypt, 74% of the students stated that they took drugs without consulting a doctor since they thought that the disease was mild. However, 71% of the students stated that they took drugs without consulting a doctor because of having knowledge based on their previous experiences (13). In a similar study conducted on medical school students, 45% of the participants stated that they used over-the-counter medication to save time, while 25% reported that they thought it was unnecessary to visit a doctor for mild diseases (8). In Brazil, 57% of the university students stated that they preferred self-medication because they knew what drugs to take for the symptoms they experienced, while 44% stated they preferred self-medication for mild diseases (17).

Of the students in the self-medication group, 38.5% stated that they offered OTC drugs to someone else. In a similar study conducted on university students, 17.8% of the students studying in a healthcare-related faculty and 17.7% of the students studying in a non-healthcare faculty stated that they recommended OTC drugs (27). It was found that 36.1% of the female students and 33.3% of the male students in medical faculty in Turkey recommended drugs to someone else (34). In Egypt, 12.6% of university students were shown to promote their close environment for self-medication (13). In a study on rational drug use in our country, 42.6% of the university students participating in the study were shown to take medication upon advice (35).

Of the students in the self-medication group 3.8%'si believe that OTC drugs had no adverse effects, while 30.5%'si think that the adverse effects would not be severe. This misconception about OTC drugs is also observed on a worldwide scale (3, 36). One of three students using OTC drugs does not have information about the adverse effects of OTC drugs. However, although the behavior of responsibility expected for self-medication is reflected by a rate of PIL reading of 82.2% and an understanding rate of 98%, the thought that there would be no adverse effects constitutes a risky situation. In fact, 8.2% of the students experienced an adverse effect due to OTC drugs they used. A major problem with OTC drugs is related to the handicaps in the reporting of adverse effects caused by these drugs. The fact that the patient does not know about the potential adverse effects of OTC

drugs may also affect the description and reporting of adverse effects for OTC drugs. Therefore, it is important that patients have sufficient information about the drugs they take (36).

CONCLUSION

In Turkey, self-medication is a prevalent behavior among university students. Self-medication is more prevalent in female students. Students mainly rely on their previous disease experiences. Drugs previously given by their physicians for similar conditions are predominantly preferred. One third of the students, which is quite a high rate, has a misconception that OTC drugs do not have adverse effects at all or only have not-serious adverse effects. For the rational use of self-medication, the healthcare system should take and prioritize measures to inform students on the adverse effects of drugs and admission to health care institutions at the right time.

Self-medication should be considered a normal and appropriate part of public health. Self-medication with OTC drugs can provide many benefits from the aspects of the patient and physician. Physicians and pharmacists should be more active in monitoring drugs and informing patients to increase the effectiveness of self-medication and to minimize current risks.

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RESEARCH ARTICLE

Erkan Melih Sahin[1]
Ozgul Ocak[2]
Cansu Demiral[1]
Busra Donmez[1]

[1] Canakkale Onsekiz Mart University Faculty of Medicine, Department of Family Medicine, Canakkale, Turkey
[2]Canakkale Onsekiz Mart University Faculty of Medicine, Department of Neurology. Canakkale, Turkey

Corresponding Author:
Erkan Melih Sahin
Canakkale Onsekiz Mart University Faculty of Medicine, Department of Family Medicine, Canakkale, Turkey
Phone: +90 5053026571
mail: emsahin@yahoo.com

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konuralptipdergi@duzce.edu.tr
konuralptipdergisi@gmail.com
www.konuralptipdergi.duzce.edu.tr

COVID-19 Symptoms at First Admission to Hospital

ABSTRACT

Objective: The aim of this study is to profile the complaints in the disease application using a symptom survey in patients presenting with the suspicion of COVID-19 disease and to determine the disease-specific and descriptive characteristics of the initial symptoms in those who were diagnosed with the disease.

Methods: In this cross-sectional study, symptoms at first admission were questioned in adult patients who applied to the Covid Outpatient Clinic between 21 December 2020 - 22 January 2021. A total of 43 complaints were analyzed in PCR test positive and negative patients.

Results: 273 (62.0%) first application and 167 (38.0%) control applications were included in the study. The PCR test was positive in 16.5% of the first admissions. The most common complaints in the first admissions with positive PCR test were fatigue (73.0%), headache (64.9%), pain (32.2%), cough (56.8%), sore throat (51.4%), loss of appetite (45.9%) while 15.9% of them were asymptomatic. Odd's rates of significant complaints for PCR positivity were calculated as 2.607 for fever, 2.724 for anorexia, 2.051 for cough, 2.594 for loss of smell, and 2.243 for loss of strength.

Conclusions: COVID-19 is a disease that affects many organs and systems. Comparing the admission symptoms with the PCR test results will contribute to the recognition of the disease at the initial stage. Fever, anorexia, cough, loss of smell and loss of strength were found to be the distinguishing complaints of PCR positivity in our study.

Keywords: COVID-19, Symptoms, PCR Test.

COVID-19 Hastalarında Başvuru Şikayetleri

ÖZET

Amaç: Bu çalışmada COVID-19 hastalık şüphesi ile başvuran hastalarda semptom sorgulaması yapıp hastalık başvurusundaki şikayetlerin profilini çıkartmak, hastalık tanısı kesinleşenlerde başlangıç semptomlarının hastalığa özgü olma ve tanımlayıcı özelliklerini belirlemek amaçlanmıştır.

Gereç ve Yöntem: Kesitsel desendeki çalışmada 21 Aralık 2020 - 22 Ocak 2021 tarihleri arasında COVID-19 Polikliniğine başvuran yetişkin hastalarda başvuru şikayetleri sorgulanmıştır. Toplam 43 şikayet PCR testi pozitif ve negatif olanlarda analiz edilmiştir.

Bulgular: Çalışmaya 273 (%62,0) ilk başvuru, 167 (%38,0) kontrol başvurusu dahil edilmiştir. PCR testi ilk başvuruların %16,5'inde pozitif sonuçlanmıştır. PCR testi pozitif ilk başvurularda en sık belirtilen şikayetler halsizlik (%73,0), baş ağrısı (%64,9), ağrı (%32,2), öksürük (%56,8), boğaz ağrısı (%51,4), iştahsızlık (%45,9) olarak sıralanırken %15,9 hasta asemptomatikti. PCR pozitifliği için anlamlı şikayetlerin Odd's oranları ateş 2,607, iştahsızlık 2,724, öksürük 2,051, koku kaybı 2,594 ve güç kaybı 2,243 olarak hesaplandı.

Sonuç: COVID-19 hastalığı birçok organ ve sistemi etkileyen bir hastalıktır. PCR test sonucuna göre başvuru semptomlarını karşılaştırılması hastalığın başlangıç aşamasında tanınmasına katkı sağlayacaktır. Çalışmamızda PCR pozitifliği ayırt edici yakınmaların ateş, iştahsızlık, öksürük, koku duyusu kaybı ve güç kaybı olduğu saptanmıştır.

Anahtar Kelimeler: COVID-19, Şikayetler, PCR Testi.

INTRODUCTION

Although the clinical profiles of COVID-19 patients have been investigated, there are still many features that are not fully disclosed. New symptoms are reported regarding COVID-19 cases. Studies should continue to understand and ease the burden of COVID-19. Information about the virus such as immunity duration, symptoms and clinical course, transmission rate, number of infected population, mutation probability changes with new reports. This prevents the creation of a clear road map about fighting with the virus and the disease, and prevents the results of epidemic management, vaccine and drug studies from being completely predictable. Thousands of people who are considered to be caught and recovered from COVID-19 continue to live with symptoms that make it difficult to return to their daily life and previous performance even after months. Some patients continue to present with atypical symptoms and clinical course (1).

COVID-19 can be asymptomatic in some cases, and in some cases may result in severe respiratory symptoms, extrapulmonary symptoms and even death (2). COVID-19 symptoms are nonspecific and disease presentation can range from asymptomatic to severe disease. Most people infected with the COVID-19 virus have mild illness and recover. Approximately 40% of the virus-infected COVID-19 cases are asymptomatic, approximately 80% of the symptomatic cases have mild symptoms that require outpatient treatment, up to 15% of the cases require hospitalization and 5% of the cases require intensive care due to respiratory failure (3).

The most frequently reported signs and symptoms at the onset of COVID-19 include intermittent or persistent fever (77-98%), cough (46-82%), myalgia or fatigue (11-52%) and shortness of breath (3-31%) (4-5). Other less reported symptoms are sore throat, headache, sputum, and cough. Some patients have been reported to experience gastrointestinal symptoms such as diarrhea and nausea before fever and lower respiratory tract signs and symptoms develop (6). In addition, ageusia (taste disorders) and anosmia (disturbances in the sense of smell) have been reported (7). In a retrospective observational study examining 214 COVID-19 positive cases, central nervous system findings were found in 53 (24.8%) of the cases (8).

In our study, we aimed to make a comprehensive symptom questioning to profile the complaints in patients presenting with the suspicion of COVID-19 at the disease onset. Thus, clinical symptoms that were not questioned before will be questioned and possible symptoms that may have been overlooked will be identified. In addition, it was aimed to determine the disease-specific and descriptive characteristics of the initial symptoms in those whose diagnosis was confirmed.

MATERIAL AND METHODS

The study is a descriptive study in a cross-sectional design. The data collection phase of the study was carried out between December 21, 2020 - January 22, 2021. Adult patients (18 years of age and over) who applied to the COVID-19 Outpatient Clinic of Çanakkale Onsekiz Mart University Hospital were invited for the study, and the study was conducted on those who gave their consent.

Patients who gave consent to the study were asked to fill in the demographic data form and the COVID-19 survey of symptoms created for the study. In order to reduce personal contact, forms were prepared as online forms and their links were sent to the mobile phones of those included in the study. The data forms were filled out by the participants in the polyclinic waiting rooms, and researchers were constantly present in the environment to answer the questions of the participants. The time required for a participant to fill out the form is between 5 and 10 minutes and is below the possible waiting time before outpatient clinic interviews.

The demographic data form includes questions about the patients' age, gender, marital status, educational status, occupation, employment status, and smoking and alcohol habits. Information regarding the COVID-19 disease processes of the patients was also questioned with this form.

The COVID-19 application complaints form was created by the researchers by scanning the literature on this subject. It includes 7 general, 6 respiratory, 5 ear-nose-throat, 4 gastrointestinal, 3 urological, 14 neurological and 4 other symptoms and their descriptive features, which are reported to be frequent, rare or atypically.

The applications are separated as first application and control applications, for those who do not have a complaint, the reason for application is recorded. Repeated applications were not included in the study. Patients were divided into positive (+) and negative (-) according to PCR test results and analyzed accordingly.

After the data obtained digitalized and corrected, descriptive information were presented with mean and standard deviation for ordinal variables and the frequency and percentage for categorical variables. Patients' application complaints were analyzed in terms of demographic characteristics and PCR test results with Chi squre and student’s t tests selected according to variable characteristics. Odd's rates were calculated for complaints that made a significant difference according to the PCR result. Test constants and absolute p values for all analyzes, 95% confidence interval (CI) limits for Odd's ratios were presented, $p < 0.05$ was accepted as the general significance limit.

RESULTS

The study consisted of data of 440 participants. 232 (52.7%) of the participants are male, 208 (47.3%) are female, their average age is 40.8 ± 15.4 (minimum 18, maximum 88). Ages are not significantly different between genders (t = 3.094; p = 0.210). 262 of the participants (59.6%) were married, 147 (33.4%) were single, 31 (7.0%) were widowed or divorced. 6 of the participants (1.4%) are illiterate, 2 (0.5%) are literate, 91 (20.7%) are primary school graduates, 35 (8.0%) are secondary school graduates, 97 (22.0%) were high school graduates, 209 (47.5%) were higher education graduates. Of the participants, 273 (62.0%) are currently working, 91 (20.7%) are housewives, not working actively like students, 60 (13.6%) are retired and 16 (3.6%) was unemployed.

Of the participants, 183 (41.6%) never smoked, 91 (20.7%) quit, and 166 (37.7%) were still smoking active. Those who quit smoking had used an average of 12.4 ± 11.6 cigarettes a day for an average of 14.5 ± 9.2 years and had stopped using it for an average of 11.3 ± 10.7 years. Those who were currently smoking were smoking an average of 12.2 ± 8.8 cigarettes per day for an average of 12.6 ± 10.0 years. PCR test result showed a significant difference according to smoking status (X^2 = 27.826 p <0.001). The Odd's rate for the positivity of the PCR test result compared to non-smokers was 0.274 (95% CI 0.156-0.481) in smokers.

214 of the participants (48.6) had never consumed alcohol, 189 (43.0%) were using alcohol in social settings, and 36 (8.2%) were using alcohol regularly. Of those who reported using alcohol regularly, 17 (47.2%) were drinking alcohol 1-3 times a month, 18 (50.0%) 1-4 times a week, and 1 (2.8%) every day. PCR test result did not show a significant difference according to alcohol use status (X^2 = 2.721 p = 0.257).

Of the participants, 273 (62.0%) were first application and 167 (38.0%) were control interviews. 26 of the first applications (9.5%) consisted of those who remained in isolation at home after contact. Of the control interviews, 96 (57.5%) were post-treatment controls, and 22 (12.7%) were post-isolation controls. 44 (16.5%) of the 266 first applications to which the PCR test was applied, 69 (44.8%) of the 154 control interviews were positive.

205 (75.1%) of the first applications, 96 (57.5%) of the control applications consisted of patients with various complaints. The distribution of the reasons for the application of those whose applications do not depend on their complaints is given in Table 1.

Table 1. Reasons of the Covid-19 Policlinic Admissions

	First admission	Control visits	Total
Symptomatic	205	96	301
After isolation/treatment	4	51	55
Patient contact	35	5	40
Requests for medical reasons	12	3	15
Official requests	7	6	13
Personal requests	6	3	9
Pre-employment	4	1	4
Before plasma donation	0	1	1
Before traveling abroad	0	1	1
Total	273	167	440

Among all applicants, there were 132 (31.4%) people who reported that they had no complaints, and their proportion was not significantly different between those who had PCR test results positive and negative (X^2 = 0.013 p = 0.908). When only the first admissions were evaluated, there were 65 (24.4%) asymptomatic people among 266 people who were tested, and the rate of asymptomatic patients was not significantly different between PCR positive and negative ones (X^2 = 2.076 p = 0.150).

When only the first applications were evaluated, the most common complaints in patients with positive PCR test were weakness (27, 73.0%), headache (24, 64.9%), pain (23, 32.2%), cough (21, 56%, 8), sore throat (19, 51.4%), and anorexia (17, 45.9%) (Figure 1).

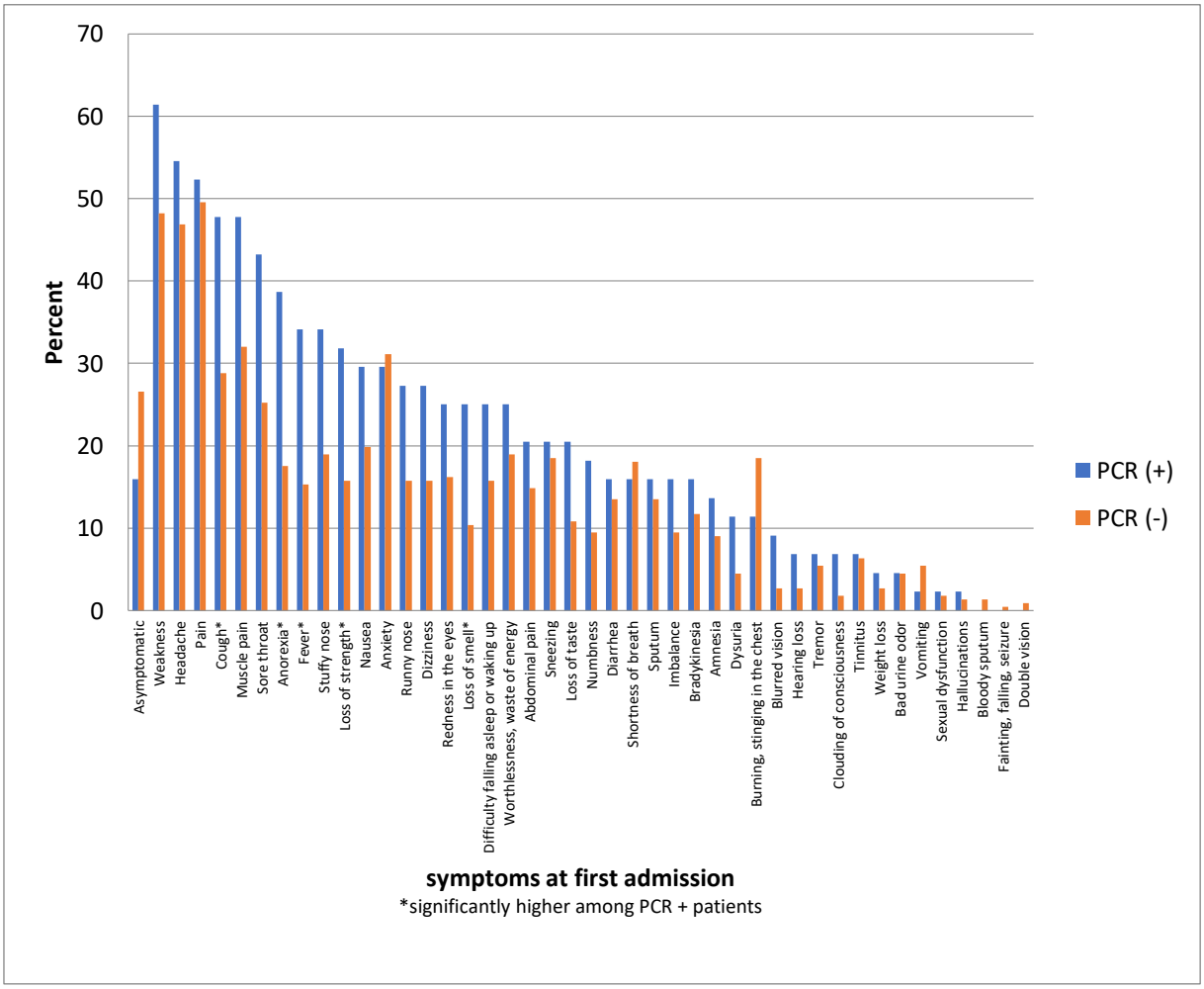

Figure 1. Incidence of symptoms at the first application

Complaints with a significant difference in the incidence between PCR test positive and negative ones were fever, anorexia, loss of sense of smell and loss of strength (Table 2). Odd's ratio for PCR positivity is 2.607 (95% CI 1.223-5.558) for fever complaints, 2.724 (95% CI 1.300-5.709) for complaints of anorexia, 2.051 (95% CI 0.996-4.222) for cough, and for loss of sense of smell. It was calculated as 2.594 (95% CI 1.129-5.956) and 2.243 (95% CI 1.047-4.808) for power loss.

DISCUSSION

COVID-19, which caused the largest known pandemic in the world, continues to be the most important topic of the world health agenda for about a year. Although it continues to be examined in all aspects, it cannot be said that the disease is adequately understood with all its features. Like similar acute respiratory diseases, COVID-19's application complaints are not distinctive. However, as information about the disease continues to be collected and examined, its unique characteristics will emerge and the recognition of the patients according to their application characteristics will increase. In our study, we aimed to reveal the characteristics of the applications made to the COVID-19 outpatient clinic in our hospital and the specificity of the application complaints to the disease. 273 of 440 patients included in the study within a month period consisted of the first applications and 44 positive cases were detected according to the PCR test results.

People with COVID-19 usually develop signs and symptoms such as mild respiratory symptoms and fever, on average 5-6 days after infection. Most cases that were asymptomatic at the time of diagnosis have continued to develop the disease. Indeed, the rate of asymptomatic infections is uncertain, but appears to be relatively rare (9). The most common symptoms reported so far in the literature are fever, cough, fatigue, and shortness of breath, similar to other viral infections, including seasonal flu (10). In the first application cases examined in our study, asymptomatic ones were seen at a rate of 24.9%, and the PCR test positivity was 15.9% in the patients who applied without complaint, but this does not reflect the asymptomatic rates in the disease because it does not reflect a community segment.

Table 2. Symptoms at the First Admission According to PCR Test Results

	PCR (+) (n=44)	PCR (-) (n=222)	Statistical analysis
Asymptomatic	7 (%15.9)	59 (%26.1)	X^2=2.076 p=0.150
Weakness	27 (%73.0)	107 (%65.2)	X^2=0.812 p=0.368
Pain	23 (%62.2)	110 (%67.1)	X^2=0.325 p=0.568
Headache	24 (%64.9)	104 (%63.4)	X^2=0.027 p=0.868
Anorexia	**17 (%45.9)**	**39 (%23.8)**	**X^2=7.380 p=0.007**
Fever	**15 (%40.5)**	**34 (%20.7)**	**X^2=6.426 p=0.011**
Nausea	13 (%35.1)	44 (%26.8)	X^2=1.025 p=0.311
Redness in the eyes	11 (%29.7)	36 (%22.0)	X^2=1.020 p=0.313
Abdominal pain	9 (%24.3)	33 (%20.1)	X^2=0.323 p=0.570
Diarrhea	7 (%18.9)	30 (%18.3)	X^2=0.008 p=0.929
Dysuria	5 (%13.5)	10 (%6.1)	X^2=2.404 p=0.121
Bad urine odor	2 (%5.4)	10 (%6.1)	X^2=0.026 p=0.872
Weight loss	2 (%5.4)	6 (%3.7)	X^2=0.241 p=0.623
Vomiting	1 (%2.7)	12 (%7.3)	X^2=1.063 p=0.303
Cough	**21 (%56.8)**	**64 (%39.0)**	**X^2=3.890 p=0.049**
Sore throat	19 (%51.4)	56 (%34.1)	X^2=3.820 p=0.051
Stuffy nose	15 (%40.5)	42 (%25.6)	X^2=3.313 p=0.069
Runny nose	12 (%32.4)	35 (%21.3)	X^2=2.073 p=0.150
Sneeze	9 (%24.3)	41 (%25.0)	X^2=0.007 p=0.932
Shortness of breath	7 (%18.9)	40 (%24.4)	X^2=0.504 p=0.478
Sputum	7 (%18.9)	30 (%18.3)	X^2=0.008 p=0.929
Burning. stinging in the chest	5 (%13.5)	41 (%25.0)	X^2=2.257 p=0.133
Bloody sputum	0 (%0.0)	3 (%1.8)	X^2=0.687 p=0.407
Muscle pain	21 (%56.8)	71 (%43.3)	X^2=2.205 p=0.138
Loss of strength	**14 (%37.8)**	**35 (%21.3)**	**X^2=4.456 p=0.035**
Dizziness	12 (%32.4)	35 (%21.3)	X^2=2.073 p=0.150
Difficulty falling asleep or waking up	11 (%29.7)	35 (%21.3)	X^2=1.204 p=0.273
Loss of smell	**11 (%29.7)**	**23 (%14.0)**	**X^2=5.298 p=0.021**
Loss of taste	9 (%24.3)	24 (%14.6)	X^2=2.066 p=0.151
Numbness	8 (%21.6)	21 (%12.8)	X^2=1.901 p=0.168
Imbalance	7 (%18.9)	21 (%12.8)	X^2=0.941 p=0.332
Bradykinesia	7 (%18.9)	26 (%15.9)	X^2=0.207 p=0.649
Tremor	3 (%8.1)	12 (%7.3)	X^2=0.027 p=0.869
Hearing loss	3 (%8.1)	6 (3.7)	X^2=1.397 p=0.237
Clouding of consciousness	3 (%8.1)	4 (%2.4)	X^2=2.886 p=0.089
Fainting. falling. seizure	0 (%0.0)	1 (%0.6)	X^2=0.227 p=0.634
Blurred vision	4 (%10.8)	6 (%3.7)	X^2=3.267 p=0.071
Double vision	0 (%0.0)	2 (%1.2)	X^2=0.456 p=0.500
Tinnitus	3 (%8.1)	14 (%8.5)	X^2=0.007 p=0.933
Sexual dysfunction	1 (%2.7)	4 (%2.4)	X^2=0.009 p=0.926
Amnesia	6 (%16.2)	20 (%12.2)	X^2=0.433 p=0.510
Anxiety	13 (%35.1)	69 (%42.1)	X^2=0.602 p=0.438
Worthlessness. waste of energy	11 (%29.7)	42 (%25.6)	X^2=0.264 p=0.607
Hallucinations	1 (%2.7)	3 (%1.8)	X^2=0.118 p=0.731

The symptoms observed during the admission of COVID-19 patients vary. While the most common complaints at presentation are fever and cough, there are fewer gastrointestinal symptoms. Symptoms such as nasal congestion, increased secretion, sputum, weakness, sore throat, hemoptysis, conjunctival hyperemia, nausea, vomiting, headache, abdominal pain, myalgia, diarrhea, rash, smell and taste disturbances may be observed in patients (11-12).

COVID-19 patients had fever (88%), dry cough (68%), fatigue (38%), sputum (33%),

shortness of breath (19%), sore throat (14%), headache (14%), myalgia or atypical symptoms like arthralgia (18%), tremors (11%), nausea or vomiting (5%), nasal congestion (5%), diarrhea (4%), hemoptysis (1%), and conjunctival congestion (1%) (13). While sore throat, fever, weakness, dry cough, nasal congestion, myalgia and headache are the most common symptoms in patients with mild clinical symptoms, dyspnea, fever, tachypnea, respiratory distress, hypoxemia, change of mental state, sepsis, multiorgan failure and death may occur (10). Headache and hemoptysis have been reported in relatively few patients (14).

In our study, the most common complaints in the first admission patients confirmed by the PCR test were fatigue, headache, pain, cough, sore throat, and anorexia, and were similar to those reported in other studies.

In COVID-19 disease, patients have upper respiratory tract infection signs and symptoms such as sore throat and rhinorrhea, as well as fatigue, fever, cough, dyspnea, myalgia (15). In one article, 44% of the patients developed headache, 41% fever, 39% myalgia, 38% cough symptoms. Patients experienced changes in smell and taste 4-5 days after the onset of the disease. Among the common symptoms, fever was the shortest (5.8 ± 8.6 days), taste and smell changes were the longest (17.2 ± 17.6 and 18.9 ± 19.7 days) (16). Anosmia and dysgeusia have also been reported in patients with COVID-19 infection.

In one study, 75% of the participants reported anosmia associated with loss or change in taste. In one confirmed case, anosmia was the only symptom (17). A cross-sectional survey study found that these symptoms are frequently reported in COVID-19 patients, and in most cases precede the onset of other symptoms (18). Odor and taste changes were observed at high rates, although not the most common symptoms in our series. It is among the complaints that show discrimination in COVID-19 patients whose loss of sense of smell is confirmed with an Odd's ratio of 2.594.

One large study, which received data from 1099 patients with laboratory-approved COVID-19 in China, showed that 44% of patients had a fever on admission, and 89% of patients developed a fever during their stay in the hospital. While the second most frequently reported symptom was cough (68%), fewer patients reported gastrointestinal symptoms such as nausea (5%) and diarrhea (4%) (11). Gastrointestinal symptoms were reported by 32% of patients, 89% defined their gastrointestinal complaints as mild. Loss of appetite (22%), nausea / vomiting (12%) and diarrhea (12%) were the most common gastrointestinal symptoms. None of the patients developed isolated gastrointestinal symptoms or gastrointestinal symptoms as the first sign of COVID-19 infection. It has shown estimates ranging from 5-50% in publications on gastrointestinal symptomatology in COVID-19 (19).

In our study, in which the presence of symptoms before the diagnostic investigation was questioned through a list, patients reported the presence of various gastrointestinal complaints at relatively low rates.

In a study involving 180 patients with positive PCR reports, 112 patients had one or more symptoms related to ENT along with widespread COVID-19 disease. While fever (95%), fatigue (93%), shortness of breath (90%), cough (83%) were the most prominent symptoms of the patients at the time of admission, the common ENT symptoms were loss of smell (54%), decreased sense of taste (51%), hearing loss (50%), sore throat (47%) and tinnitus (39%). (20) In our study group, ENT-related symptoms such as tinnitus and hearing loss were among the rarely reported complaints.

While myalgia is a common clinical feature of COVID-19, other musculoskeletal symptoms during the pandemic have rarely been described as early complaints. However, there are recent reports of COVID-19 infection and a number of neuromuscular and rheumatological complications related to the course of the disease, including myositis, neuropathy, arthropathy, and soft tissue abnormalities (21). In our study, although myalgia was among the most common complaints of 56.8% in COVID-19 patients, no specific distinction was observed for the disease. Power loss observed less frequently (37.8%) is a distinctive complaint with a Odd's ratio of 2.243 for PCR test positivity.

In a systematic review of 16 studies including a total of 575 patients, 43 patients reported lower urinary tract symptoms at the onset of the disease, and 7 patients had worsening of previous symptoms. Scrotal discomfort and swelling, pain and redness, low flow priapism, bladder bleeding, and acute urinary retention were the urological disorders (22). Urological complaints questioned in our study group were rarely reported among COVID-19 patients.

In our study, general pain was reported as a complaint by one third of the patients, but these complaints were not specific to the disease. Like most viral infections where pain is a very common symptom, COVID-19 patients commonly show headaches, sore throats, myalgia, arthralgia, or peripheral neuralgias, and pain is considered to be an important symptom (23). Recognizing that COVID-19 triggers chronic pain and exacerbates pre-existing chronic pain will be of great importance for a better understanding of the disease (24).

COVID-19 does not limit itself to just a simple lower respiratory tract infection, but can cause serious systemic disease and affect the nervous system (25). Studies in the literature have confirmed that patients with COVID-19 may have symptoms such as hearing loss, tinnitus, and

dizziness, although they are mostly mild (26). In our study, a wide set of neurological symptoms were questioned and they reported their presence at various rates for patients, but neurological symptoms seen at a higher rate in patients confirmed by PCR are limited to loss of sense of smell and muscle weakness.

There are many suspicious cases for COVID-19, and methods such as PCR tests or CT scans are used for diagnosis. However, these can be replaced by an easily accessible and cost-free general clinical diagnosis. An attempt is made to develop a rapid screening method with common clinical diagnosis results on suspicious patients. However, the differences in the diagnostic research characteristics of the patients make it difficult for these efforts to yield results (27).

It is necessary to establish a reliable method for COVID-19 patients to distinguish patients who may have critical symptoms from other patients. In a study where the diagnostic power of disease symptoms was evaluated, 11442 of 51726 COVID-19 suspect case reports had sufficient symptom data for analysis, and 16% of them were tested positive for COVID-19 (28). Among the test positive cases, cough (73%), fever (60%), myalgia (44%), headache (40%) and fatigue (38%) were the most frequently reported symptoms. While general symptoms such as fever, myalgia, arthralgia, headache and fatigue as well as gastrointestinal symptoms (diarrhea and nausea or vomiting) at the time of notification were positively associated with COVID-19, chest pain, shortness of breath and abdominal pain symptoms were not associated with a positive test result. Among the general symptoms (fever, cough, and shortness of breath), only fever (alone or with other symptoms) was strongly associated with a positive test for COVID-19, with an Odds ratio of 2.29 calculated. This rate was lower for cough, but not significant for shortness of breath. In the developed multivariate model, the presence of fever, myalgia, headache, fatigue or diarrhea was strongly associated with the result of the positive COVID-19 test result, the presence of cough or sore throat was found to be negatively correlated with diarrhea (28). In our study, presenting complaints were analyzed for the discriminatory characteristics for the disease, and fever, loss of appetite, cough, loss of sense of smell and loss of strength were found significant for PCR positivity.

Screening based on symptoms in travelers is considered defective or inadequate due to disease and patient characteristics (29). Symptom-based screening may not be an effective strategy for identifying people who should be tested for COVID-19 infection or detecting new cases of COVID-19 (30). However, as the disease is better known and the data increase, it will be possible to distinguish the disease through complaints at the initial stage.

CONCLUSION

COVID-19 disease is a disease that affects many organs and systems. Different rates are reported for application complaints in sources. Continuation of the studies evaluating the complaints at the time of application to compare the symptoms of patients according to PCR test will contribute to the recognition of the disease with initial complaints. In our study, the most common initial complaints in patients confirmed by the PCR test were listed as weakness, headache, pain, cough, sore throat, and anorexia, while PCR positivity was found to be fever, anorexia, cough, loss of sense of smell and loss of strength.

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RESEARCH ARTICLE

Eren Cam[1]
Mehmet Nurullah Kurutkan[2]
Ilknur Arslanoglu[3]
Okan Butuner[4]

[1]University of Duzce, Institute of Social Sciences, Total Quality Management, Duzce, Turkey
[2]University of Duzce Department of Health Management, Duzce, Turkey
[3]University of Duzce, Faculty of Medicine, Duzce, Turkey
[4]University of Duzce, Department of Insurance and Social Security, Duzce, Turkey

Corresponding Author:
Ilknur Arslanoglu
University of Duzce, Faculty of Medicine, Duzce, Turkey
Phone: +90 5425138858
mail: ilkilkars@yahoo.com

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konuralptipdergisi@gmail.com
www.konuralptipdergi.duzce.edu.tr

Cost of Inpatient Pediatric Type 1 Diabetes Care in Turkey: Single Center Experience

ABSTRACT

Objective: To explore the financial cost of type 1 diabetic (T1D) children and adolescents during inpatient management for various reasons.

Methods: Ten years of electronic hospital records (2009-2018) of the pediatric ward were screened retrospectively and hospitalizations with a confirmed diagnose of T1D were analyzed. Costs are grouped as laboratory tests, clinical interventions, drugs, medical supplies, and total costs before being converted to US dollars according to the mid-year index published by the Central Bank of Turkey. Descriptive statistics and comparisons against patient-specific characteristics are presented.

Results: There were 400 eligible cases. Cost per case for the hospital and for the Social Security Institution (SSI) were $268 and $309 respectively. The clinical intervention was the largest (49.84 vs 55.33 %) and that of medical supplies was the smallest (0.43 vs 0.55 %) component of the cost. Blood pH, HbA1c, having a single parent, and the number of days in the ward were parameters influencing total cost significantly ($p<0.1$).

Conclusions: With strict monitoring of social protection mechanisms for families with type I diabetic children with high social risks, cost increases stemming from social risks that can be reduced. Also, it is beneficial to closely monitor the medical risks affecting the pH and HbA1c levels. The study offers the first data about pediatric T1D hospital stays in Turkey which are expected to help to reasonable resource distribution and efficiency of care.

Keywords: Cost, Type 1 Diabetes, Pediatric, Inpatient, Turkey.

Türkiye'de Yatış Hizmeti Verilen Pediatrik Tip I Diyabetli Hastaların Maliyeti: Tek Merkezin Tecrübesi

ÖZET

Amaç: Tip 1 diyabetli (T1D) çocuk ve adolesanların değişik nedenlerle yatarak tedavisinin maliyetini ortaya koymak.

Gereç ve Yöntem: Hastanenin elektronik hasta kayıtları 10 yıl geriye kadar (2009-2018) tarandı ve T1D olduğu doğrulanan olgular irdelendi. Maliyetler laboratuvar testleri, klinik girişimler, ilaçlar, tıbbi malzeme ve total olarak gruplandı ve Merkez Bankası yıl ortası verilerine göre Amerikan dolarına çevrildi. Tanımlayıcı istatistikler ve hasta verileriyle karşılaştırmalar sunuldu.

Bulgular: Dörtyüz olgunun hastaneye ve Sosyal Güvenlik Kurumu'na ortalama maliyeti sırasıyla 268 ve 309 dolardı. En yüksek maliyet klinik girişim (% 49.84 ve 55.33), en düşük maliyet (% 0.43 ve 0.55) medikal malzemeyle ilgiliydi. Kan pH'sı, HbA1c, tek ebeveyni olmak ve hastanede yatış süresi maliyeti anlamlı olarak etkilemekteydi ($p<0.05$).

Sonuç: Sosyal riski yüksek olan ailelere yönelik sosyal koruma mekanizmalarının sıkı takip edilmesi ile sosyal risklerden kaynaklı maliyet artışları azaltılabilir. Ayrıca pH ve HbA1c düzeyini etkileyen medikal risklerin sıkı takip edilmesinde fayda vardır. Türkiye'de çocuk T1D inin yatarak tedavisi ile ilgili ilk yayın olması nedeniyle çalışmanın kaynak dağılımı ve bakım etkinliğine katkı sağlayacağını düşünmekteyiz.

Anahtar Kelimeler: Maliyet, Tip 1 Diyabet, Çocuk, Yatarak Tedavi, Türkiye.

INTRODUCTION

Type 1 diabetes (T1D) is a chronic disease related to permanent damage of pancreatic insulin-secreting cells and affecting mostly children and young adults. According to the National Diabetes Statistics reported by the Centre for Disease Control (CDC), T1D constitutes 5% of all diabetes cases (2). Epidemiological studies reveal an increase in T1D incidence especially among young children (3). The estimated increase rate of T1D incidence is around 3% (4,5). International Diabetes Federation (IDF) reports the overall number of T1D cases between 0-20 years of age as 1.106.500 with yearly 132.600 new cases (6). In the same reference, 25.669 recorded T1D cases in all age groups were reported about Turkey. But this number should be an underestimation since in a paper about all documented T1D cases even under the age of 18 years the number is above 17 000 (7). Some items are paid, partially paid, and not paid at all, according to the Health Practice communiqué on type 1 diabetes. Fully paid; It is insulins and needle tips. Partially paid items are strip, insulin pump and insulin pump set, and reservoir/patch. Non-paid items are the Glucometer, Lancet, continuous glucose measurement sensors, soothing and iPort (23).

The financial cost of diabetes care is a burden with respect to the patient and family as well as to institutions responsible for care and pay-back. In the USA 24.7 million people (approximately 7.6 % of the population and 9.7 % of adults) were diagnosed with diabetes in the year 2017. The corresponding overall cost of diabetes to the nation was 327 billion dollars, 237 billions of this (73 %) were explained by directly diabetes-related health expenses whereas the remaining 90 billion (27 %) were arising from issues like loss of working days because of diabetes, etc. (1).

Regarding this picture the importance of documenting the financial burden of T1D in every aspect is reasonable although there are not sufficient data about this issue in the literature. Especially data related to T1D, the pediatric age group, and Turkey are lacking. In the search records made on DergiPark, Google Scholar, WOS database, and the YOK thesis search site, no study was found on the cost of Type 1 diabetes-related disease of hospitalized patients. We conducted this study to compensate for the gap in this field.

MATERIAL AND METHODS

The present study relies on a retrospective review of hospitalized patients in the pediatric ward of Duzce University Teaching Hospital. Among the 783 patients whose clinical records and social risk assessment were made, those lacking the parameters given in Table 3 and Table 4 were not included in the analysis. Thus, people with missing records were not included in the cost study.

Ethics: The ethical approval for the study was obtained from Duzce University Faculty of Medicine Noninvasive Health Investigations Ethics Committee on 26 March 2018 (No: 2018/53). The application permission for the study was obtained from the Head Chief Physician. Also, permission was obtained from the patients included in the study to determine the social risk. Acted by Research and Publication Ethics.

Case Selection: At the first round hospitalizations with ICD 10 codes E10 were screened by an information technologist (IT) who is hospital staff and has access to the electronic hospital records. Ten years of electronic hospital records (2009-2018) were available. Afterward, the selected records were revised by the pediatric endocrinologist and compared with those cases files in the pediatric endocrinology departments archive. Cases without a confirmed diagnose of T1D or sufficient clinical parameters and that whit a hospitalization duration of fewer than 24 hours (i.e. hospitalized for an extensive yearly check-up) were eliminated.

Documenting of Costs: After determining the eligible hospital stays, another staff IT with access to financial documents collected data about each stay regarding the cost for the hospital and for the Social Security Institution (SSI) separately using SQL code. Costs were grouped into five categories: Laboratory tests, clinical interventions, drugs, medical supplies, and total cost. The cost data were calculated in TL. Results were then converted to US dollars according to the mid-year index published by the Central Bank of Turkey. The aim of the conversion was to facilitate international comparisons by one hand and to fix the finding against inflation effects in the country on the other hand.

Clinical Parameters: Hospitalizations were grouped in five categories according to their reasons: Newly diagnosed T1D, ketoacidosis during follow-up, revision of metabolic control, the institution of insulin pump therapy, and others. Age, sex, plasma glucose, HbA1c, venous pH, socioeconomic condition of the family, parental status (single or not) were personal parameters collected. Socioeconomic variables were collected during direct interviews with families by the same social worker who is part of the pediatric diabetes team. Although these data were available since the year of 2014, they were useful for all cases retrospectively since all cases were still on follow-up.

Statistics: Descriptive statistics and comparisons against patient-specific characteristics are presented. The values for skewness and kurtosis between -2 and +2 are considered acceptable in order to prove normal univariate distribution (19, 20). Since both the variables used in the different analyses and all the variables used in the linear

regression are between the above threshold values, the data are considered to be normally distributed. Analyses of differences between variables were made using a t-test, analyses of group differences using one way ANOVA, and those of factors directly influencing costs using linear regression. In the difference analysis, the arithmetic means, standard deviation, and confidence interval were given, and the evaluation was made.

RESULTS

Almost six out of every ten people (58.3%) are girls. The average age of the patients in the 0 to 19 age group is 11.16. The rate of single-parent people is 21.1%. The 10-14 age group (35.7%) is the most common. The family income of the children is generally low and very low. The reasons for hospitalization are mostly for metabolic regulation and diagnostic purposes (See Table 1).

Table 1. Patient characteristics (n: 400), Turkey, 2009–2018

Females n (%)	233 (58.3)
Age [years, mean (SD)]	10.45 (4.52)
HbA1c [%, mean (SD)]	11.16 (2.76)
pH mean (SD)*	7.27 (0.14)
Glucose at admission [mg/dl, mean (SD)]	342.89 (171.89)
Single parent n (%)**	59 (21.1)
Age groups in years n (%)	
• **0-4**	51(12.75)
• **5-9**	112 (28.00)
• **10-14**	143 (35.75)
• **15-19**	94 (23.50)
Socio-economic level n (%)***	
• **High**	4 (1.4)
• **Medium**	55 (19.6)
• **Low**	124 (44.1)
• **Very low**	98 (34.9)
Reason for hospitalization	
• **Diagnose**	104 (26)
• **Transition to pump**	46 (11.5)
• **Ketoacidosis**	93 (23.3)
• **Metabolic regulation**	147 (36.8)
• **Others**	10 (2.5)

*n: 279 **n: 294 ***n: 281

There were 400 children with T1D cases with a mean age of 10.54 (SD±4.52), 58.3 % of whom were girls. Mean HbA1c at or +/- 2 months prior/after hospitalization in cases already in follow-up was 11.16 (SD±2.76) %. This value is quite high in comparison to the concomitant median value of 8.59 % of the background population (i.e. all documentable cases in our center's follow-up in the year of 2018, n: 316).

Family with a single parent was observed in 20.1 % if the parental status is reported. The socio-economic level of the families was low in 44.1% and very low in 34.9% of cases. That means four out of every five families having children hospitalized for diabetes are facing difficulty in maintaining family needs essential for life! Regarding the reason for hospitalization, four out of ten hospitalizations were to improve metabolic control. Table 1 depicts case characteristics in more detail. Most of the parents (51.1 %) were graduated from gymnasium (60.7 % of mothers and 51.1 % of fathers) whereas higher grades (at least two years of university) were reported 18.7 % and 24 % in mothers and fathers respectively. The question of a number of people in the family was responded by 275 families which revealed a range of 1-11 regarding the number of children. The highest frequencies were observed in the groups of families with 2 and 3 children (40.4 and 32 % respectively).

The mean cost per person for the hospital was $268 and for the Social Security Institution (SSI) $309 between the years 2009-2018, but there was a fluctuation between years. There was a peak in the year of 2014 ($486) and a nadir in 2018 ($134) (Figure 1, Table 2).

Table 2. Costs with regard to the hospital and Social Security Institution (SSI) ($)

Year	PN	Hospital Costs						SSI Costs					
		LT	**I**	**Ph**	**MS**	**HTC**	**H-CPP**	**LT**	**I**	**Ph**	**MS**	**SSI-TC**	**SSI- CPP**
2009	3	477	289	64	0	830	277	477	404	98	0	978	326
2010	2	157	140	23	0	320	160	157	218	37	0	412	206
2011	6	413	433	98	2	946	158	413	657	153	2	1,225	204
2012	28	3.240	5.814	2.008	6	11.068	395	3.240	7.535	2205	6	12.986	464
2013	42	6.121	6.093	756	4	12.974	309	6.121	9.051	977	19	16.169	385
2014	59	10.336	12.422	1.210	99	24.067	408	10.373	16.658	1.450	208	28.688	486
2015	72	11.844	8.238	1.686	115	21.884	304	11.844	12.158	1.900	161	26.064	362
2016	81	7.185	7.887	1.451	107	16.630	205	7.154	9.460	1.591	138	18.342	226
2017	80	4.068	9.898	998	122	15.086	189	4.072	9.977	1.051	135	15.236	190
2018	27	1.166	2.303	104	10	3.582	133	1.166	2.329	111	10	3.616	134
General Sum		45.006	5.3518	8.398	464	107.386		45.017	68.446	9.573	679	123.715	

PN: Patient Number; LT:Laboratory Tests, I:Intervention; Ph:Pharmaceuticals; MS:Medical Supplies; HTC: Hospital Total Cost; H-CPP:Cost Per Person for the Hospital; SSI-TC: SSI Total Cost; SSI- CPP: Cost Per Person for SSI

From the hospital's point of view $134 (49.84 % of the cost) was that of intervention whereas laboratory tests ($113) made up the 41.91 % and pharmaceuticals ($21) 7.82 %. The lowest component of the cost was the item of medical supplies (1$) with a percentage of 0.43. On the other hand, the pay-back system (SSI in our case) paid 55.33 % for intervention and 36.39 percent for laboratory tests. Again, the portion of medical supplies was the smallest (0.55 %). Interventions, for which the SSI paid $171 made up the most important source of the hospital's profit. When we looked at the SSI costs closer, there were statistical differences between groups of sex, age, cause of hospitalization, and diabetes duration. There was a significantly higher cost of being male, 0-4 years old, and have attended for the first diagnosis. In addition, the first five years with diabetes have a relatively higher cost (according to 15-19 years group). We did not find any differences in the total cost regarding socioeconomic differences. (Table 3)

Figure 1. Distribution of mean annual cost of inpatient pediatric T1D management in Turkey between years 2009–2018

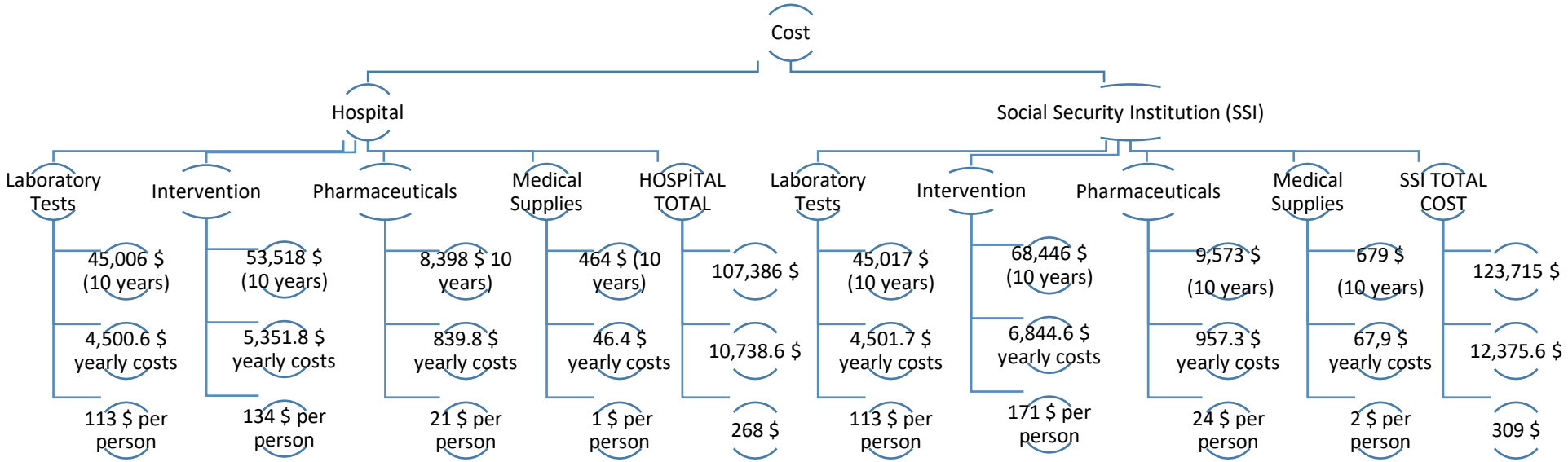

Table 3. Direct costs of type 1 diabetes by patient characteristics with regard to the Social Security Institution (Turkey 2009–2018)

	Mean (95% CI) (US$)	***P*-value**
Sex		0.018
• **Female**	278.33 (251.92- 304.74)	
• **Male**	352.47 (289.36-415.57)	
Age (Years)		**0.032**
• **0–4**	407.17 (262.53-551.80)	
• **5–9**	336.51 (265.41-407.60)	
• **10–14**	272.05 (238.64-305.45)	
• **15–19**	280.38 (245.50-315.26)	
Socio-economic level		0.463
• **High**	243.89 (-86.65-574.43)	
• **Medium**	347.62 (220.21-475.04)	
• **Low**	276.84 (240.44-313.24)	
• **Very low**	305.79 (260.42-351.16)	
Reason for hospitalization		**0.041**
• **Diagnose**	363.63 (292.84-434.41)	
• **Transition to pump**	224.14 (160.45-287.83)	
• **Ketoacidosis**	347.59 (265.63-429.55)	
• **Metabolic regulation**	274.78 (238.74-310.81)	
• **Others**	286.75 (182.43-391.08)	
Diabetes duration		**0.000**
• **<5**	312.44 (265.57-359.32)	
• **≥ 5-<10**	304.86 (272.07-337.65)	
• **≥ 10-<15**	238.22 (185.69-290.74)	
• **≥ 15**	1064.76 (-1518.14-3647.66)	

Regression is the study of the relationships between variables. Regression is a statistical method that investigates the possibility of estimating the value of parameters that establish a relationship between dependent and independent variables (21). The assumptions of the multiple linear regression model are as follows (22): Normal distribution, no autocorrelation, and no or little multicollinearity between independent variables. Linear regression analyses were made regarding both hospital and SSI costs. Total cost, which was the dependent variable was significantly influenced by the independent variables of HbA1c, and number of days in intensive care unit. Independent variables such as gender, age, first blood glucose, number of family members, a distance of residence from the hospital in kilometers, being in the emergency department for the first night of the hospital stay, number of days in intensive care unit and number of repeated hospitalizations in the same center were not found to significantly influence the total cost. These two models explained the variance in costs as 58,8% (hospital costs) and 56,2% (SSI costs) respectively. (Table 4). According to the results of autocorrelation and collinearity analysis, the results of the model can be trusted.

DISCUSSION

There are few studies focusing on T1D, especially in children. In Turkey, even any cost data about diabetes, in general, are very scarce. For example, none of 182 theses on the website of the Turkish Council of Higher Education about T1D were related to costs, as well as none of those among several papers in the database Dergipark, which comprises of periodicals in the Turkish language were related to inpatient pediatric diabetes cost (8, 9). The unique one we could find was about 211 diabetic cases, 36 from which were T1D (10). The present study is not just about the cost analysis of 400 T1D cases, moreover, it deals with a better-defined series, i.e. hospitalized T1D children and adolescents.

Turkey's National Diabetes Program (2015-2020) reports a lack of studies about T1D incidence in Turkey (11). On the other hand, there are two studies about T1D incidence under the age of 18 years in Turkey which reveal similar findings, i.e. 18 190 and 17 175 total cases and incidence around 10/100000/year (6,7). But as mentioned above data about costs of diabetes management are lacking.

According to the study of Keskek et al (10), which is about hospital stays of T1D and T2D diabetic people 54.6±16.6 years of age, the average cost of treatment was calculated as $607.4 (sum of costs of services, drugs, and equipment) which is higher than that in our study ($309). Because costs of Type I and Type II diabetes are given in total we could not compare. In this study, the cost of Type I diabetes is not given directly.

Several existing studies are reporting diabetes costs without separating T1D and T2D.

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Table 4. Parameters affecting total cost

	With regard to the hospital				With regard to the Social Security Institution			
Variable	**Coefficient**	**Std. Error**	**t-Statistic**	**Prob.**	**Coefficient**	**Std. Error**	**t-Statistic**	**Prob.**
Sex	96.99808	88.08192	1.101226	0.2765	101.8504	89.89695	1.132968	0.2631
Age	-5.495098	11.02143	-0.498583	0.6204	-5.78813	11.24854	-0.514567	0.6093
PH	-48.07541	42.17129	-1.140003	0.2602	-38.5965	43.04027	-0.896754	0.3745
Glucose	38.5355	20.40018	1.888979	0.0652	35.10055	20.82055	1.685861	0.0986
HbA1c	290.1316	108.1001	2.683915	0.0101	291.1615	110.3276	2.639062	0.0113
Single parent	-76.43895	43.62546	-1.752164	0.0864	-81.7807	44.52442	-1.836762	0.0727
Number of persons in the family	-1.434815	0.897441	-1.598784	0.1167	-1.73182	0.915934	-1.890769	0.065
Distance to the hospital (km)	-16.5861	105.7421	-0.156854	0.876	-2.16787	107.921	-0.020088	0.9841
To have the first care in emergency	-170.0193	233.9485	-0.726738	0.4711	-167.193	238.7693	-0.700229	0.4873
Number of days in intensive care unit	76.17033	12.22818	6.229081	0.000	73.66704	12.48016	5.902733	0.000
Number of days in the ward	160.8325	114.6908	1.402313	0.1675	200.7163	117.0542	1.71473	0.0931
R-squared	0.588626	Adjusted R-squared	0.499196		R-squared	0.562596	Adjusted R-squared	0.467508
	Heteroskedasticity Test: Breusch-Pagan-Godfrey				Heteroskedasticity Test: Breusch-Pagan-Godfrey			
F-statistic	1.343193	Prob. F(10.46)		0.237	F-statistic	1.222966	Prob. F(10.46)	0.3021
	Breusch-Godfrey Serial Correlation LM Test:				Breusch-Godfrey Serial Correlation LM Test:			
F-statistic	1.343193	Prob. F(10.46)		0.237	F-statistic	0.543699	Prob. F(2.44)	0.5844

The cost of T1D/person is variating from country to country. African countries Tanzania (1992-$287), Sudan (1995-$283), Somali ($357), and Burkina Faso ($185) represent the lowest (12) whereas USA and European countries the highest extremes in the spectrum (13). This might have various explanations. One of them appears to be the opportunity of the private services to determine the fees of health services in developed countries with a functioning free-market economy. The costs for this study ($ 268 and $ 309) are similar to those in countries such as Sudan, Somalia, Burkina Faso, and Tanzania. It can be said that the reason is that the prices determined in the Health Application Communiqué are set very low.

Diabetes cost/person was reported as $4,730 in a study from Texas-USA and in another one from England £3,224 (14,15). A study from the USA about newly diagnosed pediatric T1D cases reported the yearly total cost of diabetes as $12,332 if hospitalized initially and $5,053 if not, while pediatric endocrinology care cost $4,080 and $3,904 for the same groups respectively (16). Gray and Fenn (17) stated that the cost per capita in the US was $2,042. In this study, the cost per person was determined as $ 269 for the hospital and $ 309 for the social security institution. Tariffs used in health services in Turkey do not show the actual costs.

Therefore, when compared with other countries, the costs found are lower than in other countries.There is a specific situation in Turkey about health service costs. The costs announced in the Health Application Communiqué (HAC), which is the main determinant of officially covered health costs in Turkey remained stable for 11 years whereas US dollars gained considerable value against Turkish Lira during this period. This explains the relatively lower cost of health expenses in the country. Therefore the costs determined in the present study don't reflect the real market prices. The financial gap is compensated partly by the patient's own budget and partly by the hospital's income. In addition, the corresponding prices when supplied by private hospitals are many times more. The same condition explains the yearly decrease in the cost of dollars in our study. Despite the decrease of the expenses based on dollars, real expenses based on Turkish Lira are increasing to some extent due to the increase in patient numbers.

The financial burden of diabetes is expected to increase due to an increase in its prevalence. Development of more sophisticated and expensive therapeutic strategies might increase the cost per person on one hand, but in the long run, they might have an opposite effect, i.e. a decrease in the global cost for the society due to decreased complications and days out of work.

Limitations: This study is about inpatient pediatric T1D costs in a public health center. Thus the situation in private care or that during outpatient management, expenses of daily insulin as well as monitoring, the cost of adult T1D cases, medical supplies which are not covered by the insurance and the remaining indirect costs of T1D, namely transportation, working day losses, etc. are lacking. Moreover, the same items in our study should be

checked on a more extensive basis, for example in multicenter studies in different regions with different facilities.

CONCLUSION

Despite its limitations, this study offers the first data about pediatric diabetes care in Turkey. The parties concerned should be motivated to perform studies designed to highlight all the above-mentioned aspects of diabetes cost and how to structure diabetes care to be the most cost-effective and successful in reaching metabolic targets. Governments have to develop strategies such as social interactions aiming for psychosocial support and education to prevent complications and minimize medical interventions. Empowerment of primary care or empowerment of tertiary care via satellite social facilities & staff are realistic strategies as well. Studies are depicting the positive effect of structured diabetes management models as well (18)

In future studies, it would be beneficial to study according to other cost perspectives (patient, social, and lifetime cost perspectives). Also, the costs of outpatient clinic patients should be calculated. Finally, a cost study should be conducted for out-of-pocket health expenditures that are not covered by the social security institution and made by families. Besides, cost studies should be done multi-center. For the centers that are successful according to the multi-center cost results, a reward system should be developed in the reimbursement system.

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RESEARCH ARTICLE

Fatma Ciftci Kirac[1]
Seda Uyar[2]
Ramazan Kirac[3]
Sait Soyler[4]

[1] Selcuk University, Faculty of Health Sciences, Health Care Management, Konya, Turkey
[2] Selcuk University, Institute of Health Sciences, Konya, Turkey
[3] Kahramanmaras Sütçü İmam University, Faculty of Economics and Administrative Sciences, Kahramanmaras, Turkey
[4] Tarsus University, Health Services Vocational School, Mersin, Turkey

Corresponding Author:
Seda Uyar
Selçuk University, Institute of Health Sciences, Konya, Turkey
mail: seda_inan@outlook.com

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www.konuralptipdergi.duzce.edu.tr

Patient Satisfaction with Family Medicine System: A Cross-Sectional Study

ABSTRACT

Objective: Family medicine, which has an important place in the provision of health services, provides a more equitable service delivery in health, and also ensures that health expenditures are more cost-effective. In this study, it was aimed to determine the satisfaction levels with family medicine servicesof individuals who have received service from family physicians in the central districts of Turkey/Kahramanmaraş during the last year and to examine them in terms of various variables.

Methods: This is an observational study. It is also cross-sectional and descriptive. Accordingly, the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement was used in the reporting of the study. The "Family Medicine SatisfactionQuestionnaire" was used in the study. The validity and reliability of the questionnaire were carried out within the scope of the study. Before the factor analysis, Kaiser-Meyer Olkin (KMO) and Bartlett tests were conducted to examine the suitability of the data and the sample to the principal component analysis. Values of the exploratory and confirmatory factor analyzes of the study were included in the findings section.

Results: While the general satisfaction score of the participants was above the average, it was below the average in terms of family medicine physical equipment and communication sub-dimensions. On the other hand, the dimension in which the satisfaction levels of the participants were the highest was the behavior of family physician dimension. The satisfaction level regarding the benefits of the family medicine system was also above average. No significant difference was found in the general satisfaction status of the participants by gender and whether they have a chronic illness. A significant difference was determined in the satisfaction level of the participants according to the age groups, marital status, educational status, income level, number of children owned.

Conclusions: As a result of the study, it was determined that satisfaction with family medicine is generally high. In order to increase the quality of the family medicine system, which is one of the most important elements of primary health care services, patient satisfaction should be continuously evaluated and improvements should be made by detecting the disruptions in service. It is clear that the improvements to be provided in the service delivery processes will increase the satisfaction of the patients.

Keywords: Family Medicine, Satisfaction, Health Service.

Aile Hekimliği Sisteminde Hasta Memnuniyeti: Kesitsel Bir Araştırma

ÖZET

Amaç: Sağlık hizmetleri sunumunda önemli bir yeri olan aile hekimliği, sağlıkta daha eşitlikçi bir hizmet sunumu sağlamakla birlikte sağlık harcamalarının daha maliyet etkin olmasına da hizmet etmektedir. Çalışmada Türkiye/Kahramanmaraş merkez ilçelerinde son bir yılda aile hekiminden hizmet almış olan bireylerin aile hekimliği hizmetlerinden memnuniyet düzeyinin tespit edilmesi ve çeşitli değişkenler açısından incelenmesi amaçlanmıştır.

Gereç ve Yöntem: Bu araştırma gözlemsel bir araştırmadır. Aynı zamanda kesitsel ve tanımlayıcı olma özelliği de göstermektedir. Bu doğrultuda araştırmanın raporlanmasında STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) bildirimi kullanılmıştır. Çalışmada "Aile Hekimliği Memnuniyeti" anketi kullanılmıştır. Anketin geçerlilik ve güvenilirlik çalışmaları araştırma kapsamında gerçekleştirilmiştir. Faktör analizi öncesinde, verilerin ve örneklemin temel bileşenler analizine uygunluğunun incelenmesi amacıyla yapılan Kaiser-Meyer Olkin (KMO) ve Barlett testleri yapılmıştır. Araştırmaya ait açımlayıcı ve doğrulayıcı faktör analizlerine ait değerler bulgular kısmında yer verilmiştir.

Bulgular: Katılımcıların genel memnuniyet puanı ortalamanın üzerindeyken, aile hekimliği fiziki donanım ve aile hekimi iletişim alt boyutları açısından ortalamanın altındadır. Öte yandan katılımcıların memnuniyet düzeylerinin en yüksek olduğu boyut aile hekimi davranış alt boyutudur. Aile hekimliği sisteminin faydasına ilişkin memnuniyet boyutu da ortalamanın üzerindedir. Katılımcıların cinsiyetlerine ve kronik bir hastalıklarının olup olmamasına göre genel memnuniyet durumlarında anlamlı bir farklılık tespit edilmemiştir. Katılımcıların yaş grupları, medeni durumu, öğrenim durumu, gelir durumu ve sahip olunan çocuk sayısı ile memnuniyet düzeyi arasında anlamlı farklılık tespit edilmiştir.

Sonuç: Araştırma sonucunda aile hekimliğinden memnuniyetin genel olarak yüksek olduğu tespit edilmiştir. Birinci basamak sağlık hizmetlerinin en önemli unsurlarından biri olan aile hekimliği sisteminin kalitesinin artırılabilmesi için hasta memnuniyetinin sürekli olarak değerlendirilmesi ve hizmette aksayan yerlerin tespit edilerek iyileştirilmeler gerçekleştirilmesi gerekmektedir. Hizmet sunum süreçlerinde sağlanacak iyileştirmelerin hastaların memnuniyetlerini de artıracağı açıktır.

Anahtar Kelimeler: Aile Hekimliği, Memnuniyet, Sağlık Hizmeti.

INTRODUCTION

The need for family physicians came to the fore at the beginning of the twentieth century with the emergence of the necessity to provide a holistic, comprehensive and personal health service to patients as a result of excessive specialization in the field of health and medical science. The recognition of family medicine as a separate specialty in the world was first realized in England in the 1960s (1). Although there are not many definitions of family medicine in the literature, the most widely accepted one is the European Definition of Family Medicine / General Practice, published in various languages by WONCA (2002)(2). Accordingly, family medicine is the entry point of the health system and is the first medical contact point of people who want to receive health services. Health services are provided to those who want to receive service from family medicine without any discrimination. Family physicians ensure the effective use of health resources by providing primary health care services to individuals and coordinating the necessary health services. Thanks to family medicine, continuity of health services is ensured and both acute and chronic health problems can be managed. In its simplest definition, family medicine can be defined as a branch of medical science that provides a personal, primary, continuous and comprehensive health service to individuals and families (3).

Family medicine speciality was accepted as a distinct field in 1983 in Turkey and the first Department of Family Medicine was established within Gazi University Faculty of Medicine in 1984 (5).

The system, which is also included in the emergency action plan of the 58th Government, which aims a major transformation in the field of health, entered into force in 2004 with the “Law on the Pilot Implementation of Family Medicine”within the framework of the "Health Transformation Program". The system, which was previously introduced as a pilot scheme, started to be implemented throughout the country in 2010 (7).

When the family medicine system is used effectively, misdirections that may cause loss of time for both individuals and service providers, irregularities in the health system and unnecessary health expenses can be prevented. Therefore, it will be possible to prevent waste and eliminate the overcrowding and aggrievement of patients in institutions that provide secondary and tertiary health services. It is stated that most of the health problems can be solved in primary care, therefore unnecessary applications to secondary and tertiary health institutions are not economical and the possibility of unnecessary medical procedures is high due to excessive specialization in these areas. However, especially in the follow-up of chronic diseases, insufficient time in secondary care and inadequate counseling resulting from this cause repetitive interviews (7,51,52). While repetitive interviews cause financial and moral losses for the patients, it can lead to increase the waiting times of the individuals who really need to receive service and shorten the examination periods due to the overcrowding in secondary and tertiary health institutions. Furthermore, problems related to excessive workload may arise in healthcare professionals, especially in physicians.

Primary health care services are one of the services that are included in a health system and should be organized in the best way due to its various features. Well-organized primary healthcare services enable individuals to receive fast, continuous and comprehensive health services, solve many health problems before they arise within the framework of preventive healthcare services, and serve the function of “gate keper” by preventing unnecessary crowds and resulting costs to institutions that provide secondary and tertiary health services (9,10). Family physicians are also the most important factors in conducting primary health care services in terms of the training they receive and the quality of the health services they provide. In this sense, individuals' satisfaction with family physicians and their trust in them will enable them to choose primary health care services first when they need health services, and at the same time support them to act in accordance with the physician's instructions and care plan (11,12). This will contribute to the increase of the health level of the society (8,13).

Individuals' perceptions and evaluations about health services are important not only for measuring health service quality, but also for correcting and improving the disruptions or deficiencies in service delivery processes (14). In this sense, it is important to investigate the satisfaction levels of patients and the factors affecting them regarding health care processes in terms of improving the services and increasing the quality. Therefore, the main purpose of this study was to determine the satisfaction level with family medicine services of individuals who have received service from family medicine in the central districts of Kahramanmaraş duringlast year and to examine them in terms of various variables.

MATERIAL AND METHODS

This is an observational study. It is also cross-sectional and descriptive. Accordingly, the STROBE statement was used in the reporting of the study (15). The data of the study were collected by questionnaire method. The questionnaire consists of two parts. A general information form was used in the first part, and the "Family Medicine Satisfaction Questionnaire" was used in the second part. The general information form includes questions about the participants' gender, age, marital status, the place to apply first when needed, income level, education level, number of children, and whether they have a permanent / chronic illness. The questionnaire used in the second part was taken from Yalman's (2013)

study (16). The questionnaire initially consisted of 22 questions. It is a Likert type questionnaire scored between 1- strongly disagree and 5-strongly agree. The validity and reliability studies of the questionnaire were carried out within the scope of the study. Before the factor analysis, Kaiser-Meyer Olkin (KMO) and Bartlett tests were conducted to examine the suitability of the data and the sample to the principal component analysis. It was seen that KMO coefficient was 0.918 and Barlett test was significant ($p < 0.001$). The fact that the KMO coefficient was above 0.60 and the Barlett test was significant ($p < 0.001$) indicatedthe factorability and suitability of the data set for principal component analysis, and that the sample size ($n = 1039$) was sufficient (17,18). The resultsof the exploratory and confirmatory factor analyzes of the study were included in the findings section. As a result of the analysis, the questionnaire consisted of 16 questions and 4 sub-dimensions.

The population of the study consists of adults (18 years and over) residing in the city center of Kahramanmaraş. According to the data of Kahramanmaraş Provincial Directorate of Culture and Tourism, the total population of Kahramanmaraş central districts is 632 thousand 487 (19). In this context, it was calculated that it would be sufficient to include 384 people at 95% confidence level and 665 people at 99% confidence level. In the study, the questionnaire form was created through online platforms, and the participants were included in the study using convenience and purposivesampling methods. The criteria for inclusion in the study were being an adult, being literate, and having received service from family medicine in the last year. The data of the study were collected between 01/11/2020 and 01/12/2020. 1039 people whose questionnaires were answered completely were included in the study. The data of the studywas analyzed using the SPSS 21 Package program. The data was first summarized with descriptive statistics such as frequency, percentage, mean, and standard deviation, and then subjected to normal distribution analysis. In the normality test, Kolmogorov-Smirnov test was used, and as a result of the analysis, it was determined that the data was distributed normally. In this context, independent samples t test and one-way analysis of variance (ANOVA) tests were used Statistical significance value was set atp <0.05.

Ethics committee approval was obtained with the decision of Kahramanmaraş Sütçü İmam University Social and Human Sciences Ethics Committee, dated 19/10/2020 and numbered 2020/29.

The main questions of the study are as follows;

1-What is the satisfaction level of individuals who benefit from family medicine services?

2-Do the satisfaction levels of individuals who benefit fromfamily medicine services differ according to socio-demographic factors?

RESULTS

Of those included in the study, 52.4% were male, 64.6% were single and 62.1% were between the ages of 18-29. 69% of the participants were university graduates, 67.2% had no children, 57.8% had middle income, 87% did not have a permanent disease, and when 44.9% got sick, the first place they apply was a state hospital.

As seen in Table 1, there are 4 factors with an eigenvalue above 1. Values after rotation show that the scale has 4 factors. The total variance explained by the four factors together is 53.846%.

Table 1. Exploratory factor analysis total variance explained

Component	Initial Eigenvalues			Values before rotation			Values after rotation		
	Total	Variance %	Cumulative %	Total	Variance %	Cumulative %	Total	Variance %	Cumulative %
1	6.643	30.198	30.198	6.643	30.198	30.198	3.642	16.557	16.557
2	2.310	10.501	40.699	2.310	10.501	40.699	3.162	14.374	30.931
3	1.630	7.410	48.109	1.630	7.410	48.109	2.601	11.822	42.753
4	1.262	5.737	53.846	1.262	5.737	53.846	2.441	11.093	53.846

In Table 2, the factors under which the items are located, the variance explained by each factor and the factor load values of the items are given. The criterion was accepted for the item to be considered as qualified if the item factor load value was above 0.40 and not included in more than one factor with a load value above 0.40 (29). Accordingly, the 8th item, 10th item and 16th item were removed.

Table 2. Exploratory Factor Analysis Varimax Post-Rotation Values.

	Component			
	1	2	3	4
1. I am satisfied with the attitude and behavior of my family physician.	.788			
2.I can ask any question about my illness to my family physician.	.795			
3.I can easily reach my family physician whenever I want.	.718			
4.Necessary medical equipment is sufficient for patients in the FHC.				.728
5. I can get satisfactory answers to the questions I ask my family physician about my illness.	.624			
6. The physical capacity of FHC is sufficient for patients				.756
7.All necessary tests can be performed for patients in FHC.				.754
8. I can access health services more easily with the family medicine practice *	.469	.410		
9. Family medicine is apractice that will increase the quality of healthcare services.		.533		
10. I think family medicine practice reflects positively on patient health *	.486	.520		
11. I feel that the health of myself and my relatives is under control with the family medicine practice.		.482		
12. I think the density in hospital polyclinics has decreased with the family medicine practice.		.785		
13. I think family medicine practice allows more time for patients in hospital polyclinics.		.770		
14. I think everyone has the opportunity to benefit from the health system more easily and quickly in family medicine.		.690		
15. I first contact with my family physician for all my health problems.				.512
16. Family medicine allocates sufficient time to patients. *	.446	.308	.369	
17. Family medicine treats its patients as customers that should not be lost.			.689	
18. The fact that the family physician receives additional fees from each patient he cares for, affects the service quality positively.			.679	
19. Before the family medicine system, I was afraid of doctors.			.566	
20. After the family medicine system, I can establish a dialogue with my physician more easily.			.629	
21. The family medicine system has prevented physicians from being rude.			.680	
22. Family medicine generally gives the right directions.	.552			

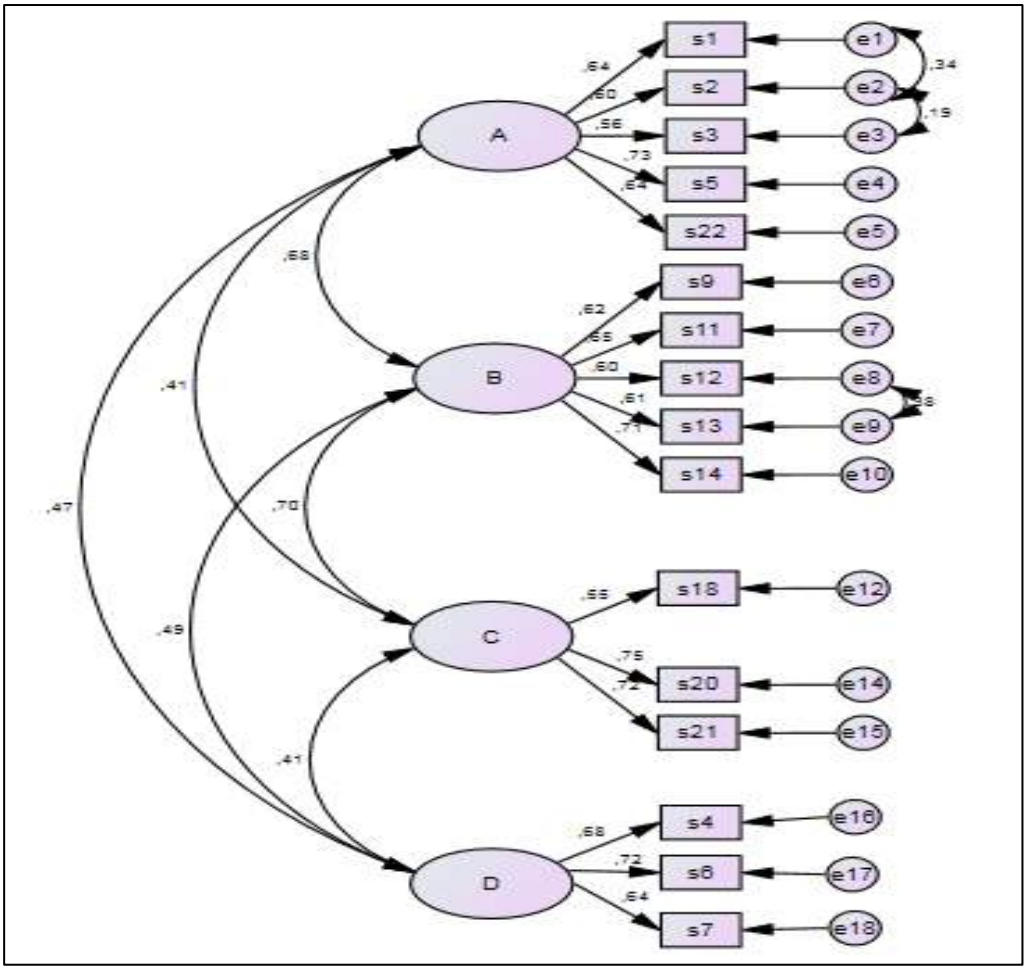

Figure 1. Confirmatory Factor Analysis Diagram(A=Family physician behavior sub-dimension, B = Family medicine system benefit sub-dimension, C = Communication sub-dimension D = Family medicine physical equipment sub-dimension)

As can be seen in Figure 1, confirmatory factor analysis was performed and standardized estimate values were given. As a result of the analysis, 3 items (2, 17, 19) with Estimate values below 0.5 were excluded. Covariance was made between 1st item, 2nd item, 3rd item, 8th item and 9th item in order to improve goodness of fitvalues. The goodness of fit values obtained were given in Table 3.

As can be seen in Table 3, the goodness of fit values of the confirmatory factor analysis are given. The goodness of fit values of the model resulting from the Path diagram are in the range of good fit and acceptable values (21,22,23,24).

Table 3. Goodness of Fit Values Used in DFA*

Index Values	Normal Value	Acceptable Value	Model Values
x2/sd	<2	<5	390.420/95= 4.110
GFI	>0.95	>0.90	0.955
AGFI	>0.95	>0.90	0.936
CFI	>0.95	>0.90	0.943
RMSEA	<0.05	<0.08	0.055
RMR	<0.05	<0.08	0.059
NFI	>0.95	>0.90	0.927

*Doğrulayıcı Faktör Analizi

Descriptive statistics for the sub-dimensions of satisfaction with family medicine are given in the Table 4. The highest mean scorebelongs to the behavior of family physician (3.37). The lowest mean scorebelongs to the physical equipment of family medicine (2.78). The general satisfaction average is 3.09. This average indicates that the participants are generally satisfied with the family medicine system.

Table 4. Descriptive Findings of Family Medicine Satisfaction Sub-Dimensions

	N	Min.	Max	Avg	Sd
Behavior of Family Physician	1039	1	5	3.37	0.82
Physical Equipment of Family Medicine	1039	1	5	2.78	0.84
Communication with Family Physician	1039	1	5	2.89	0.93
Benefit ofFamily Medicine System	1039	1	5	3.13	0.85
General satisfaction	1039	1	5	3.09	0.63

As seen in Table 5, t-test analysis was performed in independent groups. As a result of the analysis, no significant difference was found in terms of the means of family medicine sub-dimensions by gender (p> 0.05). By marital status, a difference was found from the family medicine sub-dimensions only in the means offamily medicine system benefit(p <0.05).Single participantsstated that the system is more beneficial.

One-way analysis of variance was conducted to determine the differences between the means of family physician satisfaction sub-dimensions by age and educational status of the participants. The sub-dimension of family physician behavior showed a significant difference by age (p <0.05). The means of individuals aged 50 and over were higher. There was no significant difference in the means offamily medicine physical equipment sub-dimension by age (p> 0.05).

A significant difference was found between the means ofcommunication with family physician sub-dimension by age groups (p <0.05).The communication with the family physicianaveragesof those aged 18-29 were higher than those in the 40-49 age range. There was a significant difference between themeans of the family medicine system benefitsub-dimension by age groups (p <0.05). The score of the system benefitwas found to be higher in the 18-29 age range than the others. By age groups, a difference was found between the means of family medicine general satisfaction (p <0.05), and the general satisfaction level of individuals aged 50 and over was higher.

There was no significant difference in terms of family physician behavior and communication sub-dimensions by the education level of the participants (p> 0.05)and also between the means offamily medicine general satisfaction (p> 0.05). A significant difference was found in the family medicine physical equipment sub-dimension by education level (p <0.05). The means of university graduates was lower than secondary school graduates. A significant difference was found in the family medicine system benefit sub-dimension by education level (p <0.05). The means of primary and secondary school graduates was lower than university graduates.

Table 5. Family Medicine Satisfaction Status with Social-Demographic Variables

Independent Variable	n	Behaviour of Family Phsycian (Avg±S.S.)	Physical Equipment of Family Medicine (Avg±S.S.)	Communication with Family Physician (Avg±S.S.)	Benefit of Family Medicine System (Avg±S.S.)	General satisfaction (Avg±S.S.)
Gender						
Male	544	3.41±0.81	3.11 ±0.84	2.88 ±0.97	2.78±0.86	3.10±0.64
Female	495	3.31±0.82	3.14±0.85	2.76±0.88	2.76±0.80	3.08±0.61
t		1.858	-0.547	-0.157	0.558	0.622
p		0.064	0.585	0.876	0.577	0.534
Yaş						
18-29[1]	645	3.35±0.76	2.76±0.80	2.95±0.86	3.22±0.83	3.12±0.62
30-39[2]	211	3.36±0.92	2.78±0.91	2.81±1.01	3.01±0.88	3.03±0.66
40-49[3]	112	3.32±0.91	2.74±0.86	2.66±1.02	2.94±0.83	2.97±0.65
Over 50[4]	71	3.65±0.84	2.87±0.79	2.87±1.03	2.99±0.84	3.15±0.55
F		3.173	0,394	3.789	6.347	2.811
p		**0.024**	0.757	**0.010***	**0,000***	**0.038***
Difference (scheffe)		1<4		3<1	2, 3 ve 4 < 1	2 ve 3 < 4
Marital Status						
Married	368	3.39±0.88	2.79±0.89	2.87±1.03	3.06 ±0.85	3.08±0.64
Single	671	3.35±0.78	2.76±0.80	2.90±0.86	3.17±0.83	3.17±0.83
t		0.790	0.671	-0.472	-2.047	-0.499
p		0.430	0.502	0.637	**0.041***	0.618
Education Level						
Primary School[1]	64	3.22±0.99	2.81±0.91	2.78±1.06	2.91±0.84	2.96±0.62
Secondary School[2]	87	3.32±0.81	3.00±0.74	2.80±0.91	2.91±0.77	3.03±0.52
High School[3]	171	3.29±0.87	2.90±0.85	2.93±1.05	3.12±0.84	3.09±0.64
University[4]	717	3.40±0.79	2.71±0.82	2.90±0.88	3.17±0.85	3.11±0.63
F		1.637	4.907	0.726	4.064	1.216
p		0.179	**0.002***	0.536	**0.007***	0.303
Difference (scheffe)			4<2		1 ve 2<4	

*P<0.05, t>1.96

As seen in Table 6, one-way analysis of variance was performed to examine the differences in terms of family medicine sub-dimensions averages by the income status, the number of children and the place to apply first when needed.

A significant difference was found in the means of family medicine behavior sub-dimension by income status (p <0.05). It was observed that those who stated their income status as good evaluated the family physician's behavior and attitude more positively. No significant difference was found in the physical equipment of family medicine, communication with family physician and benefit of the family medicine system sub-dimensions by income level (p> 0.05). Likewise, there was no significant difference in terms of family medicine satisfaction average by income status (p> 0.05).

No significant difference was found in the means of family physician behavior, communication with the family physician and physical equipment of family medicine sub-dimensions by the number of children (p> 0.05). A significant difference was identified in the means of family medicine system benefit sub-dimension by the number of children (p <0.05). The means of those with four or more children was higher than those without children. There was no significant difference in the average satisfaction level of the family medicine system by the number of children (p> 0.05).

A significant difference was found in terms of family physician attitude and behavior, physical equipment of family medicine, benefit offamily medicine systemsub-dimension averages by the place to applyfirst when needed (p <0.05). The family practitioners' behavior means of those who stated that the first application place was family medicine when they got sick was higher than the others. The average of family medicine physical equipment of those whose first application was a family physician was higher than those who applied to private hospitals. Likewise, those who applied

first to family medicine found the system more beneficial. There was a significant difference in the means ofsatisfaction with family medicine by the place to applyfirst when needed (p <0.05). It was observed that those whose first application place was family physicians were more satisfied than others. No significant difference was found in the means of family medicine satisfaction sub-dimensions by the status of having a permanent/ chronic disease (p> 0.05).

Table 6. Family Medicine Satisfaction Status with Socio-demographic Variables

Independent Variable	n	Behaviour of Family Phsycian (Avg±S.S.)	Physical Equipment of Family Medicine (Avg±S.S.)	Communication with Family Physician (Avg±S.S.)	Benefit of Family Medicine System (Avg±S.S.)	General satisfaction(Avg±S.S.)
Income Status						
Good[1]	277	3.44±0.84	2.71±0.90	2.89±0.98	3.17±0.85	3.12±0.67
Middle[2]	601	3.38±0.81	2.78±0.81	2.92±0.91	3.14±0.85	3.10±0.62
Bad[3]	161	3.18±0.79	2.85±0.79	2.77±0.85	3.01±0.79	2.99±0.57
F		5.597	1.382	1.601	1.786	2.507
p		0.004	0.252	0.202	0.168	0.082
Difference (scheffe)		3<1				
Number of children						
None	698	3.35±0.77	2.76±0.81	2.91±0.87	3.16±0.84	3.10±0.62
One	96	3.36±0.88	2.69±0.94	2.94±1.12	3.12±0.86	3.08±0.68
Two	111	3.47±0.88	2.74±0.87	2.85±1.04	3.18±0.83	3.13±0.68
3 and above	134	3.37±0.96	2.89±0.83	2.73±0.95	2.93±0.93	3.02±0.59
F		0.694	1.292	1.599	2.850	0.662
p		0.556	0.276	0.188	0.036	0.576
Difference (scheffe)					4<1	
Apermanent ilness						
No	904	3.37±0.82	2.75±0.84	2.87±0.93	3.14±0.85	3.09±0.63
Yes	135	3.30±0.81	2.90±0.77	2.97±0.91	3.06±0.79	3.091±0.58
t		0.890	-1.915	-1.156	1.017	-0.005
p		0.374	0.056	0.248	0.309	0.996
The place to apply first when sick						
Family Phsycian[1]	311	3.67±0.89	2.87±0.82	2.93±1.11	3.27±0.91	3.25±0.66
State Hospital[2]	466	3.24±0.74	2.76±0.82	2.91±0.84	3.12±0.80	3.05±0.59
University Hospital[3]	146	3.24±0.70	2.77±0.90	2.83±0.84	3.04±0.84	3.01±0.64
Private Hospital[4]	116	3.19±0.85	2.53±0.78	2.75±0.82	2.88±0.75	2.89±0.58
F		21.284	4.818	1.283	6.813	12.685
p		0.000	0.002	0.279	0.000	0.000
Difference (scheffe)		1>2,3 ve 4	1>4		1>4	1>2,3 ve 4

P<0.05, t>1.96

DISCUSSION

Primary health care services are one of the most important elements of a comprehensive health system with both preventive health services and diagnosis and treatment services, they also contribute greatly to the development of public health by being acceptable, accessible and affordable (4,25,26,27). In 1978, with the Declaration of Alma Ata, many health problems were revealed, and the characteristics and necessity of primary health care services were explained. In addition, a number of duties were assigned to governments for the provision of sustainable primary health services (6,28).

In this study, it is aimed to determine the satisfaction level of individuals who have received service from family medicine in Kahramanmaraş central districts in the last year and to examine them in terms of various variables. While the general satisfaction score of the participants is above the average, it is below the average in terms of family medicine physical equipment and communication with family physician sub-dimensions. Söyleyici (2010) found in his study that individuals with a high level of satisfaction with family medicine assess the physical equipment status as better. For this reason, it is considered that the perception of the physical equipment of family medicine affects satisfaction. On the other hand, the dimension in which the satisfaction levels of the participants are the highest is the family physician behavior dimension. As a result of another study, it was found that individuals who evaluated the family physician's behavior as

good had significantly higher levels of satisfaction than those who evaluated the behavior of the family physician as medium and bad (30). In a study conducted in Iran, it was found that the physical equipment of family medicine and the family physician's attitudes and behaviors affect the satisfaction of individuals (31). Similarly, Aycan et al. (2012) found in their study that satisfaction with family medicine was affected by the family physician's behavior (32). Therefore, it can be stated that an important determinant of satisfaction is the family physician's behavior. The satisfaction level regarding the benefit of the family medicine system is also above average. Similarly, in a study conducted by the Ministry of Health in 2010, it was found that satisfaction with primary health care services is quite high (33). As a result of another study, it was also concluded that most of the participants had high satisfaction with family medicine, and the insufficiency of the family health centers' infrastructure negatively affected the satisfaction. In the same study, it was stated that the participants mostly focused on the patient-physician relationship (34). When the results of other similar studies are examined, it is seen that the level of satisfaction with the family medicine system in our country is high (29,35,36,37,38). When the international literature is examined, it is also observed that satisfaction with family medicine is generally high (31,39,40,41,42,43,44).

There is no statistically significant difference in the level of satisfaction with family medicine by gender. In some studies in the literature, it was concluded that there was no difference in satisfaction by gender (37,44,45,46,47) while a difference was identified by gender in other studies (29,30). In the studies that found that satisfaction level differs by gender, women's satisfaction levels werefound higher(29,30,43). The reason for the change in the level of satisfaction by gender may be that pregnancy and post-pregnancy services, which concern women more, may alter the perception of satisfaction. Satisfaction can be expected to become standard with the standardization and adoption of these services.

General satisfaction, benefit of the family medicine system, communication with family physician and behavior of family physician averages differ among age groups. General satisfaction is below the average in the 40-49 age group, while it is above the average in the other three groups. The behavior satisfaction score average of the 50 and over age group is higher than the other groups. On the other hand, the lowest score belongs to the 18-29 age group. The reason for this may be that the young people have different expectations from family physician behavior compared to the older age group. In their studies, Lankarani et al. (2016) also reached results that match this result (43). However, the situation is different when it comes to communication satisfaction. Here, it is seen that the participants in the 18-29 age group have the highest average score. Similarly, it is observed that the satisfaction of the participants between the ages of 18-29 is quite high in terms of satisfaction with the family medicine system benefits. Thus, it can be inferred that young people have a higher perception of the family medicine system benefit and adopt the system more. According to the results of another study, elderly patients have higher communication satisfaction (48).These results do not support the results of the current study. For this reason, it is thought that the participants evaluate satisfaction with the family physician's behavior and satisfaction with their communication differently. Because, although their behaviors are satisfactory, the communication skills of physicians in the health service process are one of the important factors on satisfaction. In some studies in the literature, it was concluded that satisfaction status did not differ according to age (30,37,47, 49).

By the marital status of the participants, only a difference was found regarding family medicine system benefit. Satisfaction levels of single participants in this sub-dimension were higher than married participants. This can be explained by the age of the participants. Because in the same sub-dimension, it was determined that the younger participants have a higher level of satisfaction. In many studies in the literature, it was determined that satisfaction does not differ by marital status (30,37,44,46,53). On the other hand, Turgu et al. (2018) found that the satisfaction levels of single participants were lower. The reason for this was explained by the lack of support that family members of single individuals provide to each other (13).

According to the education level of the participants, a difference was found in the means of family medicine physical equipment and family medicine system benefits sub-dimensions. While the group with the highest satisfaction in terms of physical equipment is secondary school graduates. University graduates have the lowest average. This can be explained by the increase in the expectations of individuals as the education level increases. Similarly, in other studies in the literature, satisfaction varies according to education level (13,30,50). In some studies, it was determined that as the education level increases, the level of satisfaction decreases, and it was stated that patient expectations may increase in parallel with the education level (13,43,47). On the other hand, the highest average score regarding the benefits of family medicine system is in the university graduate group, while the lowest average is in the primary and secondary school graduates. This shows that the increase in the education level increases the perception of the family medicine system benefit.

When the family medicine satisfaction levels of the participants were examined by the income status, only a significant difference was identified in the family physician behavior dimension, and the participants who described their income status as good had the highest satisfaction level. In their study, Kırılmaz and Öztürk (2018) found that satisfaction did not differ by income level (37). On the other hand, Turgu et al. (2018) stated that the increase in income status causes a decrease in satisfaction and an increase in the living standards and therefore the expectations from health services (13). Lankarani et al. (2016) found in their study that the increasein the income level decreased satisfaction (43).

Only the sub-dimension of the family medicine system benefit differs by the number of children of the participants, and this difference was determined to stem from the participants who have no children and those with three or more children. It is estimated that the reason for the similarity with the variables of age and marital status is that there are participants with similar characteristics in these three groups. Özaras and Dil (2011) also found that those with three or more children have a higher level of satisfaction (45).On the other hand, in accordance with the current research results, Turgu et al. (2018) found that individuals who have children have a higher level of satisfaction than those who do not, but also stated that individuals who have children apply to family health centers more and being able to easily get service from the family physician when needed might have increased their level of satisfaction (13).

No difference was found in the general satisfaction sub-dimension according to whether the participants had a permanent disease or not. Durmuş et al. (2018) found that the satisfaction levels of individuals with chronic diseases are higher than those without chronic diseases (47). This result differs from the current research results. The reason for this may be that individuals with chronic diseases benefit more from family medicine services and communicate with family medicine professionals more frequently (47).

Significant differences were detected in all sub-dimensions except general satisfaction and communication with family medicine sub-dimensionsby the health institution applied when sick. Here, it is seen that those who applied to family physicians when they were sick had higher mean scores compared to the other groups in all sub-dimensions. Thus, it can be inferred that perhaps for this reason the participants with low satisfaction level did not choose family medicine as their first application place. Similarly, Söyleyici (2010) found that the satisfaction levels of those who preferred to apply to family medicine were significantly higher than the other groups (30). Turgu et al. (2018)found that as the number of applications to family physicians increased, their satisfaction score averages also increased (13). On the other hand, Kızıl et al. (2015) found that the level of satisfaction did not differ by the place applied when sick (46).

CONCLUSION

As a result of the study, it was determined that satisfaction with family medicine is generally high. In order to increase the quality of the family medicine system, which is one of the most important elements of primary health care services, patient satisfaction should be continuously evaluated and improvements should be made by detecting the disruptions in service. It is clear that the improvements to be provided in the service delivery processes will increase the satisfaction of the patients. It is important to understand the expectations of groups with low service satisfaction and the problems they face in order to increase service quality. At this point, it may be suggested to conduct studies to determine expectations from family medicine services in future studies.

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RESEARCH ARTICLE

Mervegul Kaya[1]
Ozgur Enginyurt[2]
Ahmet Karatas[3]
Tuba Gul[4]

[1] Ordu University Faculty of Medicine Training and Research Hospital Family Medicine, Ordu, Turkey
[2] Ordu University Faculty of Medicine, Family Medicine, Ordu, Turkey
[3] Ordu University Faculty of Medicine, Internal Medicine, Nephrology, Ordu, Turkey
[4] Ordu University Faculty of Medicine, Department of Neurology, Ordu, Turkey

Corresponding Author:
Mervegul Kaya
Ordu University Faculty of Medicine Training and Research Hospital Family Medicine, Ordu, Turkey
Phone: +90544 597 27 28
mail: mervegul_kaya@hotmail.com

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konuralptipdergisi@gmail.com
www.konuralptipdergi.duzce.edu.tr

Evaluation of Anemia Prevalence and Concomitant Diseases in Elderly Patients Applying to Family Medicine Polyclinic

ABSTRACT

Objective: The aim of this study was to review current approaches by evaluating anemia, which is the source of many negativities in increasingly aging population and directly affecting the quality of life, and the conditions associated with it.

Methods: The population of the study consisted of patients over 18 years old who applied to Family Medicine polyclinic in Ordu University Training and Research Hospital between May 2018 and May 2019. According to World Health Organization (WHO) criteria, a hemoglobin value below 13 g / dl in men and 12 g / dl in women is defined as anemia. The patients were divided into three groups according to their mean erythrocyte volume (MCV) as microcyte (MCV <80), normocyte (MCV 80-100) and macrocyte (MCV>100).

Results: Four hundred one participants aged 65 and over were analyzed in detail. The mean age of all patients was 78.3±8.65 years. Anemia was detected in 237 (59.1%) of 401 elderly participants. Of the elderly anemic patients, 42.6% were women and 16.4% were men. Of the elderly patients, 8.8% had microcytic anemia, 87.8% had normocytic anemia, and 3.4% had macrocytic anemia. Of the elderly patients, 32.9% had chronic disease anemia, 2% had iron deficiency anemia, and 40.5% had chronic kidney disease anemia.

Conclusions: The study conducted shows that anemia is a more frequent and greater problem than predicted in elderly patients admitted to an outpatient clinic. When the underlying cause is identified and treated, dramatic improvements can be achieved in the quality of life and life span of the elderly.

Keywords: Anemia, Geriatrics, Chronic Diseases, Family Medicine.

Aile Hekimliği Polikliniğine Başvuran Yaşlı Hastalarda Anemi Sıklığı Ve Eşlik Eden Hastalıkların Değerlendirilmesi

ÖZET

Amaç: Bu çalışmamızdaki amacımız, giderek yaşlanan nüfusumuzda birçok olumsuzlukların kaynağı olan ve yaşam kalitesini doğrudan etkileyen anemi ve ilişkili olduğu durumların değerlendirilmesi ile güncel yaklaşımların gözden geçirilmesidir.

Gereç ve Yöntem: Araştırmanın örneklemini Ordu Üniversitesi Eğitim ve Araştırma Hastanesi Aile Hekimliği polikliniğine Mayıs 2018 - Mayıs 2019 tarihleri arasında başvuran 18 yaş üzeri hastalar oluşturmuştur. Anemi tanımı, Dünya Sağlık Örgütü (DSÖ) kriterlerine göre hemoglobin değerinin erkeklerde 13 g/dl, kadınlarda 12 g/dl altında olması ile değerlendirildi. Ortalama eritrosit hacmine (MCV) göre; mikrositer (MCV<80), normositer (MCV 80-100) ve makrositer (MCV>100) olmak üzere üç gruba ayrıldı.

Bulgular: 65 yaş ve üzeri 401 katılımcı ayrıntılı olarak incelenmiştir. Hastaların yaş ortalaması 78.3±8.65 idi. 401 yaşlı katılımcının 237'sinde (%59.1) anemi tespit edilmiştir. Yaşlı anemik hastaların %42.6 'sı kadınlar, %16.4'ü erkeklerden oluşmaktadır. Yaşlı hastalarda mikrositer anemi % 8.8, normositer anemi % 87.8, makrositer anemi % 3.4 bulunmuştur. Yaşlı hastaların %32.9'unda kronik hastalık anemisi, %2 demir eksikliği anemisi, %40.5 kronik böbrek hastalığı anemisi vardır.

Sonuç: Yaptığımız çalışma ayaktan polikliniğe başvuran yaşlı hastalarda aneminin tahmin edilenden daha sık ve daha büyük bir sorun olduğunu göstermektedir. Altta yatan nedeni tespit edip tedavi yapıldığında yaşlıların yaşam kalitesinde ve yaşam sürelerinde dramatik düzelmeler sağlanabilir.

Anahtar Kelimeler: Anemi, Yaşlılık, Kronik Hastalıklar, Aile Hekimliği.

INTRODUCTION

Anemia is a global health problem due to its high prevalence and the associated significant morbidity and mortality in the elderly adult population (1).Anemia is an important public health problem in the elderly and approximately one quarter of elderly patients are anemic. The control of hematopoiesis is impaired with aging (2). There is a decrease in bone marrow in parallel with other organ functions. As the aging hematopoiesis becomes more sensitive to stress, the reduced reserve capacity of other systems with the development of anemia becomes symptomatic (3).

According to WHO criteria, a hemoglobin value below 13 g / dl in men and 12 g / dl in women is considered as anemia (4). Due to the lack of a uniform definition of anemia, the prevalence of anemia reported in older adults varies widely in the literature. It has been reported that the prevalence of anemia in older adults ranges from 2.9% to 51% in men and from 3.3% to 41% in women (5).

Aging is a physiological process, and general health and well-being are affected by several reasons. It is a condition that affects the development and results of smoking, alcohol, drugs, diet, sedentary lifestyle, age-related biological changes and functional disorders. The causes of death in the population aged 65 and over are defined as cardiovascular disease, cancer, lung disease, stroke, Alzheimer's disease, diabetes, and nephritis, respectively. In the elderly, anemia is affected by the burden of additional diseases, functional capacity, cognitive status and life expectancy. The decrease in physical and mental functions can profoundly affect the life of an elderly person and result in loss of independent life in the community (6). Quality of life is reduced when anemia is associated with specific diseases rather than alone. The improvement in anemia affects the quality of life positively regardless of the underlying disease (7).

In older adults, anemia is associated with other physical function markers, including weakness, increased frailty, muscle weakness, and falls. Anemia shows worse prognosis in elderly patients with anemia, cardiovascular and other chronic diseases. Survival benefit has been reported with the treatment of geriatric anemia in studies (8).

Causes of anemia in the elderly are basically divided into three groups. These are anemia due to nutritional deficiency, chronic disease anemia and anemia of unknown cause. There is no reason in 15-25% of them (9). The causes of anemia in hospitalized elderly are considered as chronic diseases, unexplained anemias, iron deficiency, bleeding, chronic kidney disease, liver and endocrine diseases, vitamin B12 or folic acid deficiency. In the elderly patients who are outpatient, the causes of it are listed as unexplained anemia, chronic diseases, iron deficiency, kidney and liver failure, and endocrine diseases (10).

MATERIAL AND METHODS

The study was initiated after the approval of Ordu University Faculty of Medicine Clinical Research Ethics Committee (Date: 23/05/2019; Approval No: 2019-86). Files of 520 patients aged 18 and over who applied to Ordu University Training and Research Hospital Family Medicine polyclinic between May 2018 and May 2019 were scanned. The group with active malignancy and hemoglobinopathy was not included in the study.

Hemogram measurements were performed with Cell-Dyn Ruby device. Cobas-C 501 module was used for the analysis of routine biochemical parameters Blood Urea Nitrogen (BUN) (mg / dl), creatinine (mg / dl), C-reactive protein (CRP) (reference range:0-0,5:mg / dl), serum iron, total iron binding capacity (TIBC) (mcg / dl)]. Ferritin (reference range:30-400 µg / l), vitamin B12 and folate levels were analyzed by Roche Cobas E-601.

Hemoglobin values below 13 g / dl for men and below 12 g / dl for women were accepted in the definition of anemia according to the WHO criteria. Iron deficiency was defined as serum ferritin value <20 ng / dl or serum iron <40 µg / dl and transferrin saturation <15% when serum ferritin value> 20 ng / dl. Anemia due to chronic inflammation was defined as serum ferritin value> 100 ng / dl and CRP> 0.5. Anemia due to chronic kidney disease was defined as GFR <60 ml / min / 1.73 m^2 in the calculation of GFR using the Cockcroft-Gault formula in anemic elderly. It was accepted MCV <80 fl as microcytic anemia, MCV between 80-100 fl as normocytic anemia and MCV> 100 fl as macrocytic anemia in the evaluation of erythrocyte mass.

SPSS 20 program (SPSS Inc. Released 2009. PASW Statistics for Windows, Version 20.0. Chicago: SPSS Inc.) was used for statistical analysis of the findings obtained from the study. The compliance of continuous variables to normal distribution was examined using the Kolmogorov-Smirnov test. In order to define the population, variables determined to be unsuitable for normal distribution were specified as median (minimum-maximum), and categorical variables were specified as numbers and percentages. In cases where the parametric test assumptions of the data were not provided, the non-parametric "Mann-Whitney U" test was used. Categorical data were analyzed using "Chi-square significance test". A 95% significance level (or $\alpha = 0.05$ margin of error) was used to determine the differences in the analyzes.

RESULTS

Of 520 cases included in the study, a total of 401 of those 65 years and older were examined in detail. The mean age of all patients was 78.3±8.65 years. Anemia was detected in 237 (59.1%) of 401 elderly participants ($p < 0.001$). The prevalence of anemia in the elderly was observed as 16% in men and 41.7% in women. The number of elderly

anemic patients was 237 (59.1%), and 66 of them were male (27.8%) and 171 of them were female (72.2%). When comorbid diseases were examined with respect to anemia status in the elderly, a difference was observed in terms of the presence of anemia (p = 0.004). No difference was observed with respect to drug use status (p = 0.268) (Table 1).

Table 1. Distribution of Demographic Characteristics in the Elderly According to Anemia Status

		Anemia*		
		Absent (n=164)	Present (n=237)	p**
Gender	Female	102(62.2)	171(72.2)	
	Male	62(37.8)	66(27.8)	**0.035**
Concomitant Disease	Diabetes Mellitus	9 (5.7)	14 (6.3)	**0.004**
	Hypertension	59 (37.1)	46 (20.6)	
	Cardiovascular Disease	6 (3.8)	20 (9)	
	Chronic Kidney Disease	7 (4.4)	10 (4.5)	
	Cerebrovascular Disease	7 (4.4)	22 (9.9)	
	Multiple diseases	71 (44.7)	111 (49.8)	
Drug use	No drug use	11 (6.9)	24 (10.8)	0.268
	Antiaggregant-anticoagulant	14 (8.8)	31 (13.9)	
	NSAID	3 (1.9)	6 (2.7)	
	ACE inhibitors, ARB	20 (12.6)	18 (8.1)	
	Other Antihypertensives	28 (17.6)	41 (18.4)	
	Multiple drugs	83 (52.2)	103 (46.2)	

* frequency (percentage),** Chi-square test, NSAID:Nonsteroidal antiinflammatory drugs, ACE inhibitors: Angiotensin-converting enzyme (ACE) inhibitors, ARB: angiotensin receptor blockers

Median age values differed with respect to the presence of anemia (p <0.001). While the median value was 74 for those with anemia, it was 82 for those without it. Median hemoglobin values varied according to the presence of anemia (p <0.001). While the median value was 13.7 in those with anemia, it was 11.4 in those without it. Median hematocrit values differed in terms of the presence of anemia (p <0.001). While the median value was 41.6 for those with anemia, it was 35 for those without it. Median values of MCV did not vary with respect to the presence of anemia (p = 0.713). While the median value was 88.5 in those with anemia, it was 88.3 in those without it. Median folate values did not differ according to the presence of anemia (p = 0.233). While the median value was 7.9 in those with anemia, it was 7.4 in those without it. Median values of vitamin B12 varied according to the presence of anemia (p = 0.002). While the median value was 315.2 in those with anemia, it was 378.1 in those without it. The median values of ferritin differed in terms of the presence of anemia (p = 0.044).

While the median value was 63.3 in those with anemia, it was 93.3 in those without it. Median values of iron varied with respect to the presence of anemia (p <0.001). While the median value was 79.9 in those with anemia, it was 58.7 in those without it. Median TIBC values differed according to the presence of anemia (p <0.001). While the median value was 322.9 in those with anemia, it was 288.5 in those without it. The median values of transferrin saturation varied in terms of the presence of anemia (p <0.001). While the median value was 0.19 in those with anemia, it was 0.25 in those without it. Median BUN values differed with respect to the presence of anemia (p <0.001). While the median value was 16.2 in those with anemia, it was 20.2 in those without it.

Median values of creatinine varied according to the presence of anemia (p = 0.027). While the median value was 0.8 in those with anemia, it was 0.9 in those without it. Median estimated glomerular filtration rate (eGFR) values differed in terms of the presence of anemia (p <0.001). While the median value was 80 in those with anemia, it was 68.1 in those without it. The median values of CRP varied with respect to the presence of anemia (p <0.001). While the median value was 0.3 in those with anemia, it was 0.7 in those without it (Table 2).

Table 2. Comparison of Laboratory Values in the Elderly According to Anemia Status

	No anemia*	Have anemia*	Total	p**
Age	74 (65 - 95)	82 (65 - 100)	78 (65 - 100)	**<0.001**
Hemoglobin (g / dl)	13.7 (10.2 – 17.7)	11,4 (1.7 – 14.3)	12 (1.7 – 17.7)	**<0.001**
Hematocrit (%)	41.6 (32.8 – 54.6)	35 (20 – 308.8)	37.2 (20 – 308.8)	**<0.001**
MCV (fl)	88.5 (44.3 – 101.6)	88.3 (36 – 113.6)	88.4 (36 – 113.6)	0.713
Folate (µg/L)	7.9 (2.3 - 20)	7.4 (1.8 - 941)	7.7 (1.8 - 941)	0.233
Vitamin B12 (µg/L)	315.2 (50 - 1890)	378.1 (27.2 - 2000)	349.1 (27.2 - 2000)	**0.002**
Ferritin (µg/l)	63.3 (5.1 - 1822)	93.3 (6.8 - 1845)	72.6 (5.1 - 1845)	**0.044**
Iron (µg/dl)	79.9 (30.2 – 180.1)	58.7 (2.3 – 309.2)	67.2 (2.3 – 309.2)	**<0.001**
TIBC (µg/dl)	322.9 (128 – 3410.5)	288.5 (26.4 – 499.6)	305.8 (26.4 – 3410.5)	**<0.001**
Transferrin saturation	0.25 (0.02 – 0.69)	0.19 (0.01 – 1.72)	0.22 (0 .01– 1.72)	**<0.001**
BUN (mg / dl)	16.2 (7.2 – 43.6)	20.2 (5.6 – 95.2)	18.1 (5.6 – 95.2)	**<0.001**
Creatinine (mg / dl)	0.8 (0.1 – 8.7)	0.9 (0.3 – 5.8)	0.9 (0.1 – 8.7)	**0.027**
eGFR (ml/min/1.73 m^2)	80 (28 – 122.8)	68.1 (8 - 122)	73.4 (8 – 122.8)	**<0.001**
CRP (mg/dl)	0.3 (0 – 8.5)	0.7 (0 – 27.5)	0.4 (0 – 27.5)	**<0.001**

*median (min-max), **Mann Whitney U test; MCV: Mean corpuscular volume, TIBC:Total Iron Binding Capacity, BUN: *Blood Urea Nitrogen*, *eGFR:* Estimated glomerular filtration rate, *CRP:* C-reactive protein.

The distributions of gender, B12 deficiency and folate deficiency do not differ with respect to MCV categories in the elderly (p = 0.717). The presence of anemia varies according to MCV categories in the elderly (p = 0.033). In the association between erythrocyte mass and anemia, MCV was within normal limits (80-100 fl, normocytic) in 210 (87.8%), low (<80 fl, microcyte) in 19 (8.8%) and high (> 100 fl, macrocytic) in 8 (3.4%) of 237 anemic elderly (p = 0.033).

No significant association was observed between vitamin B12 and folate deficiency and erythrocyte mass in the elderly examined. Although there were 45 participants with vitamin B12 deficiency and 9 with folate deficiency, there were no participants with MCV values> 100 fl (Table 3).

While 16% of young people had iron deficiency anemia and 8.3% of them had chronic kidney disease anemia, 32.9% of the elderly had chronic disease anemia, 2% of them had iron deficiency anemia, and 40.5% of them had chronic renal failure anemia. A significant difference was observed with respect to chronic disease anemia and chronic renal failure anemia in the elderly (p <0.001) (Table 4)

Table 3. Distributions in the Elderly according to MCV Categories

	MCV<80 fl (n=25)*	MCV:80-100 fl (n=367)*	MCV>100 fl (n=9)*	Total	p value**
Female	17 (68)	251 (68.4)	5 (55.6)	273 (68.1)	
Male	8 (32)	116 (31.6)	4 (44.4)	128 (31.9)	0.717
No anemia	6 (24)	157 (42.8)	1 (11.1)	164 (40.9)	
Have anemia	19 (76)	210 (57.2)	8 (88.9)	237 (59.1)	0.033
No B12 deficiency	23 (92)	324 (88.3)	9 (100)	356 (88.8)	
Have B12 deficiency	2 (8)	43 (11.7)	0 (0)	45 (11.2)	0.475
No folate deficiency	24 (96)	359 (97.8)	9 (100)	392 (97.8)	
Have folate deficiency	1 (4)	8 (2.2)	0 (0)	9 (2.2)	0.754

*frequency (percentage), ** Chi-square test
MCV: Mean corpuscular volume

Table 4. Anemia Classification

	Young*	Older*	p value**
Have CDA	0	78 (32.9)	
No CDA	48 (23.2)	159 (67.1)	**<0.001**
Have IDA	8 (16)	6 (2)	
No IDA	40 (84)	231 (98)	**<0.001**
Have CKD	4(8.3)	96 (40.5)	
No CKD	44 (91.7)	141 (59.5)	**<0.001**

*frequency (percentage), ** Chi-square test
CDA:Chronic Disease Anemia, IDA: Iron Deficiency Anemia, CKD: Chronic Kidney Disease

DISCUSSION

Anemia is defined as a hemoglobin value below 13 g / dl in men and below 12 g / dl in women by WHO. Anemia becomes an important health problem in the elderly population as hemoglobin values decrease with age. Anemia brings along many diseases in the elderly population. Conditions increasing in the anemic elderly can be stated as mortality, cardiovascular disease, impaired cognitive functions, decreased mobility, fall and fracture risk, hospitalizations and length of stay (6).

The prevalence of anemia is affected by many conditions. Anemia is observed more frequently in developing countries. According to WHO, it is seen at a rate of 14% in Europe and 25% in our country. The prevalence of anemia has been reported to be 1.9-14% in men and 15-64% in women in Central South America and Asian countries (11). Considering the criteria determined for the definition of anemia, the results obtained vary according to the location of the study (community, hospital, polyclinic, nursing home, etc.) and the health status of the participants. In elderly individuals, the prevalence of anemia is 12% in the community, 40% in hospital admissions and 47% in nursing home residents (12). In the literature, the prevalence of anemia has been found at quite different rates in elderly individuals. There are studies on anemia in the elderly population in our country. The prevalence of anemia was found to be 30% in the study conducted by Coban et al. on 2100 patients aged 65 and over who applied to the internal diseases polyclinic (13). Similarly, the prevalence of anemia was observed to be 32.5% in the study performed by Erkan et al. on 501 patients aged 65 and over who applied to internal diseases polyclinic (14). It was detected in the study conducted by Sahin et al. on 521 patients aged 65 and over that the frequency of anemia was 63% (15). It was found the prevalence of anemia to be

59.1% in this presented study, similar to Sahin et al. The high number of elderly and comorbid patients and the special patient referral from other health units in the region because of the fact that our hospital is a medical school hospital may be the factors for the high frequency of anemia in this study.

Memisogullari et al. investigated the types of anemia in their study. Microcytic anemia at rate of 46.9%, normocytic anemia at a rate of 52.6% and macrocytic anemia at a rate of 0.5% were found in their study (16). In a study conducted by Sahin et al. on patients admitted to the emergency service, 521 patients aged 65 and over were evaluated. Of those with anemia in the study, 76.6% was normocytic, 14.0% was microcytic, and 9.4% was macrocytic (15). It was detected in this presented study that normocytic anemia was at a rate of 87.8%, microcytic anemia was at a rate of 8.8%, and macrocytic anemia was at a rate of 3.4%. This presented study is compatible with the literature in this aspect.

One third of anemia is due to nutritional deficiency. More than half of anemias due to iron, folate and B12 deficiency also occur in this way. It was reported in the study conducted by Guralnik et al., the frequency of anemia due to nutritional deficiency was 35% in the United States. As nutrient deficiencies, iron, B12 and / or folate are the most common ones. Iron deficiency can be seen alone or together with vitamin B12 and folate deficiency (17). It was observed in the study performed by Amin et al., low ferritin (serum ferritin <12µg / l) was at a rate of 3%, iron deficiency was at a rate of 2%, and iron deficiency anemia was at a rate of 1.2% (18). The frequency of B12 deficiency in elderly patients was found as 26.4% by Sandikci et al. and 43% by Emiroglu et al. (19). In this presented study, the frequency of B12 deficiency in elderly anemic patients was observed as 11.2%. We think that B12 deficiency is lower than the literature in our patients because of the supplements of vitamin B12 in the patients who we have followed up in our hospital.

Anemia is usually caused by only one cause (for example, iron deficiency in pre-menopausal women with heavy menstrual bleeding) in younger people, whereas anemia is often multifactorial in the elderly and reflects the typical multimorbidity of older people. This often makes it difficult to examine the mechanism that causes anemia in the elderly. For instance; iron deficiency in the elderly can be seen due to malnutrition, which is often aggravated by the use of multiple drugs, and malabsorption. Losses from the gastrointestinal system can be considered as the most important cause of iron deficiency anemia. Nonsteroidal anti-inflammatory drugs (NSAIDs), antiaggregants and anticoagulants cause gastrointestinal system bleeding. With aging, the rate of use of acetylsalicylic acid and other antiaggregants and anticoagulants increases due to cardiovascular diseases. Consequently, gastrointestinal complaints and gastrointestinal bleeding increase (20). In this presented study, the rate of cardiovascular disease in anemic elderly was 9%, and 13.9% of the patients used antiaggregant and anticoagulants and 2.7% of them used NSAIDs.

Of anemic patients in the study conducted by Karakus et al., 19.8% used proton pump inhibitors (PPI), 4.5% used NSAIDs, 2.3% used aspirin, and 0.7% used NSAIDs and PPIs (21). In this presented study, 2.7% of the elderly patients used NSAIDs.

The morbidity profiles of chronic diseases were evaluated in 171 patients in the study performed by Tariq et al. Hypertension at a rate of 61.4%, anemia at a rate of 46.8% and diabetes mellitus at a rate of 34.5% were observed most frequently (22). In this presented study, diabetes mellitus was found in 6.3% and hypertension was found in 20.6% of elderly anemic patients.

In the study conducted by Yuksel et al., 714 patients who applied to the general internal medicine and geriatric polyclinics and were diagnosed with iron deficiency anemia as a result of the examinations were evaluated. Anemia was detected in 37.7% of men and 62.3% of women (20). It was detected in the study performed by Imdat et al. on 642 patients in the city of Van that the prevalence of anemia was 15.9%, of which 17.3% were women and 11.9% were men (23). Sahin et al. (2013) stated in their study conducted on patients applied to the family medicine polyclinic that the prevalence of anemia was 29.2% in men and 33.3% in women (15). In this presented study, the frequency of anemia in the elderly was observed as 16% in men and 41.7% in women.

National Health and Nutrition Examination Survey (NHANES) data was used to determine the prevalence of anemia in patients with CKD in 2007-2008 and 2009-2010. According to the data of the United States between 2007 and 2010, 14% of the population was found to have chronic kidney disease. Anemia was seen in 15.4% of patients with chronic kidney disease and 7.6% of the general population. Anemia was twice as common in patients with chronic kidney disease compared to the normal population (24). In a study conducted by Sezer SD et al. on the etiology of anemia in the elderly, inflammation was the first (54%), the second was CKD (30.6%), followed by iron deficiency anemia (29.9%), vitamin B12 deficiency (16.7%) and folate deficiency (14.7%), respectively (25). In this presented study, the rate of CKD in patients over 65 years of age was found to be 4.5%. It was found the rate of anemia due to chronic kidney disease as 23% in the elderly in this

presented study. We think that the different rates of anemia in CKD patients in our country and in the world are due to the fact that the etiology of kidney disease in geographical regions is specific to that region. The study has some limitations. The first limitation is that the study is conducted retrospectively based on the laboratory values. Therefore, it cannot be said with certainty whether the abnormal laboratory parameters are a chronic or an acute condition. The second limitation of the study is that it is hospital-based. The findings are limited to patients presenting to the polyclinic and do not determine the general population. We think that new multi-center prospective studies on this subject will be guiding in this regard.

CONCLUSION

Consequently, anemia is a frequent occurrence in patients over 65 years of age in Turkey. Anemia in elderly patients in the world and in our country requires a special approach in terms of etiology, treatment and precautions. In our study, the most common cause of anemia in patients admitted to the family medicine outpatient clinic was normocytic anemia, demonstrating that chronic disease anemia plays a key role, especially in elderly individuals. This study emphasizes the importance of anemia in elderly patients. In addition, we think that this study will contribute to the evaluation of possible etiological factors of anemia.

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RESEARCH ARTICLE

Tolga Aktan[1]
Bayram Sahin[2]

[1] Guven Healthcare Group, Strategic Budget Management Department, Ankara, Turkey
[2] Hacettepe University, Faculty of Economy, Ankara, Turkey

Corresponding Author:
Tolga Aktan
Guven Healthcare Group, Strategic Budget Management Department, Ankara, Turkey
Phone: + 90533 5650414
mail: tolgaaktan@hotmail.com

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Assessment of Relationship between Hospital Resource Management Capacity and Characteristics of Hospitals and Managers

ABSTRACT

Objective: The purpose of the study is to investigate the relationship between hospital resource management capacity and hospital and manager characteristics.

Methods: The study was conducted on 41 hospitals affiliated to the Ministry of Health of Turkey in Istanbul and Ankara and 232 hospital managers working in these hospitals. Primary and secondary data sources were used as data collection methods. In the first part of the survey, which is used as the primary data source, the questions related to the duties of the managers, gender, total management time, the period of management in the hospital, formal management training, organizational and professional commitment and identification levels and hospital capacity management levels were included. As the secondary data source, hospital statistics were applied and data related to the characteristics of the hospitals.

Results: Exploratory factor analysis was performed to determine whether the questions used to evaluate the resource management capacity of the hospitals were structurally valid. As a result of exploratory analysis, a three-factor structure consisting of equipment, workforce and facility dimensions was reached, and the confirmatory factor analysis conducted to test the accuracy of this structure was found to be acceptable for goodness of fit values. As a result of the structural equation model used in the study, the type of hospitals and the number of medical specialties and the gender of the managers have significant effects on the resource management capacity of hospitals ($p < 0.05$). However, the hospital age and the number of medical specialties and the manager roles, total management time, duration of management in the hospital, formal management training and the managers' organizational commitment and organizational identification levels do not have a significant effect on the resource management capacity of hospitals ($p > 0.05$).

Conclusions: According to the findings, resource management capacities of specialty hospitals are at a better level than general hospitals. This result shows that the type of service and the scope of service in specialty hospitals are clearly defined. Even if the number of medical specialties becomes more complex in the findings, the resource management capacity of the hospitals is managed more successfully. In the last findings, it was concluded that female managers are more successful in evaluating resource management capacity.

Keywords: Hospital Resource Management Capacity, Hospital Characteristics, Manager Characteristics.

Hastanelerin Kaynak Yönetimi Kapasitesi İle Hastane Ve Yöneticilerin Özellikleri Arasindaki İlişkinin İncelenmesi

ÖZET

Amaç: Bu çalışmada, hastanelerin kaynak yönetimi kapasitesi ile hastane ve yönetici özellikleri arasındaki ilişkinin incelenmesi amaçlanmıştır.

Gereç ve Yöntem: Çalışma, İstanbul ve Ankara illerindeki Sağlık Bakanlığı'na bağlı 41 hastane ve bu hastanelerde görevli 232 hastane yöneticisi üzerinde yapılmıştır. Çalışmada veri toplama yöntemi olarak birincil ve ikincil veri kaynakları kullanılmıştır. Birincil veri kaynağı olarak kullanılan anketin birinci bölümünde yöneticilerin görevi, cinsiyeti, toplam yöneticilik süresi, çalışmış olduğu hastanedeki yöneticilik süresi, formal yönetim eğitimi alma durumu, örgütsel ve mesleki bağlılıkları ile özdeşleşme düzeylerini belirlemeye yönelik sorulara, ikinci bölümünde ise çalıştıkları hastanelerin kaynak yönetim kapasitesini belirlemeye yönelik sorulara yer verilmiştir. Çalışmada ikincil veri kaynağı olarak ise araştırma kapsamındaki hastanelerin istatistiklerine başvurularak faaliyet süresi, türü, hizmet verdiği tıp uzmanlığı sayısı gibi özelliklerine ilişkin veriler elde edilmiştir.

Bulgular: Hastanelerin kaynak yönetim kapasitesini değerlendirmek için kullanılan soruların yapısal olarak geçerli olup olmadığını belirlemek için yapılan açımlayıcı faktör analizi sonucunda; ekipman, işgücü ve tesis boyutlarından oluşan üç faktörlü bir yapıya ulaşılmış, bu yapının doğruluğunu test etmek için doğrulayıcı faktör analizi kullanılmıştır. Çalışmada hastanelerin ve yöneticilerin özelliklerinin hastanelerin kaynak yönetimi kapasitesi üzerindeki etkisini test etmek için kullanılan yapısal eşitlik modeli sonucunda; hastanelerin türü ve tıp uzmanlığı sayısı ile yöneticilerin cinsiyetinin hastanelerin kaynak yönetimi kapasitesi üzerinde anlamlı etkileri olduğu ($p<0,05$), buna karşın hastanelerin faaliyet süresi ve tıp uzmanlığı sayısı ile yöneticilerin görevi, yöneticilik süresi, hastanedeki yöneticilik süresi, formal yönetim eğitimi ve yöneticilerin örgütsel ve mesleki bağlılık ile örgütsel özdeşleşme düzeylerinin hastanelerin kaynak yönetimi kapasitesi üzerinde anlamlı etkisinin olmadığı ($p>0,05$) tespit edilmiştir.

Sonuç: Bulgulara göre özel dal hastanelerinin kaynak yönetim kapasiteleri genel hastanelere göre daha iyi seviyededir. Bu sonuç özel dal hastanelerinde hizmet verme şeklinin ve hizmet kapsamının net bir şekilde tanımlandığını göstermektedir. Elde edilen bulgularda tıp uzmanlığı sayısı arttıkça daha karmaşık hale gelse bile hastanelerin kaynak yönetimi kapasitesi daha başarılı bir şekilde yönetilmektedir. Son olarak elde edilen bulgularda kadın yöneticilerin kaynak yönetimi kapasitesini değerlendirmede daha başarılı olduğu sonucuna ulaşılmıştır.

Anahtar Kelimeler: Hastane Kaynak Yönetimi Kapasitesi, Hastane Özellikleri, Yönetici Özellikleri.

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e-ISSN1309–3878
konuralptipdergi@duzce.edu.tr
konuralptipdergisi@gmail.com
www.konuralptipdergi.duzce.edu.tr

INTRODUCTION

The fact that most of the resources allocated to the health sector are used in hospitals has increased the importance given to measuring and monitoring the resource management capacity of hospitals. In Turkey, the share of hospital expenditures in total health expenditures in 2019 was 48.2% and showed an increase of 21% compared to 2018 (1).

As a result of the increase in health expenditures since the early 1980s, controlling costs and making the right resource management have gained great importance in both health systems and hospitals. In 2030, it is predicted that the share of health expenditures in the gross national product in OECD countries will be 10.2%. In 2018, this rate was 8.8% (2). With these numerical increases, the demand for quality healthcare services has led to the development of an economic perspective that can be described as contradictory in the health sector and the formation of a public awareness in this direction (3). The constantly increasing trend of health expenditures, the high share of hospital expenditures in total health expenditures and the increase in the demand for quality health services make it necessary to manage the resources and the factors affecting the resource management capacity.

Hospitals are now under pressure to reduce costs and increase service quality. This situation raises the need for proper management of hospital capacities. Capacity is the ability to do business at the maximum level sustainable (4).

According to another definition, capacity is the maximum number of customers that can be served in a time frame (5). Capacity in enterprises such as hospitals where products and services differ widely; It depends on the mix of products and services requested over a period of time. Based on these definitions, the capacity in hospitals is determined by measuring resources such as beds, operating rooms and intensive care units in order to determine the complexity of the patient treatment process (6). From a broader perspective, health capacity; involves the allocation of key resources such as facilities, labor and equipment (7).

Resource management in hospitals; it is to use of common resources when and where they are needed such as operating rooms, hospital beds and intensive care units. Resource management is also a complex and dynamic situation due to the existence of departments that have to provide unplanned services such as Emergency Services (8). In order to manage this situation, determining the factors affecting the resource management capacity is very important.

When the studies on the factors affecting hospital resource management capacity are examined in the literature; It was stated that the decisions taken regarding facility and technology management strongly affect resource management. And it has been stated that the facility, workforce and equipment sub-dimensions of capacity affect the selection and timing of the services provided in hospitals, service quality, service cost, patient and employee satisfaction (9).

In addition, there are studies (10) stating that improvements in hospital processes positively affect workforce and technology resource management. There are also studies stating that workforce development is an important factor affecting the quality of health care (11). In a study conducted in private hospitals, it was concluded that hospitals provide quality service as a result of a good facility management and this increases patient satisfaction (12).

In a study examining the effects of hospital characteristics (hospital size, location, training feature) on resource management capacity, a positive significant relationship was found and it was revealed that hospitals with high resource management capacity also had high cost and quality management performance. In the same study, it was also stated that workforce development and equipment/technology decisions directly affect cost management performance and quality management performance has a strong causal relationship with equipment/technology decisions (13).

As can be seen, the factors affecting the resource management capacity in hospitals have been evaluated in scientific studies from different angles. Some of these are related to administrative decisions at the hospital level, while others are related to the characteristics of hospitals and employees. In this study, after considering the characteristics of hospital and hospital managers, the effects of managers' levels of organizational commitment, professional commitment and organizational identification on hospital resource management capacity were examined.

Resource Management in Hospitals: Capacity refers to the ability of both resource and resource to be used. Healthcare capacity consists of key resources such as facilities, equipment and workforce (7). Resource management and planning is critical to creating an effective business environment in sectors and organizations that produce goods and services. Effective resource management is realized by creating a structure that can respond to rapidly changing environmental conditions while keeping the input cost low (14).

Capacity planning in health institutions has more than one dimension. These are investment in existing services, investment in expensive hardware and technology (such as magnetic resonance imaging devices), service delivery, human resource and financial resource planning. Planning of health services differs from country to country. Planning of health services differs from country to country. Therefore, the importance attached to each dimension of planning varies by country.

Most of the countries plan the number of hospitals in order to provide healthcare services at the optimum level. On the other hand, there are differences between countries in terms of service delivery and service scope planning. Some health authorities outline their health plans based on existing infrastructure only in terms of number and location of services, while other plans detail the planning. Like the number and geographic distribution of the medical specialties (15). Classification of resources in healthcare can be done in the form of physicians, nurses, biologists, pharmacists, physiotherapists and other healthcare professionals, patient rooms, equipment, consumables, implantable devices and organs, and instruments and devices in accordance with a resource-based perspective (16).

Resource management has a variety of uses. One of the most common methods is the use of shared services. In this method, resources are used jointly and it is aimed to reduce the costs. In this application, back office operations used by multiple departments are centralized and costs are reduced.

Today, many organizations use a joint service model for finance, human resource management, and information technology. Another widely used model is resource pooling. Resource pooling is used in information technology terminology to describe a situation where providers serve multiple clients or "terminals" with ad hoc and scalable services. These services can be adjusted to suit each customer's needs (14). The aforementioned methods, which can be applied in different sectors, also have applications in the health sector. However, demographic structures should be taken into consideration in the resource management planning of hospitals. First of all, the main determining factors such as disease burden and average age should be determined at the location where the planning is made during the establishment phase of the hospital. According to these factors, different types of resources such as the number of beds, technological equipment, type of hospital, training and research hospital, number of personnel, number of physicians and nurses should be planned. Resource management can be done in the short, medium and long term. Healthcare capacity planning in many countries takes place at the national, regional or local level.

In a study, the capacity planning models of different countries were examined and it was determined that planning started to take place at the regional level. This often implies the transfer of responsibility for the regulation of health services from the center to local governments, as in Denmark and Finland. Local administrations in Denmark and Finland are important actors in healthcare capacity planning (15).

In resource management and capacity planning studies, three basic dimensions can be mentioned as facility, workforce and equipment management. These dimensions are explained as measured in the study under separate headings below.

Facility Management in Hospitals: Facility management can be defined as the internal planning, implementation and management of buildings and accommodation, services and resources that contribute to the effective and efficient realization of organizational goals (17). According to another definition, facility management can be defined as the management of non-core company assets to support and increase the effectiveness of the main business of the organization (18).

According to the British Institute of Facilities Management (BIFM) definition, facility management is the integration of multidisciplinary activities in the built environment and the management of their effects on people and workplaces (19). Facility management subheadings include facility maintenance management, facility performance management, facility risk management, facility supply management and facility demand management (20).

Workforce Management in Hospitals: Workforce management is one of the most dynamic and critical jobs in health service delivery. Since a hospital cannot exist without caregivers, it is important to recruit and retain staff. Recruiting a highly skilled and qualified workforce should be a top priority in hospitals to ensure safe patient care. Qualified personnel recruited should be managed in accordance with workforce development policies with continuous training and thus workforce continuity should be ensured.

Management policies should be developed by taking into account the developments within and outside the organization in labor management. Planning according to patient treatment needs can be given as an example to the developments experienced within the organization. All health professionals such as physicians, nurses, biologists are included in this staff planning. In addition, acuity of patients admitted to the hospital should be taken into account when dealing with internal developments in the hospital (21).

In workforce management, policies should be developed by considering internal and external organizational factors. Workforce planning of physicians, nurses and other health professionals can be given as an example to the developments in the organization, depending on the patient treatment needs. In addition, the acuity of patients admitted to the hospital should be taken into account when dealing with internal developments in the hospital (21).

As examples of non-organizational developments, national labor policies, migration movements, changes in society and technological developments can be given (22). Employees can be ignored when customers are considered only as external customers in labor management. The aim is to combine the needs of the external client with the skills of the employees. Thus, the benefit of both internal and external customers is optimized (9).

Equipment and Technology Management in Hospitals: With the increasing technology investments in health, the correct use of limited resources is becoming more and more important every day. Health technology-related costs are affected by technical, economic, financial, legal, social and political factors. Since the use of technology increases costs, there is a serious pressure on hospital managers to optimize costs without sacrificing efficiency and quality. Deciding on the use of the right technologies should be considered within the scope of health policy and should be planned according to the size of the hospital, hospital region, patient demographic characteristics, disease maps and the level of development in the region throughout the country.

Medical devices occupy an important place in technology management in hospitals. With the developing technology; The role of medical devices in diagnosis, treatment and rehabilitation of patients, their place and importance in health institutions are increasing day by day. In this direction, effective use of medical devices in healthcare facilities and optimum planning can increase the quality of service and increase the level of patient satisfaction (23). Until the 1970s, exploratory surgery was used to diagnose diseases - which is both costly and health hazardous - and imaging technologies such as computed tomography, MRI (magnetic resonance imaging) and PET Scan are now being used due to the developing medical technology has been started (24).

Today, technology management plans are considered as an important element of hospitals' strategic plans (3). Technology should be considered as a key factor in business strategies. Considering that the most important resources of an organization are workforce and knowledge, technology will play a key role, enabling the maximum use of these resources and creating added value (25).

Factors Affecting Hospitals' Resource Management Capacity: In different studies examining the factors affecting the resource management capacity of hospitals, it was stated that clinical engineering has a significant effect on the procurement process of institutional equipment and the implementation of new clinical equipment, and this has an impact on resource management decisions (26). In addition, there are studies (10) state state improvements in hospital processes positively affect workforce and technology resource management, and workforce development is an important factor affecting the quality of health care (11).

In a study conducted in private hospitals, it was concluded that patient satisfaction is high in hospitals where quality service is provided as a result of a good facility management (12). A positive significant relationship was found in a study examining the effects of hospital characteristics (hospital size, location, training feature) on resource management capacity, and it was revealed that hospitals with high resource management capacity also have high cost and quality performance. In the same study, it was also stated that workforce development and equipment / technology decisions directly affect cost performance and quality performance has a strong causal relationship with equipment / technology decisions (13).

MATERIAL AND METHODS

Purpose and Hypotheses of the Study: The purpose of this study is to measure the effects of the characteristics of hospitals (type, duration of activity, number of medical expertise they serve) and the characteristics of the managers (role, gender, total management time, duration of management in the hospital where they work), organizational and professional commitment and organizational identification levels of managers on the resource management capacity of the hospitals. The following hypotheses have been tested in order to achieve the study purpose.

H1: Resource management capacity of hospitals differs significantly according to a) characteristics of hospitals (type, age, number of medical specialty), b) characteristics of managers (role, gender, total management time, duration of management in the hospital where they work, whether they received formal training in management), c) managers' organizational commitment d) professional commitment and e) organizational identification levels.

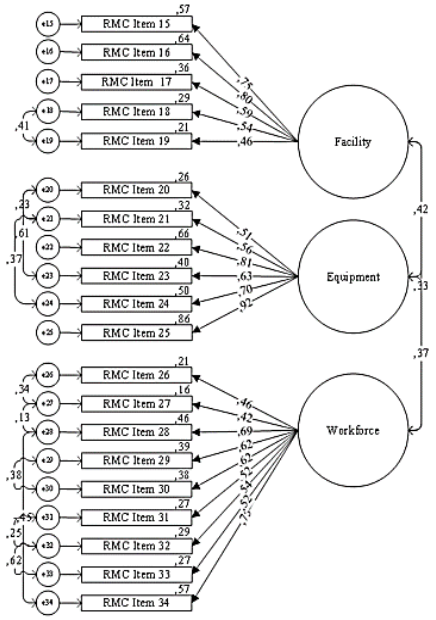
Population and Sample: The population of the study consists of the Ministry of Health of Turkey hospitals in Ankara and Istanbul. As of 2016, there are 37 Ministry of Health hospitals in Ankara and 56 hospitals in Istanbul, and permits have been obtained from a total of 41 hospitals, 23 hospitals in Ankara and 18 hospitals in Istanbul.

The sample was not selected in the study. An attempt was made to reach 437 managers (chief physicians and their deputies, administrative financial managers and their deputies, care services managers and their deputies) in 41 hospitals, however, 237 of them agreed to participate in the

study and 205 managers refused. The managers who worked in the hospital for at least 1 year were included in the scope of the study. 5 managers who did not meet this requirement were excluded and the study was completed with a total of 232 managers.

Data Collection Tool and Application: Questionnaire method was used as a data collection tool. In the first part of the questionnaire, questions related to the characteristics of the managers (role, gender, total management time, the duration of the management at the current hospital, formal education status in management) were included.

In the second part of the questionnaire, with 20 questions, managers were asked to evaluate the resource management capacity of the hospital where they work. These 20 questions are based on a 5-point Likert scale where 1 represents 'Significantly lower' and 5 represents 'Significantly higher'. For the questions in this section, Ling's (9) "Hospital Capacity Management System Survey" and Siferd's (21) study were used. 6 of the 20 questions in this section are about "equipment management capacity", 9 of them are about "workforce capacity" and 5 of them are about "facility management capacity". As a result of the exploratory factor analysis conducted to determine whether these 20 items reveal a meaningful factor structure or not, a three-factor structure has been reached in the form of equipment, workforce and facility management shown in Figure 1.



x2 (CMIN)	sd	x2/sd	TLI	CFI	NFI	RMSEA
359.456	157	2.290	0.879	0.900	0.838	0.075

Figure 1. Resource Management Capacity (RMC) Exploratory Factor Analysis Final Measurement Model and Fit Values

The data collection process in the study started in February 2017 and was completed at the end of July 2017. In the implementation of the questionnaire, the scatter and collect method was used and each hospital was visited at least three times to increase participation.

Data Analysis: SPSS 20 (IBM Statistical Package for the Social Sciences) and AMOS 23 statistical programs were used for data entry and analysis in the study. Descriptive and analytical analysis methods were used in the analysis of the research data.

The validity of the questionnaire was tested by factor analysis. Exploratory factor analysis was applied first to reach a small number of factors from the many items on the questionnaire. After reaching the reference intervals related to the exploratory factor analysis, the confirmatory factor analysis was performed to determine the accuracy of the established factors and the models were reviewed until the reference ranges were reached. After reaching the final model, reliability analysis based on Cronbach alpha coefficient was performed. The structural equation model was used to test the hypotheses of the study.

RESULTS

In this section, descriptive information about the characteristics of hospitals and managers within the scope of the study and analytical analysis about the factors affecting the resource management capacity of hospitals are included.

Table 1. Characteristics of the Hospitals within the Scope of the Research

Hospital Type	**Number**	**%**
General Hospital	27	65.9
Specialty Hospital	14	34.1
Hospital Age (Year)	**Number**	**%**
13 years and below	10	24.4
14–33 years	10	24.4
34–60 years	11	26.8
61 years and over	10	24.4
Number of Medical Speciaties (Sub-specialities are included)	**Number**	**%**
3-19	21	51.2
20 years and over	20	48.8

When the characteristics of the 41 hospitals included in the study are examined; 27 hospitals (65.9%) are general hospitals, 14 hospitals (34.1%) are private branch hospitals, the youngest hospital is 1.5 years old and the oldest hospital has been operating for 119 years. it was determined to be a hospital. In order to reveal the service diversity of the hospitals, it has been determined that the number of medical specialties served (including minor specialties) is between 3-19 in 21 of 41 hospitals, and between 20-51 in 20 hospitals.

Table 2 Characteristics of the Managers Participating in the Research

Role	**Number**	**%**
Hospital Chief Physician	20	8.6
Deputy Chief Physician	69	29.7
Administrative and Financial Services Manager	24	10.3
Administrative and Financial Services Deputy Manager	76	32.8
Health Care Services Manager	29	12.5
Health Care Services Deputy Manager	14	6.0
Gender	**Number**	**%**
Female	88	37.9
Male	138	59.5
No answer	6	2.6
Total Management Time	**Number**	**%**
Less than 5 years	136	58.6
5 years and above	84	36.2
No answer	12	5.2
Duration of management in the hospital where they work	**Number**	**%**
Less than 5 years	177	76.3
5 years and above	42	18.1
No answer	13	5.6
Formal Management Training Status	**Number**	**%**
Yes	159	68.5
No	63	27.2
No answer	10	4.3
Organizational Commitment	**Average**	**Ss**
Emotional Commitment	3.86	0.94
Continuance Commitment	2.57	0.79
Normative Commitment	3.29	0.71
Professional Commitment	**Average**	**Ss**
Emotional Commitment	3.87	0.63
Continuance Commitment	2.94	0.74
Normative Commitment	3.64	0.72
Organizational Identification	3.88	0.61

The characteristics of the managers who answered the questionnaire in the hospitals within the scope of the research are given in Table 2. Accordingly, 232 out of 437 managers in 41 hospitals agreed to participate in the study. 89 managers work in the group of chief physicians and their deputies, 100 people work in the administrative and financial services managers and deputies group, and 43 work in the positions of health care services managers and deputies.

It is observed that approximately 38% of the managers participating in the survey are women, 58.6% of them have been managers for less than 5 years, 76% of them have a management time in the hospital where they work is less than 5 years and 68.5% of them have received formal management training. 21% of the managers who received formal management training stated that they received courses and certificates, 3% associate degree, 26% undergraduate, and 49% post-graduate education.

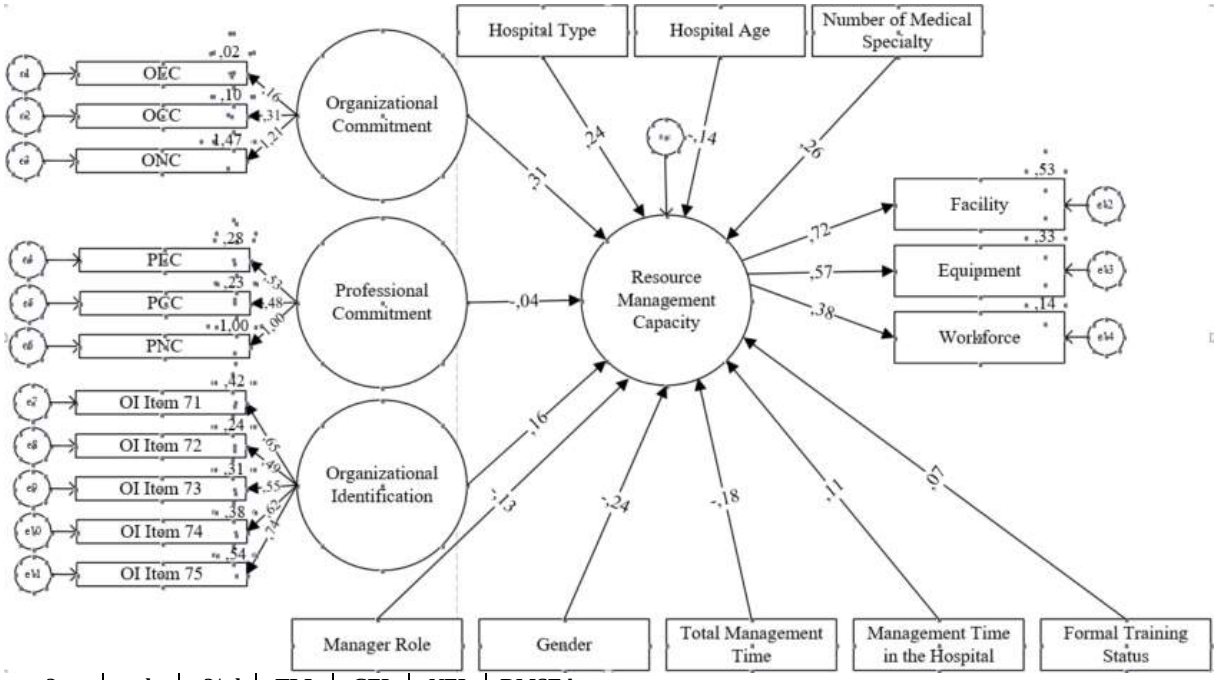
When the organizational and professional commitment and organizational identification levels of the hospital managers within the scope of the study are examined in Table 2, it is observed that their organizational emotional commitment and professional emotional commitment scores are very close to each other, professional continuance commitment levels are higher than organizational continuance commitment, and professional normative commitment levels are higher than organizational normative commitment levels.

When the organizational identification levels of the hospital managers who answered the questionnaire are examined, it is seen that the organizational identification scores (3.88 ± 0.61) are higher than the average value regarding the organizational and professional commitment levels. In a study conducted on healthcare professionals, the organizational identification level was calculated as 2.99 (27) according to the 5-point Likert scale, and in another study, the organizational identification level average of private sector employees was calculated as 3.76 (28). This situation shows that the organizational identification levels of the managers participating in the research are quite high.

In order to determine the factors affecting the resource management capacity of the hospitals

within the scope of the study, 2-stage structural equation models were created. In the initial structural model shown in Figure 2, in order to explain the resource management capacities of hospitals, the characteristics of the hospitals (type of hospital [being a general-specialty], hospital age and the number of medical specialties) and the characteristics of the managers (role, gender, total management time and duration of management in the hospital where they work and formal management training) and organizational commitment, professional commitment and organizational identification levels of managers are included as independent variables.

As seen in the initial model in Figure 2, it is seen that the goodness of fit values (x2/df = 3.665, TLI = 0.395, NFI = 0.460, CFI = 0.395, RMSEA = 0.112) are not within acceptable limits. Among the variables in the model, it is seen that the organizational commitment levels and gender of the managers, the type of the hospital and the number of medical specialties have a significant effect on the resource management capacity. On the other hand, it is observed that the professional commitment and organizational identification levels of the managers, the role of the managers, the total management time, duration of management in the hospital where they work, the formal management training status and the hospital age do not have a significant effect on the resource management capacity of the hospitals.

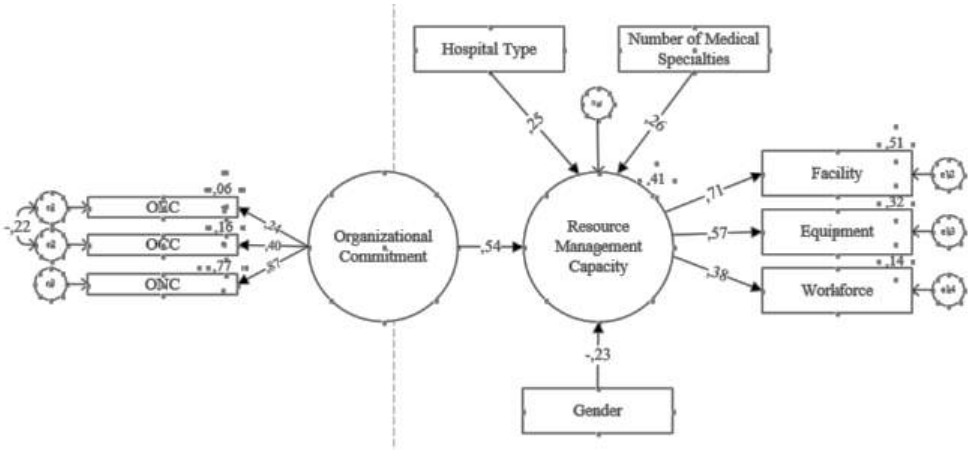


x2 (CMIN)	sd	x2/sd	TLI	CFI	NFI	RMSEA
755.055	206	3.665	0.395	0.460	0.395	0.112

Figure 2. Initial Structural Model Estimating the Resource Management Capacity of the Hospitals Under the Scope of the Research and the Fit Values

In order to obtain a model with higher fit values compared to the initial model and to increase the adaptation of the model to the data set, the second structural model in Figure 3 where the organizational commitment levels of the managers, the type of hospital, the number of medical specialties and the manager's gender were used as independent variables. The goodness of fit values of this model were calculated as x2/df = 1.364, TLI = 0.937, NFI = 0.866, CFI = 0.937, RMSEA = 0.041.

When the findings of the model were examined, it was seen that as the organizational commitment levels of the managers and the number of medical specialties of the hospitals increased, the resource management capacity of the hospitals increased/improved. It has been observed that the resource management capacity of specialty hospitals and the resource management capacity of hospitals with female managers are higher. According to this final structural model that predicts the resource management capacity of hospitals, H1a, H1b and H1c hypotheses were accepted, and H1d and H1e hypotheses were rejected.



x2 (CMIN)	sd	x2/sd	TLI	CFI	NFI	RMSEA
32.737	24	1.364	0.937	0.958	0.866	0.041

Figure 3. Final Structural Model Estimating the Resource Management Capacity of the Hospitals Under the Scope of the Research and the Fit Values

DISCUSSION

In this study, it was aimed to examine the effects of the hospital and manager characteristics and the organizational commitment, professional commitment and organizational identification levels of the managers on the resource management capacity of the hospitals.

The Organizational Commitment Scale developed by Meyer and Allen (29) was used to measure the organizational commitment of the hospital managers participating in the study, and the Professional Commitment Scale developed by Meyer, Allen and Smith (30) was used to measure the professional commitment levels. As a result of the validity and reliability analyzes, it was seen that the answers given to some questions did not conform to the original structures of the scales and were left out.

The organizational emotional commitment level of the managers participating in the study, measured with a total of three questions, was calculated as 3.86. Accordingly, it can be said that their level of commitment is above average. Organizational emotional commitment level is the positive attitude of individuals towards the organization they work with, and therefore it is desired to be at a high level. In a study conducted by Bedük and Yıldız on the mobbing and organizational commitment levels of hospital employees, the average level of organizational emotional commitment was found to be 2.89 according to the 5-point Likert scale (31). In a study conducted by Bayyurt and Kılıç, the organizational emotional commitment level of the hospital staff was determined as 2.91 according to the 5-point Likert scale (32). These results show that the organizational emotional commitment levels of managers within the scope of this study are higher than the results of similar studies.

The average level of organizational continuance commitment of the managers participating in the study was calculated as 2.57. Organizational continuance commitment refers to a negative situation and is expected to be low. In a study conducted on pharmaceutical industry managers, the organizational continuance commitment average was found to be 2.75 according to the 5-point Likert scale (33). These results show that the level of continuing commitment, which can be expressed as mandatory commitment, of hospital managers is more positive than the managers of the pharmaceutical sector. Unlike the original scale, the high level of normative commitment measured with five items in the study indicates the principal commitment of the manager to the organization she/he works with and is expected to be high.

In the research, the organizational normative commitment level of the administrators was found to be 3.29. In a study conducted on hospital staff, this average was 2.91 (32), while in another study on hospital staff, organizational normative commitment levels were found to be 2.95 according to the 5-point Likert scale (34). It is possible to interpret this difference as that managers have higher normative commitment levels compared to employees.

While 18 items were used in the original scale to measure the professional commitment levels of the managers participating in the study, it was found appropriate to use 14 items after the validity and reliability analysis of the research. The average professional emotional commitment level

of the managers participating in the study was calculated as 3.87. In a study conducted on nurses, the average of professional emotional commitment was found to be 3.5 according to the 5-point Likert scale (35). In another study conducted on hospital senior managers, the level of professional emotional commitment according to the 5-point Likert scale has an average value of 4.39 (36). These results show that the level of professional emotional commitment of the managers participating in the study is lower than the mentioned study.

The average occupational normative commitment dimension of the managers participating in the study was calculated as 3.64, in the study of Aktaş and Gürkan (35) it was 2.73 and in the study of Carlson (36) it was calculated as 2.63. These values show that the administrators participating in the research have a high level of normative commitment. The average level of professional continuance commitment, which is expected to be low, was found to be 2.94 in this study. In Carlson's (36) study, this value was calculated as 3.31. This situation shows that the managers participating in the research have a more positive value in compulsory continuation of their profession.

As a result of the validity and reliability analysis of the 5 items in the original scale in order to measure the organizational identification levels of the managers participating in the study, it was seen that the values were within the reference ranges. In the findings obtained, the organizational identification level average of the hospital managers participating in the study was calculated as 3.88. In a study conducted on healthcare professionals, the organizational identification level was calculated as 2.99 according to the 5-point Likert scale (27) and in another study, the organizational identification level of private sector employees was calculated as 3.76 (28). This situation shows that the organizational identification levels of the administrators participating in the research are quite high.

Another concept considered within the scope of the research is the hospital resource management capacity measured by the size of facility, equipment and workforce. The number of studies dealing with resource management capacity in hospitals with different dimensions is limited, as in this study. In general, human resources capacity measurements have been emphasized in studies (37) (38) (39).

In recent years, it has been observed that studies on the technological equipment dimension of resource management have been increasing due to the rapid development of health technologies on a global scale and the most important factor affecting health expenditures (40) (41).

According to the findings of the study, the type of hospital and the number of medical specialties that are among the characteristics of the hospitals significantly affect the resource management capacity of the hospital. It is thought that this result is due to the clear definition of the manner and scope of service in specialty hospitals and their better management of facilities, equipment and workforce capacities as they focus on a single area and provide services. In a study, it was stated that the type of hospital has a significant relationship with the technological level of hospitals, which is a dimension of resource management. According to this study, the use of technology is higher in specialty hospitals (42). In addition, it can be concluded that these results were reached in line with the importance given to the items of increasing the outpatient and surgery service capacity in the facility size with the highest factor load in the resource management capacity scale in specialty hospitals (0.71). Another hospital characteristic that significantly affects the resource management capacity of the hospitals covered by the research is the number of medical specialties. These findings show that as a result of the increase in the number of medical specialties served in general hospitals, the resource management capacity has also increased.

On the other hand, it has been revealed in the study that the resource management capacity of the hospitals does not differ according to their activity periods (hospital age). In the literature on the subject, there are various studies stating that the demographic characteristics of hospitals significantly affect the resource management capacity (43) (44) (13) as well as there are studies without such a relationship (9) (45). In Ling's study (9), the relationship between the training feature, one of the hospital demographic variables, and the resource management capacity was examined, but no meaningful results were obtained. Li and Benton (13) examined resource management capacity in three dimensions as facility, equipment and workforce as in this study and found that it showed significant relationships with hospital demographic characteristics (hospital size, hospital location, training feature). Li and Benton found a positive and significant relationship between the size of the hospital measured by the number of beds and the resource management capacity (13). The mentioned study stated that large hospitals manage demand changes better, they are more successful in managing workforce planning and service capacity, and that these results have a positive impact on resource management capacity. Li and Benton also stated that the most important variables affecting the resource management capacity in hospitals are the quality of outpatient services, workforce skills and information technologies (13).

According to the findings of the study, the gender of the manager, which is considered among the demographic variables of the managers, significantly affects the resource management capacity of the hospitals. According to these findings, the resource management capacity of the hospitals within the scope of the study was evaluated as more successful by female managers. There are other studies stating that female managers are more successful in evaluating resource management capacity (46) (47). In these studies conducted in different sectors, it was stated that female managers are more successful in sharing information and leadership, and they are more successful than men, especially in labor resource planning (48).

According to the findings obtained in the study, features such as the role of hospital managers, total and management time in the hospital they work, and whether they received formal training in management are not in a meaningful relationship with the resource management capacity of the hospitals they manage. The reason why managers participating in the study did not achieve success in resource management capacity, despite receiving formal management training, is thought to be due to the fact that the Ministry of Health hospitals operate under the central authority, not autonomous.

Different results have been reached in the literature regarding the effect of the management time in the organization where the manager works on the resource management capacity. In one study, it was stated that there are significant relationships between management time and resource management capacity (49), while no significant relationships were found in another study (50).

Alexander and Lee classified the time that a manager worked in the organization as short, medium and long, and stated that those in the medium-term working time were more successful in resource management capacity, attributing this to the adaptation process in short working time and the managers in the same position during long working time (49).

Alexander and Lee attributed these results to the fact that short-term managers are not able to make the right decisions about resource management capacity because they are involved in the adaptation process in their organizations. In long-term managers, he commented that if the manager stayed in the same position for a long time, this situation decreased the motivation of the employee and this negatively affected the resource management capacity decisions (49). It can be stated that the different findings of the studies are due to the fact that the resource management capacity is measured with different dimensions and methods in the mentioned studies. For example, in the study conducted by Alexander and Lee (49), it is seen that resource management capacity is measured only in terms of labor capacity. In addition, contrary to the findings obtained in this study, there are studies in the literature that found that the managerial position of hospital managers significantly affects the hospital resource management capacity (51). In their study, Currie and Procter stated that mid-level managers are more successful in human resources management than senior managers because of their decision-making power and partly involvement in operational affairs when they have an influence on strategic decisions (51).

Another important finding of the study is that there is a significant relationship between the resource management capacity of the hospitals within the scope of the study and the organizational commitment levels of the managers, whereas there is no significant relationship between the professional commitment and organizational identification levels of the managers and the resource management capacity of the hospitals. As the level of commitment of managers to the hospital they work in increases, it is observed that there are positive developments in the resource management capacity of the hospitals in terms of facility, equipment and workforce dimensions.

CONCLUSION

In this study; it is aimed to examine the relationship between hospital managers' organizational commitment, professional commitment and organizational identification levels on resource management capacity measured by manager's perceptions of workforce, facility and equipment dimensions. In addition, the institutional and managerial characteristics that may have an impact on the resource management capacities of the hospitals were also taken into consideration.

The study was conducted on 232 senior executives who have been administrators for at least one year and volunteered to participate in 41 hospitals affiliated to the Ministry of Health in Ankara and Istanbul provinces. From the findings of the study, it was concluded that the resource management capacities of the hospitals included in the study, measured by the dimensions of facilities, equipment and workforce, were significantly affected by the type of hospitals and the number of medical specialties.

The resource management capacity of specialty hospitals and hospitals with a higher number of medical specialties they serve is at a higher level. According to this result, the experience of specialty hospitals and hospitals with a higher number of medical specialties in resource management capacity can be used to improve resource management capacities. However, there is no significant relationship between the resource

management capacity of hospitals and their duration of activity (hospital age). On the other hand, while there is a significant relationship between the gender of the managers participating in the research and the resource management capacity of the hospitals, female managers better manage the equipment, work force and facility resources of the hospitals they work. The role of the managers, the total management time, the management time at the hospital where they work, and whether or not they have received formal training on management before do not have a significant effect on the resource management capacity of the hospitals. Considering that male employees do not want to take orders from female managers and that male employees' negative attitudes towards female managers have been expressed in different studies (52) (53) the success of female managers in resource management capacity should be taken into account despite these negativities. According to this result, it may be suggested that central authorities carry out studies to increase the number of female managers in hospitals.

The organizational commitment levels of the managers participating in the study, measured in terms of emotional, attendance and normative commitment dimensions, positively affect the resource management capacity of the hospitals. Managers with higher levels of commitment to their hospitals better manage equipment, labor and facility resources. Considering that the organizational commitment levels of managers positively affect the resource management capacities of hospitals, it may be beneficial to pay attention to the normative commitment dimension, which has the highest factor load among the dimensions that constitute the organizational commitment levels of managers. On the other hand, there were no significant relationships between managers' professional commitment and organizational identification levels and hospital resource management capacities.

The results of the study showed that the resource management capacity of the hospitals, measured in terms of facility, equipment and workforce dimensions, was positively affected by the type of hospitals and the number of medical specialties. According to this result, specialty hospitals perform facility management better, manage their equipment better and use human resources more efficiently than general hospitals. While providing services or focusing on a specific area enables resources to be planned, used and managed relatively more rationally, as the variety of services increases, the type and number of facilities, equipment and personnel required for each service will differ, so planning, using and managing the necessary inputs will become more difficult. Therefore, it should be noted that resource management in general hospitals is relatively more complex. On the other hand, the fact that the resource management capacity of the hospitals with a high number of medical specialties in the study seems to contradict the explanation made about the specialty and the general hospital, in fact, the increase in the number of medical specialties can be explained by the more professional management of the resource management of the hospitals.

37.9% of the managers participating in the research are women and women managers manage the resources of the hospitals they work in better. These results support the decisions regarding the need for more opportunities for female managers in public and private hospitals. Another variable that affects the resource management capacity of hospitals in the study is the organizational commitment levels of the managers. In parallel with many studies conducted on this subject (54) (55) it is observed that the level of commitment of managers to their hospitals has a positive effect on the resource management capacities of hospitals. Baird's study highlights the importance of providing adequate facilities and organizational commitment within hospitals and suggest that managers should try to enhance the provision of such resources in an attempt to elicit commitment within their hospitals (55). The finding that activities to increase the level of organizational commitment in hospitals will also affect the resource management capacities of hospitals positively should be taken into consideration especially by the central authorities.

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RESEARCH ARTICLE

Ekin Ilkeli[1]
Ali Cemal Duzgun[2]

[1]Cardiovascular Surgery, Duzce State Hospital, Duzce, Turkey
[2]Cardiovascular Surgery, Ankara Training and Research Hospital, Ankara, Turkey

Corresponding Author:
Ekin Ilkeli
Cardiovascular Surgery, Duzce State Hospital, Duzce, Turkey
Phone: +90380 529 13 00
mail: ekinilkeli@hotmail.com

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The Effectiveness of New Oral Anticoagulants in the Treatment of Lower Extremity Venous Thrombosis: A Retrospective Clinical Study

ABSTRACT

Objective: This clinical study included a retrospective evaluation of 138 patients using new oral anticoagulants (rivaroxaban, dabigatran, apixaban, edoxaban) for lower extremity deep vein thrombosis.

Methods: 138 patients using new oral anticoagulant drugs were included in the retrospective study. Demographic characteristics, diagnosis and treatment charts, radiological images, epicrisis notes of the patients were recorded. Records of each patient were reviewed during their 12 months of follow-up. New oral anticoagulant efficacy; It was evaluated by measuring thigh and calf diameters before and after treatment, whether there was recanalization in Doppler USG (recanalization> 75%), recanalization time, bleeding side effects and recovery times with treatment, and recurrence rates. The data were analyzed statistically using a statistics program.

Results: A significant difference was found when the mean thigh diameter measurements measured at the beginning of the treatment (Mean ± SD: 75,41) and the mean thigh diameter measured after the treatment (Mean ± SD: 54,63) were compared ($p<0.05$). A significant difference was found when the mean calf diameter measurements (Mean ± SD: 43.99) measured at the beginning of the treatment and the mean calf diameter measured after the treatment were compared ($p<0.05$). Post-treatment Doppler USG showed complete recanalization rate in 54% (75 patients) at 3 months and 25% (35 patients) at 6 months. At the end of the 6th month, the total recanalization rate occurred in 80% (110) patients.

Conclusions: New oral anticoagulants (rivaroxaban, dabigatran, apixaban, edoxaban) are very effective in the treatment of lower extremity deep venous thrombosis, both in providing recanalization and in terms of clinical improvement in early and midterm.

Keywords: New Oral Anticoagulants, Deep Vein Thrombosis, Thrombophilia.

Alt Ekstremite Venöz Tromboz Tedavisinde Yeni Oral Antikoagulanların Etkinliği: Retrospektif Klinik Çalışma

ÖZET

Amaç: Bu klinik çalışma alt ekstremite derin ven trombozu nedeniyle yeni oral antikoagulan ilaç (rivaroksaban, dabigatran,apiksaban, edoksaban) kullanan 138 hastanın retrospektif olarak incelenmesini içermektedir.

Gereç ve Yöntem: Retrospektif çalışmaya yeni oral antikoagulan ilaç kullanan 138 hasta dahil edildi. Hastaların demografik özellikleri, tanı ve tedavi şemaları, radyolojik görüntüleri, epikriz notları kaydedildi. Her bir hastanın kayıtları takip edildikleri 12 ay boyunca incelendi. Yeni oral antikoagulan etkinliği; tedavi öncesi ve sonrası uyluk ve baldır çaplarının ölçülmesi, doppler USG'de rekanalizasyon olup olmadığı (rekanalizasyon>%75), rekanalizasyon süresi, kanama yan etkileri ve tedavi ile iyileşme süreleri, rekürrens oranları ölçülerek değerlendirildi. Veriler istatistik programı kullanılarak istatiksel olarak incelendi.

Bulgular: Tedavi başlangıcında ölçülen uyluk çap ölçümleri ortalaması (Ort±SS:75,41) ile tedavi sonrası ölçülen uyluk çap ortalaması (Ort±SS:54,63) karşılaştırıldığında anlamlı fark bulundu ($p<0.05$). Tedavi başlangıcında ölçülen baldır çap ölçümleri ortalamaları (Ort±SS:43,99) ile tedavi sonrası ölçülen baldır çap ortalaması karşılaştırıldığında anlamlı fark bulundu. ($p<0.05$). Hastalarda tedavi sonrası doppler USG de tam rekanalizasyon oranı 3.ayda %54 (75 hasta) ,6 ayda %25 (35 hasta) da görüldü.6.ay sonunda toplam rekanalizasyon oranı %80 (110) hastada gerçekleşmiştir.

Sonuç: Yeni oral antikoagulanlar (rivaroksaban, dabigatran,apiksaban, edoksaban) alt ekstremite derin venöz tromboz tedavisinde, erken ve orta dönemde hem rekanalizasyonun sağlanmasında hem klinik düzelme anlamında oldukça etkilidir.

Anahtar Kelimeler: Yeni Antikoagülan Ajanlar, Derin Ven Trombozu, Trombofili.

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konuralptipdergi@duzce.edu.tr
konuralptipdergisi@gmail.com
www.konuralptipdergi.duzce.edu.tr

INTRODUCTION

New oral anticoagulants (NOACs) with a wider therapeutic range and less food exposure are also very current in the treatment of venous thrombosis and prophylaxis. In recent years, new oral anticoagulant agents have been preferred in the treatment of serious diseases with high thrombosis risk (such as deep venous thrombosis, pulmonary embolism, atrial fibrillation), since they have less potential for side effects and do not require routine blood tests (1).Warfarin, a vitamin K antagonist,has been replaced by new oral anticoagulants in the standard treatment of deep venous thrombosis. Studies have shown that NOACs keeps the risk of major bleeding in a more reliable range (2). Similarly, significant reductions were seen in the risk of stroke and systemic embolism (3). We retrospectively present the clinical results of NOACs that we use in the treatment of the Lower Extremity deep venous thrombosis (DVT) over 138 patients.

MATERIAL AND METHODS

138 patients who were diagnosed with DVT for the first time in the cardiovascular surgery outpatient clinic between January 2015 andJune 2018 were included in the study. After obtaining the approval of the ethics committee (Ankara Education and Research Hospital; Decision Number:368/2020, Date: September 17,2020) the patient records were examined retrospectively and the data were obtained. There were 242 patients diagnosed with DVT who were using oral anticoagulant drugs. Patients who received vitamin K antagonist (warfarin) treatment, who were heparinized with a diagnosis of acute and subacute DVT and who received endovascular therapy (venousstent, vena cava inferior filter, pharmacomechanical thrombectomy) were excluded from the study. Thus, a homogeneous patient population (138 patients) receiving only oral anticoagulant (rivaroxaban, dabigatran, apixaban, edoxaban) was created and more specific results were tried to be achieved. New oral anticoagulant efficacy; It was evaluated by measuring the thigh and calf diameters before and after the treatment, whether there was recanalization (recanalization> 75%) in the doppler USG taken at the 3rd and 6th months, recanalization time, bleeding side effects and recovery times with treatment, and recurrence rates.

Data analysis:Minitab 16 version (Minitab Inc. State College, Pennsylvania, USA) statistical program was used for analysis of patient data. The Pearson correlation coefficient was calculated for the investigation of the relationship between the parametric data, and the Spearman correlation coefficient for the investigation of the relationship between the nominal data. Student's t test was used for parametric data, and Mann-Whitney U-Wilcoxon Rank Sum W test was used for nominal data to investigate the difference between groups, and $p<0.05$ was considered significant. The X2 test was used to investigate whether there was a difference between the groups in terms of the individual distribution of the causative diseases.

RESULTS

Data of 138 patients using NOACs (rivaroxaban, dabigatran, apixaban, edoxaban) for the treatment of deep venous thrombosis were evaluated. 46% (64) of the patients were male and 54% (74) were female. The mean age of the patients was found as Mean ± SD: 56.72. Of the patients who received NOACs treatment with a diagnosis of DVT, 28% (38 patients) used apixaban, 26% (36 patients) rivaroxaban, 26% (36 patients) dabigatran, 20% (28 patients) edoxaban. When the duration of treatment was examined, it was understood that 15% (21 patients) were treated for 3 months, 49% (36 patients) received 6 months of treatment, 49% (68 patients) received 12 treatments.

A significant difference was found when the mean thigh diameter measurements (Mean ± SD: 75,41) measured at the beginning of the treatment and the mean thigh diameter measured after the treatment (Mean ± SD: 54,63) were compared ($p<0.05$). Similarly, a significant difference was found when the mean calf diameter measurements (Mean ± SD: 43.99) measured at the beginning of the treatment and the mean calf diameter measured after the treatment were compared ($p<0.05$).

Post-treatment Doppler USG showed complete recanalization rate in 54% (75 patients) at 3 months and 25% (35 patients) at 6 months. At the end of the 6th month, the total recanalization rate occurred in 80% (110) patients. Postthrombotic syndrome occurred in only 5% (7 patients) of the treated patients. The recurrence rate was 5% (7 patients) in all patients using NOACs .There was no significant difference between recurrent DVT due to etiological reasons. During the 12-month follow-up of 138 patients, the major bleeding rate was observed in 2% (3 patients), and the minor bleeding rate was observed in 4% (6) patients (Table 1).

Table 1. Patient demographic characteristics

Number of patients (138)		Number	Percent
Age			
Average age	Mean±SD: 56.72		
Age range (years)	(22-88)		
Sex			
Male		64	46
Female		74	54
Use of NOACs			
Apiksaban		38	28
Rivoksaban		36	26
Dabigatran		36	26
Endoksaban		28	20
Full recanalization time			
3 Months		75	54
6 Months		35	25
12 Months		21	15
Average thigh diameters (cm)			
Before	Mean±SD: 75.41		
After	Mean±SD: 54.63		
Average calf diameters (cm)			
Before	Mean±SD: 43.99		
After	Mean±SD: 41.13		
Postrombotic syndrome		7	5
Recurrence		7	5
Major bleeding		3	2
Minör bleeding		6	4

When the etiology of deep venous thrombosis was examined, it was seen that genetic factors played a role in 17% (24 patients) of 138 patients using NOACs. The most common cause in patients was immobilization with 30% (41 patients). Post-surgical DVT was seen in 15% to 21 patients. Cancer was observed in 12 to 16 patients in the etiology of patients using NOACs (Table 2).

Table 2. DVT etiology of patients

DVT causes	Number (n)	Percent (%)
Genetic factors Factor V Leiden mutation 13 (54 %) Protrombin mutation 6 (25%) Antithrombin III deficiency 3 (13%) Hyperhomocysteinemia 2 (8 %)	24	17
Cerrahi operasyon sonrası	21	15
Immobilization (Hemiplegia, Paraplegia, long travel)	41	30
Traumatic (vascular ınjury)	6	4
Oral contraceptives	8	6
Obesity	6	4
Cancer	16	12
Other	16	12

The most common localization of DVT was femoro-popliteal involvement with 30% (42 patients). This was followed by common femoral vein involvement in 28% (39 patients) and popliteal vein involvement in 17% (23 patients) (Table 3).

Table 3. DVT site

DVT localization	Number (n)	Percent (%)
Common femoral vein	39 left:22	28
External illac vein	13 left:8	9
Popliteal vein	23 left:14	17
Popliteal –femoral vein	42 left26	30
Femoral and illiac ven	21 left:15	15

In the statistical analysis, no significant relationship was found between the causes of the disease and recurrence rates, postthrombotic syndrome (PTS) development rates, recanalization rates and diameter measurements, and treatment durations.

DISCUSSION

Venous thromboembolism (VTE) is a multifactorial disease and patients may have more than one risk factor at the same time. The more risk factors the patient has, the higher the risk of developing venous thromboembolism (4).

Three main pathological mechanisms that facilitate the development of VTE were described by the famous pathologist Rudolf Virchow in the early 19th century. Stasis, vascular wall damage and hypercoagulability in the blood are the three main criteria and the presence of at least one criterion in the patient is sufficient to increase the risk. DVT is a disease that should be started as soon as the diagnosis is made due to its high prevalence and potentially fatal outcomes (5).

In the untreated follow-up of deep vein thrombosis, pulmonary embolism (PE), post-thrombophlebitic syndrome (PTS) with extremely high long-term morbidity and pulmonary hypertension may occur. Therefore, treatment should be started as soon as the diagnosis is made. The aim of the treatment is to prevent these three complications, as well as the prevention of relapses. Therefore, it is recommended to continue long-term treatment when necessary. Acute DVT treatment; It has two phases: initial treatment and long-term treatment after the onset. In the treatment, it is aimed to prevent new attacks in the long term by treating the acute attack and preventing the clot from spreading and embolization to the lungs (6,7,8).

Most cases of DVT are hidden and usually resolve spontaneously without complications. When symptomatic DVT is diagnosed, 40% of patients have silent PE. According to an epidemiological model, more than 370 000 deaths were caused by VTE in six European countries with a total population of 454.4 million people in 2004. 34 percent of these patients died unexpectedly or within hours of the acute incident, before treatment could begin or take effect. In 59 percent of the other patients, death was caused by acute PE, which was diagnosed after death. (9,10,11)

Symptomatic PE develops in approximately 4% of patients treated with DVT. PE develops in about 1% of postoperative patients. The long-term morbidity of DVT is the postthrombotic syndrome that develops in approximately one quarter of symptomatic proximal DVT cases. Most cases develop within 2 years afterwards. PE and DVT may progress in 13% of the patients, although they have received full treatment (9,10).

Anticoagulant therapy is recommended for 3-12 months, depending on the site of thrombosis and the presence of ongoing risk factors. Lifetime anticoagulation therapy can be recommended for recurrent episodes of dvt, chronic clotting problem, or life-threatening PE. This treatment protocol has less than 12% cumulative risk of bleeding complications. To continue long-term anticoagulant therapy, the benefit-risk ratio should be evaluated at regular intervals (11).

The purpose of long-term treatment in DVT is to prevent recurrent VTE attacks that are not directly related to the acute event. In patients with DVT that develops secondary to a transient risk factor, anticoagulation for 3 months is included in all guidelines as a very strong recommendation. Similarly, 3-month anticoagulant therapy is considered to be sufficient in patients with first distal DVT that are not triggered. The main problem is how long the treatment will continue in the first proximal DVT cases that are triggered. Long-term anticoagulant therapy is particularly beneficial in male patients, patients with moderate-to-advanced post-thrombotic syndrome and high d-dimer levels one month later. Therefore, long-term treatment is recommended if the risk of bleeding is low and effective anticoagulant follow-up can be performed in patients who have had their first attack. In the second DVT attack that is not triggered, long-term secondary protection is appropriate. Low Molecular Weight Heparin (LMWH) is recommended in the first 3-6 months of long-term anticoagulant administration in DVT and cancer patients. Then anticoagulation should be given with LMWH or warfarin until the cancer is cured or for a long time. Each patient undergoing long-term anticoagulation should be explained in detail the risk-benefit ratio of the treatment and the patient's preferences should be considered. It is recommended to evaluate the benefit-risk ratios at regular intervals for patients whose treatment period is extended (12, 13,14). In our study, which we examined rectospectively, patients using NOACs received early response in distal thrombosis within the first 3 months. Sufficient response was obtained in the first 3 months, especially in women using oral contraceptives and patients with genetic etiology at a young age.

Warfarin is the first anticoagulant drug used in the treatment of venous thromboembolism. Due to the narrow therapeutic range, routine International normalized ratio (INR) monitoring, high drug-food interaction and potential for bleeding, it has offered an alternative to the constant search for new anticoagulants. Alternative NOACs are used instead of warfarin in the treatment of deep venous thrombosis due to its wide therapeutic range, less drug-food interaction, no need for INR follow-up and less bleeding potential.

The pharmacological properties and guideline recommendations of NOACs have been defined in large studies (Table 4).

Table 4. Pharmacological properties and recommendations of new oral anticoagulants

	Rivaroksaban	Dabigatran	Apiksaban	Endoksaban
Action	Factor xa inhibitor	Factor IIa	Factor xa inhibitor	Factör xa inhibitor
Bioavailability	80-100 %	3-7 %	50-66 %	62 %
Renal elimination	33 %	80 %	27 %	50 %
Antidote	Andexanet alfa	İdaricuzimab	Andexanet alfa	Andexanet alfa
Half life (hours)	7-13	12-17	8-15	8-10
Interaction	p-glycoprotein transporter inhibitors + CYP3A4 inhibitors	p-glycoprotein transporter inhibitors	p-glycoprotein transporter inhibitors + CYP3A4 inhibitors	p-glycoprotein transporter inhibitors + CYP3A4 inhibitors
Non-bleeding side effects	Peripheral edema 5 %	Dyspepsia 35 %	Rare	Rare
Conditions and Recommendations	In the initial and continuation treatment of DVT and PE Prophylaxis after total knee and hip replacement	Treatment of DVT and PE Recurrence DVT,PE Prophylaxis after total knee and hip replacement	Treatment of DVT, PE to prevent recurrence, Prophylaxis after total knee and hip replacement	Treatment of DVT, PE to prevent recurrence, Prophylaxis after total knee and hip replacement (ın Japan) *

* The table was created as a result of meta-analysis and clinical studies. (Ref: 8,17,18)

There are many multi-population prospective, double-blind, randomized studies on NOACs. The data of 27,023 patients in all phase 3 studies comparing rivaroxaban, apixaban, edoxaban, and dabigatran with vitamin K antagonists were examined in a meta-analysis and according to the following results, VTE recurrence was found to be similar in the NOACs and warfarin groups (2.0%; 2.2%, respectively.). Major bleeding was found 39% lower in NOACs users compared to Vitamin K antagonists (VKA) users ($p = 0.02$). In the subgroup analysis, NOACs resulted in less VTE recurrence in patients 75 years of age and older and in cancer patients than in patients using warfarin. ($p = 0.003$ for 75 years old and $p = 0.02$ for cancer subgroup) As a result, studies have shown that direct thrombin and Factor Xa inhibitors are at least as successful as standard treatments in the treatment of acute VTE (15,20).

Standard doses have been established for the use of new oral anticoagulants (Table 5).

Table 5. Standard doses of new oral anticoagulants in the treatment of DVT

New oral anticoagulant	Initial treatment	During the treatment	Long-term treatment
Dabigatran	LMWH or unfractionated heparin*	Dabigatran 150 mg 2x1	Dabigatran 150 mg 2x1
Rivaroksaban	15 mg 2x1	20 mg 1x1	20 mg 1x1
Apiksaban	10 mg 2x1	5 mg 2x1	2.5 mg 2x1
Edoksaban	LMWH or unfractionated heparin *	Edoksaban 60 mg 1x1	Edoksaban 60 mg 1x1

Dabigatran and edoxaban initially need a heparin bridge. Standard treatment doses should be applied by calculating patient-based benefit / risk. (Ref:8,17,18)

However, the recommendation of clinicians is to adjust the treatment doses on patient basis by calculating benefit / risk. Dose adjustment is recommended for elderly patients, cancer patients, and patients with renal insufficiency. Clinical applications of two NOACs (dabigatran and apixaban) initially require a heparin bridge. Some antimalarial (quinidine), anti-fungal (ketoconazole), anti-tuberculosis (rifampicin), and antibiotic drugs (clarithromycin) may increase NOACs-drug interactions through P-pg or CYP3A4 pathways. LMWH treatment is recommended for VTE

patients with active cancer (16,17,18). One of the important conclusions we have drawn from the study is that age, cancer, immobilization stand out as etiological reasons (more than half of the patients) and have features in terms of treatment. One of the controversial points is which treatment option will be more appropriate in the elderly and cancer patients. With the introduction of two antidotes (idaricuzimab for dabigatran and andexanet alfa for factor Xa inhibitors), the potential for use of NOACs in patients with high bleeding risk is expected to increase. Especially in elderly patients over 75 years of age, the risk of developing DVT is higher and the risk of bleeding is much higher. Therefore, new oral anticoagulants are preferred. Because, as mentioned above, the bleeding potential is lower in patients using NOACs. Because LMWHs are preferred by clinicians due to their antitumoral effects in patients of this age, larger studies are needed on this subject. It is recommended not to use these agents in patients with creatinine clearance ≤ 15 ml / min, prefer low doses of factor Xa inhibitors rather than dabigatran in patients with 15-30 ml / min, and dose selection according to the risk of bleeding in patients with 30-50 ml / min. Similarly, low dose preference is recommended for patients over 80 years of age and patients with body weight less than 60 kg. Benefit / risk calculation should be considered especially in the elderly and cancer patients (19,21).

However, there are still some controversial points in terms of NOACs. Studies on the use of new NOACs in patients such as antiphospholipid syndrome (APS) have not been terminated. Since there are no clinical studies completed with these drugs in patients with APS, the available information on the drugs in question is still limited. Disadvantage of NOACs treatment; It is not used in children, advanced liver and kidney patients, mechanical heart valve patients and it is more costly.

CONCLUSION

As a result, as can be understood from the data of the patients included in the study, the measurements of the leg diameters of the patients and the thrombus recanalization were achieved in the ideal measurements in the 3rd and 6th months. New oral anticoagulant drugs (rivaroxaban, dabigatran, apixaban, edoxaban), which have been used for more than ten years, provide sufficient efficacy in the treatment of deep venous thrombosis due to their more advantages and clinical improvement in patients

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RESEARCH ARTICLE

Cuneyt Cam[1*]
Emrah Atay[1]
Hatice Aygar[1]
Ece Elif Ocal[1]
Saniye Goktas[1]
Burhanettin Isikli [1]
Muhammed Fatih Onsuz[1]
Selma Metintas [1]

[1] Eskisehir Osmangazi University Faculty of Medicine, Department of Public Health, Eskisehir, Turkey

Corresponding Author:
Cuneyt Cam
Eskisehir Osmangazi University Faculty of Medicine, Department of Public Health, Eskisehir, Turkey
Phone: +90 555 558 87 08
mail: drcuneytcam@gmail.com

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konuralptipdergi@duzce.edu.tr
konuralptipdergisi@gmail.com
www.konuralptipdergi.duzce.edu.tr

Evaluation of Associated Factors with Nutrition Behavior and Dietary Self-efficacy for Healthy Food Choice among Primary School Students

ABSTRACT

Objective: The aim of the study was to investigate the associated factors with nutrition behavior and dietary self-efficacy for healthy food choices among primary school students.

Methods: The study is a cross-sectional research conducted with 4th grade students in the city center of Eskisehir in the 2018 academic year. The study group consisted of 402 students studying in six primary schools in the city center of Eskisehir. Data of the study were collected using a questionnaire including socio-demographic characteristics, Food Behavior Scale (FBS), and Children Dietary Self-efficacy Scale (CDSS).

Results: The mean age of the students in the study group was 9.88 ± 0.44 years and 51.0% of the students were female. Of the participants 19.9% were overweight and 10.2% were obese. While female students in CDSS chose healthy food with a mean ± SD 65% ± 24 percentages, male students chose healthy food with a mean ± SD 55% ± 25 percentages ($p<0.001$). Medium level positive relation ($r = 0.426$, $p<0.001$) was detected between scores taken from FBS and CDSS in Spearman Correlation Analysis. In the multiple linear regression performed to determine the relationship between FBS and CDSS after controlling the effect of related factors, it was determined that nutrition behavior indicated a positive relation ((β (95% CI): 0.398 (0.301-0.495)) with CDSS score.

Conclusions: Dietary self-efficacy was determined as a factor influencing nutrition behavior. In this regard, it was concluded that monitoring the close relationship between nutrition behavior and dietary self-efficacy could be useful beginning from early ages.

Keywords: Nutrition Behavior, Dietary Self-efficacy, Primary School Students, Turkey

İlkokul Öğrencilerinin Sağlıklı Gıda Tercihlerinde Beslenme Davranışı ile İlişkili Olabilecek Faktörlerin ve Beslenme Öz-yeterliği ile İlişkisinin Değerlendirilmesi

ÖZET

Amaç: Bu çalışma, ilkokul öğrencilerinin sağlıklı gıda tercihlerinde beslenme davranışı ile ilişkili olabilecek faktörlerin ve beslenme öz-yeterliği ile ilişkisinin değerlendirilmesi amacıyla yapılmıştır.

Gereç ve Yöntem: Çalışma, 2018 eğitim-öğretim döneminde Eskişehir il merkezinde bulunan ilkokul dördüncü sınıf öğrencilerinde yapılan kesitsel tipte bir araştırmadır. Çalışma grubu, Eskişehir il merkezinde bulunan altı ilkokulda öğrenim gören 402 öğrenciden oluşmaktadır. Çalışmanın verileri sosyo-demografik özellikleri, Beslenme Davranış Ölçeği (BDÖ) ve Çocuk Beslenme Öz-yeterlik Ölçeği (ÇBÖÖ) sorularını içeren bir anket form kullanılarak toplandı.

Bulgular: Çalışma grubundaki öğrencilerin yaş ortalaması 9,88 ± 0,44 yıl olup, öğrencilerin %51,0'ı kız idi. Bireylerin %19,9'u fazla kilolu ve %10,2'si obezdi. ÇBÖÖ'de kız öğrenciler ortalama %65 ± 24 ile sağlıklı besinleri seçerken, erkek öğrenciler ortalama %55 ± 25 ile sağlıklı besinleri seçtiler ($p<0,001$). Spearman Korelasyon Analizinde BDÖ ve ÇBÖÖ'den alınan puanlar arasında orta düzeyde pozitif ilişki ($r=0,426$, $p<0,001$) saptandı. İlişkili faktörlerin etkisi kontrol edildikten sonra BDÖ ve ÇBÖÖ arasındaki ilişkiyi belirlemek için yapılan çoklu lineer regresyonda, beslenme davranışının ÇBÖÖ ile pozitif bir ilişki ((β (% 95 CI): 0,398 (0,301-0,495)) gösterdiği belirlendi.

Sonuç: Beslenme öz-yeterliği, beslenme davranışını etkileyen bir faktör olarak saptandı. Bu bağlamda, beslenme davranışı ile beslenme öz-yeterliği arasındaki yakın ilişkinin izlenmesinin erken yaşlardan itibaren faydalı olabileceği sonucuna varılmıştır.

Anahtar Kelimeler: Beslenme Davranışı, Öz-yeterlik, İlkokul Öğrencileri, Türkiye

INTRODUCTION

Nutrition is known as one of the most important environmental factors in physical and mental development in the early stages of life (1). Since childhood is a period with rapid mental and physical development, an adequate and balanced diet which is expressed as the intake of sufficient energy, protein, carbohydrate, vitamin, mineral, and other elements, has crucial importance to provide normal and healthy growth (2). In addition, a balanced diet in childhood is a decisive factor for adulthood health conditions as well (3,4). Nutrition more than necessary for healthy growth and development causes obesity starting from childhood and maintaining during all adulthood and later this leads to diseases such as diabetes mellitus, hyperlipidemia, and hypertension (5,6). Therefore healthy nutrition habits during childhood are regarded as having positive effects on life-long disease risks as well as growth and development (7).

Parents have a crucial role in shaping children's eating habits (8). They realize this through their eating behaviors and table or nutrition management practices. In addition, they provide their children to experience from first hand by determining their children's eating preferences, consumption patterns, and food that their children have access. Although when children grow up and start education, their teachers and peers become more important, the family at the heart of the social environment plays a crucial role in shaping the eating behavior of children (9,10).

Individuals are accepted as learners who both create a social environment and influenced by this. Social cognitive learning theory (SCLT) analyze individuals learning by monitoring others and process that they succeed to control their behaviors progressively by considering continuous interaction between individual and environmental determinants causing changes in individuals psychology. This theory is based on reciprocal determinism, symbolizing capability, forethought capability, vicarious capability, self-regulatory capability, self-reflective capability, and self-efficacy principles (11). SCLT heavily used in health behavioral researches is also used for interventions encouraging healthy eating among children (12-16). SCLT emphasizes the importance of individual, environmental, and behavioral factors and their roles on affecting behaviors. Faith on individuals' ability to realize a significant behavior, self-efficacy which is defined as self-confidence about realizing a behavior and one of the fundamental principles within SCLT is acknowledged as central determinants of behaviors in SCLT. Self-efficacy revealed as a key concept in SCLT by Bandura is based on four interacting information sources (17). This is explained as the first-hand experience of similar behavior (mastery experience), finding an opportunity to monitor others similar behaviors (vicarious experience), convinced by an authority (verbal or social persuasion) and perception of the individual's own physiological and emotional situation (physiological and emotional experience) (18). Self-efficacy has a crucial role in many health behaviors (4). For example, dietary self-efficacy is perceived sufficiency level in order to make healthy nutrition choices even he/she meets potential obstacles and eating habits are indicated as indirect body mass index determinants (19,20). Researches about this issue include adolescents and beyond periods and there is not enough data for the primary school period.

The aim of the study was to investigate the associated factors with nutrition behavior and dietary self-efficacy for healthy food choices among primary school students.

MATERIAL AND METHODS

The study was a cross-sectional research conducted with 4th grade students in the city center of Eskisehir in the 2018 academic year. Primary schools of the city were divided into 3 layers in line with the socio-economic conditions of the society living there. All the 4th grade students from one or more selected schools from all layers were included in the study. The selection was made with a population-weighted draw. The study group consisted of 402 students studying in six primary schools in the city center of Eskisehir.

Schools were visited an appropriate day and time. After asserting details of the study and verbally explaining about the research process in a way that they could understand, it was expressed that participation was voluntary and they could leave the research if they wanted. Verbal approvals of the students accepted participating to the research were obtained. Students themselves filled the questionnaire prepared before under the supervision of the researchers. These took about 20-25 minutes.

Research Instrument: A questionnaire was prepared for the aim of the study by using appropriate literature (3,8,21-24). The questionnaire was composed of 3 sections including socio-demographic characteristics, Food Behavior Scale (FBS), and Children Dietary Self-efficacy Scale (CDSS).

Food Behavior Scale: The food consumption of children was evaluated with FBS. The scale was composed of 14 illustrated elements consisting of low fat/salt and high fat/salt foods in order to determine the food consumption of the children. Children were showed comparable foods and asked which of them he/she eat (frequently). Scale elements took -1 for unhealthy food and took +1 for healthy food, total value is between -14 and +14. If the total score obtained from the scale was higher than 1, this indicated that healthy eating

behavior was more positive (21,22). The Turkish validity and reliability study of the scale was realized by Haney and Erdogan (23).

Children Dietary Self-Efficacy Scale: CDSS measured self-efficacy in children's habits of eating low fat and low salt food. Scale items were composed of various food and nutrient groups with oil and salt content. Foods in the scale were selected among frequently consumed foods by children in this age group. Scale measured self-confidence that allowed children to choose less fatty and less salty food in spite of fatty and salty food choices. The scale was composed of 15 items and it was a three-point Likert type. Scale items were in the range of -1 and +1 (-1: I am not sure, 0: I am a little bit sure, +1: I am very sure) and the total score was between -15 and +15. The higher point taken from the scale indicated higher self-efficacy value (21,22). Turkish validity and reliability study was realized by Haney and Erdogan (23).

Definitions: Body mass index (BMI) of children were classified as 'severe thinness, thinness, normal, overweight, and obesity' based on the definition World Health Organization (WHO) determined for this age and gender group (24). Those who were previously diagnosed with chronic disease by the physicians were considered as 'having chronic disease". The family type of students was divided into "nuclear family, extended family, and single-parent family".

Statistical Analysis: The data obtained from the research were evaluated in IBM SPSS (version 15.0) statistical package program. Descriptive statistics, Mann-Whitney U, and Kruskal Wallis tests were used for data analysis. Multiple linear regression analysis was applied to determine the factors affecting the FBS score. The logarithm of the dependent variable FBS scores were taken into consideration and adapted to normal distribution. Multiple linear regression model was applied and the model was created with statistically significant values. Gender, mother's education status, father's education status, mother's employment status, and CDSS were considered as independent variables. The statistical significance value was accepted as $p<0.05$.

RESULTS

The mean age of the students in the study group was 9.88 ± 0.44 years (min 9 - max 11) and 51.0% (205) of the students were female. The family monthly income was middle in 73.6% of students, in 85.1% of students the family type was nuclear family, in 36.3% of students the mother's education status was primary school, and in 43.8% of students the father's education status was middle&high school. While 61.9% of their mothers were working, 4.2% of their fathers were unemployed.

Of the participants 19.9% were overweight and 10.2% were obese. Furthermore, 46 (11.4%) of the students had a physician-diagnosed chronic disease.

Distribution of students according to BMI grouping was demonstrated in (Figure 1).

The distribution of student answers to FBS questions was demonstrated in (Table 1).

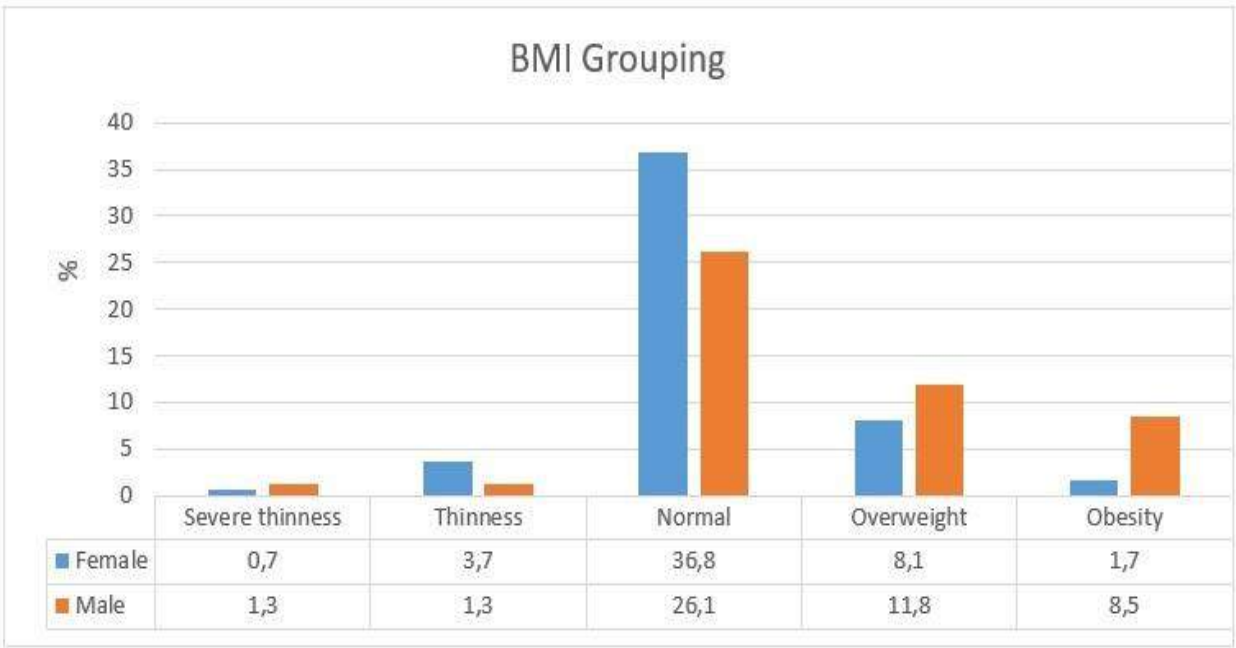

Figure 1. Distribution (%) of students according to BMI grouping and gender

Table 1. Distribution of student answers to FBS questions

FBS† questions‡			Correct Answer (%)	Wrong Answer (%)
1	Cookie	**Apple**	83.3	16.7
2	Hot Dog	**Chicken**	88.6	11.4
3	Buttered Popcorn	**Unbuttered popcorn**	63.2	36.8
4	**Bran muffin**	French toast with butter and syrup	42.5	57.5
5	Chocolate cake	**Orange**	79.4	20.6
6	**Ice cream**	Fresh fruity popsicle	71.9	28.1
7	Sweet roll	**Whole wheat roll**	67.4	32.6
8	**Turkey**	Salami, sausage	66.2	33.8
9	Whole milk	**Low fat or skimmed milk**	77.4	22.6
10	**Saltless**	Salty	57.2	42.8
11	Ice cream	**Frozen or normal yogurt**	60.9	39.1
12	**Whole wheat or brown bread**	French toast	65.9	34.1
13	**Herbal oil**	Butter	56.7	43.3
14	Regular hamburger	**Lean hamburger**	53.0	47.0

†Food Behavior Scale, ‡Each food in FBS questions was presented in illustrated form. Every question was formed like 'Which of these two foods do you prefer more frequently'. The foods specified in bold in the table are the right options.

FBS scores of the students were indicated by calculating the percentage of healthy food preferences of each child. The total nutrition behavior scores of students were between 0% and 100%. While female students in FBS chose healthy food with a mean ± SD 69% ± 22 percentages, male students chose healthy food with a mean ± SD 64% ± 23 percentages. The score of students from CDSS was stated by calculating the percentage of healthy food preferences of each child. The total dietary self-efficacy scores of students were between 0% and 100% healthy food choices. While female students in CDSS chose healthy food with a mean ± SD 65% ± 24 percentages, male students chose healthy food with a mean ± SD 55% ± 25 percentages ($p<0.001$). The distribution of average total scores of students in the study group taken from FBS and CDSS according to socio-demographic and medical characteristics was demonstrated in (Table 2).

Table 2. Distribution of average total scores of students in the study group taken from FBS and CDSS according to socio-demographic and medical characteristics

Characteristics	FBS† Total Score (%) Mean±SD	*P*	CDSS‡ Total Score (%) Mean±SD	*P*
Gender				
Female	69±22	0.055*	65±24	**<0.001***
Male	64±23		55±25	
Family type				
Nuclear family	67±23	0.809**	61±25	0.156**
Extended family	65±23		53±28	
Single-parent family	68±21		64±30	
Family income status				
Low	62±29	0.629**	47±32	0.230**
Middle	67±22		60±25	
High	65±24		62±26	
Mother education status				
Primary school	62±26[a]	**0.012****	56±26[a]	**<0.001****
Middle&High school	67±21[a]		58±25[a]	
University	72±20[b]		67±24[b]	
Father education status				
Primary school	61±27[a]	**0.027****	56±28[a]	**0.002****
Middle&high school	66±22[a]		58±24[a]	
University	71±20[b]		65±25[b]	
Mother employment status				
Employed	71±22	**0.006***	66±26	**<0.001***
Unemployed	64±23		57±25	
Father employment status				
Employed	67±23	0.224*	60±26	0.618*
Unemployed	59±27		56±17	
BMI§ grouping				
Severe thinness	71±26	0.497**	43±22	0.232**
Thinness	66±23		64±26	
Normal	65±23		60±25	
Overweight	70±22		62±23	
Obesity	69±24		60±31	
Chronic disease				
Yes	65±21	0.408*	51±26	**0.029***
No	67±23		61±25	

†Food Behavior Scale, ‡Children Dietary Self-efficacy Scale, §Body mass index.
*Mann-Whitney U, **Kruskal Wallis, a,b: The difference between groups that do not have the same letter in each column is significant ($P<0.05$).

Medium level positive relation (r = 0.426, p<0.001) was detected between scores taken from FBS and CDSS in Spearman Correlation Analysis. In the multiple linear regression performed to determine the relationship between FBS and CDSS after controlling the effect of related factors, it was determined that nutrition behavior indicated a positive relation ((β (95% CI): 0.398 (0.301-0.495)) with CDSS score.

The results of multiple linear regression analysis of variables that could have effects on FBS scores of the study group were demonstrated in (Table 3).

Table 3. The results of multiple linear regression analysis of variables that could have effects on FBS[†] scores of the study group

Variables	Unstandardized beta β±SE (95% CI[§])	Standardized beta β
Gender	-0.239±0.594 (-1.407 - 0.929)	-0.019
Mother education status	0.352±0.484 (-0.599 - 1.303)	0.045
Father education status	0.507±0.512 (-0.500 - 1.504)	0.058
Mother employment status	-0.452±0.650 (-1.731 - 0.826)	-0.034
CDSS[‡] total score	0.398±0.049* (0.301 - 0.495)	0.384*
Adjusted R^2 = 0.182, F = 17.577*		

*P<0.001, [†]Food Behavior Scale, [‡]Children Dietary Self-efficacy Scale, [§]CI: Confidence Interval

DISCUSSION

The health of children is mostly determined by their eating habits. Children with insufficient and unbalanced eating habits become resistless to diseases, they get ill frequently, they have more severe illness, in addition their perception, attention, and cognitive abilities are influenced negatively. It is crucial to prepare the ground for future generations to become healthier and stronger in order to realize the development of cognitive abilities of children. It is extremely important to gain healthy eating behavior from childhood and to maintain these habits in later ages in order to have a healthy body (25,26). Gaining eating habits is a multifactor process which starts in the family and continues in school (27).

It is demonstrated that eating habits are systematically related to various factors (such as fear of being overweight, ideal body shape and weight, low-size prestige, self-respect, and social approval). Girls taking care of their body image, eating less sugary, sweetened, and fast-food in order to lose weight, consuming fruit and vegetables more frequently rather than energy-intensive foods and choosing healthy foods are explained with their attention to nutrition more than boys (28,29). In the study, any difference could be found between girls and boys in their FBS scores. Similar results have been reported in the studies of Passos et al. and Svenson et al. (30,31). In some studies, nutritional behavior scores were reported to be higher in girls (32,33).

One of the important factors dominating a healthy lifestyle is education status and influences not only the person but also his/her environment. Education status of the parents could affect children's behavior to choose healthy food. It is asserted that parents having a higher level of education are more closely interested in a child's nutrition, have healthy food purchasing habits, care more about food variety such as fruit, vegetable, meat, and milk, etc. in the house. These factors could provide that the child's to have better-eating decisions and gain healthy eating behaviors (9,34,35). In the study, FBS scores of children whose parents' education level was university was higher than those whose parents' had lower education level. Although there are researches declaring similar results in the literature, it was reported that there were no relationship between parents' education status and children's nutrition behavior in the study conducted by Svensson et al. (31,34,36,37).

Although it is probable that the working status of the mother and father may have different effects on children, studies have mostly not focused on the working status of a single parent and they did not separate the working status of parents (38). According to traditional gender role distribution, men are perceived as ones supporting families, on the other hand, even women work full time, they are accepted as caregivers (39). In this regard, parents working especially mothers working leads mothers to have work and life stress. Moreover, their time spent with child shortens, care shown in the selection of the food offered to her child decreases, time spent to prepare food reduces, number and duration of breakfasts and family dinners realized together and periodically lessens. In addition, this causes child to consume more energy-intensive, poor quality sugary, sweetened and fast food instead of fruits and vegetables, working parents especially working mothers lead work and life stress. Therefore children especially with working mothers were indicated not to have healthy eating behavior (40,41). In this study, FBS scores of children with working mothers were determined to be higher. In addition, no difference was found between nutrition behavior scores of children with employed and unemployed fathers. In the study of Kopelman et al., it was reported that the nutrition behaviors of the children whose

parents were working were better (42). In the study executed by Jacka et al., any relationship was found between the working status of mother and children nutrition scores. In addition, this study stated that nutrition scores of children with working fathers were higher (43). The reasons for the different results were the socioeconomic and sociocultural characteristics of the country and region where the study was conducted, differences between the working order, the differences between the measurement tools used, and the differences between the age distributions of the study group.

Lots of predictor factors have been defined in the never-ending search for health-related behavior explanations. In social cognitive theory, the concept of self-efficacy and the role of self-efficacy in the prediction of health-related behaviors have been studied extensively (44,45). It is stated that self-efficacy includes a productive ability about judgments what one can do with the skills he/she has, but not with the skills he/she has. Self-efficacy reflects a person's faith in overcoming difficulties in performing a particular task in a particular situation. It is stated that self-efficacy influences the behavior preferences of people undertook such as gaining new behaviors (learning a new computer program etc.) and preventing current behaviors (reducing oily food choices etc.). In addition, self-efficacy influences people's efforts to adopt new behavior and persistence when faced with obstacles (46). In this study, a positive relationship was detected between the nutrition behavior of children and dietary self-efficacy. In the study conducted by Choi et al. and Won et al. similar results were reported (47,48). In addition, in researches, it was declared that increasing self-efficacy provides eating habits to change and boost the possibility of shaping in a healthy way (19,20,48). In this study, multivariate model in the primary school age group was found to be remarkable in terms of indicating the positive impact of dietary self-efficacy by removing the effect of socio-demographic factors on nutrition behavior.

Limitations: The study was a cross-sectional study that was conducted in six primary schools in the city center of Eskisehir and that could not be generalized to all primary school students in Turkey. While some students' body weight and height were taken based on their own statements, others' body weight and height were obtained from school records. Inclusive students with communication difficulties were not included in the study. Because these inclusive students may not understand the questions correctly and can not answer properly.

CONCLUSION

In this study, dietary self-efficacy was determined as a factor influencing nutrition behavior. SCLT is appeared to be a useful model for investigating effective structures in healthy nutrition behavior. It is crucial to address individual, environmental and behavioral factors in childhood in order to increase faith in healthy nutrition behavior. More comprehensive further researches (based on the fact that more comprehensive identification of outstanding factors for healthy lifestyles may be useful in shaping lifelong healthy eating habits) are needed in order to determine whether improvement of self-efficacy of children will transform into healthy eating behavioral changes. Individual, environmental and behavioral constraints affecting nutrition behavior and dietary self-efficacy are needed to be understood more clearly. In this regard, it was concluded that monitoring the close relationships of nutrition behavior and dietary self-efficacy could be useful beginning from early ages.

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RESEARCH ARTICLE

Tuba Sahip Karakas[1*]
Zerrin Gamsizkan[1]
Sengul Cangur[2]

[1] Department of Family Medicine, Medical Faculty, Düzce University, Duzce, Turkey
[2] Department of Biostatistics and Medical Informatics, Medical Faculty, Düzce University, Duzce, Turkey

Corresponding Author:
Tuba Sahip Karakas
Department of Family Medicine, Medical Faculty, Düzce University, Duzce, Turkey
Phone: +90 506 468 96 12
mail: tubasahip@gmail.com

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Exposure of Violence and its Effects on Health Care Workers

ABSTRACT

Objective: The aim of this study is to examine the frequency of violence that the healthcare workers of Düzce University Research and Practice Hospital encountered, situations that cause violence, post-violence attitude and the effects of violence on the personnel, and to evaluate the relationship between violence and the burnout levels of the healthcare workers.

Methods: This descriptive cross-sectional study was conducted on the physicians and nurses working in different departments at Düzce University Research and Application Hospital, between October 2020 and February 2021. A questionnaire form consisted of 24 questions including demographic information and questions about working conditions and violence and Maslach Burnout Scale consisting of 22 questions were applied to the participants.

Results: The frequency of the participants being exposed to violence throughout their professional life was found 74.4%. The most common type of violence was psychological violence (92.7%). Exposure to physical violence was more common among male healthcare workers (22.7%) ($p < 0.001$). It was found that the rate of exposure to violence increased as the time spent in the profession, the average number of duty shifts, and the number of patients examined daily increased ($p < 0.05$). Swearing and insult were the most common types of violence exposed (71.1%). In the comparison of the exposure to violence and sub-dimensions of burnout scale, it was found that "Emotional exhaustion" and "Depersonalization" subscale scores of those who were exposed to violence were significantly higher than those who were not ($p = 0.005$).

Conclusions: Violence in the health sector is a serious problem that decreases the motivation of healthcare workers and causes mental, emotional and physical problems. In order to deal with this problem, instead of ignoring the problem, we need to reveal the violence and its destructive effects through more comprehensive studies.

Keywords: Healthcare Workers, Violence, Burnout

Sağlık Çalışanlarında Şiddet Maruziyeti ve Şiddetin Çalışanlar Üzerindeki Etkileri

ÖZET

Amaç: Bu çalışmanın amacı Düzce Üniversitesi Araştırma ve Uygulama Hastanesi hekim ve hemşirelerinin şiddete uğrama sıklığı, şiddete neden olan durumlar, şiddet sonrası tutum ile şiddetin etkilerini incelemek, çalışanların tükenmişlik düzeylerini ölçerek şiddetle ilişkisini değerlendirmektir.

Gereç ve Yöntem: Tanımlayıcı kesitsel özellikte olan araştırmamız Ekim 2020-Şubat 2021 tarihleri arasında Düzce Üniversitesi Araştırma ve Uygulama Hastanesinde farklı bölümlerde çalışan hekim ve hemşirelerle yürütülmüştür. Çalışmada anket yöntemi kullanılmış olup, demografik bilgiler, çalışma koşullarıyla ilgili sorular ve son olarak şiddetle ilgili soruların olduğu 24 sorunun ardından, 22 soruluk Maslach Tükenmişlik Ölçeği ile birlikte toplam 46 soru yöneltilmiştir.

Bulgular: Araştırmamızda katılımcıların meslek hayatları boyunca şiddete uğrama sıklığı %74,4 bulunmuştur. En sık maruz kalınan şiddet türü %92,7 ile psikolojik şiddet olmuş, fiziksel şiddete maruziyet erkek cinsiyette (%22,7) daha sık rastlanmıştır ($p<0,001$). Meslekte geçirilen süre ve tutulan ortalama nöbet sayısı günlük bakılan hasta sayısı arttıkça şiddet maruziyetinin de arttığı saptanmıştır ($p<0,05$). Maruz kalınan şiddet türünde en fazla küfür hakaret (%71,1) yanıtı alınmıştır. Kişilerin şiddet maruziyeti ile tükenmişlik alt boyutları karşılaştırıldığında; şiddete maruz kalanların "Duygusal tükenme" ve "Duyarsızlaşma" alt ölçek puanları maruz kalmayanlardan anlamlı derecede yüksektir ($p=0,005$).

Sonuç: Sağlık sektöründe şiddet çalışanların motivasyonunu azaltan, ruhsal, duygusal ve fiziksel sorunlara yol açan ciddi bir sorundur. Bu sorunla başa çıkmak için sorunu göz ardı etmek yerine daha kapsamlı çalışmalar ile şiddeti ve şiddetin yıkıcı etkisi gözler önüne sermeliyiz.

Anahtar Kelimeler: Sağlık Çalışanları, Şiddet, Tükenmişlik

INTRODUCTION

Labor life is one of the areas where violence is frequently encountered. Violence in the workplace is defined as "physical or psychological assault of the employee by a person or a group, while performing his / her duty" (1). The health sector is one of the sectors in which violence is common in working life (2). Studies show that, health care workers are at higher risk of being exposed to violence than employees in other sectors (3, 4). Violence in healthcare institutions is described as "psychological, physical and sexual assault, generally created by the patients and their relatives, harmful to the physical and mental health of the healthcare worker"(5). Being exposed to violence disturbs the physical, psychological and social wellbeing of the healthcare worker, increases long-term stress, depression and anxiety levels as well as short-term effects, and causes burnout (6-8). It has been noted that although being exposed to violence is more common in the healthcare, the rate of reported cases of violence remained lower. The reason for this is that while serious situations involving injury are perceived as violence, the other types of violence are ignored (9).

When studies on violence against healthcare professionals are examined, emergency departments are the first places where violence occurs and followed by psychiatry clinics (10,11). The most important reasons for the high prevalence of violence in emergency services include, frequent admission of the patients with drug addiction, substance use, and alcohol problems, providing health service 24-hours, being the place of first intervention for patients with critical conditions, and the burden of anxiety on the workers and patients due to the working conditions in the emergency departments. The deaths in the emergency departments can be evaluated to occur due to inadequate treatment, by the relatives of the patients. Patients and their relatives may hold emergency department personnel responsible for this whole process and tend to become aggressive (12).

Frequency and type of violence in the field of healthcare may vary depending on the department and position of the healthcare worker. Although the rates of being exposed to verbal violence were similar for doctors and nurses, it was observed that nurses were exposed to physical, sexual and psychological violence more frequently (13). In some studies, it has been suggested that healthcare workers in the surgical branches are exposed to violence more frequently compared to the internal branches (14,15).

A number of psychological interactions including confusion, anger, relentlessness, insecurity, burnout, and self-blame can be observed in the healthcare workers who are subjected to violence (16). In addition, healthcare workers who are exposed to physical violence may experience post-traumatic stress disorder and the quality of the service provided to the patients may decrease consequently (17, 18).

The aim of this study is to examine the frequency of violence that the healthcare workers of Düzce University Research and Practice Hospital encountered, situations that cause violence, post-violence attitude and the effects of violence on the personnel, and to evaluate the relationship between violence and the burnout levels of the healthcare workers.

MATERIAL AND METHODS

This study was designed as a descriptive cross-sectional study and conducted between October 2020 and February 2021. Data were collected by applying a questionnaire from to the physicians and nurses working in Düzce University Research and Application Hospital. The universe of the study is 604 healthcare workers, including 292 physicians and 312 nurses, meeting the inclusion criteria. The sample size was determined to include approximately 250 individuals for a 95% confidence level, 5% margin of error, and 50% survey response rate.

Data Collection Tools: In order to collect data suitable for the aims of the study, a questionnaire form was prepared by the researcher in line with the literature and developed by consulting the expert opinion. A pilot questionnaire application was applied to a group of 15 people before the study started. After this pilot study, the questions in the questionnaire form were finalized in terms of content and form.

Maslach Burnout Scale: Maslach Burnout Scale was developed by Christina Maslach, Susan E. Jackson and CaryCherniss and used to determine the extent of burnout experienced by individuals working in professions involving intensive human relations. The scale consists of three sub-dimensions and a total of 22 questions. The emotional burnout sub-dimension evaluates the level of burnout experienced due to job and includes 9 questions. The depersonalization sub-dimension evaluates the rigid, indifferent and emotionless attitudes towards the work and people and includes 5 questions. The personal success sub-dimension evaluates the ability to cope with the problems experienced and the feelings of success and sufficiency and includes 8 questions (19). The higher scores of emotional burnout and depersonalization sub-scales and lower scores of personal achievement subscale indicate a high level of burnout.

Statistical Analysis: The data were evaluated by using SPSS (version 22.0) statistical package program. Descriptive statistics were expressed as mean± standard deviation, median, interquartile range, and percentage where appropriate. The assumptions of normality of

quantitative variables and homogeneity of variances were examined by Shapiro-Wilk and Levene tests, respectively. In the comparisons between groups, Mann Whitney U test was applied considering the conditions of providing the assumptions. The relationships between quantitative variables were evaluated by the Spearman correlation coefficient. The relationships between categorical variables were examined by Pearson's Chi-square and Fisher's Exact test. A value of $p<0.05$ was accepted as statistically significant.

RESULTS

In this study, 190 doctors (53.4%) and 166 nurses (46.6%) working in Düzce University Research and Application Hospital were included. Thirty-eight of the doctors were faculty members and 152 were research assistants. The mean age of the participants was 31.5 ± 7.1 (19 -72) and 185 (52%) participants were under 29 years of age, 120 (33.7%) were between 30 and 39 years of age, and 51 (14.3%) were 40 years of age and older. The rate of female participants was 56.5% and the rate of males was 43.5%, while 57.3% were married and 47.2% were single.

There were no statistically significant differences between the participants' exposure to violence throughout their professional life according to gender, age, task distribution, and working in internal medicine or surgery branches ($p> 0.05$). Participants' exposure to violence according to age, gender, duty and branch distribution is shown in Table 1.

The frequency of the participants being exposed to violence throughout their professional life was found to be 74.4%. The most common type of violence was psychological violence (92.7%), while exposure to physical violence was more common in men (22.7%) ($p<0.001$). When the participants who were subjected to violence were evaluated, we found that 94 (88.7%) of the research assistants, 29 (93.5%) of the faculty members, and 118 (92.2%) of the nurses had been exposed to verbal violence. Considering the physicians working in internal branches (n= 90) and surgical branches (n= 47) who were exposed to violence, 77 (85.6%) of those working in internal branches and 46 (97.9%) of those working in surgical branches had been exposed to verbal violence were exposed to verbal violence. The rate of exposure to verbal violence was significantly higher in those working in surgical branches compared to those working in internal medicine ($p = 0.034$).

It was found that the exposure to violence increased as the time spent in the profession ($r = 0.171$ $p = 0.005$) and the average number of duties ($r = 0.209$ $p = 0.001$) increased. Considering the most common type of violence exposed, we found that healthcare workers were exposed to swearing and insult (71.1%) with the highest rate.

Table 1. The distribution of exposure to violence of the participants according to age, gender, duty and branches

		I had been exposed to violence		I had not been exposed to violence		p
		n	%	n	%	
Gender	Female	155	77.1	46	22.9	0.222
	Male	110	71.4	44	28.6	
Age	≤ 29	131	71.2	53	28.8	0.280
	30-39	95	79.2	25	20.8	
	≥40	39	76.5	12	23.5	
Duty	Research assistant	106	70.2	45	29.8	0.215
	Faculty member	31	81.6	7	18.4	
	nurse	128	77.1	38	22.9	
Branch	İnternal medicine	90	69.8	39	30.2	0.220
	Surgery	47	78.3	13	21.7	

When the mean scores of the Maslach Burnout Scale were examined, it was found that the mean score of Emotional Exhaustion" sub-dimension was 18.2 ± 8.7 points, the mean score of "Depersonalization" subdimension was 6.5 ± 4.2 points, and the mean score of "Personal Achievement" subdimension was 21.8 ± 5.4 points. When the mean sub-dimension scores of Maslach Burnout Scale are compared according to the being exposed to violence, a significant difference was found in terms of the mean scores of "emotional exhaustion" and "depersonalization" sub-dimensions ($p <0.05$), while there was no significant difference in terms of "personal accomplishment" subscale score ($p> 0.05$). The "emotional exhaustion" and "depersonalization" subscale scores of those who were exposed to violence were significantly higher compared to those who were not exposed to violence.

Descriptive statistics and comparisons of sub-dimension scores of Maslach Burnout Scale according to being exposed to violence are given in Table 2.

Table 2. Descriptive statistics and comparisons of sub-dimension scores of Maslach Burnout Scale according to being exposed to violence

	Exposure to violence						
	Yes			**No**			
	Mean±SD	**Median (IQR)**	**MeanRank**	**Mean±SD**	**Median (IQR)**	**MeanRank**	**P**
Emotional exhaustion	19±8.2	18(12)	187.0	15.8±9.8	15.5(16)	151.6	**0.005**
Depersonalization	6.9±4.2	6(6)	186.2	5.4±4.1	5 (7)	151.5	**0.005**
Personal Achievement	21.7±5.4	22(8)	174.9	22.3±5.3	22 (7)	185.2	0.411

SD: StandardDeviation, IQR: InterquartileRange

We found that mean score of personal achievement sub-dimension was statistically significantly higher in males compared to females ($p < 0.05$), there were no significant differences in terms of the mean scores of emotional exhaustion and depersonalization sub-dimensions ($p > 0.05$). When the scores of physicians working in internal and surgical branches are compared, emotional exhaustion and depersonalization sub-dimension scores of physicians working in surgical branches were significantly higher compared to those working in internal medicine branches ($p < 0.05$). However, there is no significant difference between the physicians in terms of personal achievement sub-dimension scores, according to the branches they worked ($p > 0.05$).

Descriptive statistics and comparisons of sub-dimension scores of Maslach Burnout Scale according to gender and working in internal or surgery branches are given in Table 3.

Table 3. Descriptive statistics and comparisons of scores of sub-dimensions of Maslach Burnout Scale, according to gender and working in internal or surgery branches

	Gender			**Branch**		
	Female	**Male**	**p**	**Internal medicine**	**Surgery**	**p**
Emotional exhaustion	18.4±8.5*	17.9±9.1*		17.2±8.3*	19.47±7.7*	
	18 [13]#	18 [14] #	0.604	16 [11]#	20 [10.5] #	**0.040**
Depersonalization	181&	175.3&		89.9&	107.6&	
Emotional exhaustion	6.3±4*	6.8±4.5*		6.4±4*	8.1±4.4*	
	6 [6]#	6 [7]#	0.407	6 [6]#	8 [7]#	**0.012**
Depersonalization	174&	183.1&		88.7&	110.2&	
Emotional exhaustion	21.2±5.3*	22.5±5.4*		21.8±5*	22.2±5.9*	
	21 [7]#	21 [9] #	**0.027**	21 [7]#	22.5 [8.5]#	0.556
	167.4&	191.7&		93.9&	99&	

*Mean±SD, # Median [InterquartileRange], &MeanRank

When the emotional exhaustion sub-dimension scores are compared according to type of violence exposed, there was no significant difference between the mean scores of "emotional exhaustion" sub-dimension of those who were exposed to verbal violence and those who did not ($p > 0.05$), whereas the mean scores of those who were exposed to physical violence and threat were found to be significantly higher ($p < 0.05$). It was found that 109 (%41.1) of the participants who were exposed to violence had lodged a complaint to proper authorities, whereas 156 (%58.9) did not lodge any complaint. The details of the process of lodging a complaint and reasons why the participants did not make any complaint despite the violence they were subjected to are shown in Table 4.

DISCUSSION

Three quarters of the participants in our study state that they have been exposed to violence at least once in their professional life. In studies conducted in our country, the rates of exposure to violence among healthcare workers are variable. In a study conducted by Eskişehir-Bilecik Medical Association, on 1,071 healthcare workers working in Ankara, Eskişehir and Kütahya, in 2002, it was reported that 50.8% of the healthcare workers were subjected to violence at least once in their professional life (20). In a multi-center study conducted in Sivas city center, the rate of exposure of healthcare workers to violence at least once during their professional life was found to be 95.51% (21).

Table 4. Evaluation of the process of lodging a complaint after being exposed to violence

		n	%
Have you even lodged a complaint?	Yes	109	41.1
	No	156	58.9
If you did not lodge a complaint, what is the reason?	Disregarding, taking it in stride	26	16.8
	Fear of negative consequences	14	9
	Not expecting any results	106	68.4
	Being the one been complained about violence	1	0.6
	Other **	8	5.2
If you lodged a complaint, what action was taken?	No action was taken	30	27.3
	The insulter apologized	9	8.2
	The insulter was removed by security	14	12.7
	An investigation was conducted	57	51.8
If an investigation was conducted, how did it resulted?	No result was achieved	13	22.8
	The insulter paid compensation	8	14
	Disciplinary penalty was imposed	4	7
	Penalty was suspended	9	15.8
	In progress / not yet concluded	8	14
	The insulter was sentenced to prison	4	7
	Nonsuited	11	19.3

* More than one option has been marked in this question. ** Other reasons are workload, not having time, too many procedures, and obstructions by the administration.

In our study, the most common type of violence that the healthcare workers were exposed to was psychological violence, while the rate of physical violence was found to be lower. According to the review prepared jointly by WHO, ILO and ICN in 2002, in which the studies on violence towards healthcare workers in different countries are evaluated, it was reported that 3-17% of the cases were physical violence, while the rest were verbal insult (27-67%), threat (10% -23), sexual violence(0.7-8%), and ethnic violence (0.8-2.7% (22). In studies conducted in our country, the reported rates of physical violence were similar and lower than psychological violence (23,24).

There were no statistically significant differences between the participants in terms of exposure to violence throughout their professional lives according to gender, age, distribution of duties, and physicians' branches of working. In a study conducted on the ED personnel working in Kocaeli state hospital, it was found that 82% of the employees were exposed to violence and there was no relationship between being exposed to violence and gender, length of service, and age (25). In a similar study conducted in Bolu, no relationship was reported between being exposed to violence and age and gender (26). In our study, the question "What effect did the violence have on you?" was answered as "I felt anger, sadness, and disappointment" by approximately half of the participants, while one third of the participants stated that they felt insecurity and anxiety and one fifth of them stated that they felt helpless. The question 'What are the negative thoughts caused by the violence you were exposed to?" were answered as "'My motivation to work decreased" by three quarter of the participants and as "I regretted being a doctor / nurse" by approximately half of the participants'. In the study of Koristas et al., it was reported that 62.73%of the healthcare workers experienced symptoms of post-violent stress and post-traumatic stress disorder, including anxiety, fear, insecurity, stress, and hesitation, due to violence. In addition, it was reported that, the healthcare personnel who were exposed to violence avoided working in the place where the violence occurred and their job satisfaction decreased, concentration impaired, and ability to listen to patients decreased (27).

When the sub-dimension scores of Maslach Burnout Scale were compared according to being exposed to violence, "Emotional exhaustion" and "Depersonalization" subscale scores of those who were exposed to violence were found to be significantly higher compared to those who were not. However there was no significant difference

between those who were exposed to violence and those who were not, in terms of subscale scores of personal accomplishment. Similar to our study, in another study conducted in our country, sub-dimension scores of "emotional exhaustion" and "depersonalization" were found to be significantly higher in those who were exposed to violence, while no difference was found between the scores of "personal accomplishment" (8).

When the scores of sub-dimension Maslach Burnout Scale were evaluated according to genders, there was no difference between males and females in terms of the mean scores of “emotional exhaustion” and “depersonalization” sub-dimensions. Personal achievement subscale scores of males were higher than females. It is similar to our study results concluding that the dimension of "personal accomplishment" is high in men (28).

When physicians working in internal medicine and surgical branches are compared, “Emotional exhaustion” and “depersonalization” subscale scores of physicians working in surgical branches were found to be significantly higher. There were no significant differences between physicians working in internal medicine and surgical branches in terms of personal success sub-dimension. In the literature, conflicting results about the relationship between working in internal medicine and surgical branches and burnout levels have been reported. In a study conducted at Hacettepe University, similar to our study, "depersonalization" subscale scores of the physicians working in surgical branches were found to be significantly higher (29). However, there are studies reporting that "emotional exhaustion" subscale scores were higher in physicians working in internal branches and there were no differences in terms of "depersonalization" and "personal success" subscales (30). More than half of the employees exposed to violence stated that they did not lodge a complaint to proper authorities. The most common reason for not lodging a complaint was "not expecting any results ". Other reasons were " disregarding, taking it in stride”, “fear of negative consequences”, and “being the one been complained about violence”, respectively.

Half of the participants, who lodged a complaint, stated that an investigation was initiated, and a quarter stated that no action was taken. In the most of the studies conducted in our country, it was reported that healthcare workers continued to provide service, especially after experiencing psychological violence, and did not lodged any legal complaints. The rate of reporting being exposed to physical violence was found to be higher compared to verbal insult and psychological violence. This situation was suggested to be due to the fact that the healthcare workers think that verbal and other types of psychological violence are inherent in the healthcare profession, they do not care, they believe that they cannot achieve any results or even themselves can be the one who is blamed (31,32).

Limitations: The results cannot be generalized since the study was conducted in a single healthcare institution. Due to the limitations arising from the fact that the study was conducted by questionnaire method and only quantitative comparisons were made, the effects of violence on the workers may not be fully reflected. Although variable results were reported by the studies, it is obvious that violence leads to negative thoughts and problems in varying rates in all employees.

CONCLUSION

In our study, the healthcare workers’ frequency of being exposed to violence throughout their professional lives was found to be considerably high. The most common type of violence experienced was psychological violence, while physical violence was more common in male gender. Participants generally stated that they did not think the measures taken against violence, by the institution they work were sufficient. As a result, healthcare workers suffer from violence either being exposed to personally or witnessing their colleagues in the workplace. In addition to difficulties of the profession, violence increases the risk of burnout syndrome. Healthcare workers should be informed about burnout syndrome, and those who show symptoms or seek help should be provided with the necessary support. It is necessary for each institution to develop an action plan for incidents of violence, facilitate legal complaint process, and provide legal support to employees.

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RESEARCH ARTICLE

Seyda Toprak Celenay[1*]
Serap Ozgul[2]
Funda Demirturk[3]
Ceren Orhan[2]
Emine Baran[2]
Turkan Akbayrak[2]

[1]Department of Physiotherapy and Rehabilitation, Faculty of Health Sciences, Ankara Yildirim Beyazit University, Ankara, Turkey
[2]Department of Physiotherapy and Rehabilitation, Faculty of Physical Therapy and Rehabilitation, Hacettepe University, Ankara, Turkey
[3] Department of Physiotherapy and Rehabilitation, Faculty of Health Sciences, Gaziosmanpasa University, Tokat, Turkey

Corresponding Author:
Seyda Toprak Celenay
Ankara Yildirim Beyazit University, Health Sciences Faculty, Department of Physiotherapy and Rehabilitation, Ankara-Turkey,
Phone: +90 3129061000
mail: sydtoprak@hotmail.com

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Comparison of Physical Activity, Quality of Life and Menstrual Symptoms by Menstrual Pain Intensity in Turkish Women with Primary Dysmenorrhea

ABSTRACT

Objective: The aim of this study was to compare physical activity level, quality of life (QoL), and menstrual symptoms by pain intensity in Turkish women with primary dysmenorrhea.

Methods: Women with primary dysmenorrhea (n = 333) were assigned to three groups based on pain intensity. Physical and demographic characteristics were asked. Pain intensity, physical activity level and QoL were evaluated with Visual Analogue Scale, International Physical Activity Questionnaire-7 (IPAQ-7) and Short Form-36 Health Survey Questionnaire (SF-36), respectively. The menstrual symptoms was recorded.

Results: IPAQ-7 scores did not show significant difference among three groups ($p > 0.05$). Physical functioning, bodily pain, vitality, role limitations because of emotional and physical problems scores of SF-36 in the severe-pain group were lower than in the mild-pain group ($p < 0.05$). Physical functioning and bodily pain scores of SF-36 in the moderate-pain group were lower than in the mild-pain group ($p < 0.05$). Role limitations because of emotional problems and bodily pain scores of SF-36 in the moderate-pain group were higher than in the severe-pain group ($p < 0.05$). Severe-pain group had a greater number of menstrual symptoms than other groups ($p < 0.05$).

Conclusions: In this study, it was observed that there was no difference between physical activity level and menstrual pain intensities in Turkish women having primary dysmenorrhea. In addition, women with higher menstrual pain intensity had lower QoL and higher frequency of menstrual symptoms. Therefore, these parameters should be considered for management of primary dysmenorrhea.

Keywords: Dysmenorrhea, Exercise, Quality of Life

Primer Dismenoreli Türk Kadınlarda Ağrı Şiddetine Göre Fiziksel Aktivite Düzeyi, Yaşam Kalitesi ve Menstrüel Semptomların Karşılaştırılması

ÖZET

Amaç: Bu çalışmanın amacı primer dismenoreli Türk kadınlarda ağrı şiddetine göre fiziksel aktivite düzeyini, yaşam kalitesini ve menstrüel semptomlarını karşılaştırılmaktı.

Gereç ve Yöntem: Primer dismenoreli kadınlar (n = 333) ağrı şiddetine göre hafif, orta ve şiddetli-ağrı gruplarına ayrıldı. Fiziksel ve demografik özellikler sorgulandı. Ağrı şiddeti, fiziksel aktivite düzeyi ve yaşam kalitesi sırasıyla Görsel Analog Skalası, Uluslararası Fiziksel Aktivite Anketi-7 (UFAA-7) ve 36-Maddelik Kısa Form Sağlık Anketi (KF-36) ile değerlendirildi. Menstrüel semptomlar kaydedildi.

Bulgular: UFAA-7 skorları üç grup arasında fark göstermedi ($p > 0,05$). Şiddetli-ağrı grubunda KF-36'nın fiziksel fonksiyon, vücut ağrısı, emosyonel ve fiziksel problemlere bağlı rol kısıtlaması skorları hafif-ağrı grubundan daha azdı ($p < 0,05$). Orta-ağrı grubunda KF-36'nın fiziksel fonksiyon ve vücut ağrısı skorları hafif - ağrı grubundan daha azdı ($p < 0,05$). Orta-ağrı grubunda KF-36'nın emosyonel problemlere bağlı rol kısıtlaması ve vücut ağrı skorları şiddetli-ağrı grubundan daha fazlaydı ($p < 0,05$). Şiddetli ağrı grubunda diğer gruplardan daha fazla sayıda menstrüel semptom vardı ($p < 0,05$).

Sonuç: Bu çalışmada primer dismenoreli Türk kadınlarda fiziksel aktivite düzeyi ve menstrüel ağrı şiddeti arasında fark olmadığı görüldü. Ek olarak daha yüksek menstrüel ağrı şiddetine sahip olan kadınlar daha düşük yaşam kalitesi ve daha yüksek menstrüel semptom sıklığına sahipti. Böylece primer dismenorenin yönetiminde bu parametreler dikkate alınmalıdır.

Anahtar Kelimeler: Dismenore, Egzersiz, Yaşam Kalitesi

INTRODUCTION

Primary dysmenorrhea, one of the most common gynecologic problems, has been defined as a menstrual pain related to a normal ovulatory cycle and without a pelvic pathology (1). It is characterized by spasmodic cramps in the lower abdomen that can spread to the back and thighs, and is generally accompanied by some typical symptoms (2). Prevalence of primary dysmenorrhea, generally among menstruating young adults and adolescents, ranges between 20 and 90% (1,3). This pain causes recurrent short-term school and work absenteeism in this population (4).

Primary dysmenorrhea has been attributed to excessive prostaglandin production, leading uterin hyper-contraction, during menstruation (5). Physical activity or exercise may be effective in the frequency and/or severity of dysmenorrhea. The increasing endorphin levels, decreased stress or sympathetic over-activity and increased local blood flow at the pelvic region through exercise might cause changes in pain perception (6,7). Although physical exercise has been advocated as a non-medical intervention for the relief of dysmenorrhea, there are insufficient and contradictory datas related to dysmenorrhea and physical activity level. Exercise or physical activity has been linked with reduced prevalence of dysmenorrhea and associated symptomatology in some studies; whereas in some published articles, no correlation was found between physical activity level and dysmenorrhea (8-10).

The prevalence of primary dysmenorrhea, which is also a significant health problem, is high among the female adolescents (11). Lots of women with very severe menstrual pain have some systemic symptoms including nausea, vomiting, nervousness, and insomnia (13). Menstrual pain and its accompanying symptoms affect quality of life (QoL) (12-15). In this way, the effects of the menstrual pain intensity on QoL and the existence of its accompanying symptoms should be evaluated. In literature, previous studies have reported lower QoL in women with dysmenorrhea; however, they did not adequately elucidated associations between the intensity of the menstrual pain and QoL (16-18).

Accordingly, this study aimed to compare the physical activity level, QoL and menstrual symptoms in women with primary dysmenorrhea who had different pain intensities. The following hypothesis was investigated: Physical activity level, QoL and menstrual symptoms would be different among women with mild, moderate and severe menstrual pain intensity.

MATERIAL AND METHODS

Subject: Nulliparous women, aged 18–25 years, referred to the physiotherapy clinics of the three different universities, with a history of primary dysmenorrhea, with no previous history of gynecological diseases and a normal pelvic examination, having regular menstrual cycles (28 ± 7 days), and being volunteer were recruited in this study. Participants who had history of secondary dysmenorrhea, urogynecologic disease, neuropsychiatric or metabolic disease, pelvic surgery, and positive pregnancy test were excluded. The University's Ethics Committee approved the protocol of the present study (Approval date and number: 27.03.2013 and GO 13/60-17) and conducted within the framework of the Helsinki Declaration principles. Written informed consent forms were provided to participants.

Assessments: Physical characteristics such as age, height, and weight were recorded. In menstrual examination, age of menarche, menstrual cycle duration length and onset of menstrual pain were asked. Information about oral contraceptive or intrauterine device use, parity, history of gynecological diseases, family history, smoking and alcohol use status were also collected.

The intensity of menstrual pain was evaluated with the Visual Analog Scale (VAS) (consisting of a 10 cm horizontal line in length, in which "0" remarks "no pain" and "10" remarks "excruciating pain''). Clark et al (19) demonstrated its reliability in the assessment of pain intensity. Pain scores of ≤ 3 cm were defined as "mild pain", 3.1 cm to 6.9 cm "moderate pain", and ≥7.0 cm as "severe pain" on VAS (20). According to the pain intensity, the participants were assigned to mild (n=60), moderate (n=141) and severe (n=132) pain groups. Moreover, the presence of systemic menstrual symptoms including nausea, vomiting, nervousness, headache, dizziness, fatigue and insomnia were recorded as "yes" or "no".

The International Physical Activity Questionnaire-7 (IPAQ-7), a valid and reliable questionnaire in Turkish people, was used to assess the physical activity level of the participants (21). The total score of the IPAQ-7 is obtained based on the duration and frequency of weekly vigorous and moderate intensity physical activities and walking activities.

The Short Form-36 Health Survey Questionnaire (SF-36), a valid and reliable questionnaire in Turkish people, was used to measure the QoL (22). The SF-36 consists 1) physical functioning, 2) role limitations (due to physical problems), 3) bodily pain, 4) general health, 5) vitality, 6) social functioning, 7) role limitations (due to emotional problems), and 8) mental health domains. The domain scores range from 0 (the worst QoL) to 100 (the best QoL) individually for each domain separately.

Statistical Analysis: The sample size calculation was used the G*Power package software program (G*Power Version 3.0.10, Franz Faul, Universität Kiel, Germany). According to the IPAQ-7 scores, it was calculated that 159 subjects

(53 per group) was needed to obtain 80 % power with f = 0.25 effect size, α = 0.05 type I error, and β = 0.20 type II error (23).

IBM SPSS Statistics 22.0 (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.) was used for data analysis. The distribution of normality was examined several methods such as visual (histograms, probability plots) and analytical (Kolmogorov-Simirnov test). Descriptive statistics were presented by mean±standard deviation (X±SD), frequency (n), or percentage (%).

The Chi-square tor the Fisher's exact tests were used for comparisons of the categorical variables. Parametric quantitative variables were analyzed by the one-way ANOVA. The homogeneity of the variances was assessed with Levene test. Tukey's test was used to conduct pair-wise analyses if it was found an overall significance. A p-value <0.05 was considered statistically significant.

RESULTS

Three hundred and seventy women were asked and/or evaluated (12 not willing to participate in the research, 10 having urogynecologic disease, 5 having neuropsychiatric, and 10 having a history of secondary dysmenorrhea). As a result, 333 women were participated in the present study. It was found no statistical difference among the physical characteristics of the groups (p > 0.05), except the menstrual pain intensity, smoking and alcohol consumption parameters (p < 0.05) (Table 1).

Table 1. Physical and menstrual characteristics of the groups

Characteristics	Mild-pain group (n = 60)	Moderate-pain group (n = 141)	Severe-pain group (n = 132)	p
Age (year, X±SD)	20.36 ± 1.62	20.60 ± 1.75	20.86 ± 1.66	0.147[a]
Body mass index (kg/m2, X±SD)	21.32 ± 3.20	21.32 ± 3.24	20.68 ± 2.65	0.172[a]
Menarche age (year, X±SD)	13.63 ±1.27	13.33 ± 1.31	13.33 ± 1.21	0.273[a]
Menstrual cycle (days, X±SD)	29.26 ± 5.17	29.29 ± 5.21	30.10 ± 1.40	0.655[a]
Duration of menstruation (days, X±SD)	5.88 ± 1.12	5.87 ± 1.18	6.00 ±1.18	0.642[a]
Menstrual pain intensity (VAS, cm, X±SD)	2.92 ± 0.08	5.02 ± 1.13	8.47 ± 1.02	< 0.001[a]*
Family history (n, %)				
Yes	30, 50.0	80, 56.7	84, 63.6	0.184[b]
No	30, 50.0	61, 43.3	48, 36.4	
Smoking (n, %)				
Yes	1, 1.7	13, 9.2	17, 12.9	0.046[c]*
No	59, 98.3	128, 90.8	115, 87.6	
Alcohol consumption ((n, %)				
Yes	3, 5.0	16, 11.3	23, 17.4	0.047[b]*
No	57, 95.5	125, 88.7	109, 82.6	

*p < 0.05, X: Mean, SD: Standart deviation, VAS: Visual Analog Scale, [a]: One-way ANOVA test, [b]: Chi-square test, [c]: Fisher's exact test

It was seen that there were no difference among the three groups in terms of IPAQ-7 and social functioning, mental health and general health scores of the SF-36 (p > 0.05) (Table 2). It was found a difference in physical functioning, role limitations due to emotional problems and physical problems, bodily pain, and vitality items of the SF-36 among three groups (p < 0.05) (Table 2). The scores of physical functioning, role limitations due to emotional problems and physical problems, bodily pain and vitality in severe dysmenorrhea group were lower than the mild group (p < 0.05) (Table 2). Also in mild group, physical functioning and bodily pain scores were higher than moderate group (p < 0.05) (Table 2). The scores of role limitations because of emotional problems and bodily pain in moderate group were higher compared to severe group (p < 0.05) (Table 2). Moreover, it was shown that women in severe group had higher frequency of nervousness, headache, nausea, vomiting, fatigue and insomnia symptoms than those in mild and moderate group (p < 0.05, Table 3)

DISCUSSION

The study put forward that some parameters of the quality of life such as physical functioning and role limitations, bodily pain and vitality of women with severe pain were more affected than those with mild pain. Additionally, women with moderate pain demonstrated a lower physical functioning and bodily pain than those with mild pain. Furthermore, women with moderate pain indicated greater role limitations because of emotional problems and bodily pain than those with severe pain. Based on the findings regarding the symptoms of dysmenorrhea, women with severe pain had higher frequency of some menstrual symptoms than those with mild and moderate-pain. However, no difference was detected in physical activity level and social functioning, mental health and general health perception domains of QoL among three groups.

Table 2. Physical activity levels and quality of life variables in the groups

Variable	Mild-pain group (n = 60)	Moderate-pain group (n = 141)	Severe-pain group (n = 132)	**Δ1**	**Δ2**	**Δ3**	**p1**	**p2**	**p3**	**F**
IPAQ-7	1470.93 ± 2348.57	1241.48 ± 1452.38	1565.76 ±1804.23	229.45 (-569.23,1028.14)	-94.83 (-926.53,736.86)	-324.28 (807.04,158.46)	0.864[d]	0.990 [d]	0.289 [d]	1.146[a]
SF-36 Physical functioning	90.85 ± 12.61	84.32 ± 20.13	82.57 ± 21.25	6.53 (0.86,12.20)	8.27 (2.33,14,21)	1.74 (-4,28,7.77)	0.018[d]*	0.003[d]*	0.866[d]	3.798[a]
Social functioning	70.62 ± 21.69	66.99 ± 18.10	64.86 ± 23.32	3.63 (-4.11, 11.38)	5.75 (-2.01, 14.13)	2.12 (-3.97, 8.22)	0.590[d]	0.268 [d]	0.788[d]	1.567[a]
Role-emotional	65.90 ± 38.27	61.34 ± 41.15	49.07 ± 42.81	4.55 (-10.08, 19.18)	16.82 (1.85, 31.80)	12.27 (0.002, 24.52)	0.836[d]	0.022 [d]*	0.049 [d]*	4.587[a]
Role-physical	80.45 ± 30.55	75.86 ± 33.63	65.45 ± 40.0	4.58 (-7.19, 16.35)	14.99 (2.25, 27.72)	10.41 (-0.41, 21.23)	0.723[d]	0.015 [d]*	0.064[d]	4.632[a]
Bodily pain	71.63 ± 20.20	60.80 ± 19.06	51.44 ± 21.80	10.82 (3.42, 18.22)	20.18 (12.71, 27.66)	9.36 (3.54, 15.17)	0.002[d]*	<0.001 [d]*	0.001 [d]*	21.115 [a]
Vitality	63.05 ± 59.71	54.63 ± 16.08	51.70 ± 19.06	8.41 (-2.41, 19.25)	11.35 (0.40, 22.29)	2.93 (-5.58, 11.44)	0.162[d]	0.040[d]*	0.696[d]	2.998[a]
Mental health	58.68 ± 15.28	57.93 ± 16.27	57.64 ± 17.95	0.74 (-5.35, 6.84)	1.03 (-5.11, 7.19)	0.29 (-4.49, 5.08)	0.956[d]	0.917[d]	0.988[d]	0.079[a]
General health	63.23 ± 14.84	58.53 ± 17.50	59.24 ± 18.35	4.69 (-1.62, 11.01)	3.99 (-2.38, 10.37)	-0.70 (-5.66, 4.26)	0.188[d]	0.305[d]	0.941[d]	1.595[a]

*p < 0.05, IPAQ-7: International Physical Activity Questionnaire-7, SF-36: Short Form-36 Health Survey Questionnaire, Δ1: Change in outcome variables from mild group and to moderate group, Δ2: Change in outcome variables from mild group and to severe group, Δ3: Change in outcome variables from moderate group, and to severe group, p1: Comparison of changes between mild and moderate group, p2: Comparison of changes between mild and severe group, p3: Comparison of changes between moderate and severe group, a: One-way ANOVA test, d: Pairwise post-hoc test with Tukey's test

Table 3. Menstrual symptoms of the groups

Menstrual symptoms	Mild-pain group (n = 60)	Moderate-pain group (n = 141)	Severe-pain group (n = 132)	**p**
Nervousness (n, %)				
Yes	38, 63.3	88, 62.4	105, 79.5	0.005[b]*
No	22, 36.7	53, 37.6	27, 20.5	
Headache (n, %)				
Yes	4, 10.0	40, 28.4	46, 34.8	0.002[b]*
No	56, 90.0	101, 71.6	86, 65.2	
Dizziness (n, %)				
Yes	9, 15.0	25, 17.7	30, 22.7	0.380[b]
No	51, 85.0	116, 82.3	102, 77.3	
Nausea (n, %)				
Yes	14, 23.3	56, 39.7	81, 61.4	< 0.001[b]*
No	46, 76.7	85, 60.3	51, 38.6	
Vomiting (n, %)				
Yes	4, 6.7	16, 11.3	36, 27.3	< 0.001[b]*
No	56, 93.3	125, 88.7	96, 72.7	
Fatigue (n, %)				
Yes	40, 66.7	89, 63.1	104, 78.8	0.015[b]*
No	20, 33.3	52, 36.9	28, 21.2	
Insomnia (n, %)				
Yes	14, 23.3	57, 40.4	104, 78.8	< 0.001[b]*
No	46, 76.7	84, 59.6	28, 21.2	

*p < 0.05, [b]: Chi-square test

Physical activity or exercise has been shown to reduce the intensity of dysmenorrhea with various mechanisms (6,7). Recent studies in the literature have focused on different exercise interventions to deal with dysmenorrhea symptoms. Mahvash et al. (7) investigated the effect of an 8-week physical activity program on primary dysmenorrhea. The results of the current study suggested that performing regular physical activity reduces the symptoms of primary dysmenorrhea. Ortiz et al. (24) evaluated the efficacy of a physiotherapy program, consisting of stretching, Kegel, jogging and relaxation exercises, in primary dysmenorrhea. They stated that this program is effective for reducing dysmenorrhea symptoms when they are regularly performed. In another study, Vaziri et al. (25) compared the effects of exercises (aerobic and stretching) on severity of primary dysmenorrhea. They reported that both interventions resulted in a significant reduction in dysmenorrhea severity. In addition, some studies also showed that there was no association between dysmenorrhea and physical activity level. Blakey et al. (26) put forward no association between participation in physical activity and primary dysmenorrhea. Maruf et al. (27) demonstrated no association between physical activity level and adiposity in school adolescents with primary dysmenorrhea. Our study also found that there was no difference in physical activity levels according to menstrual pain intensity. These results might suggest that the physical activity level may be insufficient on changing menstrual pain level. And also, doing exercise regularly may be needed for decreasing the severity of dysmenorrhea or menstrual pain intensity.

Many pain conditions are related to reducing QoL (16, 17, 28-31). Primary dysmenorrhea is also a recurrent pain condition linked to menstruation (1). To our knowledge, there are few studies related to the associations between the menstrual pain intensity and QoL (16-18, 31). Unsal et al. (18) investigated the dysmenorrhea prevalence and determined its effect on QoL among female university students. They observed a significant decrease in most items of QoL as the intensity of dysmenorrhea increased. Weisberg et al. (17) declared severe menstrual pain with heavy menstrual bleeding affects all aspects of women's QoL much more than heavy menstrual bleeding alone. Iacovides et al. (18) showed that severe menstrual pain associated with primary dysmenorrhea impacts QoL. Tanmahasamut and Chawengsettakul (31) stated that dysmenorrhea in university students has high prevalence and moderate to severe dysmenorrhea have negative impact on daily and academic activities, and QoL. Similarly, our study also put forward that the on many parameters of the QoL show change according to menstrual pain intensity in women with primary dysmenorrhea. Our results suggest that management of menstrual pain might improve QoL. And also, increasing QoL may be a significant indicator of improvements in dysmenorrhea managements. Moreover, the menstrual pain together with the increasing the menstrual symptoms could be related to the intensity of dysmenorrhea.

According to our knowledge, there was no study investigating the menstrual symptoms in terms of menstrual pain intensity. In this study, it was seen that the women with severe menstrual pain intensity had more menstrual symptoms such as nervousness, headache, nausea, vomiting, fatigue and insomnia than those with mild and moderate pain. Therefore, in clinical practice, it should be considered that the menstrual pain intensity may be marker for the frequency and severity of menstrual symptoms in women with primary dysmenorrhea.

There were some limitations in this study. First limitation was the inclusion of women having primary dysmenorrhea with similar characteristics to the study. Because, most of them were university students and their age was changing between 18 and 25. They had also similar physical activity level. To increase generalizability, the students from three different universities were included. Especially for the physical activity level in different groups of the menstrual pain intensity, a population includes individuals with a wide range of physical activity level should be included in further studies. On the other hand, we evaluated the physical activity level using self-reported measures. However, the Turkish version of the IPAQ-7 was a valid and reliable questionnaire. More objective assessment methods for the measurement of physical activity level may be used in future studies.

CONCLUSION

In the current study, it was shown that there was no difference between physical activity level and menstrual pain intensities in women having primary dysmenorrhea. Moreover, women with higher menstrual pain intensity had lower QoL and higher frequency of menstrual symptoms. In clinics, these findings should be considered for the management of women with primary dysmenorrhea. However, there is a need for further studies linked to this condition.

Conflict of Interest: The authors declare no conflict of interest.

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RESEARCH ARTICLE

Gurkan Muratdagi[1]
Elif Sarica Darol[2]
Elif Kose[3]
Serap Ungan[4]
Muhammet Rasit Aydin[5]
Abdulkadir Aydin[6]
Elif Akar[6]
Ahmet Talha Turkmen[6]
Erkut Etcioglu[7]
Emine Melike Arslan[6]
Aslihan Arikan[6]
Ahmet Oksuz[8]
Yildiz Buyukdereli Atadag[9]

[1] Bahçelievler Family Health Center, Sakarya, Turkey
[2] Sakarya University Faculty of Medicine, Department of Neurology, Sakarya, Turkey
[3] Sakarya University Faculty of Medicine, Department of Public Health, Sakarya, Turkey
[4]Sakarya University Faculty of Medicine, Department of Internal Medicine, Sakarya, Turkey
[5]Sapanca State Hospital, Sakarya, Turkey
[6]Sakarya University Faculty of Medicine, Department of Family Medicine, Sakarya, Turkey
[7]Osmaneli State Hospital, Bilecik, Turkey
[8] Mimar Sinan Family Health Center, Sivas, Turkey
[9] Baglarbasi Family Health Center, Gaziantep, Turkey

Corresponding Author:
Gurkan Muratdagi
Bahçelievler Family Health Center, Sakarya, Turkey
Phone: +90 2642753708
mail: drgm54@gmail.com

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konuralptipdergi@duzce.edu.tr
konuralptipdergisi@gmail.com
www.konuralptipdergi.duzce.edu.tr

The Evaluation of the News Related to Coronavirus in National Media before and after the First Declared Case in Turkey

ABSTRACT

Objective: We aimed to investigate the content of Covid-19 news in the media before and after the declaration of the first Covid-19 case in Turkey, as well as the compatibility of their medical massages with World Health Organisation (WHO) data.

Methods: In this descriptive cross-sectional study, Covid-19 news in Turkey's most visited webpages of five newspapers and five internet news sites was examined retrospectively for two months categorized as the periods of one month before and one month after the first Covid-19 case declaration in Turkey. The news was evaluated according to their content, sources, content and headline compatibility, evidence and accuracy levels in terms of WHO reports, its potential to evoke social negative emotions such as anxiety, fear, panic, and to produce negative bias against China. Statistical analysis was performed by using the SPSS 21 program and the results were expressed as numbers and percentages.

Results: It was determined that in total of 7915 news, the most content was about the protection and prevention methods. In the news before and after the first case declaration in Turkey, the content-headline incompatibility rates were 50,8% and 1,1%; incompatibility rates of the medical information in the news with WHO reports were 7,1% and 2,9%; the rates of referencing were 74,3% and 66,9%, the rates of the news having the potential to produce anxiety and fear in the reader were 56,9% and 19,6% and to produce prejudice and negative attitudes towards China were 19,7% and 4,6%, respectively.

Conclusions: It seems that the declaration of the first Covid-19 case changed the news making pattern of the media to a more responsible behaviour for the public. We suggest that it is a rational approach to use the power of the media correctly in enhancing public awareness towards Covid-19 pandemic.

Keywords: Covid-19, Media, Analysis

Türkiye'de Görülen İlk Koronavirüs Vakasından Önce ve Sonra Ulusal Medyada Yer Alan Koronavirüs Haberlerinin Değerlendirilmesi

ÖZET

Amaç: Bu çalışmada ülkemizdeki ilk vakanın görülmesinden önce ve sonra medyadaki Covid-19 haberlerinin içerikleri ile topluma verdikleri tıbbi mesajların DSÖ verileriyle uyumunu araştırmak amaçlanmıştır.

Gereç ve Yöntem: Kesitsel tipte tanımlayıcı olarak tasarlanan bu çalışma için Türkiye'de ilk Covid-19 vakasının görüldüğü tarihten önceki ve sonraki birer aylık toplam iki aylık zamanda en çok ziyaret edilen beş gazetenin web sayfası ile beş haber sitesindeki Covid-19 haberleri geriye dönük olarak incelenmiştir. Haberler, içeriklerine, kaynaklarına, haber ile başlık uyumuna, DSÖ verilerine göre kanıt ve doğruluk düzeylerine, sosyal kaygı, korku, panik gibi negatif duygular ve Çin'e karşı ön yargı oluşturma potansiyellerine göre değerlendirilmiştir. Verilerin tanımlayıcı istatistikleri, SPSS 21 programı kullanılarak sayı ve yüzde şeklinde ifade edilmiştir.

Bulgular: İncelenen toplam 7915 haberin en fazla hastalıktan korunma ve önleme yollarına ait içeriğe sahip olduğu tespit edilmiştir. Türkiye'de ilk Covid-19 hastasının tespit edilmesinin öncesindeki ve sonrasındaki haberlerde başlık ile içeriklerinin uyumsuzluk oranlarının %50,8 ve %1,1; içerdikleri tıbbi bilginin DSÖ kaynaklarıyla uyumsuzluk oranlarının %7,1 ve %2,9; kaynak belirtme oranlarının %74,3 ve %66,9 olduğu tespit edilmiştir. İlk vakanın görülmesinden önceki haberlerin %56,9'unun, sonraki haberlerin %19,6'sının okuyucuda kaygı ve korku hisleri oluşturabilecek özellikte olduğu; ilk vakadan önceki haberlerin %19,7'sinin; sonraki haberlerin ise %4,6'sının Çin'e karşı önyargı ve negatif tutumlara neden olabilecek türde haberler olduğu belirlenmiştir.

Sonuç: Covid-19 vakasının ilk kez görülmesinden sonra medyanın yaklaşımını değiştirip daha sorumlu haberler yapmaya başladığı görüldü. Covid-19 salgınında halkın bilinçlendirilmesinde medyanın gücünü doğru kullanmanın akılcı bir yaklaşım olduğunu düşünüyoruz.

Anahtar Kelimeler: Covid-19, Medya, Analiz

INTRODUCTION

News about the new type of coronavirus pandemic that emerged in Wuhan, China and later called Covid-19 has recently taken a large place in the media. Although the news increases the awareness of the public about the coronavirus, it can also cause pollution of information due to various concerns of media outlets. Incorrect or incomplete contents of the news due to rating concerns can also lead to a negative orientation of the society in the field of health. People can develop false behavior patterns due to this misinformation. In this context, difficulties can be experienced by healthcare providers during the implementation of evidence-based and scientific applications and it may be limited or impractical to make correct medical interventions (1). The term 'infodemic' which was first used in the SARS epidemic, has a meaning of 'the rapid spread of both true and false information about a subject to large masses. This term was used again by the World Health Organization (WHO) in the Covid-19 outbreak. In Covid-19, a lot of unfounded and fearful information has reached wide masses through the media (2). There have been negative consequences of unfounded news such as prevention methods resulting in death, trial of various treatment methods that have no effect. In Covid-19 disease, scientists have limited knowledge about the prevention, treatment and many other aspects due to being a newly encountered microorganism (3,4). The pandemic started in China and spread rapidly all around the World. Negative attitudes towards the Chinese government were experienced in all countries of the World. This situation has caused a racism and discrimination towards Chinese people living in many countries of the World (5).

Investigating the content of the news about coronavirus in the written or visual media can allow to determine the information reached the society and the awareness they have about coronavirus. Studies in this area have been focused in examining the types of coronavirus-related news published in certain date intervals addressing the coronavirus or the information about the coronavirus they convey to the public. The scientific relevance of the news was not evaluated in these studies.

The purpose of this study is to evaluate the accuracy and reliability of the health information conveyed by the news to the reader by examining the contents and sources of coronavirus-related news published in national newspapers and news sites with high circulation in Turkey.

MATERIAL AND METHODS

In this descriptive cross-sectional study, the news related to coronavirus was retrospectively analyzed in the web pages of the five most visited newspapers and five news sites between the dates of 11.02.2020-11.03.2020 and 12.03.2020-12.04.2020 which are the periods of one month before and one month after the first coronavirus case declaration in Turkey on March 11, 2020, respectively. The most visited newspapers and news sites in the internet environment were selected by searching the sub-headings of "Newspapers" and "News" under the "Turkish Press and Publication" category on www.alexa.com. Accordingly, the top five most visited newspapers were Hürriyet, Milliyet, Sözcü, Akşam and Yeniakit; and the top five news websites were www.ensonhaber.com, www.haberturk.com, www.haberler.com, www.haber7.com and www.superhaber.tv. Using the "Google Advanced Search" option in webpages of selected newspapers and news sites, 3859 news items that include the words "coronavirus" and "COVID-19" between 11.02.2020 - 11.03.2020 before the first case was declared and 4056 news between 12.03.2020 - 12.04.2020 after the first case was declared were reviewed. Thus, a total of 7915 news was assessed.

Independent variables in the news before the announcement of the first Covid-19 case in Turkey were determined as 'the type of the news', 'whether the news creates negative situations such as anxiety, fear, panic', 'whether the news constitutes negative bias against China', 'whether the news containing medical information is compatible with WHO sources' 'whether the information given is referenced', 'the origin of the source of the news', 'whether the headline is compatible with the content of the news'. In addition to these variables; 'news prepared by the Ministry of Health for the purpose of informing the public', 'whether the news consists of measures taken throughout the country', 'whether the news emphasizes social solidarity', 'news about penalties that are imposed on people who do not comply with the restrictions', 'news about violence against healthcare workers', 'news with positive criticism towards the health system' were considered as independent variables in the news after the announcement of the first Covid-19 case in Turkey.

The news was analyzed by the researchers simultaneously with the video conference meetings. The decision of the absolute majority has been decisive in the categorization of the news content in order to minimize the personal differences. The data obtained were evaluated using the SPSS 21 (Statistical Packageforthe SocialSciences) program. Descriptive statistics were given as number (n) and percentage (%).

RESULTS

The Distribution of the News Content: There were 11.254 pieces of content in total of all news. In the news both before and after the the declaration of the first case in Turkey, it was seen that the content was mostly about the measures to be taken against the disease and the ways of protection (1837 (32.9%), 1868 (33.1%),

respectively). The least content in the news before the first case declaration was about the clinical information for the disease (478 (8.6%)); while it was about the economic effects of the disease (394 (6.9%)) in the news after the first case declaration (Table 1).

Table 1. The distribution of coronavirus news by content

Content of the news	Before the first case		After the first case	
	Number (n)	Percentage (%)	Number (n)	Percentage (%)
Advice on the prevention and protection	1837	32.9	1868	33.1
Epidemiological data	1670	29.9	1633	28.8
Magazine	968	17.2	1135	20.1
Economic effects of the disease	638	11.4	394	6.9
Information on the clinic of the disease	478	8.6	633	11.1
Total number of the contents	5591	100	5663	100

The Compatibility of the Titles with the Contents of the Corovirus-related News: It was determined that in 1961 (50.8%) of the 3859 news before the first case declaration, the title and the news content were completely incompatible. The number of news having titles completely compatible with the content was 212 (5.5%), mostly compatible was 82 (2.1%) and mostly incompatible was 1604 (41.6%). It was seen that, of the 4056 news articles examined after the first case declaration, 43 (1.1%) were completely incompatible, 904 (22.3%) were completely compatible, 2466 (60.7%) were mostly compatible, 643 (15,9%) were mostly incompatible (Table 2).

Table 2. The compatibility of the titles with the contents of the coronavirus-related news

The compatibility of the news title with the content	Before the first case		After the first case	
	Number (n)	Percentage (%)	Number (n)	Percentage (%)
Completely compatible	212	5.5	904	22.3
Mostly compatible	82	2.1	2466	60.7
Mostly incompatible	1604	41.6	643	15.9
Completely incompatible	1961	50.8	43	1.1
Total	3859	100	4056	100

Compliance of medical information in the news with WHO Sources: There were 1733 (21.9%) news containing medical information among the 7915 news. It was observed that the medical information given in 312 (27.1%) of the 1150 news articles published in the period before the first case declaration in Turkey, was completely compatible with WHO sources, while 626 (54.4%) was mostly compatible, 82 (7.1%) was completely incompatible with WHO sources, and 130 (11.4%) was mostly incompatible.

The medical information given in 150 (25,7%) of the 583 medical news published in the period after the first case declaration in Turkey, was completely compatible with WHO sources, 355 (60,9) was mostly incompatible, 61 (10,5%) was mostly incompatible, 17 (2,9%) was completely incompatible. It was observed that the number of the news containing completely incompatible medical information with WHO sources was decreased to 17 (2,9%) after the declaration of the first Covid-19 case in Turkey (Table 3).

Table 3. Compliance of medical information in the news with WHO Sources

Compatibility of Medical Content with WHO Resources	Before the first case		After the first case	
	Number (n)	Percentage (%)	Number (n)	Percentage (%)
Completely compatible	312	27.1	150	25.7
Mostly compatible	626	54.4	355	60.9
Mostly incompatible	130	11.4	61	10.5
Completely incompatible	82	7.1	17	2.9
Total	1150	100	583	100

Referencing Status of the News: Regardless of the content of the news, 1579 (40.9%) of the news referenced in the news examined before the first case declaration. Eight hundred and fifty five (74.3%) of the news containing medical information before the first declared case in Turkey; and 390 of (66.9%) of the news containing medical information after the first case declaration, presented references for the medical information in their context. It was determined that no source was specified in 295 (25.7%) of the news before the first case declaration; and in 193 (33.1%) of the news after the first case declaration. In 192 of these news (12.2%), both Chinese and non-Chinese sources were given as references. Besides; it has been

determined that 1161 (73.5%) news reports used non-Chinese sources and 226 (14.3%) news reports used Chinese-based sources.

In the news examined after the first case declaration, it was observed that the number of the news referring to the source decreased to 1153 (28.4%). Among them, 14 (1.2%) were both from China and outside of China, 1087 (94.3%) were from outside of China, and 52 (4.5%) were from China (Table 4).

Table 4. Referencing status of the news

	Before the first case		After the first case	
	Number (n)	Percentage (%)	Number (n)	Percentage (%)
Source of the medical news				
Source Available	855	74.3	390	66.9
No Source	295	25.7	193	33.1
Total	1150	100	583	100
Origin of the source in all cited news				
Chinese sources	226	14.3	52	4.5
Chinese and non-Chinese sources	192	12.2	14	1.2
Non-Chinese sources	1161	73.5	1087	94.3
Total	1579	100	1153	100

News with A Potential to Evoke Negative Thoughts and Prejudice: According to the evaluations made by the researchers in our study; 2196 (56.9%) of the news before the first case declaration; 796 (19.6%) of the news after the first case declaration had content that could create negative thoughts such as fear, anxiety and panic in the readers. It was evaluated that 760 (19.7%) of the news before the first case declaration and 186 (4.6%) of the news after the first case declaration had content that could create prejudice against the citizens of Public Republic of China, the place where the pandemic started.

Some Features of the News After the Declaration of the First Case in Turkey: 379 (9.3%) of the news after the declaration of the first case, consisted of daily developments shared by the Minister of Health in order to inform citizens. 1594 (39.3%) of the news was related to the current measures taken by the government; 870 of them (21.4%) emphasized social solidarity; 179 of them (4.4%) mentioned the punishments as a result of not complying with the measures, 9 of them (0.02%) were about violence in health. It was determined that 232 of the news (5.7%) consisted of positive and appreciative news about health workers and the health system.

DISCUSSION

In this study, we evaluated the data obtained from newspapers and news publishing sites on the internet. We observed that the contents of the news published both before and after the declaration of the first Covid-19 case in Turkey, were about "prevention and protection", "epidemiological data" and "tabloid" in similar proportions, mostly about "prevention and protection". Media, which is an important source of information on health for people, usually targets to make news that will attract public attention rather than medical professional news (6). In a study investigating the role of the media in China, it was reported that in the early days of the pandemic, the contents of the news were mostly about the preventative and control procedures, the process of medical treatment and the economic effects of the disease, the most content was about the preventative and control procedures (7). These results are completely in accordance with the results of our study. In a study investigating the search behaviors of people on the internet related to Covid-19 in Italy, it was determined that the most searched topics were face masks, disinfectants, Covid-19 symptoms, coronavirus vaccine (8). Since the media aims to cover the news that mostly attracts the attention of people, we suggest that the disease prevention aspects are mostly selected subjects for the news.

The title of a news item can be different from its content. Such situations may occur as a result of the media's desire to attract more readers' interest and increase the reading rates (7). In our study, when we evaluated the compatibility of the news titles with the contents; we observed that the rate of completely or mostly incompatible news titles before the first case declaration, was 92.4%, and this rate decreased to 17% after the first case declaration. We also observed that the rate of completely or mostly compatible titles with the contents which was 7.6% before the declaration of the first case, increased to 83% after the first case declaration. We suggest that these alterations in the rates are due to the fact that the Covid-19 disease was perceived as a more serious situation in our country after the first case was declared, and the enhanced awareness of the news creators prevented rating concerns and led them to make news with compatible titles and contents.

In this study, we assessed the compatibility of the contents of the news containing medical information with the medical announcements published by WHO in terms of the medical messages they give to the reader. We observed that the rate of the news completely compatible with WHO sources which was 27,1 before the declaration of the first case decreased to 25.7%

after the first case declaration, the rate of the mostly compatible news increased from 54.4% to 60.9%, and the rate of completely incompatible news decreased from 7.1% to 2.9%. We may suggest that WHO was considered as a reliable source by the media about a disease seen for the first time in the World. On the other hand, we observed that no source was given to the reader in the news containing medical information (25.7% before the first case declaration and 33.1% after the first case declaration). In a study evaluating the medical messages of cancer news in the media in terms of evidence-based medicine, it was determined that 36.5% of the news, similar to our study, consisted of news that did not indicate the source (9). Although making news that would attract the attention of people is a reporting method, the accuracy of the news and especially the consistency of the information they contain with the scientific data is very important. It is also important to inform the public about a disease with a pandemic characteristic with the cooperation of health service providers and media, to serve the public with news that has scientific value and reliable source, in order to raise the awareness of the public and to help them to act correctly on this issue. In this context, it is essential for the journalists who make the news to receive opinions from experts in their field during the preparation of the news, and to convey up-to-date and correct messages to the public (9). The media has a great impact on alleviating the effects of a pandemic and reducing the speed of its spread (10). It is vital to reach people with medical information prepared from the right sources. In the Covid-19 pandemic, there were sad events that resulted in death due to misunderstanding from some of the news which led misuse of methanol for the purpose of coronavirus protection (3). As a result of some of the news with incorrect message content, many negative consequences such as refusing or delaying treatment, resorting to wrong protection from the disease were encountered (4).

When we evaluated all the news, we observed that 14.3% of the news with a mentioned source before the first case was of Chinese origin, while this rate decreased to 4.5% in the period after the first case declaration. Since the pandemic started in China and spread all over the world, most newsworthy events related to the disease were seen in China at the beginning of the pandemic. However, we suggest that this rate decreased due to the fact that the events in the news also originated from countries in the world other than China, as the cases spread to other countries of the world over time.

As a result of the evaluation of the researchers in our study, it was determined that the news content with a potential to cause negative emotions such as fear and anxiety in the readers was 56.9% before the first case declaration and 19.6% after the first case declaration. At this point, many countries of the world have encountered such situations and made efforts to overcome these problems. Combating the unfounded rumors and fear-inducing news about the coronavirus spreading all over the world has been an important public health problem (11). We consider that the decrease that we observed in this rate after the first case declaration may be due to the fact that the efforts have yielded results in our country, similar to the efforts to fight against unfounded news, especially leaded by WHO.

The fact that China is the source of the pandemic, has led to the formation of racism and prejudices associated with the pandemic all over the world. Especially fake news content resulted in the negative attitudes and behaviors to Chinese people living in many parts of the World (8). In Italy, a Chinese origin person was so affected by this situation that he tried to give a message to all people with a banner saying "I am not a virus, I am a human being." (12). In our study, we determined that the rates of the news that could create bias against China wer 19.7% before the first case declaration and 4.6% after the first case declaration. We suggest that calling for an anti-racist approach in our country, as in the whole world, was effective in the lower rates observed after the first case declaration.

It is essential for the states to interact and communicate with the public through media in emergencies involving public health. In this regard, it is very important for the governments to lead a war like a pandemic (13). In addition to taking many measures in accordance with the health policies of the country since the first case was seen in our country, the people of the country were informed daily by the Minister of Health through the media. In this study, we observed that the rate of news with this feature was 9.3%.

It is very important for societies to act as a unit and in solidarity under the leadership of health authorities in public health problems that affect the whole country, in order to minimize the negative impact. We evaluated the news in this aspect and observed that the news after the first case declaration in our country, had a rate of 21.4%. The occupational group that has the highest priority in combating the pandemic is healthcare professionals. All healthcare workers who work more devotedly than ever to control the disease and treat patients in the best way, have been supported by many societies in our country (14). Similar to this situation, which is one of the results of social solidarity, the rate of news that appreciates healthcare professionals and their activities was found to be 5.7% of the news after the first case declaration. Violence against healthcare professionals is one of the main problems that are tried to be eliminated by health policies in many countries of the world. In the news after the first

case declaration, we observed that the rate of the news on violence against healthcare workers was 0.02%. We consider that this low rate rate is associated with the social solidarity and awareness that has developed in our country with the pandemic.

CONCLUSION

Health education gains great importance when encountering major problems such as the pandemic that concern the whole World. Using the media as a tool in health education is a rational approach. In the fight against Covid-19, people's high health literacy is one of the important ways to be least affected by the pandemic. The basic requirement of high health literacy is to have the right health information. Accordingly, the publication frequency and content standards of Covid-19 news can be determined by making some legal arrangements for the internet media. In addition, efforts should be made to understand the importance of health journalism and to ensure that news creators have a high level of health literacy.

Experts and journalists must cooperate in making news that contain accurate and reliable information. Thus, both the awareness of the society on Covid-19 can be enhanced and the correct information can be provided. The Ministry of Health and public health organizations will convey the right messages to large masses through the media in the fight against the public health problem that concerns every segment of the society such as the pandemic.

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RESEARCH ARTICLE

Ibrahim Ates[1]
Turgay Tugay Bilgin[2]

[1] Erzurum Technical University, Faculty of Engineering and Architecture, Department of Mechanical Engineering, Erzurum, Turkey
[2] Bursa Technical University, Faculty of Engineering and Natural Sciences, Department of Computer Engineering, Bursa, Turkey

Corresponding Author:
Ibrahim Ates
Erzurum Technical University, Faculty of Engineering and Architecture, Department of Mechanical Engineering, Erzurum, Turkey
Phone: +90 444 5 388 (2302)
mail: ibrahim.ates@erzurum.edu.tr

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The Investigation of the Success of Different Machine Learning Methods in Breast Cancer Diagnosis

ABSTRACT

Objective: The aim of this study is to identify cancer earlier in life using machine learning methods.

Methods: For this purpose, the Wisconsin Diagnostic Breast Cancer dataset was classified using Naive Bayes, decision trees, artificial neural networks algorithms and comparison of these machine learning methods was made. KNIME Analytics Platform was used for applications. Before the classification process, the dataset was preprocessed. After the pre-processing stage, three different classifier methods were applied to the dataset. Accuracy, sensitivity, specificity and confusion matrices were used to measure the success of the methods.

Results: The results show that Naive Bayes and artificial neural network methods classify tumors with 96.5% accuracy. The success of the decision tree method in classification was 92.6%.

Conclusions: The machine learning algorithms can be used successfully in breast cancer diagnosis to determine whether the tumors are malign or benign.

Keywords: Breast Cancer Diagnosis, Machine Learning, Naive Bayes, Decision Trees, Artificial Neural Networks, KNIME

Meme Kanseri Tespitinde Farklı Makine Öğrenmesi Yöntemleri Başarısının İncelenmesi

ÖZET

Amaç: Bu çalışmanın amacı, makine öğrenimi yöntemlerini kullanarak kanseri yaşamın erken dönemlerinde belirlemektir.

Gereç ve Yöntem: Bu amaçla, Wisconsin Diagnostic Breast Cancer veri setinin Naive Bayes, karar ağaçları, yapay sinir ağları ile sınıflandırılması yapılmış ve söz konusu makine öğrenme yöntemleri karşılaştırılmıştır. Uygulamalar için 'KNIME Analytics Platform' u kullanılmıştır. Sınıflandırma işlemi yapılmadan önce veri seti ön işlemeden geçirilmiştir. Ön işleme aşamasından sonra, verilere üç farklı sınıflandırıcı yöntem uygulanmıştır. Yöntemlerin başarısını ölçmek için doğruluk, duyarlılık, özgüllük, hata matrisleri ve ROC eğrileri kullanılmıştır.

Bulgular: Uygulama sonuçları, Naive Bayes ve yapay sinir ağı yöntemlerinin tümörleri %96.5 doğrulukla doğru olarak sınıflandırdığını göstermektedir. Karar ağacı yönteminin sınıflandırmadaki başarısı %92.6 olarak elde edilmiştir. Sonuç olarak, her üç modelin üstün doğruluğa sahip sınıflandırma yaptığı söylenebilir.

Sonuç: Makine öğrenme algoritmaları, meme kanseri teşhisinde tümörlerin kötü huylu veya iyi huylu olup olmadığını belirlemek için başarıyla kullanılabilir.

Anahtar Kelimeler: Meme Kanseri Teşhisi, Makine Öğrenmesi, Naive Bayes, Karar Ağaçları, Yapay Sinir Ağları, KNIME

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e-ISSN1309–3878
konuralptipdergi@duzce.edu.tr
konuralptipdergisi@gmail.com
www.konuralptipdergi.duzce.edu.tr

INTRODUCTION

According to the data of the World Health Organization, approximately 2.3 million women in the world were diagnosed with breast cancer in 2020, and this number corresponds to 11.7% of the total cancer cases. The number of women who died of breast cancer in 2020 was reported to be approximately 685000 (1). This means that one out of every three cases results in death. In our country, it was reported by the World Health Organization that 24175 of 101018 cancer cases seen in women in 2020 were breast cancer (Figure 1). This rate corresponds to approximately 24% of the total cancer cases in women. Despite the high rate of breast cancer cases, researchers have stated that this type of cancer is among the types of cancer that can be treated if diagnosed at an early stage (3). Therefore, early diagnosis and subsequent determination of the appropriate cancer treatment helps to significantly eliminate the risk of death. Breast cancers are classified as benign and malignant according to their radiological and pathological examination. Doctors need support and conducive mechanisms to differentiate these tumors. However, there are cases where the distinction between benign and malign is contradictory. Therefore, automatic diagnosis systems will help for classification of tumors (4).

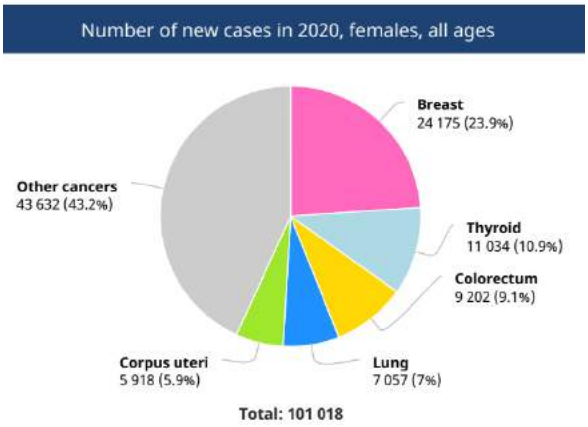

Figure 1. Distribution of cancer cases in women in Turkey (2)

Recently, many studies have been conducted in the era of artificial intelligence to diagnose breast cancer and classify them as benign or malignant. Machine learning algorithms have been applied by the researchers for the diagnosis of cancer and the detection of the tumor type and it has been stated that these algorithms are generally successful (5, 6). When the literature is reviewed, it is seen that various classification methods have been developed and applied for the diagnosis of breast cancer (3-8,15-26). Most studies used the Wisconsin Diagnostic Breast Cancer (WDBC) and Breast Cancer (BC) dataset from the UCI machine learning depository.

Rodrigues (7) examined the performance of Naive Bayes and J48 decision tree machine learning techniques in breast cancer diagnosis using the WDBC dataset containing missing data. It was stated that with the Naive Bayes algorithm, 97.8% accuracy in predictions was achieved while the accuracy was 96.05% with the J48 decision tree algorithm. It was stated that the dataset should be pre-processed before running the Naive Bayes algorithm because it does not operate with lost values, and normalization should be done to achieve better results.

Asri et al. (8) compared the performances of four different machine learning algorithms, which are the Support Vector Machine, C4.5 decision tree, Naive Bayes and k-Nearest Neighborhood, in the diagnosis of breast cancer using the WDBC dataset. The success of each algorithm in classification was evaluated using the values of accuracy, precision, sensitivity and specificity. The experimental results have shown that the Support Vector Machine gives the highest accuracy with a value of about 97.13%. All analyzes were carried out in a simulation environment using WEKA data mining program.

Saygılı (9) classified the WDBC dataset with machine learning methods such as Support Vector Machine, k-Nearest Neighborhood, Naive Bayes, J48 decision tree, random forest and MLP artificial neural networks. After the pre-processing stage, six different classifiers were applied to the dataset with 10-fold cross validation method. Accuracy, sensitivity, specificity, ROC area values and confusion matrices were used to measure the performance of the methods. As a result of the simulations, it was seen that the most successful method was random forest with 98.77% accuracy. The second most successful method is MLP artificial neural network method with 98.41% accuracy.

Ünal and Başçiftçi (10) made an empirical comparison of 10 popular machine learning models for breast cancer prediction. WDBC dataset was used to train the models and advanced accuracy metrics were used for comparison. The experimental results have shown that all models have high accuracy, but the Support Vector Machine algorithm has slightly better performance than other methods. In addition, Logistic Regression, K-Nearest Neighborhood, and artificial neural networks have also been found to be powerful classifiers for predicting breast cancer.

Mohammed et al. (11) targeted to increase the accuracy of the classification made in the diagnosis of breast cancer by processing the missing data in WDBC and BC datasets with the resampling technique. In the study, Decision Trees (J48), Naive Bayes, Sequential Minimal Optimization machine learning algorithms are used. The results obtained showed that the use of the resampling filter in the preprocessing stage increased the performance of the classifier. In this study, the performance of different machine

learning methods to classify tumors as benign or malignant was examined on breast cancer dataset. Data mining has been done with three classification algorithms. Naive Bayes, Decision Trees and MLP Artificial Neural Networks were used as classification algorithms. The application was implemented in version 4.2.3 of the KNIME Analytics Platform data mining program. Accuracy, sensitivity, specificity, precision, confusion matrices and ROC curves were used to measure the success of the methods examined.

METHOD

Dataset: The original dataset (WDBC) used in this study is located in the Machine Learning Repository of the University of California, Irvine (UCI). The dataset was created by Dr. Wolberg at the University of Wisconsin Hospital in the United States of America (12). The WDBC dataset used in this study was taken from Kaggle and consists of 569 samples and 30 cytologic features (13). The features derived from a digital scan of fine needle aspirate (FNA) slides (ref). For digital analysis examinations on the cytology slide, an area containing the most abnormal cells was selected and an image was obtained from this area. Ten major nuclear features were measured for each cell in this image. These features are radius, texture, circumference, area, smoothness, compactness, concave, concave points, symmetry, fractal dimension of the cell nucleus. High values of these features was modeled to correlate with malignancy. The average value of each feature, the worst (average of the three largest values) and standard error were evaluated for each image, resulting in a total of 30 features for each case. The details of the characterization procedures of each nuclear features can be found in (14). Of the 569 samples in the dataset, 357 were classified as benign and 212 as malignant. The summary of the WDBC dataset is shown in Table 1. An example for image of a benign and malignant breast fine needle aspirates is given in Figure 2 and 3, respectfully.

Table 1. The summary of the WDBC dataset (15)

Feature no	Feature name	Average	Standart error	Maximum
1	Radius	6.98-28.11	0.112-2.873	7.92-36.06
2	Texture	9.71-39.28	0.36-4.89	12.02-49.54
3	Circumference	43.79-188.50	0.76-21.98	50.41-251.20
4	Area	143.50-2501.00	6.80-542.20	185.20-4254.00
5	Smoothness	0.053-0.163	0.002-0.031	0.071-0.223
6	Compactness	0.019-0.345	0.002-0.135	0.027-1.058
7	Concave	0.000-0.427	0.000-0.396	0.000-1.252
8	Concave points	0.000-0.201	0.000-0.053	0.000-0.291
9	Symmetry	0.106-0.304	0.008-0.079	0.157-0.664
10	Fractal dimension	0.050-0.097	0.001-0.030	0.055-0.208

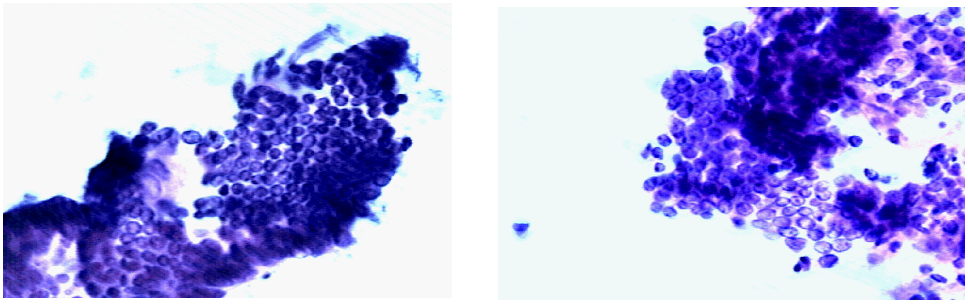

Figure 2. Benign cancer cell sample images (16)

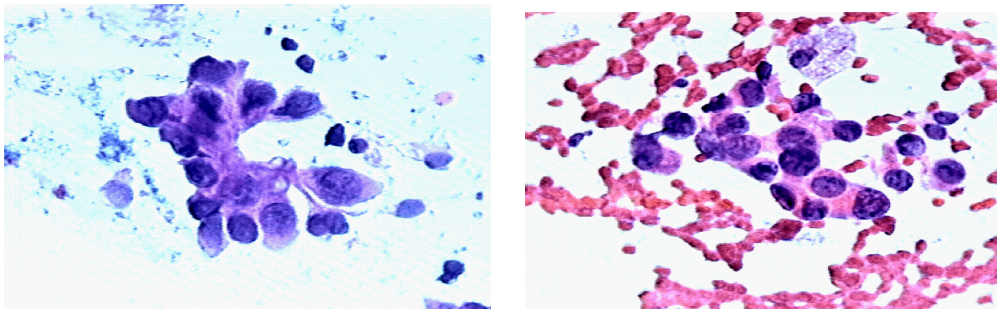

Figure 3. Malignant cancer cell sample images (16)

Machine Learning Methods: The Naive Bayes classifier is based on Bayes' theorem. Bayes theorem was found by Thomas Bayes in 1812 and is based on the conditional probability calculation formula. In the Naive Bayes algorithm, the probability of occurrence of each situation is calculated for a sample and the classification process is made according to the one with the highest probability value.

The basic idea in decision tree algorithms is based on dividing the input dataset into groups with the help of a clustering algorithm. The clustering process continues in depth until all the elements of the group have the same class label. In other words, a decision tree is a structure used to divide a dataset containing a large number of sample into smaller groups by applying a set of decision rules. Decision trees have a predefined target variable. In terms of their structure, they offer a strategy from top to bottom. How the split takes place in decision tree algorithms is one of the factors affecting the accuracy of the tree.

The artificial neural network is a model created by taking into account the working structure of the human nervous system, such as the brain that processes information. Neural networks can be used to model and identify trends that are too complex to be noticed by humans or other computer techniques, with their extraordinary ability to extract meaning from complex or imprecise datasets (4). Unlike the real biological neural network structure, many artificial neural network models have been created with some simplifications. Such simplifications are indispensable for understanding the properties under study and for any mathematical analysis.

KNIME Analytics Platform: KNIME includes modular data flow design and various tools for machine learning and data mining, called nodes. By making associations between nodes, dataset can be processed, visualized, interpreted and reported. Applications in this study were carried out in KNIME 4.2.3 program.

As stated before, the applications have been made on the WDBC file downloaded from Kaggle. First, the dataset was pre-processed. The related file has been transferred to the program with the "File Reader" node under the "IO" category. The 30 features of the sample taken from the patient were measured in the dataset and as a result, it was determined whether the tumor was benign or malignant. Secondly, the total data is divided into two parts in the "Partitioning" node under the "Manipulation" category, as 70% training sets and 30% test sets. The separation of the dataset into two parts was done by random sampling. As a result of the partitioning process, 398 data lines were determined as training sets, while the remaining 171 data lines were determined as training sets. At this stage, the dataset has become suitable for classification algorithms. The training set obtained in the partitioning node is processed in “Learner” node in which the learning takes places. The test set output of the partitioning node is sent to the “Predictor" node. Both nodes are in the "Mining" category. On the other hand, the learning experience gained from the “Learner” node also comes to “Predictor” node. Thus, the “Predictor" node has two entry points. Finally, the "Scorer" node in the "Mining" category was added to evaluate the success of the classifiers. The "Scorer" node provides the assessment of other success criteria, especially the confusion matrix. Also, "ROC Curve (local)" node has been added to view ROC curves.

Figure 4 shows the selections used in the configuration of the "Decision Tree Learner" node related to the decision tree method. This node is the section where the decision tree algorithm performs learning. It is stated that the class to be decided is the "diagnosis" column. While creating the decision tree, Gini index was used as the quality measure in the division process. The tree building process is set to continue until only one item remains on each node, and no pruning will be performed. In addition, multipath splits have been applied instead of binary nominal splits.

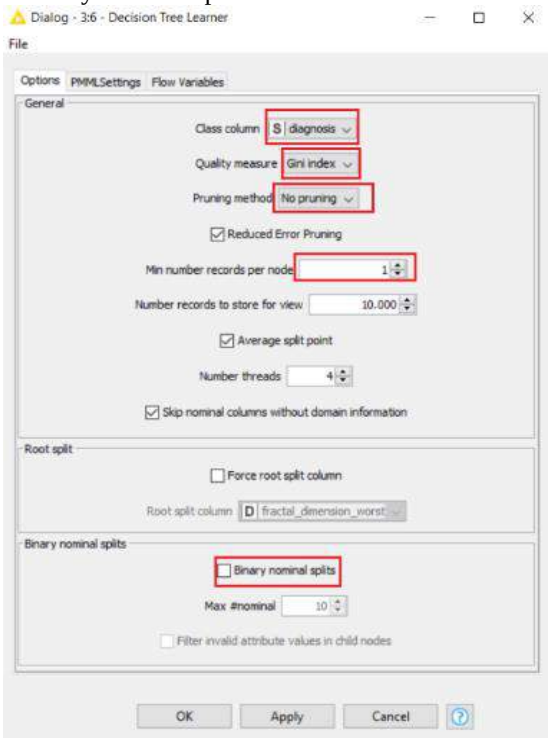

Figure 4. Decision Tree Learner configuration window

In this study, the Multilayer Perceptron (MLP) algorithm also is used as neural networks method. For this purpose, "RProp MLP Learner" and "Multilayer Perceptron Predictor" nodes, which are under the "Mining" category in the KNIME

program, have been used. Prior to this, each set obtained after the Partitioning node is normalized in the "Normalizer" node. Thus, it is aimed to prevent the effect of feature values that may be in different orders to the results. All dataset is subjected to the Min-Max normalization process and arranged so that their values are between 0-1. The normalized training set is connected to the "RProp MLP Learner" node. The values entered in "RProp MLP Learner" configuration are shown in Figure 5. A maximum of 100 iterations will be made to determine the weight coefficients in the learning process. The number of hidden layers is determined as 5 and the number of hidden neurons per layer is determined as 10. The class column to be trained is specified as "diagnosis".

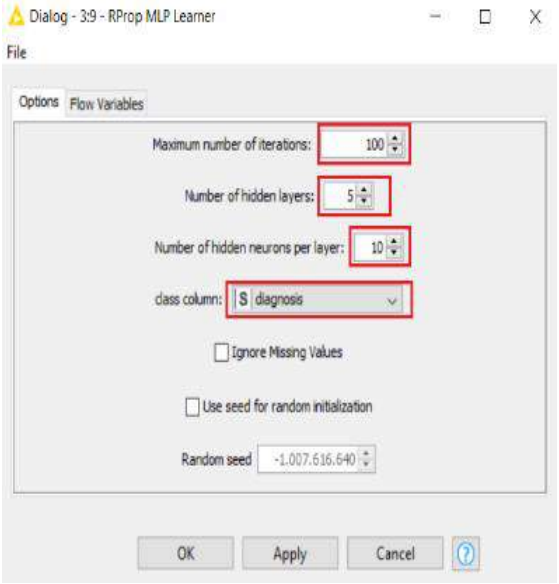

Figure 5. RProp MLP Learner dialog window

Performance Metrics: In this study, the error matrix, accuracy, specificity, sensitivity, precision, F score and ROC curve were used as performance metrics. Confusion matrix is used to measure the performance of machine classification algorithms when the number of class labels is two or more. The confusion matrix is a table made up of four different combinations with predicted and actual values when the number of class labels is two. With the confusion matrix table, the values predicted by the model and the actual values are compared.

Various performance metrics have been developed using the values in the confusion matrix. The most commonly used of these is accuracy. Accuracy is a measure of the correct predictions made by the classifier and provides general information about how many samples were classified as true or false. The accuracy is calculated with the following equation.

$$\text{Accuracy} = \frac{TP + TN}{FP + FN + TP + TN} \quad (1)$$

Sensitivity or Recall is a metric that shows how much of the values that are actually positive are predicted positively and is obtained from Equation 2.

$$\text{Sensitivity, Recall} = \frac{TP}{TP + FN} \quad (2)$$

Another metric derived from the confusion matrix is precision. Precision shows how many of the values are predicted positively are actually positive and is calculated by Equation (3).

$$\text{Precision} = \frac{TP}{TP + FP} \quad (3)$$

Specificity, on the other hand, is an indicator of how much of the values that are actually negative are predicted negatively and is calculated from Equation 4.

$$\text{Specificity} = \frac{TN}{TN + FP} \quad (4)$$

The F-score (F-measure) shows the harmonic mean of the precision and sensitivity values. It is a more successful metric compared to accuracy, especially in datasets that are not evenly distributed. F score can be calculated from Equation 5.

$$F - \text{score}\,(F - \text{measure}) = \frac{2 \times \text{Precision} \times \text{Sensitivity}}{\text{Precision} + \text{Sensitivity}} \quad (5)$$

Another important performance criterion used outside of the above metrics derived from the confusion matrix is the ROC curve. The ROC curve is basically a metric that shows whether the obtained classification models are working well and is calculated as follows.

$$\text{ROC} = \frac{\text{True Positive Rate (TPR)}}{\text{False Positive Rate (FPR)}} = \frac{\text{Sensitivity}}{1 - \text{Specificity}} \quad (6)$$

RESULTS

Figure 6 shows the image of the workflow chart created in the KNIME program within the scope of this study.

The confusion matrices and performance metrics of the three methods are shown together in Table 2. When Table 2 is examined, it is seen that the Naive Bayes algorithm and MLP artificial neural networks algorithm had the same accuracy with 96.5%. In two algorithms, they made 165 correct classifications and 6 incorrect classifications. At the same time, the F-score values were the same in both methods. On the other hand,

the classification accuracy percentage of the decision tree algorithm was obtained as 92.4%. It classified 13 samples of dataset incorrectly and classified 158 samples of dataset correctly. The performance criteria of the decision tree were lower than the other two algorithms.

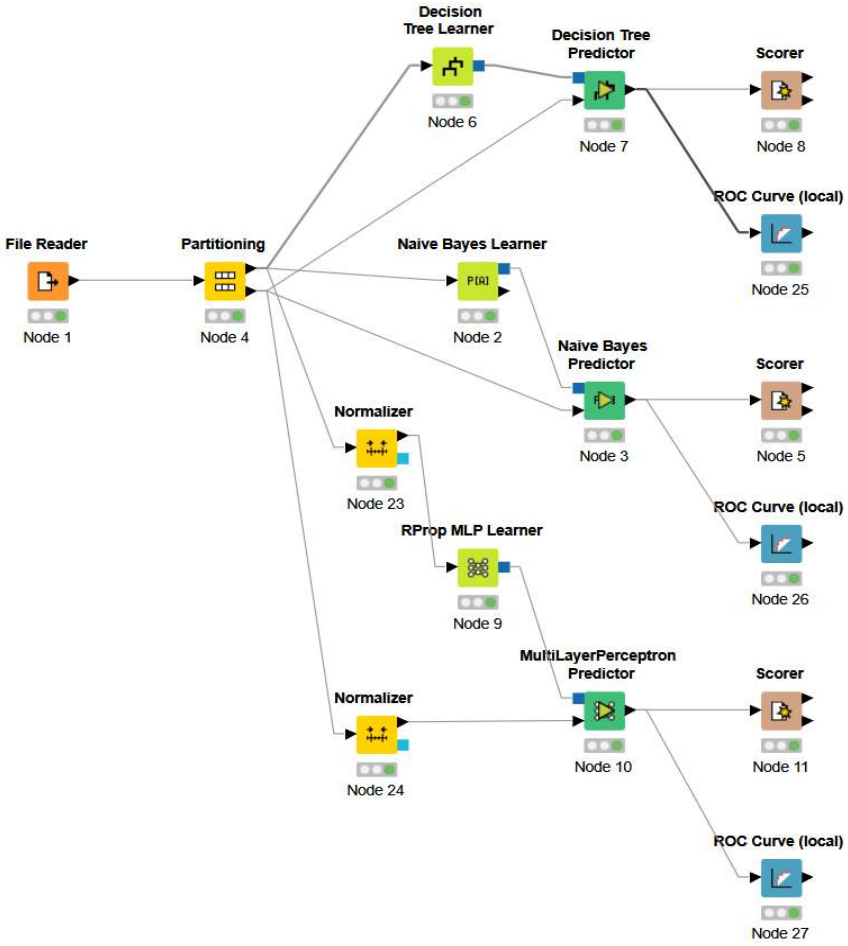

Figure 6. Workflow chart created in KNIME

Table 2. Confusion matrices and performance metrics

Naive Bayes		**Predicted value**		**Performance metrics**				
		Malign	Benign	Accuracy	Sensitivity	Specificity	Precision	F-score
Actual value	Malign	59	4	0.965	0.937	0.981	0.967	0.952
	Benign	2	106		0.981	0.937	0.964	0.972
Decision Tree		**Predicted value**		**Performance metrics**				
		Malign	Benign	Accuracy	Sensitivity	Specificity	Precision	F-score
Actual value	Malign	58	5	0.924	0.921	0.926	0.879	0.899
	Benign	8	100		0.926	0.921	0.952	0.939
MLP Artificial Neural Network		**Predicted value**		**Performance metrics**				
		Malign	Benign	Accuracy	Sensitivity	Specificity	Precision	F-score
Actual value	Malign	60	3	0.965	0.952	0.972	0.952	0.952
	Benign	3	105		0.972	0.952	0.972	0.972

Figure 7 shows the ROC curves obtained in each algorithm for malign and benign tumor classes. The ROC curves of Naive Bayes and MLP artificial neural network algorithms are quite similar to each other. The two curves have a fairly steep slope. The area value under the ROC curve was found to be 0.996 and 0.989 for the Naive Bayes and MLP artificial neural network method, respectively. So it can be said that the Naive Bayes algorithm is slightly more successful than the MLP

artificial neural network algorithm. In the decision tree method, the speed of convergence to 1 is slower than the other two algorithms. In Figure 8, the classified decision tree structure is shown. It is seen that there is a lot of branching in the decision tree. This can affect accuracy as well as complicate the classification algorithm. Here, a simpler tree can be obtained by pruning. In addition, the classification process was made by considering 30 features of the tumor samples. By applying feature selection algorithms, the most effective of those on classification can be selected. Therefore, the decision trees can be created having simple tree structure with more accurate classification.

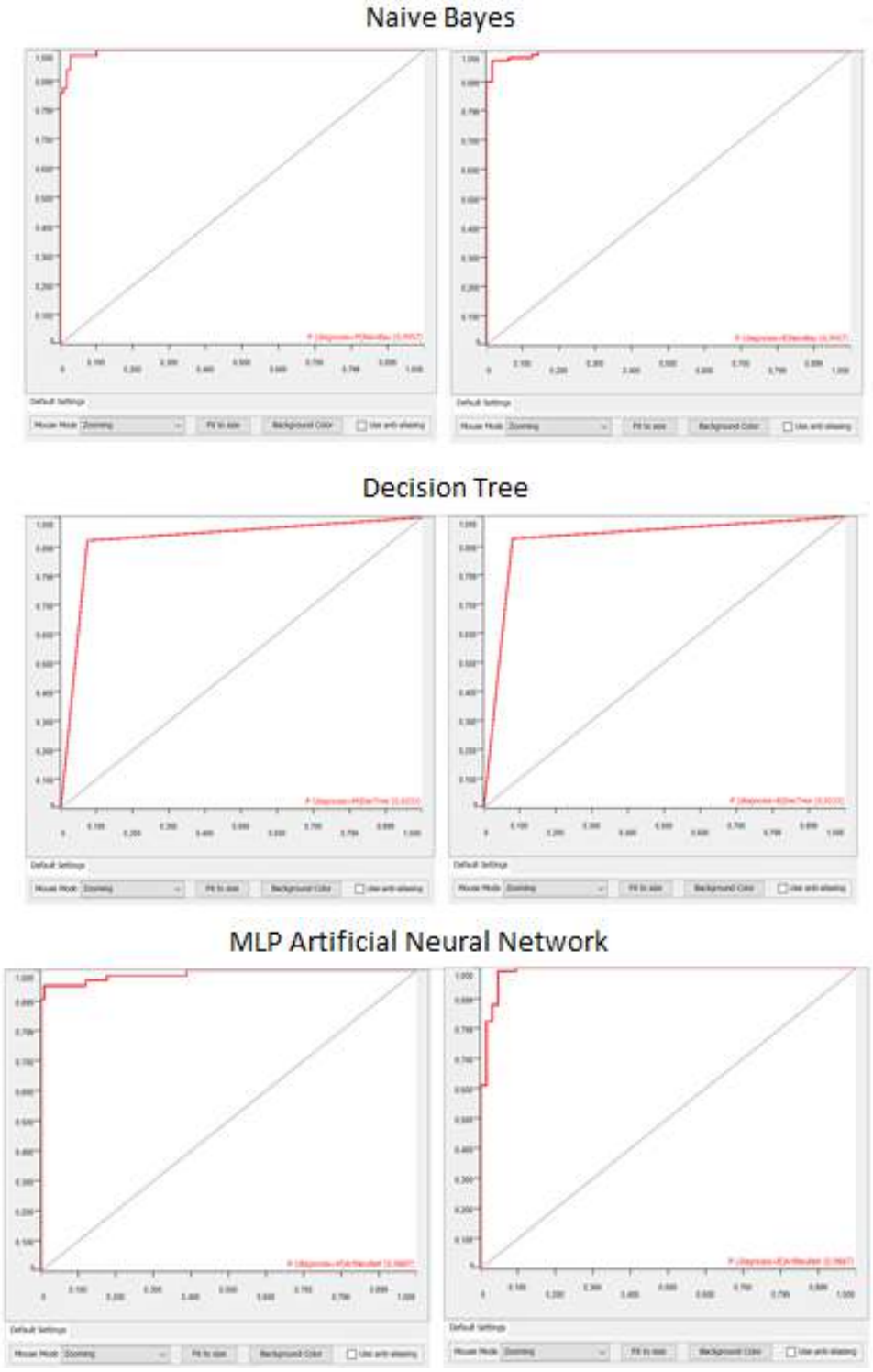

Figure 7. ROC curves

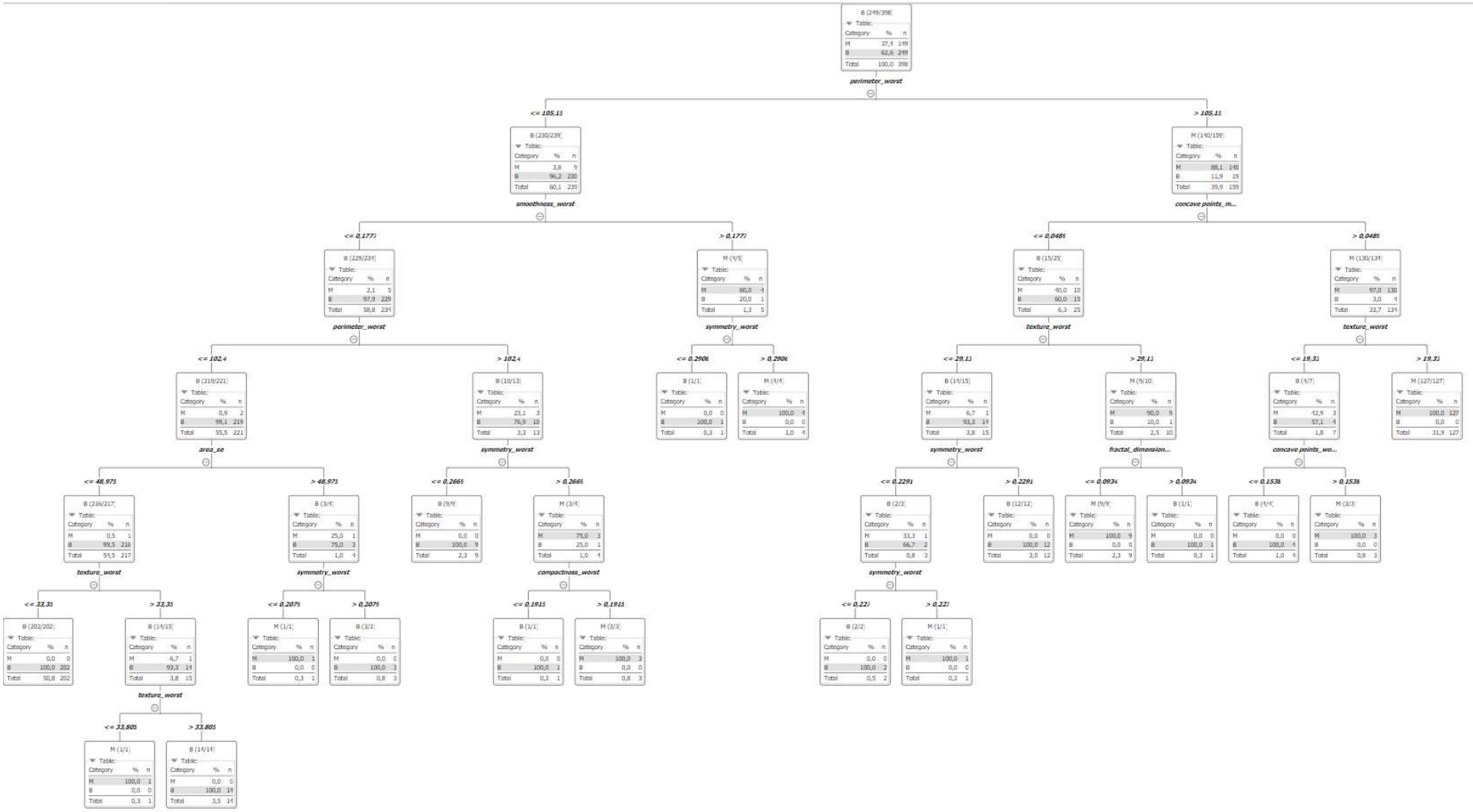

Figure 8. Decision tree structure (M: Malign, B: Benign)

DISCUSSION

In this section, the success rates achieved with various techniques on the WDBC data set in recent years are included. The classification accuracy of the existing studies in Table 6 varies between approximately 88% and 97%. Considering the 92.6% and 96.5% classification accuracies obtained in this study, it can be said that it has a high success among the existing studies in the literature.

Table 3. Methods and classification accuracy rates used in literature

Reference	Method	Classification accuracy (%)
Miao et al. (17)	Rough co-training	88.6
Lavanya and Rani (18)	Decision tree	94.84
Maldonado et al. (19)	Support vector machine	95.25
Koloseni et al. (20)	Differantial evolution	93.64
Astudillo ve Oommen (21)	Tree-based topology oriented self-organizing maps	93.32
Tabakhi et al. (22)	Naive Bayes/Decision tree	93.2/92.94
Lim and Chan (23)	Bandler-Kohout Subproduct	95.26
Rodrigues (7)	Naive Bayes/Decision tree	97.08/96.05
Asri et al. (8)	Support vector machine	97.13
Kong et al. (24)	Jointly sparse discriminant snalysis	93.85
Xu et al. (25)	Particle swarm optimisation	94.74
Nilashi et al. (15)	Fuzzy logic	93.2
Yavuz and Eyupoglu (26)	Generalized Regression Neural Network - Feed Forward Neural Network	94.54

As can be seen in Table 3, the studies have been conducted on the prediction of breast cancer diagnosis of many different machine learning techniques in the literature. It is noteworthy that despite the use of similar machine learning algorithms, the classification accuracies reported by researchers are different. The reason for that the machine learning is still an area with limitations and needs not only knowledge of data mining engineers but also the experience of the domain experts (27). Designing an effective machine learning model requires successful preprocessing, feature selection and classification processes (28). Each process includes different parameter selections and accordingly different solutions (27). Since there are no analytical approaches for parameter selection, the success of the model still depends on the choice of the expert performing the analysis. Therefore, setting the parameters and design of machine learning methods automatically has not been solved yet (28).

CONCLUSION

In this study, the performance of different machine learning methods to classify tumors as benign or malignant was examined on a breast cancer dataset. Data mining has been done with three classification algorithms. Naive Bayes, Decision Trees and Artificial Neural Networks algorithms were used as classification algorithms. The application was implemented in version 4.2.3 of the KNIME Analytics Platform data mining program. Accuracy, sensitivity, specificity, error matrices and ROC curves were used to measure the success of the methods examined. The key results from the study are listed below.

- Naive Bayes algorithm and MLP artificial neural network algorithm have shown similar classification performance. The accuracy value of both methods in classification was found to be 96.5%.
- Decision tree method classified the dataset correctly with 92.4% accuracy.
- Decision tree's success criteria are lower than the other two algorithms.
- It has been observed that the ROC curves of Naive Bayes and MLP artificial neural network algorithms are quite similar to each other and the two curves have a very steep slope. In the decision tree, the speed of convergence to 1 is slower than the other two algorithms.

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RESEARCH ARTICLE

Ozlem Coskun[1]
Yavuz Selim Kiyak[1]
Dilek Oztas[2]
Ozgur Erdem[3]
Isil Irem Budakoglu[1]

[1] Department of Medical Education and Informatics, Gazi University Faculty of Medicine, Ankara, Turkey
[2] Department of Public Health, Ankara Yıldırım Beyazıt University Faculty of Medicine, Ankara, Turkey
[3] General Directorate of Public Health, Ministry of Health, Ankara, Turkey

Corresponding Author:
Ozlem Coskun
Gazi University Faculty of Medicine, Department of Medical Education and Informatics, Ankara, Turkey
Phone: +90 312 202 7445
mail: drozlemcoskun@gmail.com

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konuralptipdergisi@gmail.com
www.konuralptipdergi.duzce.edu.tr

Skills in National Core Curriculum: National Survey of Primary Care Physicians in Turkey

ABSTRACT

Objective: Core curriculum describes the basic standard of medical education. In this study, we aimed to investigate primary care physicians' views on the minimum level of competency required in a general practitioner about skills listed in the National Core Curriculum for Undergraduate Medical Education-2014 (NCC-2014) and whether they feel competent in these skills.

Methods: Between October 1, 2017 and September 1, 2018, 27652 primary care physicians who work in Turkey were surveyed about the skills listed in the NCC-2014. The participants rated the minimum competency for every skill on 0–4 level, and also stated whether they felt that the primary care physicians were competent.

Results: 4117 (14.9%) participants answered entire questions. Out of 136 skills, "Level3—Should be able to do the skill in cases which are frequent and not complex" was the most selected category for 123 (90.4%) skills, "Level2—Should be able to do the skill according to the guidelines in a state of emergency" was the most selected category for 10 (8.1%) skills, and "Level4—Should be able to do the skill even in complex cases" was the most selected category for 3 (2.2%) skills by participants.

Conclusions: The participants are generally willing to perform skills, but according to them, some of the skills are complex. There are differences between the required competency levels in the NCC-2014 and the opinions of participants. Since physicians' views are important for curriculum development, medical curriculum developers around the world would benefit from findings of this study.

Keywords: Primary Care Physicians, Core Curriculum, National Survey, Skills

Ulusal Çekirdek Eğitim Programındaki Klinik Beceriler: Türkiye'deki Birinci Basamak Hekimlerinin Ulusal Çapta Araştırılması

ÖZET

Amaç: Çekirdek eğitim programı, tıp eğitiminin temel standartlarını ifade eder. Bu çalışmada; birinci basamak hekimlerinin Ulusal Çekirdek Eğitim Programı-2014'teki (UÇEP-2014) beceriler hakkında bir pratisyenin sahip olması gereken asgari yeterlilik seviyesi hakkındaki görüşlerinin ve kendilerini bu becerilerde yeterli hissedip hissetmediklerinin araştırılması amaçlanmıştır.

Gereç ve Yöntem: Türkiye'de çalışan 27652 birinci basamak hekimine 1 Ekim 2017 ile 1 Eylül 2018 arasında, UÇEP-2014'teki beceriler hakkında anket gönderildi. Katılımcılar, her bir beceriyi, olması gereken asgari yeterlilik düzeyini belirtmek için 0-4 arasında puanladı. Ayrıca bu becerilerde kendilerini yeterli görüp görmediklerini de belirttiler.

Bulgular: 4117 (%14.9) katılımcı bütün soruları cevapladı. 136 beceriden 123'ünde katılımcıların en çok seçtiği kategori "Seviye3— Karmaşık olmayan, sık görülen, durumlarda/olgularda uygulamayı yapar." iken, 10 (%8.1) beceride "Seviye2— Acil bir durumda kılavuz/yönergeye uygun biçimde uygulamayı yapar.", 3 (%2.2) beceride ise "Seviye4— Karmaşık durumlar/olgular da dahil uygulamayı yapar." en çok seçilen kategoriydi.

Sonuç: Birinci basamak hekimleri becerileri gerçekleştirmekte genel olarak isteklidir. Fakat onlara göre bazı beceriler karmaşıktır. UÇEP-2014 ile hekimlerin görüşleri arasında farklılıklar vardır. Hekimlerin görüşleri program geliştirme açısından önemli olduğundan, dünyanın dört bir yanındaki tıp eğitimi programı geliştiricileri bu çalışmanın bulgularından yararlanabilir.

Anahtar Kelimeler: Birinci Basamak Hekimleri, Çekirdek Eğitim Programı, Ulusal Anket, Beceriler

INTRODUCTION

The development of core curriculum is a wise solution to overcome the problem of content overload. After the World Summit on Medical Education in Edinburgh in August 1993, many medical schools around the world embarked on developing their core curricula (1). One of them, which is also on a national level, is in Turkey. Developing a National Core Curriculum (NCC) is an important step in describing the basic standard of the undergraduate medical education in Turkey. The attempts in this direction started in 2001. After a solid effort, the first NCC in Turkey was released in 2002 (NCC-2002). Since then, so many changes have occurred about the issues related to the health system in years that the core curriculum needed an overhauling. As a result, an attempt to develop a new NCC started in 2013. The last NCC was declared in 2014 based on the contributions from academic members of medical faculties and other stakeholders. Also, the Council of Higher Education (YÖK) declared that every medical school should structure its programs in line with the NCC-2014 to strengthen the standardization across the country (2,3).

The four primary factors of NCC-2014 included: (a) the frame of national competencies, (b) symptoms and conditions, (c) core illnesses/clinical problems, and (d) basic skills. In the list of basic skills in NCC, there are 136 items that include a wide range of skills ranging from taking a psychiatric history to performing a lumbar puncture and from conducting a neurological examination to performing a gastric lavage. These 136 skills are grouped under six titles. These titles include: (a) history taking; (b) general and local physical examination; (c) recording, reporting, and notifying; (d) laboratory tests; (e) invasive and non-invasive procedures; and (f) preventive and community medicine (3).

The minimum competency levels, which a graduate is supposed to have, are determined for these 136 skills. There are four competency levels of these skills (3):

Level 1: A graduate should be able to know how the skill is supposed to be done and explain the procedure to the patient.

Level 2: A graduate should be able to do the skill according to the guidelines in a state of emergency.

Level 3: A graduate should be able to do the skill in cases that are frequent and not complex.

Level 4: A graduate should be able to do the skill, even in complex cases.

According to the NCC-2014, a newly graduated student (undergraduate years) should have the ability to perform skills in one of four competency levels. For example, in accordance with the criteria of the NCC-2014, a graduate should be able to perform pleural puncture according to the guidelines in a state of emergency (Level 2). But the NCC-2014 requires students to possess a higher level of competency (Level 4) for providing the basic life support. (3)

Even if the NCC-2014 determined it, the primary care physicians actively working in the field could think differently according to their personal experience because individuals “internally make sense of what they have experienced” (4) Hence, we believe that it is important to reveal a general tendency of their opinions about these competency levels and identify their self-perceptions about their competency in these skills.

There are two studies that investigate the skills in the NCC. One of them aims to explore the views of primary care physicians about skills in the NCC-2014. However, the participants in this study were limited to 55 family physicians (5). The other study’s participants are residents, not primary care physicians, and the skills are from the NCC-2002 (6).

There are studies that investigate primary care physicians’ self-perception of competency in some skills. These studies are about skills that are limited to just one field such as dermatology (7) and life-threatening emergencies (8). Besides, the numbers of the participants in these studies were 40 and 213, respectively. There is a study that is not limited to just one field. This study is based on the skills from the national list for the training of family physicians; however, this study surveyed only 170 primary care physicians (9). Moreover, there are studies that investigate what primary care the physicians want to know. One of them is a content analysis of the questions asked by 88 primary care practitioners (10) and the other one aims to compare primary care physicians’ learning needs regarding 71 clinical skills useful in private and public sectors and includes 129 participants (11).

To our knowledge, no study examines all the skills that are listed in the NCC for undergraduate medical education. So, there is a gap to fill in this field in terms of the skills (all skills in the NCC) and the sample size (the number of the participants).

In this study, we aimed to investigate the following:

1. What are the primary care physicians’ views on the minimum required level of competency at undergraduate level in a primary care physician in terms of the skills listed in the NCC-2014?

2. Do primary care physicians feel competent in these skills?

3. Is there a significant difference in self-perceived competency levels between 0-5 years’ graduates and 5+ years’ graduates?

Since core curriculum in medical education is a global issue—it cannot be limited by countries’ borders—and physicians’ views are important for

every medical curriculum developer (12), the readers from outside Turkey can benefit from our results when they attempt to develop their national core curricula. We hope our study enlightens the way for development of medical curriculum.

MATERIAL AND METHODS

We conducted this descriptive study in Turkey. We prepared a form containing demographical questions and the list of medical skills specified in the National Core Curriculum (NCC-2014) for undergraduate medical education. In this questionnaire, we asked primary care physicians about the minimum required level of competency in primary care physicians and their current competency levels in these skills.

We provided the participants five options to rate every skill listed in the NCC-2014:

Level 0: It is not necessary.

Level 1: A primary care physician should be able to know how the skill is supposed to be done and explain the procedure to the patient

Level 2: A primary care physician should be able to do the skill according to the guidelines in a state of emergency

Level 3: A primary care physician should be able to do the skill in cases that are frequent and not complex

Level 4: A primary care physician should be able to do the skill, even in complex cases

Levels 1-4 have been extracted from the NCC-2014 as a copy. Level 0 was not in the NCC-2014 but we have added as an option because primary care physicians could think that a skill is totally redundant.

For the same skills, to learn the physicians' self-evaluation, we provided three options to the participants. The options were: (a) I feel competent, (b) I do not feel competent, and (c) I cannot decide whether I feel competent or not.

Some of the replies that the participants can give in response to the questions are as follows:

1. A primary care physician should be able to know how a lumbar puncture is supposed to be practiced and explain the procedure to the patient. I do not feel competent in performing a lumbar puncture.

2. I think a primary care physician should be able to provide the basic life support even in complex cases. I feel competent in basic life support.

We sent a web-based questionnaire to all primary care physicians who work for the Health Ministry in Turkey (N=27652). The participation was voluntary; the physicians who did not provide the informed consent were excluded. We collected the data between October 1, 2017 and September 1, 2018. We analyzed the data by using the Statistical Package for Social Sciences (SPSS) v.22.0 for Windows (Chicago, IL, USA). Descriptive statistics and Pearson's Chi-Squared Test were used. Significance level is accepted as 0.05.

Gazi University Ethical Board approved the study on September 11, 2017.

RESULTS

4,117 (14.9%) of the primary care physicians surveyed answered all the questions of the questionnaire. Of them, 1,364 (33.1%) were female participants, 3,741 (90.1%) general practitioners, and 376 (9.1%) specialists. In Table 1, we have provided the descriptive data of the participants.

Table 1. Demographic characteristics of participants.

Characteristics	**n (%)**
Gender	
Female	1364 (33.1)
Male	2753 (66.9)
Age (years)	
18-30	740 (18.0)
31-40	1078 (26.2)
41-50	1443 (35.0)
51≤	856 (20.8)
Years have passed after graduation from medical faculty	
0-5	708 (17.2)
More than 5	3409 (82,8)
Status	
General Practitioner	3741 (90.9)
Specialist	376 (9.1)
Specialties	
Family Medicine	278 (6.8)
Public Health	63 (1.5)
Microbiology	10 (0.2)
Other	25 (0.6)

Level 3 was the most selected category for 123 (90.4%) skills. Level 1 and Level 0 were not the most selected categories for any skill. Level 2 was the most selected category for 10 (8.1%) skills. The participants mostly selected Level 4 for just 3 (2.2%) skills.

"Level 2—Should be able to do the skill according to guidelines in a state of emergency" was the most selected category for these skills (The numbers placed next to skill names show competency levels, which are determined in the NCC-2014.):

- Performing pericardiocentesis-1
- Performing lumbar puncture-1
- Performing and repairing episiotomy-2
- Performing paracentesis-2
- Performing pleural puncture-2
- Performing blood transfusions-2
- Performing suprapubic bladder puncture-2
- Assisting with normal spontaneous delivery-2
- Stabilizing emergency psychiatric patients-3
- Using Galveston orientation scale-3.

"Level 4—Should be able to do the skill even in complex cases" was the most selected category for these skills (The numbers placed next to skills show competency levels in the NCC-2014.):

- Hand washing-4
- Providing basic life support-4
- Taking blood pressure-4

Table 2 contains the top ten skills that were classified as "Level 0—It is not necessary". Table 3 contains the top ten skills in which the participants felt the most competent and the least competent and the top five skills in which they did not decide whether they feel competent.

The following data help in analyzing the results when the participants who could not decide their competency were excluded:

- For 28 skills, the percentage of the 0-5 years' graduates who did not feel competent is significantly higher than 5+ years' graduates.
- For 47 skills, the percentage of the 0-5 years' graduates who did not feel competent is significantly lower than 5+ years' graduates.
- For 61 skills, there is no significant difference in the percentage between 0-5 years and 5+ years' graduates who do not feel competent.

The detailed data about all these skills are provided in the Appendix. We also reported all percentages on the minimum competency levels that primary care physicians selected for 136 skills require and the current competency levels that they perceive themselves. (See the Appendix.)

Table 2. Top ten skills which were classified as "Level 0- It is not necessary" by participants.

Skills	Participant numbers (%)	Competency Levels in NCC-2014
Performing pericardiocentesis	1041 (25.3%)	1
Performing pleural puncture	990 (24.0%)	2
Performing lumbar puncture	970 (23.6%)	1
Determining and evaluating the chlorine level in water	950 (23.1%)	3
Workplace visits and conducting workplace inspection	950 (23.1%)	3
Building a genetic tree and referring the patient to genetic counseling when it is necessary	900 (21.9%)	3
Preparing faecal smear and evaluating it under microscope	876 (21.3%)	3
Obtaining water sample	859 (20.9%)	4
Preparing dry-wet slide for microscopic evaluation and evaluating it under microscope	855 (20.8%)	3
Performing suprapubic bladder puncture	846 (20.5%)	2

DISCUSSION

In our study, Level 3 was the most common answer (123/136) received from the participants for skills. Moreover, the most selected category was Level 3 for 49 skills that were classified as Level 4 in the NCC-2014. This could mean that primary care physicians perceived their role as being just a first-step or coordinator of providing the patient care.

A research, which was conducted in Israel, found that 95.7% of primary care physicians considered that coordination of all patient care would be a very appropriate role for them (13).

Table 3. Top ten skills which were felt most competent and less competent and top five skills which were not decided whether feel competent by participants.

Skills	Participant numbers (%)	Competency Levels in NCC-2014
Felt most competent by participants, top ten.		
Taking blood pressure	3506 (85.2%)	4
Hand washing	3458 (84.0%)	4
Writing a prescription	3419 (83.0%)	4
Evaluating general condition and vital signs	3337 (81.1%)	4
Measuring blood sugar using a glucometer and evaluating its result	3307 (80.3%)	4
Teaching breast-feeding techniques	3277 (79.6%)	4
Teaching how to do breast examinaton by oneself	3254 (79.0%)	4
Abdominal examination	3235 (78.6%)	4
Conducting immunization services	3198 (77.7%)	4
Respiratory system examination	3184 (77.3%)	4
Felt least competent by participants, top ten.		
Performing pericardiocentesis	476 (11.6%)	1
Performing pleural puncture	557 (13.5%)	2
Performing lumbar puncture	674 (16.4%)	1
Using Galveston orientation scale	825 (20.0%)	3
Preparing faecal smear and evaluating it under microscope	856 (20.8%)	3
Evaluating vaginal samples	862 (20.9%)	3
Performing suprapubic bladder puncture	870 (21.1%)	2
Performing paracentesis	880 (21.4%)	2
Preparing dry-wet slide for microscopic evaluation and evaluating it under microscope	911 (22.1%)	3
Performing and repairing episiotomy	919 (22.3%)	2
Not decided whether felt competent, top five.		
Managing suicide attempt	1651 (40.1%)	2
Evaluating suicide risk	1607 (39.0%)	2
Identifying, protecting and transporting of forensic evidence	1517 (36.8%)	3
Following principles of working with a biological material	1509 (36.7%)	4
Identifying problems related to health in community by using epidemiologic methods and offering solutions for these problems	1491 (36.2%)	3

This finding supports our "primary care physician as a coordinator" argument. Our findings also indicate that primary care physicians are willing to do most of the skills until the skills become complex, and they know that there are others after them who would handle these complex cases. But the meaning and extent of complexity are uncertain because the NCC-2014 does not provide any further explanation about this.

There are other differences in competency levels between NCC-2014 and the opinions of primary care physicians. Although some skills classified as Level 2 by the NCC-2014, for 7 of these skills, the most selected category by the participants was Level 3. There is the same condition for Level 1 skills in NCC; the participants classified all of them as Level 2. These findings show that primary care physicians believe they should do more than what the NCC-2014 expects from them.

The participants encountered difficulties in two main topics: surgical procedures and microscopic evaluation.

Of the top 10 skills that were classified as Level 0, four (pericardiocentesis, pleural puncture, lumbar puncture, suprapubic bladder puncture) were surgical procedural skills. We also see that these four skills along with "performing paracentesis" and "performing and repairing episiotomy" are grouped in the list of top 10 skills in which the participants felt the least competent. A study that examines the self-perceived surgical skills of novice doctors (interns) supports our findings; the study revealed that the "interns did not feel adequately prepared to perform independent surgical skills" (14). Another study that states similar findings as ours states: thoracentesis is one of the skills in which the physicians perceive limitations to perform (8).

However, we can conclude that some primary care physicians have problems with performing some of the surgical procedures, which are listed in the NCC. Also, they do not think that these skills are necessary. The reason why they think these skills to be unnecessary could be a result of seeking an excuse for their incompetence. On the other hand, it is possible that they do not improve themselves on these skills because they consider them to be unnecessary.

The same possibilities are valid for skills related to the microscopic evaluation because there is the same situation. "Preparing fecal smear and evaluating it under a microscope" and "preparing dry-wet slide for microscopic evaluation and evaluating it under a microscope" are listed as unnecessary skills. Besides, both of them and "evaluating vaginal samples" are at the list of the top 10 skills in which the participants felt the least competent.

Our findings are similar to the research that was conducted on internal medicine residents. In this research, the researchers found that 37.0% of the internal medicine residents did not correctly prepare the specimen for a microscopic urinalysis, and many residents were not proficient in performing this (15). In our study, 41.6% of the primary care physicians perceive themselves as competent in performing the complete urinalysis (including microscopic evaluation).

The top five skills in which it was not decided whether primary care physicians felt themselves competent are discouraging. Approximately two out of five primary care physicians could not decide whether they felt competent in managing the suicide attempt and evaluating the suicide risk. Although the awareness of one's own performance is essential for improving clinical performance (16), they were not able to reflect even on these kinds of vital skills.

Another discouraging finding is about global diseases. Although "every medical student should carry a basic understanding of the major diseases that affect humans worldwide" (17), just 36.2% of the primary care physicians perceive themselves as able to identify the problems related to health in the community by using epidemiologic methods and offering solutions for these problems.

"Determining and evaluating the chlorine level in water," "obtaining water sample" and "workplace visits and conducting workplace inspection" are placed in the list of the top 10 skills that were classified as of Level 0. It should be noted that all these skills are obliged to be performed away from the institution's building. Besides, the technicians can contribute to this kind of skills. The primary care physicians consider these skills unnecessary because they might think that health service is confined to health institution's building walls, or these skills should be performed by technicians. However, the studies that were conducted in Canada support the first of these arguments. These studies show that the "proportion of 'office-only' general practitioners and family physicians rose from 14% in 1989 – 90 to 24% in 1999 – 2000" (18), and the billing outside office hours of family physicians decreased by 38.5% from 1991 to 2010 (19).

The significance of the differences on feeling not competent in some skills between 0-5 years' graduates and more than 5 years' graduates could mean that compared to junior primary care physicians, the experienced (more than 5 years after graduation) primary care physicians feel less incompetent in skills that they frequently perform in their professional life. The significantly lower rates of incompetence in pregnancy follow-ups and conducting immunization services can be seen as an indicator of this. It also could mean that experienced physicians become incompetent if they do not perform some skills for a long time. The significantly higher rates of incompetence in experienced primary care physicians, in comparison

with juniors' competence levels, on digital rectal examination and Rinne-Weber test can support this argument. Because physicians who actively work in the field rarely perform these skills and it could bring about lose their competence.

This study has some limitations. Although 27,652 primary care physicians who work for the Health Ministry in Turkey, just 4117 (14.9%) of them answered all the questions. Our findings may not be generalizable to Turkey because 23,535 (85.1%) primary care physicians were not taken into consideration. Another limitation of this study is the uncertainty of "complexity" classification. Since complexity of a case is relative and not determined by a consensus, every participant pictured a different "complex case" in his or her mind. They answered the questions according to their self-classification; hence this limitation might affect our findings.

CONCLUSION

To our best effort, this is the first study to investigate the opinions and self-perceived competencies of primary care physicians about all the skills listed in the NCC. We found that the participants are generally willing to perform skills, but they find some of them to be complex. Their self-perceived competency levels vary from skill to skill, but surgical procedures and microscopic evaluation are two of the weakest parts. Even if some opinions of primary care physicians are consistent with the NCC-2014, there are differences regarding the most selected categories by primary care physicians and the categories determined by the NCC-2014. Since primary care constitutes the basis of the healthcare system and a curriculum must consider the views of primary care physicians, curriculum developers around the world would benefit from the findings of our study.

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Appendix: Percentages of opinions of 4117 primary care physicians about competency levels on skills and their answers about self-perceived competencies, from National Survey about National Core Curriculum-2014 in Turkey, 2017-2018. (Cells with grey backround show competency levels determined by National Core Curriculum-2014 for each skill)

	All participants					All participants			Participants who cannot decide her/his competency were excluded		
	Level 4- Should be able to do the skill even in complex cases	Level 3- Should be able to do the skill in cases which are frequent and not complex	Level 2- Should be able to do the skill according to guidelines in a state of emergency	Level 1- Should be able to know how the skill is supposed to be done and explain the procedure to patient	Level 0- It is not necessary	I feel competent	I do not feel competent	I cannot decide whether I feel competent	Proportion of who do not feel competent, 0-5 years graduates	Proportion of who do not feel competent, 5+ years graduates	Significance of the difference between 0-5 and more than 5 years graduates (p)
A- History Taking											
History taking	31.2	42.9	13.0	11.6	1.2	76.2	6.6	17.1	9.0	7.8	0.33
Obtaining a psychiatric history	16.2	43.5	19.9	17.9	2.4	47.5	19.4	33.1	15.5	16.6	0.56
Evaluating mental status	21.1	43.8	19.5	13.7	1.8	62.4	12.2	25.3	62.8	72.6	<0.001*
B- General and Local Physical Examination											
Examination of a forensic case	14.5	37.9	26.8	14.6	6.1	39.3	31.1	29.6	44.3	44.1	0.95
Antropometric measurements	14.2	37.4	20.3	19.6	8.5	45.8	23.7	30.4	28.9	35.2	0.007*
Head and neck, ENT examination	20.2	56.1	13.6	9.0	1.0	77.0	6.3	16.8	8.4	7.3	0.37
Abdominal examination	23.3	53.3	14.3	8.1	1.0	78.6	5.5	15.9	6.9	6.5	0.74
Evaluating consciousness and mood examination	20.1	48.8	19.5	10.3	1.3	62.0	12.4	25.6	15.8	16.9	0.55
Child and newborn examination	18.3	52.6	17.8	10.3	1.1	54.8	17.9	27.3	42.1	21.3	<0.001*
Skin examination	17.5	55.2	14.9	11.1	1.3	64.1	13.1	22.8	26.1	15.2	<0.001*
Digital rectal examination	11.6	37.8	21.4	18.6	10.5	38.3	32.4	29.3	26.4	50.1	<0.001*
Examination of a pregnant	14.6	49.6	20.8	13.2	1.8	46.2	23.4	30.3	51.2	30.0	<0.001*
Evaluating general condition and vital signs	33.7	44.4	13.0	8.0	0.9	81.1	5.1	13.8	4.6	6.2	0.11
Eye and fundus examination	11.6	38.8	25.9	18.0	5.7	27.6	40.9	31.4	59.5	59.7	0.93
Gynaecological examination	10.0	36.2	26.0	20.0	7.7	30.7	38.9	30.5	62.8	54.4	0.001*
Cardiovascular system examination	17.8	49.5	21.4	10.1	1.2	55.1	16.1	28.8	17.5	23.7	0.002*
Musculoskeletal examination	16.9	54.4	16.9	10.7	1.1	71.1	8.4	20.5	9.8	10.7	0.54
Breast and auxiliary region examination	16.0	52.0	17.3	13.0	1.7	65.8	11.0	23.2	16.4	13.9	0.14
Neurological examination	17.3	49.2	21.1	10.9	1.5	51.6	18.6	29.8	15.0	29.1	<0.001*

Crime scene investigation	10.1	29.3	26.0	16.9	17.7	25.7	42.1	32.1	64.5	61.6	0.23
Forensic examination of a dead	13.5	39.0	23.6	14.9	9.0	44.6	25.7	29.7	31.7	37.6	0.01*
Respiratory system examination	22.3	53.3	14.6	8.8	0.9	77.3	6.1	16.6	6.5	7.4	0.44
Urological examination	13.0	47.5	22.3	13.8	3.4	46.7	19.4	33.9	32.1	28.8	0.16
C- Recording, Reporting and Notifying											
Writing a forensic report	15.2	36.5	26.6	14.3	7.3	44.5	26.7	28.8	41.9	36.5	0.02*
Taking informed consent	20.8	41,3	19.2	15.9	2.8	60.1	14.9	24.9	13.3	21.3	<0.001*
Writing an epicrisis report	20.2	41.2	19.5	14.1	5.0	58.7	15.7	25.6	17.9	21.9	0.04*
Preparing a patient file	20.6	40.9	17.8	14.1	6.6	58.7	15.1	26.2	11.6	22.5	<0.001*
Appropriate referral of patients	27.0	42.1	17.1	12.0	1.8	70.1	10.0	19.9	18.3	11.3	<0.001*
Issuing a death certificate	21.3	42.0	18.7	12.1	5.9	65.4	13.2	21.4	17.4	16.7	0.68
Reporting and notifying	20.0	43.4	18.7	13.6	4.2	56.1	16.0	27.9	25.4	21.5	0.056
Writing a prescription	34.4	44.6	10.7	9.0	1.3	83.0	4.9	12.0	7.6	5.2	0.01*
Preparing refusal of treatment form	25.5	40.1	17.3	13,9	3.2	52.2	19.3	28.5	24.4	27.5	0.13
D- Laboratory Tests											
Following principles of working with a biological material	11.1	32.5	23.6	21.4	11.4	31.8	31.6	36.7	40.2	51.9	<0.001*
Performing decontamination, disinfection, sterilization, antisepsis	20.0	40.6	20.5	15.3	3.6	52.4	19.1	28.5	28.5	26.3	0.29
Preparing faecal smear and its evaluation under microscope	8.1	26.1	22.5	22.0	21.3	20.8	47.3	31.9	71.8	69.0	0.21
Evaluation of direct radiography	17.5	47.3	19.3	12.2	3.5	48.3	20.8	30.8	22.0	31.9	<0.001*
Performing electrocardiogram and its evaluation	22.0	45.7	19.0	11.0	2.3	49.7	20.2	30.1	17.6	31.4	<0.001*
Performing fecal occult blood test	15.2	37.1	19.8	18.2	9.7	52.8	22.0	25.2	42.7	26.7	<0.001*
Measuring blood sugar using a glucometer and evaluating its result	28.6	42.3	14.9	11.6	2.6	80.3	5.9	13.8	6.7	6.9	0.83
Evaluating bleeding and clotting times	15.0	33.6	23.2	16.7	11.5	38.6	29.0	32.4	35.6	44.5	<0.001*
Filling out request forms for laboratory requests	26.9	42.6	14.5	12.0	3.9	75.8	8.1	16.1	11.8	9.2	0.054
Taking and transferring laboratory specimens to a laboratory under appropriate conditions	21.0	38.7	19.1	14.7	6.5	59.8	14.1	26.0	19.5	19.0	0.80
Using a microscope	13.9	34.9	21.4	16.6	13.2	37.1	31.3	31.6	39.5	47.1	0.002*

Preparing dry-wet slide for microscopic evaluation and evaluating it under microscope	10.2	28.3	22.0	18.7	20.8	22.1	46.1	31.8	62.9	68.6	0.01*
Using a peak-flow meter and evaluating its result	12.1	34.2	23.2	17.4	13.1	30.0	37.3	32.6	62.8	53.8	<0.001*
Preparing and evaluating a peripheral smear	10.8	31.7	21.0	19.2	17.3	24.2	44.2	31.6	55.4	66.5	<0.001*
Performing water disinfection	11.6	28.5	23.7	18.6	17.6	27.5	40.0	32.5	64.7	58.1	0.007*
Obtaining water sample	11.2	26.9	22.5	18.5	20.9	34.9	35.6	29.6	55.9	49.4	0.007*
Determining and evaluating the chlorine level in water	9.8	25.7	22.5	18.8	23.1	26.0	42.3	31.7	62.0	61.9	0.95
Performing complete urinalysis (including microscopic evaluation)	14.9	35.9	21.4	16.4	11.4	41.6	29.1	29.3	35.6	42.4	0.004*
Evaluating results of screening and diagnostic tests	18.6	44.9	18.0	14.0	4.4	57.4	15.7	26.9	18.1	22.2	0.03*
Measuring and evaluating of transcutaneous bilirubin level	10.8	29.2	23.0	18.9	18.1	24.2	43.4	32.4	62.5	64.6	0.36
Evaluating vaginal samples	9.7	27.9	21.5	20.8	20.1	20.9	46.9	32.2	70.9	68.7	0.34
E- Invasive and Non-Invasive Procedures											
Stabilising emergency psychiatric patients	13.7	32.2	34.0	15.2	4.9	35.2	29.8	35.0	41.9	46.6	0.06
Identifying and managing forensic cases	17.0	38.2	27.4	13.0	4.4	45.3	22.6	32.1	30.7	33.8	0.17
Placing an oropharyngeal airway	31.1	34.3	25.4	8.2	2.0	61.4	16.4	22.2	15.9	22.2	0.001*
Rational drug use	31.4	43.6	14.3	9.3	1.4	74.7	7.0	18.2	11.1	8.1	0.01*
Preparing and applying splints	18.1	36.0	28.7	12.0	5.2	47.5	25.5	27.0	20.0	38.3	<0.001*
Applying bandaging and tourniquet	26.4	38.4	24.6	9.1	1.5	72.9	8.4	18.8	8.7	10.6	0.17
Applying and removing nasal tamponade	22.5	38.9	26.6	9.5	2.4	59.9	16.1	24.0	19.8	21.4	0.41
Following up child growth and development (percentile charts, Tanner stages)	26.1	45.3	15.6	11.6	1.3	74.6	8.1	17.3	13.0	9.2	0.006*
Establishing vascular access	28.0	38.8	22.4	8.7	2.1	63.2	14.2	22.6	21.6	17.7	0.03*
Performing defibrillation	30.4	34.9	24.5	8.2	1.9	50.8	21.3	27.9	25.3	30.4	0.02*
Identifying, protecting and transporting of forensic evidence	15.0	31.6	27.5	15.3	10.6	28.0	35.1	36.8	47.7	57.3	<0.001*
Draining soft tissue abscesses	17.8	41.0	25.5	11.5	4.3	56.5	17.5	26.0	30.8	22.2	<0.001*
Taking precautions to stop or limit external bleeding	30.1	38.1	22.0	8.2	1.7	71.5	8.4	20.1	13.1	10.0	0.02*
Providing maternal care following birth	19.0	41.9	22.7	13.1	3.4	51.8	17.3	30.8	40.4	22.1	<0.001*
Providing newborn care in the delivery room	19.7	42.4	22.1	12.6	3.3	53.0	16.9	30.1	39.7	21.3	<0.001*
Hand washing	43.3	34.2	12.0	9.1	1.5	84.0	4.4	11.6	4.9	5.0	0.91

Performing intubation	29.2	34.2	25.9	8.3	2.4	45.1	26.1	28.7	33.9	37.2	0.15
Performing and repairing episiotomy	13.4	27.4	30.3	15.7	13.2	22.3	49.2	28.5	71.2	68.3	0.18
Using Galveston orientation scale	11.5	27.3	29.4	17.9	13.9	20.0	45.7	34.2	66.7	70.1	0.13
Pregnancy and puerperal follow-ups	21.8	43.7	19.3	12.8	2.4	65.4	12.8	21.8	32.5	13.4	<0.001*
Using Glasgow coma scale	28.5	35.3	23.5	9.7	3.1	55.4	17.4	27.2	12.4	26.5	<0.001*
Collecting biological sample	14.8	33.3	26.5	15.3	10.1	35.9	28.7	35.3	33.8	46.8	<0.001*
Evaluating illness / trauma severity score	19.3	34.3	29.4	12.4	4.6	36.9	27.1	36.0	29.7	45.1	<0.001*
Providing appropriate transportation of a patient	29.1	36.9	22.5	9.4	2.0	67.5	10.0	22.5	12.3	13.0	0.67
Putting patient in recovery position	30.7	34.7	23.6	9.0	2.1	62.3	13.1	24.7	19.4	16.9	0.17
Removing foreign body from respiratory tract	29.1	33.2	28.2	7.9	1.7	52.0	17.2	30.8	22.0	25.4	0.11
Determining legal competence	15.0	34.7	25.8	16.6	7.9	34.1	30.8	35.1	49.7	47.1	0.30
Performing IM, IV, SC, ID injection	31.3	38.0	20.5	8.3	1.9	72.4	8.9	18.8	11.0	10.9	0.95
Inserting a urinary catheter	28.4	39.5	20.9	8.6	2.6	76.8	7.6	15.6	5.7	9.8	0.001*
Providing advanced life support	25.6	33.6	26.5	10.0	4.4	45.1	23.1	31.8	26.8	35.4	<0.001*
Evaluating suicide risk	15.9	35.5	30.3	14.1	4.2	30.4	30.6	39.0	44.4	51.3	0.009*
Managing suicide attempt	17.1	32.5	32.2	13.2	4.9	27.3	32.6	40.1	49.3	55.5	0.01*
Taking blood pressure	43.0	34.9	13.1	7.7	1.3	85.2	4.7	10.1	5.0	5.3	0.76
Performing blood transfusions	12.8	24.7	29.1	16.9	16.6	24.0	46.3	29.7	59.8	67.2	0.001*
Capillary blood sampling	21.1	32.3	23.8	13.2	9.6	54.7	21.1	24.3	22.8	28.9	0.004*
Removing tick (insect)	26.5	36.4	25.3	9.3	2.5	61.2	15.7	23.1	28.3	18.8	<0.001*
Delivering bad news	28.4	36.0	21.1	11.5	3.1	56.2	14.2	29.6	18.1	20.6	0.20
Taking sample for culture	19.7	36.1	23.3	13.3	7.7	50.1	20.5	29.4	20.5	31.0	<0.001*
Performing enema	20.3	33.5	23.5	13.6	9.2	58.7	16.3	25.0	16.8	22.9	0.002*
Performing lumbar puncture	9.2	21.1	25.5	20.7	23.6	16.4	59.8	23.8	75.4	79.2	0.04*
Performing gastric lavage	18.0	31.6	29.8	11.6	9.0	50.2	24.4	25.3	25.7	34.2	<0.001*
Mini mental state examination	19.5	39.1	24.4	12.7	4.3	55.0	16.7	28.4	19.3	24.1	0.02*
Inserting nasogastric tube	22.6	35.9	27.1	9.4	5.1	62.3	15.5	22.1	10.4	22.1	<0.001*
Assisting with normal vaginal spontaneous delivery	15.7	31.2	33.6	12.0	7.4	27.6	39.6	32.8	62.9	58.1	0.05
Oxygen and nebulizer-inhalation treatment	27.7	39.2	21.9	9.1	2.1	75.6	7.9	16.5	10.2	9.3	0.50

Administration of medications in oral, rectal, vaginal or topical ways	26.7	38.5	20.8	10.2	3.8	73.0	8.9	18.1	12.1	10.6	0.27
Performing paracentesis	10.0	23.1	28.3	19.2	19.5	21.4	51.1	27.5	59.0	73.0	<0.001*
Performing pericardiocentesis	8.1	18.5	26.2	22.0	25.3	11.6	64.7	23.7	84.0	85.0	0.54
Performing pleural puncture	8.5	18.8	26.9	21.7	24.0	13.5	62.5	24.0	82.2	82.2	0.98
Administering PPD skin test	14.6	31.8	24.5	17.8	11.3	40.4	29.9	29.7	41.2	42.8	0.51
Using puls oximeter	29.5	36.3	20.7	9.9	3.6	72.7	10.1	17.2	5.6	13.6	<0.001*
Evaluation of patient's capacity to consent	16.3	33.3	24.7	16.7	8.9	39.1	26.2	34.7	36.2	40.9	0.06
Administering Rinne-Weber and Schwabach tests	11.7	30.5	24.5	19.4	14.0	28.3	36.6	35.1	38.5	60.4	<0.001*
Applying servical collar	28.4	34.4	24.7	9.3	3.3	66.2	12.7	21.2	14.5	16.4	0.27
Providing appropriate protection and transportation according to cold chain process	30.1	38.6	18.4	10.7	2.3	74.3	8.8	16.9	18.6	9.1	<0.001*
Evaluating respiratory function test	17.2	39.3	24.4	14.0	5.1	40.0	28.1	31.9	25.6	44.7	<0.001*
Using alcoholmeter	15.4	31.2	26.1	15.0	12.3	43.5	29.5	27.0	43.6	39.8	0.11
Building a genetic tree and referring the patient to genetic counseling when it is necessary	10.8	25.5	19.3	22.5	21.9	29.1	38.8	32.1	42.1	60.6	<0.001*
Performing suprapubic bladder puncture	10.1	21.7	27.7	20.0	20.5	21.1	51.3	27.6	69.4	71.1	0.43
Providing basic life support	33.2	32.2	23.8	8.2	2.6	60.8	15.2	24.0	13.2	21.4	<0.001*
Finding solution for the ethical problems in medical practices	23.0	38.6	20.3	14.1	4.0	49.6	16.4	34.0	24.0	25.1	0.62
Heel lance for blood sampling	24.3	37.5	20.1	13.7	4.5	70.8	11.1	18.1	20.8	12.1	<0.001*
Providing appropriate transportation of limbs which are amputed after trauma	26.4	31.9	27.9	10.3	3.5	47.3	23.2	29.5	26.3	34.3	<0.001*
Appropriate preparation of medications to be administred	25.9	37.8	21.5	10.8	4.0	64.3	11.8	23.9	19.9	14.7	0.003*
Taking vaginal and servical samples	16.3	34.8	23.5	16.1	9.3	45.4	26.2	28.5	39.2	36.0	0.17
Performing wound-burn care	24.7	42.0	21.3	9.8	2.3	70.1	10.0	19.9	13.0	12.4	0.67
Neonatal resuscitation	23.9	32.5	29.5	10.3	3.8	33.9	33.9	32.2	53.4	49.3	0.09
Performing and removing superficial sutures	29.7	39.3	20.5	8.3	2.2	75.5	8.6	15.9	7.5	10.8	0.01*
F- Preventive and Community medicine											
Organizing emergency aids	27.8	34.1	25.5	10.2	2.4	59.0	12.8	28.3	18.0	17.7	0.86
Family counseling	22.4	41.0	18.0	15.8	2.7	63.7	12.0	24.4	19.6	15.0	0.009*

Family planning counseling	24.3	43.3	15.9	14.5	2.0	73.0	8.2	18.8	18.4	8.5	<0.001*
Conducting immunization services	28.0	44.4	14.4	12.0	1.3	77.7	6.5	15.9	13.3	6.6	<0.001*
Teaching breast-feeding techniques	29.9	42.0	13.6	12.8	1.7	79.6	6.1	14.3	12.7	6.0	<0.001*
Workplace visits and conducting workplace inspection	13.7	26.5	19.5	17.3	23.1	39.7	29.6	30.7	37.5	43.8	0.009*
Teaching how to do breast examinaton by oneself	28.1	42.5	14.2	13.4	1.8	79.0	5.9	15.1	8.0	6.7	0.26
Applying contraception techniques	24.8	42.3	15.6	14.6	2.6	69.0	10.0	21.0	18.6	11.5	<0.001*
Providing health service in unusual situations	23.4	36.7	25.7	11.4	2.7	49.5	15.4	35.1	25.9	23.4	0.24
Periodic examination and control (Cardiac risk calculation, adolescent counseling, smoke counseling, cancer screening)	21.9	41.7	18.7	14.8	2.9	57.0	15.0	28.0	19.4	21.2	0.37
Taking precautions for preventing infections acquired from health service	24.9	42.8	18.3	12.3	1.7	62.4	11.4	26.3	16.0	15.3	0.69
Taking precautions for preventing infections at public places	23.8	41.5	19.2	13.0	2.5	59.9	12.2	27.8	6.0	5.5	0.82
Providing health education to community	25.9	41.5	16.1	13.9	2.6	66.9	10.1	23.0	4.3	5.0	0.79
Fighting infectious disease in community	25.4	42.2	17.9	12.6	1.9	60.4	12.1	27.5	16.8	16.7	0.99
Identifying problems related to health in community by using epidemiologic methods and offering solutions for these problems	19.5	37.8	21.3	15.8	5.6	42.2	21.6	36.2	29.6	34.8	0.03*