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Website

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

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Orjinal Araştırma / Original Article

Evaluation of Pediatric Patients Admitted to the Emergency Department with Head Trauma

Acil Servise Kafa Travması Nedeniyle Başvuran Çocuk Hastaların Değerlendirilmesi

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Abstract

Aim: Head trauma is the most frequent reason for trauma related child deaths. Minor head traumas (MHT) form a considerable part of pediatric head traumas. Brain Computed Tomography (CT) is the gold standard for demonstrating intracranial pathologies in patients with head trauma. It is necessary to avoid having unnecessary CT scans in order to reduce the cost and the harms of radiation. We aim to assess the pediatric patients that applied to the emergency service with complaints of head trauma in the light of Prediction of Important Clinical Events (CHALICE) clinical decision-making rules.

Material and Method: 200 patients under 18 years old who applied to the emergency service with complaints of head trauma between 2016 and 2019 are included in this retrospective study.

Results: 200 patients in total were included in the study; of them, 128 are males and 72 are females. Of the patients, 3 have a Glaskow Coma Score (GCS) of 3-8, 2 have a GCS of 9-13, and the remaining 195 patients have a GCS of 14-15. Considering the symptoms, 35 patients had a headache, 28 patients had subcutaneous hematoma, and 26 patients had nausea-vomiting. The reason for trauma is motor vehicle accident for 99 patients and falling down from height for 95 patients. Four patients died. CHALICE (+) rate was found 67.82% in the patients having a brain CT scan. 41.95% of asymptomatic patients had a brain CT scan.

Conclusion: Most of the patients participating in our study applied to the emergency service with minor head trauma. 32,18 percent of the patients who had brain CT were CHALICE (-) and 41.95% of the patients who had no symptoms showed us that unnecessary CT is performed at a high rate in pediatric MHT.

Keywords: Pediatric head trauma, CHALICE, computed brain tomography, defensive medicine, traumatic brain damage, minor head trauma

Öz

Amaç: Kafa travması travmaya bağlı çocuk ölümlerinin en sık sebebidir. Minör kafa travmaları (MKT) çocukluk kafa travmalarının önemli bir kısmını oluşturmaktadır. Beyin Bilgisayarlı Tomografisi (BT) kafa travması ile gelen hastalarda intrakraniyal patolojileri göstermek için altın standarttır. Ancak MKT'lerin küçük bir kısmında ciddi kafa içi hadise olduğu düşünüldüğünde maliyet ve radyasyonun zararlarını azaltmak için gereksiz tomografi çekmekten kaçınmak gerekir. Biz bu çalışmada acil servise kafa travması ile başvuran çocuk hastaları CHALICE klinik karar verme kuralları ışığında değerlendirmeyi amaçladık.

Gereç ve Yöntem: Bu retrospektif çalışmaya 2016-2019 tarihleri arasında 18 yaş altında acil servise kafa travması nedeniyle başvuran 200 çocuk hasta dahil edilmiştir.

Bulgular: Çalışmaya 128 erkek ve 72 kız olmak üzere toplam 200 hasta alınmıştır. Bunlardan 3'ünün GKS 3-8 arasında, 2'sinin GKS 9-13 arasında ve kalan 195 hastanın GKS 14-15 arasındadır. Semptomlara bakıldığında ise 35 hastada baş ağrısı, 28 hastada cilt altı hematom ve 26 hastada bulantı-kusma görülmüştür. Travma şekli 99 hastada araç içi trafik kazası ve 95 hastada yüksekten düşme şeklindedir. 39 hasta hastaneye yatırılarak tedavi edilmiştir. Exitus olan 4 hasta vardır. Beyin BT çekilenlerde CHALICE (+) oranı %67,82 olarak tespit edilmiştir. Hiçbir semptomu olmayan hastaların %41,95'ine beyin BT çekilmiştir.

Sonuç: Çalışmamıza katılan hastaların büyük çoğunluğu minor kafa travması ile acile servise başvurmuştur. Beyin BT çekilen hastaların %32,18'i CHALICE (-) olması ve hiç bir semptomu olmayan hastaların %41,95'ine beyin BT çekilmesi bize göstermiştir ki çocuk MKT'lerinde yüksek oranda gereksiz BT çekilmektedir.

Anahtar Kelimeler: Çocuk kafa travması, CHALICE, bilgisayarlı beyin tomografisi, defansif tıp, travmatik beyin hasarı, minör kafa travması

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INTRODUCTION

Trauma is the most significant reason for morbidity and mortality in children. Head trauma is the most frequent reason for trauma related child death at the rate of 80%.[1] Childhood head traumas may lead to various clinical conditions ranging from mild to severe. However, most of the pediatric head traumas are mild.[2] The most common reasons for pediatric head traumas are motor vehicle accidents, falling, assaults, bicycle accidents, and sports trauma. The most frequent reason for head trauma in babies under one year old is abuse.[3,4]

Minor head traumas (MHT) form a considerable part of pediatric head traumas. While incidence of intracranial pathologies in MHT varies between 3% and 5%, the rate increases in younger children.[5] Yet, such pathologies rarely require surgical intervention and proper management of such patients is still a controversial topic.[5,6]

Brain computed tomography (CT) is the gold standard for demonstrating intracranial pathologies in patients with head trauma. It enables early diagnosis and treatment of intracranial cases. However, it is a high-cost process for minor head traumas, in particular.[7] On the other hand, it is indicated that exposure to ionizing radiation during computed tomography (CT) scanning increase the rates of brain tumor and leukemia in children.[8] Considering that only <1% of MHT is a severe intracranial case,[5] one must be very careful in taking the risk of cost and radiation. Many decision-making rules were developed in making the decision for having a brain CT scan for such patients. The criteria of the Pediatric Emergency Care Applied Research Network (PECARN), Canadian Assessment of Tomography for Childhood Head Injury (CATCH), and Children's Head Injury Algorithm for the Prediction of Important Clinical Events (CHALICE) are the most frequently accepted clinical decision-making criteria that were developed for selective CT requests.[5]

In this study, we aim to assess the pediatric patients that applied to the emergency service with complaints of head trauma in the light of CHALICE clinical decision-making rules.

MATERIAL AND METHOD

200 patients under 18 years old who applied to the emergency service with complaints of head trauma between 2016 and 2019 are included in this retrospective monocentric study. Patient data were obtained retrospectively from patient files and hospital electronic information system. The ethics committee approval required for the study was obtained from the local ethics committee. (Ahi Evran University Clinical Research Ethics Committee's decision dated 22.05.2018 and numbered 2018-10 / 89)

All patients under 18 years old who were diagnosed with head trauma in emergency service and for which brain CT scanning was performed and the patients under 18 years old who were kept under observation for 8 hours and above without brain CT scanning are included in the study. We reached the patients, who were kept under observation and then discharged, by phone whenever possible and obtained information on their later medical conditions. Those whom we failed to reach and obtain information are excluded from the study.

Demographic information, presenting symptoms, Glaskow Coma Score (GCS), Trauma mechanisms, CT images, hospitalization-discharge-death findings of all patients were recorded.

The patients with GCS>13 were evaluated as having a head trauma and 195 patients were evaluated in this category. The patients were also evaluated from the point of view of CHALICE clinical decision-making rules (**Table 1**).[9]

Table 1. CHALICE Clinical Decision Rule

History
1. Witnessed LOC >5minutes
2. History of amnesia >5 minutes
3. Abnormal drowsiness
4. Over 3 discrete vomits
5. Physician's suspicion of nonaccidental injury
6. First ever seizure after injury
Examination
1. GCS<14 or <15 if under 1 year
2. Suspicion of penetrating or depressed skull injury or tense fontanelle
3. Sign of basil skull fracture
4. Positive focal neurological finding
5. Presence of bruise, swelling or laceration >5 cm if <1 year old
Mechanism
1. Dangerous mechanism (MVA) >40 mph
2. fall >3 meters
3. High speed projectile injury.

Statistical analyses were performed by using the program SPSS version 17.0. Conformity of variables to normal distribution was examined by histogram charts, and Kolmogorov-Smirnov test. Mean, standard deviation, and median values were used in presenting descriptive analyses. Categorical variables were compared by using Chi Square Test. While Mann Whitney U Test was used in evaluation of nonnormal (nonparametric) variables between two groups, Kruskal Wallis Test was used in evaluation of them among more than two groups. The conditions under which p-value is below 0.05 were valuated as statistically significant results.

RESULTS

A total of 200 patients were included in the study; of them, 128 are males and 72 are females. Of the patients, 3 have a GCS of 3-8, 2 have a GCS of 9-13, and the remaining 195 patients have a GCS of 14-15. Considering the symptoms, 35 patients had a headache, 28 patients had subcutaneous hematoma, and 26 patients had nausea-vomiting. Form of trauma is motor vehicle accident in 102 patients and falling down from height in 95 patients. 199 patients had blunt trauma and the remaining patient had a blunt and penetrating trauma. Spread of trauma is isolated head trauma in 105 patients and multisystem trauma in 95 patients. 39 patients were hospitalized. 4 patients died. Distribution of gender and clinical findings of the patients are given in **Table 2**.

Mean age of the participants of this study is 8.66±5.47 years. Mean length of hospital stay is 1.05±4.20 days. Age and laboratory values of the patients are given in **Table 3**.

The patients were also evaluated by CHALICE clinical decision-making rules. CHALICE (+) rate was found 67.82% in patients with brain CT scan. 18 (15.25%) of 118 CHALICE (+) patients having a brain CT scan was evaluated as CT (+); 100 (84.75%) were evaluated as CT (-).

Table 2. Distribution of patients by gender and clinical findings

		n	%
Gender	Male	128	(64.50)
	Female	72	(36.50)
GCS	3-8	3	(1.50)
	9-13	2	(1.50)
	14-15	195	(97.50)
Symptom	Headache	35	(17.50)
	Nausea-vomiting	26	(13.50)
	Changes in consciousness	17	(8.50)
	Subcutaneous hematoma	28	(14.50)
	No symptoms	93	(46.50)
	Cardiac arrest	1	(.50)
Form of trauma	Falling from height	95	(47.50)
	Traffic accident-in-vehicle	99	(49.50)
	Injury by foreign body	2	(1.50)
	Battery-abuse	1	(.50)
	Traffic accident-extravehicular	3	(1.50)
Trauma mechanism	Blunt	199	(99.50)
	Blunt + Penetrating	1	(.50)
Spread of trauma	Isolated head trauma	105	(52.50)
	Multisystem trauma	95	(47.50)
Brain CT	Bone fracture	8	(4.50)
	SAH	4	(2.50)
	Subdural hemorrhage	3	(1.50)
	Contusio cerebri	3	(1.50)
	Normal Brain CT	154	(77.50)
	Brain CT not scanned	26	(13.50)
	SAH + Subdural hemorrhage	1	(.50)
	Fracture in maxillofacial bones	1	(.50)
Treatment	Outpatient treatment	161	(80.50)
	Hospitalization	39	(19.50)
Result	Recovery	195	(97.50)
	Transfer	1	(.50)
	Dead	4	(2.50)
CT finding	Present	20	(10.00)
	Absent	180	(90.00)

Brain CT scanning of the patients were compared to the forms of trauma, symptoms, spread, treatment, results, and the rates of CT findings (**Table 4**). Accordingly, while the rate of falling down from height is higher in the patients with brain CT scan, the rate of traffic/ in-vehicle accidents as form of trauma is higher in the patients without brain CT scan. The rate of patients with brain CT scan who show the symptoms of headache and nausea-vomiting is higher compared to those without brain CT scan. The rate of isolated head trauma is higher in the patients with brain CT scan compared to those without brain CT scan. The rate of hospital stay is higher in the patients with brain CT scan compared to those without brain CT. No significant correlation was found between the presence of results and CT findings and the brain CT scans. In addition, it is remarkable that 41.95% of the asymptomatic patients had a brain CT scan.

Table 4. Comparison of Brain CT scanning of the patients to the rates of forms of trauma, symptoms, spread of trauma, treatment, result, and CT finding

		Brain CT				P*
		Scanned		Not Scanned		
		n	%	n	%	
Form of trauma	Falling from height	90	(51.72)	5	(19.23)	0.019
	Traffic accident-in-vehicle	78	(44.83)	21	(80.77)	
	Injury by foreign body	2	(1.15)	0	(.50)	
	Battery-abuse	1	(.57)	0	(.50)	
	Traffic accident-extravehicular	3	(1.72)	0	(.50)	
Symptom	Headache	31	(17.82)	4	(15.38)	0.001
	Nausea-vomiting	25	(14.37)	1	(3.85)	
	Changes in consciousness	17	(9.77)	0	(.50)	
	Subcutaneous hematoma	28	(16.09)	0	(.50)	
	No symptoms	73	(41.95)	20	(76.92)	
	Cardiac arrest	0	(.50)	1	(3.85)	
Spread of trauma	Isolated head trauma	98	(56.32)	7	(26.92)	0.005
	Multisystem trauma	76	(43.68)	19	(73.08)	
Treatment	Outpatient treatment	136	(78.16)	25	(96.15)	0.031
	Hospitalization	38	(21.84)	1	(3.85)	
Result	Recovery	170	(97.70)	25	(96.15)	0.717
	Transfer	1	(.57)	0	(.50)	
	Dead	3	(1.72)	1	(3.85)	
CT finding	Present	20	(11.49)	0	(.50)	0.068
	Absent	154	(88.51)	26	(100.00)	

*Chi Square Test

Table 3. Age and laboratory value of the patients

	Mean	±s.d.	Median	Min.	Max.
Age (years)	8.66	±5.47	8.50	.50	17.50
WBC (/µL)	11336.62	±4514.53	10125.50	4330.00	27610.00
Neutrophile (/µL)	5913.20	±3638.18	4935.50	810.00	23940.00
Lymphocyte (/µL)	4168.25	±2338.59	3620.00	920.00	14550.00
Basophile (/µL)	34.50	±41.38	10.00	.50	300.00
Eosinophile (/µL)	158.40	±299.45	44.50	.50	1990.00
HGB (g/dL)	12.68	±1.59	12.70	5.50	16.80
HTC (%)	37.59	±4.57	37.60	14.50	48.40
PLT (/µL)	309530.00	±92740.95	298500.00	32000.00	526000.00
NA (mmol/L)	138.51	±3.03	138.50	127.50	153.50
K (mmol/L)	4.13	±.45	4.10	3.50	5.50
Cl (mmol/L)	103.07	±3.59	103.50	94.50	130.00
CRP (mg/L)	3.02	±8.09	.31	.50	73.50
Length of Hospitalization (days)	1.05	±4.20	.50	.50	48.50

The correlation among GCS and form of trauma, symptom, trauma mechanism, spread, brain CT, treatment, and result were examined. Accordingly, we found that there is a significant correlation among GCS and symptom, brain CT, treatment, and result (p<0.001 for all of them). While the rate of headache is higher in the patients with GCS of 14-15, the rate of changes in consciousness is higher in those with GCS of 3-8 and GCS of 9-13. While the rate of bone fracture is higher in the patients with GCS of 14-15; the rate of SAH is higher in those with GCS of 3-8; the rate of subdural hemorrhage is higher in those with GCS of 9-13. The rate of hospital stay is lower in the patients with GCS of 14-15 compared to those with GCS of 3-8 and GCS of 9-13. Mortality rate is higher in the patients with GCS of 3-8 compared to those with GCS of 9-13 and GCS of 14-15. GCS is 14-15 in the patients with changes in consciousness compared to those with other symptoms. The rate of bone fracture is higher in the patients with Subcutaneous Hematoma compared to those with Nausea-Vomiting and Changes in Consciousness. The rate of hospital stay is higher in the patients with changes in consciousness compared to those with Nausea-Vomiting and Subcutaneous Hematoma. Death rate is lower in the patients with Nausea-Vomiting compared to those with Changes in Consciousness and Cardiac Arrest (p<0.001).

The rate of isolated head trauma as spread of trauma is higher in the patients with the form of trauma due to falling from height as compared to those with the form of trauma due to in-vehicle traffic accident and extravehicular traffic accident (p<0.001). The rate of brain CT bone fracture is higher in the patients with the form of trauma due to falling from height compared to those with the form of trauma due to in-vehicle traffic accident (p=0.01). Distribution of GCS, symptoms, form of trauma, trauma mechanism, spread of trauma, treatment, and result rates of the patients by brain CT is given in **Table 5**.

When brain CT findings of the patients are sorted out as present/absent, the number of patients with GCS of 3-8 and GCS of 9-13 in CT findings are higher than the patients without CT findings. The rate of changes in consciousness is higher in the patients with CT findings compared to those without CT findings (p<0.001 for all of them).

Table 5. Comparison of Clinical Findings and Trauma Characteristics of the Patients to Brain CT

		Brain CT															
		Bone fracture		SAH		Subdural hemorrhage		Contisuo cerebri		Normal Brain CT		Brain CT Not scanned		SAH+ Subdural hemorrhage		Fracture in maxillofacial bones	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
GKS	3-8	0	(.50)	2	(50.00)	0	(.50)	0	(.50)	0	(.50)	0	(.50)	1	(100.00)	0	(.50)
	9-12	1	(12.50)	0	(.50)	1	(33.33)	0	(.50)	0	(.50)	0	(.50)	0	(.50)	0	(.50)
	13-15	7	(87.50)	2	(50.00)	2	(66.67)	3	(100.00)	154	(100.00)	26	(100.00)	0	(.50)	1	(100.00)
Symptom	Head ache	0	(.50)	0	(.50)	0	(.50)	0	(.50)	31	(20.13)	4	(15.38)	0	(.50)	0	(.50)
	Nausea-vomiting	1	(12.50)	0	(.50)	0	(.50)	1	(33.33)	21	(13.64)	1	(3.85)	1	(100.00)	1	(100.00)
	Changes in consciousness	1	(12.50)	4	(100.00)	3	(100.00)	2	(66.67)	7	(4.55)	0	(.50)	0	(.50)	0	(.50)
	Subcutaneous hematoma	4	(50.00)	0	(.50)	0	(.50)	0	(.50)	24	(15.58)	0	(.50)	0	(.50)	0	(.50)
	No symptoms	2	(25.50)	0	(.50)	0	(.50)	0	(.50)	71	(46.10)	20	(76.92)	0	(.50)	0	(.50)
	Cardiac arrest	0	(.50)	0	(.50)	0	(.50)	0	(.50)	0	(.50)	1	(3.85)	0	(.50)	0	(.50)
Form of trauma	Falling from height	5	(62.50)	1	(25.50)	2	(66.67)	1	(33.33)	81	(52.60)	5	(19.23)	0	(.50)	0	(.50)
	Traffic accident-in-vehicle	2	(25.50)	3	(75.50)	1	(33.33)	1	(33.33)	69	(44.81)	21	(80.77)	1	(100.00)	1	(100.00)
	Injury by foreign body	1	(12.50)	0	(.50)	0	(.50)	0	(.50)	1	(.65)	0	(.50)	0	(.50)	0	(.50)
	Battery-abuse	0	(.50)	0	(.50)	0	(.50)	0	(.50)	1	(.65)	0	(.50)	0	(.50)	0	(.50)
	Traffic accident-extravehicular	0	(.50)	0	(.50)	0	(.50)	1	(33.33)	2	(1.30)	0	(.50)	0	(.50)	0	(.50)
Trauma mechanism	Blunt	8	(100.00)	4	(100.00)	3	(100.00)	3	(100.00)	153	(99.35)	26	(100.00)	1	(100.00)	1	(100.00)
	Blunt + Penetrating	0	(.50)	0	(.50)	0	(.50)	0	(.50)	1	(.65)	0	(.50)	0	(.50)	0	(.50)
Spread of trauma	Isolated head trauma	5	(62.50)	1	(25.50)	2	(66.67)	1	(33.33)	89	(57.79)	7	(26.92)	0	(.50)	0	(.50)
	Multisystem trauma	3	(37.50)	3	(75.50)	1	(33.33)	2	(66.67)	65	(42.21)	19	(73.08)	1	(100.00)	1	(100.00)
Treatment	Outpatient treatment	3	(37.50)	0	(.50)	0	(.50)	0	(.50)	132	(85.71)	25	(96.15)	0	(.50)	1	(100.00)
	Hospitalization	5	(62.50)	4	(100.00)	3	(100.00)	3	(100.00)	22	(14.29)	1	(3.85)	1	(100.00)	0	(.50)
Result	Recovery	8	(100.00)	1	(25.50)	3	(100.00)	3	(100.00)	154	(100.00)	25	(96.15)	0	(.50)	1	(100.00)
	Transfer	0	(.50)	1	(25.50)	0	(.50)	0	(.50)	0	(.50)	0	(.50)	0	(.50)	0	(.50)
	Dead	0	(.50)	2	(50.00)	0	(.50)	0	(.50)	0	(.50)	1	(3.85)	1	(100.00)	0	(.50)

*Chi Square Test

DISCUSSION

We found that 32.18% of the patients in the study had a brain CT scan although they turned out CHALICE (-) and 15.25% of CHALICE (+) patients turned out CT (+). 154 (88.5%) out of 174 patients in total for which tomography scanning was performed were evaluated as normal. In addition, it is remarkable that brain CT scan was performed for 41.95% of the asymptomatic patients. The National Cancer Institute and the Food and Drug Administration have recommended a decrease in radiation exposure by eliminating unnecessary CT scans, with special emphasis on the pediatric population.[10] The findings make us think that brain CT scan is not reasonable in examination of pediatric head traumas considering the side effects of radiation and the cost. The plans required to minimize unnecessary CT scans in children must be made without delay.

The need for reduce unnecessary CT scans while minimizing the risk of missing the symptoms of clinically significant traumatic brain injury (TBI) led to development of clinical estimate rules designed to guide the clinicians in CT decision-making process.[11] The 3 most frequently used decision-making rules (PECARN, CATCH, and CHALICE) are hard to compare with each other as they have different objectives and target population. For example, CHALICE includes all children with head trauma; PECARN includes the children with head trauma and GCS of 14-15; CATCH includes the children with head trauma and GCS of 13-15.[11] The reason for using CHALICE decision-making rules in this study is the fact that the study contains patients from all groups. Clinical estimate rule for CHALICE head trauma was derived for evaluation of head traumas of all degrees in a prospective cohort analysis consisting of 22,722 children that applied to emergency service in The United Kingdom between 2000 and 2002.[12] It was reported that this decision-making rule indicates traumatic brain damage with of 98.6% sensitivity and 86.9% specificity.[11]

In this study; It is noteworthy that 32.18% of CHALICE (-) patients had CT performed, 88.5% of patients underwent CT scan had normal results, and 41.95% of asymptomatic patients had CT scans. This situation made us think of clinicians perform unnecessary CT scans for pediatric head traumas with a defensive medicine approach without utilizing any of the clinical decision-making rules.

In defensive medicine, a physician avoids unnecessary use of medical practices for diagnosis and treatment and the practices that are highly likely to result in a malpractice case by behaving overprotectively or reservedly in order not to encounter any criminal or legal action, pay damage or increase the premiums on insurance policy.[13] In a compilation published in 2019, the reasons for defensive medicine are specified as physician-patient communication, medical error and malpractice cases, the effect of media, lack in professional experience, violence, healthcare system, patient complaints, patient density, and the desire to become a perfect physician.[14] We think that it is very important to minimize the reasons that push the physicians to adopt defensive medicine approach as well as the trainings for physicians in order to reduce unnecessary CT scans for pediatric patients with head trauma.

GCS is one of the oldest and most common scoring systems that are used for evaluation of the patients with head trauma. Besides, GCS is frequently used in separating the patients with head trauma into subgroups, diagnosis and treatment methods, and repetitive evaluation of patients.[15] It was reported in many previous studies that low GCS values and changes in consciousness are related to mortality due to brain damage and head trauma.[16-18] In addition, GCS and changes in consciousness are common physical examination findings that indicate a high risk in PECARN, CATCH, and CHALICE which are the most frequently used decision-making rules for MHTs in children.[9] This study indicates in line with the literature that GCS and changes in consciousness are related to clinical condition, brain damage, intracranial case, hospital stay and mortality of the patients. A previous study on 29,433 pediatric patients with head trauma reported that 63.7% of the patients are males and 95.4% have a GCS of 15. In addition, 70.1% of the patients in this study applied to the hospital with complaints of falling. The most frequent presenting symptoms were reported to be headache and vomiting. Only <1% of the patients needed surgical intervention.[9] The data in the literature are also similar.[19] In this study, 64% of the patients are males and 36% are females. 97.5% of the patients have a GCS of >13. The patients applied to the hospital with complaints of head ache at the rate of 17.5% and nausea-vomiting at the rate of 13%. 49.5% of the patients applied to the hospital due to motor vehicle accident and 47.5% applied due to falling from height. CT findings were found in 10% of the patients. Only 4 patients died. The data in this study are consistent with the literature.

Limitations

The study is limited to being monocentric, retrospective, and the limited number of patients. We think of supporting the study findings with later prospective and multicentric studies with more patients in the future. Besides, studying the reasons that push physicians to defensive approach in making the decision in performing tomography scanning for pediatric head traumas may be beneficial in developing approaches to reduce the rate of unnecessary tomography scans in the future.

CONCLUSION

The fact that there are lots of CHALICE(-) patients for which CT scanning is performed in this study, results of a great majority of the patients for which CT scanning is performed are normal and CT scanning is performed for 41.95% of the asymptomatic patients make us think that physicians don't utilize any of the clinical decision-making rules due to their

defensive medicine approach. We think that it is important to investigate and minimize the reasons that push the physicians to adopt defensive medicine approach as well as the trainings for physicians in order to reduce unnecessary tomography scans for MHTs in pediatric patients.

ETHICAL DECLARATIONS

Ethics Committee Approval: Ahi Evran University Clinical Research Ethics Committee's decision dated 22.05.2018 and numbered 2018-10 / 89

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

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Orjinal Araştırma / Original Article

Analysis of Hospitalized Geriatric Patients from an Emergency Department

Acil Servis Başvurusu Sonrası Hastaneye Yatırılan Yaşlı Hasta Grubunun Analizi

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Abstract

Objective: The increase in the geriatric population in industrialized countries also increases the rate at which this group utilizes emergency services. Evaluation of this patient group is not specific to a single discipline, but requires a multidisciplinary approach. Information obtained by examining emergency service use among geriatric patients can inform us of approaches to improve hospital efficiency and potentially reduce the morbidity and mortality rates.

Material and Method: This study investigated the retrospective records of geriatric patients who presented to emergency services during 2016 Kütahya Evliya Çelebi Training and Research Hospital, Turkey. Demographic characteristics, diagnoses, hospitalization rates, hospitalization according to clinics, seasonal characteristics, duration of hospital, and patient outcomes were evaluated. Study data were evaluated using the SPSS 20.00 statistical program.

Results: A total of 314.178 patients opted for emergency services during 2016, and 29.163 (9.2%) were 65 years old and older. Among these patients, 10.545 were hospitalized, of whom 4.246 (40.2%) were aged 65 years or older. The most frequently utilized hospital units were the cardiology (n=723, 17.02%), the neurology (n=717, 16.88%), and the chest diseases (n=674, 15.87%).

Conclusion: The geriatric population requires that necessary changes should be made in healthcare structures. Our study, which evaluates hospitalization rates and health status in geriatric population at a provincial which can also provide a regional level, can help in making patient admission, follow-up, and rehabilitation more comprehensive.

Keywords: Geriatric assessment, emergency department, hospitalization

Öz

Amaç: Sanayileşmiş ülkelerde geriatrik yaş popülasyonunun artış göstermesi bu yaş grubu hastaların acil servislere başvuru oranını da arttırmaktadır. Ayrıca bu grubun değerlendirilmesi tek bir branşa özgü olmayıp multidisipliner bir yaklaşım gerektirmektedir. Dolayısıyla bu hasta grubunun acil servis başvurularının incelenmesiyle elde edilecek veriler müdahele zamanını kısaltabileceği gibi takiplerinde de hastane kaynaklarının verimli kullanılmasını ve bunun sonucunda morbidite ve mortalite oranlarını azaltılması için yol gösterici olabilir.

Gereç ve Yöntem: Bu çalışma Kütahya Evliya Çelebi Eğitim Araştırma Hastanesi Acil Servisi'ne 01.01.2016 – 31.12.2016 tarihleri arasında başvuran geriatrik hastaların geriye dönük kayıtları incelenerek gerçekleştirilmiştir. İncelemede hastaların demografik özellikleri, tanıları, hastaneye yatış oranları, kliniklere göre dağılımı, mevsimsel özellikleri, hastanede yatış süreleri ve sonlanım durumları değerlendirilmeye alınmıştır. Çalışmada elde edilen veriler SPSS 20.00 programı kullanılarak değerlendirilmiştir.

Bulgular: Çalışmanın yapıldığı süre içerisinde acil servise yapılan başvuru sayısı 314.178 olup 29.163'ü (%9,2) atmışbeş yaş ve üzeri olduğu tesbit edildi. Bu dönem içerisinde acil servisten diğer servislere yatan hasta sayısı 10.545 olup, bunların 4246'sı (%40,2) 65 yaş ve üstü hasta grubunu oluşturdu. Yatış yapılan geriatrik hastaların klinik dağılımına bakıldığında en sık üç kilnik kardiyoloji (n=723, %17,02), nöroloji (n= 717, %16,88) ve göğüs hastalıkları (n=674, %15,87) olarak tespit edildi.

Sonuç: Geriatrik hasta popülasyonunun hastaneye başvuru ve yatış oranlarının bölgesel olarak belirlenip değerlendirilmesi, ihtiyaca göre gerekli sağlık yapılanmasına yol göstererek, bu hastaların yatışı, takibi ve rehabilitasyonlarının daha nitelikli yapılmasına yol gösterebilir.

Anahtar Kelimeler: Geriatrik değerlendirme, acil servis, hastaneye yatış

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INTRODUCTION

Geriatric patients represent a special community for emergency services and although there is no clearly defined age range, many countries consider this cohort to begin from 65 years of age.[1] Human life span is longer in industrialized countries. In the last 100 years, human life span has been extended by more than 25 years. Due to decreasing birth rates and improved medical care, the proportion of individuals aged over 80 years shows a particularly noticeable increase in the overall population.[2] Life expectancy data from the World Health Organization shows that the estimated average lifespan in Turkey is 71 years for men and 75 years for women.[3] According to the Turkish Statistical Institute, in 2014, the geriatric population in Turkey was 6,192.962, i.e., 8% of the total population. The male population constitutes 43.6% and the female population constitutes 56.4% of the geriatric population. According to population projections, it is estimated that the geriatric population will increase to 10.2% of the total population by 2023, 20.8% by 2050, and 27.7% by 2075.[4] Consistent with this increase, it has been estimated that rates of hospital presentation and emergency service utilization by geriatric population will grow when compared to those by the non-geriatric patient population.[5,6]

Physiological changes that occur with aging in the geriatric population result in a decrease in the functional capacity. These contribute to the emergence or exacerbation of many diseases, such as cardiovascular, nervous system, metabolic, and endocrine diseases. Chronic diseases present in older patients are exacerbated because of reduced physiological resources or electrolyte imbalances.[7,8]

It has been shown that at least 75% of the geriatric population is under drug treatment for one or more illnesses and that clinicians are more cautious when evaluating patients 9. Emergency departments are specialized units that provide initial and timely evaluation of patients when they first arrive at the hospital. Physiological changes that occur among older individuals and the effects of existing chronic diseases and drug treatment regimens can prolong the evaluation process in emergency services. Accordingly, mortality and morbidity rates can be increased. Knowing these risks among geriatric patients, the emergency physician endeavors to make a prompt and accurate diagnosis, facilitate appropriate treatment, and use existing facilities efficiently as part of a multidisciplinary care team.

The hospital where the present research was undertaken is the only public hospital in the center of the Kutahya city in Aegean Region of Turkey. It provides 750 medical and care beds and 90 intensive care beds. This study evaluates the rates of hospitalization of geriatric patients in the rural hospital in Aegean Region of Turkey in order to inform more efficient use of hospital resources, diagnostic and treatment services, and follow-up and rehabilitation according to patients' level of need.

MATERIAL AND METHOD

This study was undertaken to investigate the retrospective records of geriatric patients who presented to emergency services at Kütahya Evliya Çelebi Training and Research Hospital between 01.01.2016 and 31.12.2016. The medical records of our patients were accessed via the hospital's data automation system. The study protocol conformed to the ethical guidelines of the Declaration of Helsinki and was reviewed and approved by the Clinical Research Ethics Committee of Dumlupınar Universty (Permission granted: 18.01.2017, Decision no:2017/06 2018/8-1).

Statistical Analysis

The study population consisted of geriatric patients (>65 years old). The demographic characteristics of patients, hospitalization rates, hospitalization according to clinics, seasonal characteristics, and length of stay and outcomes of patient hospitalization were evaluated using SPSS (Version 20.0, SPSS Inc., Chicago, IL). Descriptive statistics (mean±SD) and percentage were calculated for all variables.

RESULTS

A total of 314.178 patients were enrolled in the study during 2016, and 29.163 (9.2%) of these patients were aged 65 years and more. The number of patients hospitalized to emergency services during the study was 10,546. Among this group, 4.246 (40.2%) patients were aged over 65 years. The sample of 4.246 patients over 65 years had a mean age of 76.1±7.0 (range, 65-102). The study sample comprised 2.027 (47.7%) females and 2.219 (52.3%) males (**Table 1**). The average age of female patients was 76.8±7.1, while that of male patients was 75.4±6.8 .When the referral complaints of patients admitted to the clinics were evaluated, the three most common symptoms were dyspnea, chest pain, and general impairment. The most common diagnoses were respiratory system disorders, cardiac disorders and neurological diseases. Patients were admitted to the appropriate clinics following a review of their symptoms and examinations performed at the end of the study. Accordingly, 3.352 (78.9%) patients were admitted to internal clinics, and 894 (21%) patients were admitted to surgical clinics.

The most common symptoms were chest pain, general impairment, and shortness of breath when considering presentations to the emergency unit of internal clinics. Most common patient diagnoses included respiratory system disorders, cardiac disorders and neurological diseases. Commonly attended internal medicine clinics included cardiology, neurology, chest diseases, and internal diseases in the order of frequency. Patients hospitalized to the emergency unit of surgical clinics were found to most commonly have abdominal pain, trauma, and chest pain. The most common diagnoses of these patients were acute abdominal problems, trauma-related fractures, and cardiac diseases among patients who were awaiting a surgery. The most common

of hospitalized clinics were general surgery, orthopedics, traumatology, cardiovascular surgery, and neurosurgery according to frequency of the patients who were admitted to surgical clinics. When the service and intensive care rates of patients were examined, 2.640 (62.2%) were hospitalized and 1.606 patients (37.8%) were admitted to intensive care. The average duration of hospitalization was 9.9 days in intensive care and 12.1 days in other services. When seasonal rates of patient admissions were examined, geriatric patients visited the chest diseases unit and intensive care unit commonly during spring (n=203) and winter (n=259), and the internal disease unit common during autumn (n=185). Patient admission to the cardiology unit and coronary intensive care unit also increased during autumn (**Table 1**). When the outcomes of the patients were examined, 714 patients (16.9%) were discharged due to life termination, 41 patients (1%) were referred for further examination and treatment, and 3.491 patients (82.1%) were discharged (**Table 2**).

DISCUSSION

With aging, functional capacity decreases and chronic disease prevalence increases. This often leads to the emergence of acute diseases, either independently or in association with existing illness.[10] A multidisciplinary approach is needed to determine the etiologic basis of acute or chronic diseases that are encountered in emergency services.[10,11] Multidisciplinary teams are necessary as it takes time and diverse skills to complete the necessary examinations and consultations.[11-13]

In studies of geriatric patients, the rates of admission to emergency services have been shown to vary considerably from 11.5% to 50%.[11-14] In our study, the rate of admission was 9.2%. This rate appears to be affected by the characteristics of the geographical region and the local population. In the Agean Part of Turkey, the sampling frame for the current study, 11% of the provincial population constitutes the age group defined as geriatric, as determined in 2013.[4] Therefore,

Table 1. Distribution of the patients according to diagnoses, Demographic features and Seasonal distiribution

		Gender		Seasons				Total
		Female	Male	Spring	Summer	Autumn	Winter	
Respiratory system disorders	Service	291	410	212	104	120	265	926
	İntensive Care	97	128	66	49	43	67	
Cardiac disorders	Service	78	78	35	31	24	66	865
	İntensive Care	316	393	169	180	202	158	
Neurological diseases	Service	234	247	110	126	123	122	839
	İntensive Care	199	159	98	72	95	93	
Gastrointestinal system disorders	Service	256	227	106	119	150	108	578
	İntensive Care	40	55	32	21	18	24	
Trauma	Service	188	131	75	87	87	70	360
	İntensive Care	15	26	7	12	15	7	
Nephrological disorders	Service	83	93	32	57	42	45	260
	İntensive Care	43	41	14	22	25	23	
Endocrine and metabolic disorders	Service	46	31	21	22	16	18	106
	İntensive Care	14	15	8	7	7	7	
Infectious disorders	Service	20	29	16	12	10	11	68
	İntensive Care	7	12	5	7	2	5	
Hematologic disorders	Service	22	19	16	9	9	7	48
	İntensive Care	5	2	2	1	2	2	
Urologic disorders	Service	22	62	26	20	13	25	91
	İntensive Care	1	6	1	0	4	2	
Cardiovascular disorders	Service	20	16	10	13	5	8	58
	İntensive Care	9	13	4	5	6	7	
Others	Service	17	20	13	7	8	9	47
	İntensive Care	4	6	3	2	2	3	
Total		**2219**	**2027**	**1081**	**985**	**1028**	**1152**	**4246**

Table 2. Distribution of the patients according to diagnoses and outcome of patients

Diagnosis		Outcome of patients				Total
		Discharged	Exitus	Transport	Refuse	
Respiratory system disorders	Service	607	78	3	13	701
	İntensive Care	116	100	4	5	225
Cardiac disorders	Service	141	14	1	0	156
	İntensive Care	581	103	8	17	709
Gastrointestinal system disorders	Service	413	52	15	3	483
	İntensive Care	57	35	2	1	95
Neurological diseases	Service	436	39	5	1	481
	İntensive Care	227	126	2	3	358
Trauma	Service	289	22	7	1	319
	İntensive Care	26	14	1	0	41
Nephrological disorders	Service	150	24	0	2	176
	İntensive Care	39	44	0	1	84
Endocrine and metabolic disorders	Service	71	6	0	0	77
	İntensive Care	17	12	0	0	29
Infectious disorders	Service	37	12	0	0	49
	İntensive Care	8	10	1	0	19
Hematologic disorders	Service	36	4	1	0	41
	İntensive Care	5	2	0	0	7
Urologic disorders	Service	76	5	0	3	84
	İntensive Care	7	0	0	0	7
Cardiovascular disorders	Service	31	2	1	2	36
	İntensive Care	17	5	0	0	22
Other	Service	32	4	1	0	37
	İntensive Care	8	1	0	1	10
Total		**3427**	**714**	**52**	**53**	**4246**

the geriatric population admitted to hospital was found to be in proportion to the overall population. One noteworthy element of this study is that it provides evidence for the current patient population in the provincial center because Kütahya Evliya Çelebi Training and Research Hospital can present large scale of population due to its location.

Several studies regarding the utilization of emergency hospital services by geriatric patients have been undertaken internationally. In a study conducted by Kekeç et al.[15] the three most common causes of admission were metabolic or systemic diseases, cardiovascular diseases, and cerebrovascular diseases. In another study, Ünsal et al.[10] assessed the emergency service presentations of older patients and determined that the most frequent causes of admission were hypertension, cardiac and pulmonary diseases, and upper respiratory tract and urinary tract infections. In a study performed by Castella et al.[16] it was reported that cardiovascular diseases were the main cause of admission to hospitals in older patients across the both sexes. In our study, the three most common causes of admission were chronic pulmonary diseases, cardiovascular diseases, and cerebrovascular diseases. In addition to cardiovascular and respiratory system diseases, studies have reported fall-related injuries among older adults as frequent causes of admission.[17,18] In our study, trauma was ranked seventh in general prevalence among the referrals of older patients and second in surgical cases.

In the literature, emergency hospitalization rates among the geriatric age group range from 11.5% to 61%.[14,15] Vanpee et al.[11] reported a 69% hospital admission rate in their study of a patient population over 75 years of age. The wide range of hospital admission rates among older adults is explained by the fact that countries have different definitions of geriatric population.[11] In our study, the hospitalization rate of the geriatric patient population increased in proportion with the other age groups (40.2%), which is consistent with the literature. When the patient group that was admitted to the emergency department was evaluated, it was determined that one out of every three patients was in the geriatric age group.

Two ways in which our findings differ from the international literature relate to length of hospital stay and outcomes of geriatric age group hospitalization. The average duration of hospitalization was 12.1 days for intensive care and 9.9 days for other services among the geriatric group of patients.

When presentations of the geriatric age group were evaluated in relation to emergency department admissions, reasons for illness included the presence of co-existing diseases accompanying the presenting condition, deterioration of cognitive function, and slowness of movement.[2,19] In addition to these reasons, all necessary tests for geriatric patient diagnoses and determination of appropriate treatments could not always be made. Barriers to diagnosis and treatment

included the lack of adequate equipment and the inappropriate physical conditions of the emergency room. For this reason, the recommended service model for older patients is the geriatric emergency service, where appropriate equipment, physical environment, and well-trained multidisciplinary staff are available.[20]

Comprehensive assessment to guide diagnosis is important for geriatric care. In their evaluation of the efficacy of geriatric assessment in emergency services, Garf et al.[21] concluded that comprehensive geriatric assessment reduced the requirement of functional assistance, re-admission to hospital, and needs for long-term care. However, rapid circulation in the emergency department prevents comprehensive geriatric assessment. For this reason, different methods have been suggested in the literature to admit older patients to emergency services.[21-25] In recent times, hospitals have begun to restructure their physical environments for older patients, and some have set up geriatric monitoring departments with bed capacities of four to seven.[20]

CONCLUSION

In these conditions, we believe that geriatric age group admission rates and health status can lead to the establishment of regional geriatric care centers, even if they are not provincial, so that the admission, follow-up, and rehabilitation of these patients can be more comprehensive.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study protocol was approved by the Medical Ethics Committee of Dumlupınar Universty (Permission granted: 18.01.2017, Decision no:2017/06 2018/8-1).

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

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Orjinal Araştırma / Original Article

Effect of Body Mass Index on the Prognosis in Lipophilic Drug Intoxication

Lipofilik İlaç Zehirlenmesinde Vücut Kitle İndeksinin Prognoza Etkisi

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Abstract

Introduction: The aim of this study was to investigate the effects of body mass index (BMI)c on the prognosis of lipophilic drug intoxication in patients who are admitted to the emergency units.

Material and Method: The files of the patients who presented to the emergency department with lipophilic drug poisoning between January 2014 and August 2016 were reviewed. Demographic characteristics, medications taken, complaints at the time of admission, and physical examination findings were recorded. BMIs of the patients were calculated. The group was created according to their BMI. These groups were compared.

Results: 202 patients were included in the study. Among the participants, 75 (37,1%) were in the 18-24,9 BMI interval, and 127 (62,9%) were ≥25. A statistically significant difference was observed between BMI groups regarding age, active complaint, hypertension, coronary artery disease, psychiatric disease, atrial fibrillation, need for atropine, need for pralidoxime (PAM), duration of mechanical ventilation and duration of intensive care unit stay (p<0,05).

Conclusions: The need for atropine and PAM, duration of mechanical ventilation and intensive care unit stay were observed to be higher in patients with high BMI. BMI maybe used as a prognostic factor for the prognosis of patients with lipophilic drug intoxication; however, more comprehensive studies are needed to support the finding.

Keywords: Lipophilic drug, body mass index, poisoning, emergency medicine

Öz

Giriş: Bu çalışmanın amacı, acil servislere başvuran hastalarda vücut kitle indeksinin (VKİ) lipofilik ilaç zehirlenmesinin prognozuna etkisini araştırmaktır.

Gereç ve Yöntem: Ocak 2014 - Ağustos 2016 tarihleri arasında lipofilik ilaç zehirlenmesi nedeniyle acil servise başvuran hastaların dosyaları incelendi. Demografik özellikler, alınan ilaçlar, başvuru anında şikayetler ve fizik muayene bulguları kaydedildi. Hastaların vücut kitle indeksleri hesaplandı. BMI'lerine göre grup oluşturuldu ve karşılaştırıldı.

Bulgular: Çalışmaya 202 hasta dahil edildi. Katılımcıların 75'i (%37,1) 18-24,9 VKİ aralığında, 127'si (%62,9) ≥25 idi. VKİ grupları arasında yaş, aktif yakınma, hipertansiyon, koroner arter hastalığı, psikiyatrik hastalık, atriyal fibrilasyon, atropin ihtiyacı, pralidoksim ihtiyacı (PAM), mekanik ventilasyon süresi ve yoğun bakımda kalış süresi açısından istatistiksel olarak anlamlı farklılık gözlendi (p<0,05).

Sonuç: VKİ'si yüksek hastalarda atropin ve PAM ihtiyacı, mekanik ventilasyon süresi ve yoğun bakımda kalış süresinin daha yüksek olduğu görüldü. BMI, lipofilik ilaç intoksikasyonu olan hastaların prognozu için prognostik bir faktör olarak kullanılabilir; ancak bulguyu desteklemek için daha kapsamlı çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Lipofilik ilaç, vücut kitle indeksi, zehirlenme, acil tıp

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INTRODUCTİON

Intoxication is the functional impairment of an organism that meets a specific agent.[1,2] Drug intoxications are emergencies that are frequently observed in emergency units and accompanied by high mortality and morbidity rates. One of the most important factors that define the prognosis is the time between drug intake and treatment; the treatment should be begun as soon as possible. Toxic agent elimination methods that are performed at the correct timing are life-saving.[3,4] Factors that affect the absorption in drug intoxication are: the route of agent administration or exposure, chemical and physical characteristics of the agent (molecular size, lipid solubility (lipophility), and the degree of ionization).[4]

Direct measurements of one's body composition include underwater weighing, skin folding measurement, bioelectric impedance analysis, and double energy X-ray absorptiometry. These direct methods are practical; however, they are not applicable for most health workers. Therefore, indirect methods have been developed, which include measurements of height and weight of the patients according to gender. BMI, body surface area, ideal body mass, non-fat body mass, and recently defined normal mass are frequently used weight and height definers in clinical practice and pharmacokinetic studies. BMI is a value that is obtained by division of the patient's body weight (kg) to the square of the height of the patient (m) (BMI=kg/m^2).[5]

Since lipophilic drugs accumulate in adipose tissue, the duration of their stay in the body increases, and then they may undergo redistribution. Accordingly, intoxication status may take longer and more severe in lipophilic drug intoxication.6 Since lipophilic agents such as verapamil, organophosphate compounds, clomipramine, propranolol, bupropion, lamotrigine, sertraline, quetiapine, haloperidol and, local anesthetics are highly soluble in fat tissue, BMI would have an important prognostic role in intoxications.[6-8] However, the prognostic significance of BMI in lipophilic drug intoxication is not known. In our study, we aimed to determine the prognostic significance of BMI in lipophilic drug intoxication.

MATERIAL AND METHOD

The study was conducted in compliance with the 1975 Declaration of Helsinki and approved by Necmettin Erbakan University School of Medicine, Scientific Research Evaluation Committee with a decision no: 2016/16-96. Written or verbal informed consent was obtained from each patient included in the study.

Patients who had been hospitalized in the toxicology intensive care unit of Konya Research and Training Hospital due to lipophilic drug intoxication between January 2014 and August 2016, were retrospectively investigated. The inclusion criteria were: 18 years of age and older, admission to the emergency unit due to lipophilic drug intoxication, hospitalization in the toxicology intensive care unit of emergency medicine clinics. The exclusion criteria were: age younger than 18 years, pregnancy, non-lipophilic drug intoxications, and discharge before 48 hours due to completed therapy or patient's desire.

The BMIs of the patients included in the study were calculated and the effects on the prognosis were investigated. The demographic characteristics, age, gender, weight, height, type of the drug exposed, clinical symptoms and findings, vital signs on admission, time from drug intake to admission to the emergency unit, complete blood count results, biochemical indicators, pH, HCO_3, lactate and pCO_2 levels in the venous blood of the patients who had been admitted to the emergency unit with lipophilic drug intoxication and for whom a judicial patient file was formed, were evaluated. GCSs were calculated from medical records The Fakir Hercules weighing machine was used in the intensive care units. The weight and height information were used to calculate the BMIs of the patients. The duration of hospital stay and status of discharge or exitus were checked from the records. Two groups were created and compared according to BMI.

The data were analyzed using the SPSS 15.0 program package. Compliance with the normal distribution was investigated using visual and analytic methods. The numerical data obtained from descriptive analysis were expressed as mean±standard deviation if normally distributed, and as interquartile range (IQR) if non-normally distributed. The nominal data were expressed as percentages. Differences between the groups were compared using chi-square or Fisher's tests. The Mann-Whitney U test was used for comparisons between paired groups if the data were not normally distributed. A P value of <0.05 was accepted as statistically significant.

RESULTS

A total of 5583 patients were examined in the toxicology intensive care unit of Konya Research and Training Hospital between January and August 2016. Among these, 202 were included in the study following the file investigation.

The patient group was composed of 97 (48%) males and 105 (52%) females. The median age (IQR) was 32.5 (21) years. Among the participants, 87 (43.1%) were aged between 18-30, 98 (48.5%) were aged between 31-60 and 17 (8.4%) were over 60 years. The patient distribution according to BMI revealed 75 patients (37.1%) within the 18-24.9 BMI interval, and 127 (62.9%) ≥25 BMI. Glasgow Coma Scale classification revealed 4 patients (2%) in the 3-9 interval, 16 (7.9%) in the 10-12 interval and 182 (90.1%) in the 13-15 interval. Among the participants, causes of intoxication were organophosphate in 106 (52.5%), sertraline in 49 (24.3%), quetiapine in 28 (13.9%), propranolol in 9 (4.5%), haloperidol in 7 (3.5%), clomipramine in 2 (1%), local anesthetic agents in 2 (1%), bupropion in 1 (0.5%), lamotrigine in 1 (0.5%) and verapamil in 1 (0.5%). Active complaints were present in 136 of 202 patients. Among these, the complaint was nausea/vomiting in 108 patients, chest pain or discomfort in 2, and confusion in 24. The remaining 30 patients had other complaints.

Among the 202 patients, mechanical ventilation was needed in 22 (10.9%), and all were administered standard fluid infusion. Atropine was needed in 35 (17.3%), PAM was needed in 36 (17.8%), naloxane or anexate was needed in 3 (1.5%), and other treatments were needed in 5 (2.5%).

The patients included in the study were classified in two groups according to the BMIs in obesity classification of the World Health Organization, as the 18-24.9 interval group and the ≥25 group. Statistical calculations that also comprised organophosphate intoxication demonstrated 36 (17.8%) males and 39 (19.3%) females in the BMI 18-24.9 interval group, and 61 (30.2%) males and 66 (32.7%) females in the BMI ≥25 group, which revealed no significant difference ($p>0.05$). A statistically significant difference was observed between the BMI groups regarding age, active complaint, hypertension, coronary artery disease, psychiatric disease atrial fibrillation, need for atropine, need for pralidoxime (PAM), duration of mechanical ventilation, duration of intensive care unit stay, age, clinical termination, WBC, Hb, pCO_2, troponin, 48th hour urea, and 48th hour AST and ALT ($p<0.05$).

Organophosphate intoxication was observed in 106 (52.5%) of 202 patients included in the study. The group with organophosphate intoxication was then excluded and a subgroup analysis was performed according to BMI. In this new analysis excluding organophosphate intoxication, the BMI 18-24.9 group included 18 (18,8%) males and 30 (31.3%) females, and the BMI ≥25 group included 18 (18.8%) males and 30 (31.3%) females. A statistically significant difference was observed between the groups formed according to BMI regarding age, psychiatric disease, duration of intensive care unit stay, clinical termination, pCO_2, and 48th hour ALT level ($p<0.05$). All patients who needed mechanical ventilation were in the BMI ≥25 group. **Table 1** demonstrates the comparison of the patient population that were grouped according to the BMI, including other types of lipophilic drug intoxication.

Table 1. Comparison of the patient population in which other lipophilic drug intoxications are included and grouped according to BMI

	BMI 18-24,9	BMI ≥25	P value
Age, year, median (IQR)	22 (6)	35.5 (13)	<0.001
Gender, n (%)			
Male	18 (18.8)	18 (18.8)	1.00
Female	30 (31.3)	30 (31.3)	
Diabetes mellitus, n (%)	0 (0)	1 (100)	1.00
Hypertension, n (%)	0 (0)	2 (100)	0.49
CAD, n (%)	0 (0)	2 (100)	0.49
Psychiatric illness, n (%)	5 (22.7)	17 (77.3)	0.004
COPD or asthma, n (%)	0 (0)	3 (100)	0.24
Other disease, n (%)	5 (55.6)	4 (44.4)	1.00
GCS, median (IQR)	15 (0)	15 (1)	0.09
Active complaints, n (%)	23 (41.8)	32 (58.2)	0.06
Nausea, vomiting, n (%)	19 (43.2)	25 (56.8)	0.21
Blur of consciousness, n (%)	3(37.5)	5 (62.5)	0.71
Other complaints, n (%)	4 (50)	4 (50)	1.00
Normal ECG, n (%)	45 (52.9)	40 (47.1)	0.19
Ventricular extra systole, n (%)	0 (0)	1 (100)	1.00
Tachycardia or bradycardia, n (%)	3(37.5)	5 (62.5)	0.71
Atrial Fibrillation, n (%)	0 (0)	3 (100)	0.24
Naloxane or anexate need, n (%)	0 (0)	3 (100)	0.24
Intubation/mechanical ventilation requirement, n (%)	0 (0)	4 (100)	0.11
ICU stay day, median (IQR)	2 (0)	3.5 (1)	<0.001
Connecting to a mechanical ventilator, n(%)	0(0)	4(100)	
Clinical outcome,n (%)			
Discharge	47 (49)	41 (42.7)	0.05
Transfer	1 (1)	7 (7.3)	
Ex	0 (0)	0 (0)	

DISCUSSION

In this study, we investigated the prognostic significance of BMI by comparing obese and non-obese groups in poisoning with lipophilic drugs. In our study, active complaints were more common in the obese group; hypertension coronary artery disease, psychiatric disease, atrial fibrillation were more common; the need for atropine and PAM is higher; longer stayed in intensive care; their clinical outcomes were worse. In addition, all of the patients on mechanical ventilators were in the group with BMI ≥25.

In drug intoxications, distribution of the drug into different sites of the body depends on the physicochemical characteristics of the drug, such as its molecular size, ionizing degree, lipid solubility, and the ability to be carried through biological membranes.[9,10] In drug intoxications with high lipophilic property, the agents are accumulated in the liver, kidneys, and fat tissue. They are then re-distributed, which may lead to further side effects. Starting at that point, the effects of a drug will depend on the weight of a patient. The patients may have the same weight while having different heights. Thus, the fat amounts will differ, and BMI may be important in the follow-up of patients in intoxications with high lipophilic drugs.

Koo Young Jung et al.[11] demonstrated that the duration of mechanical ventilation, the need for intensive care and the total duration of hospital stay were higher in obese patients (BMI≥25) in the high lipophilic drug group, and that in organophosphate intoxication, in particular, the high BMI was significantly related to a bad prognosis. Yusuke Sasabuchi et al.[12] demonstrated that the total duration of stay in the intensive care unit and hospital was longer in this group. In our study, patients accepted as obese according to BMI were found to remain on mechanical ventilation and in the intensive care unit longer, for both organophosphate intoxication-included and -excluded groups.

Akalın et al.[13] demonstrated in their study that patients with low GCS among those who had been admitted to the hospital due to organophosphate intoxication, had stayed in the hospital for a longer duration. They also reported that values such as GCS, p.cholinesterase, and creatinine were independent predictive values and that the need for atropin and PAM for patients with diabetes mellitus, hypertension,

obesity, coronary artery disease, cardiac arrhythmias (atrial fibrillation, etc) and comorbidities were higher. In our study, a history of hypertension, coronary artery disease and a.fibrillation in obese patients in the group that included organophosphate intoxication was higher compared to other groups and the need for atropine and PAM were higher.

Yaegashi et al.[14] reported that obese patients needed interim care units to a higher extent. James et al.[15] used conventional risk adjustment methods including disease severity and comorbidities, and found no correlation between the BMI category and extubation or transfer to interim care unit, or death risk.[15-17] In our study, the obese patient group stayed in intensive care 1.75 times longer. In addition, the rate of transfer to another clinic was 7 times higher in the obese patient group. There was a significant difference was observed between with and without organophosphate intoxication groups regarding BMIs and clinical terminations.

In the current literature, there are studies demonstrating that psychiatric diseases are more common among obese patients.[18-20] In our study, a history of the psychiatric disease was observed to be more common among obese patients according to BMI.

There is no clear evidence in the current literature indicating more common active complaints in the obese group with lipophilic drug intoxication. In our study, the presence of active complaints were observed to be more common among obese patients in the group with organophosphate intoxication.

In the current literature, there is no clear evidence showing the relationship between high BMI and high laboratory values in lipophilic drug intoxication. In our study, Wbc, Hb, PCO_2, troponin, ALT and 48th hour urea, 48th hour AST and 48th hour ALT values were found to be higher in the obese group. In the subgroup analysis in which organophosphate intoxications were excluded, PCO_2, 48th hour ALT values were found to be higher in the obese group.

CONCLUSION

Examination of the BMI of a patient may provide useful information for physicians to predict the clinical progression and maybe a guide for the re-evaluation of patients with lipophilic drug intoxication. BMI may be considered as a prognostic factor for the follow-up of patients with lipophilic drug intoxication; however, further studies are needed to clear the subject.

Limitations

Our study is the first to investigate the effect of BMI on the prognosis in lipophilic drug intoxication comprehensively. However, it was a retrospective study and the data of the patients were obtained in a limited manner. The sample size was limited as well.

In our study, BMI was calculated according to the weight and height of the patients. However, in order to correctly measure obesity, prospective studies that use body fat analyzers are needed.

Since factors such as insufficient sample size for patients admitting with bupropion, lamotrigine, verapamil, clomipramine and local anesthetic agent intoxication, and the fact that organophosphate group drug intoxication formed the majority of the patient population (52,5%) may lead to a misevaluation that the data seemed to belong to a single drug group, further studies that include sufficient sample size for each patient group are needed for more accurate outcomes.

ETHICAL DECLARATIONS

Ethics Committee Approval: Necmettin Erbakan University School of Medicine, Scientific Research Evaluation Committee with a decision no: 2016/16-96.

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

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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

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Orjinal Araştırma / Original Article

The Expression of Angiogenic Protein Cyr61 Significantly Increases in the Urine of Early-Onset Preeclampsia Patients

Anjiyojenik Protein Cyr61'in Ekspresyonu, Erken Başlangıçlı Preeklampsi Hastalarının İdrarında Önemli Ölçüde Artar

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Abstract

Aim: This study sought to compare the expression of the Cysteine-rich 61 (Cyr61) protein in the urine of early-onset preeclampsia (PE) patients with that of the urine of normotensive healthy pregnant women.

Material and Method: A total of 80 patients who gave birth from June 2019 to December 2019 were enrolled in this prospective study. The study group comprised 40 pregnant women at 20-34 weeks of gestation who presented with early-onset PE. Gestational age- and body mass index-matched, 40 healthy normotensive pregnant women without proteinuria were included in the control group. We recorded demographic characteristics and urine Cyr61 concentrations of the participants.

Results: The urine Cyr61 protein levels were significantly higher in the early-onset PE group (922.6±1263.1 pg/mL) than those of the control group (499.2±270.2 pg/mL, p<0.001). As a result of the ROC analysis, the area under the curve (aHR=0.690, 95% CI=0.556-0.813) was found to be significant (p=0.003). So, it was seen that Cyr61 could be used for the diagnosis of early-onset PE. The values 981.52 pg/mL and above, corresponding to 67.5% of sensitivity and 72.5% of specificity points, can be used as a cut-off which is calculated by the Youden index, can be used to diagnose early-onset PE.

Conclusion: This study found an increased Cyr61 protein level in the urine of the early-onset PE patients compared with the urine of healthy pregnancies. The increased presence of Cyr61 protein in the urine could serve as a predictive tool for the early diagnosis of early-onset PE and renal ischemia.

Keywords: Cysteine-rich protein 61, early-onset preeclampsia,renal ischemia.

Öz

Amaç: Bu çalışma, erken başlangıçlı preeklampsi (PE) hastalarının idrarındaki Sistein açısından zengin 61 proteinin (Cyr61) ekspresyonunu normotansif sağlıklı hamile kadınların idrarıyla karşılaştırmayı amaçladı.

Gereç ve Yöntem: Bu prospektif çalışmaya Haziran 2019 ile Aralık 2019 tarihleri arasında doğum yapan toplam 80 hasta dahil edildi. Çalışma grubu, erken başlangıçlı PE ile başvuran 20-34. gebelik haftalarındaki 40 gebe kadından oluşturuldu. Kontrol grubuna, gebelik yaşı ve vücut kitle indeksi uyumlu, proteinürisi olmayan 40 sağlıklı normotansif gebe alındı. Katılımcıların demografik özelliklerini ve idrar Cyr61 konsantrasyonlarını kaydettik.

Bulgular: İdrar Cyr61 protein seviyeleri erken başlangıçlı PE grubunda (922,6±1263,1 pg/mL) kontrol grubuna (499,2±270,2 pg/mL, p<0,001) göre anlamlı ölçüde daha yüksekti. ROC analizi sonucunda, eğri altındaki alan (aHR=0,690, %95 CI=0,556-0,813) anlamlı bulundu (p=0,003). Böylece, Cyr61'in erken başlangıçlı PE tanısında kullanılabileceği görüldü. Youden indeksi ile hesaplanan, %67,5 sensitivite ve %72,5 özgüllük noktalarına karşılık gelen 981,52 pg/mL eşik değeri erken başlangıçlı PE'yi teşhis etmek için kullanılabilir.

Sonuç: Bu çalışmada, erken başlangıçlı PE hastalarının idrarında sağlıklı gebelerin idrarına kıyasla daha yüksek Cyr61 protein düzeyi bulunmuştur. İdrarda artan Cyr61 protein düzeyi, erken başlangıçlı PE ve renal iskeminin erken teşhisi için öngörücü bir belirteç olarak kullanılabilir.

Anahtar Kelimeler: Sistein açısından zengin protein 61, erken başlangıçlı preeklampsi, renal iskemi

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INTRODUCTION

Preeclampsia (PE) is defined as a new onset of hypertension following 20 weeks of pregnancy in a previously normotensive gravid co-occurring either proteinuria or end-organ dysfunction.[1,2] This pregnancy complication constitutes one of the major causes of maternal and fetal morbidity and mortality, affecting 2-8% of all pregnancies worldwide.[3] PE is associated with adverse pregnacy outcomes, including maternal end-organ damage, growth restriction, oligohydramnios, preterm birth, and fetal and neonatal mortality.[4,5]

In a healthy pregnancy, highly invasive extravillous trophoblast (EVT) cells migrate through the uterine wall, erode the spiral arteries, remodel these arteries by replacing the vascular endothelial and muscle cells, and transforming them into the low resistant vessels to provide high blood flow capacity.[6,7] If any EVT cells' migration and invasion characteristics are defected or disturbed, it could result in a shallow invasion of EVT cells into the decidua and vessels, accompanied by inadequate remodeling of the maternal vascular structures seen in the preeclamptic placenta.[8-12] This incomplete remodeling induces uteroplacental insufficiency and fetal growth restriction, which could affect placental development and angiogenesis.[13]

Cysteine-rich 61 (Cyr61, CCN1), a component of the CCN protein family, is a secreted matricellular protein expressed by stromal cells, vessel's endothelial cells, and interstitial EVT giant cells, and implicated in diverse cellular processes, including angiogenesis, adhesion migration, formation, proliferation, and apoptosis.[14] Also, Cyr61 is highly expressed in the human placenta during embryogenesis.[14,15] However, the immunohistochemical examination of preeclamptic placental tissues and the analysis of serum samples of preeclamptic patients showed reduced expression of Cyr61.[16,17]

During a healthy pregnancy, the kidney experiences significant physiologic and anatomic adaptive alterations performing a pivotal role in gestation. These changes make the kidney vulnerable to conclusions happening in PE.[18] The kidney is one of the organs targeted by PE, causing abnormal renal histology, proteinuria, renal ischemia, and renal dysfunction.[19,20] Cyr61 is considered to aid in numerous events, including neovascularization, wound healing, and organ development.[21] Prior researches have identified the low secretion level of Cyr61 in a healthy kidney and high secretion of Cyr61 in the ischemic kidney, which recommends that Cyr61 might be a potential marker for diagnosis of renal ischemia.[22] Therefore, we assumed that we might detect Cyr61 in the urine following renal ischemia caused by PE.

This study sought to compare the expression of the Cyr61 protein in the urine of early-onset PE patients with that of the urine of normotensive healthy pregnant women.

MATERIAL AND METHOD

This prospective study was conducted at the XX Hospital. A total of 80 patients who gave birth from June 2019 to December 2019 were enrolled in the study. The study group comprised 40 pregnant women aged between 18-35 years at 24-34 weeks of gestation who presented with early-onset PE. Gestational age- and body mass index (BMI)-matched 40 healthy pregnant normotensive patients without proteinuria were included in the control group. The control group consisted of pregnant women who did not experience any adverse outcomes associated with pregnancy in the later weeks of pregnancy and had given birth at term.

We used the ACOG criteria for PE definition.[23] Early-onset PE were defined after 20th week of pregnancy as hypertension (systolic blood pressure [BP] of ≥140 mm Hg, or diastolic BP of ≥90 mm Hg on two times at least 4 hours apart [unless antihypertensive therapy is started at this point]), and the presence of proteinuria (≥300 mg/24 h urine collection [or this amount extrapolated from a timed collection], or protein/creatinine ratio of ≥0.3 mg/dL, or dipstick examination of 2+ [practiced only if other quantitative techniques not accessible]). In the absence of proteinuria, if the pregnant women suffered from gestational hypertension present with any of the following characteristics, they were diagnosed as preeclampsia: impaired liver function as shown by abnormally elevated blood concentrations of liver enzymes (to twice the higher limit standard concentration), thrombocytopenia (platelet count $<100{,}000\times10^9$/L), and severe persistent right upper quadrant or epigastric pain unresponsive to medication, renal insufficiency (serum creatinine concentration >1.1 mg/dL or a doubling of the serum creatinine concentration in the lack of other renal disorder), visual disturbances, new-onset headache unresponsive to medication and not considered for by alternative diagnoses, and pulmonary edema.

We excluded patients with multiple pregnancies, eclampsia, HELLP syndrome, ruptured amniotic membranes, anemia, infections, fever, and co-existing morbidities, including diabetes mellitus, thyroid disorders, chronic hypertension, renal disease, hepatic disease, collagen vascular disease, and known malignancy. Patients at the active phase of labor, a previous history of gestational hypertensive disorders, patients with incomplete or unavailable medical records were also excluded.

We collected blood and urine samples of the patients at the PE diagnosis period before any treatment for the study group, and during routine antenatal care before labor for the control group. At the time of the maternal urine sample collection, the gestational age and BMI of the patients were matched, and the two groups were similar in terms of gestational age and BMI. We recorded maternal age, parity, BMI, gestational age at urine sample collection, systolic and diastolic BP, amount of proteinuria, white blood cell (WBC) count, hemoglobin value, platelet count, blood urea nitrogen (BUN), creatinine, AST, ALT, birth week, birth weight, and urine Cyr61 levels of the patients.

The urine concentration of Cyr61 was measured in duplicate using an enzyme-linked immunoassay (ELISA) kit (Catalog Number: SEG313Hu; Cloud-Clone Corp. 23603 W. Fernhurst Dr., Unit 2201, Katy, TX 77494, USA) according to the manufacturer's protocol. The intra- and interassay coefficients of variations were < 10% and < 12% respectively.

The ethics committee of the Kanuni sultan Süleyman Training and Research Hospital approved the study (2019.04.83). An informed consent form was obtained from all patients. .

Statistical Analysis

We used IBM SPSS 21.0 for Windows (SPSS Inc., Chicago, IL, USA) statistical package program for statistical evaluation of our research data. We presented measured variables as mean±standard deviation (std), and categorical variables as numbers and percentages (%). The Kolmogorov-Smirnov test was used to determine whether the numerical data matched the normality distribution. The Chi-square and Fisher exact tests were used for pairwise comparisons. We used the Mann-Whitney U test to compare the non-normally distributed data. Differences were considered statistically significant at P-value <0.05. We used a receiver operating characteristic (ROC) curve to evaluate the sensitivity and specificity performance characteristics of Cyr61, and estimated a cut-off value by using the index of Youden.

Group sample sizes of 40 and 40 achieve 80% power to detect a difference of 35% between the control and early-onset PE groups with estimated group standard deviations of 270.2 and 280.0 and with a significance level (alpha) of 0.05 using a two-sided two-sample t-test.

RESULTS

Throughout the study period from June 2019 to December 2019, 63 patients suffered from early-onset PE were admitted to our hospital. Four patients had a history PE in their previous pregnancies. Four patients were at the active phase of labor. Three patients had chronic hypertension. Two patients did not wish to participate and withdrew from the study. We also excluded ten patients per the other exclusion criteria. A total of 40 pregnant patient suffered from early-onset PE entirely fulfilled the inclusion criteria for the final analysis (**Figure 1**).

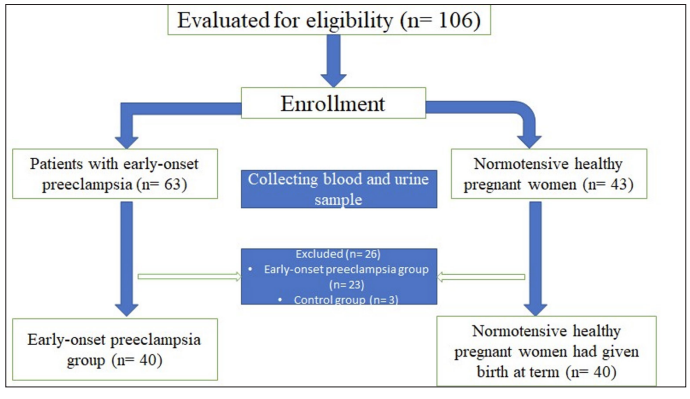

Figure 1. Flow diagram of the study

We summarized the demographic and clinical characteristics of the participants in **Table 1**. There were no significant differences between the two groups in terms of maternal age, number of nulliparous patients, BMI, and gestational age at urine sample collection.

The urine Cyr61 protein levels were significantly higher in the early-onset PE group (922.6±1263.1 pg/mL) than those of the control group (499.2±270.2 pg/mL, p<0.001, **Table 1**).

Table 1. Demographic and clinical details, and urine Cyr61 expression of early-onset preeclampsia patients and the matched healthy control group

	Early-onset preeclampsia group (n=40)	Control group (n=40)	P value
Maternal age, years	25.2±3.1	26.3±2.9	0.618
Nulliparous, n (%)	26 (65%)	21 (52.5%)	0.223
Body Mass Index, kg/m^2	24.7±2.2	23.6±2.7	0.464
Systolic Blood Pressure, mmHg	146.8±6.2	114.2±6.7	**<0.001**
Diastolic Blood Pressure, mmHg	97.1±3.4	73.2±3.9	**<0.001**
Gestational age at urine sample collection, weeks	30.2±4.2	30.5±3.9	0.813
WBC, /mm^3 ×10^3	12.26±3.16	11.82±2.83	0.336
Hemoglobin, g/dL	11.94±1.27	11.32±1.51	0.728
Platelet, /mm^3 ×10^3	241.17±72.19	271.27±56.43	**<0.001**
BUN, mg/dL	13.78±4.63	10.16±3.22	0.165
Creatinine, mg/dL	0.89±0.47	0.51±0.26	0.094
AST, U/L	40.66±78.77	23.17±9.25	**<0.001**
ALT, U/L	35.57±67.90	19.43±7.71	**<0.001**
Proteinuria, mg/24-hour	4929.37±6682.38	N/A	N/A
Birth week	30.6±3.9	38.4±1.2	**<0.001**
Birth weight	1558.9±686.9	3352±346.1	**0.006**
Urine Cyr61, pg/mL	922.6±1263.1	499.2±270.2	**<0.001**

Data are presented as mean ± standard deviation, or number (percentage)

As a result of the ROC analysis, the area under the curve (aHR=0.690, 95% CI=0.556-0.813) was found to be significant (p= 0.003). So, it was seen that Cyr61 could be used for the diagnosis of early-onset PE. The values 981.52 pg/mL and above, corresponding to 67.5 sensitivity and 72.5 specificity points, can be used as a cut-off which is calculated by the Youden index, can be used to diagnose early-onset PE (**Table 2**, **Figure 2**).

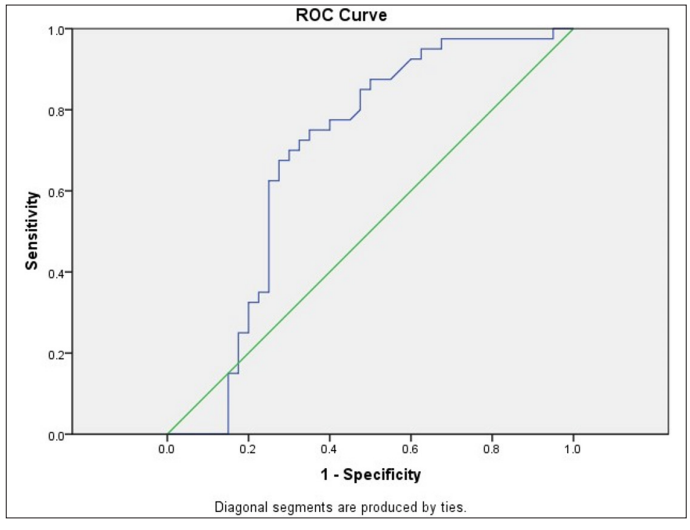

Figure 2. ROC curve for Cyr61 value for predicting early-onset preeclampsia

Table 2. The area under the curve of Cyr61 value

	ROC	St.Error	95% Confidence Interval		p
			Lower	Upper	
Cyr61	0.690	0.063	0.566	0.813	0.003

DISCUSSION

Our study indicates that the Cyr61 protein demonstrated significantly increased secretion levels in the urine of patients suffering from early-onset PE compared with normotensive gestational age- and BMI-matched controls. The excess of molecules involved in the PE pathogenesis suggests that a single mechanism may not describe the development of this disease, and it could stem from several reasons.[16] Therefore, it isn't easy to discover a proper marker among these molecules for PE, and until presently, a useful marker has not yet been developed. Since the Cyr61 urine protein level was discovered to be noticeably increased in early-onset PE patients, we could serve this protein as a new biomarker for this disease.

Previous data proposes that PE and other gestational hypertensive diseases are a significant contributor to the burden of renal ischemia.[24] A recent study reported that PE, especially severe PE, is the most common cause of renal ischemia during pregnancy.[25] Researchers formerly considered that the organ dysfunction that occurs with PE reversed after delivery. However, current studies reported that PE is related to an increased risk of chronic or future renal disease.[26] The histopathological examination of PE patients' kidneys during the antepartum or postpartum period showed protein casts in the tubules, proliferation of mesangial cells, vacuolation of podocytes, and endotheliosis.[27]

The imbalance in the production of growth and angiogenic factors at the placenta and their secretion into the maternal blood may drive to the clinical sign of PE, including proteinuria and hypertension.[15] Vascular endothelial growth factor (VEGF) seems to perform a pivotal role in the connection between endotheliosis and proteinuria development.[28] The podocyte-derived VEGF binds to endothelial cells, inducing the maturity and the structural integrity of the glomerular endothelium, and maintaining glomerular filter integrity by binding on podocytes.[18] In PE, the reducing levels of VEGF damage the ECs and the glomeruli. These ECs begin to produce endothelin-1 (ET1), which has a potential connection between endothelial dysfunction and altered podocyte integrity and function. ET1's release causes following podocyte-associated protein shedding from podocytes.[29] The shedding of the podocytes is related to the severity of PE, and the urine levels of podocyte-associated proteins are correlated with the amount of proteinuria.[30]

Cyr61 can be observed in healthy embryonic glomeruli and human podocytes. Cyr61 is a secreted protein that acts as a matricellular signaling factor competent for many functions, including migration, proliferation, adhesion of fibroblasts and ECs, and wound healing, and increases in the inflammatory response and other injury circumstances.[31] Li et al.[22] reported that Cyr61 protein significantly increased at 3 h following renal ischemia, reached the basal level at 24 h, and could be detected early after ischemia in the rat urine. They stated that urine Cyr61 protein is an outstanding biomarker of renal ischemia, and better than the serum creatinine (Scr) for early diagnosis of renal ischemia. Because of the physiological alterations and increase in glomerular filtration rate (GFR), a decrease of Scr occurs during pregnancy, causing the correct and immediate diagnosis of renal ischemia more difficult and masks the renal function changes. It is not always possible to compare the renal function parameters with the patient's baseline values. Furthermore, pregnant women may have a 30-40% reduction in GFR without significant increases in Scr.[25,32] In our study, urine Cyr61 expression levels in the placentas of PE (922.6±1263.1 pg/mL) were higher than those in healthy pregnancy (499.2±270.2 pg/mL, $p<0.001$). This result suggests that Cyr61 may be a new marker for the diagnosis of early-onset PE and also could be used to diagnose renal ischemia early.

Lai et al.[33] stated that the inhibition of Cyr61 reduces renal inflammation and fibrosis after renal ischemia. Liu et al.[34] pointed out that Cyr61 was related to fibrosis in the long-term of ischemia, that the Cyr61 expression was positively associated with renal fibrosis after renal ischemia. These consequences confirm that PE increases the risk of chronic or future renal disease and may cause permanent kidney damage without preexisting renal disease. However, it is not evident whether Cyr61 can be utilized as a potential marker of the progression of acute to chronic renal disease.[22]

The main limitation of this study is that we did not compare the urine Cyr61 values with patients' GFR. The main strength of this study is that, to the best of our knowledge, this study, for the first time, provides evidence that Cyr61 protein upregulates in the urine of PE patients. Further studies of Cyr61 signaling pathways are required to clarify its mechanisms of action in PE and future renal disease.

CONCLUSION

In this study, we found an increased Cyr61 protein level in the urine of the early-onset PE patients compared with the urine of gestational age-matched healthy pregnancies. The increased presence of Cyr61 protein in the urine could serve as a predictive tool for the early diagnosis of early-onset PE and renal ischemia.

ETHICAL DECLARATIONS

Ethics Committee Approval: The ethics committee of the Kanuni sultan Süleyman Training and Research Hospital approved the study (2019.04.83). An informed consent form was obtained from all patients.

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

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Orjinal Araştırma / Original Article

Evaluation of the Duration of Peripheral Venous Catheter in Vein in Hospitalized Children

Hastaneye Yatan Çocuklarda Periferik Venöz Kateterin Vende Kalma Süresinin Değerlendirilmesi

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Abstract

Aim: This study was conducted to evaluate the duration of the peripheral venous catheter in vein, which is employed in the treatment of children who are hospitalized in pediatric clinics.

Material and Method: The study was conducted as a prospective and observational-descriptive study. The sampling of the study consisted of the 249 child, who were admitted to the pediatric clinic and who underwent peripheral venous catheter insertion. Institution and ethics committee permission was obtained for the study. The data were collected with the "Peripheral Venous Catheter Monitoring Form" and "Phlebitis Scale", which were prepared according to the literature.

Results: It was determined that a total of 57.8% of the children who were included in the study were 1-36 months old, 60.6% were male, and 66.7% were hospitalized for more than 6 days. It was also determined that the duration of the catheter in children was 58.76±28 hours and catheter was inserted 3.61±1 times during hospitalization. The negative correlation between "durations of peripheral ıntravenous catheters in veins" and "number of peripheral intra venous catheters inserted from hospitalization to discharge" was found to be statistically significant. It was determined that 73.5% of the catheters were removed because of the obstruction.

Conclusion: As a result of the present study, it was determined that the peripheral venous catheter in children under three years of age had a shorter duration of remaining in the veins, and children were subjected to repeated peripheral venous catheter attempts because of obstructions before their treatments were completed.

Keywords: Peripheral venous catheter, child, intra venous practice, pediatric clinic, nursing

Öz

Amaç: Bu araştırma, pediatri kliniklerinde yatan çocukların tedavisinde kullanılan periferik venöz kateterin vende kalma süresini değerlendirmek amacıyla yapılmıştır.

Gereç ve Yöntem: Çalışma, prospektif ve gözlemsel-tanımlayıcı olarak yapılmıştır. Araştırmanın örneklemini, pediatri kliniğinde yatan ve periferik venöz kateter uygulanan 249 çocuk oluşturmuştur. Araştırma için etik kurul ve kurum izinleri alınmıştır. Veriler, literatüre göre hazırlanmış olan "Periferik Venöz Kateter İzlem Formu" ve "Flebit Ölçeği" ile toplanmıştır.

Bulgular: Araştırma kapsamına alınan çocukların %57,8'inin 1-36 aylık, %60,6'sının erkek ve %66,7'sinin 6 günden fazla hastanede yattığı belirlenmiştir. Çocuklara uygulanan kateterin vende kalma süresinin 58,76±28 saat ve yatış süresince kateter uygulama sayısının ortalama 3,61±1 olduğu saptanmıştır. "Periferik venöz kateterin vende kalma süresi" ve "çocuğun yatışından çıkışına kadar takılan kateter sayısı" arasında istatistiksel olarak negatif yönde ilişki olduğu belirlenmiştir (p<0,05). Periferik venöz kateterlerin %73,5'inin tıkanma nedeniyle çıkarıldığı bulunmuştur.

Sonuç: Bu çalışma sonucunda üç yaş altı çocuklarda periferik venöz kateterin vende kalma süresinin daha kısa olduğu ve çocukların henüz tedavileri sonlanmadan özellikle tıkanma nedeniyle tekrarlı periferal venöz kateter girişimlerine maruz kaldıkları bulunmuştur.

Anahtar Kelimeler: Periferik venöz kateter, çocuk, intra venöz uygulama, pediatri kliniği, hemşire

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INTRODUCTION

Nowadays, administering fluids, drugs, and electrolytes with peripheral intra venous catheters (PIVC) to veins is a widely used technique. PIVC application is an indispensable element for modern medicine and is the most common invasive intervention at hospitals.[1-4] PIVC are frequently used in cases such as diarrhea and vomiting that can lead to dehydration, in patients to whom liquid electrolytes cannot be given orally, in preoperative and postoperative periods, in continuous or intermittent drug administration, to provide blood and blood products, to ensure total parenteral nutrition, facilitate access to the vein in emergencies, and for hemodynamic monitoring and diagnostic assisting applications.[1,5,6] However, if the treatment period is more than 6 days, it is recommended to use central catheter or peripherally inserted central catheter (PICC) instead of PIVC.[7] In case of clinical indications such as phlebitis, infiltration, obstruction, accidental removal, suspicious infection and completion of therapy, catheters need to be removed or replaced.[4,8] Rickard et al.[9] (2012), in a randomized controlled study, it was determined that there was no additional increase in catheter-related bloodstream infections (CRBSI) compared to the routine replacement of the changed PIVCs in case of clinical indication development. Therefore, PIVCs should not be changed unless clinical indications develop. However, children are subjected to repeated peripheral catheter applications for the completion of unfinished treatments before they recover because of phlebitis, catheter displacement, obstruction, infiltration or even extravasation.[10,11] In addition, since the diameters of the appropriate veins are small and difficult to find in children, recurrent peripheral catheter applications provide the ground for pain, trauma, and infection in children, cause disruption of treatments, create intense anxiety and stress in the family, and causes stress and loss of labor and corporate cost losses in nurses.[1,12] In addition, peripheral catheter applications are a stressful procedure that requires being in close proximity with the patient in clinics of diseases such as covid 19 that are at risk of intensive transmission.[13,14]

Safe initiation, execution, and termination of intra venous treatment is a very significant practice for pediatric nurses and requires specialization. Variables such as appropriate dilution of the drugs, the use of the infusion pump, the nature of the area where the PIVC is inserted, the determination of the area, the care of the area, the age of the child and the child's disease, dressing, knowledge and experience of the nurse, may affect the duration of the catheter in the vein and complications.[5,10,15] Prevention of infiltration/extravasation (I/E) in pediatric patients is important. A study has examined the effect of an education program, which aims to prevent and manage pediatric I/E, on I/E rates in pediatric patients. The study has led to an improvement in nursing care, an improvement in the quality of patient care and has helped progress toward increased patient safety.[16] For this reason, the main aim of pediatric nurses in monitoring, maintenance, security and management of infusion must be taking the necessary precautions to increase the duration of the catheters in veins without complications.[17,18] Because, as mentioned before, finding the right vascular pathway is difficult and traumatic in children. On the other hand, atraumatic care is an important concept in nursing literature and is a healthcare philosophy aiming to minimize physical and psychological difficulties for children and their families in healthcare settings. The main target in atraumatic care is not to cause any damage.[19] Most pediatric patients have at least one PIVC insertion during their hospitalisation. Despite the important function of PIVC for delivery of intra venous therapy, failure and complications rates are widely reported; however these results have not been synthesised. PIVC failure and complications in paediatrics patients are a significant problem globally. Therefore, continued efforts from health care providers are required to decrease the incidence of these complications.[15]

Purpose of the Study

This study was conducted for the primary purpose of examining the duration of the PIVC in the vein, the number of PIVC inserted until discharge, and the causes of removals of PIVC, which are used at children hospitalized in pediatric clinics.

Research Questions

1. What is the duration of the PIVC in the vein and number of times the PIVC was inserted until discharge in pediatric patients?
2. Does the child's age, gender, catheter type and catheterized area of the child affect the duration of the PIVC in the vein and the number of PIVC placed in the child until discharge?
3. Is there a relationship between duration of the PIVC in the vein and the number of PIVC placed in the child until discharge?
4. What are the reasons for removing the PIVC?

MATERIAL AND METHOD

Study Type

The study was conducted as a prospective and observational-descriptive study.

Place and Sampling of the Study

The universe of the research consists of children treated with PIVC implantation in the pediatric clinic. The sampling of the study consisted of the children (n=249), who were admitted to the pediatric clinic and who underwent peripheral venous catheter insertion.The study was based on the monitoring of children who were treated with peripheral venous catheters in pediatric clinic of a University Hospital in Turkey between January and June 2018. In the pediatrics clinic, patients who need medical treatment of acute and chronic diseases between the ages of 1-18 are hospitalized and there are no surgical patients. The minimum sample size was calculated with the G*Power 3.1.9 program based on the literature.[20] Accordingly, the total number of samples that should be included in the

study was calculated as n=246 for 80% statistical power, 0.16 effect size and 0.05 type 1 error. The research was completed with n=249 people. The cases were determined according to the inclusion and exclusion criteria in the study and there was no data loss.

Criteria for the Study

Inclusion criteria: Those who were treated with peripheral venous catheters in pediatric clinic in the study were included in this study.

Exclusion criteria: The children who had an immune deficiency, who had severe circulatory disorders and dehydration, who received chemotherapy, who had central catheters, who had dibetes mellitus, who had blood inserted, who had total parenteral nutrition, who previously participated in this study, who catheter inserted in another unit and who did not want to participate in the study were excluded.

Variables of Research

Dependent variables: Duration of the PIVC in the vein and number of times the PIVC was inserted until discharge in pediatric patients.

Independent variables: Child's age, gender, catheter type and catheterized area of the child.

Data Collection Forms

The data were collected with the "Peripheral Venous Catheter Monitoring Form" and "Phlebitis Scale", which were prepared according to the literature.

Peripheral Venous Catheter Monitoring Form, includes the child's age, gender, disease type, number of days in hospital, catheter type, use of heparin cap, catheterization site, type of drug given from catheter, fluid intake, fluid delivery method, duration of catheter in vein, number of catheters inserted while in hospital, the reasons for catheter removal.

The Phlebitis Scale was developed by Schultze and Gallant (2006). The scale, which involves the rating stages of the related symptoms in the observation of the catheters in terms of possible risks and/or phlebitis in patients undergoing catheter, consists of 5 stages, which are; Stage 1, the stage in which symptoms like pain, redness, and edema, which are the symptoms of phlebitis, are absent. Level 2 is the stage when early symptoms of phlebitis are seen. In this stage, there is redness less than 2.5 cm around the catheter and pain appearing with palpation. Stage 3 is the middle stage of phlebitis. In this level, there are signs of redness bigger than 2.5 cm and between 2.5 cm and 5 cm around the intra venous region, pain that occurs with palpation in the area, and stiffness around it. Stage 4 is the stage of advanced phlebitis or initial thrombophlebitis. In this stage, there are 5 cm or more redness in the area, pain, and stiffness appearing with palpation in or around the area. Stage 5 is the advanced stage of thrombophlebitis. In this stage, there are 4th stage phlebitis and purulent drainage findings.[21,22]

Data Collection

Observations were made in the patient room by the pediatric clinical nurse (GY) before drug/fluid administration through the catheter and shift changes (average; 5 times/day). In cases where fluid infusion is given through the catheter; observation frequency (average; 1 time/hour) varied according to the type and amount of fluid administered. During the observation, the PIVC site; It was evaluated in terms of phlebitis, infiltration, dislocation, and occlusion. If these complications developed, the patient was taken to the intervention room for PIVC removal and re-application of PIVC. The area of the catheter in the body, the color/number of the catheters, and the control of the catheter area in terms of phlebitis were evaluated and recorded in the Phlebitis Scale by making observations. In addition, the insertion and removal times of these catheters, the number of the hospitalization days of the child, the number of the catheter interventions from the hospitalization to the discharge, the age, gender, medical diagnosis of the children, and other information like the medication and fluid that were applied during this catheter were obtained from the patient file. Applications such as catheter insertion stages, selection of the insertion area, selection of the color/number of the catheter, drug and fluid application stages, were made within the routine practices of the pediatric service. Thus, the reliability of the study was provided. No additional applications that may affect the results of the study were made, and the study was conducted in the observational and descriptive fashion.

Data Analysis

The data were recorded and analyzed by using the SPSS 22 Software. The fitness of the data to normal distribution was tested. The quantitative data were expressed with mean and standard deviation (SD); and the qualitative data were expressed with numbers and percentages. For the comparison of the quantitative data between the groups, the significance test for the difference between two mean values and the Pearson Correlation Test was used. $p<0.05$ was considered to be significant in statistical terms.

Ethical Considerations

The study was conducted in line with the principles of the Helsinki Declaration. The permission of the institution for the study and the approval of the Ethics Committee were obtained from the Tokat Gaziosmanpasa University Ethics Committee of Clinical Research (2017/6, 17-KAEK-052); and oral consents were obtained from the children/parents who met the inclusion criteria for the study.

RESULTS

It was determined that a total of 57.8% of the children who were included in the study were 1-36 months old, 60.6% were male, 90.8% were because of an acute illness, and 66.7% were hospitalized for more than 6 days. It was also found that the most frequently used catheter was the yellow/24

number catheter (87.6%), none of them had heparin valves, the most frequently used area was the area above the hand (47.8%), 83.1% were given medicine, 51.8% were given fluid, and 62% of these were given fluid with infusion pump. It was determined that 13.3% of the catheters that were inserted to children remained in the vein for 2-24 hours, 25.7% remained for 25-48 hours, 30.1% remained for 49-72 hours, 20.5% remained for 73-96 hours and 10.4% remained for 97-144 hours; and 73.5% of the catheters were removed because of the lack of the fluid/medicine flow (obstruction), 12.9% of the catheters were displaced, 4% were removed because of infiltration, 2% were removed because of phlebitis (1st and 2nd levels), and 7.6% were removed because of the termination of the treatment/discharge (**Table 1**).

Table 1. Distribution of variations on peripheral venous catheter use (n=249)

	Number	%
Age		
1-36 month	144	57.8
37 month -15 years	105	42.2
Gender		
Female	98	39.4
Male	151	60.6
Disease type		
Acute illness	226	90.8
Acute and chronic illness	23	9.2
Number of days in hospital		
1-5 days	83	33.3
6 days and +	166	66.7
Catheter type		
Yellow/24	218	87.6
Blue/22	31	12.4
Heparin valves		
Used	-	-
Not used	249	100
Catheterized area		
Hand	119	47.8
Arm	88	35.3
Foot	41	16.5
Head	1	0.4
Medicine administration status from catheter		
Antibiotic	203	81.5
Other	4	1.6
Did not take medicine	42	16.9
Fluids administration status from catheter		
Took fluids	129	51.8
Did not take fluids	120	48.2
Fluids application method *		
With infusion pump	80	62.0
With drop setting set	49	38.0
Durations of peripheral venous catheters in veins		
2-24 hours	33	13.3
25-48 hours	64	25.7
49-72 hours	75	30.1
73-96 hours	51	20.5
97-144 hours	26	10.4
Reasons for catheter removal		
Lack of the fluid/medicine flow (obstruction)	183	73.5
Catheter dislocation	32	12.9
Infiltration	10	4.0
Phlebitis	5	2.0
Termination of the treatment/discharge	19	7.6

*The percentage was taken from children (n=129) who were given fluid through the catheter

It was determined that the duration of the catheter in veins was 58.76±28 hours, the catheter was inserted 3.61±1 times during hospitalization. The duration of the catheter in the veins in children between 1-month-old-36-month-old (55.62±25 hours) was shorter than the children who were older than 37 months (63.06±30 hours); and the difference between the averages of these periods was statistically significant ($p<0.05$). It was also determined that the number of catheters inserted from the hospitalization to discharge of the children who were 1-36 months old (3.76 ±1) were higher than the children who were older than 37 months; however, there were no statistically significant differences between the groups ($p>0.05$). It was determined that the duration of the catheter in the vein and the number of catheters inserted from the hospitalization to discharge, according to the gender of the children, the area where the catheter was inserted, and the color/number of the catheter were not statistically significant ($p>0.05$). It was determined that the catheters that were inserted in the foot/head vein (52.98±27) were shorter hours than those that were inserted in the hand/arm area (59.93±28) ($p>0.05$). In addition, it was also determined in terms of the color/number of the catheters that the duration of the yellow/24 catheters in the veins (57.51±27) was shorter than the blue/22 catheters (67.52±31), the number of the catheters inserted from the hospitalization to the discharge was higher ($p>0.05$) (**Table 2**).

Table 2. According to some variables, the means of durations of PIVC in veins (hour), number of PIVC inserted from hospitalization to discharge

	Durations of PIVC in veins (hour)	Number of PIVC inserted from hospitalization to discharge
Age	Mean±SD	Mean±SD
1-36 month	55.62±25.68	3.76 ±1.71
37 month -15 years	63.06±30.65	3.41±1.63
p	**0.039**	0.112
Gender		
Female	57.87±28.51	3.52±1.53
Male	59.33±27.85	3.68±1.78
p	0.689	0.461
Catheter type		
Yellow/24	57.51±27.46	3.66±1.70
Blue/22	67.52±31.0	3.25±1.52
p	0.063	0.205
Catheterized area		
Hand-Arm	59.93±28.01	3.57±1.72
Foot-Head	52.98±27.95	3.83±1.51
p	0.144	0.367
Overall average	58.76±28.07	3.61±1.68

Data are shown as mean±standard deviation. For the comparison of the quantitative data between the groups, the significance test for the difference between two mean values were used. $p<0.05$ was considered to be significant in statistical terms.

The poor negative correlation between "durations of PIVC in veins" and "number of PIVC inserted from hospitalization to discharge" was found to be statistically significant ($p<0.05$) (**Table 3**).

Table 3. Correlation between durations of PIVC in veins (hour) and number of PIVC inserted from hospitalization to discharge (n=249)

	Mean±SD	p	r
Number of PIVC inserted from hospitalization to discharge	3.61±1.68	0.014	-0.156
Durations of PIVC in veins (hour)	58.76±28.07		

r: Pearson Correlation Test

DISCUSSION

Vascular access devices are commonly inserted devices that facilitate the administration of fluids and drugs, as well as blood sampling. Despite their common use in clinical settings, these devices are prone to occlusion and failure, requiring replacement and exposing the patient to ongoing discomfort/pain, local vessel inflammation and risk of infection.[1-3,23] In order to prevent these complications, observation of the catheter area by nurses is very important, especially in irritant drug infusions.[20] However, it was seen that studies conducted on catheter vein duration and frequency of interventions especially in children are in a limited number in the literature. It is difficult to find, follow up and care peripheral vessels, especially in infants and young children. In a study, it was determined that children who underwent PIVC mostly developed complications (67.7%) below the age of 3 years.[24] Since verbal and cognitive development in the 0-3 age group is not sufficient compared to the older age groups, cooperation is also difficult. Cognitive development accelerates in children over the age of 3 with the start of pre-school education.[5] For these reasons, in this study, a grouping was made as over 3 years old and under. As a primary result of the present study, it was determined that the peripheral venous catheter in children under three years of age had a shorter duration of remaining in the veins, and children were subjected to repeated peripheral venous catheter attempts because of obstructions before their treatments were completed (**Table 1** and **Table 2**). In this study, the fact that there was a statistically significant decrease in the number of catheters inserted from the hospitalization to the discharge of the children as the duration of the peripheral venous catheters in the veins increased in the children who were included in the study is an important result at this point (**Table 3**).

These primary findings are an important result showing that hospitalized children are frequently exposed to catheter applications, which is one of the traumatic procedures. Repeated traumatic procedures can lead to pain, stress, problems in the child's psychosocial development, loss of labor and cost. It is an important issue for healthcare professionals to take measures against repeated invasive procedures and to increase such studies.[12,18,23]

Jeong et al. (2017) determined that the mean PIVC dwell time was 55.62±27 hours, mostly at 24–72 hours intervals, in 1596 pediatric patients.[20] In another study conducted on children who were between the ages 3-18, it was found that the mean duration of catheterization was 83.53 hours.[25] It is considered that the inclusion of children under 3 years of age in this study may have caused a lower catheterization time (58.76±28 hours). In this study, it was found that the catheter duration in the veins was shorter when yellow/24 number catheter was used especially in children under 36 months who had catheters inserted in the foot/head veins. In the period that passed from the hospitalization of the children to the discharge, the number of catheters was higher in children who were under 36 months, in those with catheters in the foot/head veins, and when yellow/24 number catheters were used. As the age decreases in children, so does the vascular lumen, and the catheter may be dislocated because of the natural movements of children and the lack of cooperation, which can cause infiltration and extravasation. It was also reported in studies that catheter insertion from lower extremity veins increased complication risk.[11,20,24] In addition, it is also known that catheters that are commonly used in pediatric patients (yellow/24 number; 87.6% for this study) with smaller internal lumen have decreased stay is the veins in fluid and/or drug administration especially in case internal lumen is exposed to damage due to intense, acidic and irritant drugs. In the present study, antibiotics (81.5%) were the most commonly used drug type. In addition, previous studies showed that antibiotics are a risk for phlebitis formation and other complications.[20,24] In another study, it was found that the mean duration of the peripheral venous catheter in the veins of pediatric patients was 68.82±35 hours, and the duration of remaining in the veins decreased due to similar risk factors.[10] In a similar study, the rate of developing complications regarding peripheral venous catheter in pediatric patients was 49.7%, 6% phlebitis developed and complications developed under 3 years of age at the highest rate as in this study.[24] In the present study, it was found that the incidence of phlebitis was low (2%) among the causes of catheter removal. In this study, the phlebitis rates being low may be associated with short catheter vein durations in children who were included in the study. Jacinto et al.[26] (2014) aimed at a study to identify risk factors for phlebitis related to PIVC in children. Similarly, conducted the study with 338 children, nine (2.7%) developed phlebitis. Laudenbach et al.[27] (2014) conducted a study with 80 children between the ages of 2 and 17 and reported that 22.5% of the children developed peripheral intra venous catheterization complications, and the most common complications were obstruction and infiltration. Similarly, in the present study, it was also observed that obstruction was a major problem as a catheter complication (73.5%).

The findings obtained in the study show that innovative studies must be conducted to solve the problem of designing the material (other variables; catheter type, heparinous valve, flushing, drug density, dilution, dressing, etc.) in the case of failure in fluid/drug flow given from the catheter (obstruction and catheter dislocation) to reduce the number of catheter interventions in children and to increase the duration of the catheter in veins before treatment end.[2,17,18,23,28] A study aimed at examining the effectiveness of IV House UltraDressing for protecting PIVCs in pediatric patients was conducted. This randomized controlled trial comprised 60 pediatric patients

(aged 2–24 months): 30 in the experimental group and 30 in the control group. IV House UltraDressing has been determined to be a useful device that can be used in pediatric patients to increase catheter waiting time and to protect and stabilize PIVCs.[18] To protect and stabilize PIVCs is an important nursing care. Because, as mentioned above, it is difficult and traumatic to find the right vascular pathway in children. The reasons for the difficulty in inserting catheters in pediatric patients are associated with the adipose tissue being more, the veins being small, and the cooperation being insufficient. For this reason, it must be the main target to ensure that the catheters that are inserted in children with difficulty remain in the vein for a long time unless clinical indications develop.[4,8] Because decreasing the traumatic procedures that are associated with pain in children is an approach intended for the philosophy of atraumatic care. For this reason, it is recommended that innovative and experimental studies are conducted to increase the duration of the catheter in the veins of children and to reflect these findings to the literature and pediatric clinics. The scientific developments and practices regarding this procedure, which is the responsibility of nurses, must be closely followed, and new knowledge and skills must be transferred to practice.

Limitations

The study was conducted in the Pediatric Clinic of a University Hospital. For this reason, the data were limited to the children in this clinic and cannot be generalized to all clinics. This research is limited by some variables shown in this study that can affect the length of time the catheter remains in the vein.

ETHICAL DECLARATIONS

Ethics Committee Approval: The permission of the institution for the study and the approval of the Ethics Committee were obtained from the Ethics Committee of Clinical Research (2017/6, 17-KAEK-052)

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

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Orjinal Araştırma / Original Article

Early Postoperative Complications in Primary Cleft Lip and Palate Repair: A Retrospective Analysis of 328 Cases

Dudak Damak Yarıklarının Primer Onarımında Erken Postoperatif Komplikasyonlar: 328 Olgunun Retrospektif Analizi

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Abstract

Aim: Primary cleft lip and palate (CLP) repair is the most critical stage throughout lifetime. CLP surgery involves risks of surgery and anesthesia related complications. In this study, it was aimed to evaluate the complications occur in the early period after primary CLP surgery and to determine early factors that trigger these conditions.

Material and Method: In this study 328 surgeries of 271 CLP patients were included. Complications such as fever occurring in the first 3 days were classified as minor complications. Complications that could not be treated with palliative care or that had to be transferred to intensive care were considered as major complications. The epidemiology and causal link of early complications were statistically evaluated.

Results: Early complications were seen in 19% (n: 63) of all cases that were operated for cleft lip and palate. Among them, rate of minor complications was 9% (n: 25). It was determined that prolongation of anesthesia caused an increase in minor complications such as inadequate oral nutrition. Major complications were observed in 11% (n: 38). These major complications were more common in patients with bilateral cleft lip, cleft palate, syndromic cases, and male patients. Complicated cases' mean length of stay in hospital was 3.35 days. When compared with noncomplicated cases, there was increase in hospitalization time ($p<0.05$).

Conclusion: Minor complications can be prevented with careful intubation and shortening the surgery duration. Despite all these precautions, major complications are still very important problems in bilateral cleft lip, syndromic and male patients. Therefore, it is mandatory to perform these surgeries in centres where management of these complications is possible.

Keywords: Cleft lip and palate, early, postoperative, complications

Öz

Amaç: Primer dudak damak yarığı (DDY) onarımı, yaşam boyu en kritik aşamadır. DDY ameliyatı, ameliyata ve anesteziye bağlı komplikasyon risklerini içerir. Bu çalışmada, primer DDY cerrahisi sonrası erken dönemde meydana gelen komplikasyonların değerlendirilmesi ve bu durumları tetikleyen erken dönemdeki faktörlerin belirlenmesi amaçlanmıştır.

Gereç ve Yöntem: Bu çalışmaya 271 DDY hastasının 328 ameliyatı dahil edildi. İlk 3 günde ortaya çıkan ateş gibi komplikasyonlar minör komplikasyon olarak sınıflandırıldı. Palyatif bakımla tedavi edilemeyen veya yoğun bakıma transfer edilmesi gereken komplikasyonlar ise majör komplikasyonlar olarak kabul edildi. Erken komplikasyonların epidemiyolojisi ve nedensel bağlantısı istatistiksel olarak değerlendirildi.

Bulgular: Dudak damak yarığı nedeniyle ameliyat edilen tüm olguların %19'unda (n: 63) erken komplikasyonlar görüldü. Bunlar arasında minör komplikasyon oranı %9 (n: 25) idi. Anestezinin uzamasının ağızdan beslenmede yetersizlik gibi minör komplikasyonların artmasına neden olduğu belirlendi. Majör komplikasyonlar %11 (n: 38) oranında görüldü. Bu majör komplikasyonlar, bilateral dudak yarığı olanlarda, sendromik olgularda, damak yarığı olanlarda ve erkek hastalarda daha sıktı. Komplike vakaların ortalama hastanede kalış süresi 3,35 gündü. Komplike olmayan vakalarla karşılaştırıldığında hastanede kalış süresinde artış vardı ($p<0,05$).

Sonuç: Dikkatli entübasyon ile anestezi ve ameliyat süresinin kısaltılması minör komplikasyonları önleyebilir. Tüm bu önlemlere rağmen iki taraflı dudak yarıklarında, sendromlu hastalarda ve erkek hastalarda majör komplikasyonlar hala çok önemli problemlerdir. Bu nedenle bu komplikasyonların yönetiminin mümkün olduğu merkezlerde dudak damak yarığı ameliyatlarının yapılması zorunludur.

Anahtar Kelimeler: Dudak damak yarığı, erken, postoperatif, komplikasyonlar

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INTRODUCTION

Cleft lip and palate patients need many operations throughout their lives. In this patient group, complications related to surgical procedures can be seen, as well as different complications that may threaten patient's life in early postoperative period. Primary operations in cleft lip and palate make risks of general anaesthesia more pronounced than surgery procedure risks due to it's being done in infantile period. It is known that anesthesia risks are higher in early childhood and especially in newborns.[1] At the same time risk of general anesthesia is higher in patients with cleft lip and palate compared to normal patient population.[2] Moreover, many additional anomalies and syndromes may accompany cleft lip and palate.[3] This increases the complication rate during and after the operation. Management of the early complications has to be done by plastic surgeons.

In this study, early complications after primary cleft lip and palate repair in children were investigated retrospectively. It is aimed to determine factors that cause complications in primary cleft lip and palate surgery (first surgery) that involve surgery and anesthesia related complications risks together. Preventive measures are discussed in the light of the literature.

MATERIAL AND METHOD

A total of 328 surgeries of 271 cases with cleft lip or palate between January 2012 and October 2018 were retrospectively analyzed. Data were obtained from ENLİL® hospital information management system and anesthesia course form. The study was approved by the Ethics Committee of the Selcuk University Faculty of Medicine (no: 2018/23) and performed in accordance with the Declaration of Helsinki and protection of personal data.

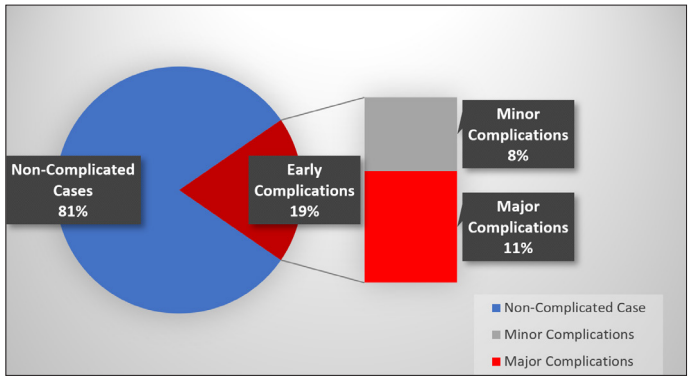
All surgeries were performed under elective conditions and were preoperatively consulted with an anaesthesiologist and a paediatrics physician. Complications seen in first three days from the day of the operation were included in the study. Patients over 2 years old were excluded. Ages, weights of the patients and duration of anesthesia were recorded from hospital data system. Type of the deformity was classified as bilateral and unilateral for the cleft lip and as complete and incomplete for the cleft palate.

Postoperative fever, mechanical airway destruction, respiratory tract infection, ischemia / dehiscence in flap and bleeding were recorded. Complications such as fever that was treated with simple methods, partial wound separation, temporary hypothermia and hospitalization period less than two days were classified as minor complications. Respiratory tract infection, airway destruction, excessive postoperative bleeding and complete wound dehiscence or patients with hospitalization period longer than 2 days or requirement to transfer to intensive care unit, were defined as major complications.[4]

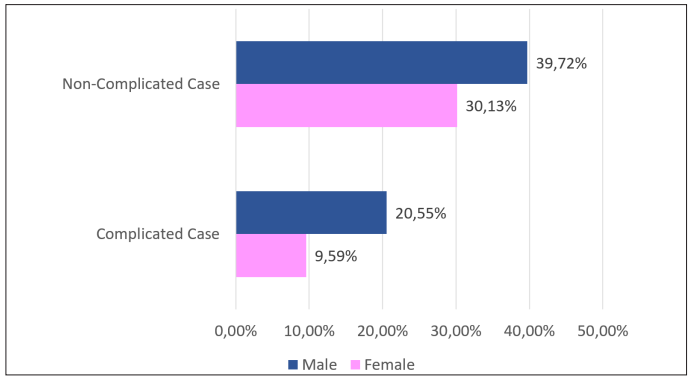
Relationship between all complications and gender, weight, cleft type, duration of anesthesia, duration of hospitalization and additional anomalies were statistically evaluated. Chi-square and t test were used for evaluation and a value of $p<0.05$ was considered significant for all analyses. SPSS® statistics program was used for statistical analysis (version 21.0 for Windows; Armonk, NY: IBM Corp.)

RESULTS

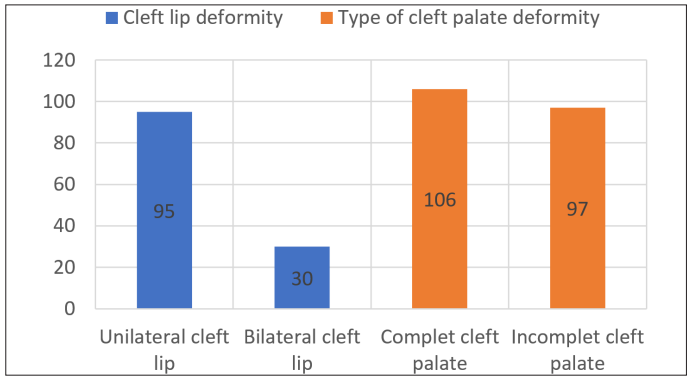
Patients' age ranged from 4 months to 24 months (mean: 11.19 months). It was observed that 76% (n: 95) of cleft lip patients had unilateral lip deformity. Bilateral cleft lip percentage was 24% (n: 30). Complete cleft palate deformity was observed in 52.2% (n: 106) of the patients and incomplete deformity was seen in 47.8% (n: 97) of the patients. Early complications were detected in 19% of the primary 328 operations (n: 63). While 11% (n: 38) of all complications were major complications, 8% (n: 25) percent of complications were minor complications (**Graphic 1**). The most common major complications were respiratory tract infection (n: 10) and airway destruction (n: 10) in primary palate repair patients. Ratio of treatment requiring respiratory infection was determined as 4.27%. Severe bleeding requiring transfusion was detected in only one patient after primary palate repair. Both major complications and minor complications were more common in male cases than in female and it was a statistically significant difference (**Graphic 2**). Early complications were found to be higher in patients with cleft palate compared to primary lip repair patients ($p<0.05$). More major complications were observed in patients with bilateral cleft lip than unilateral cleft lip patients. The difference was statistically significant ($p<0.05$) (**Graphic 3**).



Graphic 1. Early complication rate



Graphic 2. Patient Distribution Rate by Gender



Graphic 3. Early Complication Numbers

In patients without any complications, mean anesthesia duration was 124 minutes. On the other hand, average anesthesia duration was observed as 134 minutes in palate repair surgeries with major complications. There was no statistically significant difference in duration of anesthesia with major complicated and non-complicated palate repair patients (p>0.05). However, it was observed that duration of anesthesia was significantly effective in development of minor complications (p: 0.039).

In major complications with cleft lip patients, anesthesia duration was not an effective factor (p>0.05). Similar to palate repair patients, general anesthesia time was an efficient factor in the development of minor complications (p: 0.047).

Although mean weight of complicated cleft lip patients was lower than uncomplicated cases, no statistical difference was observed (p>0.05). As low weights were similarly observed in complicated cleft palate patients (**Table 1**), there was no statistically significant difference (p>0.05). Major complications were significantly increased in patients with additional anomalies or syndromes (p<0.05). Cardiac anomaly was present in 65% of the patients who developed major complications (**Table 2**).

Table 1. Average weights by deformity

Deformity	Mean weight (±SD) (Min. – Max. weight)
Complicated cleft lip	6743.31 g (±1762.25)
Non-Complicated cleft lip	7131.62 g (±1133.59)
Complicated cleft palate	8462.74 g (±1353.90)
Non-Complicated cleft palate	9513.88 g (±1880.10)

SD: Standart deviation

Table 2. Distribution of additional anomaly or syndrome

Additional Anomaly or Syndrome	Number of Patients
Cardiac anomaly	11
Down syndrome	3
Other syndromes	4
Microcephalia	3
Laryngomalacia	1
Renal agenesis	1
Asthma	1
Status epilepticus	1
History of intensive care units	5

Mean length of hospital stay was 1.27 days in cleft palate patients without complications, and 1.67 days in non-complicated cleft palate patients. The duration of hospitalization was 3.17 days and 3.54 days, respectively in cleft lip and palate patients that complications occurred. It was found that complication development significantly increased the duration of hospitalization (p<0.05).

DISCUSSION

Many organs are immature in early years of life. This situation causes a predisposition to complications during surgery.[5] Although most of these early complications are related to anesthesia, they are also important for plastic surgery practice. Early diagnosis and treatment are critical. Moreover, it is urgent to identify complications in this group of patients who are often discharged on the first postoperative day.[6] There are factors affecting early postoperative complications in all three periods including preoperative evaluation, during anesthesia and postoperative care.

Continuous contact of the nasal cavity with food and saliva causes frequent upper respiratory infections in children with cleft lip and palate.[7] Presence of infection in any part of respiratory system triggers anesthesia related complications.[1] At the same time, nutritional deficiency, micrognathia, macroglossia and glossoptosis cause an increased risk for general anesthesia. Many centres reported different postoperative complication rates ranging from 3% to 38%.[3,8-12] This situation is mostly related to classification system of complications and diagnostic methods. Early postoperative complications can be classified as two parts as major life-threatening complications that require advanced treatments, and minor complications that can be eliminated with palliative treatments such as fluid replacement and antipyretic therapy.[4]

Complications have been reported to be associated with age in literature. Therefore, the most important factors that determine the operation timing are the weights and ages of the children's. Even in the 'Rule of 10s' proposed by Wilhelmsen and Musgrave, the two main rules that determine the timing of the surgery are the weights and ages of the patients.[13] Nowadays, patients in young age and low weight in weight in parallel to the development of anesthesia techniques can be operated safely. Nevertheless, in the current literature has been shown to be no significant difference between the effects of the ages of the patients to the overall complication rates.[1,14] Similarly, in our study, there was no relationship between the development of early complications and age and weight.[9,15]

In literature, it was shown that cleft lip and palate can be associated with more than 150 syndromes or anomalies.[11] For this reason, some preliminary evaluations are made for prevention of complications. Especially for patients with additional anomalies or syndromes, preoperative evaluations are more valuable because of high rate of complications. As a

result of our study, general anesthesia increases complication rates in patients who have cardiac anomalies and these complications tend to be serious. It has been suggested in the literature that cases with cardiac problems should be operated in the late periods of life to reduce the negative effects of complications.[16] Similarly, increased rate of complications are also observed due to additional anomalies in male patients and bilateral cleft patients.

To prevent early postoperative respiratory complications; diagnosing viral upper respiratory tract infections, questioning vaccination, and bleeding disorders history are essential and postponing the surgery when necessary is the most important measure.[1] Otolaryngology consultation may be required for asymptomatic serous otitis media and possible ventilation tube applications.

Anatomical variability of the upper airways of cleft lip and palate patients causes intubation difficulties.[12] It has been shown that respiratory problems may be related to recurrent intubation trials. Especially in this group of patients; false intubation, difficult intubation, tube separation or compression, desaturation, laryngeal spasm, and bronchospasm have been reported frequently.[12] In order to prevent breathing problems, reinforced cuff-free ventilation tubes should be used, gentle intubation should be performed, and irritation should be avoided. Another issue to be considered in early years of life is the amount of intravascular fluid. While body weight is between 5 kg and 10 kg, total blood volume is 400-700 ml. Therefore, even small volume blood losses or dehydration can result in hemodynamic disorders. Intraoral surgery creates intubation and laryngoscopy difficulties. Significantly major complications are higher in palate repairs than lip repairs. In the literature, this situation is associated with the amount of blood loss.[11] In the literature, meticulous surgery performed in experienced hands, has been shown to be especially related to low bleeding rates.[15]

Our study shows that prolonged operation time has negative effects on palate cleft repair, especially for major complications. However, we think that this situation is mostly related to already difficult cases or intubation problems (difficult intubation, separation of the tube, pressing the tube ...) caused to long surgery time.

In the postoperative period, airway irritation can be reduced with cold steam. Routine body temperature measurement during and after surgery are also important and measurement being 38°C and above is an indicators for early intervention to prevent complications. Insufficient analgesia or reflux after starting feeding too early may result in apnea as a result of vagal stimulation.[17] At the same time, parents' reservations about feeding may cause inadequate fluid intake too. Therefore, education of parents and nurses about nutrition is effective in correcting this situation.

Fillies et al.[11] suggested that early complications were more common in children between 4000-6000 gr. However, it was demonstrated with this study that weight was not associated with the triggering of early complications due to the fact that primary surgery was not performed under 6000 gr. in our clinic. Therefore, performing the surgery at the appropriate weight will not increase major complications in cleft lip and palate surgeries.

CONCLUSION

Most similar retrospective studies show that complications seen in primary surgeries of patients with cleft lip and palate have decreased over the years. With data of non-profit medical organisations such as Operation Smile, in which a large number of cleft lip and palate surgeries are performed, it has been shown that there is a decrease in many early complications with the above mentioned prevention measures.[15]

The development of minor complications can only be prevented by taking history, doing a physical examination, performing surgery at appropriate weight and shortening the general anesthesia duration. Significant parts of the minor complications that cause prolongation in hospital stay can be prevented with routine, strict measures. However, major complications remain as an important problem for in bilateral cases, patients with anomaly or syndrome, and male patients with cleft palate. Extended operative time is also a significant problem. In central hospitals, experienced surgical team with the appropriate equipment will reduce the morbidity by facilitating the treatment of major complications that may develop.

ETHICAL DECLARATIONS

Ethics Committee Approval: Selcuk University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (Date: 17.01.2018, Number: 2018/23)

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

Referee Evaluation Process: Externally peer-reviewed.

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Orjinal Araştırma / Original Article

Risk Factors for Nosocomial Infections in Children

Çocuklarda Nozokomiyal Enfeksiyonlar İçin Risk Faktörleri

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Abstract

Aim: To determine the frequency of healthcare associated infections (HCAIs) developed within a year in patients admitted to a tertiary pediatric hospital.

Material and Method: Between February 1996 January 1997 the patients hospitalized at Dr Sami Ulus Children's Hospital and diagnosed as HCAI during their follow up were included in the study. The diagnosis of 'nosocomial infection' was made on the basis of Center for Disease Control (CDC) diagnostic criteria . Clinical, laboratory and imaging findings were recorded.

Results: HCAIs were detected in 311 (9.1%) of the 3420 hospitalized patients. Some of these patients experienced more than 1 episode, and thus, the total HCAI episodes were 353. Of the patients with HCAI; 77.8% were younger than 1 year old, 60.5% (n= 188) were male. HCAI was detected to occur after 10.9±10 days of hospitalization. The most frequent HCAIs were acute gastroenteritis, sepsis, urinary tract infections and lower respiratory system infections. Gram-negative organisms were the most frequently isolated agents. Of the 311 patients with HCAIs, 38 (12.2%) died.

Conclusion: HCAI is an important cause for mortality and morbidity in pediatrics clinics. HCAI surveillance, detection of the problems and taking precautions for infection control are important steps.

Keywords: Health care-associated infections, child, risk factors

Öz

Amaç: Üçüncü basamak bir çocuk hastanesine yatırılan hastalarda bir yıllık süre içinde gelişen sağlık bakımı ile ilişkili enfeksiyon (SBİE) sıklığının belirlenmesidir.

Gereç ve Yöntem: Şubat 1996 – Ocak 1997 tarihleri arasında Dr. Sami Ulus Çocuk Hastanesine yatırılan ve izlemlerinde SBİE tanısı alan hastalar çalışmaya alındı. SBİE tanısı, CDC (Center for Disease Control and Prevention) tanı kriterleri esas alınarak konuldu. Klinik kayıtlar, laboratuar ve görüntüleme bulguları kaydedildi.

Bulgular: Hastaneye yatırılan 3420 hastada 311 (%9,1) SBİE saptandı. Bu hastalardan bazılarında 1'den fazla enfeksiyon epizotu saptandı.Toplam SBİE epizodları 353 idi. Olguların %77,8'i bir yaş altında, %60,5 (n=188) erkek idi. SBİE yatıştan sonraki 10,9±10 günlerde ortaya çıktığı saptandı. En sık görülen SBİE; akut gastroenterit , sepsis, üriner sistem enfeksiyonu ve alt solunum yolu enfeksiyonları idi. Gram negatif organizmalar en sık izole edilen ajanlardı. SBİE tanısı alan 311 hastanın 38'i kaybedildi (%12,2).

Sonuç: SBİE çocuk servislerinde önemli mortalite ve morbidite nedenidir. SBİE sürveyansı sorunların saptanması ve enfeksiyon kontrolü için önlemler alınması çok önemli basamaktır.

Anahtar Kelimeler: Sağlık bakımı ilişkili enfeksiyon, çocuk, risk faktörler

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INTRODUCTION

Hospital-acquired infections (HCAI), also known as healthcare-associated infections (HCAI), are nosocomially acquired infections that are typically not present or might be incubating at the time of admission. These infections are usually acquired after hospitalization and manifest 48 hours after admission to the hospital. HCAIs can happen in any health care facility, including hospitals, ambulatory surgical centers, end-stage renal disease facilities, and long-term care facilities. Bacteria, fungi, viruses, or other, less common pathogens can cause HCAIs. HCAIs are a significant cause of illness and death — and they can have serious emotional, financial, and medical consequences.[1,2] Patients hospitalized in pediatric services and pediatric intensive care units (PICUs) have a higher risk of HCAIs. Prolonged hospitalization, invasive interventions, congenital malformations, and total parenteral nutrition are significant factors that increase the risk of nosocomial infections in pediatric patients. Prolonged hospitalization, invasive interventions, congenital malformations, and total parenteral nutrition are significant factors that increase the risk of HCAI in pediatric patients.The incidence, prevalence, morbidity and mortality rates of HCAIs varies depending on factors such as the type of the hospital, age of the patient, diagnosis at hospitalization, hospitalization service, diagnosis and treatment interventions.[3] HCAIs are a frequent problem, particularly in Intensive Care Units (PICU). In Europe, incidence of nosocomial infections was reported as 1-2.5% in general pediatric services and as 6.1-15.1% in pediatric intensive care units (PICU).[4,5] In developing countries, HCAI rates of PICUs were reported - much higher 13.6-15.4%.[7,8]

Healthcare-associated infection is to be a significant cause of morbidity and mortality worldwide and in Turkey. HCAI frequency is reported as 3.02% to 9.3% in the pediatric age group in Turkey.[3,9] Since 2005 every hospital has "National Nosocomial Infections Surveillance and Control Unit".[10] Since then there has been significant decrease in HCAI rates, where the particular decrease in year 2007 should be noted.[3]

The aim of this research is to find out the frequency of nosocomial infections in one year period in Dr. Sami Ulus Pediatric Hospital and to compare the changes in surveillance studies of nosocomial infections in children in different years with the derived data.

MATERIAL AND METHOD

In the present study, the data of healthcare-associated infections detected at Dr. Sami Ulus Children's Training and Research Hospital -a tertiary hospital-, were collected in the period January 1996- December 1996. The pediatric hematology-oncology service was excluded from the study. The diagnosis of Healthcare-associated infections (HCAI) have been assessed according to the Centers for Disease Control and Prevention (CDC) criteria. For HCAIs, questionnaires included information on the type of infection, onset of infection, any device relationship (e.g. whether a urinary catheter had been fitted before onset of infection), and other details. Information on whether the nosocomial infection had already been present on admission or had been acquired during the current hospital stay, and the pathogen that had caused the infection, were also recorded. Culture samples obtained from patients were studied in the microbiology laboratory using traditional manual methods. Infection sites, responsible microorganisms and their effect on prognosis were studied. For prophylactic antibiotic use, the type of antibiotic, route of administration, indication, and whether the indication was listed in the patient's medical record were recorded. The Statistical Package for the Social Sciences (SPSS) for Windows version 10.1 was used for the statistical analysis. The study was approved by the Ethics Committee of Dr.Sami Ulus Maternity and Children's Training and Research Hospital, Ankara, Turkey (Date: 17.01.2020, No:73799008).

RESULTS

In the 1-year period, 3420 patients were hospitalized. HCAIs were detected in 311 (9.1%) of the patients. Thirty-eight (13.5%) of these patients experienced more than 1 episode, and thus, the total number of HCAI episodes was 353. 39.5% (n=123) of the patients were female and 60.5% (n= 188) of them were male. The relationship between gender and HCAI was found statistically significant ($p<0.05$). 77.8% of the patients were younger than 1 year of age. HCAI frequency was higher in the 0–1-year-old age group than the other age groups. This difference was found statistically significant ($p<0.05$) (**Table 1**).

Table 1. Distribution of HCAI by age groups n (%)

Diagnosis / age	0-12 months	1-4 age	5-9 age	10-14 age	Total n (%)
Gastroenteritis	79 (88.7)	9 (10.1)	1 (1.2)		89 (28.6)
Sepsis	67 (84.8)	9 (11.3)	2 (2.5)	1(1.2)	79 (25.4)
Urinary tract infection	61 (83.6)	12 (16.4)			73 (23.4)
Pneumonia	20 (51.2)	9 (23.0)	7 (17.9)	3 (7.7)	39 (12.5)
Peritonitis			3 (30.0)	7 (70.0)	10 (3.2)
Omphalitis	9 (100.0)				9 (2.8)
Skin infection	3 (42.8)	4 (57.1)			7 (2.2)
Conjunctivitis	3 (60.0)	2 (40.0)			5 (1.6)
Total, n (%)	242 (77.8)	44 (14.1)	13 (4.1)	12 (3.8)	311 (100.0)

HCAI distribution in terms of diagnosis was as follows: 28.6% (n=89) of them were GE, 25.4% (n=79) were sepsis, 23.4% (n=73) were UTI, 12.5% (n=39) were pneumonia, 3.2% (n=10) were peritonitis, 2.8%(n=9) were omphalitis, 2.2% (n=7) were skin infection and 1.6% (n=5) were conjunctivitis. HCAI-GE was high because of the *Salmonella* Gastroenteritis epidemic during May-June period.

Patients were diagnosed with HCAI on the average of 10.9 ± 10^{th} (383^{rd}) day of their hospitalization - in HCAI-Sepsis it was 16.1±6.7, urinary tract infection 19.2±13.1, pneumonia 22.8±13.9 and GE 14.6±8.9 days. Although the day of diagnosis for HCAIs differed, this was not found statistically significant ($p>0.05$).

Table 2. Distribution of the causative microorganisms of HCAI

	n	%
Klebsiella spp.	99	40.2
Salmonella spp.	58	23.5
E. coli	29	11.7
CoNS	14	5.6
S. aureus	8	3.2
Pseudomonas spp.	10	4.0
Candida	8	3.2
Enterococcus spp.	7	2.8
Enterobacter spp.	7	2.8
Group B *streptococcus*	6	2.4
Total	246	100

CoNS: Coagulase negative *staphylococcus*

The comorbid diseases were malnutrition 50.4% (n=178), congenital heart diseases 17.5% (n=62), Immunodeficiency 15.8% (n=56), chronic kidney disease (CKD) 2.8%(n=10) and neuromuscular disease1.4% (n=5). Nine of HCAI-Peritonitis cases (n=10) were the patients who were applied continuous ambulatory peritoneal dialysis (CAPD) because of CKD. Existence of CAPD in Peritonitis cases was found to be statistically significant ($p<0.05$).

The HCAI diagnosis was established by clinical features in 107 (34.4%) patients whose cultures were negative or not available. Various organisms were isolated in 246 (69.6%) of the cultures in the 353 HCAIs episodes. Gram-negative organisms were more frequently isolated (58.9%) than Gram positive- organisms (41.0%). The most frequently isolated organisms were *Klebsiella* spp. 99 (40.2%), *Salmonella* spp. 58 (23.5%), *E. coli* 29 (11.7%), coagulase-negative *staphylococcus* (CoNS) 14 (5.6%), *Pseudomonas aeruginosa* 10 (4 %), *Candida* 8 (4.0%), *Enterococcus* spp. 7 (2.8%), *Enterobacter* spp. 7 (2.8%) and Grub B *Streptococcus* 6 (2.4%).

When the distribution of detected organisms and infection site was examined, in HCAI-sepsis and UTI cases, the most frequently detected agent was *K. pneumonia*. In HCAI-UTI cases, *E. coli* was the second most frequently detected agent. In all of the culture-positive HCAI-GE cases, *Salmonella* spp was detected as the agent (**Table 3**).

In vitro antibiotics susceptibility of the isolated microorganisms were as follows: *Klebsiella* spp; amikasin 45%, sulperazon 59%, *Escherichia* spp; sulperazone 45%, seftriakson 60%, *Salmonella* spp.; amikasin and netilmisin 45%, *P. aeruginosa*; sulperazone 56%, netilmicin sulfate 49%, *S. aureus*; vancomycin 80%, CoNS; ceftazidime 55%. Grub B *Streptococcus* was found susceptible to Amoxycillin- Clavulanic Acid with the ratio of 80%. In all agents, imipenem susceptibility was 100%.

Thirty-eight of the 311 patients (12.2%) died. 32 of them were HCAI-sepsis and 6 of them were HCAI-pneumonia. 14 of the patients who died of sepsis were the premature newborns who had been hospitalized in neonatal intensive care unit (NICU). In NICU, premature newborn mortality was 28.5% (14/49) and term neonatal was 12.1% (5/41).

During the period that this research was conducted, in the services, there was 1 washbasin in every room and no isolation room in any of the services. During daytime working hours there was 1 nurse per 6-7 patients and 1 nurse per 15-20 patients during nighttime working hours.

DISCUSSION

Healthcare-associated infections (HCAIs), or nosocomial infections, are a significant cause of morbidity and mortality. HCAI surveillance is important for effective infection control.[12,13] The frequency of HCAIs varies according to the type of hospital. The rates have been determined as 4.4% in primary care hospitals; 7.1% in tertiary care hospitals and 19.2% in intensive care units.[14] In our study, the HCAIs rate was found to be 9.1%. During the period of our study, in the studies of Campins et al.[15] from Spain, and Starling et al.[16] from Brasil, the frequency of nosocomial infection was reported as 9.7% and 10.2%, respectively. In 2009, Özçetin et al.[9] reported the frequency of HCAIs as 5,3% in the pediatric service of the university hospital (excluding the neonatal service) covering a one year period. In the study of Maraş et al.[17] published in 2015, the frequency of nosocomial infection was reported as 9.3%. Although studies have been conducted in different countries and in different years, the HCAI rate in pediatric services is similar.

Table 3. The distribution of the detected organisms according to the infection site

HCAI-microorganisms	The HCAI-Site								
	GE (n=89)	Sepsis (n=79)	Pneumonia (n=39)	UTI (n=73)	Peritonitis (n=10)	Omphalitis (n=9)	Skin infection (n=7)	Conjunctivitis (n=5)	Total
Klebsiella spp.		43		41	4	9		2	99
E. coli		1		28					29
Salmonella spp.	58								58
CoNS		4	1		4	3		2	14
S. aureus		2	2		2		2		8
Pseudomonas spp.		4		1			3	2	10
Candida				3					8
Enterococcus spp.		3		4					7
Enterobacter spp.		2		5					7
Group B *streptococcus*		2		4					6

GE: Gastroenteritis, UTI: Urinary tract infection, CoNS: Coagulase negative *staphylococcus*

The frequency of the HCAIs in children is inversely correlated with age.[18] It was found in our study that approximately ⅔ of the HCAI cases were under twelve months. HCAI incidence in the pediatric intensive care unit (PICU) was high: long-term monitoring, invasive interventions, total parenteral nutrition, and the use of high-spectrum antibiotics are factors that increase the risk of infection among patients who are treated and monitored in pediatric clinics, especially in PICUs.[20] In our study, 28.9% of all HCAIs were detected in the neonatal intensive care unit. In parallel with the findings of earlier studies, the frequency of nosocomial infections was highest in our study among PICU patients.[21]

In our study, the most frequently observed HCAIs were bloodstream infections, urinary tract infections and pneumonia when *Salmonella* gastroenteritis in May and June is excluded.

HCAI microorganisms differ between the hospitals and in different units within the same hospital.[4,22] In our study, gram negative bacilli such as *Klebsiella* spp., *Salmonella* spp. and *E. coli* were detected as responsible in more than half of the HCAI cases. The results of our study are similar to those of studies conducted in following years in Turkey.[3,9,23,24] In our study, common HCAIs-microorganisms were detected to have low susceptibility to aminoglycoside and third-generation cephalosporins. This situation was thought to be related to the frequent preference of these antibiotics in empirical treatment or to Extended-Spectrum Beta-Lactamases (ESLB) Producing *Escherichia coli* and *Klebsiella* spp. All of the microbiological agents were detected as highly susceptible to imipenem (100%). Since carbapenems (imipenem) were not widely used during the years of our study, it was thought that they were highly susceptible especially against ESLBs.

In our study, 12.2% of HCAIs cases (n=311) died. All of these cases had risk factors that facilitated the development of infection (Age, male gender, congenital heart disease, Chronic Kidney Disease, malnutrition, prematurity). Kepenekli et al.[24] found that HCAIs cause considerable morbidity and mortality in pediatric intensive care units (PIUCs). The research indicates that the mortality rate of HCAIs in PICUs is 13%. Similar findings about mortality and morbidity were noted in our study.

The number of patients per nurse and nurse care are important in preventing HCAIs.[25] Özçetin et al.[9] reported in their study that as the number of patients per nurse increased, the frequency of HCAI increased. In our hospital during daytime working hours there was 1 nurse per 6-7 patients and 1 nurse per 15-20 patients during nighttime working hours. The relationship between the number of patients per nurse and the state of HCAI development has not been evaluated.

It is not easy to determine the additional costs that HCAIs bring to hospitals. Annually, approximately 2 million patients suffer with healthcare-associated infections (HCAIs) in the USA, and nearly 90,000 are estimated to die. The overall direct cost of HCAIs to hospitals ranges from US $28 billion to 45 billion.[26] In our country, the studies conducted by Yalçın et al.[27] had reported that the duration of hospital stay due to nosocomial infection increased by 20 days per patient and the cost per patient increased by 1582 dollars. Carbapenem antibiotics (imipenem) were generally used in our study due to low susceptibility to other antibiotics. In the one year period, the additional cost of the antibiotics alone was calculated as about 75000 USD.

CONCLUSION

Healthcare-acquired infections (HCAIs) are significant causes of mortality and morbidity, and may lead to prolonged hospitalization as well as increased costs throughout the world. The surveillance of HCAIs may help in decreasing the incidence of infections and reducing costs.

ETHICAL DECLARATIONS

Ethics Committee Approval: University of Health Sciences, Dr Sami Ulus Maternity and Children's Education and Research Hospital Evaluation Committee approval was obtained for this study (approval number: 73799008/ 17-01-2020)

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

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Orjinal Araştırma / Original Article

The Relationship Between C-Reactive Protein/Albumin Ratio and Radiological Findings in Patients with COVID-19

COVID-19 Hastalarında C-Reaktif Protein/Albümin Oranı ile Radyolojik Bulgular Arasındaki İlişki

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Abstract

Aim: Our aim in this study is to determine the C-reactive protein/Albumin ratio (CAR) values of computed tomography (CT) -positive COVID-19 patients and CT-negative COVID-19 patients and to investigate the relationship between C-reactive protein/Albumin ratio and radiological images of patients.

Material and Method: A-hundred COVID-19 patients over the age of 18 were included in our study. C-reactive protein (CRP), albumin levels and lung CT scan were collected. We divided the patients into two sections: CT-positive and CT-negative. We investigated the relationship between CT and CAR in patients, with and without comorbidity.

Results: The measured CRP levels and CAR in the CT-positive group were significantly higher than CT-negative group (37.76±64, 9.05±22, p=0.001, 11.8±23.2, 2.12±5.42, p=0.0 01). The measured albumin levels of CT-positive group were significantly lower than the CT-negative group (4.12±0.63, 4.53±0.36, p=0.001). When we evaluate the patients by excluding those with comorbidity; CRP levels and CAR measured in the CT-positive group were significantly higher than in the CT-negative group. (15.94±19.2, 6.07±7.38, p=0.013, 4.57±6.82, 1.38±1.75, p=0.016). Although the albumin values of CT-positive patients were lower than those of CT-negative patients, no statistically significance was found.

Conclusion: In general, we found that CAR levels in CT-positive patients were significantly higher than in CT-negative patients. In cases where CT is contraindicated (such as pregnancy), CAR can be used to indicate lung involvement or to follow-up patients with pulmonary involvement.

Keywords: COVID-19, C-reactive protein/albumin ratio, radiological finding

Öz

Amaç: Bu çalışmada amacımız, bilgisayarlı tomografi (BT) -pozitif COVID-19 hastalarının ve BT-negatif COVID-19 hastalarının C-reaktif protein/Albümin oranı (CAO) değerlerini tespit etmek ve COVID-19 hastalarının C-reaktif protein/Albümin oranı ile radyolojik görüntüleri arasındaki ilişkiyi araştırmaktır.

Gereç ve Yöntem: Çalışmamıza 18 yaş üstü yüz COVID-19'lu hasta dahil edildi. C-reaktif protein (CRP), albümin seviyeleri ve akciğer BT taraması toplandı. Hastaları iki bölüme ayırdık: BT-pozitif ve BT-negatif. Komorbidite dışlanmadan ve dışlanarak CAO ve BT taraması arasındaki ilişkiyi araştırdık.

Bulgular: BT pozitif grupta ölçülen CRP seviyeleri ve CAO değerleri, BT negatif gruba göre anlamlı olarak yüksekti (37,76±64, 9,05±22, p=0,001, 11,8±23,2, 2,12±5,42, p=0,001). Ölçülen albümin seviyeleri BT-pozitif grupta, BT negatif gruba göre anlamlı derecede düşüktü (4,12±0,63, 4,53±0,36, p=0,001). Komorbiditesi olanları dışlayarak hastaları değerlendirdiğimizde; BT-pozitif grupta ölçülen CRP seviyeleri ve CAO, BT-negatif gruba göre anlamlı olarak yüksekti (15,94±19,2, 6,07±7,38, p=0,013, 4,57±6,82, 1,38±1,75, p=0,016). BT-pozitif hastaların albümin değerleri BT-negatif hastalarınkinden daha düşük olmasına rağmen, istatistiksel olarak anlamlı fark bulunmamıştır.

Sonuç: Genel olarak CAO düzeylerini BT-pozitif hastalarda, BT-negatif hastalara göre anlamlı olarak yüksek bulduk. Ancak komorbiditeyi dışladığımızda C-reaktif protein/albümin oranının azaldığını da göz önünde bulundurmak gerekir. BT'nin kontrendike olduğu durumlarda (gebelik gibi) olası akciğer tutulumunu işaret etmede veya akciğer tutulumu olan hastaların takiplerinde CAO kullanılabilir.

Anahtar Kelimeler: COVID-19, C-reaktif protein/albümin oranı, radyolojik bulgu

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INTRODUCTION

COVID-19 pandemic has affected the entire world in a short time. The presence of COVID-19 can present with a variety of clinical symptoms ranging from asymptomatic/mild symptoms to severe illness and death. Clinical diagnosis of COVID-19 is based on clinical signs, molecular diagnosis of the viral genome by RT-PCR, lung x-ray or CT scanning, and blood tests.[1,2] The most important involvement place of COVID-19 is the lung.[3] Therefore, it is very important to show lung involvement radiologically. Although the gold standard in the disease's diagnosis is the RT-PCR test, radiological imaging has been used intensively because of the inadequacy of the test in some places and the fact that it may show false negativity in the early period.[4,5] It should be kept in mind that radiological methods are not screening tests in the diagnosis of COVID-19, but should be used as a method to help diagnose and monitor the disease. In imaging, chest radiography, thoracic CT and thoracic ultrasonography in some limited centers are used for this purpose. Chest radiography is the first choice imaging method for demonstrating COVID-19 pneumonia. Since patients are exposed to lower doses than CT, they should be preferred, especially in young and pediatric age groups. However, it should be kept in mind that the limited ground-glass involvement in the lungs, especially in the early phase of the disease, cannot be seen on radiography. It reported the sensitivity of chest radiography in demonstrating disease involvement to be between 30-6%.[6] In studies, the sensitivity of the RT-PCR test in the early period of the disease was found to be 71%, and thoracic CT was 98%.[4,5] However, it should be kept in mind that thoracic CT may be normal in the early period of the disease. It recommended thorax CT to be used primarily in patients with symptomatic and suspicious chest radiography and in cases with suspected complications. However, what should not be forgotten is that it should evaluate the CT result in the light of clinical findings.

CRP is an acute phase protein released from hepatocytes after stimulation by various cytokines in response to infection, ischemia, trauma, and other inflammatory conditions.[7] CRP levels are correlated with the level of inflammation, and its concentration level is not affected by factors such as age, sex, and physical condition.[8] It is an important index for the diagnosis and assessment of severe pulmonary infectious diseases.[9] High CRP levels have been found in critically ill patients in relation to prognosis and mortality.[10,11] Albumin is the main protein in the blood and a negative acute phase reactant produced in the liver.[12] COVID-19 have distinct hypoalbuminemia, which is likely due to hepatotoxicity of cytokine storm.[13] It is known that low serum albumin is associated with poor prognosis and mortality.[13-15]

The CRP/Albumin ratio, which is the result of the ratio of these two parameters to each other, is the parameter that has just started to be used. The CRP/ALB ratio was first reported to identify patients with serious illness on an acute medical ward.[16] The CRP/Albumin ratio is believed to be a more reliable predictor of inflammatory status than CRP or albumin alone.[17] In this study, we examined the CRP/Albumin ratios of CT-positive COVID-19 patients and CT-negative COVID-19 patients with and without comorbidity.

MATERIAL AND METHOD

We performed this study with respect to the recommendations put forward via the Declaration of Helsinki. Harran University Ethics Committees approved the study protocol (Reference No HRU/20.20.26). We carried it out in Şanlıurfa Research and Training Hospital. We performed a retrospective study. One hundred COVID-19 patients regardless of additional diseases over the age of 18 who applied to hospital were included in our study. These data include the laboratory and radiological findings of patients at the time of first admission to the hospital. CRP, albumin levels, other data and lung CT scan were collected in this study. We divided the patients into two sections: CT-positive group and CT-negative group. We investigated the relationship between CT and CAR in patients with COVID-19 patient, first without comorbidity and then with comorbidity (such as diabetes, hypertension, COPD, asthma, heart failure, and cancer).

Statistical analysis

We completed statistical analysis using IBM SPSS 25.0 (SPSS for Windows, SPSS Inc., Chicago, IL, USA). Kolmogorov–Smirnov test was used for normality testing of CRP, albümin and CRP/Albumin ratios. The groups were not displayed normal distribution. Mann-Whitney U Test, among nonparametric tests, was used to investigate whether there were considerable differences between the groups. $P<0.05$ was accepted as statistically significant.

RESULTS

Out of A-hundred patients with positive RT-PCR test, thirty-nine patients were CT-negative and sixty-one patients were CT-positive. The gender distribution and average age of the CT-negative group and the CT-positive group included in our study are shown in **Table 1**. Thirty-two patients had additional diseases that would alter the level of parameters such as diabetes, hypertension, COPD, asthma, heart failure, and cancer. When we without comorbidity, thirty-five of sixty-eight patients with COVID-19 were CT-positive and thirty-three of them were CT-negative.

Table 1. Gender and average age of the patients

Groups	Gender (Male/Female)	Age (years)
CT Negatif	19/20	38.90±14.09
CT Pozitive	28/33	41.70±15.76

The CRP, albumin levels and CAR measured in the CT-positive patient group and the CT negative patient group included in our study are shown in **Table 2**. Our results without excluding comorbidity: The measured CRP levels in the CT-positive patient group were significantly higher than CT-negative patient group (37.76±64, 9.05±22, p=0.001). The measured albumin levels CT-positive patient group were significantly lower than CT-negative patient group (4.12±0.63, 4.53±0.36, p=0.001). The measured CAR in the CT-positive patient group were significantly higher than CT-negative patient group (11.8±23.2, 2.12±5.42, p=0.001). CT scans of patients with COVID-19 with high CAR levels showed common lung involvement. We show the CT scans of some of our patients with high CAR in **Figure 1**.

Table 2. Statistical comparison of C Reactive Protein (CRP), Albumin and CRP/Albumin levels of patients with CT positive and CT negative COVİD-19

Groups	CRP (mg/L)	P value	Albumin (g/dL)	P value	CRP/Albumin Ratio	P value
CT Negatif (39)	9.05±22	0.001	4.53±0.36	0.001	2.12±5.42	0.001
CT Pozitive (61)	37.76±64		4.12±0.63		11.8±23.2	

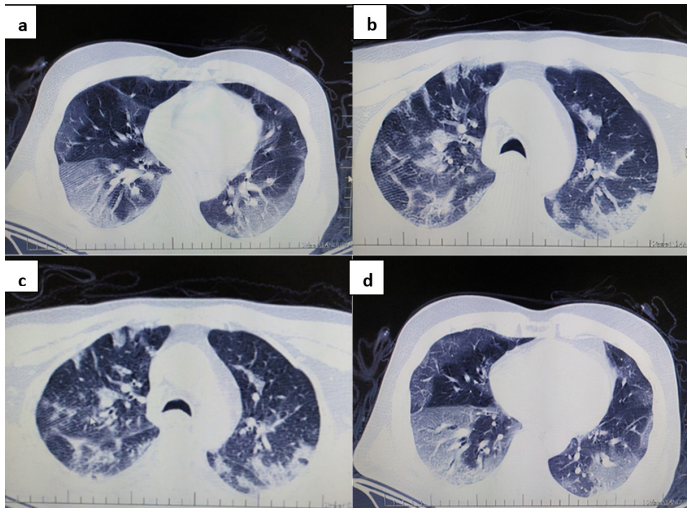

Figure 1. CT positive scans of COVİD-19 positive patients (C-reactive protein/Albumin ratio levels respectively a: 24,56, b: 26,00, c: 18,98, d: 16,96. a: A 44-year-old patient who presented with the complaints of cough, shortness of breath and weakness had peripherally located ground glass areas in both lung lobes. b: A 58-year-old patient who presented with the complaints of shortness of breath, fever and cough had ground glass densities scattered in both lungs upper lobes. c: A 39-year-old patient who presented with the complaints of cough, shortness of breath, and loss of taste and smell had ground glass densities scattered in the upper and lower lobes of both lungs. d: A 50-year-old patient who presented with the complaints of shortness of breath, weakness and malaise had diffuse ground glass densities in both lungs).

The results we got by excluding the comorbidities are shown in **Table 3**. When we evaluate patients without comorbidity the measured CRP levels and CAR in the CT-positive group were significantly higher than CT-negative group (15.94±19.2, 6.07±7.38, p=0.013, 4.57±6.82, 1.38±1.75, p=0.016). Although the albumin values of CT-positive patients were lower than those of CT-negative patients (4.25±0.58, 4.55±0.35, p:0.057), we found no statistically significant significance.

Table 3. Statistical comparison of C Reactive Protein (CRP), Albumin and CRP/Albumin levels of patients without comorbidities with CT positive and CT negative COVİD-19

Groups	CRP (mg/L)	P value	Albumin (g/dL)	P value	CRP/Albumin Ratio	P value
CT Negatif (33)	6.07±7.38	0.013	4.55±0.35	0.057	1.38±1.75	0.016
CT Pozitive (35)	15.94±19.2		4.25±0.58		4.57±6.82	

DISCUSSION

COVID-19 infection is a global pandemic, which has caused many deaths worldwide. Inflammation is the cellular immune response that occurs to remove damaged tissues caused by bacterial or viral infections and the causative agent from the environment. Some viruses infect lymphocytes and increase their destruction, causing lymphopenia and a decrease in serum albumin, which is a negative acute phase reactant, while increasing the levels of CRP and ferritin, which are positive acute-phase reactants.[18,19] CRP is a type of protein produced by the liver that rises in response to inflammation. CRP levels have been associated with a variety of conditions, including severe sepsis, heart failure, and other inflammatory disease.[10] In a study by Wang et al.[20] many COVID-19 patients showed high CRP levels, which is consistent with other studies. The aggravated cases in this study showed significantly higher CRP levels than non-serious patients. This result suggested that CRP may be a serum marker of disease severity in 22 patients with COVID-19. Liu et al.'s[21] study suggested that serum levels of IL-6 and CRP have a significant correlation with the severity of COVID-19 and that these parameters can independent factors to predict disease risk. Several studies have reported data on Hypoalbuminemia in COVID-19 patients.[22-24] Low serum albumin reflects poor nutritional status, liver and kidney dysfunction, and has been an independent predictor of poor survival in critically ill patients.[25]

In previous studies, the effectiveness of CAR as a prognosis and mortality marker, especially in malignant diseases, has been studied.[10,15,17] CAR is an effective parameter not only as a mortality marker but also in the selection of patients to be treated aggressively. In previous studies conducted with inflammatory bowel diseases, they have shown that CAR is a useful marker for determining disease activity and who should be given early steroid treatment.[7,20] The CAR a prognostic score to evaluate outcomes in patients with cancer, inflammation, and sepsis.[26] Kim et al.[27] reported that the CAR at admission positively correlated with prognosis in patients with severe sepsis or septic shock treated with early targeted therapy. In a study, they have shown CAR as a predictor of mortality in patients with acute pancreatitis. It has been emphasized that CAR is a comprehensive and effective form of CRP and albumin rather than a simple ratio of CRP to albumin.[28]

CONCLUSION

In our study, we found that CRP levels and CAR values were significantly higher in CT-positive patients compared to CT-negative patients, and albumin levels were significantly lower in CT-positive patients. Although CRP levels and CAR values decreased numerically when we excluded patients with comorbidity, it was statistically significant. In conclusion, where CT is contraindicated (such as pregnancy), CAR can be used to indicate lung involvement or to follow-up patients with pulmonary involvement. We have not found any publications in the literature comparing the ratio of lung CT and CAR in COVID-19 patients (with or without comorbidity). Therefore, it should be supported by similar studies to strengthen this view.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study was approved by the Harran University Ethics Committees. Sanliurfa Research and Training Hospital (Reference No. HRU/20.20.26).

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

Referee Evaluation Process: Externally peer-reviewed.

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Evaluation of the Knowledge and Attitudes of Patients Admitted to COVID-19 Outpatient Clinic about Traditional and Complementary Medicine

COVID-19 Polikliniğine Başvuran Hastaların Geleneksel ve Tamamlayıcı Tıp Uygulamaları Hakkında Bilgi ve Tutumlarının Değerlendirilmesi

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Abstract

Objective: During the coronavirus-19 (COVID-19) pandemic, an effective treatment method for the treatment and prevention of the disease has not been determined yet. Promising results have been achieved in the treatment of COVID-19 with a holistic approach in addition to conventional medical methods in traditional and complementary medicine practices (TCM), which are increasing in popularity today. This study was aimed to evaluate the view, attitude and behavior of the participants who applied with the suspicion of COVID-19 in the treatment and protection of COVID-19.

Material and Method: A 12-question questionnaire was applied to the volunteers among the patients who applied to the outpatient clinic with the suspicion of COVID-19. Participants were asked multiple choice questions questioning their beliefs and previous experiences in TCM and their views, beliefs and behaviors in the treatment and prevention of COVID-19.

Results: 145 (77,5%) of the participants say that they have knowledge about TCM and 71,7% of them believe in TCM applications. In addition, 33.2% of the participants have applied to TCM applications before. During the pandemic period, phytotherapy (22,46%) was the second cupping treatment (12,83%), which was the most beneficial application. Although 27,7% of the participants thought that TCM would not be more beneficial than conventional COVID-19 drugs, 19,79% believed that it would be beneficial with routine medications.

Conclusion: In Turkey increased knowledge and beliefs about TCM applications in all walks though the COVID-19 in the treatment and prevention holistic approach to conventional medicine has still not accepted enough belief in society.

Keywords: Coronavirus, traditional medicine, holistic approach, pandemic

Öz

Amaç: Koronavirüs-19 (COVID-19) pandemisi sürecinde hastalığın tedavisinde ve korunmada halen etkin bir tedavi metodu belirlenememiştir. Günümüzde popülaritesi giderek artan geleneksel ve tamamlayıcı tıp uygulamalarında (GETAT) klasik tıbbi yöntemlere ilaveten bütüncül yaklaşımla COVID-19 tedavisinde umut verici sonuçlar elde edilmiştir. Kesitsel tipteki bu çalışmada COVID-19 şüphesi ile başvuran katılımcıların COVID-19 tedavi ve korunmasında GETAT'a bakışı, tutum ve davranışlarının değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntem: COVID-19 şüphesi ile polikliniğe başvuran hastalardan gönüllü olanlara 12 soruluk anket yapılmıştır. Katılımcılara GETAT'a inanışları ve daha önceki deneyimleri ile COVID-19 tedavi ve korunmasında GETAT'a bakışları, inanışları ve davranışlarını sorgulayan çoktan seçmeli sorular yöneltilmiştir.

Bulgular: Katılımcıların 145 (%77,5)'i GETAT hakkında bilgisini olduğunu ve %71,7'si de GETAT uygulamalarına inandığını söylemektedir. Ayrıca katılımcıların %33,2'si ise daha önce GETAT uygulamalarına başvurmuştur. Pandemi döneminde en sık faydalı olduğu düşünülen uygulama fitoterapi (%22,46), ikinci kupa tedavisi (%12,83) olmuştur. Katılımcıların %27,7'si GETAT'ın klasik COVID-19 ilaçlarından daha faydalı olmayacağını düşünmesine rağmen %19,79 katılımcı ise rutin ilaçlarla birlikte faydalı olacağına inanıyordu.

Sonuç: Türkiye'de her kesimde GETAT uygulamaları hakkında bilgi ve inanış artmış olsa da COVID-19 tedavisi ve korunmasında klasik tıbba bütüncül yaklaşımlarına olan inanış halen toplumda yeterli kabul görmemiştir.

Anahtar Kelimeler: Koronavirüs, geleneksel tıp, bütüncül yaklaşım, pandemi

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INTRODUCTION

The new type of coronavirus (COVID-19) outbreak, which has spread rapidly since December 2019 and has become a pandemic, remains the leading medical health problem for the world. Despite all efforts, there is still no effective treatment method. Therefore, treatments often focus on the treatment of symptoms and prevention of transmission of the disease. These uncertainties in its treatment have played a role in the orientation of some patients towards traditional and alternative therapies, especially medicinal plants. As a matter of fact, numerous studies have been published examining the effects of phytotherapy and ozone therapy on COVID-19. [1-3] In fact, positive effects of acupuncture, phytotherapy (zinc, garlic, green tea, etc.) and systemic ozone treatment on COVID-19 complications and the course of the disease have been reported.[4-9] It is not yet clear what the trend is like in the COVID-19 pandemic and the patients' view of these practices in the treatment of COVID-19 is not yet clear, especially in eastern countries where belief in traditional medicine is widespread.

To evaluate the views, experiences and attitudes of patients who apply to traditional and complementary medicine practices (TCM) frequently referred to in the COVID-19 pandemic with suspicion of COVID-19 and their attitudes and opinions about its effectiveness in the treatment of COVID-19.

MATERIAL AND METHOD

Universe and sampling

The study is of a cross-sectional type and people over the age of 18 constitute the universe of the study. Within the scope of pre-study research on COVID-19, scientific research permission was obtained from the Ministry of Health and ethical approval numbered 2021/005 from KTO Karatay University.

Participant Selection

This study was performed in accordance with the declaration of Helsinki protocol. Patients who applied to XXX Hospital COVID-19 outpatient clinics with suspicion of COVID-19 between November 2020 and January 2021 were asked to participate in the survey during the COVID-19 diagnostic tests and the volunteers were surveyed. A total of 214 participants were included in the study. 27 (12.6%) of them who were incomplete or not consistently filled out in the questionnaire form were excluded in the study. The study was conducted with the data of 187 participants. Participants were randomly selected from all applicants on a voluntary basis regardless of age, gender and sociodemographic characteristics. All participants received voluntary questionnaires and informed consent forms for data protection.

Survey Form

In addition to sociodemographic factors in the study, a total of 12 questionnaires were applied that evaluated the participants' knowledge about TCM practices, awareness and TCM practices during the pandemic period (**Form 1**). Eight of the questions are multiple choice, three can be selected multiple options, and one is open-ended. The educational status of the participants was categorized in 5 different groups. The form, which was created to evaluate the sociodemographic characteristics of the participants, includes age, gender, educational status, working status. Occupations are collected in 6 main categories according to socioeconomic status. Participants were asked to choose information, attitudes, behaviors and attitudes and beliefs about TCM practices during the pandemic period in a multiple choice: 1- yes, 2- partly, 3-undecided, 4-no. In addition, TCM practices, which are frequently used to describe which TCM practices they applied to before and after the pandemic, are given to allow them to select multiple options. The study was conducted in the 1st year of the COVID-19 pandemic and at a time when the positive effects of systemic ozone, acupuncture and mug treatment practices on COVID-19 were socially known.

Statistical Analysis

As a descriptive statistic; number, percentages, median, minimum, and maximum value; Chi-Square in single analyses, multiple logistic regression analysis was used in multiple analyses. SPSS 22.0 package program was used to evaluate the data.

TRADITIONAL AND COMPLEMENTARY MEDICINE (TCOM) IN THE TREATMENT OF COVID-19

1. Age | **2. Sex**: ☐ Male ☐ Female

3. Education Status

☐ Illiterate ☐ Primary school ☐ Middle School ☐ High school ☐ University and above

4.Your Job?

☐ Unemployed ☐ Retired ☐ Housewife ☐ Civil Servant ☐ Academician ☐ Self-employed ☐ Worker

5. Which of the Traditional and Complementary Medicine (TCOM) practices do you know about? (You can check multiple options)

☐ None ☐ Cupping ☐ Acupuncture ☐ Mesotherapy ☐ Ozone Therapy ☐ Phytotherapy

6. Do you believe that traditional and complementary Medicine (TCOM) practices are beneficial for your health?

☐ Yes ☐ No ☐ Partially ☐ Undecided

7. Have you done any of the following Traditional Medicine practices before? (You can check multiple options)

☐ None ☐ Cupping ☐ Acupuncture ☐ Mesotherapy ☐ Ozone Therapy ☐ Phytotherapy

8. Have you experienced the benefits of Traditional and Complementary Medicine (TCOM) applications for your health before?

☐ Yes ☐ No ☐ Partially ☐ Undecided

9. Do you believe that Traditional and Complementary Medicine (TCOM) practices are beneficial for preventing or healing coronavirus (COVID-19) disease?

☐ Yes ☐ No ☐ Partially ☐ Undecided

10. Which of the TCOM applications do you plan to apply to prevent or recover from coronavirus (COVID-19) disease? (You can check multiple options)

☐ None ☐ Cupping ☐ Acupuncture ☐ Mesotherapy ☐ Ozone Therapy ☐ Phytotherapy

11 Do you believe that Traditional and Complementary Medicine (TCOM) applications are more beneficial than drugs used for the disease in the treatment of coronavirus (COVID-19) disease?

☐ Yes ☐ No ☐ Partially ☐ Undecided

12. Do you believe that Traditional and Complementary Medicine (TCOM) applications together with medicines in the treatment of coronavirus (COVID-19) will cure the disease better?

☐ Yes ☐ No ☐ Partially ☐ Undecided

Form 1. Survey Form

RESULTS

Sociodemographic data of the participants are given in **Table 1**. 63.6% of the participants are male and the average age is 36. When evaluated according to educational status, it was found that only 2 (1.07%) participants were literate, with the majority (33.16%) studying in high school and above. According to the professions, 41.71% of the participants are in the working group and the civil servants (19.79%) come in second place.

The majority of those who were familiar with TCM applications were women (86.7%, p=0.02%). 145 (77.5%) participants said they had information about TCM practices; participants with knowledge stated that they had the most knowledge about trophy treatment (35.3%). In addition, 17.7% of respondents reported having information about more than one application.

Table 1. Sociodemographic characteristics of participants

		n	%
Gender	Female	68	36.36
	Male	119	63.64
Education Status	Literate	2	1.07
	Primary school	30	16.04
	Secondary school	34	18.18
	High School	62	33.16
	University and above	59	31.55
Profession	Unemployed	16	8.56
	Retired	4	2.14
	Housewife	30	16.04
	Officer	37	19.79
	Academics	5	2.67
	Self-employed	17	9.09
	Workers	78	41.71
		Mean± SD	**Min-max**
Age		36.00± 10.07	18-64

The mean age of patients with no knowledge of TCM practices was 36.53± 10.09, while the average age of those with knowledge of any of them was 36.29±9.55 and was statistically similar (p=0.882). Participants had similar knowledge levels about TCM practices based on their educational status and occupation (p=0.730, p=0.140, respectively).

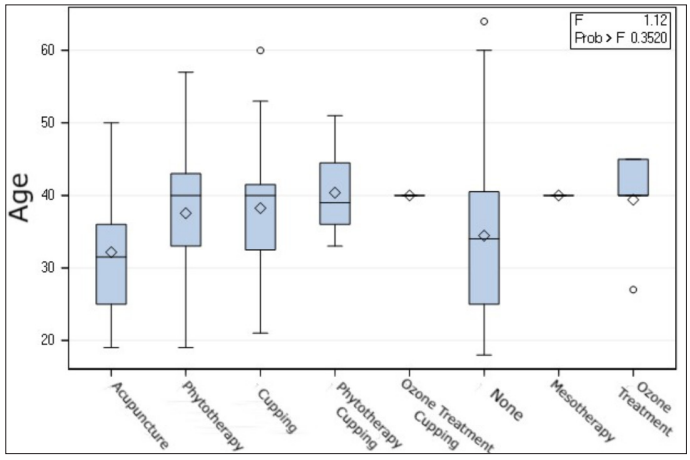
71.7% of respondents said they believed TCM, but 6.4% said they did not. Participant's gender, educational status and occupation and their belief in TCM practices were similar (p=0.155, p=0.451, p=0.938, respectively). In addition, 57.2% of patients with knowledge about TCM practices believe in TCM.

31.01% of respondents to any TCM practices; 2.13% have applied to more than one TCM practice. Most respondents (66.8%) had never applied to any TCM practices before. Participants' gender, educational status and occupation and their application rates for TCM practices were similar (p=0.638, p=0.161, p=0.535, respectively).

Although the number of participants who previously benefited from TCM practices, did not see and were undecided was equal 27 (27.9%), 30 (16.1%) benefited in part from participating applications (**Table 2**). TCM practices was cup treatment where participants had the most knowledge (35.3%) and applied most frequently (17.1%). In addition, 33 (16.7%) of the participants were familiar with two or more applications. More than half (50.27%) of respondents believed TCM practices were beneficial. There was no difference between the gender, educational status and occupation of the participants and their previous benefits from TCM practices (p=0.963, p=0.223, p=0.535, respectively). Applications for TCM practices were found to be partially older (**Figure 1**).

Table 2. Evaluation of participants' knowledge and attitudes about TCM practices before the COVID-19 pandemic

		Participant n (%)	Male n (%)	Female n (%)	p
Which of the TCM practices do you know about?	None	42 (22.5)	33 (27.7)	9 (13.2)	
	Cupping	66 (35.3)	40 (33.6)	26 (38.2)	
	Acupuncture	12 (6.4)	6 (5.0)	6 (8.8)	
	Mesotherapy	3 (1.6)	1 (0.8)	2 (2.9)	
	Ozone Treatment	3 (1.6)	3 (2.5)	0 (0)	
	Phytotherapy	28 (15.0)	14 (11.8)	14 (20.6)	
	Cupping-Ozone Treatment	2 (1.1)	2 (1.7)	0 (0)	
	Cupping-Acupuncture	9 (4.8)	5 (4.2)	4 (5.9)	
	Cupping- Phytotherapy	2 (1.1)	1 (0.8)	1 (1.5)	
	Cupping-Ozone - Phytotherapy	2 (1.1)	0 (0)	2 (2.9)	
	Cupping-Acupuncture-Ozone	1 (0.5)	1 (0.8)	0 (0)	
	Cupping-Acupuncture-Phytotherapy	11 (5.9)	8 (6.7)	3 (4.4)	
	All	6 (3.2)	5 (4.7)	1 (1.5)	
Have you had any of the TCM practices done?	None	125 (66.8)	81 (68.1)	44 (64.7)	
	Cupping	32 (17.1)	20 (16.8)	12 (17.6)	
	Acupuncture	6 (3.2)	4 (3.4)	2 (2.9)	
	Mesotherapy	5 (2.7)	2 (1.7)	3 (4.4)	
	Ozone Treatment	4 (2.1)	3 (2.5)	1 (1.5)	
	Phytotherapy	11 (5.9)	7 (5.9)	4 (5.9)	
	Acupuncture-Phytotherapy	1 (0.5)	1 (0.8)	0 (0)	
	Cupping-Acupuncture-Phytotherapy	3 (1.6)	1 (0.8)	2 (2.9)	
Do you believe that TCM practices are beneficial for your health?	Yes	94 (50.27)	63 (52.9)	31 (45.6)	
	Partially	40 (21.39)	25 (21.0)	15 (22.1)	
	I'm undecided.	41 (21.93)	21 (17.6)	20 (29.4)	0.156
	No	12 (6.42)	10 (8.4)	2 (2.9)	
TCM practices has you benefited from its applications for your health?	Yes	52 (27.96)	32 (26.9)	20 (29.9)	
	Partially	30 (16.13)	20 (16.8)	10 (14.9)	
	I'm undecided.	52 (27.96)	33 (28.4)	19 (28.4)	0.964
	No	52 (27.96)	34 (65.4)	18 (26.9)	



Graphic 1. Early complication rate

Participants' views and attitudes on TCM practices in the COVID-19 outbreak are given in **Table 3**. Phytotherapy (22%, 46%) was the second cup treatment (12.83%). Female participants were more likely to believe that TCM practices were beneficial for COVID-19 prevention and treatment (p=0.04). At the same time, 27.7% of respondents thought TCM would be no more beneficial than conventional COVID-19 drugs, while 19.79% believed it would be beneficial with routine medications.

Table 3. Evaluation of participants' knowledge and attitudes about TCM practices during the COVID-19 pandemic

Survey Questions	Answers n (%)			
	Yes	Partially	Undecided	No
Do you believe that TCM practices are useful to protect against COVID-19 or to cure the disease?	53 (28.34)	47 (25.13)	61 (32.62)	26 (13.90)
Do you believe that TCM practices are more beneficial in the treatment of COVID-19 than the drugs used for the disease?	27 (14.44)	44 (23.53)	65 (34.76)	51 (27.27)
Do you believe that getting TCM practices together with drugs in the treatment of COVID-19 will better treat the disease?	37 (19.79)	61 (32.62)	57 (30.48)	32 (17.11)

DISCUSSION

With the onset of the coronavirus pandemic, intensive studies on COVID-19 treatment and prevention methods continue to be carried out all over the world. Although proven vaccines have been widely applied for prevention, the treatment options currently proven effective in the treatment of COVID-19 are unclear.[10,11] Therefore, there has been increased interest in both classical TCM practices in order to protect against COVID-19.[12-15]

In this study, we aimed to evaluate the knowledge, awareness, and attitudes of patients with suspected COVID-19 about TCM. It was generally previously thought that the perspective on TCM practices was lower and the belief was more less.[16] However, we found that most (77.5%) of respondents had knowledge of TCM practices and believed in TCM practices (71.7%). In addition, it was found that the level of knowledge about TCM practices was similar between education and sociocultural levels among the participants. For this reason, we see that TCM practices are now homogeneously distributed in society and that there is an increasing interest in TCM practices by the whole society regardless of profession and education.

During the pandemic period, the positive integrative effects of TCM practices, especially phytotherapy and ozone treatment, on classical medicine in the treatment of COVID-19 have been proven.[1,17] In our study, although phytotherapy was most used in the prevention and treatment of COVID-19, it was found that the participants did not show the appropriate rates of interest in the literature in ozone treatment. Interestingly, although there were no studies evaluating the effectiveness of cup therapy in the treatment and protection of COVID-19, it was determined that the participants applied increasing interest in cup treatment. We think that the reason for this situation is that cup treatment is the most common TCM practices and because the positive effects of cup treatment on the immune system are known to society, it is a frequently used method.

A few studies was reported that acupuncture treatment has anti-inflammation, immunity activation and nervous system modulation were primary therapeutic pathways of acupuncture against COVID-19.[18-20] In addition, it has been claimed that acupuncture treatment relieves symptoms associated with COVID-19 and has an effect on relieving symptoms associated with anxiety after COVID-19 treatment.[19,21] However, more studies are needed to prove the effects of acupuncture on COVID-19 treatment. Acupuncture therapy has not become widespread in society, despite its ever-increasing trend. In our study, 39 (20.8%) of the participants stated that they knowed to acupuncture and only 4.8% of them reported that they applied to it. Therefore, there is a need to raise awareness of the effectiveness of acupuncture in the treatment of COVID-19 in the society.

It was previously reported that women's attitudes to TCM practices were more positive.[22,23] In this study, it is seen that awareness of TCM practices in the treatment of COVID-19 and protections more positive in middle-aged women and supports the literature. Complementary medicine treatments are widely accepted in adults today. Especially in the last two decades, studies on TCM have gained momentum all over the world and their effective results have been accepted. Complementary medicine offered people opportunities for both regression of functional complaints and anti-aging effects. Functional complaints (sweating, palpitations, fatigue and anxiety, etc.) and aging anxiety are frequently observed in middle-aged women in the perimenopausal period. For this reason, we think that middle-aged women are more aware of TCM and they resort to those treatments more frequently.

More than half (53.47%) of respondents believe that TCM practices are partially or completely beneficial in COVID-19 recovery. However, most participants (27.27%) also confirmed that it was no more effective than conventional medical

treatments. Nevertheless, it is more accepted that it is useful for the purpose of complementary treatment of classical medicine (52.41%). Therefore, it shows that society applied TCM practices as holistic treatment during the pandemic period and believes that it would be more beneficial to treat COVID-19 with a holistic approach.

The fact that TCM practices are believed to be beneficial for health (50.27%) and that TCM practices are beneficial for the prevention of COVID-19 disease or for the recovery of the disease (28.24%) may be due to the fact that TCM practices are not yet widely used in the holistic treatment of COVID-19. Therefore, holistic treatment results are needed in the near future.

CONCLUSION

This study was conducted at a time when COVID-19 pandemic cases were intense in Turkey and revealed awareness, attitudes and behaviors about TCM practices of participants at risk of COVID-19, although they have limitations in terms of representation and generalization. Although TCM practices have become very common in our country, the importance of holistic approaches to protection from COVID-19 and the improvement of the disease has not yet reached sufficient prevalence in society.

ETHICAL DECLARATIONS

Ethics Committee Approval: Ethical approval numbered 2021/005 was obtained from KTO Karatay University.

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

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Orjinal Araştırma / Original Article

Do Obstetric Factors Have an Effect on Success of Medical Treatment of Anal Fissure Seen in Women?

Kadınlarda Görülen Anal Fissürün Medikal Tedavi Başarısında Obstetrik Faktörlerin Etkisi Var Mıdır?

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Abstract

Objective: The aim of this study is to examine the effect of obstetric factors on the medical treatment success of anal fissure in women.

Material and Method: A total of 324 women, who were diagnosed with anal fissure, who applied to the General Surgery outpatient clinic between 2015 and 2020, were included in the study. The patients were divided into two groups; group I (medical treatment was successful) and group II (medical treatment failed - surgery performed). Both groups were compared in terms of age, body mass index (BMI), number of births, delivery type, birth weight, breastfeeding rate, constipation, diarrhea, smoking and anal fissure symptoms.

Results: Medical treatment was applied to all of the 324 patients we included in our study, and it was observed that 45.7% of them had successful medical treatment and 54.3% had undergone surgical treatment (lateral internal sphincterotomy) because of unsuccessful medical treatment. It was found that age, BMI, number of births, number of vaginal births, breastfeeding rate, constipation rates were higher in those who failed medical treatment ($p<0.05$). The number of cesarean sections, birth weight, diarrhea and smoking were found to be similar between the two groups ($p>0.05$). While gas incontinence was observed in 44.1% of those who underwent surgical treatment, this rate was found to be 1.4% in those who benefited from medical treatment.

Conclusion: In our study, it was found that while maternal age, number of births, vaginal delivery and breastfeeding rates had a negative effect on the success of anal fissure medical treatment, cesarean delivery and baby birth weight were not effective.

Keywords: Anal fissure, pregnancy, delivery, obstetrics, medical therapy

Öz

Amaç: Bu çalışmanın amacı, kadınlarda görülen anal fissürün medikal tedavi başarısında obstetrik faktörlerin etkisinin incelenmesidir.

Gereç ve Yöntem: Çalışmaya2015-2020 yılları arasında Genel Cerrahi polilliniğine anal bölge rahatsızlığı nedeni ile başvurup anal fissür tanısı almış 324 kadın dahil edildi. Hastalar iki gruba ayırıldı; grup I (medikal tedavi başarılı) ve grup II (medikal tedavi başarısız - cerrahi yapılan). Her iki grup yaş, vücut kitle indeksi (VKİ), doğum sayısı, doğum şekli, bebek doğum ağırlığı, emzirme oranı, kabızlık, ishal, sigara içme ve anal fissür semptomları açısından karşılaştırıldı.

Bulgular: Çalışmamıza aldığımız 324 hastanın tümüne medikal tedavi uygulanmış olup bunlardan %45,7'sinde medikal tedavi başarılıyken, %54,3'ünde ise medikal tedavi başarısız olduğundan dolayı cerrahi tedavi (lateral internal sfinkterotomi) uygulandığı gözlendi. Medikal tedavi başarısız olanlarda yaş, VKİ, doğum sayısı, vajinal doğum sayısı, emzirme oranı, kabızlık oranlarının daha fazla olduğu tespit edildi ($p<0,05$). Sezaryen sayısı, bebek doğum ağırlığı, ishal ve sigara kullanımının iki grup arasında benzer olduğu bulundu ($p>0,05$). Cerrahi tedavi uygulananlarda %44,1 gaz inkontinansı görülürken medikal tedaviden yarar görenlerde bu oran %1,4 saptandı.

Sonuç: Çalışmamızda gebelik sürecinde oluşan anal fissür medikal tedavi başarısında obstetrik etkenlerden maternal yaş, doğum sayısı, vajinal doğum ve emzirmenin olumsuz yönde etki ettiği görülürken sezaryenle doğum ve bebek doğum kilosunun etkili olmadığı saptandı.

Anahtar Kelimeler: Anal fissür, gebelik, doğum, obstetrik, medikal tedavi

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INTRODUCTION

Anal fissure is one of the frequently recurring, quite disturbing anorectal diseases that are quite common in society. While it often leads to severe pain and itching, it may rarely bleed. The diagnosis is made by anamnesis and anal canal examination.[1] If the patient's complaints continue for more than 1-1.5 months, the disease is considered chronic.[2] Fissures are occurred at the same rate in both gender groups.[3] Most women complain of anal disorders during pregnancy and birth-process. While the most common disease among these lesions is haemorrhoids, the second disease is anal fissure.[4] The main cause of these lesions has been shown as injury to the anal mucosa due to constipation. In addition to the most common risk factor being constipation, it has been emphasized that the birth weight of the child, the time elapsed during the termination of pregnancy and perianal diseases are also important.[5,6]

Acute anal fissure patients recover at a rate of 40-80% with the treatment of mainly constipation-preventing diet with dense fiber, abundant oral fluid intake, sitz baths in the anal area and drugs containing calcium channel blockers, diltiazem, nifepidine or glyceryl trinitrate.[7,8] However, if the symptoms of the patients persist for more than six months, the medical recovery rate decreases to 8%.[7,9] Especially in women, the disease is diagnosed late because they tell their complaints of anal fissure late or do not tell their complaints at all because of the sociocultural and environmental effects, and this reduces the medical treatment success rate.[10] An incurable anal fissure can cause severe discomfort, especially during pregnancy and post-partum, causing severe pain that may disturb the pregnancy and the delivery process.[11]

This study aims to examine the effect of obstetric factors in the success of medical treatment of anal fissure seen in women.

MATERIAL AND METHOD

324 patients who presented to the General Surgery polyclinic and were diagnosed with anal fissure, dating between 2015 and 2020, were included in the study. The study was conducted in accordance with the Declaration of Helsinki, after the approval of the Niğde Ömer Halisdemir University Medical Faculty Non-interventional Ethic Committee dated 27/08/2020 and numbered 2020/41.

All female patients included in the study were examined by the same physician in the general surgery clinic. Physical examination of the patients was performed by paying attention to the presence of ulcers, skin tags and pseudo polyps in the anal region in the prone position. Rectal examination was not performed avoid pain. Anal fissure was diagnosed in patients who have at least one of the complaints of pain, bleeding, itching or swelling in the anal area and has a rupture in anal area on physical examination. Inclusion criteria in the study was determined as having a diagnosis of anal fissure with a pregnancy history between the ages of 18 and 60 and being or not being recovered after receiving a medical treatment and receiving surgical treatment (lateral internal sphincterotomy), exclusion criteria were determined as having a history of chronic gastrointestinal disease (ulcerative colitis, Crohn's, malignancy), anal canal surgery without anal fissure, and having a psychiatric disease.

Patients with anal fissure were divided into two groups as those who benefited from medical treatment (Group-I) and those who received surgical treatment (due to medical treatment failure) (group-II). The treatment was considered successful in patients who did not have any complaints due to anal fissures within at least six months after medical treatment. The information of all participants included in the study was recorded by asking their age, body mass index (BMI), number of births, mode of delivery, infant's weight, breastfeeding time, complaints when diagnosed (bleeding, pain, swelling, itching), constipation and diarrhoea complaints, and whether they had post-surgical faecal incontinence. This information was compared among two groups.

Statistical analysis was carried out with SPSS (SPSS Statistics version 22.0, SPSS inc.) statistical software. While t-test was used for parametric values in statistical comparisons, Pearson chi-square and Fisher's Exact test were used for categorical variables. Categorical variables were shown as number and percentage (n; %), while numeric variables as mean ± standard deviation (mean ± SD). $P<0.05$ was accepted statistically significant.

RESULTS

Medical treatment for anal fissure was administered to all 324 patients included in the study and the success rate was 45.7% (148/324), while the rate of not benefiting from medical treatment and applying surgical treatment was recorded as 54.3% (176/324). When the two groups were compared in terms of demographic characteristics, age and body mass index (BMI) were determined to be lower in Group-I according to group-II ($p<0.05$). When the comparison was made in terms of obstetrics, the total number of births, the number of vaginal deliveries and the breastfeeding rate were determined to be lower in Group-I ($p<0.05$), while there was no statistically significant difference between the two groups in terms of the number of caesarean deliveries and baby birth weight ($p>0.05$). While constipation was more common in group-II, there was no statistically significant difference found between the two groups in terms of diarrhoea and smoking (**Table 1**).

While pre-treatment bleeding and pain symptom presence was of lower rate in Group-I, both groups had similar characteristics in terms of the presence of swelling and itching symptoms. While fluctuation complication rate after medical treatment (Group-I) was 1.4%, this rate was determined to be 44.1% after surgical treatment (group-II) ($p<0.001$).

It was found that 324 patients with anal fissure (AF), which we included in our study, recovered at a rate of 45.7% with medical treatment, however 54.3% did not respond to medical treatment and were administered surgical treatment. In medical treatment failure, age, BMI, parity, vaginal parity, breastfeeding rate, constipation had negative effects.

However, it was observed that the C-section parity, birth weight of the baby, diarrhoea and smoking did not affect. Gas incontinence was observed in 44.1% of those who were administered surgical treatment, while it was seen in 1.4% of those who received medical treatment.

Table 1: Comparison of demographic, obstetric features and symptoms

	Group I (n=148)	Group II (n=176)	p-value
Demographic characteristics			
Age	35.2±9.8	40.1±9.2	<0.001
BMI	20.4±2.5	21.1±3.5	0.044
Smoking	48.3%	51.7%	0.846
Constipation	41.6%	%58.4	<0.001
Diarrhoea	72.7%	27.3%	0.120
Obstetric features			
Number of Births	2.0±1.2	2.3±0.9	0.008
Vaginal Delivery	1.5±1.3	2.0±1.1	0.004
C/S	0.4±0.7	0.3±0.5	0.246
Infant Weight	3472±366	3475±450	0.952
VD Infant Weight	3464±377	3413±443	0.393
Lactation	41.4%	58.6%	<0.001
Symptoms			
Bleeding	29.4%	70.6%	<0.001
Itching	42.1%	52.2%	0.182
Pain	42.1%	57.9%	0.004
Swelling	34.8%	65.2%	0.114
Complication			
Faecal Incontinence	1.4%	44.3%	<0.001

BMI: Body Mass Index, C/S: C-section, VD: Vaginal Delivery

DISCUSSION

Vaginal delivery causes deep and superficial injuries to the anal mucosa and muscles depending on the duration and number of births, ending up in anal fissure.[12,13] Trauma in the anal canal has been detected in approximately 50% of women who performed vaginal delivery.[14] In women who gave birth by C-section, anal fissure is quite low, rating around 1.2-15.2%.[11] In our study, it was found that the vaginal births and its parity affect to anal fissure treatment; a direct relationship was found between the high number of vaginal deliveries and the patients who were not benefiting from medical treatment and going to surgical treatment.

Although etiological factors in anal fissure formation are controversial, it has been shown that they are associated with increased pressure in the anal canal.[15] Internal sphincter pressure increases due to obesity, constipation, sitting for a long time, and prolonged straining. It has been asserted that this increase in internal sphincter pressure may cause anal fissure by causing ischemia in the posterior anal canal mucosa by compressing the branches of the inferior rectal artery.[16,17] In our study the medical treatment success rate of anal fissure in breastfeeding mothers with high BMI was found to be low. It suggests that this is related to the fact that the situation may become chronic due to the increase in the pressure in the anal area caused by the mothers who sit for a long time every two hours and breastfeed their child and repeat this frequently. Because, studies have reported that 33-44% of women experience discomfort due to anal region lesions in the first months after birth.[18] For this reason, frequent breastfeeding by sitting may make anal region lesions chronic.

Age is important in medical treatment success, and a higher success rate has been reported, especially in young patients with anal fissure compared to older patients.[19] In our study, medical therapy was found to be unsuccessful in elderly patients, in accordance with the literature. The reason for the traumatization of the anal canal as a result of hard defecation, constipation, and long-lasting straining, paves the way for anal fissure formation.[20] In women, it has been reported that traumatization of the anal area mucosa due to constipation, diarrhoea, and anorectal sexual intercourse is effective in the formation of anal fissure.[21] If constipation which causes anal fissure is not diagnosed early and treated, it makes the situation chronic and reduces the response to medical treatment.[22,23] In our study, it was found that constipation has a statistically significant effect on failure of medical treatment of anal fissure.

The long duration of anal pain, itching and bleeding symptoms seen in anal fissure indicate that the disease becomes chronic and this reduces the response to medical treatment.[24] Similarly, in our study, it was found that the presence of clinical symptoms contributed to the failure of the medical treatment.

The limitations of our study are that it is a retrospective study and not evaluating the presence of pelvic organ prolapse and urinary incontinence, while the strength of our study is that it is the first study to mention the medical treatment failures of anal fissure during pregnancy.

CONCLUSION

In our study, among obstetric reasons, number of pregnancies and vaginal deliveries and breastfeeding were negative factors in the success of the medical treatment of anal fissure during pregnancy. Also age and excess body weight are among other important reasons. Anal area lesions can be reduced by taking precautions such as diet, sitting bath, and receiving early medical treatment before pregnancy and delivery in order to reduce this negative condition that women experience, which is mostly ignored.

ETHICAL DECLARATIONS

Ethics Committee Approval: Approval of the Niğde Ömer Halisdemir University Medical Faculty Non-interventional Ethic Committee dated 27/08/2020 and numbered 2020/41.

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

Referee Evaluation Process: Externally peer-reviewed.

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Orjinal Araştırma / Original Article

Evaluation of Management of Patients who Admit to Emergency Service with Dyspeptic Complaints

Acil Servise Dispeptik Yakınmalarla Müracaat Eden Hastaların Yönetiminin Değerlendirilmesi

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Abstract

Aim: Dyspepsia means difficulty in the digestive process and consists of symptoms of bloating, pain, burning, early satiety, nausea and burping. Dyspepsia is one of the leading causes of admission to emergency services. Medical workups are overdone since there is still no consensus about the management of dyspeptic patients in emergency service. The aim of this article is to evaluate what is done for the management of patients with dyspeptic complaints in the emergency service.

Material and Method: This study was conducted by retrospective file scanning method and consisted of 2798 cases who admitted to the emergency service between 1 January – 31 December 2019 with dyspeptic complaints.

Results: Most of the patients included in the study were female (58.1%) and the mean age was 39.73±17.34. 77.8% of the included patients were treated in yellow area while 54.8% were diagnosed with gastritis. While 98.5% of the patients were discharged with outpatient treatment in the emergency observation room, only 1.5% were hospitalized. One case admitted with dyspepsia diagnostic code and presented with epigastric pain died.

Conclusion: In this study, it was found that patients with dyspeptic complaints presented to the emergency department at a very high rate and almost all patients benefited from outpatient treatment. In medical care, careful history taking and detailed physical examination of patients with dyspeptic complaints are considered important to avoid unnecessary investigations in the diagnostic process and to utilize resources appropriately as a developing country.

Keywords: Emergency service, dyspepsia, patient management, gastritis

Öz

Amaç: Dispepsi sindirim işleminin zorluğu anlamına gelip üst batında hissedilen şişkinlik, ağrı, yanma, erken doyma, bulantı ve geğirti semptomlarından oluşur. Dispepsi acil servislere başvurunun önde gelen nedenlerinden bir tanesidir. Dispeptik hastaların acil serviste yönetimi hakkında halen bir uzlaşmanın olmaması nedeni ile gereğinden fazla tetkikler yapılmaktadır. Bu makalede amaç bir acil serviste dispeptik yakınma ile başvuran hastaların yönetiminde nelerin yapıldığını incelemektir.

Gereç ve Yöntem: Bu çalışma, retrospektif dosya taraması yöntemi ile yapılmış olup; 1 Ocak-31 Aralık 2019 tarihleri arasında acil servise dispeptik yakınma nedeni ile başvuran 2798 vaka üzerinde yapılmıştır.

Bulgular: Çalışmaya dahil edilen hastaların çoğunluğu (%58,1) kadın olup yaş ortalaması 39,73±17,34 yıldır. Dahil edilen hastaların %77,8'i sarı alanda tedavi edilirken,%54,8'i gastrit tanısı aldı. Hastaların %98,5'i acil servis gözleminde günübirlik tedavi alarak taburcu olurken sadece %1,5'ine hastane yatışı yapılmıştır. Dispepsi tanı kodu ile kabul edilen ve epigastrik ağrı ile başvuran 1 vaka vefat etmiştir.

Sonuç: Bu çalışmada dispeptik yakınmalı hastaların acil servise çok yüksek oranda başvurduğu ve hastaların neredeyse tamamına yakınının ayaktan tedaviden fayda gördüğü tespit edilmiştir. Sağlık hizmet sunumunda dispeptik yakınmalı hastalardan alınacak dikkatli bir öykü ve ayrıntılı fizik muayene, tanı sürecinde gereksiz tetkiklerin önlenmesi ve gelişmekte olan bir ülke olarak kaynakların yerinde kullanılması açısından önemli olduğu değerlendirilmektedir.

Anahtar Kelimeler: Acil servis, dispepsi, hasta yönetimi, gastrit

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INTRODUCTION

The term dyspepsia derives from words "Dys" and "pepsis" and means difficulty in the process of digestion. Dyspepsia is not a diagnosis but a combination of symptoms which are bloating, pain, burning, early satiety, nausea and burping felt in the upper abdomen.[1] While dyspeptic complaints may stem from an underlying organic cause (gastritis, peptic ulceration, duodenal ulceration or gastric duodenal cancers), there are dyspepsia cases (functional dyspepsia) which doesn't have any underlying organic, systemic or metabolic cause.[1-3] Most of the dyspeptic complaints (75%) are functional dyspepsia; and it is more common in females, smokers, non-steroid anti-inflammatory drug users and people with *Helicobacter pylori* infection.[4,5]

Dyspeptic complaints are very common in our country and the world during our daily life. The prevalence of dyspepsia varies from region to region, and rates varying between %3 and %40 have been reported in Europe, North America and Ocean countries.[6,7] In a study conducted in Thailand, the public prevalence rate of dyspepsia was reported as 66%.[8] Death is not expected in dyspeptic complaints, except for complications.[4,9] However, it is very important because it is a common disease, has a chronic process, adversely affects daily life and quality of life, and increases unjustifiable costs related to health system.[10-13] In the United States, the annual cost of dyspepsia is more than $ 18 billion.[4,13]

Emergency services are healthcare centers, which are easily accessible to receive healthcare services and provide free service to every patient with social security insurance in our country. Thus dyspeptic patients admit frequently which cause an increasing both in the workload in emergency services and unnecessary costs in health service delivery. The aim of this study is to determine whether the resources in health service provision are used in a cost-effective way by analyzing the management of patients who admitted to the emergency service with dyspeptic complaints.

MATERIAL AND METHOD

This study was conducted by retrospective file review method. The study was conducted on 2798 cases who admitted to the emergency service of a training and research hospital between 1 January – 31 December 2019 with dyspeptic complaints such as epigastric pain, bloating, early satiety, burping and for whom ICD diagnosis codes K21 (Gastro-esophageal reflux disease), K25 (Gastric ulcer), K27 (Peptic ulcer, site unspecified), K28 (Gastrojejunal ulcer), K29.0 (Acute gastritis) and K30 (Dyspepsia) codes were entered. Laboratory tests, imaging methods, diagnoses and treatments of the patients included in the study were obtained from the Hospital Information Management System (HIMS). In addition, data on whether the patients were hospitalized or not and which clinic the patients were admitted to were also included. Five different groupings were made in terms of the time of diagnosis related to dyspeptic complaints from the file scans of the patients as earlier (diagnosed before admitting to the emergency room with dyspepsia), at the time of admission, recurrent admission to the emergency room, later (After admission to the emergency room, at another date and by a gastroenterologist) and pre-diagnosis (treated with pre-diagnosis in the emergency department). No written informed consent was obtained from the patients due to retrospective study design. Patients over 18 years of age and whose ICD code was K21, K25, K27, K28, K29.0 and K30 were included. Those under 18 years of age and other diagnostic codes were excluded. All admissions of the patients who had more than one admissions during the study process were examined, but only the first admissions was included. A p value of <0.05 was considered significant.

The study protocol was approved by Ahi Evran University Faculty of Medicine on 29.01.2019 with the decision number of 2019-02/29. The study was conducted in accordance with the Declaration of Helsinki.

Statistical Method

Statistical analysis of the study was performed using Statistical Package for Social Sciences version 21.0 software for Windows (IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp., USA). Normality assumption was tested by Kolmogorov-Smirnov and Shapiro-Wilk tests. Explanatory statistics of the variables are given as Mean±standard deviation, Median (interquartile at the 25th and 75th percentiles, IQR), and frequencies n (%). For the univariate analyzes of variables in the study; Chi Square, Repeated Measures Analysis of Variance (RMANOVA), Friedman and Mann-Whitney U tests were used according to the type of variable and state of assumptions.

RESULTS

58.1% of the patients included in the study were women and 41.9% were men. The mean age of the patients is 39.73±17.34 years; age distribution is between18-85 years. According to the triage category, most of the patients who admitted to the emergency department with dyspeptic complaints were admitted to the yellow area and received treatment with a rate of 77.8%, while 54.8% patients were diagnosed with gastritis (ICD code: K29) (**Table 1**). 98.5% of the patients who admitted with dyspeptic complaints were discharged from the emergency room with outpatient treatment, while only 1.5% of them were hospitalized. Most of the patients hospitalized were hospitalized in the gastroenterology clinic and received medical treatment, while only 2 cases were diagnosed with appendicitis and were received emergency operation. A pregnant patient was referred to another center due to the need for Endoscopic Retrograde Cholangiopancreatography (ERCP), (**Table 1**). A 74-year-old patient, who was included in our study and presented with epigastric pain, was diagnosed with acute coronary syndrome and died in coronary intensive care he was hospitalized.

When diagnosis and laboratory findings of patients with dyspeptic complaints are compared; a statistically significant difference was found between the Hemoglobin (Hgb), White blood cell (Wbc), Platelet (Plt), Glucose (Gluc), C-reactive protein (CRP), Estimated glomerular filtration rate (eGFR),

Alanine aminotransferase (ALT), Gamma-glutamyl transferase (GGT), Bilirubin (Bil) levels among the groups of earlier, at the time of admission or recurrent admission (p<0.01) (**Table 2**). Among patients with dyspeptic complaints, Hgb, Plt and eGFR values of at the time of admission group are lower than other diagnosis times. Wbc, CRP, Gluc, ALT, Aspartate aminotransferase (AST), GGT, Bilirubin and Troponin values were higher in at the time of admission group (**Table 2**).

Table 1. Distribution of sociodemographic characteristics, triage categories, ICD diagnosis code and time of diagnosis of the patients

Variables	Time of diagnosis				Pre-diagnosis n=2466	Total n=2798
	Earlier (in the past) n=144	At the time of admission* n=61	Recurrent admission n=17	Later** n=110		
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Gender						
Female	90 (62.5)	31 (50.8)	10 (58.8)	73 (66.4)	1423 (57.7)	1627 (58.1)
Male	54 (37.5)	30 (49.2)	7 (41.2)	37 (33.6)	1043 (42.3)	1171 (41.9)
Age (years)	47.5 (18-82)	56 (18-87)	31 (21-81)	41.5 (18-92)	35 (18-95)	37 (18-95)
Triage Categories						
Green Zone	34 (23.6)	5 (8.2)	2 (11.8)	15 (13.6)	559 (22.7)	611 (21.8)
Yellow Zone	108 (75.0)	55 (90.2)	15 (88.2)	95 (86.4)	1903 (77.2)	2176 (77.8)
Red Zone	2 (1.4)	5 (8.2)	-	-	4 (.2)	11 (.4)
ICD Codes						
21	26 (18.1)	14 (23.0)	6 (35.3)	22 (20.0)	624 (25.3)	692 (24.7)
25	-	-	1 (5.9)	-	-	1 (0.0)
27	13 (9.0)	3 (4.9)	1 (5.9)	4 (3.6)	130 (5.3)	151 (5.4)
28	1 (.7)	10 (16.4)	1 (5.9)	2 (1.8)	10 (.4)	24 (.9)
29	89 (61.8)	27 (44.3)	4 (23.5)	70 (63.6)	1344 (54.5)	1534 (54.8)
30	15 (10.4)	7 (11.5)	4 (23.5)	12 (10.9)	358 (14.5)	396 (14.2)
Decision for the patient						
Outpatient	141 (97.9)	33 (54.1)	15 (88.2)	107 (97.3)	2461 (99.8)	2757 (98.5)
Admission	3 (2.1)	28 (45.9)	2 (11.8)	3 (2.7)	5 (.2)	41 (1.5)

* Patients diagnosed during admission to the emergency department. Recurrent Admission group is the patient group who admitted to our emergency service again with the same complaint in a week after admitting to the emergency department with dyspepsia.
** ICD Codes: K21 (Gastro-esophageal reflux disease), K25 (Gastric ulcer), K27 (Peptic ulcer, site unspecified), K28 (Gastrojejunal ulcer), K29.0 (Acute gastritis) and K30 (Dyspepsia)
*** The patients defined as "later group" are patients who were referred to a gastroenterology specialist and diagnosed by a gastroenterologist.

Table 2. Comparison distribution of laboratory findings and diagnosis time of patients

Variables	Time of Diagnosis					Pre-diagnosis n=2466	p
	Earlier (in the past) n=144	At the time of admission* n=61	Recurrent admission n=17	Later** n=110	Total n=2798		
	M.±SS	M.±SS	M.±SS	M.±SS	M.±SS	M.±SS	
Hgb	12.8±2.2	10.23±3.7	13.0±1.3	13.3±2.0	13.7±2.2	14.0±1.9	0.001
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	
Wbc	8.4 (3.3-16.4)	10.6 (5.6-35.1)	10.1 (9.8-10.1)	8.2 (3.9-10.8)	8.6 (2.3-73)	8.9 (2.3-19.0)	0.001
Plt	285.8±83.6	271.2±85.9	325.6±78.9	246.6±75.5	270.6±82.1	269.6±81.3	0.001
Gluc	135 (75-421)	140.9 (98-224)	101.6 (96-113)	131.1 (83-250)	108 (64-505)	126.5 (64-302)	0.001
CRP	0.3 (0.11-0.71)	0.75 (0.33-2.18)	0.77 (0.6-1.91)	0.23 (0.10-0.58)	0.38 (0.15-0.99)	0.35 (0.14-0.92)	0.001
eGFR	86.38 (42-121)	76.4 (9-114)	127.3 (120-131)	83.4 (34-120)	95 (1-153)	83.8 (8.7-138)	0.001
ALT	15 (5-53)	24 (6-184)	23 (11-359)	18 (5-101)	17 (5-904)	16 (6-96)	0.001
AST	22 (12-43)	35 (12-275)	21 (13-549)	24 (12-66)	21 (0-549)	20 (6-160)	0.012
GGT	16.5 (7-64)	49 (9-764)	28 (15-437)	28 (8-97)	19 (3-1584)	19.5 (5-261)	0.001
BIL	0.4 (0.1-1.3)	0.5 (0.1-10.4)	1.1 (0.5-2.7)	0.4 (0.1-1.8)	0.4 (0-10.4)	0.4 (0-5)	0.001
LIPAZ	30.5 (4-66)	33 (12-1362)	37 (16-137)	37 (17-60)	30 (3-1362)	28 (3-439)	0.008
Trop	7 (0-55)	9.5 (0-276)	3.2 (3-8.9)	6.2 (0-44)	6 (0-276)	5.8 (0-194)	0.200

* Patients diagnosed during admission to the emergency department.
** The patients defined as "later group" are patients who were referred to a gastroenterology specialist and diagnosed by a gastroenterologist.
*** Hgb: Hemoglobin, Wbc: White blood cells, Plt: Platelet, Gluc: Glucose, CRP: C reactive protein, eGFR: Estimated glomerular filtration rate, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, GGT: Gamma glutamyl transferase, BIL: Bilirubin, LIPAZ: Lipase, Trop: Troponin I.

For the patients who admitted with dyspeptic complaints; complete blood count was requested for 24.69% (n=691) of patients, routine biochemical test combined with CRP for 24.51% (n=686) and troponin test for 13.75% (n=385). Electrocardiography (ECG) was performed in 22.83% (n=639) of the patients and abdominal x-ray (AXR) was taken in 23.73% (n=664) of the cases in terms of imaging methods. In addition, 85 cases had abdominal tomography, 16 cases had endoscopy and 24 cases had abdominal ultrasonography (USG).

H2 receptor blocker was administered in 65.43% (n=1831), spasmolytic in 59.5% (n=1664), antiemetic in 55.78% (n=1561), and PPI (proton pump inhibitor) in 49.1% (n=1374) and liquid anti-acid in 7.46% (n=209) of patients presenting with dyspeptic complaints. Intravenous fluid therapy was initiated in 40.2% (n=1125) of the patients, and a total of 678900 mL fluid therapy was administered. Intramuscular treatment was applied for 25.19% (n=705) of the patients, and 27.09% (n=758) of the patients were discharged with a prescription.

It was found that the majority of patients (87.99%, n=2462) who admitted to the emergency department with dyspeptic complaints were treated with a pre-diagnosis of dyspepsia. It was found that a diagnosis related to dyspeptic complaint was made by a gastroenterologist for 5.14% (n=144) of patients before emergency service admission, 0.85% (n=24) of them during emergency service admission and in recurrent admissions and 3.93% (n=110) of them after the emergency service admission (**Table 3**). Of the 2798 cases presenting with dyspeptic complaints, 2.07% (n=58) of them were diagnosed with a disease in the differential diagnosis group of dyspepsia.

Cholecystitis was diagnosed in 26, cholelithiasis in 12 and pancreatitis in 9 patients who admitted to emergency service with a dyspeptic complaint. Gastrointestinal system (GIS) bleeding was the most observed complication of peptic ulcer. Also, 16 of the patients were diagnosed with GIS bleeding during their emergency admission and 2 of them during their recurrent admissions to the emergency service. 3 of the patients were diagnosed with acute coronary syndrome (ACS) and 1 of them readmitted with epigastric pain 6 hours after being discharged from the emergency room and died in the intensive care unit where (s)he was hospitalized due to cardiac arrest in the emergency department. Also, 3 of the patients who admitted with dyspepsia were diagnosed with acute appendicitis and 3 were diagnosed with pregnancy (**Table 3**).

Most of our patients have benefited from the treatment they received from the emergency department, only 0.6% of them (n=17) were partially relieved when they were treated in the emergency service and admitted to the same emergency service again with similar complaints within the first week after their discharge from the emergency service. When these patients were reevaluated; 4 were diagnosed with cholelithiasis, 9 with cholecystitis, 1 with pancreatitis, 2 with GIS bleeding and 1 with appendicitis. Except for the case with a pre-diagnosis of dyspeptic complaint and presented with epigastric pain and diagnosed with a pre-diagnosis of ACS at the age of 74, no case died, including delayed cases (**Table 3**).

Outpatient groups and hospitalized groups of patients with dyspeptic complaints were compared in terms of age, gender, triage category and laboratory parameters (**Table 4**). The mean age of the patients treated by hospitalization was found to be statistically significantly higher than those treated as outpatients (p=0.001). In addition, the rate of hospitalization was found to be statistically significantly higher in male patients comparing to women (p=0.001). In terms of laboratory parameters, Hgb, Plt and eGFR values were low in those who were hospitalized, while Wbc, Glucose, CRP and GGT parameters were found to be high (p<.01).

Table 3. The distribution of the definite diagnoses of the patients in relation to the time of diagnosis

Diagnosis	Time of Diagnosis				Total n=2798	p
	Earlier (in the past) n=144	At the time of admission* n=61	Recurrent admission n=17	Later** n=110		
	n (%)	n (%)	n (%)	n (%)	n (%)	
Gastritis, Pangastritis	101 (49.5)	3 (0.01)	-	100 (49.0)	204	0.001
Peptic ulcer	34 (75.6)	3 (6.6)	-	8 (17.8)	45	
GER	4 (100)	-	-	-	4	
Cholelithiasis	1 (8.38)	5 (41.7)	4 (33.3)	2 (16.7)	12	
Cholecystitis	-	17 (67.8)	9 (32.1)	-	26	
Pancreatitis	-	8 (88.9)	1 (11.1)	-	9	
Gastric cancer	4 (66.7)	-	-	2 (33.3)	6	
GIS bleeding	-	16 (88.8)	2 (11.2)	-	18	
MI, ACS		3 (100)			3	
Appendicitis		2 (66.7)	1 (33.3)		3	
Pregnancy	2 (66.7)	1 (33.3)	-	-	3	
Zollinger Ellison syndrome	1 (50.0)	-	-	-	1	

* Patients diagnosed during admission to the emergency department.
** The patients defined as "later group" are patients who were referred to a gastroenterology specialist and diagnosed by a gastroenterologist.
GER: Gastro-esophageal reflux, GIS: Gastrointestinal system, MI: Myocardial infarction, ACS: Acute coronary syndrome.

Table 4. Comparison of variables in patients in hospitalization and outpatient settings

Variables	Outpatient M. (Min. - Max.)	Hospitalization M. (Min. - Max.)	p
Age (year)	36 (18-95)	64 (21-88)	0.001
	n (%)	n (%)	
Gender			
Female	1610 (58.5)	15 (36.6)	0.001
Male	1143 (41.5)	26 (63.4)	
Triage Category			
Red Zone	4 (.1)	7 (17.1)	
Yellow Zone	2140 (77.7)	33 (80.5)	0.001
Green Zone	609 (22.1)	1 (2.4)	
Laboratory parameters			
HGB	13.80 (7-20)	12.70 (3-18)	0.001
WBC	8.5 (7.08-10.82)	9.65 (7.30-13.67)	0.001
PLT	263 (0.0-896)	226 (109-515)	0.001
GLUC	108 (64-505)	134 (76-297)	0.001
CRP	0.36 (0.14-0.91)	0.99 (0.51-2.83)	0.001
E GFR	96 (1-153)	85.5 (22-137)	0.005
ALT	16.5 (5-359)	16 (6-184)	0.881
AST	21 (6-549)	21 (12-275)	0.289
GGT	20 (5-437)	30 (9-764)	0.008
BIL	0.4 (0.04-3.20)	0.48 (0.13-1.60)	0.011
LIPASE	28.5 (9-496)	32.5 (4-1362)	0.130
TROP	6.14 (0-194)	11.55 (0-276)	0.029

Hgb: Hemoglobin, Wbc: White blood cells, Plt: Platelet, Gluc: Glucose, CRP: C reactive protein, eGFR: estimated glomerular filtration rate, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, GGT: Gamma glutamyl transferase, BIL: Bilirubin, LIPAZ: Lipase, Trop: Troponin I.

DISCUSSION

As a result of the data, we obtained from our study, it was determined that there were too many patient admissions related to dyspeptic complaints among emergency room admissions. It was determined that 98.5% of these patients were discharged because they benefited from outpatient treatment in the emergency department and 87.9% of these patients were treated with a pre-diagnosis and discharged without a definitive diagnosis. Since mortality is not expected in patients presenting with dyspeptic complaints,[4,9] while symptomatic treatment is performed in emergency departments, on the other hand complications of diseases that cause dyspepsia and diseases with high mortality in the differential diagnosis group of dyspepsia are tried to be ruled out. For these reasons, workups are planned for patients in terms of urgent and high mortality diseases. In our study, it was found that there were laboratory findings that would lead to diagnosis in 1.7% (n=12) of the patients who had a hemogram test, and in 3.35% of the patients who had a routine biochemical test. As emergency department physicians, low Hgb in hemogram test led to diagnosis of gastrointestinal bleeding, and high ALT, AST, GGT, Lipase parameters in biochemical test led to cholecystitis and pancreatitis diagnosis. As determined in the results of our study, the use of significant and unnecessary costs in resources of healthcare is increasing for the management of patients who admit to emergency service with dyspeptic complaints. In an article previously published in the literature, diseases causing dyspeptic complaints were found to be 54% more costly than other diseases even at the stage of diagnosis.[14]

In our study, it was found that 87.9% of the patients were not diagnosed with the endoscopic method. These cases are accepted as uninvestigated cases in the literature.[5,15] Uninvestigated cases are observed with a rate of 7-45% in the world depending on geographical location and their definition.[15] In an earlier study conducted in the emergency department in Turkey, it was stated that only one third of the cases who admitted to the emergency department with dyspeptic complaints applied to a gastroenterology specialist.[16] In a meta-analysis conducted by Ford et al.[5] the global prevalence of uninvestigated dyspepsia was found as 21%. As it is understood from that study, the majority of dyspeptic cases are uninvestigated dyspepsia cases that are not established final diagnosis via endoscopic method and these cases frequently admit to emergency services or family physicians due to their complaints rather than admitting to a gastroenterology specialist.

With a good history and detailed physical examination, a differential diagnosis of many diseases such as cardiac and vascular diseases, cholecystitis, pancreatitis, acute abdomen, ileus, malignancy and gastroenteritis can be made in patients who present to the emergency department with dyspeptic complaints. If there are cases in doubt, further examinations are planned accordingly. In a previously published study in the literature, it was stated that the incidence of cholelithiasis is high in patients with dyspeptic complaints, but dyspepsia does not cause cholelithiasis.[17] Yet in another study, ultrasonography was performed in all patients with dyspepsia and it was reported that more than half of these patients had fatty liver and 12.8% had biliary diseases.[18] In our study, gall bladder diseases (cholelithiasis, cholecystitis) were found to be the most common accompanying disease in patients with dyspeptic complaints. Cardiac and vascular diseases are the diseases with the highest mortality in the differential diagnosis group. Cardiac diseases such as myocardial infarction and acute coronary syndrome, and vascular diseases such as aortic dissection and aneurysm should definitely be evaluated in this patient group. In our study, one of our patients died and (s)he was a patient with a diagnosis of ACS. The most important complications of dyspeptic diseases are peptic ulcer perforation and gastrointestinal bleeding, and these should definitely be evaluated in differential diagnosis. Due to disagreements in the treatment management of dyspeptic diseases and the serious economic burden on the health insurance system[9] guidelines were published on this issue in the USA, Canada and Europe.[4,19] In our country, there is a guide published by Ozden[1] however, these guidelines have been prepared specifically for gastroenterology specialists. In our

country, at least three times the number of patients presenting to a gastroenterologist with dyspeptic complaints apply to emergency services and family physicians in family health centers.[16] However, there is no guideline that physicians of the emergency services can use for the management of these patients who admit to emergency departments.[20] In a study conducted by Kim et al.[21] for family physicians, it was found that raising clinical awareness about functional dyspepsia would reduce unnecessary treatments and costs.

Patients who present to the emergency department with dyspeptic complaints respond well to symptomatic liquid antacid, H2 receptor blocker and PPI treatment. Thus, it has been found that the majority of patients were discharged after an outpatient treatment in the emergency department. In two previous studies, it was stated that H2 receptor blocker treatment had the same effectiveness with two different intravenous PPI preparations.[20,22] Also, in the same study, it was determined that the cost of dyspepsia treatment with PPIs is 3 times that of the H2 receptor blockers treatment and 11 times that of the liquid antacid's treatment. In another study conducted in the emergency department, it was reported that PPI treatment did not have additional contribution to liquid antacid treatment.[22] However, in our study, PPI treatment was started as the first choice in many patients and the rate of PPI/H2 receptor blocker use was found 75.04%. Also, we found that the use of liquid antacids in the emergency department was very low in our study. Thus, it is considered that the selection of economical preparations, which have similar effectiveness in dyspepsia treatment, will reduce treatment costs in general. In diseases that cause dyspeptic complaints, usually no abnormalities are observed in laboratory findings, except for complications. Rather, laboratory tests are required for differential diagnosis and complications. Thus, as it can be understood from the results of the study, unnecessary workups in the management of dyspeptic complaints may cause a serious increase in costs. One of the results that makes this study noteworthy is that there are very few similar studies in the literature.

CONCLUSION

As a result of the data, we obtained from our study, it was determined that there were a lot of patient admissions to emergency services due to dyspeptic complaints, 98.5% of these patients could be discharged with outpatient treatment in the emergency department and 87.9% of these patients were treated with a pre-diagnosis of dyspepsia. It is considered that taking a careful history and performing a detailed physical examination for the diagnosis of patients with dyspeptic complaints presenting to the emergency department, and cost-effective behavior in the planning of treatment and the workups for dyspeptic complications and diseases with high mortality in the differential group of dyspepsia are important for preserving the national wealth as a developing country.

Limitations

The most important limitation of our study was that the rate of patients presenting to the emergency service due to dyspeptic complaints may be lower than it actually was. The cause of this situation is usage of "Unspecified Abdominal Pain" and "Nausea with Vomiting" as ICD diagnosis code for patients who present to emergency services with dyspeptic complaints.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study protocol was approved by Ahi Evran University Faculty of Medicine on 29.01.2019 with the decision number of 2019-02/29. The study was conducted in accordance with the Declaration of Helsinki.

Informed Consent: Since our article was conducted with the retrospective file screening method, the voluntary consent form was not signed by the patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest: No conflict of interest was declared by the authors.

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Orjinal Araştırma / Original Article

Evaluation of Geriatric Fractures Admitted to the Emergency Department According to Years and Seasons

Acil Servise Başvuran Geriatrik Kırıkların Yıllara ve Mevsimlere Göre Değerlendirilmesi

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Abstract

Objective: With the rapidly increasing and diversifying elderly population of industrialized countries, the incidence of geriatric fractures is gradually increasing. The aim of this study is to evaluate the distribution of geriatric fractures according to the prevalence, age, sex, season and years.

Material and Method: Analyzes of geriatric fractures in patients aged 65 and over who were admitted to our emergency department between January 2015 and December 2020 were performed according to the most common fracture locations (hip, distal forearm, proximal humerus and ankle). The distribution of these fractures by age, gender, seasonal characteristics and years was evaluated

Results: A total of 370 cases (168 male, and 202 female patients) with an average age of 79.5± 9.02 years were included in the study. The most common fracture stypes in order of decreasing frequency were fractures of the hip (51.7%), distal forearm (25.1%), proximal humerus (12.4%) and ankle (10.8%). The incidence of distal forearm fractures was significantly higher in females than males (p=0.001), but any statistically significant difference was not found between genders regarding other fractures (p> 0.05). It was observed that the incidence of hip fractures was significantly higher in the people aged 86 years and over, while the other fractures were more frequently seen in the 65-75 age group. A seasonal feature was not observed in all fractures. The highest rate of hip fractures was seen in the year 2020. There was no difference in the distribution of other types of fractures over the years

Conclusion: It has been concluded that the incidence of geriatric fractures increases relatively in conditions of social isolation and does not show seasonal characteristics in our region. We are of the opinion that a good management strategy should be determined characterized with both the isolation of these patients and their early treatment and discharge in disasters as pandemics, and the incidence of geriatric fractures that can be mortal with advancing age should be very well known.

Keywords: Geriatric fractures, hip, distal forearm, weather, elderly

Öz

Amaç: Günümüzde sanayileşmiş ülkelerin hızla artan ve çeşitlenen yaşlı nüfusa sahip olması ile beraber bu kırıkların görülme sıklığı giderek artmaktadır. Bu çalışmanın amacı geriatrik kırkların görülme sıklığı, yaş, cinsiyet, mevsim ve yıllara göre dağılımını değerlendirmektir.

Gereç ve Yöntem: Ocak 2015- Aralık 2020 yılları arasında acil servisimize başvuran 65 yaş ve üstü geriatrik kırıklı hastaların en sık görülen kırık lokalizasyonuna göre (kalça, distal önkol, proksimal humerus ve ayakbileği kırıkları) analizleri yapıldı. Bu kırıklar yaş, cinsiyet, mevsimsel özellik ve yıllara göre dağılımları değerlendirildi.

Bulgular: Çalışmaya alınan 370 hastanın 168 tanesi erkek 202 tanesi kadın olup yaş ortalaması 79,5±9,02 idi. En sık görülen kırık tiplerinin görülme sıklığına göre sırasıyla; kalça (%51,7), distal önkol(%25,1), proksimal humerus (%12,4) ve ayak bileği kırığı (%10,8) olduğu görüldü. Distal önkol kırıklarının kadınlarda erkeklere oranla istatistiksel olarak anlamlı bir şekilde yüksek olduğu (p=0,001), ancak diğer kırıklarda cinsiyetler arasında istatistiksel olarak fark görülmemiştir (p>0,05). Kalça kırıklarının 86 yaş ve üzeri gurubunda anlamlı olarak yüksek olduğu, diğer kırıkların ise 65-75 yaş aralığında daha yüksek olduğu görülmüştür. Tüm kırıklarda mevsimsel bir özellik görülmemiştir. Kalça kırıklarının 2020 yılında en yüksek oranda görülmüştür. Diğer kırıklarda ise yıllar arasında kırık dağılımı açısından fark görülmemiştir.

Sonuç: Geriatrik kırıkların sosyal izalosyonda rölatif olarak arttığı ve yöremizde mevsimsel özellik göstermediği sonucuna varılmıştır. Yaşın ilerlemesi ile mortal olabilecek geriatrik kırıkların insidansının iyi bilinmesi ve pandemi gibi durumlarda bu hastaların hem izolasyonu hem de erken tedavi edilip taburcu edilmesi ile birlikte iyi bir yönetim stratejisi belirlenmesi gerektiği kanaatindeyiz.

Anahtar Kelimeler: Geriatrik kırıklar, kalça, distal önkol, hava durumu, yaşlılar

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INTRODUCTION

Geriatric fractures emerge as an important public health problem and are among the frequent reasons for admissions to the emergency services.[1] These fractures mostly occur in osteoporotic individuals as a result of simple falls during daily activities. Along with poor vision and decreased reflexes, many causative factors as well as the presence of osteoporosis predispose to the development of fractures. Today, with the rapidly increasing elderly population of industrialized countries, an increase in the incidence of these fractures is anticipated.[2,3] It has been also reported that the incidence of these fractures show a seasonal change.[4] Especially older age, gender, the presence of additional diseases, and the type of fracture can affect daily living activities and quality of life of the geriatric patients.[5]

It is very important to carry out studies on the incidence of geriatric fractures and to update information on this issue. Considering the health expenditures and intensive care burden, it can be thought that this burden can be partially reduced by plans to be performed at aiming at prevention of geriatric fractures. The aim of this study is to examine the frequency of fractures in geriatric patients admitted to our center and the distribution of these fractures by age, sex, season and years. Another feature of our study is that patients who applied since the first implementation of social restrictions during the pandemic were included in the evaluation.

MATERIAL AND METHOD

The data related to the extremity fractures of patients aged 65 and over, who were admitted to the emergency service between January 2015 and December 2020 and consulted to the orthopedics-traumatology clinic, were scanned from the automation records of our hospital using the International Classification of Diseases-10 (ICD-10) system. These fractures were classified according to their anatomical location. Among 563 patients diagnosed with fractures, 370 cases that had four most common types of fractures (hip, distal forearm, proximal humerus and ankle) were evaluated. The distribution of these fractures by age, sex, season and years was evaluated. The patients were divided into 3 groups in terms of age distribution as 65-75, 76-85 and 86 years and above. Patients with missing data in the automation system and cases that were not evaluated by the orthopedic clinic, and patients with pathological fractures and multiple fractures were excluded from the study.

The study was carried out with the permission of Van Yüzüncü Yıl University Non-Invasive Clinical Research Ethics Committee (Permission granted: 16.10.2020, Decision no: 2020/07-02).

Statistical analysis

The sample size of this study which was carried out for the analysis of common fractures in geriatric patients, was determined for each variable by considering the minimum statistical power of the test as 80% with type 1 error of 5%. Categorical variables in the study were expressed as numbers and percentages. Chi-square test was used to determine the relationship between "fracture type groups" and categorical variables. In the calculations, the statistical significance level was taken as (a) 5% and the SPSS (IBM SPSS for Windows, ver.24) statistics package program was used for analysis.

RESULTS

A total of 370 cases (168 male, and 202 female patients) with an average age of 79.5± 9.02 were included in the study. The most common types of fractures in order of decreasing frequency were fractures of the hip (51.7%), distal forearm (25.1%), proximal humerus (12.4%) and ankle (10.8%). Demographic data of our patients are given in **Tables 1** and **2**.

Table 1 is examined, it is seen that the rates of distal forearm fractures are statistically significantly higher in women compared to men, but there is no statistically significant difference between genders in terms of other fractures.

Table 2 is examined, it is seen that the rates of hip fractures are statistically significantly higher in the age group of ≥ 86 years, while the other fractures are seen at a significantly higher in the 65-75 age group.

Table 3 is examined any seasonal difference is not seen in terms of all fractures.

As seen in **Table 4**, the highest rate of geriatric hip fractures was seen in 2020, while any difference is not noted in the distribution of other fracture types over the years.

Table 1. Gender difference according to the location of the fractures

	Male		Female		*p.
	n	%	n	%	
Hip	106	55.5	85	44.5	0.129
Distal forearm	21	22.6	72	77.4	0.001
Proximal humerus	21	45.7	25	54.3	0.555
Ankle	20	50.0	20	50.0	1.00

* Levels of significance according to one sample chi-square test

Table 2. Difference between fracture types according to age groups

	65-75 years		76-85 years		86+ years		*p.
	N	%	N	%	N	%	
Hip	45	23.6	70	36.6	76	39.8	0.014
Distal forearm	52	55.9	26	28.0	15	16.1	0.001
Proximal humerus	24	52.2	12	26.1	10	21.7	0.024
Ankle	31	77.5	7	17.5	2	5.0	0.001

* Levels of significance according to one sample chi-square test

Table 3. Seasonal differences according to the location of the fractures

	Winter		Spring		Summer		Autumn		*p.
	N	%	N	%	N	%	N	%	
Hip	58	30.4	48	25.1	48	25.1	37	19.4	0.202
Distal forearm	26	28.0	22	23.7	30	32.3	15	16.1	0.152
Proximal humerus	7	15.2	8	17.4	18	39.1	13	28.3	0.082
Ankle	10	25.0	14	35.0	10	25.0	6	15.0	0.362

* Levels of significance according to one sample chi-square test

Table 4. The difference in the distribution of fractures within a period of 6 years

	2015		2016		2017		2018		2019		2020		*p.
	N	%	N	%	N	%	N	%	N	%	N	%	
Hip	40	20.9%	32	16.8%	20	10.5%	25	13.1%	27	14.1%	47	24.6%	0.007
Distal forearm	16	17.2%	17	18.3%	18	19.4%	21	22.6%	10	10.8%	11	11.8%	0.329
Proximal humerus	7	15.2%	4	8.7%	7	15.2%	10	21.7%	9	19.6%	9	19.6%	0.693
Ankle	9	22.5%	6	15.0%	8	20.0%	6	15.0%	7	17.5%	4	10.0%	0.806

* Levels of significance according to one sample chi-square test

DISCUSSION

In this study, in which the distribution of geriatric fractures by age, sex, localization, seasonal characteristics and years was investigated hip fractures ranked on top, followed by distal forearm, proximal humerus and ankle fractures in decreasing order of frequency. It was observed that these fractures were more common in women and also distal forearm fractures were seen at significantly higher rate in women than men.

Considering the seasonal variation of the incidence rates of fractures, any significant change was not detected in our region. The distribution of fractures by years revealed that the incidence of hip fractures increased compared to previous years with the pandemic restrictions in 2020, while incidence of fractures in other localizations did not vary by years.

Similar to our study, geriatric fractures have attracted considerable attention in the literature and many studies have been conducted in this area.[1,3,6] Geriartric fractures, which constitute a serious public health problem, have been investigated and many preventive methods have been defined due to their relationship with osteoporosis. In these studies, especially effects of osteoporosis on the incidence, mortality and health expenditures of hip fractures were highlighted.[7,8] In our study, fracture localization, age-gender distribution, and the long-lasting winter season in our region on fractures were examined in more detail rather than the relationship between these fractures and osteoporosis.

According to the location of the fractures, hip fractures were seen more frequently, especially in the patient population aged 86 years and over (P=0.014). When we reviewed the relevant literature similar to our study, a large-scale national study conducted in Ukraine indicated that, the incidence of hip fractures at the age of 80 and over was 10 times higher than the lower geriatric age groups, indicating a statistically significant intergroup difference. It has been also reported that this result is related to increases both in the incidence of osteoporosis and the population of this age group.[9] In a study conducted on geriatric hip fractures, Lewiecki EM et al.[10] reported that the hip fracture rates were higher than predicted and this rate increased significantly, especially at the age of 80 and over. They also recommended conduction of further studies to evaluate all factors contributing to this important change in hip fracture rates and to develop strategies for the treatment of osteoporosis.

Distal forearm fracture is another common fracture type seen in geriatric patients. We observed that these fractures were statistically significantly more often seen in women than men. In a study conducted in 2020, Zakroyeva et al.[11] reported that distal forearm fractures were more common in women than in men (female / male ratio = 3.5). In their study, the incidence of fractures in women increased at the age of 69, and then decreased with age. In men, its incidence decreased with increasing age. Gül et al.[12] reported that women had more often suffered from distal forearm fractures than men. In a large -scale case series conducted on patients with geriatric osteoporosis, distal forearm fractures were reported to be more frequently seen in women than men.[13] In our study, it was found that these fractures were more common in the 65-75 age group, and forearm fractures decreased in both genders with increasing age. It is thought that increasing osteoporosis in postmenopausal women may be related to this result.

It was observed that the rates of proximal humerus and ankle fractures we also encountered in our study, were close to each other. Although these fracture types have not attracted much attention as hip and distal forearm fractures in the literature, it should be kept in mind that the localization of these two fractures is important, and that especially long-term immobilization of patients with ankle fractures will bring along fatal risks such as embolism, etc. In a study conducted on ankle fractures of elderly populations, it was emphasized that these patients constituted a heterogeneous group of cases with diabetes, neuropathy, osteopenia which created difficulties in treatment.[14] In our study, these fractures were more frequently seen in the 65-75 age group and the incidence of ankle fractures decreased in both genders with aging.

In present study, the seasonal distribution of geriatric fractures also did not differ among types of fractures. In a previous study; it was reported that hip fractures were seen with a higher rate in the winter months.[15] Some studies have indicated that falls due to slippery ground covered with snow and ice may play an important role in the incidence rates of seasonal fractures.[16] In another study, it was reported that hip fractures in women over the age of 50 did not convey seasonal characteristics, and the incidence rates of hip and wrist fractures were higher in men in winter.[17] It has been indicated that incidence rates of the hip, distal forearm, humerus and ankle fractures increase in the winter in elderly individuals, but hip fractures show less seasonality than other fractures, and these fractures mostly develop as a result of domestic falls.[4] The incidence of fractures of the proximal humerus increases with age and have been observed more frequently in the winter months.[18]

In another study, it was reported that there was no statistically significant relationship between the incidence of geriatric fractures and weather conditions (seasonal characteristics).[19]

Considering the distribution of fractures by years in our study, it was seen that the fractures other than hip fractures did not show any statistical change over the years. It was determined that hip fractures were most common in 2020, when social isolation measures were applied. Different studies have been reported in the literature on variations inthe incidence rates of geriatric fractures over the years. In a national data-based study published in 2017; declining trends in the incidence of lower body (hip, pelvic and lower spine) and wrist fractures have been suggested over the past 11 years (2004-2014). In another study, it was reported that in 2011 720,000 cases with geriatric fractures were seen in Germany and that its rates will increase by 28% by 2030.[20]

Another common problematic issue of geriatric fractures is related to comparative incidence rates of indoor and outdoor fractures. Geriatric distal forearm fractures tend to occur in relatively active individuals due to slipping during strolling outside, whereas hip fractures usually occur indoors in more fragile elderly patients.[21] It has been reported that indoor fractures were seen more frequently in geriatric patients subjected to domestic restrictions during the pandemic period, and especially the number of cases with hip fractures increased in hospital admissions, It has been indicated that inadequate support received by these individuals from relatives and caregivers because of the social isolation policy may have been presumably held responsible for increasing rates of hip fractures.[22] In our study, which analyzed fractures seen within a period of 6 years extending from 2015 to 2020 (incl.), similarities in annual rates of geriatric fractures were observed, but statistically significantly greater number of hip fractures were found in the period when social restrictions were imposed.

The most important limitation of this study is that it was conducted in a single center and with a relatively small number of patients. Retrospective design of our study was its another limitation, thus the relationship between fractures and Bone Mineral Density (BMD) and Body Mass Index (BMI) could not be evaluated.

CONCLUSION

In this study, it was concluded that geriatric fractures increase relatively in social isolation and do not show seasonal variations in our region. Another important result derived from our study is that, while the distal forearm, proximal humerus and ankle fractures caused by simple falls in partially more active geriatric individuals aged 65-75 years are associated with lower mortality rates, hip fractures are more often indoor fractures with higher mortality rates in older patients. With increasing age a good management strategy can be determined based on isolation, early treatment and discharge of these patients in pandemic periods and being very knowledgeable about the incidence of potentially mortal geriatric fractures.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Van Yüzüncü Yıl University Non-Invasive Clinical Research Ethics Committee (Permission granted: 16.10.2020, Decision no: 2020/07-02).

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

Referee Evaluation Process: Externally peer-reviewed.

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Orjinal Araştırma / Original Article

Effects of COVID-19 Pandemic on the Mental Health of Pregnant Women

COVID-19 Pandemisinin Gebe Ruh Sağlığı Üzerine Etkileri

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Abstract

Objective: The negative consequences of coronavirus disease 2019 (COVID-19) pandemic on the mental health of pregnant women and the mental disorders it may trigger pose risks for the physical, cognitive and psychological development of infants as well as having risks in terms of the general health and functionality of the mother. This study aimed to investigate the effects of COVID-19 pandemic on the mental health of pregnant women and to evaluate the prevalence of psychiatric symptoms.

Material and Method: The study included a total of 112 pregnant women who agreed to fill an online survey which was provided to them via e-mail. Online survey consisted of sociodemographic data form, questions related to COVID-19, Depression Anxiety Stress Scale-Short Form (DASS-21), and Posttraumatic Stress Disorder (PTSD) Checklist for Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition (DSM-5) (PCL-5).

Results: The mean age of the participants was 31.06 years. The DASS-21 subscale score for depression was 4.20 (±3.91) whereas it was 3.75 (±3.50) for the anxiety subscale and 5.68 (±3.81) for the stress subscale. Total PCL-5 score was 31.29 (±16.85). Those diagnosed with COVID-19 during the pandemic were observed to show a higher rate of anxiety symptoms. Those who believed that they needed professional support for mental health during the pandemic showed higher rates of depression, anxiety, and stress symptoms. The prevalence of PTSD symptoms were found to be higher among participants who were not health care professionals and who thought they needed professional support for mental health during the pandemic.

Conclusion: Determining the effects of the COVID-19 pandemic on the mental health of pregnant women will be important to put early intervention methods in action and implement evidence-based practices.

Keywords: Pregnant, COVID-19, mental health

Öz

Amaç: COVID-19 pandemisinin gebe ruh sağlığı üzerinde yaratabileceği olumsuz sonuçlar ve tetikleyebileceği ruhsal bozukluklar, annenin genel sağlığı ve işlevselliği açısından riskler barındırmasının yanında bebeklerin fiziksel, bilişsel ve psikolojik gelişimleri açısından da risk oluşturmaktadır. Bu çalışmada COVID-19 pandemisinin gebe ruh sağlığı üzerine etkilerini araştırmak ve psikiyatrik semptomların yaygınlığını değerlendirmek amaçlanmıştır.

Gereç ve Yöntem: Çalışmaya kendilerine e-mail yolu ile iletilen online anketi doldurmayı kabul eden 112 gebe dahil edildi. Online anket; sosyodemografik veri formu, COVID-19 ile ilgili sorular, Depresyon Anksiyete Stres Ölçeği-Kısa Form (DASS-21) ve DSM-5 için Travma Sonrası Stres Bozukluğu Kontrol Listesi 'nden (PCL-5) oluşmaktaydı.

Bulgular: Katılımcıların yaş ortalaması 31,06 idi. DASS-21 depresyon alt ölçek puanı 4.20 (±3,91), anksiyete alt ölçek puanı 3,75 (±3,50), ve stres alt ölçek puanı 5,68 (±3,81), PCL-5 toplam puanı ise 31,29 (±16,85) olarak saptandı. Pandemi sırasında COVID-19 tanısı alanların daha yüksek oranda anksiyete semptomları sergiledikleri; pandemi sürecinde ruh sağlığı açısından profesyonel bir destek alma ihtiyacı olduğunu düşünenlerin ise daha yüksek oranda depresyon, anksiyete ve stres semptomları sergiledikleri saptandı. Sağlık çalışanı olmayanların ve pandemi sürecinde ruh sağlığı açısından profesyonel bir destek alma ihtiyacı olduğunu düşünenlerin daha yüksek oranda travma sonrası stress bozukluğu semptomları sergilediği görüldü.

Sonuç: COVID-19 pandemisinin gebe ruh sağlığı üzerine etkilerini saptamak, erken müdahale yöntemlerini harekete geçirebilmek ve kanıta dayalı uygulamalar gerçekleştirebilmek adına önemli olacaktır.

Anahtar Kelimeler: Gebe, COVID-19, ruh sağlığı

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) was first reported in Wuhan, China in December 2019 and was declared as a pandemic by the World Health Organization (WHO) on 11 March 2020. The first COVID-19 case in Turkey was reported on 11 March 2020. As a major public health problem, the COVID-19 pandemic not only poses a major threat to human life but also significantly affects community mental health. Psychosocial stress factors that may be encountered during pandemics include health threats to ourselves and our loved ones, major changes in daily life routines, separation from family and friends, loss of income, economic impacts domestically and worldwide, disruptions in health services, and implementation of quarantine and social isolation measures.[1] During the pandemic, people face not only the risk of themselves becoming infected but also the burden of coping with the illness or death of their relatives. Fear of catching the disease, being worried about contracting the disease or family members contracting the disease, concerns regarding how the disease will progress, and uncertainty in the overall process are intense sources of anxiety and stress response is inevitable. Factors such as previous experiences, personality traits, gender, age, and medical history may be effective in the various mental reactions shown in such periods. There are many potential sources of stress with a potential effect on mental health in the context of the current COVID-19 pandemic. Along with these stressors; anxiety, depression, fear, psychological stress, post-traumatic stress symptoms, and sleep problems are observed during the COVID-19 pandemic.[2] As the negative effects of COVID-19 pandemic, which is widespread and has various effects, on the mental health of the community are so evident, it is possible to mention groups that can be considered special in terms of mental health, such as those with previously known psychiatric illnesses, children, individuals over 65 years of age, health care professionals or refugees. Pregnant women can also be considered as one of these special groups.[3]

Although most women consider pregnancy to be the most enjoyable period of their life, some women may experience periods that may result in various mental disorders, even in the normal course of pregnancy. Mental disorders that may be encountered during pregnancy pose risks for the physical, cognitive and psychological development of infants as well as having risks in terms of the general health and functionality of the mother. Results of meta-analysis on the mental disorders that may be encountered during pregnancy have shown that the prevalence of depression in the perinatal period is 11.9%.[4] whereas the prevalence of antenatal anxiety disorder is 15.2%.[5] The results of a systematic review and meta-analysis evaluating the perinatal consequences of anxiety during pregnancy have shown that anxiety during pregnancy increases the risk of spontaneous preterm birth, low birth weight, small for gestational age, and small head circumference.[6] Another meta-analysis has revealed that premature birth is associated with maternal depression.[7]

Pandemics that have affected the world, such as severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), has demonstrated that the mental health of pregnant women is more likely to be affected by such disease outbreaks.[8,9] The weakening of social support systems with the restriction measures taken, financial difficulties, risk of infection, disruptions in daily routine, and frightening information about the epidemic negatively affect maternal mental health during pregnancy. These potential sources of maternal stress have been identified as risk factors for mental health problems during the COVID-19 pandemic.[10] For these reasons, it can be said that pregnant women are in the higher risk group as their mental health is negatively affected during the COVID-19 pandemic.[11] In a study conducted by Saccone et al.[12] involving 100 pregnant women, the authors reported that the psychological effects of COVID-19 among pregnant women were moderate and two-thirds of the participants had higher anxiety levels than normal. According to the results of another cross-sectional study, the prevalences of anxiety and depression symptoms were found to be 34.4% and 39.2%, respectively.[13] Wu et al.[14] evaluated the mental health status of pregnant women before and after the pandemic and found that the rates of depressive symptom, anxiety scores, and self-harm thoughts of pregnant women were higher in the post-pandemic period compared to the pre-pandemic. The authors further reported that depressive symptoms increased among pregnant women as the number of COVID-19 cases, suspicious infection, and daily mortality rates increased.[14] Besides the results supporting that the COVID-19 pandemic causes anxiety and depressive symptoms in pregnant women, the presence of post-traumatic stress disorder (PTSD) symptoms have been also evaluated. In a study involving 1,123 women who were pregnant or recently gave birth during the COVID-19 pandemic, 10.3% of the participants were observed to have PTSD symptoms.[15] In another study comparing the women, who were pregnant during the COVID-19 pandemic, with those who were pregnant before the COVID-19 pandemic; the prevalence of anxiety, depression, dissociative, and PTSD symptoms were observed to be higher in women who were pregnant during the pandemic period.[16] In addition to the effects of the pandemic process on mental health during pregnancy, the rates of depression and anxiety in the early postpartum period are reported to be also high among women who are pregnant during the outbreak.[17]

The negative consequences of COVID-19 pandemic on the mental health of pregnant women and the mental disorders it may trigger pose risks for the physical, cognitive and psychological development of infants as well as having risks in terms of the general health and functionality of the mother. Existing data on the effects of COVID-19 on the mental health of pregnant women are limited. This study aimed to investigate the effects of COVID-19 pandemic on the mental health of pregnant women and to evaluate the prevalence of psychiatric symptoms.

MATERIALS AND METHODS

Participants

A total of 113 women who were over 18 years of age, agreed to answer the online questionnaire prepared for the study and were pregnant at the time of completing the online questionnaire, were literate to answer the questions, were not mentally retarded, and did not have a neurological disease affecting cognitive functions were included the study. One of these participants was excluded from the study due to providing incomplete data. Therefore, 112 pregnant women were taken into account for further analyses.

Procedure

The study was conducted as an online cross-sectional study and conducted between January 1 and February 1, 2021. The online questionnaire created by the researchers using Google Forms was sent to the participants via e-mail. The first part of the questionnaire consisted of questions about socio-demographic characteristics and COVID-19. It was followed by the Depression Anxiety Stress Scale–Short Form (DASS-21) and PTSD Checklist for Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition (DSM-5) (PCL-5).

Instruments of Assessment

Depression Anxiety Stress Scale-21- Short Form (DASS-21): This scale has been developed from DASS-42, the longer version.[18,19] The short-form consists of three subscales, each containing seven questions. There are a total of 21 questions aiming to measure depression, anxiety, and stress levels. It is a four-point Likert-type scale (0="never", 1="sometimes and occasionally", 2="quite often", and 3="always"). The Turkish version of the scale was used in this study.[20]

PTSD Checklist for Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition (DSM-5) (PCL-5): It is a five-point Likert-type (0="Not at all", 1="A little bit", 2="Moderately", 3="Quite a bit" and 4="Extremely") scale designed to measure PTSD symptoms and the severity of these symptoms according to DSM-5 diagnostic criteria.[21] The 20-item scale has four subscales namely re-experiencing, avoidance, negative alterations, and hyper-arousal. The scale also provides a total score and cut-off score for evaluating the frequency of symptoms. In the Turkish population, the cut-off point of the scale was found to be 48 for community samples. The Turkish version of the scale was used in this study.[22]

Statistical Analysis

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 15.0 software. Descriptive statistical methods (such as mean, standard deviation, median, minimum, maximum, frequency, percentage) were used for the expression of data. Mann Whitney U test was used for the comparison of two groups whereas the Kruskal-Wallis test and post-hoc Dunn test were used for the comparisons of more than two groups. Spearman's correlation coefficient was used for correlation analysis. Results were evaluated at a 95% confidence interval and a p value of <0.05 was considered statistically significant.

Ethics Statement: Approval for the study was granted by the Sakarya University Ethical Committee with Approval no:71522473/050.01.04/631, dated December 28, 2020. All patients signed informed consent for participation in this study, and their anonymity is preserved.

RESULTS

A total of 112 pregnant women with a mean age of 31.06 (±4.19) years were included in the study. The week of gestation ranged from five to 40 weeks, and the number of children ranged from zero to two. All participants were married and most of them (81.3%) were living in a metropolitan area. Majority of the participants (93.8%) were university graduates. Of pregnant women, 25.9% were health care professionals, 8.9% stated that they were working actively during the pandemic. This rate was 20.7% among health care professionals and 4.6% among those who were not health care professionals. Of the pregnant women, 3.6% stated that they were still smoking but they decreased their consumption during the pandemic. None of them were using alcohol or drugs. There was a systemic disease (thyroid disease being the most common)requiring follow-up during pregnancy in 13.4% of the pregnant women while 18.8% had previously applied to a psychiatry clinic and 7.1% had a diagnosed mental illness (anxiety being the most common). The proportion of participants diagnosed with COVID-19 during the pandemic was 11.6% (n=13), and only one of these patients received inpatient treatment. Of the participants, 69.6% had a relative diagnosed with COVID-19 during the pandemic and 46.4% knew someone who died due to COVID-19. The rate of pregnant women who thought they need professional support for mental health during the pandemic was 22.3% and the rate of those who felt anxious about the pregnancy process due to the COVID-19 pandemic was found to be 73.2% (**Table 1**).

Scores obtained from DASS-21 and PCL-5 scales are shown in **Table 2**. The DASS-21 subscale score for depression was 4.20 (±3.91) whereas it was 3.75 (±3.50) for the anxiety subscale and 5.68 (±3.81) for the stress subscale. Total PCL-5 score was 31.29 (±16.85).

The comparison of DASS-21 scale scores according to the sociodemographic characteristics of the participants revealed that there was no statistically significant difference in DASS-21 subscale scores according to the week of gestation, number of children, occupation, working during the epidemic, presence of a systemic disease requiring follow-up during pregnancy, previous application to a psychiatry clinic, a diagnosed psychiatric illness, having a relative diagnosed with COVID-19, knowing someone who died due to COVID-19, and feeling anxious about pregnancy due to COVID-19 pandemic (p>0.05). Participants who were living in districts and smaller settlements were observed to have statistically significantly higher DASS-21 anxiety and stress subscales scores compared

Table 1. Demographic Characteristics of Participants

	mean/n	sd/%
age	31.06	4.19
week of gestation		
first trimester (1–13 weeks)	12	10.7
second trimester (14–26 weeks)	38	33.9
third trimester (27–40 weeks)	62	55.4
number of children		
0	69	61.6
1	31	27.7
2	12	10.7
place of residence		
metropolitan city	91	81.3
other provinces	12	10.7
districts and smaller settlements	9	8.0
educational status		
primary school graduate	1	0.9
secondary school graduate	1	0.9
high school	5	4.5
university graduate	105	93.8
profession		
health care professional	29	25.9
not a health care professional	83	74.1
employment status during the pandemic		
I am not working	45	40.2
I am working from home	34	30.4
My working hours are flexible	22	19.6
I am actively going to work	10	8.9
no answer	1	0.9
health care professional		
I am not working	10	34.5
I am working from home	1	3.4
My working hours are flexible	11	37.9
I am actively going to work	6	20.7
no answer	1	3.4
not a health care professional		
I am not working	35	42.2
I am working from home	33	39.8
My working hours are flexible	11	13.3
I am actively going to work	4	4.6
having systemic disease requiring follow-up during pregnancy		
yes	15	13.4
Thyroid diseases	11	73.3
MS	2	13.3
Allergy	1	6.7
Rheumatism	1	6.7
no	97	86.6
smoking		
still smoking but less during the pandemic	4	3.6
no	108	96.4
applying to psychiatry in the past		
yes	21	18.8
no	91	81.3
a diagnosed psychiatric illness		
yes	8	7.1
anxiety disorder	5	62.5
depressive disorder	2	25.0
anorexia nervosa	1	12.5
no	104	92.9
Diagnosed with COVID-19 during the pandemic		
yes	13	11.6
no	99	88.4
Type of treatment for those diagnosed with COVID-19 during the pandemic		
did not take medication	12	92.3
inpatient treatment	1	7.7
having a relative diagnosed with COVID-19 during the pandemic		
yes	78	69.6
no	34	30.4
knowing someone died of COVID-19 during the pandemic		
yes	52	46.4
no	60	53.6
thinking about receiving professional mental health support during the pandemic process		
yes	25	22.3
no	87	77.7
feeling anxious about pregnancy due to COVID-19 pandemic		
yes	82	73.2
no	30	26.8

Note. Results are presented as mean (standard deviation) or count (percentage).

Table 2. DASS-21 and PCL-5 scale scores of the participants

	Mean	SD	median	min	max
Total DASS-21 score					
depression subscale score	4.20	3.91	3	0	14
anxiety subscale score	3.75	3.50	3	0	14
stress subscale score	5.68	3.81	5.5	0	16
Total PCL-5 score	31.29	16.85	28	1	67
re-experiencing	6.82	4.11	7	0	15
avoidance	3.31	2.07	3	0	8
negative alterations	11.73	6.34	11.5	0	25
hyper-arousal	9.42	5.54	8	0	23

Note. DASS-21: Depression Anxiety Stress Scale-21, PCL-5: Posttraumatic Stress Disorder (PTSD) Checklist for Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition

to those who were living in other settlements (p=0.020 and p=0.028, respectively). The anxiety subscale score was found to be statistically significantly higher in those who were diagnosed with COVID-19 during the pandemic than those who were not (p=0.23). All DASS-21 subscale scores were significantly higher in those who thought they needed professional support for mental health during the pandemic than those who did not (**Table 3**).

The comparison of PCL-5 scale scores according to the sociodemographic characteristics of the participants revealed that there was no statistically significant difference in PCL-5 subscale scores according to the week of gestation, number of children, place of residence, working during the epidemic, presence of a systemic disease requiring follow-up during pregnancy, previous application to a psychiatry clinic, a diagnosed psychiatric illness, being diagnosed with COVID-19 during the pandemic, having a relative diagnosed with COVID-19, knowing someone who died due to COVID-19, and feeling anxious about pregnancy due to COVID-19 pandemic (p>0.05). The PCL-5 scale score was found to be statistically significantly higher in participants who were health care professionals than those who were not and in those who thought they needed professional support for mental health during the pandemic than those who did not (p=0.041 and p=0.001, respectively) (**Table 4**).

When the sociodemographic characteristics of the participants and PCL-5 subscale scores compared, no statistically significant

difference was observed in PCL-5 subscale scores according to the week of gestation, number of children, place of residence, working during the epidemic, presence of a systemic disease requiring follow-up during pregnancy, previous application to a psychiatry clinic, a diagnosed psychiatric illness, knowing someone who died due to COVID-19, and feeling anxious about pregnancy due to COVID-19 pandemic (p>0.05). Negative alterations subscale score was found to be statistically significantly higher among those who were not health care professionals than health care professionals (p=0.047). The re-experiencing subscale score was statistically significantly higher in those who were diagnosed with COVID-19 during the pandemic compared to those who were not and in those who had a relative diagnosed with COVID-19 compared to those who do not (p=0.046 and p=0.042, respectively). All PCL-5 subscale scores were significantly higher in those who thought they needed professional support for mental health during the pandemic than those who did not (**Table 5**).

Table 3. Comparison of DASS-21 subscale scores according to the characteristics of the participants

	depression subscale score				anxiety subscale score				stress subscale score			
	Mean	SD	median	p	mean	SD	median	p	mean	SD	median	p
week of gestation												
first trimester (1–13 weeks)	4.58	4.68	3		3.92	3.90	2		5.83	4.82	4	
second trimester (14–26 weeks)	3.21	3.60	1.5	0.191	3.34	3.10	2.5	0.839	5.16	3.48	4	0.434
third trimester (27–40 weeks)	4.73	3.89	4		3.97	3.68	3		5.97	3.82	6	
number of children												
0	4.23	3.90	3		4.28	3.65	4		5.78	3.91	5	
1	3.84	3.68	3	0.830	2.71	2.88	2	0.116	5.26	3.43	5	0.801
2	4.92	4.74	3.5		3.42	3.73	3		6.17	4.34	6.5	
place of residence												
metropolitan city	4.14	3.86	3		3.52	3.42	2		5.40	3.49	6	
other provinces	3.58	3.78	2	0.657	3.00	2.73	2	0.020	5.08	4.74	4	0.028
districts and smaller settlements	5.56	4.75	7		7.11	3.69	7		9.33	4.09	9	
profession												
health care professional	4.28	4.04	3	0.926	3.24	2.90	2	0.623	5.59	4.00	5	0.802
not a health care professional	4.17	3.89	3		3.93	3.69	3		5.71	3.76	6	
employment status during the pandemic												
I am not working	3.96	4.25	2		3.62	3.43	3		5.24	3.40	5	
I am working from home	4.06	3.80	3	0.522	4.06	3.98	2	0.844	5.59	4.38	4	0.439
My working hours are flexible	4.64	3.72	4		3.41	3.42	2.5		6.36	3.89	6	
I am actively going to work	4.90	3.70	5		4.10	2.73	4		6.60	3.63	6.5	
having systemic disease requiring follow-up during pregnancy												
yes	4.87	4.32	3	0.475	4.00	3.68	3	0.673	6.53	3.60	6	0.289
no	4.09	3.86	3		3.71	3.49	3		5.55	3.84	5	
applying to psychiatry in the past												
yes	4.71	4.43	4	0.617	4.62	3.80	5	0.216	6.52	4.15	6	0.321
no	4.08	3.80	3		3.55	3.42	2		5.48	3.72	5	
a diagnosed psychiatric illness												
yes	3.75	4.27	2	0.724	3.50	3.63	2.5	0.878	6.25	4.65	5.5	0.829
no	4.23	3.90	3		3.77	3.51	3		5.63	3.76	5.5	
Diagnosed with COVID-19 during the pandemic												
yes	6.38	4.70	6	0.060	5.62	3.43	5	0.023	7.00	2.20	7	0.067
no	3.91	3.73	3		3.51	3.45	2		5.51	3.94	5	
having a relative diagnosed with COVID-19 during the pandemic												
yes	4.05	3.73	3	0.662	3.60	3.55	2.5	0.310	5.51	3.21	5.5	0.995
no	4.53	4.35	3		4.09	3.41	3		6.06	4.95	5	
knowing someone died of COVID-19 during the pandemic												
yes	3.79	3.59	3	0.313	3.46	3.49	2.5	0.258	5.75	3.85	6	0.888
no	4.55	4.17	3		4.00	3.51	3		5.62	3.80	5	
Thinking about receiving professional mental health support during the pandemic												
yes	6.92	4.61	6	0.0003	5.56	3.80	6	0.004	7.48	3.47	9	0.005
no	3.41	3.33	2		3.23	3.25	2		5.16	3.76	5	
feeling anxious about pregnancy due to COVID-19 pandemic												
yes	4.11	3.62	3	0.819	3.71	3.49	3	0.794	5.85	3.68	6	0.324
no	4.43	4.69	2		3.87	3.57	2		5.20	4.16	4	

Note. DASS-21: Depression Anxiety Stress Scale-21

Table 4. Comparison of total PCL-5 scores according to the characteristics of the participants

	Mean	SD	median	p
week of gestation				
first trimester (1–13 weeks)	32.50	13.98	33	
second trimester (14–26 weeks)	27.61	16.76	25.5	0.265
third trimester (27–40 weeks)	33.31	17.27	30.5	
number of children				
0	32.83	18.04	30	
1	27.42	14.37	26	0.348
2	32.42	15.23	35.5	
place of residence				
metropolitan city	31.99	16.62	29	
other provinces	27.17	15.79	20	0.527
districts and smaller settlements	29.67	21.34	22	
profession				
health care professional	25.72	13.83	24	0.041
not a health care professional	33.23	17.45	30	
employment status during the pandemic				
unemployed	27.87	19.13	22	
working from home	33.24	13.12	31	0.187
flexible working	34.41	19.12	31	
actively working	34.30	10.40	37.5	
having systemic disease requiring follow-up during pregnancy				
yes	31.00	14.22	37	0.912
no	31.33	17.29	27	
applying to psychiatry in the past				
yes	31.14	15.77	30	0.768
no	31.32	17.18	27	
a diagnosed psychiatric illness				
yes	30.62	17.19	26.5	0.874
no	31.34	16.91	28	
Diagnosed with COVID-19 during the pandemic				
yes	40.38	21.30	57	0.076
no	30.09	15.93	27	
having a relative diagnosed with COVID-19 during the pandemic				
yes	32.69	16.63	29	0.201
no	28.06	17.16	23.5	
knowing someone died of COVID-19 during the pandemic				
yes	30.15	17.61	27.5	0.460
no	32.27	16.25	28	
Thinking about receiving professional mental health support during the pandemic				
yes	41.32	16.42	45	0.001
no	28.40	15.93	26	
feeling anxious about pregnancy due to COVID-19 pandemic				
yes	31.59	16.41	28	0.660
no	30.47	18.27	27.5	

Note. PCL-5: Posttraumatic Stress Disorder (PTSD) Checklist for Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition

DISCUSSION

Effects of the pandemic on the mental health of pregnant women are as very important as the effects of COVID-19 on the physical health of pregnant women and babies. In the present study investigating the effects of the COVID-19 pandemic on the mental health of pregnant women, the DASS-21 depression subscale score was 4.20 (±3.91), the anxiety subscale score was 3.75 (±3.50), and the stress subscale score was 5.68 (±3.81), and the PCL-5 total score was 31.29 (±16.85). Anxiety and stress symptoms were higher among those who were living in districts and smaller settlements whereas those diagnosed with COVID-19 during the pandemic were observed to have higher anxiety symptoms and those who thought they needed professional support for mental health during the pandemic had higher depression, anxiety and stress symptoms. The prevalence of PTSD symptoms were found to be higher among participants who were not health care professionals and who thought they needed professional support for mental health during the pandemic. Women who were not health care professionals were observed to exhibit symptoms of PTSD listed under the negative alterations more while those who were diagnosed with COVID-19 during the pandemic and those who had a relative diagnosed with COVID-19 were observed to exhibit re-experiencing symptoms more. Those who thought they needed professional support for mental health during the pandemic process were found to have higher PTSD symptoms in all areas.

The evaluation of studies investigating the effects of pandemic on the mental health of pregnant women at the level of anxiety, depression, stress and PTSD symptoms shows that the results generally support that mental health is affected negatively; however, there are differences between the rates. In a study by Berhelot et al.[16] involving two groups who were pregnant before the COVID-19 pandemic and who were pregnant during the pandemic period, those who were pregnant during the pandemic period showed more severe depression, anxiety, and PTSD symptoms. Results of a cross-sectional study involving a total of 819 participants (544 pregnant women and 315 non-pregnant women) revealed that the prevalence of depression, anxiety, physical discomfort, insomnia, and PTSD symptoms in the pregnant group were 5.3%, 6.8%, 2.4%, 2.6%, and 0.9%, respectively, while these rates were 17.5%, 2.5%, 5.4%, and 5.7% in the non-pregnant group, respectively. Following the adjustment for other covariates, the authors observed that pregnancy was associated with a reduced risk of depression (OR = 0.23; 95% CI: 0.12–0.45), anxiety (OR = 0.26; 95% CI: 0.16–0.42), insomnia (OR = 0.19; 95% CI: 0.06–0.58), and PTSD (OR = 0.15; 95% CI: 0.04–0.53).[23] A meta-analysis including eight studies showed that the prevalence of anxiety symptoms was significantly increased during the COVID-19 pandemic compared to before and there was an increase in scale scores related to depressive complaints; however, it was suggested that this increase was not significant compared to the pre-pandemic period.[8] In the present study, 73.2% of the pregnant women stated that they felt anxious about the pregnancy process due to the COVID-19 pandemic and their scale scores showed that they exhibited subthreshold depression, anxiety, stress, and PTSD symptoms. These differences in results may be due to the fact that the evaluation scales used are different, and the studies are mostly cross-sectional and have been conducted at different stages of the epidemic.

In a study by Saccone et al.[12] anxiety levels were higher and the psychological impact of the COVID-19 outbreak was more severe in women in the first trimester of pregnancy compared to those who were in the second or third trimester

Table 5. Comparison of PCL-5 subscale scores according to the characteristics of the participants

	re-experiencing score				avoidance subscale score				negative alterations subscale score				hyper-arousal subscale score			
	Mean	SD	median	p	mean	SD	median	p	mean	SD	median	p	mean	SD	median	p
week of gestation																
first trimester (1–13 weeks)	7.58	4.36	9		3.42	2.19	4		12.17	6.10	10		9.33	3.58	7	
second trimester (14–26 weeks)	5.95	4.08	4.5	0.220	2.95	2.00	3	0.425	10.26	5.90	10	0.249	8.45	5.71	7.5	0.299
third trimester (27–40 weeks)	7.21	4.07	7		3.52	2.09	4		12.55	6.57	13		10.03	5.73	9	
number of children																
0	7.32	4.28	8		3.58	2.19	4		12.28	6.79	12		9.65	5.81	8	
1	5.87	3.82	5	0.268	2.74	1.90	2	0.200	10.26	5.46	10	0.331	8.55	5.01	7	0.581
2	6.42	3.68	6		3.25	1.60	4		12.42	5.50	13		10.33	5.47	10	
place of residence																
metropolitan city																
other provinces	7.04	4.13	7	0.490	3.37	1.98	4	0.697	11.91	6.34	12	0.567	9.66	5.49	9	0.565
districts and smaller settlements	5.58	3.87	4.5		3.17	2.25	2		10.00	4.86	8.5		8.42	5.55	7	
	6.22	4.38	4		2.89	2.89	1		12.22	8.23	10		8.33	6.44	7	
profession																
health care professional	5.72	3.32	5	0.110	2.79	1.76	2	0.120	9.52	5.02	9	0.047	7.69	5.20	7	0.056
not a health care professional	7.20	4.31	7		3.49	2.15	4		12.51	6.59	13		10.02	5.56	9	
employment status during the pandemic																
I am not working	6.04	4.48	5		2.82	2.28	2		10.60	7.32	9		8.40	5.88	7	
I am working from home	7.41	3.63	8	0.346	3.65	1.65	4	0.193	12.26	5.46	12.5	0.312	9.91	4.33	10	0.404
My working hours are flexible	7.55	4.44	7		3.64	2.40	3		12.68	6.33	13		10.55	6.82	10	
I am actively going to work	7.30	2.58	7.5		3.90	1.10	4		13.10	4.23	12.5		10.00	4.78	9	
having systemic disease requiring follow-up during pregnancy				0.735				0.629				0.703				0.827
yes	7.00	3.85	9		3.07	2.05	4		11.87	4.84	14		9.07	4.96	7	
no	6.79	4.17	6		3.35	2.08	3		11.71	6.56	10		9.47	5.65	8	
applying to psychiatry in the past																
yes	7.05	3.58	8	0.759	3.38	1.75	4	0.786	11.71	6.25	10	0.829	9.00	5.05	9	0.931
no	6.77	4.24	6		3.30	2.15	3		11.74	6.39	12		9.52	5.67	8	
a diagnosed psychiatric illness																
yes	7.50	4.28	6	0.626	3.50	2.00	3	0.754	11.37	6.30	9.5	0.799	8.25	5.15	8	0.606
no	6.77	4.12	7		3.30	2.08	3		11.76	6.37	12		9.51	5.58	8	
Diagnosed with COVID-19 during the pandemic																
yes	9.15	5.16	13	0.046	4.08	2.50	6	0.113	15.23	8.21	22	0.075	11.92	5.91	16	0.087
no	6.52	3.88	6		3.21	2.00	3		11.27	5.95	10		9.09	5.44	8	
having a relative diagnosed with COVID-19 during the pandemic				0.042				0.299				0.657				0.148
yes	7.33	4.07	7		3.44	2.04	4		11.97	6.22	11.5		9.95	5.53	9	
no	5.65	4.02	4		3.03	2.14	3		11.18	6.66	11		8.21	5.45	7	
knowing someone died of COVID-19 during the pandemic																
yes	6.23	4.15	5	0.163	3.13	2.12	3	0.378	11.13	6.49	10.5	0.387	9.65	5.97	9	0.865
no	7.33	4.05	8		3.47	2.03	4		12.25	6.20	12.5		9.22	5.18	8	
Thinking about receiving professional mental health support during the pandemic																
yes	9.44	3.69	10	0.0003	4.44	2.00	5	0.002	15.56	6.08	16	0.001	11.88	5.67	13	0.015
no	6.07	3.93	5		2.99	1.99	3		10.63	6.00	10		8.71	5.33	8	
feeling anxious about pregnancy due to COVID-19 pandemic				0.784				0.526				0.688				0.974
yes	6.87	3.90	7		3.40	2.02	4		11.84	5.96	12		9.48	5.65	8	
no	6.70	4.72	5		3.07	2.23	3		11.43	7.37	10		9.27	5.33	8.5	

Note. PCL-5: Posttraumatic Stress Disorder (PTSD) Checklist for Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition

of pregnancies. In the present study, there was no statistically significant difference in terms of DASS-21 and PLC-5 scale scores according to the week of gestation.

Interestingly, the results of the present study showed that the prevalence of PTSD symptoms was higher among those who were not health care professionals. In many studies conducted during the COVID-19 pandemic, in which health care professionals who were playing an active role in combating pandemic and at higher risk of being infected were included, this group were reported to have significantly higher depression, anxiety and PTSD symptoms compared to the normal population.[24-26] The differences in the present results may be attributed to the fact that the occupational distribution of the study population is not homogeneous and that the group mostly consists of those who are not health care professionals.

Furthermore, people infected with COVID-19 are exposed to many stressors and traumatic events, such as hospitalization, isolation, infection or death of their relatives, besides the symptoms of the disease. In a cross-sectional study involving patients who were hospitalized due to COVID-19 infection and discharged, the prevalence of moderate-to-severe anxiety, moderate-to-severe depression, and PTSD was found to be 10.4%, 19% and 12.4%, respectively.[27] Another study involving 714 individuals who were hospitalized due to COVID-19 infection reported the prevalence of significant PTSD symptoms associated with COVID-19 to be 96.2%.[28] In another study involving 307 patients who were hospitalized due to COVID-19 infection, the authors reported that 18.6% of the participants exhibited depressive symptoms and 13.4% exhibited anxiety symptoms.[29] Compatible with the literature, we found that anxiety symptoms were higher in those diagnosed with COVID-19 during the pandemic. Furthermore, participants who were diagnosed with COVID-19 during the pandemic and those who had a relative diagnosed with COVID-19 exhibited the symptoms of re-experiencing more.

Studies have shown that psychiatric symptoms worsen in patients with previously known mental disorders.[30,31] Berthelot et al.[16] reported that among women who were pregnant during the COVID-19 pandemic, those with a previous psychiatric diagnosis exhibited a higher rate of stress and psychiatric symptoms. In the present study, the rate of those with a previous psychiatric diagnosis was quite low (7.1%). The comparison of the scale scores showed that there was no statistically significant difference between these participants and those without a known psychiatric disorder. However; depression, anxiety, stress, and PTSD symptoms were observed to be higher among women who thought they needed professional support for mental health during the pandemic. Given that these individuals may be more likely to receive a diagnosis when they apply to a psychiatry outpatient clinic, we can say that this is an expected finding.

This study has some limitations. First of all, it was designed as a cross-sectional study and therefore, a cause-effect analysis could not be performed among study variables. Other limitations include collecting data with an online questionnaire using self-report scales and not conducting a diagnostic clinical interview. On the other hand, the fact that it is one of the few studies investigating the effects of the COVID-19 pandemic on the mental health of pregnant women in Turkey is one of its strengths. Most of the studies on COVID-19 in pregnancy have focused on the physical effects of the pandemic on infected mothers and probability of transmission of the virus from mother to baby. Mental health problems of pregnant women are just as important as physical problems and should not be ignored.

CONCLUSION

This study has provided a cross-sectional overview of the effects of the COVID-19 pandemic on the mental health of pregnant women. In conclusion, pregnant women diagnosed with COVID-19 during the pandemic have been observed to exhibit a higher rate of anxiety symptoms and those who believe that they need professional support for mental health during the pandemic show higher rates of depression, anxiety, and stress symptoms. The prevalence of PTSD symptoms has been observed to be higher among participants who are not health care professionals and who believe they need professional support for mental health during the pandemic. The negative consequences of COVID-19 pandemic and the mental disorders it may trigger pose risks for the physical, cognitive and psychological development of infants as well as having risks in terms of the general health and functionality of the mother. Therefore, determining the effects of the COVID-19 pandemic on the mental health of pregnant women will be important to put early intervention methods in action and implement evidence-based practices.

ETHICAL DECLARATIONS

Ethics Committee Approval: Approval for the study was granted by the Sakarya University Ethical Committee with Approval no:71522473/050.01.04/631, dated December 28, 2020.

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

Referee Evaluation Process: Externally peer-reviewed.

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Orjinal Araştırma / Original Article

Effects of Perinatal Factors on Platelet Indices in Late Preterm and Term Newborns

Geç Preterm ve Term Yenidoğanlarda Perinatal Faktörlerin Trombosit İndeksleri Üzerindeki Etkileri

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Abstract

Aim: This study aimed to compare platelet indices between late preterm and term newborns, and to analyze their relationship with perinatal conditions.

Material and Method: Ninety-eight late preterm and 102 term newborns admitted to the neonatal intensive care unit between 2018 and 2020 were retrospectively evaluated. Platelet indices including platelet count (PLT), mean platelet volume (MPV), plateletcrit (PCT), and platelet distribution width (PDW) were measured in blood samples taken on the first day of life.

Results: There was no significant difference in the PLT, MPV, PCT, and PDW values between late preterm and term newborns. In late preterm newborns, multivariable analysis showed that maternal hypertension was significantly related to lower PLT (p=0.001). In term newborns, multivariable analysis showed that being small for gestational age (SGA), male sex, and maternal hypertension were significantly related to lower PLT (p<0.001, p=0.001 and p=0.017, respectively). In addition, SGA and male sex were related to lower PCT (p=0.001). In all studied patients, MPV was significantly different between infants with and without prolonged rupture of membrane (PROM) (9.8 fL vs. 9.2 fL, p=0.001).

Conclusion: The obtained results show that various perinatal features influence the platelet indices in late preterm and term newborns.

Keywords: Platelet indices, late preterm infants, platelet count

Öz

Amaç: Bu çalışmanın amacı geç preterm yenidoğanlar ve term yenidoğanlarda trombosit indekslerini karşılaştırmak ve perinatal faktörlerle ilişkisini incelemektir.

Gereç ve Yöntem: 2018-2020 yılları arasında akademik bir merkezin Yenidoğan Yoğun Bakım Ünitesine kabul edilen 98 geç preterm ve 102 term yenidoğan retrospektif olarak değerlendirildi. Yaşamın ilk gününde alınan kan örneklerinde trombosit sayısı (PLT), ortalama trombosit hacmi (MPV), plateletkrit (PCT) ve trombosit dağılım genişliği (PDW) dahil olmak üzere trombosit indeksleri ölçüldü.

Bulgular: Geç prematüre ve term yenidoğanlar arasında PLT, MPV, PCT ve PDW değerleri açısından anlamlı fark yoktu. Geç prematüre yenidoğanlarda, çok değişkenli analiz, maternal hipertansiyonun düşük PLT ile anlamlı şekilde ilişkili olduğunu gösterdi (p=0,001). Term yenidoğanlarda, çok değişkenli analiz, gebelik yaşına küçük (SGA) olmak, erkek cinsiyet ve maternal hipertansiyonun düşük PLT ile anlamlı şekilde ilişkili olduğunu gösterdi (sırasıyla p<0,001, p=0,001 ve p=0,017). Ayrıca, SGA ve erkek cinsiyet daha düşük PCT ile ilişkiliydi (p=0,001). Çalışılan tüm hastalarda, MPV, uzamış membran rüptürü (PROM) olan ve olmayan bebekler arasında önemli ölçüde farklıydı (9,8 fL ve 9,2 fL, p=0,001).

Sonuç: Elde edilen sonuçlar, çeşitli perinatal özelliklerin geç preterm ve term yenidoğanların trombosit indekslerini etkilediğini göstermektedir.

Anahtar Kelimeler: Trombosit indeksleri, geç preterm, trombosit sayısı

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INTRODUCTION

Platelets have a role in various physiological and pathological process. The main function of platelets is to provide hemostasis, and they also have several immunological functions.[1-3] Platelet indices including total platelet count (PLT), mean platelet volume (MPV), plateletcrit (PCT), and platelet distribution width (PDW) are biomarkers of platelet activation. Platelet production is characterized by proliferation and differentiation of megakaryocytes with stimulation of thrombopoietin. Newborns, particularly preterm newborns have immature platelets. Several studies have shown that platelet count decreases with gestational age and birth weight.[4] Previous research has shown that the risk of thrombocytopenia increases almost 2.5 times in low birth weight infants.[5] Besides, MPV, PCT and PDW have been related to neonatal sepsis and intraventricular hemorrhage.[6,7] Among neonates born <32 weeks' gestation, higher MPV has been related with mortality.[8]

Late preterm newborns (LPN), born between 34 and 36 weeks of gestation, constitute 75% of all preterm births, and they are the fastest growing preterm group.[9] Although generally not considered to be high risk, late-preterm infants have increased mortality and morbidity compared to term infants.[10] A recent study showed reduced PLT and PCT in LPN compared with term newborns (TN).[11] However, studies regarding the impact of perinatal conditions on platelet indices in late preterm and term newborns are limited. Additionally, some studies have found that maternal complications including prolonged rupture of membrane (PROM) and maternal hypertension (HT) can affect platelet indices.[12,14] In this study, we aimed to analyze the relationship between perinatal factors and platelet indices at birth in late preterm and term newborns.

MATERIAL AND METHOD

This study was approved by Hospital Ethics Committee (No: 2021/0063). Medical records of 1118 newborns admitted to the neonatal intensive care unit of an academic center between January 2019 and December 2020 were retrospectively screened. Of these infants, 98 late preterm and 102 term (born at 37 and 41 weeks of gestation) newborns were included in the study. Exclusion criteria were congenital infections, alloimmune thrombocytopenia, major congenital malformations, metabolic diseases, clinically or laboratory confirmed early onset sepsis, and infants not tested within 6 hours of birth.

Blood samples were obtained from peripheral veins during admission. For each patient, PLT, MPV, PCT, and PDW values were recorded. Patient's demographics including sex, birth weight, mode of delivery, Apgar scores at 5 minutes as well as prenatal factors including maternal HT and PROM were noted. Gestational age was estimated based on the last menstrual period and ultrasound in the first trimester. Small for gestational age (SGA) was defined as birth weight below the 10th percentile according to Fenton growth charts.

Statistical analysis

Data were analyzed by SPSS version 22 (SPSS Inc., Chicago, IL). Platelet indices were presented as median and interquartile range (IQR) as non-normality of distribution and compared by Mann–Whitney U test. Categorical variables were compared by Chi-squared test. Correlations between platelet indices and gestational age, birth weight and 5 minute Apgar scores were analyzed by using Spearman's rank test. Variables with $p<0.05$ in univariate tests were included in multivariate linear regression. Significance was set at $p<0.05$.

RESULTS

The median gestational age was 35.4 (IQR: 35-36.2) weeks in late preterm and 38.6 (IQR: 37.6-39.3) weeks in term newborns. Birth weight was 2340.5 (IQR:2020-2765) g and 2840 (IQR: 2595-3325) g in late preterm and term newborns, respectively.

Table 1 describes the platelet indices in LPN and TN. There were no significant differences in platelet indices between LPN and TN. No significant correlation was observed between gestational age, birth weight and PLT (**Figure 1** and **Figure 2**).

Table 1. Platelet indices in late preterm and term newborns

	Late premature (n=98) Median (IQR)	Term (n=102) Median (IQR)	P value
GA (weeks)	35.4 (34.6-36.2)	38.8 (38-39.3)	<0.001
BW (grams)	2340.3 (2020-2765)	2840 (2595-3325)	<0.001
SGA, n (%)	29 (29.6%)	20 (19.6%)	0.101
PLT (×103/μL)	250 (211-326)	262.5 (225-309)	0.526
MPV (fL)	9.3 (8.9-9.7)	9.3 (9-9.6)	0.674
PCT (%)	0.3 (0.2-0.3)	0.3 (0.2-0.3)	0.372
PDW	16.3 (16.1-16.5)	16.3 (16.1-16.4)	0.976

GA, gestational age; BW, birth weight; PLT, platelet count; MPV, mean platelet volume; PCT, plateletcrit; PDW, platelet distribution width; IQR, median interquartile range, SGA, small for gestational age.

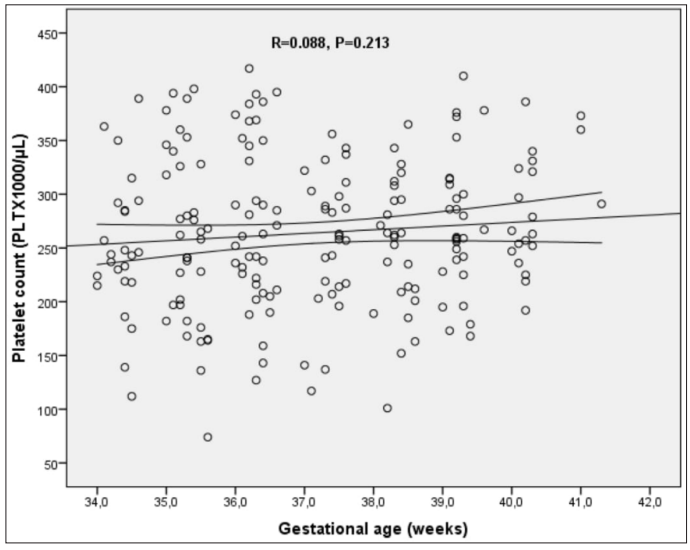

Figure 1. Correlation between platelet count and gestational age. R is Spearman's correlation coefficient.

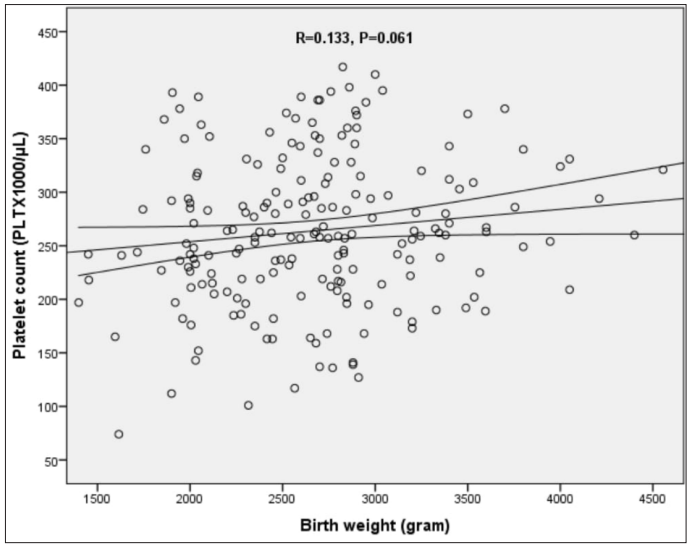

Figure 2. Correlation between platelet count and birth weight. R is Spearman's correlation oefficient.

Table 2 and **Table 3**, respectively, describes the platelet indices according to patient's characteristics in late preterm and term newborns. In late preterm newborns, infants of hypertensive mothers showed significantly lower PLT (208x10^3/µL vs. 265x10^3/µL, p=0.035) and PCT (0.2% vs. 0.3%, p=0.047) compared to infants of mothers without HT. Infants born by cesarean section had a lower PLT (236.5x10^3/µL vs. 272.5208x10^3/µL, p=0.031). Compared to non-SGA infants, SGA infants presented lower PLT (203x10^3/µL vs. 263x10^3/µL, p=0.030) and PCT (0.2% vs. 0.2%, p=0.033). Multivariate analysis revealed that Maternal HT was significantly related to lower PLT (β=-0.336, p=0.001) while no factors related to PCT and PDW were found.

In term newborns, males presented lower PLT (258x10^3/µL vs. 277x10^3/µL, p=0.013) compared to female newborns. Multivariate analysis showed that being SGA (β=-0.377, p<0.001), male sex (β=-0.281, p=0.001) and maternal HT (β=-0.209, p=0.017) were significantly related to lower PLT. In addition, SGA (β=-0.401, p=0.001) and male sex (β=-0.307, p=0.001) were associated with lower PCT.

In all studied patients, MPV was significantly different between infants with and without PROM (9.8 fL vs. 9.2 fL, p=0.001).

DISCUSSION

This study demonstrated that platelet indices did not differ between late preterm and term newborns. Previous studies reported that LPN present lower PLT and PCT compared to TN.[11,15] Alicja et al.[11] evaluated platelet parameters of 71 TN and 58 LPN and found that PLT correlated with gestational age and birth weight. In our study, there was no correlation between PLT and gestational age or birth weight. On the other hand, Rolim et al.[16] evaluated hematologic profile in 2662 newborns including 193 late preterm, and showed that platelets remained nearly constant during gestation. These variations can be explained by differences in patient characteristics and sample size.

The present study demonstrated that various patient's characteristics have an impact on platelet indices in late preterm and term newborns. Term SGA newborns showed lower PLT and PCT than non-SGA infants, as previously reported.[17-19] Reduced platelet count indicates the immaturity of platelet production in SGA newborns.[20] Thrombopoietin, the main regulator of platelet production, is produced by liver. The original location of fetal thrombopoiesis is the

Table 2. Platelet indices according to patients characteristics in late preterm infants.

Factor (n)	PLT (x103/µL) Median (IQR)	MPV (fL) Median (IQR)	PCT (%) Median (IQR)	PDW Median (IQR)
Maternal HT (15)	208 (165-238)	9.6 (8.7-9.8)	0.2 (0.1-0.25)	16.4 (16.2-16.6)
non-maternal HT (83)	265 (222-345)	9.3 (8.9-9.3)	0.3 (0.2-0.3)	16.3 (16.1-16.5)
	P=0.035	P=0.790	P=0.047	P=0.451
PROM (23)	239.5 (208-283)	9.75 (9-10.5)	0.2 (0.2-0.3)	16.4 (15.9-16.6)
non-PROM (75)	257.5 (217-335.5)	9.2 (8.9-9.6)	0.2 (0.2-0.3)	16.3 (16.1-16.5)
	P=0.376	P=0.034	P=0.958	P=0.307
Cesarean delivery (66)	236.5 (202-296)	9.4 (8.9-9.7)	0.2 (0.2-0.3)	16.4 (16.1-16.6)
Vaginal delivery (32)	272.5 (236.5-351.5)	9.25 (8.9-9.75)	0.2 (0.2-0.3)	16.2 (16-16.45)
	P=0.031	P=0.693	P=0.068	P=0.128
Male (54)	237.5 (187.7-293.3)	9.2 (8.8-9.7)	0.2 (0.2-0.3)	16.3 (16.1-16.5)
Female (44)	261.5 (219.5-310.7)	9.2 (8.7-9.7)	0.2 (0.2-0.3)	16.3 (16.1-16.5)
	P=0.123	P=0.694	P=0.131	P=0.755
SGA (29)	203 (159-221.5)	9 (8.8-9.5)	0.2 (0.1-0.2)	16.2 (16-16.4)
non-SGA (69)	263 (218.5-318.5)	9.2 (8.7-9.7)	0.2 (0.2-0.3)	16.6 (16.5-16.8)
	P=0.030	P=0.176	P=0.033	P=0.500
Gestational age	r =0.030	r =-0.114	r =0.053	r =-0.198
	P=0.776	P=0.264	P=0.603	P=0.092
Birth weight	r =0.206	r =-0.120	r =0.219	r =-0.096
	P=0.042	P=0.238	P=0.031	P=0.347
5 min Apgar score	r=0.123	r=-0.136	r=0.061	r =- 0.127
	P=0.226	P=0.182	P=0.0.552	P=0.213

PLT, platelet count MPV, mean platelet volume PCT, plateletcrit; PDW, platelet distribution width; IQR, median interquartile range; MH, maternal hypertension; SGA, small for gestational age; PROM, premature rupture of membranes. Significant correlation between gestational age, birth weight, Apgar scores and platelet indices were analyzed using Spearman's rank correlation (r).

Table 3. Platelet indices according to patients characteristics in term infants.

Factor (n)	PLT (x103/µL) Median (IQR)	MPV (fL) Median (IQR)	PCT (%) Median (IQR)	PDW Median (IQR)
Maternal Ht (6)	211 (163-266)	9.3 (8.6-9.9)	0.2 (0.2-0.2)	16.3 (161-16.4)
Non-maternal HT (96)	265 (236-313.5)	9.3 (9-9.6)	0.2 (0.2-0.3)	16.3 (16.1-16.5)
	P=0.011	P=0.928	P=0.037	P=0.874
PROM (7)	283 (231-328)	9.9 (9.3-10.3)	0.3 (0.2-0.3)	16.5 (16.2-16.6)
Non-PROM (95)	263 (226.5-299)	9.2 (9-9.6)	0.3 (0.2-0.3)	16.3 (16.1-16.4)
	P=0.385	P=0.014	P=0.176	P=0.085
Cesarean delivery (66)	260 (237-299)	9.15 (8.5-9.6)	0.2 (0.2-0.3)	16.3 (16.1-16.5)
Vaginal delivery (36)	286 (243.7-318)	9.05 (8.7-9.3)	0.3 (0.2-0.3)	16.3 (16-16.4)
	P=0.167	P=0.577	P=0.313	P=0.358
Male (52)	258 (221-286.5)	9.3 (9-9.75)	0.2 (0.2-0.3)	16.3 (16.1-16.5)
Female (50)	277 (236-332)	9.2 (9-9.6)	0.2 (0.2-0.3)	16.25 (16.1-16.4)
	P=0.013	P=0.673	P=0.009	P=0.069
SGA (20)	210.5 (185-247)	9.2 (9-9.5)	0.2 (0.2-0.2)	16.3 (16-16.4)
Non-SGA (82)	278.5 (239-317.5)	9.3 (9-9.7)	0.3 (0.2-0.3)	16.3 (16.1-16.5)
	P<0.001	P=0.297	P=0.004	P=0.980
Gestational age	r =0.134	r =-0.061	r =-0.153	r =-0.002
	P=0.180	P=0.540	P=0.112	P=0.984
Birth weight	r =0.170	r =0.064	r =0.170	r =-0.086
	P=0.087	P=0.525	P=0.088	P=0.391
5 min Apgar score	r=0.170	r=-0.076	r=0.143	r=-0.095
	P=0.088	P=0.477	P=0.152	P=0.344

PLT, platelet count MPV, mean platelet volume PCT, plateletcrit; PDW, platelet distribution width; IQR, median interquartile range; MH, maternal hypertension; SGA, small for gestational age; PROM, premature rupture of membranes. Significant correlation between gestational age, birth weight, Apgar scores and platelet indices were analyzed using Spearman's rank correlation (r). Spearman's rank correlation (r).

liver and spleen.[21] Intrauterine growth restriction disturbs the development of internal organs as a result of the redistribution of blood to the brain. Hiett et al.[22] reported that SGA infants had fewer circulating megakaryocytes in cord blood. Moreover, in present study, infants born to mothers with hypertension showed lower PLT and PCT. Maternal hypertension has been reported to be associated with neonatal thrombocytopenia.[12,23] Although the pathogenesis of neonatal thrombocytopenia in maternal hypertension is not well-established, one potential mechanism is that chronic fetal hypoxia caused by maternal hypertension may impair megakaryocyte proliferation.[24]

This study showed that MPV was high in newborns born from pregnancies with PROM. Chen et al.[25] found that MPV correlates with intrauterine infection in newborns with combined leukopenia and thrombocytopenia. MPV was also associated with the development of intracranial hemorrhage, chronic lung disease and necrotizing enterocolitis in preterm very low birth weight infants.[26] High MPV and PDW values were reported in late neonatal sepsis.[27] In this study, there was no case diagnosed with late sepsis.

We also found that term male newborns present lower platelet values. Though studies on the relationship between sex and PLT are very limited, a previous study[28] reported higher PLT in females compared to males in full term infants. However, the mechanism of PLT changes by sex are not clearly established. Some researchers suggested that males may have a restricted maturity of thrombopoiesis.[15] Several studies reported a significant relationship between low Apgar scores and thrombocytopenia.[29,30] In a study of preterm infants between 27 and 35 weeks of gestation, Beiner et al.[31] found that lower gestational age, low 5 min Apgar, SGA, and cesarean delivery were risk factors for neonatal thrombocytopenia. In a murine model, severe hypoxia was shown to be related to shortened platelet survival.[32] In our study, there was no relationship between platelet indices and 5 minute Apgar scores. This might be due to the small number of cases with severe birth asphyxia in our study population.

This study has certain limitations. Given the retrospective nature of this study, the timing of blood samples was not sufficiently standardized which might affect platelet indices. Additionally, this was a single-center study involving a small sample size, which limits to generalize available results to other centers. Also, term infants in our study had various complications such as hypoglycemia or transient tachypnea of the newborns. The blood samples should have been collected from healthy term infants for comparison of platelet indices between late preterm and term newborns.

CONCLUSION

The present study shows that several perinatal conditions influence the platelet indices in late preterm and term newborns. Particularly, SGA, maternal hypertension, and male sex were related to reduced PLT and PCT. Moreover, MPV was found to be associated with PROM. Thus, it is important to evaluate platelet parameters in newborns with different perinatal factors since these neonates might have

impaired platelet parameters which could lead to hemostatic disorders and infectious diseases. Further studies regarding the consequences of late prematurity and perinatal factors on platelet indices are required.

ETHICAL DECLARATIONS

Ethics Committee Approval: Medeniyet University Goztepe Training Hospital Ethics Committee (No: 2021/0063).

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

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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

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Orjinal Araştırma / Original Article

Evaluation of Our Neuronavigation Assisted Biopsy Results According to Lesion Location and Size

Nöronavigasyon ile Biyopsi Sonuçlarımızın Lezyon Yeri ve Boyutuna Göre Değerlendirilmesi

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Abstract

Purpose: Since neuronavigation assisted intracerebral biopsy is an often-used method in deeper and smaller lesions, it may cause radiological and neurological complications in patients. Also, since it is a minimally invasive method, tissue sampling is limited, and a definite histopathological diagnosis may not be possible for every biopsy. In this study, we aimed to examine how NNAB results is affected by the lesion's localization and size.

Material and Method: The files of 41 patients who underwent neuronavigation assisted intracerebral tissue biopsy between 2016 and May 2021 were reviewed retrospectively. Patients who underwent biopsy with frameless neuronavigation were included in the study. The determined parameters were evaluated according to the localization of the lesions, presence in the eloquent area, and lesion size.

Results: 20 (63.41%) lesions out of 41 patients included in the study were localized in the eloquent area, while the lesions of 15 (36.58%) were outside the eloquent area. The mean lesion size was 34×27.76 mm. The tissue samples of 38 (92.68%) patients received a diagnosis. Postoperative control CT scans showed radiological complications in 4 (9.75%) patients. Three (7.31%) patients had postoperative neurological complications. No biopsy-related mortality was observed.

Conclusion: Adequate planning and examination of radiological images by both the radiologist and the surgeon before surgery reduce the risk of radiological and neurological complications caused by the lesion's small size and eloquent area localization. Biopsy of the target tissue from more than one quadrant provides sufficient tissue for histopathological diagnosis and helps to make a more accurate diagnosis.

Keywords: Biopsy, frameless, ıntracerebral, neuronavigation

Öz

Amaç: Nöronavigasyon ile intraserebral biyopsi sıklıkla daha derindeki ve ufak boyuttaki lezyonlarda kullanılan bir yöntem olduğu için hastalarda radyolojik ve nörolojik komplikasyonlar oluşturabilmektedir. Ayrıca minimal invaziv bir yöntem olduğu için kısıtlı doku örneği alınabilir ve buna bağlı histopatolojik tanı koyulmayabilir. Biz de bu çalışmayla nöronavigasyon ile intraserebral biyopsi sonuçlarımızın lezyon lokalizasyonuna ve boyutuna bağlı ne kadar etkilendiğini ortaya koymaya çalıştık.

Gereç ve Yöntem: 2016 ve Mayıs 2021 yılları arasında bu yöntem ile opere edilmiş 41 hastanın dosyaları retrospektif olarak incelendi. Çalışmaya çerçevesiz nöronavigasyon ile biyopsi alınan hastalar dahil edildi. Belirlenen parametreler lezyonların yerine, hassas bölgede olup olmamasına ve boyutlarına göre değerlendirildi.

Bulgular: Çalışmaya dahil edilen 41 hastanın 26 (%63,41)' sının lezyonu hassas bölge, 15 (%36,58)' nin lezyonu ise hassas bölge dışı yerleşimliydi. Lezyon boyutları ortalama 34×27,76 mm idi. 38 (%92,68) hastanın doku örneklerine tanı koyulabildiği tesbit edildi. Operasyon sonrası çekilen kontrol BT' lerde 4 (%9,75) hastada radyolojik olarak komplikasyon görüldü. 3 (%7,31) hastada ise operasyon sonrası nörolojik komplikasyon mevcuttu. Cerrahiye bağlı mortaliteye rastlanmadı.

Sonuç: Cerrahi öncesi iyi planlama ve radyolojik görüntülerin hem radyolog hem de cerrah tarafından iyi incelenmesi lezyonun hassas bölgede ve küçük boyutta olmasının getirdiği radyolojik ve nörolojik komplikasyon riskini azaltmaktadır. Hedef dokudan birden fazla kadrandan biyopsi alınması histopatolojik tanı için yeterli doku elde edilmesini sağlar ve doğru tanı koyulmasına çok daha fazla yardımcı olur.

Anahtar Kelimeler: Biyopsi, çerçevesiz, intraserebral, nöronavigasyon

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INTRODUCTION

Neuronavigation assisted biopsy (NNAB) is a minimally invasive method that has been used more frequently with the development of technology for cerebral lesions that cannot be operated on with open surgery or that do not require surgery but need tissue diagnosis.[1] Excision with craniotomy is very convenient in patients with a deep-localized lesion, lesions located in more eloquent areas, small lesions, and/or high comorbidities. Besides, it helps to obtain accurate tissue diagnosis of diseases with challenging diagnosis and whose primary treatment is not surgical, such as primary central system lymphoma or neurodegenerative diseases. In particular, NNAB procedures performed without a stereotaxy frame have become highly preferred due to the patient's comfort and less complication risk.[2]

Through this method, it is imperative to take a sufficient amount of tissue sample from the right place without harming the patient. Although special magnetic resonance imaging (MRI) is used for this purpose and pre-intervention plans are made, neurological and/or radiological complications may develop due to the small lesion sizes and lesion localization such as the motor cortex, basal ganglia, thalamus, or corpus callosum.[3] Also, inadequate or inaccurate pathological results may occur.

To the best of our knowledge, we did not find such a detailed study about frameless NNAB, especially based on the location and size of the lesion. In this study, we examined how the success of NNAB procedures performed in our clinic is affected by the localization and size of the lesion.

MATERIAL AND METHOD

The study was carried out with the permission of Selcuk University Rectorate Local Ethics Committee (Date: 09.06.2021, Decision no: 2021/35). All procedures were performed adhered to the ethical rules and the Helsinki Declaration of Principles.

The files of 41 patients who underwent neuronavigation assisted intracerebral biopsy in our clinic between 2016 and May 2021 were reviewed retrospectively. Patients who underwent NNAB without stereotaxy frame were included in the study. The gender, age, pre-operative presence of neurodeficiency, anatomical localization, and size of the intracerebral lesion/lesions were evaluated. The anatomical localization of the lesions was divided into two groups as the eloquent area or not the eloquent area. Deeply located lesions, such as the motor cortex, basal ganglia, internal-external capsule, thalamus, caudate nucleus, corpus callosum, and Wernicke-Broca that are likely to cause neurodeficiency in the patient, were defined as eloquent areas (**Figure 1**). Also, whether the lesions were multiple, whether the primary of the lesion was known or not, the reported MR spectroscopy results before the operation, and the pathology reports of the tissue samples were examined. Postoperative computed tomography (CT) scans were performed to determine whether there were radiological complications and how much the cystic contents of cystic lesions could be evacuated. Additionally, it was determined by examining the neurological examinations after the operation whether there were neurological complications related to the procedure. The presence of any wound complication was also examined. Patients' postoperative length of hospitalization in Neurosurgery Clinic and in the hospital was also determined.

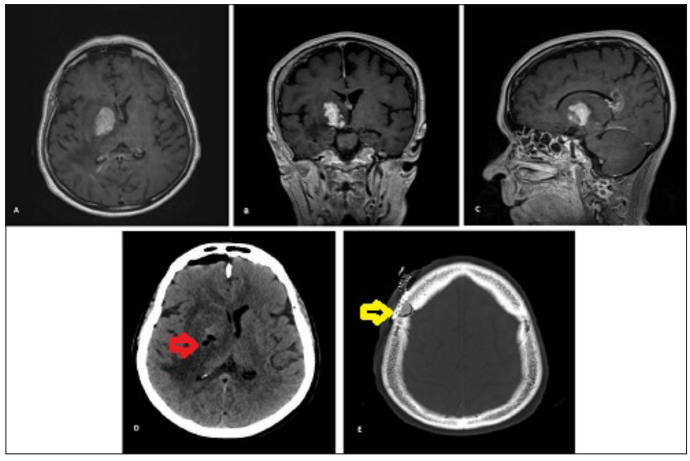

Figure 1. (A) Hyperintense lesion in the right basal nucleus on contrast-enhanced T1 sequence axial MRI, **(B)** coronal MRI, **(C)** sagittal MRI, **(D)** The area of the biopsy taken from the lesion in the postoperative early control cranial CT (red arrow), **(E)** Visualization of the entry point and burr hole plaque in the bone section of postoperative early control cranial CT (yellow arrow)

Surgical Technique

Standard procedure was used for each patient. Appropriate images were selected after the navigation compatible MRI taken the evening before the operation of the patients and were loaded into the neuronavigation device. Planning was done by selecting the entry point and the target point in a way that the lesion could be reached in the shortest possible way without causing any complication to the patient on the device's computer. During the planning, special attention was paid to the absence of intracerebral vascular structures in the trace reaching the target. Under general anesthesia, the patients' heads were fixated by a 3-pin spiked Mayfield to prevent disruption in navigation planning. The patients were given the appropriate position. Image matching was performed with the neuronavigation device.

The operation area of the patients was shaved, and the lesion was marked in this area. Patients were not administered any anti-cerebral edema medication during the surgical procedure. A linear incision of approximately 3 cm was made by centering the lesion. After reaching the bone tissue, the lesion location was confirmed by neuronavigation, and one burr hole was opened to this area with the help of an electric motor. After the dura was opened in the form of an envelope, the biopsy arm was fixed to minimize the margins of error indicated by the navigation device. The biopsy needle length was adjusted according to the distance to the lesion indicated

by the neuronavigation device, and the biopsy needle was introduced through the cannula. Tissue samples were taken from 4 quadrants of the lesion and were sent to pathology for histopathological examination. While removing the cannula and biopsy needle, attention was paid to the presence of blood at the ends regarding the risk of hemorrhage. The opened dura was sutured if possible. In all cases, a hemostatic sponge was placed on this area. The bone powder obtained during the opening of the burr hole was filled in this area, and the round bone plate was fixed in the bur hole area. Galea was unconditionally sutured (**Figure 2**). The patients were extubated in the operating room and taken to the Neurosurgery Intensive Care Unit.

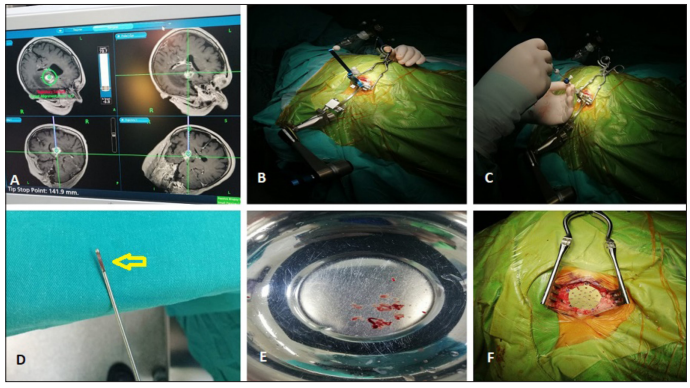

Figure 2. (A) Targeting and trajectory of the lesion on the monitor of the peroperative neuronavigation device, **(B)** Fixation of the biopsy arm by targeting the lesion, **(C)** Taking a biopsy with a biopsy needle, **(D)** Tissue sample taken at the tip of the biopsy needle, **(E)** Quantity of tissue samples from 4 quadrants, **(F)** Closure of the burr hole with a plaque after the completion of the biopsy

Statistical Analysis

Statistical analyzes were performed using SPSS version 18.0. The Chi-square test was used to compare categorical measurements. Fisher's Exact test result was interpreted in the presence of a cell with less than 5 in frequency in 2×2 tables in the chi-square test. Likelihood Ratio statistic was interpreted if there was no 2×2 table and less than five frequencies. The Mann-Whitney U test was used for comparisons with the pathology results since the variables of age, lesion size, and length of stay in the hospital were quantitative data.

RESULTS

The mean age of 41 patients included in the study was 57.31 (minimum 11, highest 78) years. Twenty-five patients (60.97%) were female, and 16 were male (39.02%). Preoperatively, 22 (53.65%) patients had low Glasgow Coma Score (GCS) and/or neurodeficiency. Intracerebral lesions were multiple localized in 10 (24.39%) patients. Lesion biopsy localizations were as follows; corpus callosum localization in 7 (17.07%), right basal ganglia in 4 (9.75%), left basal ganglia in 1 (2.43%), the right caudate nucleus in 2 (4.87%), left caudate nucleus in 1 (2.43%), right thalamus in 5 (12.19%), and left thalamus in 3 (7.31%). Also, lesion biopsies were taken from right frontal in 3 (7.31%) patients, left frontal in 6 (14.63%) patients, right parietal in 3 (7.31%) patients, left parietal 1 (2.43%) patient, left occipital in 2 (4.87%) patients, the right temporooccipital in 1 (2.43%) patient, and left temporal in 2 (4.87%) patients. 26 (63.41%) of these lesions were in the eloquent area, and 15 (36.58%) were outside the eloquent area. When the cerebral region of the lesion and whether the tissue samples were histopathologically diagnosed or not, no statistically significant relationship was found between two of them (p>0.05) (**Table 1**). When we examine the relationship according to the presence of the lesion in the eloquent area or outside of the eloquent area and whether the tissue samples were histopathologically diagnosed or not, no significant relationship was found statistically again (p>0.05) (**Table 2**).

Table 1. The statistical relationship between the location of lesions that have been biopsied and whether these lesions have a pathological diagnosis

			Pathological Diagnosis		Total
			No	Yes	
Lesion location	Corpus Callosum	n	0	7	7
		%	0.0%	100.0%	100.0%
	Right Basal Nucleus	n	0	4	4
		%	0.0%	100.0%	100.0%
	Right Frontal Lobe	n	1	2	3
		%	33.3%	66.7%	100.0%
	Right Caudat Nucleus	n	0	2	2
		%	0.0%	100.0%	100.0%
	Right Occipital Lobe	n	0	2	2
		%	0.0%	100.0%	100.0%
	Right Parietal Lobe	n	1	2	3
		%	33.3%	66.7%	100.0%
	Right Thalamus	n	0	5	5
		%	0.0%	100.0%	100.0%
	Right Temporooccipital	n	0	1	1
		%	0.0%	100.0%	100.0%
	Left Basal Nucleus	n	0	1	1
		%	0.0%	100.0%	100.0%
	Left Frontal Lobe	n	0	6	6
		%	0.0%	100.0%	100.0%
	Left Caudat Nucleus	n	0	1	1
		%	0.0%	100.0%	100.0%
	Left Parietal Lobe	n	0	1	1
		%	0.0%	100.0%	100.0%
	Left Thalamus	n	0	3	3
		%	0.0%	100.0%	100.0%
	Left Temporal Lobe	n	1	1	2
		%	50.0%	50.0%	100.0%
Total		n	3	38	41
		%	7.3%	92.7%	100.0%

Likelihood Ratio=11.054 p=0.606

Table 2. Statistical relationship between the presence of lesions in the sensitive area and whether these lesions can have pathological diagnosis

			Pathological Diagnosis		Total
			No	Yes	
Eloquent Region	No	n	1	14	15
		%	6.7%	93.3%	100.0%
	Yes	n	2	24	26
		%	7.7%	92.3%	100.0%
Total		n	3	38	41
		%	7.3%	92.7%	100.0%
Fisher's Exact Test p=1.000					

The mean lesion size was 34×27.76 mm. There was no statistically significant difference between the size of the lesions and the adequacy of the amount of tissue sample for histopathological diagnosis. (p>0.05) (**Table 3**). The primary diagnosis of 3 (7.31%) patients was lung cancer; the rest of the patients were undiagnosed. When the results of MR spectroscopy taken before the operation were examined, it was found that the preliminary diagnosis of 11 (29.72%) lesions was undecided (3 grade 3 glial masses, 2 grade 2 glial masses, 2 lymphomas, 3 metastases, 1 vasculitis), and the diagnosis of 26 (70.27%) lesions was sure (17 glioblastoma multiforme (GBM), 4 metastases, 2 lymphomas, 1 grade 2 glial masses, 1 abscess, 1 demyelinating disease). It was determined that 4 patients did not undergo MR spectroscopy before the operation. When the pathology results were examined, it was seen that the tissue diagnosis of 3 (7.31%) patients was uncertain (2 necrotic tissue, 1 insufficient sample), tissue samples taken by NNAB of 38 (92.68%) patients were found to be able to diagnose (19 GBM, 2 grade 2 glial masses, 6 lymphomas, 3 grade 3 glial masses, 4 metastases, 2 demyelinating diseases, 2 abscesses). When the diagnoses of the patients who had both MR spectroscopy and pathology results were compared, the radiological and pathological diagnoses of 27 (72.9%) patients were compatible with each other. The lesions of 8 (19.51%) patients were cystic. It was determined that the cystic lesions of 6 (75%) patients were evacuated grossly by the NNAB procedure. CT scans taken in the first 24 hours after the operation revealed radiological complications in 4 (9.75%) patients (2 site hematoma, 1 ventricular hemorrhage, 1 trace hematoma). No relationship was found between the radiological complications after the operation and the location of the lesion and whether it was in the eloquent area or not (p>0.05) (**Table 4, Table 5**). In the postoperative neurological examinations of the patients, neurodeficiency was detected in 3 (7.31%) patients; permanent in 1 patient and temporary in 2 patients. No significant relationship was found between the neurological complications after the operation and the location of the lesion and whether it was in the eloquent area or not (p>0.05) (**Table 4, Table 5**). Of the three patients with neurological deficit, 2 (66%) patients had radiological complications. Besides, it was statistically shown that the size of the lesion was not associated with the development of neurologic and radiological complications after the operation (**Table 3**). No procedure-related mortality was detected in the patients included in the study. Postoperative wound complications were detected in 2 (4.87%) patients, 1 of whom was cerebrospinal fluid (CSF) leakage, and the other was local wound infection. It was observed that these wound problems were resolved with simple interventions. The mean postoperative length of hospital stay of the patients was 9.91 days. There was a significant difference between the length of hospital stay of the patients and the length of stay in the Neurosurgery Clinic since approximately 56% of the patients included in the study were consulted from other clinics and were taken over from these clinics before the procedure and transferred back to these clinics after the procedure. Considering the length of hospital stay due to the NNAB procedure, it would be more accurate to evaluate the length of stay in the Neurosurgery Clinic (**Table 6**). This period was an average of 4.39 days. No statistically significant difference was found when the length of stay in Neurosurgery Clinic was compared according to whether the lesion was in the eloquent area or the size of the lesion (p>0.05).

Table 3. Statistical relationship between size of biopsy lesions and presence of postoperative radiological complication, postoperative neurological complication and pathological diagnosis

Lesion Size (mm^2)		n	Mean	Median	Mann-Whitney Test (p)
Postoperative Radiological Complication	No	37	806	450	0.629
	Yes	4	1886	875	
Postoperative Neurological Compliacation	No	38	928	497	0.920
	Yes	3	704	420	
Pathological Diagnosis	No	3	454	497	0.652
	Yes	38	947	437	

Table 5. The statistical relationship between the presence of lesions in the sensitive area and whether postoperative radiological complication and postoperative neurological complication

			Postoperative Radiological Complication		Total	Postoperative Neurological Complication		Total
			No	Yes		No	Yes	
Eloquent Region	No	n	14	1	15	15	0	15
		%	93.3%	6.7%	100.0%	100.0%	0.0%	100.0%
	Yes	n	23	3	26	23	3	26
		%	88.5%	11.5%	100.0%	88.5%	11.5%	100.0%
Total		n	37	4	41	38	3	41
		%	90.2%	9.8%	100.0%	92.7%	7.3%	100.0%
			Fisher's Exact Test p=1.000			Fisher's Exact Test p=0.287		

Table 6. The statistical relationship between the presence of lesions in the eloquent area and stay in neurosurgery clinic, lesion size and stay in neurosurgery clinic.

			Stay in Neurosurgery Clinic (Day)	Fisher's Exact Test
Eloquent Region	No	n:15 %: 36.5	4.33	p>0.05
	Yes	n: 26 %: 63.5	4.41	
Lesion Mean Size (mm^2)		n<911mm^2 n>911mm^2	4.39	p>0.05

Table 4. The statistical relationship between the location of lesions that have been biopsied and whether postoperative radiological complication and postoperative neurological complication

			Postoperative Radiological Complication		Total	Postoperative Neurological Complicaiton		Total
			No	Yes		No	Yes	
Lesion Location	Corpus Callosum	n	6	1	7	7	0	7
		%	85.7%	14.3%	100.0%	100.0%	0.0%	100.0%
	Right Basal Nucleus	n	3	1	4	3	1	4
		%	75.0%	25.0%	100.0%	75.0%	25.0%	100.0%
	Right Frontal Lobe	n	3	0	3	3	0	3
		%	100.0%	0.0%	100.0%	100.0%	0.0%	100.0%
	Right Caudat Nucleus	n	2	0	2	2	0	2
		%	100.0%	0.0%	100.0%	100.0%	0.0%	100.0%
	Right Occipital Lobe	n	2	0	2	2	0	2
		%	100.0%	0.0%	100.0%	100.0%	0.0%	100.0%
	Right Parietal Lobe	n	3	0	3	3	0	3
		%	100.0%	0.0%	100.0%	100.0%	0.0%	100.0%
	Right Thalamus	n	4	1	5	5	0	5
		%	80.0%	20.0%	100.0%	100.0%	0.0%	100.0%
	Right Temporooccipital	n	1	0	1	1	0	1
		%	100.0%	0.0%	100.0%	100.0%	0.0%	100.0%
	Left Basal Nucleus	n	1	0	1	1	0	1
		%	100.0%	0.0%	100.0%	100.0%	0.0%	100.0%
	Left Frontal Lobe	n	6	0	6	6	0	6
		%	100.0%	0.0%	100.0%	100.0%	0.0%	100.0%
	Left Caudat Nucleus	n	1	0	1	1	0	1
		%	100.0%	0.0%	100.0%	100.0%	0.0%	100.0%
	Left Parietal Lobe	n	1	0	1	1	0	1
		%	100.0%	0.0%	100.0%	100.0%	0.0%	100.0%
	Left Thalamus	n	2	1	3	1	2	3
		%	66.7%	33.3%	100.0%	33.3%	66.7%	100.0%
	Left Temporal Lobe	n	2	0	2	2	0	2
		%	100.0%	0.0%	100.0%	100.0%	0.0%	100.0%
Total		n	37	4	41	38	3	41
		%	90.2%	9.8%	100.0%	92.7%	7.3%	100%
			Likelihood Ratio Value= 7.151 p= 0.894			Likelihood Ratio Value=13.147 p=0.437		

DISCUSSION

The most important criteria that distinguishes NNAB from surgery performed by craniotomy is to obtain sufficient tissue samples from lesions in deep-seated, small-sized, and so-called eloquent areas. Also, it does not cause additional morbidity or mortality in patients with high comorbidity/comortality. Although the use of this method has increased considerably in these respects, morbidity rates vary between 1.3% and 27.8%, and mortality rates vary between 0.7% and 3.9%.[2,3] In our study, there was no mortality related to the biopsy procedure, and the morbidity rate was 7.1%. Although our morbidity rates were not statistically significant according to the location of the lesions and their presence in the eloquent area, they were lower than most of those reported in the literature.[2] Since more than half of the patients included in the study [22 (53.65%) patients] had pre-operative neurodeficiency and 63.41% of the biopsy taken lesions were in the eloquent area, we believe that it is important that our morbidity remains at 7.1%.

Especially in the biopsy of lesions located in eloquent areas, the possibility of morbidity increases as the size of the lesion decreases.[2] In our study, it was found that postoperative neurological complications developed in 2 (13.3%) out of 15 patients, especially with lesions of 20×20 mm or smaller. This rate is above our general morbidity rate. The lesion of 1 of these patients was located in the basal nuclei, while the other was located in the thalamus. In more than 90% of the studies in the literature, the sizes of the lesions that were biopsied were over 1 cm, which is also consistent with our study.[2] However, contrary to our study, there are also studies stating that biopsies performed using a framed head may be more efficient and safe since the lesion size is small.[4-7] This also applies to the deeply located lesions and lesions in eloquent areas.[4,8,9] However, the advantages of the two methods over each other are not clear in the literature due to the fact that the results of the frameless method in recent studies are as good as the frame-based method results and that the frame-based method has disadvantages for patient comfort, difficulty in imaging, prolonging the surgical time, and the risk of infection.[1,2,10]

Radiological complications can also be seen in patients without postoperative neurologic complications. As a radiological complication, hemorrhage in the biopsy trace or bleeding into the biopsy taken lesion can be seen (**Figure 3**).[1] Although these bleedings do not increase most of the time, they can lead to dramatic results such as hematoma needing discharge by craniotomy, neurodeficiency, and even death.[11] Therefore, control cranial CT is performed in the first 3 hours after biopsy in our clinic for early diagnosis, follow-up, and treatment. In this study, we detected hematoma in 4 (9.75%) patients after the process. However, 2 of them (1 intralesional hematoma, 1 contusion on trace line) had neurological complications. None of these patients required reoperation since there was no increase in hematoma and neurodeficiency in the follow-up CT scans. Special attention should be paid to biopsy targeting and the absence of vascular formation in the trace to be passed, apart from considering the use of anticoagulant or antiaggregant in patients to prevent such bleeding. Hence, it is necessary to examine the MR images adequately while making the plan. Also, the nature of the lesion from which the biopsy was taken should be considered.[2] The MRI must be taken before the surgery should be interpreted correctly in this respect. In lesions of unknown primary, accurately interpreted radiological examinations can give clues to the surgeon whether the lesion is bleeding or not.

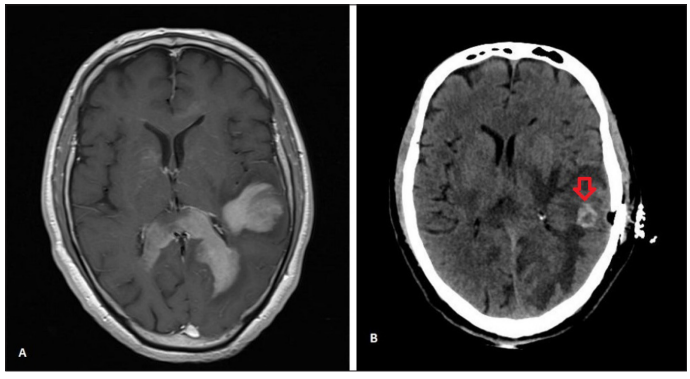

Figure 3. (A) The appearance of the lesions as hyperintense in contrast-enhanced T1 axial MRI, **(B)** Hematoma appearance in the biopsy area in postoperative early control cranial CT.

In our study, the harmony between the preliminary diagnosis stated in MRI spectroscopy and the histopathological diagnosis after the biopsy was approximately 73%. In order to make the correct tissue diagnosis, it is necessary to take sufficient tissue samples from the right part of the lesion. Accurate histopathological diagnosis of the lesion and accurate grading of neuroglial masses is vital for patients to receive valid oncological treatment.[1] However, the amount of tissue samples that can be taken with the NNAB method is very limited due to the thinness of the biopsy needle (**Figure 2**).

Therefore, if the biopsy is not taken from the targeted lesion are with sufficient quantity, tissue samples can be taken from the cerebral tissue, necrotic part, or areas where the mass grade is low. To prevent this, tissue samples should be taken from different quadrants of the target point (**Figure 2**). However, there are not enough deterministic studies on this subject in the literature.[2] Our practice is to take a biopsy by rotating the biopsy needle 360 degrees in 4 quadrants. This situation brought the success of histopathological diagnosis with a rate of 92.68% (**Figure 1**). Although there are different statements about this rate in the literature, the highest rates vary between 84% and 100%.[2,10] We think that the correct interpretation of current MR images by the neuroradiologist is important to increase the accurate histopathological tissue diagnosis. It is also very useful to define the highest graded part of the lesion to the surgical team and plan the biopsy target accordingly. Besides, a plan can be made by determining the target in more than one way from a single burr hole to increase the histopathological accuracy of the biopsy. However, it should not be forgotten that each additional intervention to the cerebral tissue increases the risk of complications.[2]

The cerebral tissue in which the lesion is located and the size of the lesion are also important for the accuracy of histopathological diagnosis.[10] When the lesion is located in the eloquent area and/or is small in size, the complication risk increases; therefore, sampling from more than one quadrant can be avoided.[2,10] Also, the deeper the lesion and the farther from the cortical area, the greater the amount of cerebral tissue to be passed. Besides, the inconsistency of the cortical anatomy, which corresponds to the entry point in the shortest route plan to reach the lesion, may cause the location of the cortical entry point to be changed and increase the distance to the target. In this respect, some centers perform the biopsy planning on functional MR images to protect the more functional areas of the brain.[3]

Also, depending on the patient's brain tissue structure (atrophicity, large cisterna, etc.), the ventricle, and important vascular structures close to the lesion, there may be shifts in different directions from the targeted area on the lesion. In our study, 2 (66.6%) lesions out of the three patients who could not get a histopathological diagnosis were in an eloquent area and deeply located. Besides, the mean size of lesions that could not be diagnosed histopathologically (454 mm^2) was smaller than the mean sizes of all lesions in the study (911 mm^2).

Obtaining sufficient tissue samples with NNAB can be challenging when the solid part of the lesion is too small, and the lesion is dominantly cystic. The cystic part was more common in the lesions of 8 patients in our study. 2 (66.6%) out of the three lesions that could not be diagnosed due to insufficient tissue samples had cystic structure. One of these lesions was in the eloquent area, and the other was not. Also, 2 of these lesions did not have an apparent solid component. Hence, if the cystic content aspirated by the NNAB method is not histopathologically diagnostic, it may unfortunately also be a disadvantage. However, we have experienced that cystic contents could be drained totally with the NNAB method; 6 (75%) of the cystic lesions in our study were almost totally

drained in the early control CT scans taken after the operation. The lack of studies in the literature on the approach to cystic lesions with the NNAB method is also noteworthy.

In multiple lesions, having more options to obtain sufficient tissue and reaching the target without any problems is an advantage. The lesion should be chosen according to its proximity to the cortex, distance from important structures in the cerebral tissue. Also the largest lesion or the lesion with the most suitable nature for accurate diagnosis should be preferred if possible.[1-3,10] In our study, the mean size of the multiple lesions was 963.8 mm^2, which was close to the overall mean size of all lesions. Therefore, biopsy tissues taken from this group were sufficient in quantity, and pathological diagnoses could be made in all of them. In addition, there was only one patient (10%) with multiple lesions who had postoperative radiological and/or neurological complications. The lesion that could not be diagnosed due to insufficient tissue sample was not present in this group.

Although there is not enough data in the literature, the mean length of hospital stay of the patients who underwent the NNAB method included in our study was 4.39 days, which was significantly below the mean existing data.[10] This indicates that the procedure-related morbidity is low. Despite the multiplicity of lesions located in the eloquent area from which the biopsy was taken, the average length of hospital stay in our study makes the procedure's minimal invasiveness even more significant.

The results of our study include many important details that will lead to other studies related to the NNAB method. However, no statistically significant difference was found due to insufficient sample size in most of the parameters. According to our literature review, that this situation was also experienced in other trials.[1]

CONCLUSION

Although many factors affect the success of neuronavigation and intracerebral biopsy, the lesion's location, adjacency, and the size of the lesion are also important, as supported by the numerical data results of our study. Good planning before surgery and a detailed examination of radiological images by both the radiologist and the surgeon reduces the risk of radiological and neurological complications caused by the lesion's small size and eloquent localization. Through frameless NNAB, it is possible to achieve the same success as frame-based NNAB without causing additional morbidity and mortality. As in our study, a biopsy of the target tissue from more than one quadrant provides sufficient tissue for histopathological diagnosis and helps to make a more accurate diagnosis. With this method, it is also possible to drain cystic lesions significantly regardless of their location and size.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Selcuk University Rectorate Local Ethics Committee (Date: 09.06.2021, Decision no: 2021/35).

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

Referee Evaluation Process: Externally peer-reviewed.

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

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Orjinal Araştırma / Original Article

The Volume of Trauma-Related Emergency Department Visits During the COVID-19 Pandemic

COVID-19 Salgını Sırasında Travmaya Bağlı Acil Servis Başvurularındaki Değişimler

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Abstract

Aim: After the first case in Wuhan, China in late 2019, COVID-19 quickly spread and affected the whole world. While it had been recommended to postpone healthcare services for non-emergency cases, several studies showed that many emergency cases were decreased as well. In this study, we aimed to investigate whether the trends in visits to the emergency department (ED) were altered during the COVID period.

Material and Method: We evaluated the ED visits between July 1, 2019 and June 30, 2020 due to transport injuries, falls, interpersonal violence and self-harm using International Classification of Diseases, 10th revision codes. Pre-COVID period was defined as July 2019-Mar 2020 and COVID period was defined as April-June 2020. To show whether there was a significant change between pre-COVID and COVID periods (monthly), we used piecewise regression analyses.

Results: In total, there were 14,958 ED visits due to transport injuries, falls, interpersonal violence and self-harm during the study period. Piecewise regression analysis revealed that ED visits for transport injury (p=0.028), falls (p=0.006) and interpersonal violence (p=0.007) significantly decreased, whereas, there was a significant increase in visits for self-harm (p<0.001) in COVID period, when compared with pre-COVID period.

Conclusion: This is the first study showing that the number of ED visits for transport injury, falls and interpersonal violence were decreased and those for self-harm were increased during the COVID-19 pandemic. A maximum effort should be made by authorities to understand the reason behind these trends, particularly for self-harm behaviors.

Keywords: COVID-19, wounds and injuries, accidental falls, violence, self-injurious behavior, traffic accidents

Öz

Amaç: 2019'un sonlarında Çin'in Wuhan kentinde yaşanan ilk vakanın ardından COVID-19 hızla yayıldı ve tüm dünyayı etkiledi. Acil olmayan vakalar için sağlık hizmetlerinin ertelenmesi önerilmiş olsa da, birkaç çalışmada birçok acil vakanın da azaldığı gösterilmiştir. Bu çalışmada, travma kaynaklı acil servis başvurularının COVID-19 pandemisi sırasındaki değişimini araştırmayı amaçladık.

Gereç ve Yöntem: ICD-10 kodları kullanılarak 1 Temmuz 2019 - 30 Haziran 2020 tarihleri arasında trafik kazası, düşme, darp ve özkıyım nedeniyle acil servis başvuran hastalar belirlendi. COVID öncesi dönem Temmuz 2019-Mart 2020, COVID dönemi ise Nisan-Haziran 2020 olarak tanımlandı. COVID öncesi ve COVID dönemleri arasındaki değişimin değerlendirilmesi için parçalı regresyon analizleri kullanıldı.

Bulgular: Çalışma döneminde trafik kazası, düşme, darp ve özkıyım nedeniyle toplam 14.958 acil servis başvurusu yapılmıştı. COVID döneminde, COVID öncesi döneme kıyasla trafik kazası (p=0,028), düşme (p=0,006) ve darp (p=0,007) sebebiyle yapılan acil servis başvurularında anlamlı azalma, özkıyım sebebiyle yapılan başvurularda ise anlamlı artma olduğu görüldü (p<0,001).

Sonuç: COVID-19 salgını sırasında trafik kazası, düşme ve darp nedeniyle yapılan acil servis başvurularının azaldığı, özkıyım nedeniyle yapılan başvuruların ise arttığı görülmektedir. Başvuru sıklıklarındaki bu değişimlerin arkasındaki nedenlerin anlaşılması için azami çaba gösterilmelidir.

Anahtar Kelimeler: COVID-19, düşme, darp, özkıyım, trafik kazası

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INTRODUCTION

After the first case in Wuhan, China in late 2019, COVID-19 quickly spread and affected the whole world. By the end of August 2020, almost 25 million cases and 800,000 deaths were reported worldwide.[1] Under these circumstances, Center for Disease Control (CDC) have recommended postponing healthcare services for non-emergency cases in an attempt to prevent new cases and to compensate the increasing workload of healthcare professionals.[2] In the meantime, governments around the world had implemented measures such as stay-at-home orders, postponing all kinds of scientific, cultural and artistic activities and shutting down the entertainment facilities to prevent the spread of the pandemic.

Scientific reports have confirmed that hospital admissions due to non-COVID related reasons were significantly decreased upon these implementations. A recently published article from the United States showed that visits to emergency departments (ED) were decreased in the first months of the COVID-19 pandemic.[3] Several other studies reported a decline in admissions and hospitalizations due to acute myocardial infraction.[4-7] Another study utilizing public vehicle collision data showed that the number of vehicle related injuries were decreased.[8] These trends suggest that the number of admissions to ED due to trauma might also have been decreased. Recent studies showed that the trends in trauma related hospital admissions during the COVID-19 pandemic were decreased.[9,10]

In this study, we aimed to investigate the trends in trauma-related visits to ED during the COVID-19 era. Furthermore, we sought to evaluate whether the hospitalization rates of these patients were altered.

MATERIAL AND METHOD

Study design and patient selection

The data for this retrospective observational study were obtained from electronic health records at Ankara City Hospital, a medical institution with the highest bed capacity (3,704 beds) in Europe. The study reports were prepared according to the STROBE guidelines.[11] The study was approved by the Local Ethics Committee (Approval No: E1/1076/2020).

We evaluated the ED visits between July 1, 2019 and June 30, 2020 due to transport injuries, falls, interpersonal violence and self-harm, as these external causes account for one of the most frequent causes of deaths in Turkey.[12] The International Classification of Diseases, 10th revision (ICD-10) codes were used to separate admissions into their respective groups. The ICD-10 codes were derived with respect to Global Burden of Disease Study 2013.[13] Such that, codes V00-V86.99, V87.2, V87.3, V88.2, V88.3, V91-V91.9, V93-V98.8 and Z04.1 were categorized as "transport injuries", W00-W19.9 as "falls", "X85-Y08.9, Y87.1, Y87.2, Z04.4-Z04.5, W50, W51" as "interpersonal violence" and X60-X84.9 as "self-harm". We investigated the number of ED visits for these predefined categories on a monthly basis. Monthly rates of hospitalization were also analyzed for each category to evaluate the potential impact of aforesaid measures on clinical practice. In-hospital mortality were derived from electronic health records and presented for each predefined category.

Study Periods

The study period was designed as one year, starting from July 1, 2019 (the start date of full-capacity work in ED at our hospital) to June 30, 2020.

The first confirmed COVID-19 case in Turkey was announced on March 11, 2020 and a national stay-at-home order was declared for persons over 65 years of age on March 21, 2020. These measures were expanded on April 3, 2020.[14] In addition, several other national precautions including cancellation of large-scale social activities had also been implemented by the end of March 2020. As of June, these measures had been gradually reduced, signaling the beginning of normalization period in Turkey.[15] For these reasons, in this study, "pre-COVID period" was defined as July 2019-March 2020, "COVID period with restrictions" was defined as April-May 2020 and "normalization period" was defined as June 2020.[16]

Statistical Analysis

Continuous variables were demonstrated as mean ± standard deviation (SD) and categorical variables as frequencies and percentages. Number of visits to ED and hospitalization rates were presented according to quartiles of the study period. Trends for the ED visits due to above-mentioned reasons were plotted for pre-COVID (July 2019-March 2020), COVID (April-May 2020) and normalization (June 2020) periods. Accordingly, hospitalization rates for each subcategory were plotted for the same period.

To show whether there was a significant alteration between pre-COVID and COVID periods (monthly), we used piecewise regression analyses, a useful statistical method to compare the trends of two separate periods,[17,18] for each trend including the number of ED visits and hospitalization rates in transport injury, falls, interpersonal violence and self-harm. STATA version 16.1 (STATA Corporation, College Station, Texas) was used for all statistical analysis. Statistical significance was defined as $p<0.05$.

RESULTS

In total, there were 14,958 ED visits due to transport injuries, falls, interpersonal violence and self-harm during the study period. The mean (SD) age of study population was 34.5 (24.4) years. Of the study population, 8,938 (59.8%) were male. The major reason for ED visits was fall (62.7%), followed by transport injury (25.9%), interpersonal violence (10.7%) and self-harm (1.0%).

Numbers of ED visits per each quartile of the study period were presented in **Table 1**. While the number of visits were relatively stable before the COVID period (n=3,941 in Jul-Sep 2019, n=4,371 in Oct-Dec 2019, n=3,892 in Jan-Mar 2020), there was a decrease to 2,754 in COVID period (Apr-Jun 2020). Numbers of hospitalization due to trauma per each quartile of the study period were presented in **Table 2**. Of 14,958 ED visits, 3,645 (24.4%) were hospitalized. Most of the hospitalized patients were male (61.7%, n=2,250).

In total, 196 patients died in hospital within a median (25th-75th) of 18 (6-87) days. The mean (SD) age of these 196 patients was 75.58 (17.89) years and more than half of them (n=102, 52.0%) were female. Out of these 196 patients, 19 died due to transport injury, 172 due to falls and 5 due to interpersonal violence. None of the patients died due to self-harm. The trends of mortality rates were similar for each quartile of the study period (**Table 3**).

The mean (SD) number of monthly ED visits due to transport injury was 371.7 (55.7) in the pre-COVID period. However, the number of ED visits due to transport injury declined in the COVID period with restrictions (n=90 (75.7% decrease) in April 2020, n=144, (61.0% decrease) in May 2020), compared with the mean number of monthly visits in pre-COVID period. The number of ED visits due to transport injury was similar in the normalization period (June 2020) and pre-COVID period. Piecewise regression analysis revealed that this trend was significant (p=0.028). However, there were no significant alterations in hospitalization rates throughout the study period (p=0.921) (**Figure 1**).

While the mean (SD) number of monthly ED visits due to falls was 847.2 (113.9) in the pre-COVID period, the number of ED visits decreased by 66.0% in April 2020 (n=284). As shown in **Figure 2**, piecewise regression analyses showed that trends in the number of visits (p=0.006) and hospitalization rates (p=0.665) due to falls were similar with transport injury.

Table 1. Emergency Department visits due to trauma according to quartiles of the study periods

	Total n=14,958	Jul-Sep 2019 n=3,941	Oct-Dec 2019 n=4,371	Jan-March 2020 n=3,892	Apr-June 2020 n=2,754
Age, mean (SD)	34.5 (24.4)	35.4 (23.7)	33.4 (24.5)	34.9 (24.5)	34.6 (25.2)
Sex					
Male, n (%)	8,938 (59.8%)	2,389 (60.6%)	2,558 (58.5%)	2,257 (58.0%)	1,734 (63.0%)
Female, n (%)	6,020 (40.2%)	1,552 (39.4%)	1,813 (41.5%)	1,635 (42.0%)	1,020 (37.0%)
Admission reason to Emergency Department					
Transport injury, n (%)	3,870 (25.9%)	1,006 (25.5%)	1,245 (28.5%)	1,050 (27.0%)	569 (20.7%)
Falls, n (%)	9,378 (62.7%)	2,496 (63.3%)	2,639 (60.4%)	2,413 (62.0%)	1,830 (66.4%)
Self-harm, n (%)	144 (1.0%)	33 (0.8%)	18 (0.4%)	23 (0.6%)	70 (2.5%)
Interpersonal violence, n (%)	1,601 (10.7%)	412 (10.5%)	476 (10.9%)	410 (10.5%)	303 (11.0%)

Table 2. Hospitalization due to trauma according to quartiles of the study periods

	Total n=3,645	Jul-Sep 2019 n=796	Oct-Dec 2019 n=944	Jan-March 2020 n=1,090	Apr-June 2020 n=815
Age, mean (SD)	40.6 (26.7)	41.5 (25.8)	40.5 (27.0)	39.9 (26.5)	40.9 (27.5)
Sex					
Male, n (%)	2,250 (61.7%)	506 (63.6%)	583 (61.8%)	650 (59.6%)	511 (62.7%)
Female, n (%)	1,395 (38.3%)	290 (36.4%)	361 (38.2%)	440 (40.4%)	304 (37.3%)
Admission reason to Emergency Department					
Transport injury, n (%)	1,107 (30.4%)	249 (31.3%)	319 (33.8%)	362 (33.2%)	177 (21.7%)
Falls, n (%)	2,274 (62.4%)	494 (62.1%)	558 (59.1%)	636 (58.3%)	586 (71.9%)
Self-harm, n (%)	45 (1.2%)	12 (1.5%)	7 (0.7%)	12 (1.1%)	14 (1.7%)
Interpersonal violence, n (%)	233 (6.4%)	42 (5.3%)	64 (6.8%)	81 (7.4%)	46 (5.6%)

Table 3. In-hospital mortality according to quartiles of the study periods

	Total n=196	Jul-Sep 2019 n=51	Oct-Dec 2019 n=57	Jan-March 2020 n=48	Apr-June 2020 n=40
Age, mean (SD)	75.58 (17.89)	71.41 (20.40)	77.59 (16.85)	78.10 (11.31)	75 (21.62)
Sex					
Male, n (%)	94 (1%)	30 (1.2%)	28 (1%)	15 (0.6%)	21 (1.2%)
Female, n (%)	102 (1.6%)	21 (1.3%)	29 (1.5%)	33 (2%)	19 (1.8%)
Admission reason to Emergency Department					
Transport injury, n (%)	19 (0.4%)	4 (0.3%)	5 (0.4%)	3 (0.6%)	7 (1.2%)
Falls, n (%)	172 (1.8%)	45 (1.8%)	49 (1.8%)	45 (1.8%)	33 (1.8%)
Self-harm, n (%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Interpersonal violence, n (%)	5 (0.3%)	2 (0.4%)	3 (0.6%)	0 (0%)	0 (0%)

As shown in **Figure 3**, the mean (SD) number of monthly ED visits due to interpersonal violence was 145 (18.1) in the pre-COVID period. In the piecewise regression analyses, we showed that trends in the number of visits (p=0.007) and hospitalization rates (p=0.931) due to interpersonal violence were similar with transport injury and falls.

The mean (SD) number of monthly ED visits due to self-harm was 8.4 (2.9) in the pre-COVID period. However, there was a dramatic increase in the number of ED visits due to self-harm (176.3%) (p<0.001) with a decreasing hospitalization rate (p=0.019) in the COVID period compared with pre-COVID period (**Figure 4**).

DISCUSSION

In the "COVID period with restrictions", ED visits due to transport injury, falls and interpersonal violence were decreased when compared with pre-COVID period. Indeed, the number of ED visits due to transport injury, falls and interpersonal violence were similar in the pre-COVID and normalization periods. While the number of ED visits due to self-harm were increased in the COVID period, the hospitalization rates were decreased when compared with pre-COVID period. To the best of our knowledge, this is the first study showing the trends of ED visits due to specific reasons including transport injury, falls, interpersonal violence and self-harm during the COVID-19 pandemic. Understanding the underlying causes of these changes will enable the development of appropriate healthcare strategies and more effective management of the high patient volume in emergency departments.

A research by Sutherland et al.[8] supports our findings regarding the visits related to transport injury. In that study, authors reported that total vehicle collisions and vehicle related injuries decreased during the COVID-19 pandemic, which is similar to our findings. It has been shown that less drivers on the road declined the chance of traffic injury.[19] Since many countries have implemented various restrictions to prevent the spread of infection, the density of traffic and volume of accidents may have been decreased. In this regard, Badr et al.[20] showed that the mobility decreased in the United States during the COVID period.

Falls are yet another important reason for trauma-related ED visits. One out of five falls are reported to cause a serious injury such as fractures or a head trauma.[21] Each year, 3 million elderly visit emergency departments due to falling.[22] At least 800,000 patients are hospitalized each year because of fall-related injuries, most frequently head trauma or hip

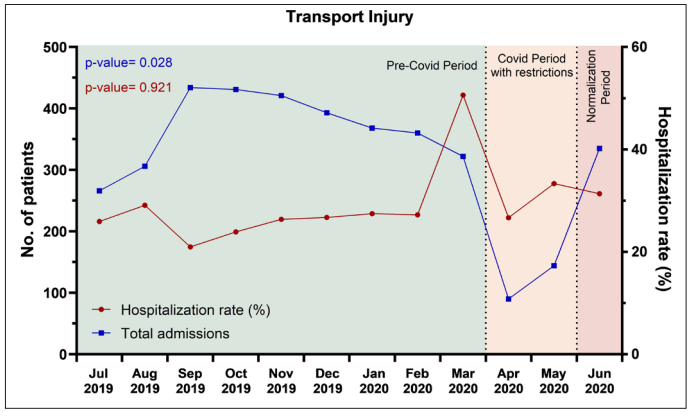

Figure 1. ED visits and hospitalization rates due to transport injury during the study period

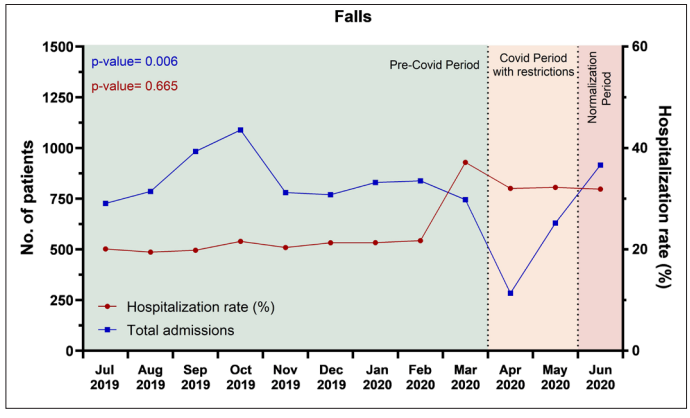

Figure 2. ED visits and hospitalization rates due to falls during the study period

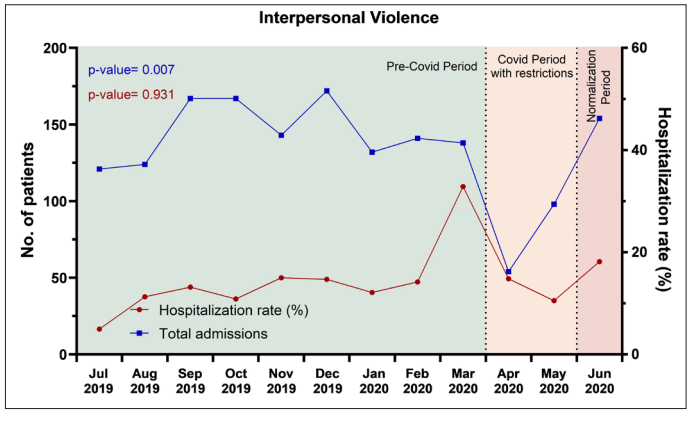

Figure 3. ED visits and hospitalization rates due to interpersonal violence during the study period

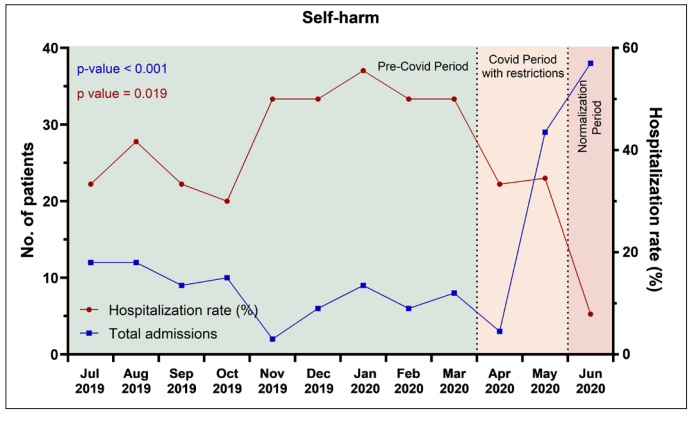

Figure 4. ED visits and hospitalization rates due to self-harm during the study period

fractures.[23] Our results show a significant decrease in fall-related ED visits in the COVID period with restrictions. Indeed, the number of fall-related visits were back to pre-COVID levels in the normalization period.

In this study we found that interpersonal violence decreased during the first two months of COVID period when compared to pre-COVID period. Interpersonal violence (violence between individuals) is subdivided into two categories; domestic violence (child maltreatment, intimate partner violence, elder abuse) and community violence (violence and/or assault by acquaintance or strangers). According to "The Shadow Pandemic" report published by the United Nations Entity for Gender Equality and the Empowerment of Women, domestic violence in France has increased by 30% during the COVID lockdown period. Contrary to this, a domestic violence helpline in Italy is reported to receive 55% fewer calls, as asking for help might have been found to be harder during the lockdown. Thus, the decline in interpersonal violence in this study during the first two months of COVID era might be attributed to a reduction in help requests.[24]

Similar to our findings that demonstrate the increase in ED visits due to self-harm, Cheung et al.[25] reported that suicides increased in Hong Kong during the 2003 severe acute respiratory syndrome (SARS) epidemic. A recent study utilizing Google Trends data showed that acute anxiety queries were 11% higher than expected.[26] It is known that the increased anxiety is associated with suicide behaviors,[27] so the increased number of ED visits due to self-harm might be related to increase anxiety during pandemic spreading. On the other hand, our results indicate that hospitalizations due to self-harm decreased during the restrictions and normalization periods. As most of the in-patient care capacity of our institute was reserved for the COVID-19 patients, self-harm admissions might have been followed-up and discharged from within the emergency department.

This study provided information about trends in ED visits due to transport injury, falls, interpersonal violence and self-harm. However, this might not represent the true reason of alterations shown in the number of ED visits. Interestingly, ED visits due to self-harm were found to be increased in COVID period. This study can be regarded as a trigger for the actions to prevent self-harm behaviors. Otherwise, a "suicide pandemic" may also arise along with the COVID-19 pandemic due to possible economic adversities, increased fear and anxiety and uncertainty of the future.

There are several limitations to our study. Firstly, this is a retrospective, single center study and may not be adaptable to nationwide trends. Besides, the normalization period analyzed in this study covers only a 1-month period, thus the accuracy of data for this period can be questioned. It is also unknown whether these findings arose from a real drop in the number of incidents, or merely from a drop in ED visits due to concerns of infection. Considering the fact that our hospital has been transformed into a pandemic hospital, it is also possible that patients have applied to different institutions. Since, July 2019 was the start date of full-capacity work in our hospital, we were not able to capture previous years. As previous studies reported controversial findings about the seasonal trends of injuries, it remains unclear whether these trends were seasonal or not.[28-30] Finally, diagnoses were derived from ICD-10 codes, thus, there might be subject to inaccuracies in coding.

CONCLUSION

This is the first study showing that the number of ED visits for transport injury, falls and interpersonal violence were decreased and those for self-harm were increased during the COVID-19 pandemic. However, no difference was observed in the hospitalization rates between pre-COVID and COVID periods. Similar hospitalization rates despite the decreased number of admissions might be due to the fact that minor cases did not necessarily apply to ED, while only severe cases in need of hospitalization applied to the ED. It was notable that the number of ED visits in the normalization period were similar to pre-COVID era. Further studies examining a longer period and utilizing nationwide data are needed for a better understanding of the reasons behind these trends.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ankara City Hospital Ethics Committee (Approval No: E1/1076/2020).

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

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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

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Orjinal Araştırma / Original Article

Retrospective Evaluation of Liver Injuries in Children: Ten Years Experience of a Single Centre

Çocuklarda Karaciğer Yaralanmalarının Geriye Dönük Değerlendirilmesi: Tek Bir Merkezde On Yıllık Deneyim

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Abstract

Objective: We aimed to evaluate the causes of trauma that result in liver injury and additional solid organ injuries, management types and results of management in children referred to our clinic for liver injuries in last ten years.

Material and Method: The records of 47 patients managed for liver injuries owing to blunt abdominal trauma between July 2010 and May 2020 were reviewed retrospectively.

Results: The patients were 1-17 (7.8±5.8) years old; 30 (63.8%) were male and 17 (36.2%) were female. Causes of injuries included pedestrian and passenger traffic accidents (29, 61.7%), falls from height (12, 25.5%), bicycle accidents (4, 8.5%), objects falling on the body (1, 2.1%), after a physical assault (1, 2.1%). Isolated liver injury was present in 27 patients (62%), while 20 patients (38%) had other organ injuries. Liver injuries were grade I in 8 patients (17.3%), grade II in 12 (26%), grade III in 18 (38.2%), grade IV in 8 (17%), and grade V in 1 (2%). Thirty-nine patients (83%) were managed conservatively in these series of liver injuries, whereas 8 patients (17%) had unstable vital signs managed surgically. The mortality rate, duration of stay in intensive care and hospital, and the number of blood transfusions were higher in surgically managed patients, while hemodynamic parameters were considerably lower in surgically managed patients.

Conclusion: Conservative treatment methods should be chosen in patients with a liver injury who are hemodynamically stable. The shorter duration of hospital stay, less blood transfusion requirement, and lower morbidity, mortality percentages are indispensable reasons for this method to be preferred.

Keywords: Children, injury, liver, management, trauma

Öz

Amaç: Son on yılda kliniğimize başvuran çocuklarda karaciğer hasarı ve ek solid organ yaralanmaları ile sonuçlanan travma nedenlerini, tedavi tiplerini ve tedavinin sonuçlarını değerlendirmeyi amaçladık.

Gereç ve Yöntem: Temmuz 2010-Mayıs 2020 tarihleri arasında künt karın travmasına bağlı karaciğer yaralanmaları nedeniyle tedavi edilen 47 hastanın kayıtları retrospektif olarak incelendi.

Bulgular: Hastalar 1-17 (7,8±5,8) yaşında olup; 30 (%63,8)'u erkek, 17 (%36,2)'si kadındı. Yaralanmaların nedenleri yaya ve yolcu trafik kazaları (29, %61,7), yüksekten düşme (12, %25,5), bisiklet kazaları (4, %8,5), vücuda düşen cisimler (1, %2,1), fiziksel saldırı sonrası yaralanmadır (1, %2,1). Hastaların 27 (%62)'sinde izole karaciğer hasarı, 20 (%38)'sinde başka organ yaralanmaları vardı. Karaciğer yaralanmaları hastaların 8 (%17,3)'inde grade I, 12'sinde (%26) grade II, 18 (%38.2)'inde grade III, 8 (%17)'inde grade IV ve 1'inde (%2) grade V idi. Bu seride karaciğer yaralanması olan hastaların 39 (%83)'u konservatif olarak takip edilirken, vital bulguları stabil olmayan 8 (%17)'ine cerrahi müdahale yapıldı. Cerrahi müdahale ile takip edilen hastalarda mortalite oranı, yoğun bakım, hastanede kalış süresi ve kan transfüzyonu sayısı daha yüksekken, hemodinamik parametreler önemli ölçüde düşüktü.

Sonuç: Hemodinamik olarak stabil karaciğer yaralanması olan hastalarda konservatif tedavi yöntemi seçilmelidir. Hastanede daha kısa kalış süresi, daha az kan transfüzyonu gereksinimi ve daha düşük morbidite, mortalite yüzdeleri bu yöntemin tercih edilmesinin vazgeçilmez nedenleridir.

Anahtar Kelimeler: Çocuklar, yaralanma, karaciğer, tedavi yönetimi, travma

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INTRODUCTION

Liver trauma is one of the most common abdominal lesions in severely injured trauma patients.[1] The prevalence of blunt liver injury has been reported to increase especially in the last 3 decades.[2,3] In recent years, as a result of improvements in the imaging methods used to diagnose solid organ injuries, and in the conditions of intensive care units, the treatment approach in hemodynamically stable cases with blunt liver trauma has changed from surgical intervention to non-operative therapy.[4,5] It is thought that patients with liver injury, and hemodynamically stable can be followed up with controlled ultrasonography (US) or contrast abdominal computed tomography (CT) if there is no other emergency surgical pathology.[6] Follow-up of vital signs, whether or not there are acute abdominal symptoms by physical examination, changes in hemoglobin and hematocrit, liver enzyme levels are important follow-up tools in non-operative patients.[5,6] We aimed to evaluate the causes of trauma that result in liver injury and additional solid organ injuries, management types and results of management in children referred to our clinic for liver injuries in last ten years.

MATERIAL AND METHOD

This study was conducted by ethics committee approval obtained from Karamanoğlu Mehmetbey University Faculty of Medicine (02-03/07.12.2020). The records of 47 patients managed for liver injuries owing to blunt abdominal trauma between July 2010 and May 2020 were examined. In addition to demographic features of the patients such as age and gender, duration of stay in the hospital, causes of trauma, additional organ injuries, and treatment methods were evaluated. Hemodynamic status was determined with blood pressure at referral, hemoglobin levels, and essential for blood transfusion. Contrast CT determined which solid organs were injured and the degree of injury. The amount of blood transfusion required, duration of hospital stay, and the status of injuries in the control CT were examined in the patients followed up with surgically or conservatively. All patients in the conservatively treated group were controlled by contrast abdominal CT between 7 and 10 days of hospitalization. Possible changes in lesions were controlled and the final condition of the injury was radiologically demonstrated for comparison purposes in previous findings. These patients were given 15 to 20 days rest after clinical and radiological improvement. Anatomy and severity of the injury, hemoperitoneum level, other abdominal organs, retroperitoneal structures, and the gastrointestinal system can be evaluated with contrast abdominal CT. It provides a remarkable contribution staging of trauma liver, spleen, kidney, pancreas, and digestive tract, treatment, and follow-up,[6] so after 1 and 6 months, patients were called to outpatient clinic control with contrast abdominal CT. The severity of liver injuries has been universally classified according to the American Association for the Surgery of Trauma (AAST) grading scale. In determining the optimal treatment strategy, however, the hemodynamic status and associated injuries should be considered. Thus, the management of liver trauma is ultimately based on the anatomy of the injury and the physiology of the patient.[7]

RESULTS

The patients were aged between 1-17 (7.8±5.8) years; 30 (63.8%) were male, 17(36.2%) were female involved in this study. The patients that have liver injuries were 8 (17%) grade I, 12 (25.6%) grade II, 18 (38.3%) grade III, 8 (17%) grade IV, 1 (2.1%) grade V (**Table 1**).

Table 1. Hepatic injuries according to AAST

Grade	The size of liver laceration	*n	** %
1	Small subcapsular hematoma or superficial laceration	8	17
2	Subcapsular hematoma covering 10-50% of surface area or a 1-3 cm laceration less than 10 cm in length	12	25.6
3	Large (>50%) ruptured subcapsular hematoma, an intraparenchymal hematoma >2 cm, or a laceration >3 cm in depth	18	38.3
4	Ruptured intraparenchymal hematoma or lobar parenchymal disruption involving 25-50% of the lobe	8	17
5	Lobar parenchymal disruption >50% or juxta-hepatic venous injury	1	2.1
6	Hepatic avulsion	0	

*Number of cases, **Percentage

We have assessed the liver injuries according to the AAST classification while the anatomic gravity of the associated injuries was defined the Injury Severity Score (ISS) system (**Table 2**)

The causes of injuries were involved a pedestrian and passenger traffic accidents (29, 61.7%), falls from height (12, 25.5 %), bicycle accidents (4, 8.5%), objects falling on the body (1, 2.1%), and 1 (2.1%) after a physical assault. While 8 (17%) of these patients were managed surgically, 39 (83%) of them were managed conservatively (**Table 2**).

Conservative follow-up was preferred over surgical intervention in the patients with hemodynamic instability and hollow organ injury. Twenty-eight (59.6%) of the patients had isolated liver injuries and 19 (40.4%) of them had other intraabdominal organ injuries. The patients who had liver injuries also present with 8 (42.1%) kidney, 7(36,9%) spleen, 3(15.8%) hollow organs, 1 (5.2%) pancreatic injuries. There were 7 (14.9%) head, 6 (12.8%) thorax, 4 (8.5%) limb and 3 (6.4%) multiple organs (**Table 2**).

Table 2. Frequencies of several variables for both treatment modes (conservative and laparotomy.)

Variable	Conservative	Laparotomy
Male	24 (80%)	6 (20%)
Female	15(88.2%)	2 (11.8%)
Traffic accidents	24 (82.8%)	5 (17.2%)
Falls from height	10 (83.3%)	2 (16.7%)
Bicycle accidents	3 (75%)	1 (25%)
Objects falling on the body	1 (50%)	1 (50%)
Assault	1 (100%)	0

While all the patients of grade I and II were managed conservatively, 4 patients (22.2%) grade III, 3 patients (37.5%) grade IV, and 1 patient (100%) grade V were managed surgically. There was also an ileum perforation in 2 patients in grade III, and 1 patient in grade IV undergone surgery. As a surgery we used primary repair for the laceration in 5 (62.5%) patients and pringle maneuver (portal triad blockage), local hypothermia application to the liver that we used it to our one patient in grade V. Also, perihepatic packing and planned reexploration as a part of damage control surgery. We used it it to our two patients in grade IV and V in cases of hemodynamic instability or coagulopathy. One patient died during surgery (2.1%) owing to excessive bleeding that induced respiratory and circulatory failure. One case in grade IV (2.1%) observed with delayed bleeding was treated surgically.

The data according to the grades of liver injury are summarized in **Table 3.** Thirty-nine patients (83%) were managed conservatively in this study. All of these patients survived.

Table 3. The data according to the grades of liver injury

Grade	Hemoglobin Level * (g/dl)	Blood transfusions (n)**
1	11.8 (9-12.5)	2 (25%)
2	11.5 (10.7-13)	6 (50%)
3	11 (10.7-11.8)	13 (72.7%)
4	10.2 (9-10.8)	8 (100%)
5	6.8	+

*Median (min-max), **Number of the patient

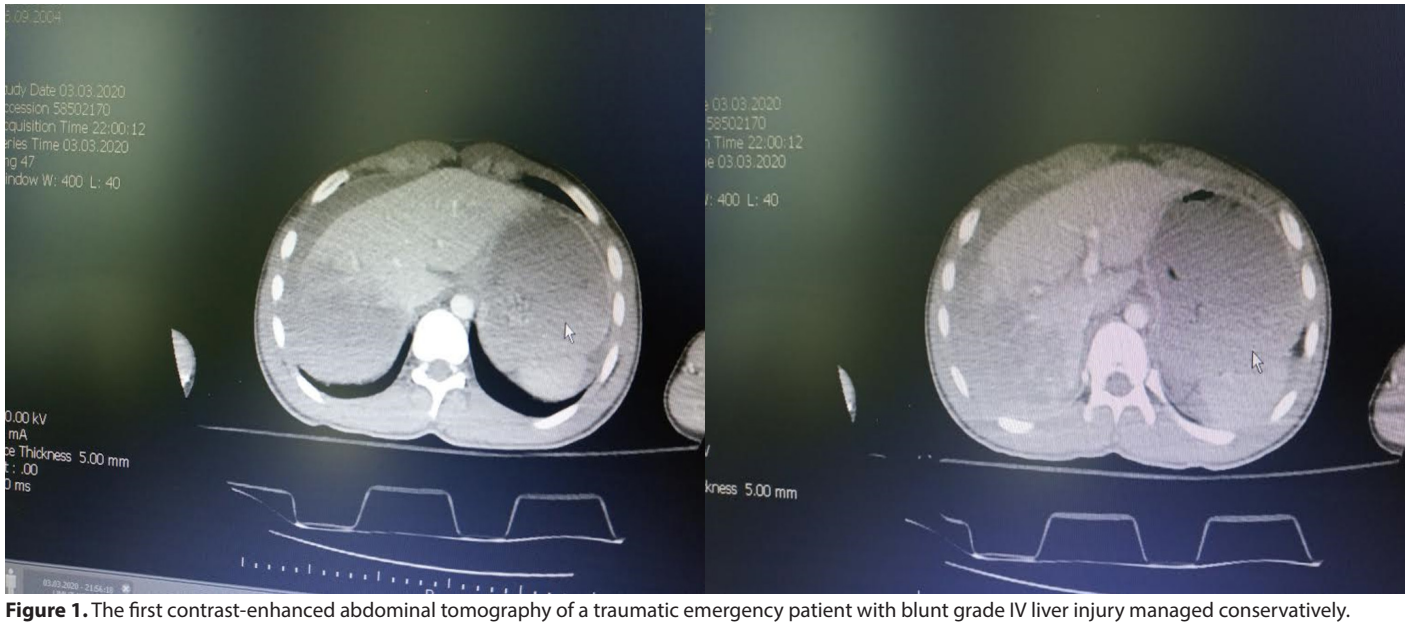

Figure 1. The first contrast-enhanced abdominal tomography of a traumatic emergency patient with blunt grade IV liver injury managed conservatively.

Figure 2. A contrast-enhanced abdominal tomography of the patient was managed conservatively with a blunt grade IV liver injury after 3 months.

In the conservatively managed group 3 (7.6%) patients had atelectasis, 1 (2.6%) developed pneumonia, 1 (2.6%) had a subhepatic abscess, 3 (7,6%) had a secondary hemorrhage and bile leakage, 1 (2.6%) had a hemobilia. Hollow organ injuries and biliary peritonitis were the most complications that treated surgically. The duration of the mean hospital stay was 7.2 days for our patients.

DISCUSSION

The liver is the second most commonly injured intraabdominal organ after abdominal traumas. The amount of liver injury after blunt abdominal traumas is 2-3%. Most liver injuries appear owing to motor vehicle accidents and falls from heights. Penetrative injuries are uncommon in children. Surgical treatment is not necessary for 70-90% of patients. The aim of non-operative management of liver injuries in children is to restrict operative morbidity and mortality.[8] As in the literature, most liver injuries were appeared owing to traffic accidents 29 (61.7%), falls from height 12 (25.5%) in this study.

The right diagnosis and treatment of liver injuries are very necessary for children because liver injury after blunt abdominal traumas is the most significant cause of mortality.[9,10] In several studies, AST and ALT levels over 150 IU/L suggested liver parenchymal damage in 43-61% of patients, but were unable to declare the degree of parenchymal damage.[11,12] However, in this study, all patients had parenchymal damage, and 8 (17%) of them had enzyme levels lower than 150 IU/L. As in the literature, there was no relation between enzyme levels and injury grade in this study. On the other hand, it has been noted that one can rule out liver parenchymal damage if enzyme levels are normal.[11,12] As in the literature, in this study, except for three patients with grade I injuries, increased AST and ALT levels were determined and all patients had liver parenchymal damage.

Abdominal contrast CT is the recommended method for finding out and grading injuries. Today, the most important criterion for patient selection for non-operative treatment of trauma centres and surgeons has been hemodynamic stability rather than visual rating.[13,14] In these patients, hemodynamic stability may break down rapidly and an emergency surgical procedure may be needed without optimal patient preparation. A difference between the liver and the spleen is that delayed bleeding is uncommon in the liver. It is noticed in less than 2% of non-operative treated patients.[15,16] As in the literature, one patient in grade IV (2.1%) was noticed with delayed bleeding, and this case was managed surgically.

Monitoring in intensive care is seen as a prudent and sensible approach so that the clinician can determine which patient will fail the non-operative treatment. Angiography and embolization should be considered if the active hemorrhage is seen or suspected during tomography if technical facilities and experience are sufficient. With an experienced, well-equipped multidisciplinary team, it is possible to achieve a success rate of over 90% by remaining non-operative. The mortality of all hepatic injuries is around 10%. Fortunately, 70-90% of hepatic injuries are minor injuries. Complicated hepatic injuries are around 10-30% and mortality has decreased to 10% in the last decade with major changes in follow-up and treatment of complicated liver injuries.[17] As in the literature, 8 (17%) patients who had unstable vital signs managed surgically. One patient (2.1%) in grade V died during the surgery due to excessive bleeding that caused the respiratory and circulatory failure. The most important changes for liver surgery are:

1. The effect of CT on non-operative treatment of the adult with blunt hepatic trauma,[18]
2. Pringle maneuver (portal triad blockage), local hypothermia application to the liver[19] that we used to our one patient;
3. Perihepatic packing and planned reexploration as part of damage control surgery in cases of hemodynamic instability or coagulopathy[20] that we used it to our two patients;
4. Treatment of juxtahepatic venous injuries with various intracaval shunts that we haven't used in any of our patients, yet.

The most important decision to be made after the first resuscitation is whether or not the patient will be operated on. After two liters of intravenous liquid substitution, it should be regarded that bleeding continues in the patient whose hemodynamic stability is not achieved. Pachter et al. in the series of 495 diseases, the success rate of this treatment was 94%. This success was achieved with an average blood transfusion of 1.9 units, 6.2% complications, of which only 2.8% were related to bleeding, and an average hospital stay of 13 days.[18] Suchlike outcomes are also seen in the series of multicentric study groups containing 404 cases.[21] In these series, 98.5% of injuries were treated non-operative and the complication rate was only 5%. Ongoing bleeding was the most common complication in 14 patients (3.5%) and only 3 (0.7%) patients were operated on to stop the bleeding. Other complications, perihepatic abscesses, and bile collections were rare and most of them regressed spontaneously, while those that did not regress spontaneously were drained accompanied by CT. Only one patient needed surgery after his intrahepatic abscess failed to be percutaneous drained. But the fact that 1 liver injury-related death (0.5%) and 2 omitted small bowel injuries (0.5%) in this study suggest that more work should be done on conservative treatment protocols. In the literature, it was reported that 50 to 80% of laparotomies due to blunt liver trauma had no active bleeding and negative laparotomy was performed.[22,23]

Many studies have been managed to define specific criteria to facilitate the application of non-operative therapy and patient selection in cases with blunt trauma.[1,24,25] These criteria were determined as hemodynamic stability, absence of peritoneal findings, less than 500 ml of hemoperitoneum. The most important critical factor here is not the degree of liver injury

or hemoperitoneum, but the hemodynamic stability of the cases after application or resuscitation.[1,26] Another factor to be considered is the presence of another intraabdominal solid or hollow organ injury that requires surgical intervention. As in the literature, there was an additional ileum perforation in 2 (11%) patients in grade III and 1(12.5%) patient in grade IV liver injuries managed surgically in our study.

After discharge, absolute bed rest for 7-10 days and limited physical activity for 4-6 weeks are recommended.[11,22] Thirty-nine of 47 (%83) patients were managed conservatively in the present study. Twenty (100%) of them were with grade I and II injuries, 14 (77.8%) with grade III injuries, and 5 (62.5%) with grade IV injuries were managed conservatively. There was a transfusion reaction in 3 patients (7%) in the follow-up period.

Surgical management of liver injury has a higher mortality rate than conservative management because liver resection increases the risk of perioperative and postoperative mortality.[11,26] Kepertis et al.[27] managed 9 of 34 patients (26%) surgically. Two of these patients had grade IV injuries, one had grade V and one had grade VI; two of the other five patients underwent surgery for splenic laceration, two for a head injury, one for diaphragmatic rupture, and one for extremity fracture. There was 1 (11%) mortality in the surgically managed patients and no incidence of mortality in the conservatively managed patients in the study of Kepertis et al.[27] Similarly, in the present study, the mortality rate was high in the surgically managed patients, as one out of eight patients (12.5%) died. The mortality rate, duration of stay in intensive care and hospital, and the number of blood transfusions were higher in surgically managed patients, while hemodynamic parameters were considerably lower in surgically managed patients.

On the other hand, there were no complications in the 6 surviving patients managed surgically. However, the lower complication rate remarked in surgically managed patients in this study was probably owing to the low patient numbers. The occurrence of intrahepatic or subhepatic abscess is 0.5-3% (11,28). As in the literature, 1 (2.6%) patient managed conservatively had a subhepatic abscess in this study.

Potential disadvantages of nonoperative treatment and early or late period complications in blunt liver traumas recovered as delayed bleeding, biliary fistula, and liver abscess, hemobilia, and extrahepatic biliary tract strictures seen in 3-5% cases.[28] Missed delayed bleeding and hollow organ injuries lead to life-threatening and negative effects on the success of non-operative therapy. Nonoperative treatment was recommended in our 5 (62.5%) cases with hemodynamically stable stage IV liver injury. We observed that there were almost no signs of trauma left after one and six months later in the contrast abdominal CT. This suggests that non-operative treatment may be more frequent, especially in selected cases, without being dependent on the degree of trauma.

In this study, the duration of stay was 1, 1.5, 2, and 3 days in intensive care and 4, 5, 6, 7 days in the hospital for grades I, II, III, and IV, respectively. There was a statistically remarkable association between grade of injuries, and duration of stay in intensive care and in-hospital ($p<0.05$). Nellensteijn et al.[29] declared that durations of stay were 0, 0, 0, and 1 day in intensive care and 2, 3, 4, and 5 days in the hospital for grades I, II, III and IV, respectively. In this study, there was also a connection between the grade of injury and duration of stay in intensive care and hospital. However, durations of stay in intensive care and hospital were longer determined in this study than Nellenstein et al.[29] This may have been owing to more severe traumas.

Although surgery is primarily considered in high-grade liver trauma, hemodynamically stable cases such as grade III and IV can be treated conservatively with close follow-up. It was determined that there was no exitus in the nonoperative treatment group. One patient died from the operated group, and that the causes of exitus were related to additional injuries. This study disclosed that the current approaches in the diagnosis and treatment of solid organ injuries determined after blunt abdominal trauma have been successfully applied in our hospital emergency surgery department.

Conclusion: Management of liver injury after blunt abdominal trauma is multidisciplinary. Conservative treatment should be preferred in children with blunt liver trauma provided that hemodynamic stability is maintained. It appears that the degree of liver damage is not as important as the hemodynamic balance in deciding non-surgical treatment. Therefore, clinical condition, degree of anatomical injury and associated injuries should be considered together in determining the best option. Conservative treatment has advantages such as shorter hospital stay, less need for blood transfusion, lower morbidity, and mortality..

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Karamanoğlu Mehmetbey University School of Medicine Ethics Committee (Permission granted: 07.12.2020, Decision no: 02-03).

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

Referee Evaluation Process: Externally peer-reviewed.

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Attitudes of The Different Occupational Groups About Parenting

Değişik Meslek Gruplarında Ebeveynlikle İlgili Tutumların İncelenmesi

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Abstract

Objective: The purpose of this study is to evaluate the point of view in different occupational groups against the parenting with a biopsychosocial approach.

Material and Method: A questionnaire consisting of 48 questions about Scale of Outlook to Parenting and demography was administered to individuals from different occupational groups at the age of parenting.

Results: It is established that the scores of attitudes to marriage of scale of Outlook to Parenting is affected by the occupation of individual's parent. The mean scores for the Attitudes to Marriage factor are found to be higher for health professionals group than security group, educator group and housewives group. It is established that regular reading habit effects Family Environment, Attitudes to Children and point of Attitudes to Marriage factors positively. Duration of education is found to effect Social Attitude factor positively.

Conclusions: Scale of Outlook to Parenting shows that there are statistical differences between the occupational groups.

Keywords: Occupations, parenting, sociology

Öz

Amaç: Bu çalışmanın amacı, biyopsikososyal yaklaşım çerçevesinde, değişik meslek gruplarında ebeveynliğe bakışı değerlendirmektir.

Gereç ve Yöntem: Farklı meslek gruplarından çocuk sahibi olma konumunda olan bireylere demografik sorular ve Ebeveynliğe Bakış Ölçeği ile ilgili toplam 48 soru içeren anket uygulandı. Uygun şekilde doldurulan 227 anket değerlendirmeye alındı.

Bulgular: Ebeveyn mesleğinin, ebeveynliğe bakış ölçeğindeki evliliğe bakış faktörünü etkilediği saptanmıştır. Sağlıkçıların evliliğe bakış faktör ortalama skorları emniyet personeli, eğitimci ve ev hanımın skorlarından yüksektir. Teknik personelin evliliğe bakış faktör ortalama skorları emniyet personelinden yüksektir. Düzenli kitap okumanın, aile ortamı, çocukla ilgili görüşler ve evliliğe bakış faktörlerini olumlu yönde etkilediği tespit edilmiştir. Toplam eğitim süresinin, sosyal tutum faktörünü olumlu yönde etkilediği saptanmıştır.

Sonuç: Meslek grupları arasında, Ebeveynliğe Bakış Ölçeğinin değişik faktörlerinin skorları bakımından istatistiksel farklılık mevcuttur.

Anahtar Sözcükler: Meslekler, ebeveynlik, sosyoloji

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INTRODUCTION

Family is a social institution in which the members interact with each other. The psychosocial status of the family is affected by the parents. Therefore, the parents are one of the focal points of the professionals who work with the families.[1,2] Individuals play new roles in families as a partner of each other. Another role of the partners is to be mother-father (parenting).[3] Family attitudes and behaviors towards to child are significant regarding the shaping child's future and development of the personality.[4]

The family life cycle characterizes the family as a changing system over time and describes the phases in this change process.[5] One of the changes of this cycle is parenting process the attitude to parenting of persons is significant in order to fulfill the parenting duties properly. Their attitudes can be affected by some factors. These factors are family environment, aims and ideals, personal skills, attitudes to marriage, physical competency, and attitudes to children, economic condition and social attitude.[6] It is observed that the entering the parenting period is affected by various natural phenomenon and social status such as some personal characteristics as well as marital and familial expectations, experiences, age, educational level, occupation and security, psychological, social and economic resources. Problem solving skills of the mothers who are socially supported by their spouses develop significantly.[7] The aim of this study to observe the possible effects of the profession which is an important element of family on the attitudes relating the parenting period which constitutes an important period in family life cycle.

MATERIAL AND METHOD

This is observational, analytical and prospective study. It was approved by Ankara Training and Research Hospital Ethics Committee with date: 05.10.2011, meeting no: 0435, decision no: 3609. The individuals who applied to the Ankara Training and Research Hospital Family Practice Clinic between the dates October 2011- February 2013, from different professions who were in the position of having children, and agreed to participate are included in the study. The data was collected by questionnaire method. Before starting the survey, the written consents are obtained from the participants. Six different occupational groups are included in this study. These occupational groups are designated as health professionals (41 individual), technicians (39 individuals), security (34 individuals), educator (45 individuals), self-employed (33 individuals) and housewives (35 individuals). Samples are collected by quota sampling considering the occupational groups. Several questions which comprise the name, surname, age, gender, number of children, regular reading habit, profession, number of family members, total education duration, educational level and 48 questions in Scale of Outlook to Parenting were asked to the individuals constitute the sampling. The data were evaluated according to the Scale of Outlook to Parenting points table. Comprising the 8 factors and 48 attitude sentences, the Scale of Outlook to Parenting is a scale which validity and reliability is reviewed. The Cronbach's Alfa value of the overall reliability of the scale is 0,893 (revised as 0,890) and considering the revised value, the scale is "high" level reliable scale.[6] The factors of the scale are Family Environment (FE), Aims and Ideals (AI), Attitudes to Children (AC), Physical Competency (PC), Attitudes to Marriage (AM), Economic Condition (EC), Social Attitude (SA), and Personal Skills (PS). During the evaluation of the attitude sentences the 5 point Likert Scale is preferred.

The data is evaluated by SPSS version 16.00. First, the average scores of the factors were calculated. Then, the features of the research group such as distribution by the occupational group, age, etc. are revealed by the descriptive type of analysis. Then, gender comparisons of the factor average scores of the each occupational group are performed with Mann Whitney U independent groups test. The possible effects of the other factors (age, profession, gender, regular reading habit, number of children, and number of family members and duration of education) which may affect the Scale of Outlook to Parenting Factors were evaluated with Factorial ANOVA test. The effects of factors that are deemed significant were evaluated with the Spearman correlation and Mann Whitney U independent groups test. The factors of which p value is lower than 0.05 are considered as significant statistically.

RESULTS

All 227 individuals (98 men, 129 women) were included the study. Mean age was 35.23 years in men and 35.57 years in women (**Table 1**).

The average scores of the factors according to gender Scale of Outlook to Parenting are compared with the Mann Whitney U independent groups test. In comparison of factor average scores regarding gender in Health Professionals group, statistically significant differences were detected between the men and women in terms of Physical Competency and Economic Condition factors (**Table 2**).

In comparison of factor average scores regarding gender in Security group, statistically significant differences were detected between men and women's in terms of Attitudes to Children (p=0.023). The scores of men were higher than women's regarding AC factor (3.78±0.74, 2.82±1.12, p=0.023). In comparison of Technician group, any statistically significant data were not detected. In comparison of factor average scores regarding gender in Educator group, statistically significant differences were detected between men and women in terms of Personal Skills (p=0.01). The scores of women were higher than men's regarding PS factor (4.03±0.76, 3.08±0.75, p=0.01). In comparison of factor average scores regarding gender in Self-Employed group, statistically significant differences were detected between

Table 1. Demographic characteristics of study group

Parameter	Man		Women		Total	
	n	(%, mean±SD)	n	(%, mean±SD)	n	(%, mean±SD)
Age	98	35.23±7.26	129	37.57±7.14	227	36.56±7.27
Number of children	98	1.21±0.91	129	1.52±1.00	227	1.39±0.97
Number of family members	98	3.48±1.20	129	3.53±1.01	227	3.51±1.09
Total education duration	98	13.52±3.45	129	12.73±4.20	227	13.07±3.91
Regular Reading Habit						
Reading	38	(35.5)	69	(64.5)	107	(100)
Not reading	60	(50)	60	(50)	120	(100)
Educational Level						
Primary school	2	(10.5)	17	(89.5)	19	(100)
Secondary school	8	(47.1)	9	(52.9)	17	(100)
High school	35	(50)	35	(50)	70	(100)
University	52	(44.8)	64	(55.2)	116	(100)
PhD degree	1	(20)	4	(80)	5	(100)

SD: Standart Deviation

Table 2. Factor average scores in health professionals group considering gender

Profession	n	Man mean±SD	n	Women mean±SD	p	n	Total mean±SD
Healthy professionals							
FE	15	4.28±0.67	26	4.35±0.52	NS	41	4.32±0.57
AI	15	4.55±0.46	26	4.61±0.40	NS	41	4.59±0.42
AC	15	3.43±0.71	26	3.27±0.84	NS	41	3.33±0.79
PC	15	4.54±0.63	26	3.65±0.91	0.002	41	3.98±0.92
AM	15	4.29±0.53	26	3.96±0.94	NS	41	4.38±0.82
EC	15	3.50±0.69	26	3.90±0.47	0.025	41	3.75±0.59
SA	15	4.60±0.35	26	4.60±0.38	NS	41	4.60±0.36
PS	15	3.88±076	26	3.91±0.91	NS	41	3.90±0.85

FE: Family Environment, AI: Aims and Ideals, AC: Attitudes to Children, PC: Physical Competency, AM: Attitudes to Marriage, EC: Economic Condition, SA: Social Attitude, PS: Personal Skills, NS: Nonspesific, SD: Standart Deviation

men and women in terms of Attitudes to Children. The scores of men were higher than women's regarding AC factor (3.88±0.68, 3.05±0.73, p=0.003). The factorial ANOVA analysis was applied in order to evaluate the possible effects of the other independent factors (gender, regular reading habit, occupation, number of children, number of family member, education duration) and scores which were gained from the each factors of the scale by the participants together. When the other factors which may affect the Family Environment factor were analyzed together, it has been observed that the regular reading habit was effective (p=0.004). In pairwise comparison, the Family Environment factor average scores of the participants who have regular reading habit was higher than the participants who do not have (4.18±0.65, 3.81±0.80 p<0.001). When the other factors which may affect the Aims and Ideas factor were analyzed together, any statistically significant data were not detected. When the other factors which may affect the Attitudes to Children factor were analyzed together, it has been observed that the gender and regular reading habit factors were effective (respectively; p=0.005, p=0.009).

In pairwise comparison, the attitudes to children factor scores of men were higher than women's (3.64±0.79, 3.38±0.89, p=0.016). The attitudes to children factor scores of the participants who have regular reading habit were higher than the participants who do not have (3.61±0.80, 3.39±0.90, p=0.71). When the other factors which may affect the Physical Competency factor were analyzed together, it has been observed that the gender and number of children factors were effective (respectively, p=0.004, p=0.020). In pairwise comparison, the physical competency factor scores of men were higher (4.26±0.79, 3.84±0.77 p<0.001). In correlation analysis, the number of children affected the PC factor score negatively (Spearman's rho=- 0.224, n=227, p=0.01). When the other factors which may affect the Attitudes to Marriage factor were analyzed together, it has been observed that the regular reading habit and occupation factors were effective (respectively; p=0.005, p=0.029). In pairwise comparison, the scores of the participants who have regular reading habit was higher than the participants who do not have (3.87±0.86, 3.52±1.01, p=0.01). In pairwise comparison among the profession groups regarding the AM factor, statistically differences were detected between Health Professions and Security (4.38±0.82, 3.45±0.89 p=0.002), Health Professions and Educator (4.38±0.82, 3.57±0.92, p=0.003), Health Professions and Housewives (4.38±0.82, 3.37±1.16, p=0.006), Security and Technician (3.45±0.89, 3.90±0.72, p=0.018). When the other factors which may affect the Economic Condition factor were analyzed together, any statistically significant data were not detected. When the other factors which may affect the Social Attitude factor were analyzed together, it was observed that the total education duration was effective (p=0,008). In correlation analyze the total education duration affected the SA factor score positively (Spearman's rho=0.185, n=227, p=0.005). When the other factors which may be affect the Personal Skills factors were analyzed together, any statistically significant data were not detected.

DISCUSSION

In our study, the factors which may affect the Scale of Outlook to Parenting factors are examined together with the occupations of the parents. When considered from this point of view, it is observed that the occupation of parents affects the attitudes to marriage independently. Regarding the attitudes to marriage factor, the scores of health professionals are higher than the scores of security, housewives and educator, as well as the scores of technicians are higher than the scores of security group. It is admissible that the health professionals who have life time education chance and communication skills can easily fit into their marriage and parenting evolvements due to these abilities. Thus, in our study parallel to previous studies, the attitudes to marriage scores of the health professionals are higher than the scores of security and educator groups. The studies conducted previously detects that the security groups are in significant psychological breakdown. The initial sources of stress are lack of communication, inspection frequency, heavy responsibilities and workload, facing with the danger and victims of crime, constant mobility and pressures of lawyers.[8]

Similar to our study, concerning the occupational groups, the factor scores of attitudes to marriage of security group is significantly lower than the other groups. The previous study which examines the attitudes to parenting of the future mother's fathers reveals that the gender has impact on the economic condition, physical competency, aims and ideals factors, and women should receive support.[6] In another study it has been revealed that the marital adjustment level is higher among the men than women.[9] Similarly, in our study it has been observed that the factor average scores of men regarding the attitudes to children and physical competency are higher than the women's significantly. In our study, it has been detected that as an independent factor the total education duration affects the social attitude factor positively. In a previous study, it has been detected that the education duration affects the economic condition, physical competency, personal skills and social attitudes factors positively.[6] In our study, positive impact of total duration of education on social attitude is considered to be consistent with the earlier studies. In our study, it has been detected that as an independent factor the regular reading habit affects Family Environment, Attitudes to Children and Attitudes to Marriage factors positively. Reading shapes the individual's behavior and relationships with others, enriches the inner world, expands the perspective, enables to be unprejudiced, unbiased and tolerant, increases the level of appreciation, enables to gain freedom of thinking and creation and evaluation habits.[10] In our study, it has been detected that the number of children factor has negative impact on the Physical Competency. As the number of children is increasing, the father participation rate decreases and the physical punishment applications are increased.[11] According to the results of a study conducted by Mehall, increasing number of children brings into view a father who is less interested in his babies.[12]

The findings of our study can provide guidance service to the groups which are risky in terms of attitudes to parenting. Discovering with our study that the Scale of Outlook to Parenting is effective on the Attitudes to Marriage factor independently, it can be stated that the occupation factor is effective on the overview on the attitude to parenting as initially predicted. For this reason, considering the occupational groups is significantly important regarding the scientific surveys on parenting, social planning and the related service policy to be planned.

This study reflects only the characteristics of Turkish society. For this reason, in order to reach international results, the similar studies should be conducted in other societies and cultures.

CONCLUSION

Our study reveals the importance of the factors which affect the attitude to parenting such as occupation, regular reading habit, and number of children, gender, and duration of education. Our study might shed light on various researches to be done in the future.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ankara Training and Research Hospital Ethics Committee (Date: 05.10.2011, Decision no: 0435-3609).

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

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Orjinal Araştırma / Original Article

Seroprevalence of HBsAg, Anti-HBs, Anti-HCV and Anti-HIV in Behçet's Disease

Behçet Hastalığı'nda HBsAg, Anti-HBs, Anti-HCV ve Anti-HIV Seroprevalansı

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Abstract

Introduction: Behçet's disease defined by Turkish dermatologist Hulusi Behçet is an inflammatory disease of unknown etiology and characterized by recurrent oral aphthous ulcers, genital ulcers, uveitis and skin lesions. We aimed to evaluate hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV) seroprevalence in Behçet's Disease.

Material and Method: Patients diagnosed with Behçet's disease and followed up by the dermatology outpatient clinic during 12-years period between July 2008 and July 2020 were retrospectively analyzed. Demographic datas and hepatitis B surface antigen (HBsAg) , hepatitis B surface antibody (anti-HBs) , hepatitis C antibody (anti-HCV), human immunodeficiency virus antibody (anti-HIV) results of the patients were recorded.

Results: 359 patients with Behçet's disease were been evaluated in this study. Of these patients, 189 (52.6%) were female, 170 (47.4%) were male and the mean age was 37.7±12.3 years. HBsAg was positive in 6 (1.6%) patients and Anti-Hbs ab in 82 (7.7%) patients. Anti HIV ab was negative in all patients. Anti-HCV antibodies were found positive in only one case (0.2%), and this was confirmed by testing for hepatitis C virus-ribonucleic acid (HCV RNA). HCV RNA was negative in this patient.

Conclusion: When compared with the general population, seropositivity rates were not detected to be high in Behçet's patients. In fact, the immunity rates were found very low. Based on such a finding, it was concluded that screening is required due to increasing immunosupressive treatments today, and individuals should be vaccinated in cases where HBV indicators are negative. In the other studies, investigating the entity, seropositivity rates have been found similar to those in the population. Considering that serological data show regional differences, we thought that, our study will contribute to the literature both national and international grades due to large patient population in our region.

Keywords: Behçet's disease, hepatitis B virus, hepatitis C virus, human immunodeficiency virus, seroprevalence

Öz

Giriş: Behçet hastalığı bir Türk dermatoloğu olan Hulusi Behçet tarafından tanımlanmış; etyolojisi bilinmeyen, tekrarlayan aftöz ülserler, genital ülserler, üveit ve deri lezyonları ile karakterli inflamatuar hastalıktır. Çlışmamızda Behçet hastalarında HBV, HCV ve HIV seroprevalansını değerlendirmeyi amaçladık.

Gereç ve Yöntem: Temmuz 2008 ile Temuuz 2020 tarihleri arasında dermatoloji polikliniğinde takip edilen Behçet hastalarının dosya bilgileri retrospektif olarak analiz edildi. Demografik verileri ile HBsAg, anti-HBs, anti-HCV, Anti-HIV sonuçları kaydedildi.

Sonuçlar: 189'u kadın (%52,6) ve 170'i erkek (%47,4) olmak üzere yaş ortalamaları 37,7±12,3 olan 359 Behçet hastası değerlendirildi. 6 hastada (%1,6) HBsAg pozitif olduğu görülürken, 82 hastada (%7,7) Anti-Hbs antikorunun pozitif olduğu görüldü. Anti HIV antikorunun tüm hastalarda negatif olduğu görülürken, anti-HCV antikorunun ise sadece 1 hastada pozitif olduğu görüldü (%0,2) ve sonucun HCV-RNA ile kontrol edildiği ve negatif olduğu görüldü.

Tartışma: Genel popülasyonla karşılaştırıldığında Behçet hastalarında seropozitiflik oranının yüksek olmadığı görüldü. Esasen immünite oranlarının düşük olduğu görüldü. Elde edilen sonuca göre immünsupresif tedavilerin arttığı günümüzde seroprevalans değerlendirmesinin Behçet hastalarında önemli olduğu düşünüldü. Ayrıca HBV göstergelerinin negatif olduğu hastalarda aşılama düşünülmelidir. Çalışma sonuçlarının genel olarak normal popülasyon ve diğer Behçet hastalığı ile ilgili seroprevalans çalışmalarından farklı olması ülkemizdeki ve bölgemizdeki farklılıklara bağlı olduğu düşünüldü.

Anahtar Kelimeler: Behçet hastalığı, hepatit B virüs, hepatit C virüs, insan immünyetmezlik virüsü

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INTRODUCTION

Behçet's disease (BD), defined by Hulusi Behçet who is a Turkish dermatologist, is an inflammatory disease of unknown cause characterized by recurrent oral aphthous ulcers, genital ulcers, uveitis and skin lesions.[1,2] BD is not a persistent inflammatory disease, but a disease consisting of recurrent acute inflammation attacks.[3,4] The disease should be followed up regularly for lifetime. It should be kept in mind that BD is a systemic disease and may affect many organs.

Therefore, it requires a multidisciplinary approach. In general, there is no treatment that cures all symptoms in Behçet's disease. For this reason, treatment must be arranged to the leading symptom. The planned treatment should be started as early as to prevent irreversible organ damages. A wide range of drugs are valid for treatment like colchicine, systemic steroids, azathioprine, cyclophosphamide, dapson, talidomid and the others.[5] Seroprevalence of global and Turkey rates are respectively; for HBV is 3,5% and 3,3%, for HCV is 2,4% and 2,5%, for HIV is 0,004% and 0,0012 in population. Pre-treatment screening for HBV, HCV and HIV is becoming a current issue due to the risk of reactivate latent infections with the use of immunosuppressive agents. All patients undergoing immunosuppressive drug therapy or monoclonal antibody therapy should be screened, prophylactic antiviral therapy should be initiated when necessary and the patient group not receiving immunosuppressive treatment should be closely monitored.[6-8]

Many patients infected with HBV are unaware of the infection or the risk of immunosuppressive treatments. Serological tests should include HBsAg, anti-HBs ab, anti-HCV ab and Anti HIV ab. Further screening is required for suspicious patients. HBeAg, anti-HBe ab and Hepatitis B virus-deoxyribonucleic acid (HBV DNA) must be screened in HBsAg positive cases.[9,10] In addition to these parameters, anti-HCV ab and anti-HIV serology should be checked before immunosuppressive treatment.[6]

In our study, we aimed to evaluate HBV, HCV and HIV seroprevalence in Behçet's Disease.

MATERIAL AND METHOD

It's a single center, retrospectively designed study. Local ethic committee approval was obtained. Medical records of dermatology outpatient clinic patients between July 2008 and July 2020 retrospectively scanned with hospital information management system (HBYS). Patients diagnosed with Behçet's disease were retrospectively analyzed. Demographic datas of patients and HBsAg, Anti-HBs ab, Anti-HCV ab, Anti HIV ab results were recorded. HBsAg, Anti-HBs and Anti HCV serological tests were studied in our laboratory using the chemiluminescence immunoassay technique with Advia Centaur (Siemens) autoanalyzer. All recorded data belonges to different patient and duplicate results are not included. Patients under 18 years of age are excluded.

Results were accepted as positive if HBsAg s/co ≥1, anti-HBs ab ≥10 IU/L, anti HCV ab s/co ≥1, anti-HIV ab s/co ≥1. Intermediate results were repeated. Patients remaining with intermediate values were not included in the study.

The study was carried out with the permission of Konya Provincial Health Directorate (Date: 04.03.2021, Decision no: E86737044-806.01.03).

RESULTS

In this study, 359 patients with Behçet's disease were included. All patients had serological tests. Of these patients, 189 (52.6%) were female, 170 (47.4%) were male and the mean age was 37.7±12.3 years (**Table 1**). HBsAg was positive in 6 (1.6%) patients and Anti-Hbs in 82 (7.7%) patients. Anti HIV was negative in all patients. Anti-HCV antibodies were found positive in only 1 patient (0.2%), and this was confirmed by testing for HCV RNA. HCV RNA was negative in this patient (**Figure 1**).

Table 1. Patient characteristics of the study

Patients, n	359
Male	170
Female	189
Age, mean	37.7 years (±12.3)

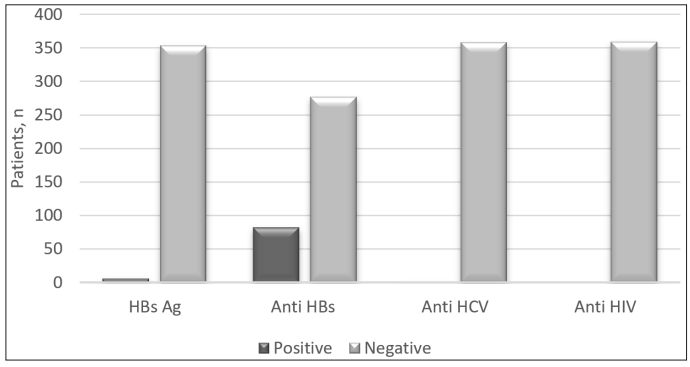

Figure 1. Seroprevalence of patients

DISCUSSION

HBsAg was positive in 6 (1.6%) patients and anti-Hbs in 82 (7.7%) patients, anti HIV was negative in all patients and anti-HCV antibodies were found positive in only 1 patient (0.2%) in our study. Due to the increase in the use of immunosuppressive drug therapy or monoclonal antibodies in chronic diseases, it has been required to perform serological screening before treatment.[6] Considering the use of immunosuppressive drugs in Behçet's patients, although the seropositivity rates are not found to be high,[11,12] sporadic cases related to hepatitis B, hepatitis C or human immunodeficiency virus (HIV) have been reported in Behçet's patients based on the literature.[13-17] However, it should be kept in mind that immunosuppressive treatment may lead to hepatitis B virus reactivation (HBVr) and result in mortality.[6,19,20] In the study performed by Roberto et al.[18] HBVr was found in a patient

with Behçet's disease after the use of tumor necrosis factor alpha (TNF-alpha) inhibitors. In the seroprevalence studies conducted in our country, the positivity of HBsAg was found to be 4.22%, 10%, 12.6%, 3.96% and 4.6% respectively.[21-25] Farajzadeh et al.[11] reported that HBsAg was detected to be positive in one patient in 48 patients with Behçet's disease. In another study performed in Konya – Turkey, blood donor participants were screened in terms of HBsAg and the positivity rate was found as 1.53%.[26] In our study HbsAg positivity was found to be quite low (1.8%) in patients with Behçet's disease. Considering that our study was regionally performed, our findings were determined as similar to the positivity rate in the society.

The first community-based investigation of hepatitis B prevalence in Turkey has recently been carried out by Turkish Association for the Study of the Liver (TASL). 5,471 people were screened in this study, the positivity of anti-HBs was found as 32%.[27] Aksu et al.[28] reported that positivity rates of HBsAg and anti-HBs in patients with Behçet's disease were measured to be 4 and 31%, respectively. Anti-HBs positivity was found to be quite low with a 7.7% rate in our study. Given the requirement for immunosuppressive treatment, the vaccination has been started to be considered a necessity for patients with Behçet's disease. The fact that such a widely-ranging rate was found in our study suggested that the regional differences. Although hepatitis B vaccination has been accepted to be safe and effective for the general population, the recommendations for hepatitis B vaccination in those with Behçet's disease still remain unclear.[29] If HBV indicators are negative in a patient, the vaccination program should be initiated before administering immunosuppressive treatment, if possible.[6] The response of the vaccine will probably be low in patients administered with immunosuppressive therapy.[30] Vaccines with higher doses or enhanced-efficacy may be required to provide anti-HBs response in patients receiving immunosuppressive treatment.[6] As seen in our study, anti-HBs seropositivity was found to be low in those with Behçet's disease and therefore these patients are considered appropriate to be screened and included in the vaccination program. The prevalence of anti-HCV and anti-HIV 1/2 have been reported as 0.16-5.2% and 0.007-0.130% in our country, respectively.[31] There are various studies about seropositivity of HCV in patients with Behçet's disease both supporting relationship or not.[13-15] Farajzadeh et al.[11] reported that there isn't any anti-HCV positivity was found in 48 patients with Behçet's disease. However, in another study, Etem et al.[12] assessed 56 patients with Behçet's disease and stated that anti-HCV positivity was found in one patient while no anti-HIV positivity was detected. As compatible with the finding in the study by Etem et al.[12] anti-HCV positivity was detected only in only one case (0.8%) in our study and the reading of HCV RNA test was also negative. Since various HIV infection-related vasculitis syndromes have been encountered recently, it has been suggested that Behçet's disease may also be associated with HIV infection.[16,17] In one HIV case, Behçet's disease was seen to be cured completely with antiretroviral treatment.[32] Although no anti-HIV positivity was detected in our study, such an evidence-based relationship between Behçet's disease and HIV cannot be ignored, and therefore we consider that the patients with Behçet's disease should be screened in terms of anti-HIV positivity.

CONCLUSION

When compared with the general population, seropositivity rates were not detected to be high in patients with Behçet's disease. In fact, the immunity rates were found very low. Based on such a finding, it was concluded that screening is required due to increasing immunosuppressive treatments today and individuals should be vaccinated in cases where HBV indicators are negative. In most of the studies investigating the entity, seropositivity rates have been found similar to those in the population. Considering that serological data show regional differences, it is clear that our study will contribute to the literature at both national and international levels due to large patient population in our region.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Konya Provincial Health Directorate (Date: 04.03.2021, Decision no: E86737044-806.01.03).

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

Referee Evaluation Process: Externally peer-reviewed.

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

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

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Orjinal Araştırma / Original Article

Clinical Features of Myasthenia Gravis Patients': The Assessment of 138 Patients

Myastenia Gravis Hastalarının Klinik Özellikleri: 138 Hastanın Değerlendirilmesi

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Abstract

Aim: The aim of this study was to evaluate the demographic characteristics, clinical presentation, antibody, and electrophysiological characteristics of patients with the diagnosis of Myasthenia Gravis (MG).

Material and Method: The demographic characteristics, clinical presentation, antibody, electrophysiological and radiological (thoracic tomography) characteristics of the patients who were followed in the Neuromuscular and Muscular Diseases Polyclinic of the hospital between 2014-2019 were analyzed.

Results: The mean age of the patients was 53.8±16.67 years. The mean disease duration was 4.8±5.05 years. Ptosis was the most common complaint in 79% (n=109) of our patients. The number of patients followed as pure ocular MG was 61.6% (n=85). There were 26 patients who presented with ptosis or diplopia at the first presentation and follow-up generalized MG with bulbar findings and weakness. Acetylcholine receptor antibody (AntiAChRAb) positivity was found in 78.3% (n=108) of the patients and thymus pathology was detected in thorax tomography in 37.7% (n=52).

Conclusions: The initial complaint provides little insight into the course of the disease. The important factor is clinical follow-up. Although MG treatment is known, the pathophysiology of MG remains to be elucidated, and other autoimmune conditions cause changes in treatment choice. Therefore, an important point in MG management; is the choice of individualized therapy.

Keywords: Acetylcholine receptor antibody, Myasthenia Gravis, pyridostigmine, thymoma

Öz

Amaç: Bu çalışmanın amacı, Myastenia Gravis (MG) tanısı ile izlenen hastaların demografik özellikleri, ilk başvuru şikayeti ile klinik seyir, antikor ve elektrofizyolojik özelliklerini değerlendirmektir.

Gereç ve Yöntem: 2014-2019 yılları arasında, hastanemiz Nöromusküler ve Kas Hastalıkları Polikliniği'nde takip edilen yüz otuz sekiz MG hastasının demografik özellikleri, ilk başvuru şikayeti ile klinik seyri, antikor, elektrofizyolojik ve radyolojik (toraks tomografi) özellikleri incelendi.

Bulgular: Hastaların yaş ortalaması 53,8±16,67 idi. Ortalama hastalık süresi 4,8±5,05 yıl idi. Hastalarımızın en sık, ilk başvuru şikayeti %79 (n=109)'unda ptozis idi. Saf oküler MG olarak takip edilen hasta sayısı %61,6 (n=85) kişiydi. İlk başvurusunda ptozis veya diplopi şikayetiyle gelip, daha sonrasında bulber bulgular ve güçsüzlük eklenerek jeneralize MG düşünülen 26 hasta bulunuyordu. Hastaların %78,3 (n=108)'ünde asetil kolin reseptör antikoru (AntiAChRAb) pozitifliği ve %37,7 (n=52)'sinde toraks tomografide timüs patolojisi bulundu.

Sonuç: İlk başvuru şikayeti hastalığın seyri hakkında çok az fikir vermektedir. Asıl önemli olan, klinik yakın takiptir. Her ne kadar MG tedavisi bilinse de MG'in patofizyolojisi halen tam olarak aydınlatılamamıştır ve diğer otoimmun durumlar tedavi seçiminde değişikliğe neden olmaktadır. Bu nedenle de MG yönetiminde önemli bir nokta; bireyselleştirilmiş tedavi seçimidir.

Anahtar Kelimeler: Asetilkolin reseptör antikoru, Myastenia Gravis, pridostigmin, timoma

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INTRODUCTION

MG symptoms occur with an autoimmune attack or damage to the neuromuscular junction (NMJ). Its clinical feature is a symptomatic weakness that is predominant in some muscle groups and typically fluctuates with increased effort and a decrease in response to rest. The diagnosis of MG is primarily based on the clinical history and examination findings that show this apparent pattern of weakness and can be confirmed using a series of diagnostic tests. However, not all patients have this classic clinical feature, and variable or atypical presentations may be seen.[1]

Although MG is a relatively rare disease, its prevalence rates have approached 20 per 100,000 in the US population and have increased over time with recent estimates.[2] Recent studies show that MG is becoming increasingly widespread, particularly in the elderly.[1,3]

The incidence of MG is between 9 and 30 in 1 million, while the prevalence is between 100 and 140 in 1 million. However, last reports have shown that its prevalence is more than 200 per 1 million.[1,4,5] While in the first five decades of women's lives diagnosed have MG is higher men are more likely to be diagnosed MG after the age of 50.[1,6] Patients with ocular MG and prepubertal juvenile MG are more common, particularly in people of Asian descent and men with late-onset MG. Anti-muscle-specific tyrosine kinase (Anti-MuSK) positive MG is more common in young women and possibly in the non-white population.[1,6]

MG physiopathology is still not fully understood, but it is known that neuromuscular transmission is inhibited by the formation of antibodies against proteins at the neuromuscular junction. Antibodies opposite to AChR, the most common antigenic target in MG, are present in 85% of patients with generalized MG and 50% of patients with ocular MG and prevent neuromuscular transmission.[1,7,8] In more than half of antiAChRAb negative generalized MG patients, antibodies target other proteins in the NMJ. The first described and still most common antibodies against MuSK.[1,9] More recently, antibodies against lipoprotein receptor-associated protein 4 (LRP4), cortactin, and agrin have been described, but a group of patients without antibodies are still defined as seronegative myasthenia gravis (SNMG).[10]

Most antiAChRAb positive MG patients have pathological thymic involvement, either thymic hyperplasia or thymoma. Thymic hyperplasia occurs in 50-80% of postpubertal adolescents and in cases of early-onset AntiAChRAb positive MG. Thymic hyperplasia is rare in Anti-MuSK positive MG. It is less common in seronegative and late-onset MG, where the thymus is usually found in the normal, atrophic, or thymoma form.[1,11,12] An important source of anti-AChR antibodies is the hyperplastic thymus. Thymoma is found in 10-20% of patients with MG, and MG is seen in 30-50% of thymoma cases.[1,11,13] The prevalence of other autoimmune diseases, particularly thyroid, has increased in MG patients and their family members. While it occurs between 13-30% in patients with MG, it is between 5-8% in the general population. A genetic effect is mentioned in autoimmune diseases, MG is the least common disease among them.[1,14,15] Widely used in the classification of MG; The American Myasthenia Gravis Foundation Clinical Classification is a useful scale for both research and general clinical purposes (**Table 1**).[16]

Table 1. American Myasthenia Gravis Foundation Clinical Classification

Class I	MG is characterized by the following: i. any ocular muscle weakness. ii. may have weakness of eye closure. iii. all other muscle strengths are normal
Class II	MG is characterized by the following: i. mild weakness affecting muscles other than ocular muscles, ii. may also have ocular muscle weakness of any severity
Class IIa	MG is characterized by the following: i. predominantly affecting limb, axial muscles, or both ii. may also have lesser involvement of oropharyngeal muscles.
Class IIb	MG is characterized by the following: i. predominantly affecting oropharyngeal, respiratory muscles, or both, ii. may also have lesser or equal involvement of limb, axial muscles, or both.
Class III	MG is characterized by the following: i. moderate weakness affecting muscles other than ocular muscles, ii. may also have ocular muscle weakness of any severity.
Class IIIa	MG is characterized by the following: i. predominantly affecting limb, axial muscles, or both, ii. may also have lesser involvement of oropharyngeal muscles.
Class IIIb	MG is characterized by the following: i. predominantly affecting oropharyngeal, respiratory muscles, or both, ii. may also have lesser or equal involvement of limb, axial muscles, or both.
Class IV	MG is characterized by the following: i. severe weakness affecting muscles other than ocular muscles, ii. may also have ocular muscle weakness of any severity.
Class IVa	MG is characterized by the following: i. predominantly affecting limb, axial muscles, or both, ii. may also have lesser involvement of oropharyngeal muscles.
Class IVb	MG is characterized by the following: i. predominantly affecting oropharyngeal, respiratory muscles or both, ii. may also have lesser or equal involvement of limb, axial muscles, or both.
Class V	MG is characterized by the following: i. intubation with or without mechanical ventilation, except when employed during routine postoperative management, ii. the use of feeding tube without intubation places the patient in class IVb.

*MG: Myasthenia Gravis

Previous studies have indicated clinical predictions for MG prognosis. Age, gender, thymus anomaly, autoimmune diseases, and initial symptoms of the disease were selected as potential clinical markers for MG prognosis.[17] When MG is diagnosed, treatment usually begins with cholinesterase inhibitors, but most patients will need immune-focused therapy.

In this study, the demographic, clinical, radiological characteristics, prognostic factors, and treatment approaches of MG patients were evaluated.

MATERIAL AND METHOD

The study was carried out with the permission of Health Sciences University Dışkapı Yıldırım Beyazıt Training and Research Hospital Clinical Research Ethics Committee (Date: 25.01.2021, Decision no: 103-05). All procedures were performed adhered to the ethical rules and the Helsinki Declaration of Principles.

In 2014-2019, the demographic characteristics, first application complaint, and clinical course, antibody status, electrophysiological and radiological (thoracic tomography) characteristics, and main treatment data of one hundred thirty-eight MG patients who were followed up in the Neuromuscular and Muscular Diseases Polyclinic of our hospital were retrospectively analyzed.

As diagnostic criteria; It was taken into consideration that in EMG; the decrement response exceeding 10% in repetitive stimulation or the presence of electrophysiological abnormality in the form of prolonged jitter in single-fiber EMG, clinical response to anticholinergic drugs, showing positivity of Ach receptor antibodies in serological tests.[18,19]

The demographic characteristics of the patients and first application complaints were evaluated. The patients' neurological examinations, the results of hemogram, routine biochemistry, hormone, and AchRAb laboratory tests were examined. The treatments of the patients who were diagnosed with electrophysiological (ASUT and SFEMG if necessary) examinations were recorded. Records of the patients who were followed up with neurological examinations at regular intervals at the control visits were obtained. These cross-sectional data obtained from MG patients were compared with the literature.

Statistical Analysis

Statistical analyzes were performed by transferring the data to the SPSS® (Statistical Package for Social Sciences) 22.0 program. While evaluating the study data, frequency distributions for categorical variables and descriptive statistics (Mean±SD) for continuous variables were given. Independent Sample T-test was used to determine whether there was a difference between two independent groups for normally distributed variables, and Mann Whitney U test was used for variables that were not normally distributed. Chi-square analysis was used to examine the relationship between two independent categorical variables. N (%) values were given for categorical variables, mean (standard deviation) for normally distributed variables, and median (minimum-maximum) values for non-normally distributed variables. A p-value of less than 0.05 was considered significant.

RESULTS

Eighty-three female patients with a mean age of 49.6±16.13 and fifty-five male patients with a mean age of 60±15.63 were included in the study. The mean duration of disease was 4.8±5.05 years.

The first application complaint and initial symptom of the patients were ptosis in 79% (n=109). 16 of them had diplopia as the initial complaint and accompanied by ptoses, dysphagia, and weakness. However, in only 1 of them, the first application complaint was just diplopia. Dysphagia and/or difficulty swallowing in 7.2% (n=10) of the patients, limb weakness in 8% (n=11), weakness in the form of weakness of the neck muscles, and drop head in 5.8% (n=8) were found as the first application complaint.

According to the Myasthenia Gravis American Clinical Classification Foundation, 79.7% (n=110) of them were ocular and 20.3% (n=28) were generalized MG in the first application. During their follow-up, 26 patients continued their follow-ups as generalized MG in 38.4% (n=53) of all patients in an average of 12.6±6.81 (2-28 months) months. At the first diagnosis, stage they diagnosed with; 78.3% (n=108) were AchRAb positivity, 31.9% (n=44) with decrement response in ASUT, and 35.5% (n=49) with SFEMG findings.

Thymus pathology was found in the thoracic tomography of 37.7% (n=52) of the patients. 33.3% (n=46) of the patients had thymectomy. The pathology results of them were thymoma in 8% (n=11), thymus hyperplasia, or thymic residue in 26.1% (n=36). One of the patients with thymoma received radiotherapy in addition to thymectomy because of parenchymal invasion.

38.4% (n=53) of the patients had the additional autoimmune systemic disease. The most common of these were diabetes mellitus, thyroid diseases, rheumatoid arthritis (RA), Sjögren Syndrome. The clinical course of those with additional autoimmune diseases worsened more often and required additional treatment (intravenous immune globulin). With the initiation of methotrexate in patients with RA, significant clinical benefit was achieved like the literature.[20] After the diagnosis of MG, 4 (2.8%) patients who experienced pregnancy were closely followed up by adjusting their medications. One of the patients was pregnant twice during MG disease. The patient, who was followed up closely in her first pregnancy, was delivered by a healthy cesarean section. In her second pregnancy, she stopped MG medication herself and did not come to follow up. Her pregnancy resulted in abortion due to fetal growth restriction and fetal death in the gynecological follow-up. Later, he continued his follow-up in our polyclinic.

DISCUSSION

MG is a relatively rare disease. The incidence of MG has been reported between 9-30 in 1 million (5). When the patients in this study were examined within the years included, 7.2% (n=10)-17.3% (n=24) of the patients were those who were newly diagnosed annually. The patients included in this study were those who were followed up in the Neuromuscular and Muscular Diseases Polyclinic of the hospital, and it was noticed that the number of newly diagnosed patients increased every year compared to the previous years. The reason for this is that the Neuromuscular and Muscular Diseases Polyclinic of our hospital is considered to be the reference center.

In recent studies, it has been stated that MG is more common especially in the elderly (1,3), the average age of our patients was 53.8±16.67 (19-89), 57.2% of them were over 50 years old. In accordance with the literature, 51.9% of the patients diagnosed with MG after the age of 50 were male. Female patients were statistically significantly younger (49.6±16.13 years, p=0.000).

In 79% (n=109) of our patients, the first application complaint was the most common ptosis. The first symptom that occurs in 15% of the patients; bulbar weakness is known to occur with difficulty speaking, chewing, or swallowing, and can sometimes occur without obvious ocular signs or symptoms in older adults.[1] Bulbar onset was present in 20 (14.4%) patients in our patients included in study. Although rare, the first complaints in MG can occur with focal weakness in single muscle groups. Defined as "dropped head syndrome", which is rare in the literature, it mainly arises as a result of the weakness of the extensor group neck muscles.[21,22] 5.8% (n=8) of our patients presented with complaints of severe head incontinence. As in the patients included in the study, the complaints increase with fatigue, there is usually accompanying ptosis, chewing, and swallowing difficulties.

Autonomic findings such as urinary-fecal incontinence and erectile dysfunction, which are very rare in MG, requiring the exclusion of other causes in case of existence, were present in 3.6% (n=5) of our patients. Additional examinations and investigations were also performed for patients with these complaints to exclude other causes, and it was concluded that MG had autonomic findings. These complaints completely resolved within 3 months to 1 year in follow-up. It was stated by the patients that especially urinary and fecal incontinence differed during the day, and some days seemed to be completely recovered.

During the 4.5-year follow-up period, 5 patients were followed in intensive care units due to the need for a mechanical respirator. 3 of them recovered and became extubated, and their follow-up continues. Two of the patients died due to pneumonia, respiratory failure, and developing autonomic findings. The etiological cause of the MG crisis and respiratory failure of the patients who died was thought to be an infection.

According to the Myasthenia Gravis American Clinical Classification Foundation, while 79.7% (n=110) of them were ocular MG patients at the first application, 26 of them were followed up as generalized MG within an average of 12.6±6.81 months (2-28 months) months. MG is one of the first diagnoses that come to mind in every patient presenting with ptosis. The physiopathology of the conditions related to the involvement of the autonomic system in MG and the different responses of the drugs used in the treatment have not been fully elucidated yet. Therefore, prospective, larger controlled studies are needed. Treatment decisions and patient follow-up frequency should be individualized according to the severity of MG and coexisting disease, and patient participation in these decisions is crucial for successful management. Few patients can have complete remission in MG. Most patients do not have complete pharmacological remission. Prospective, controlled studies comparing treatments in MG patients are few. With current knowledge and treatments, care must be taken to find the most suitable treatment for each patient. In our study, 33.3% of the patients had thymectomy. One of the patients with thymoma received radiotherapy in addition to thymectomy because of parenchymal invasion. When MG is diagnosed, treatment is usually started with cholinesterase inhibitors. However, in most patients, it may be necessary to add immune-focused therapy. Physical therapy and rehabilitation, either outpatient or inpatient, are also part of the treatment and are very effective. Another treatment method is surgery. Treatment of maximal thymectomy with sternotomy or minimally invasive approaches can be applied.

The limitation of our study is that we could not determine the pathogenicity of existing and newly identified antibodies in seronegative MG patients. The reason for this was that the testing of antibodies was paid and the patients did not want it.

Over time, specific diagnostic procedures and expert follow-up improve treatment outcomes. This is particularly important because MG is a potentially reversible disease with treatment options that can make a huge difference to the patient. With the close follow-up and appropriate treatment, the majority of MG patients are able to perform daily living activities and maintain a normal quality of life.

CONCLUSION

In the diagnosis, follow-up, and treatment process of MG patients; evaluation of the patient by the same clinician team, taking into account other diseases of the patient, individual immunological treatment, and follow-up at a certain frequency constitute the most important parts.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Health Sciences University Dışkapı Yıldırım Beyazıt Training and Research Hospital Clinical Research Ethics Committee (Date: 25.01.2021, Decision no: 103-05).

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

Referee Evaluation Process: Externally peer-reviewed.

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

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Orjinal Araştırma / Original Article

How much does the Level of Physical Activity Change in Patients with Physical Disabilities Hospitalized for Rehabilitation?

Rehabilitasyon İçin Hospitalize Edilen Fiziksel Engelli Bireylerde Fiziksel Aktivite Düzeyi Nekadar Değişiyor?

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Abstract

Objective: This study aimed to examine the short term effect of inpatient rehabilitation program on self –reported physical activity in participants with physical disabilities.

Material and Method: The patients were divided into groups as group 1: individuals with physical disability due to musculoskeletal diseases, and group 2: individuals with physical disability due to neurological diseases. The results of Physical Activity Scales for Individuals with Physical Disabilities (PASIPD) at one month after discharge (PA2) compared with the results of PASIPD at hospitalization (PA1). The first assessment was done face-to face, but the assessment after discharge were made using phone.

Results: There was a significant difference between PA2 and PA1 in group 1, group 2, and among all participants (p=0.001). The change in physical activity level from hospitalization to one month after discharge was similar in the two groups (p=0.564).

Conclusion: While people learn to live with a disability, quickly integrating physical activity with rehabilitation program into their new daily routine can be seen as a good strategy.

Keywords: disability, physical activity, rehabilitation, televisit

Öz

Amaç: Mevcut çalışmada fiziksel engelli bireylerde hospitalize edilerek uygulanan rehabilitasyon uygulamalarının kısa dönem etkisinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntem: Hastalar grup 1: kas-iskelet sistemi hastalıkları nedeniyle fiziksel engelli bireyler ve grup 2: nörolojik hastalıklar nedeniyle fiziksel engelli bireyler olarak gruplara ayrıldı. Hospitalizasyonlarının ilk günündeki Fiziksel Engelli Bireyler için Fiziksel Aktivite Ölçek (FEBFAÖ) sonuçları (FA1) taburculuktan bir ay sonraki ile (FA2) karşılaştırılmıştır. İlk değerlendirme yüz yüze yapıldı ancak taburcu olduktan sonraki değerlendirme pandemi nedeniyle telefon aracılığıyla yapıldı.

Bulgular: Grup 1'deki, grup 2'deki ve tüm katılımcıların FA2 ve FA1 arasında anlamlı fark vardı (p = 0,001). İki grup arasında fiziksel aktivite düzeyinin değişimi açısından anlamlı fark saptanmadı (p = 0,564).

Sonuç: İnsanlar fiziksel bir engelle yaşamayı öğrenirken, fiziksel aktiviteyi rehabilitasyon programıyla hızlı bir şekilde yeni günlük rutinlerine entegre etmek iyi bir strateji olarak görülebilir.

Anahtar Kelimeler: disabilite, fiziksel aktivite, rehabilitasyon, televisit

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INTRODUCTION

The World health organization (WHO) describes physical activity as any body movement produced by skeletal muscles that results in energy expenditure in daily life activities above resting level.[1] The implications of physical inactivity on health has been the subject of many studies recently.[2] An inactive lifestyle is accompanied by higher risks for morbidity and mortality of a great number of chronic diseases such as coronary artery disease, diabetes, colon cancer, and osteoporosis.[2,3] Physical activity levels can be measured by accelerometers, pedometers, heart rate monitors and various types of questionnaires.[4]

Disability was defined by WHO as a restriction or lack of ability to perform daily activity, but this definition was later changed to problems in functioning in the WHO classification of Functioning, Disability and Health (ICF).[5] Disability is used as an umbrella definition that includes 3 components of health: body functions and structures, activity limitations, and participation restrictions.[6] Thirteen to 20 % of the western population has one or more disabilities.[2] Osteoarthritis, back pain, neck pain, rheumatologic diseases, neurologic disorders (stroke, spinal cord injury, multiple sclerosis, Parkinson diseases) can cause physical disabilities.[3,6] Recent studies have shown that; high levels of disability is related with low levels of physical activity.[3,7] Also, compared to non-disabled individuals, it has been observed that disabled individuals do less physical activity in their leisure time and less physical activity of at least 30 minutes of moderate intensity five days a week.[2,7] This result may not be surprising; environmental barriers, pain, embarrassment, transportation problems, inadequate accommodations, and unsuitable sports may be some possible barriers to physical activity for individuals with disability.[8,9]

Individuals with disability are commonly hospitalized in inpatients clinics for rehabilitation, which aims to achieve optimal functional level of patients within their own limitations.[10] A rehabilitation program can be an excellent opportunity to integrate post-rehabilitation physical activity into their lifestyle.[11]

In previous studies, the effect of structured outpatient rehabilitation program on physical activity, or the effect of inpatient rehabilitation program on only participants with neurological disorders like as: spinal cord injury were investigated.[2,12]

This study aimed to examine the short term effect of inpatient rehabilitation program on self –reported physical activity both participants with physical disabilities due to musculoskeletal and neurological disorders.

MATERIAL AND METHOD

Study population and design

This study was designed as a prospective cohort study in the physical medicine and rehabilitation (PMR) inpatients clinic.

This study was approved by the University of Health Sciences Dışkapı Yıldırım Beyazıt Training and Reserach Hospital Institutional Ethics Committee (Approval number: 94/06), and was conducted in accordance with the Declaration of Helsinki guidelines Signed informed consent was obtained from each participants prior to starting data collection.

Ninety-two patients with physical disabilities, due to neurologic or musculoskeletal diseases and hospitalized in PMR clinic for rehabilitation between September 2020 and March 2021 were included in this study. Twelve patients who could not be followed up at the end of the first month were excluded from the study and the study was completed with 80 patients.

Inclusion criteria were patients over 18 years of age with cognitive functions able to fill the forms and patients with medical stabilization for neurological diseases.

Patients under 18 years of age, patients with additional hearing, visual and mental disabilities, patients with metabolic instability for neurological diseases, history of malignancy and pulmonary and cardiac failure, and patients with recurrent hospitalization in the PMR clinic were excluded from the study.

Demographic Data

It includes demographic and disease characteristics including age, gender, job, marital status, and comorbidities, and diagnosis requiring hospitalization.

Self-reported Physical Activity Measure

The physical activity scale for individuals with physical disabilities (PASIPD) was used to evaluate the physical activity level of the patients. The PASIPD was developed by Washburn et al.[13], and consists of 13-items: 6 leisure time, 6 households, and 1 occupational activity item. The number of days participated in these activities in the past 7 days was asked as never, seldom (1–2 d/week), sometimes (3–4 d/week), or often (5–7 d/week) and the average of how many hours a day they participated (<1 hour, >1 but >2 hour, 2–4 hour, > 4hour). The response to the occupational item was categorized as <1hour, >1 but < 4 hour,> 5 but< 8 hour, >8 hour. The score for each item was found by multiplying a MET value associated with the activity intensity using the daily average hours for each item, and the total score was obtained by adding the scores of the items between 2-13. The first item, which requests information about sedentary life, wasn't scored.

Interventions

At the first day of hospitalization, all participants were examined by the same physiatrist. After that, a rehabilitation program was planned for each patient according to the current functional status of these patients. Rehabilitation programs included two or more electrotherapies, heat treatments, stretching-strengthening exercises, walking-balance exercises, sitting exercise and transfer training one session/a day, 5 days/week during 4 weeks. The intensity of physical therapy and duration of hospitalization were determined according to the age, disease, functional status, comorbidities, and secondary complications of each patient.

The patients were divided into groups as group 1: individuals with physical disability due to musculoskeletal diseases, and group 2: individuals with physical disability due to neurological diseases the participants in both groups were evaluated two times (PA1, PA2). The first assessment (PA1) was made on the second day of hospitalization, the second assessment (PA2) one month after discharge. At the first evaluation, demographics (age, gender, job, comorbidities…), diseases characteristics, and the level of self-reported physical activity were examined. The first assessments was done face-to face, but the assessment after discharge were made by telephone (**Figure 1**).

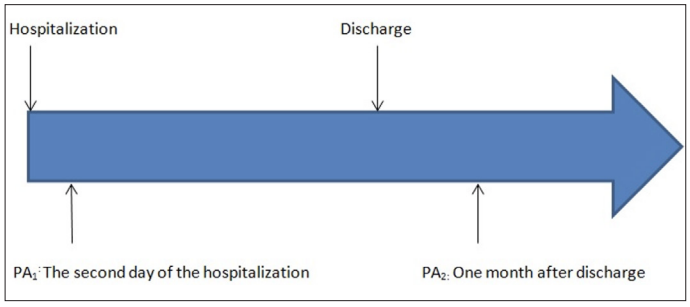

Figure 1. Study Protocol

Comparisons

The changes in PASIPD scores were compared between groups, within groups, and among all participants.

Statistical Analyses

The data analyses were conducted using Statistical Package for the Social Sciences (SPSS 22.0 for Windows) software. The variables were investigated using visuals (histograms, probability plots) and a Kolmogorov-Smirnov test. In reporting descriptive statistics, data were expressed as mean ± standard deviation (SD) and median (minimum-maximum) for continuous variables, and as frequencies and percentages (%) for nominal and categorical variables. PA2 and PA1, were compared with Wilcoxon signed rank test in group 1, group 2, and among all participants. The χ^2 tests and Fisher's exact tests were used to compare nominal and categorical variables as well as the independent sample T and Mann-Whitney U tests were used to compare the continuous values between group 1 and 2. A p-value of < 0.05 was considered statistically significant.

RESULTS

The mean age of all patients was 60.76 ± 15.71 years, 48 (60%) were female and 32 (40%) were male. Half of the patients (group 1, n = 40) had musculoskeletal diseases and the other half (group 2, n = 40) had neurological diseases. Demographics and disease data of the patients are shown in **Table 1** and **Table 2**.

According to the results comparing the demographic characteristics of the two groups, there was no significant difference in age, job, marital status and comorbidities (p>0.05). The gender of the participants in group 1 was significantly different from group 2 (p=0.006).

At the beginning of the hospitalization participants in group 1 had higher self-reported physical activity level comparing participants in Group 2 (p=0.01). The PASIPD scores were statistical similar between two groups at the one month after discharge (p>0.05).

Table 2. Disease data of patients

Group 1 n=40, n(%)	Group 2 n=40, n(%)
Rheumatoid arthritis 2 (5)	TBI 5 (12.5)
Gonarthrosis 4 (10)	ALS 1 (2.5)
IVD 24 (60)	Stroke 21 (52.5)
Artroplasty 3 (7.5)	GBS 4 (10.0)
Shoulder problems 6 (15)	Brachial plexus 1 (2.5)
Anykilosing Spondylitis 1 (2.5)	Parkinson diseases 2 (5.0)
	SCI 6 (15.0)

IVD: intervertebral disc diseases, TBI: traumatic brain injury, ALS: amyotrophic lateral sclerosis, GBS: Guillain- Barre Syndrome, SCI: spinal cord injury

Table 1. Demographics data of patients

		Total n=80	Group 1 n=40	Group 2 n=40	P
Age (years) mean±SD		60.76±15.71	63.26±17.66	58.26±17.66	0.16*
Gender n (%) Female/Male		48 (60)/32(40)	30 (75)/10 (25)	18 (45)/ 22 (55)	0.006**
Job n(%)	Unemployed	39 (48.8)	25 (62.5)	14 (35)	0.09***
	Workman	17 (23.1)	7 (17.5)	10 (25.0)	
	Driver	6 (7.5)	3 (7.5)	3 (7.5)	
	Shopkeeper	2 (2.5)	0	2 5()	
	Officer	15 (18.8)	5 (12.5)	10 (25.0)	
	Student	1 (1.3)	0	1 (2.5)	
Marital status n (%)	Single	7 (8.8)	1 (2.5)	6 (15.0)	0.09***
	Divorced	20 (25.0)	12 (30.0)	8 (20.0)	
	Married	53 (66.3)	27 (67.5)	26 (65.0)	
Comorbidities n (%)	HT	50 (62.5)	26 (65)	24 (60)	0.65**
	DM	23 (28.75)	10 (25.0)	13 (32.5)	0.82**
	Cardiac	18 (22.5)	10 (25.0)	8 (20.0)	0.59**
	Hyperlipidemia	12 (15.0)	5 (12.5)	7 (17.5)	0.54**

SD: standard deviation, p value shows comparison of group 1 and group 2, *: independent sample t test, **: Pearson's χ^2 test, ***:Fisher's exact test

The change in PASIPD from hospitalization to one month after discharge was similar in the two groups (p=0.564) (**Table 3**).

Table 3. Comparison of physical activity level at the beginning of the hospitalization and one month after discharge, and changing of physical activity level between two groups

	Group 1, n=40 median (min-max)	Group 2, n=40 median (min-max)	p value
PA1 MET h/day	1.94 (0-29.99)	0.0 (0-8.84)	0.001
PA2 MET h/day	7.31 (0.49-54.92)	5.83 (0.93-19.18)	0.138
PA2-PA1 MET h/day	4.69 (0/47.12)	3.82 (0.33/17.44)	0.564

Min-max: minimum-maximum, PA1: Physical activity level one day after hospitalization, PA2: Physical activity level at one month after discharge. Mann-Whitney U test were used.

There was a significant difference between PA2 and PA1 in group 1, group2, and among all participants (p=0.001) (**Table 4**).

Table 4. Changes in self- reported physical activity of participants

	Group 1 n=40 median (min-max)	p1	Group 2 n=40 median (min-max)	p2	Total n=80 median (min-max)	p3
PA1 MET h/day	1.94 (0-29.99)	0.001	0.0 (0-8.84)	0.001	0.69 (0-29.99)	0.001
PA2 MET h/day	7.31 (0.49-54.92)		5.83 (0.93-19.18)		6.66 (0.49-51.92)	

Min-max: minimum-maximum, PA1: Physical activity level at one day after hospitalization, PA2: Physical activity level at one month after discharge, p1 shows comparison of PA1 and PA2 in group 1, p2 shows comparison of PA1 and PA2 in group 2, p3 shows comparison of PA1 and PA2 in all patients. Wilcoxon signed rank test were used.

DISCUSSION

This study analyzed the impact of the rehabilitation program on self- reported physical activity levels of participants with physical disabilities. This study determined that the self-reported physical activity levels increased significantly from the onset of hospitalization to one month after discharge. These results were obtained both in patients with physical disabilities due to musculoskeletal diseases and in patients with physical disabilities due to neurological diseases. Although the self- reported physical activity levels of patients with physical disabilities due to musculoskeletal diseases were higher than patients with physical disabilities due to neurological diseases at the beginning of hospitalized, the improvement in self-reported physical activity from hospitalization to one month after discharge was similar in the two groups.

Exercising large muscle groups at a frequency of 3–5 times a week, for a period of 20–60 min (or multiple 10-min sessions), at an intensity of 40–70% heart rate reserve (HRR) was recommended by the American Colleague of Sport Medicine to persons with chronic conditions or disabilities (stroke, amputation, spinal cord injury…) in order to improve aerobic fitness.[14] Different results have been obtained in studies investigating the aerobic effects of rehabilitation programs.[10,14-16]

Self-reported (subjective) or device-based (objective) measurements are the instruments that measure physical activity. PASIPD, which is a self-reported questionnaire, was used to investigate the physical activity levels in this study. The reliability and validity of PASIPD, comparable to a well-established self-reported questionnaire for healthy people, was demonstrated.[2,17] Although there was a correlation between hip accelerometers and PASIPD with correlation coefficients varying between 02.23 and 0.30, it was stated that it would not be correct to compare these two different methods.[2,17]

In our study, we investigated the effects of routine rehabilitation programs on the self- reported physical activities of participants with disabilities. All participants continued their rehabilitation program in the inpatients clinic, so the impact of the environment was standardized for all patients. One month after discharge, self- reported physical activity was improved with rehabilitation among all participants and in both groups. In order to make our second evaluation, we preferred to do it one month after discharged when the patients returned to their normal daily life, because PASIPD is generally a questionnaire that evaluates housework and leisure activities, we thought that the evaluation made during the hospitalization of the patients might lead to incorrect evaluations.

During pandemic, our methods of evaluation patient were changed as all our habits changed. We preferred televisit method which is made over telephone to evaluate the self-reported physical activity level of participants due to transfer problems and pandemic.[18]

In a randomized controlled study, weekly self-reported physical activity levels increased with home or community-based exercise programs in women with mobility problems.[18] In this study, the weekly self-reported physical activity level and fitness parameters at the onset and end of the study (28 weeks later) were evaluated in the intervention group. However, in the control group, the weekly self-reported physical activity level was not investigated.[19] No significant difference was found between the intervention group and control group in fitness parameters such as weight, body mass index, peak heart rate, and blood pressure.[19] Increased physical activity nine weeks after rehabilitation was examined in a multicenter study.[11] They divided the participants into 3 groups, including those who had one of the following diagnoses: amputation, stroke, neurologic disorders, back disorders, rheumatic related disorders, and whiplash. Only a routine rehabilitation program was applied to the first group, sport counseling was given in addition to the routine rehabilitation program during the rehabilitation sessions in the second group, and sport counseling was initiated for the third group after nine weeks of rehabilitation. PASIPD scores increased significantly only in the group of patients who continued sport counseling after the rehabilitation program compared to the beginning of the study.[11] No difference was found between a routine rehabilitation program and a routine rehabilitation program that adds sport counseling. Similar results were obtained by

extending the study to one year; only in the group where sports counseling was continued after rehabilitation, a significant increase was found in PASIPD after one year when compared to the beginning of the study.[20]

Zbogar et al.[12] investigated the effect of structured therapy on physical activity in patients with paraplegia or tetraplegia due to spinal cord injury. They recorded physical activity through a self-reported questionnaire and with 2 real-time accelerometers worn on the dominant wrist or hip for ambulatory individuals. According to the results of this study, there was no significant change in self –reported physical activity from discharge to admission. However, physical activity evaluated by accelerometers was significantly increased.

Although there are similar results to our study in the literature, there are different results in the change of physical activity with rehabilitation. This may be attributed to the different patient spectrum involved and assessment method.

We found that the physical activity levels increased with in patients rehabilitation program, but the continuation of post-rehabilitation counseling services is important in order to increase physical activity for a longer time or to try to transform physical activity into a lifestyle.

Some potential problems underlying improving physical activity behavior after rehabilitation were found to include psychosocial problems, as well as several barriers such as health conditions, limited environmental opportunities, lack of time, lack of motivation, lack of money, lack of motivation, and transportation problems.[21]

The first limitation of our study was the short follow-up period. A longer follow-up period is necessary to assess how much we can integrate the physical activity of participants who have started living with disabilities into their daily life. The second limitation was that PASIPD was a subjective measure. The combination of objective and subjective measures of physical activity can increase the reliability of our results. Another limitation of our study was that the duration of disability, which may be a factor in changing physical activity, wasn't evaluated. Since our study was conducted during the pandemic period, the number of our participants remained limited due to the fact that hospitalization of patients was reduced in this period within the framework of pandemic conditions.

CONCLUSION

The rehabilitation program seemed to provide an important opportunity to start promoting a physically active lifestyle. While people learn to live with a disability, quickly integrating physical activity with rehabilitation program into their new daily routine can be seen as a good strategy. Beneficial ways to continue increasing physical activity after rehabilitation are counseling services and longer follow-up periods. Therefore, it is important to plan and structure rehabilitation activities in these patients according to psychosocial factors and environmental barriers in their daily lives.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study was approved by the University of Health Sciences Dışkapı Yıldırım Beyazıt Training and Reserach Hospital Institutional Ethics Committee (Approval number: 94/06).

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

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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

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Orjinal Araştırma / Original Article

Esophageal Involvement and Gastroesophageal Reflux Disease in Systemic Sclerosis: A Tertiary Center Experience

Sistemik Skleroz'da Özofagus Tutulumu ve Gastroözofageal Reflü Hastalığı: Üçüncü Basamak Deneyimi

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Abstract

Aim: In this study, we investigated the demographic features, endoscopic, manometric, and 24-hour pH monitoring findings of patients with SS.

Materials and Method: Twenty-six patients with SS who presented with dysphagia or heartburn complaints were identified. Patients' files, endoscopic, manometric, and 24-hour ph monitoring findings of the esophagus were examined.

Results: All of the patients were symptomatic. The average age of 26 patients was 47.9 years and 96% were women. 46.1% of them applied with the complaint of heartburn and 53.9% with the complaint of dysphagia. The frequency of esophagitis in patients with SS was found to be significantly higher (p=0.005). Pathological reflux was detected in 90% of the patients with SS who underwent 24-hour pH monitoring and it was significantly higher (p=0.013). The mean esophageal body resting pressure in the patient with SS group was -0.73 mmHg and was significantly lower than that of control group (p<0.001). The mean resting LES pressure in the patient with SS group was 3.3 mmHg and was significantly lower than that of control group (p=0.028).

Conclusion: Esophageal involvement is a hallmark manifestation of SS and typically occurs secondary to heartburn and dysphagia. In our society, the incidence of Gastroesophageal Reflux Disease (GERD) and GERD-related complications is high in SS patients with esophageal symptoms. It is important to refer these patients to experienced gastroenterology centers to be evaluated by endoscopic and then other diagnostic methods.

Keywords: Esophageal motility disorder, gastroesophageal reflux disease, systemic sclerosis.

Öz

Amaç: Bu çalışmamızda Sistemik Skleroz (SS) tanılı hastaların demografik özelliklerini, endoskopik, manometrik ve 24 saatlik ph monitorizasyonu bulgularını araştırdık.

Gereç ve Yöntem: Disfaji veya heartburn şikayetleri ile başvurmuş olan 26 SS tanılı hasta tespit edildi. Hastaların, dosyaları, endoskopik, manometrik ve özofagusun 24 saatlik ph monitorizasyonu bulguları incelendi.

Bulgular: SS tanılı hastaların tamamı semptomatikti, 26 Hastanın yaş ortalaması 47,9 idi, %96'sı kadındı. %46,1 'i heartburn şikayetiyle, %53,9'u disfaji şikayetiyle başvurmuştu. SS tanılı hastalarda özofajit sıklığı anlamlı ölçüde yüksek saptandı (p=0,005). SS tanılı hastalarda, 24 saatlik ph monitorizasyonu yapılan hastaların %90'ında patolojik reflü tespit edilmişti ve anlamlı derecede yüksekti (p=0,013). SS tanılı hastaların ortalama Özofagus Gövde Dinlenim Basıncı -0,73 mmHg olup kontrol grubuna göre anlamlı olarak düşüktü (p<0,001). SS tanılı hastaların ortalama LES Dinlenim Basıncı 3,3 mmHg olup anlamlı derecede düşüktü (p=0,028).

Sonuç: Özofageal tutulum SS' nin karakteristik tutulumlarından biridir. Özofagus tutulumu, heartburn ve disfaji gibi şikayetler ile kendini gösterir. Toplumumuzda, özofagus semptomları olan SS hastalarında Gastroözofageal Reflü Hastalığı (GÖRH) ve GÖRH ile ilişkili komplikasyonların görülme sıklığı yüksektir. Bu hastaların endoskopi ve diğer tanı yöntemleriyle değerlendirilmesi için deneyimli gastroenteroloji merkezlerine yönlendirilmesi önem arz etmektedir.

Anahtar Kelimeler: Gastroözofageal reflü hastalığı, özofagus motilite bozuklukları, sistemik skleroz

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INTRODUCTION

Systemic Sclerosis (SS) is a rare multisystemic disease of an unclear etiology, characterized by microvascular damage and excessive collagen synthesis and deposition in the skin and visceral organs.[1] The gastrointestinal tract (GI) is affected in almost 90% of the patients with SS and the disease may also involve any part of the GI, from the oral aperture to the rectum.[2] Esophageal motility disorder (EMD), lower esophageal sphincter (LES) incompetence, and the accompanying gastroparesis in some patients are considered as the primary causes of increased frequency of acid reflux. Additionally, dysphagia and gastroesophageal reflux disease (GERD) are commonly seen serious comorbidities in patients with SS.[3] GERD may result in numerous complications including esophagitis, peptic stricture, and Barrett's esophagus (BE).[4] Moreover, if left uncontrolled, GERD may form a basis for recurrent aspiration pneumonia, thereby leading to pulmonary fibrosis.[5] GER and dysphagia have been found to be associated with depressive symptoms in patients with SS.[6] In patients with SS, early assessment of esophageal involvement may create awareness of aggressive treatments for GERD. Additionally, administering treatment protocols involving antacid and prokinetic agents and taking simple precautions such as bedhead elevation may prevent long-term complications including recurrent aspirations and lung injury, thereby improving patients' quality of life.[7] The aim of this study was to evaluate the demographic, endoscopic, manometric, and 24-hour esophageal pH test results in SS patients presenting with esophageal symptoms in our society.

MATERIAL AND METHOD

This study was approved ethically by the local ethics committee (Date: 27.11.2019, Study No: 12) of from Ministry of Health Ankara City Hospital Clinical Research Ethics Committee, Ankara, Turkey. The study retrospectively reviewed the medical records of 1,827 patients that underwent conventional esophageal manometry at Ankara Training and Research Hospital Gastroenterology Department Motility Polyclinic over the period between January 2008 and December 2018. Twenty-six patients diagnosed with SS were included in the study. For each patient, medical records were reviewed for demographic characteristics including age, gender, and body mass index (BMI) and also for clinical characteristics including 24-hour esophageal pH test results and endoscopic and manometric findings. The patients included in the study had a diagnosis of SS, underwent esophageal manometry, and were aged over 18 years. Patients aged under 18 years and those with no prior manometric evaluation, suspicious signs of other esophageal motility disorders, active cardiovascular, cerebrovascular and psychopathological disorders, morbid obesity, thyroid diseases, malignancies, other rheumatological diseases involving the esophagus, and a history of surgery for reflux, esophagus, and stomach were excluded from the study. Additionally, a control group of 26 age- and gender-matched patients was also included in the study, who were randomly chosen from among patients that presented to the same department with similar complaints and had normal manometry results.

Statistical analysis

Data were analyzed using SPSS for Windows version 22.0 (IBM SPSS Inc., Armonk, NY, USA). Continuous variables were expressed as mean±standard deviation (SD) and categorical variables were expressed as frequencies (n) and percentages (%). Two groups were compared using Pearson's Chi-square test and Fisher's Exact Test. A p value of <0.05 was considered significant.

RESULTS

The 26 patients in the patient group comprised 25 (96.2%) women and 1 (3.8%) man with a mean age of 47.9 years. All of these patients were symptomatic and the most common presenting complaint in the patients was dysphagia (53.9%) followed by heartburn (46.1%). The mean BMI in the patient group was 24.1 kg/m^2 and was significantly lower than that of control group (p=0.017). **Table 1** presents the demographic characteristics of the patients in both groups.

Table 1. Demographic characteristics of patients.

	SS group (n=26)	Control group (n=26)	p
Mean age (± SD) (years)	47.9±1.43	48.4±1.53	0.90
Female n (%)	25 (96.1%)	25 (96.1%)	0.75
Presenting Symptom n (%)	Heartburn=12 (46.1%) Dysphagia= 14 (53.9%)	Heartburn=13 (50%) Dysphagia=13 (50%)	0.78
Mean BMI (kg/m^2) (± SD)	24.1±5.6	28.1±5.1	0.017

SS: Systemic Sclerosis SD: standard deviation, BMI: body mass index

Endoscopy and 24-hour esophageal pH test results

In the patient group, 18 (69.2%) patients underwent endoscopic evaluation. Endoscopic findings indicated that the frequency of esophagitis was significantly higher in the patient group compared to the control group (61.1% vs. 18.2%) (p=0.005). In the patient group, 54.5% of the patients had Los Angeles (LA) grade A and B esophagitis and 45.5% of them had LA grade C and D esophagitis. Moreover, no patient had peptic stricture and the frequency of hiatal hernia was almost significantly higher in the patient group compared to the control group. On endoscopy, only one patient was detected with BE and no significant difference was found between the two groups with regard to the frequency of LES incompetence (p>0.05).

Only 10 (38.5%) patients had 24-hour esophageal pH test results. Of these, 9 (90%) patients were detected with reflux, including 6 (60%) patients with distal reflux and 3 (30%) patients with both distal and proximal reflux. In the control group, however, reflux was detected in 9 (42.9%) out of 21

patients, including 8 (38.1%) patients with distal reflux and 1 (4.8%) patient with both distal and proximal reflux. The frequency of pathological reflux was significantly higher in the patient group compared to the control group (p=0.013). **Table 2** and **3** present the endoscopic and 24-hour esophageal pH test results in both groups.

Table 2. Endoscopic findings of patients.

	SS group (n=18)	Control group (n=22)	p
Esophagitis n (%)	11 (61.1%)	4 (18.2%)	0.005
Peptic stricture n (%)	-	-	-
Barrett's esophagus (%)	1 (5.5%)	-	-
Hiatal hernia n (%)	6 (33.3%)	2 (9.1%)	0.57
LES incompetence n (%)	7 (38.9%)	5 (22.7%)	0.31
Gastric ulcer n (%)	0 %	2 (9.1%)	0.18
Duodenal ulcer n (%)	0 %	2 (9.1%)	0.18

SS: Systemic Sclerosis

Table 3. 24-hour esophageal pH test results of patients.

	SS group (n=10)	Control group (n=21)	p
Reflux	9 (90%)	9 (42.9 %)	0.013
Distal reflux	6 (60%)	8 (38.1%)	
Distal + Proximal reflux	3 (30%)	1(4.8%)	

SS: Systemic Sclerosis

Esophageal manometry findings

In manometric evaluation, the LES was situated at a mean distance of 43.6 cm in the patient group and 43.03 cm in the control group (p>0.05). The mean esophageal body resting pressure in the patient group was -0.73 mmHg and was significantly lower than that of control group (p<0.001). The mean resting LES pressure in the patient group was 3.3 mmHg and was significantly lower than that of control group (p=0.028). **Table 4** presents the esophageal manometry findings in both groups.

Table 4. Esophageal manometry results of patients.

	SS group (n=26)	Control group (n=26)	p
Resting LES pressure (mm/Hg) (± SD)	3.3±3	20.3±4.94	<0.001
Esophageal body resting pressure (mmHg) (± SD)	-0.73±2.4	0.46±1.21	0.028
LES distance (cm) (± SD)	43.6±3.6	43.03±2.1	0.43

SS: Systemic Sclerosis LES: Lower esophageal sphincter

DISCUSSION

In the present study, GERD and complications were detected in most of the patients with SS. Moreover, a significant portion of the patients presented with both distal and proximal reflux. Given that all the patients were symptomatic, it is tempting to consider that reflux could be the primary cause of these complications.

Literature indicates that patients with SS have a higher frequency of GERD complications such as reflux esophagitis, esophageal stricture, and BE compared to the general population.[8] Katzka et al.[9] reported that patients with scleroderma are at increased risk of BE and esophageal adenocarcinoma. Wipff et a.[10] also noted that patients with SS have an increased risk of esophageal adenocarcinoma and should be closely monitored. Lahcene et al.[11] detected reflux esophagitis in 38% and esophageal stricture and BE in 10% of their patients. In our patients, although the frequency of reflux was higher compared to those reported in the literature and esophageal reflux was detected in 61% of the patients, no esophageal stricture was detected in any patient and BE was detected in only one patient.

Some previous studies found no significant association between esophageal symptoms and EMD.[12,13] Another study reported that some patients presented no manometric signs of esophageal involvement despite presenting numerous esophageal symptoms and concluded that esophageal symptoms have low sensitivity, specificity, and predictive values in the diagnosis of SS.[14] In contrast, Lahcene et al.[11] reported that the frequency of esophageal symptoms was significantly higher in the presence of esophageal dysmotility and, therefore, these symptoms could be a simple warning sign necessitating prompt search of EMDs by manometry.[12] Similarly, in our study, all the patients with SS were symptomatic and were detected with EMD on manometry. It is commonly known that patients with SS mostly present to or are referred to gastroenterology polyclinics when their complaints of dysphagia and heartburn become symptomatic. Accordingly, in these patients, an assessment of esophageal involvement in the symptomatic period may allow early diagnosis and treatment of the patients and also prevent potential complications.

Patients with EMD are likely to experience numerous clinical problems such as early satiety, food regurgitation, progressive weight loss, malnutrition, and food impaction.[15] Unintentional weight loss is the most sensitive indicator of malnutrition and should be monitored at regular intervals. Moreover, a low BMI (<18.5 kg/m^2) is an indicator of protein-energy malnutrition.[16] In a 2009 study, Savarino et al.[17] evaluated a total of 40 patients with SS including 35 women and 5 men and reported the mean BMI of the patients as 23 kg/m^2. Another study evaluated a group of patients with SS awaiting lung transplantation and reported that the mean BMI was 23.3 kg/m^2 and the men comprised 10% of the patients (18). In our study, the mean BMI in the patient group was 24.1 kg/m^2 and was significantly lower than that of control group. However, depending on the mean BMI in the patient group, it would be wise to assert that malnutrition could not be considered in our patients with SS. Additionally, the high frequency of reflux and other esophageal complications in such patients, as seen in our patients, could be the primary cause of food avoidance and the lower mean BMI compared to that of control subjects. Based on these findings, we suggest that an initial evaluation of esophageal involvement and nutrition

status is essential for the assessment of malnutrition in patients with SS that present to the gastroenterology clinic after the onset of first symptoms.

Literature indicates that the normal range for the resting LES pressure in response to wet swallows on esophageal manometry is 16.6-35.4 mmHg. Additionally, the reported normal ranges for mean distal and proximal amplitude are 64-154 and 33-91 mmHg, respectively.[19] The esophageal manometry findings of SS are associated with decreased esophageal motility with or without LES incompetence. Esophageal symptoms and manometric anomalies are commonly seen in patients with SS.[20] In our study, the mean resting LES pressure and the mean esophageal body resting pressure in the patient group were 3.3 mmHg and -0.73 mmHg, respectively, and were significantly lower than those of control group. In all the patients with SS, the resting LES pressure was below 10 mmHg and EMD was detected. In our study, manometric abnormalities were common in symptomatic patients, in accordance with the literature. Based on these findings, we consider that in patients with SS, a manometric evaluation of esophageal involvement followed by a 24-hour esophageal pH test in the symptomatic period will be beneficial for the detection of GERD and its complications.

The association between gender and GI involvement in SS remains controversial in the literature. A previous study found a significant association between GI manifestations and gender in SS.[21] In contrast, Abu-Shakra et al.[22] found no significant relationship between GI manifestations and demographic characteristics including gender, age at diagnosis, and disease type in patients with SS. However, a previous retrospective study that was conducted with 257 Greek patients with SS indicated that the frequency of GI involvement was higher in women than in men.[14] Our study, unlike previous studies, had a female preponderance (96%). This situation may be related to the fact that women in our society visit hospitals more than men. Taken together, all these findings implicate that SS mostly affects women and esophageal involvement may also lead to more frequent and serious complications in Turkish women.

Our study was limited in several ways. It had a retrospective design and had a small patient population since SS is a rare disease. However, no information was available in the study regarding the durations of the disease and the use of antacid-proton pump inhibitors and analgesic drugs by the patients.

CONCLUSION

Esophageal involvement is a hallmark manifestation of SS and typically occurs secondary to heartburn and dysphagia. SS commonly causes EMD and LES incompetence, thus precipitating patients towards reflux. Reflux also leads to EMD and as this vicious circle continues, the frequency of complications increases. In conclusion, GERD and GERD-related complications have a high incidence in SS patients with esophageal symptoms in our society. It is important to refer these patients to experienced gastroenterology centers to be evaluated by endoscopic and other diagnostic methods.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study was approved ethically by the local ethics committee (Date: 27.11.2019, Study No: 12) of from Ministry of Health Ankara City Hospital Clinical Research Ethics Committee, Ankara, Turkey.

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

Referee Evaluation Process: Externally peer-reviewed.

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Orjinal Araştırma / Original Article

Evaluation of Hematological Parameters in Predicting Short-Term Mortality for COVID-19 Patients with Gastrointestinal Symptoms: A Case-Control Study

Gastrointestinal Semptomları Olan COVID-19 Hastalarında Kısa Süreli Mortaliteyi Öngörmede Hematolojik Parametrelerin Değerlendirilmesi: Bir Vaka Kontrol Çalışması

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Abstract

Introduction: Due to local and systemic pathological mechanisms, laboratory parameters, especially hematological parameters of patients with gastrointestinal symptoms may differ from those without these symptoms. We aimed to investigate the differences between the hematological parameters of COVID-19 patients with and without gastrointestinal symptoms.

Material and Method: Our study was designed as a retrospective case-control study. The case group consisted of COVID-19 patients with confirmed gastrointestinal symptoms, and the control group consisted of those without gastrointestinal symptoms. The hematological parameters of the patients were compared statistically.

Results: In this study, 130 patients were included in the case group and 130 patients in the control group. There was no statistical difference between the groups in terms of the white blood cell count, neutrophil count, lymphocyte count, platelet count, hemoglobin, hematocrit, mean platelet volume, mean corpuscular volume, neutrophil-lymphocyte ratio, platelet-lymphocyte ratio values (p values: 0.642, 0.987, 0.132, 0.835, 0.306, 0.430, 0.057, 0.735, 0.321, and 0.031, respectively).

Conclusion: There was no significant difference between the COVID-19 patients with and without gastrointestinal symptoms in the terms of hematological parameters.

Keywords: Case-control study, COVID-19, gastrointestinal symptoms, mortality, SARS-CoV-2

Öz

Giriş: Lokal ve sistemik patolojik mekanizmalar nedeniyle, gastrointestinal semptomları olan hastaların laboratuvar parametreleri -özellikle hematolojik parametreleri olmayanlardan farklı olabilir. Çalışmamızda gastrointestinal semptomları olan ve olmayan COVID-19 hastalarının hematolojik parametreleri arasındaki farkı araştırmayı amaçladık.

Gereç ve Yöntem: Çalışmamız retrosfektif vaka kontrol çalışması olarak dizayn edildi. Vaka grubunu doğrulamış gastrointestinal semptomu olan COVİD 19 hastaları oluşturdu. Kontrol grubunu ise gastrointestinal semptomu olmayan COVİD 19 hastaları oluşturdu. hastaların hematolojik parametreleri istatistiksel olarak karşılaştırıldı.

Bulgular: Vaka grubuna 130 olgu grubuna 130 hasta dahil edildi. gruplar arasında beyaz kan hücresi sayısı, nötrofil sayısı, lenfosit sayısı, trombosit sayısı, hemoglobin, hematokrit, ortalama trombosit hacmi, ortalama korpüsküler hacim, nötrofil-lenfosit oranı, trombosit-lenfosit oranı açısından istatistiksel fark yoktu (p değerleri 0,642, 0,987, 0,132, 0,835, 0,306, 0,430, 0,057, 0,735, 0,321, 0,031 sırasıyla)

Sonuç: Gastrointestinal semptomları olan COVID-19 hastaları ile olmayanlar arasında hematolojik parametreler açısından anlamlı bir fark yoktur.

Anahtar Kelimeler: vaka kontrol çalışması, COVID-19, gastrointestinal semptomlar, mortalite, SARS-CoV-2

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INTRODUCTION

Following an unknown pneumonia outbreak in the city of Wuhan, China in December 2019, a new coronavirus was isolated and named severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses on January 7, 2020.[1] Pneumonia caused by this virus was named Coronavirus Disease 2019 (COVID-19) by the World Health Organization on February 11, 2020[2] and declared a pandemic on March 11, 2020. The SARS-CoV-2 pandemic has had serious effects not only on the health system but also on economic and social systems around the world.[3]

COVID-19 predominantly occurs as a respiratory system infection, and the most common symptoms are fever, fatigue, and dry cough.[4] In addition, various symptoms such as joint and muscle pain, sore throat, nausea, vomiting, diarrhea, conjunctivitis, headache, loss of taste or smell, and skin rash may be observed.[4] Symptoms listed in patients may occur individually or in different combinations.[4] Although SARS-CoV-2 is a virus that is mostly effective in the respiratory system, it can also affect the gastrointestinal system and cause gastrointestinal symptoms, such as nausea, vomiting, and diarrhea.[5] The pathogenesis of gastrointestinal symptoms has been discussed in the literature, and several mechanisms have been reported,[5] with the primary factors being replication and local inflammatory response in the gastrointestinal mucosa, followed by gastrointestinal response to systemic increased cytokines, gastrointestinal effects of systemic hypoxia, and gastrointestinal microthrombus.[5] We hypothesized that due to these pathological mechanisms, laboratory parameters, especially hematological parameters of patients with gastrointestinal symptoms might differ from those without these symptoms.

In this study, we aimed to investigate the differences between the hematological parameters of COVID-19 patients with and without gastrointestinal symptoms.

MATERIAL AND METHOD

Study Design

This retrospective case-control study was conducted at University of Health Sciences Ümraniye Training and Research Hospital, a 686-bed tertiary education hospital with an annual emergency department (ED) census of 453,000. We retrospectively collected the data of patients with corrected COVID-19 who presented to ED between March 01, 2021 and May 01, 2021.

Study Population

Our study population consisted of COVID-19 patients presenting to ED between March 01, 2021 and May 01, 2021. All patients had a positive reverse transcription polymerase chain reaction (rt-PCR) test for SARS-CoV-2 were included in the study. Patients with missing data were excluded.

The case group consisted of COVID-19 patients with gastrointestinal symptoms, and the control group comprised those without these symptoms. Patients of the same age and gender in the case group were selected from the list of confirmed COVID-19 cases for the control group if possible. If there was no case of the same age and gender, most similar patients were included as controls.

Data Collection

Demographics, comorbidities, and symptoms, vital parameters at admission, laboratory findings, and ED outcomes were noted from the hospital computer-based patient data system. Comorbidities were noted as coronary artery disease, diabetes mellitus, chronic obstructive pulmonary diseases, hypertension, congestive heart failure, chronic renal failure, and malignancy. Symptoms of the disease were recorded as fever, cough, sputum, dyspnea, weakness, muscle-joint pain, headache, sore throat, vomiting-nausea, and diarrhea. Systolic blood pressure, diastolic blood pressure, pulse pressure, body temperature, respiratory rate, and peripheral oxygen saturation were recorded as vital parameters. The documented laboratory parameters were blood urea nitrogen, creatinine, C-reactive protein, D-dimer, troponin, albumin, white blood cell count, neutrophil count, lymphocyte count, platelet count, mean platelet volume, and mean corpuscular volume. Lastly, the neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio were calculated.

Statistical Analysis

SPSS version 22.0 for Windows (SPSS Inc, Chicago, IL, USA) was used for statistical analyses. The normality analysis was undertaken using the Kolmogorov-Smirnov test for continuous data. Categorical data were shown with numbers (%) and compared with the chi-squared test. Quantitative variables were shown with interquartile range (25th-75th percentile) and median values, and then compared between the two groups using Student's t-test or the Mann-Whitney U test according to the normality of distribution. To identify parameters associated with 30-day mortality, the univariate analysis was conducted using the chi-square, Fisher's exact, Student's t or Mann-Whitney U test, where appropriate. To counteract the problem of multiple comparisons, the Bonferroni correction was used. Statistical significance was defined at $p<0.05$.

Ethics

Ethical approval for the study was obtained from the Ethics Committee of University of Health Sciences Ümraniye Training and Research Hospital (approval number: 153, date: May 27, 2021). We retrospectively reviewed the data obtained from the computer-based system of the hospital. However, the recorded data did not include any personal identifiable data; it only included clinical information. Therefore, informed consent was waived by the ethics committee.

RESULTS

Of the 260 patients included in the study, 130 were included in the case group and 130 in the control group. The mean of age of the case group was 43±15 years and that of the control group was 40±10 years. A total of seven patients, five in the case group and two in the control group, died within 30 days of ED presentation. The rates of 30-day mortality for the whole study cohort, case group, and control group were 2.7%, 3.8%, and 1.5%, respectively. There was no statistically significant difference between the case and control groups in terms of mortality (p=0.447). In the case group, 91 patients were discharged, 35 were hospitalized, and four were admitted to the intensive care unit. In the control group, 103 patients were discharged, 26 were hospitalized, and four were admitted to the intensive care unit. There was no statistically significant difference between the case and control groups in terms of ED outcomes (p=0.076). **Table 1** presents the comparison of demographic characteristics, clinical outcomes within the first 24 hours, comorbid diseases, symptoms, vital parameters at presentation, and mortality data between the case and control groups. The comparison of initial laboratory findings between the groups is shown in **Table 2**. Accordingly, no statistically significant difference was observed between the case and control groups in terms of hematological parameters.

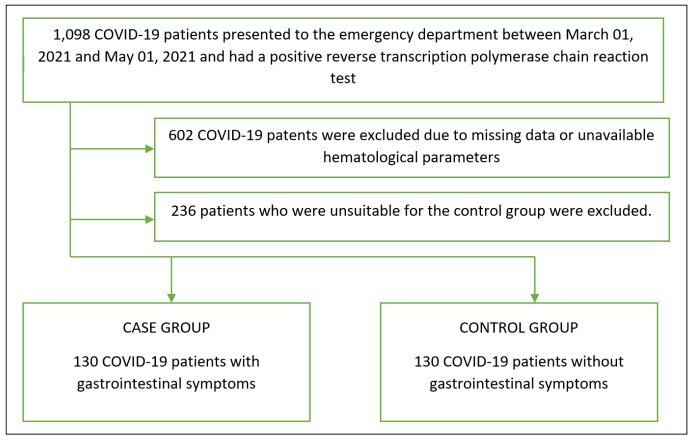

Figure 1. Flowchart of the study

Table 1. Baseline characteristics of the enrolled patients and their comparison between the case and control groups

Variables	Total	Case group (with gastrointestinal symptoms)	Control group (without gastrointestinal symptoms)	p values
	n=260 (%)	n=130 (%)	n=130 (%)	
Age, years	41±12	43±15	40±10	0.144
Gender				0.529
Male	153 (58.8%)	74 (56.9%)	79 (60.8%)	
Female	107 (41.2%)	56 (43.1%)	51 (39.2%)	
Clinical outcome within the first 24 hours				0.076
Discharge	194 (74.6%)	91 (70%)	103(79.2%)	
Admission to inpatient clinics	61 (23.5%)	35 (26.9%)	26 (20%)	
Intensive care unit admission	5 (1.9%)	4 (3.1%)	1 (0.8%)	
Comorbidities (+%/-%)				
Chronic obstructive pulmonary diseases	7 (2.7%)	4 (3.1%)	3 (2.3%)	0.702
Hypertension	25 (9.6%)	19 (14.6%)	6 (4.6%)	0.006
Diabetes mellitus	22 (8.5%)	16 (12.3%)	6 (4.6%)	0.026
Coronary artery disease	4 (1.5%)	4 (3.1%)	0	0.122
Congestive heart failure	3 (1.2%)	3 (2.3%)	0	0.247
Chronic kidney disease	4(1.5%)	3 (2.3%)	1 (0.8%)	0.622
Frequency of symptoms (n/%)				
Fever	89 (34.2%)	43 (33.1%)	46 (35.4%)	0.695
Cough	170 (65.4%)	84 (64.6%)	86 (66.2%)	0.794
Sputum	6 (2.3%)	4 (3.1%)	2 (1.5%)	0.176
Shortness of breath	78 (30%)	44 (33.8%)	34 (26.2%)	0.684
Weakness	47 (18.1%)	23 (17.7%)	24 (18.5%)	0.872
Muscle-joint pain	34 (13.1%)	20 (15.4%)	14 (10.8%)	0.270
Loss of taste or smell	13 (5%)	7 (5.4%)	6 (4.6%)	0.776
Headache	11 (4.2%)	5 (3.8%)	6 (4.6%)	0.758
Sore throat	29 (11.2%)	13 (10%)	16 (12.3%)	0.555
Nausea-vomiting	65 (25%)	65 (50%)	0	
Diarrhea	78 (30%)	78 (60%)	0	
Vital parameters				
Systolic blood pressure	123±17	126±17	116±13	0.015
Diastolic blood pressure	74±9	75±10	73±7	0.372
Pulse pressure	89±17	88±17	89±17	0.706
Body temperature	36.5 (36.3-37)	36.6 (36.4-37)	36.5 (36.2-36.8)	0.030
Respiratory rate	20 (16-22)	20 (18-22)	18 (16-20)	0.143
Oxygen saturation	97 (95-98)	96 (94-98)	97 (96-98)	0.044
Mortality	7 (2.7%)	5 (3.8%)	2 (1.5%)	0.447

Table 2. Laboratory parameters of the enrolled patients and their comparison between the case and control groups

Variables	Total	Case group (with gastrointestinal symptoms)	Control group (without gastrointestinal symptoms)	p values
	n=2012 (%)	n=1971 (%)	n=41 (%)	
Glucose, mg/dL	102 (91-117)	106 (94-119)	99 (89-109)	0.027
Blood urea nitrogen, mg/dL	25.68 (12.84-29.96)	25.68 (17.12-29.96)	23.54 (3.21-29.96)	0.190
Creatinine, mg/dL	0.82 (0.68-0.95)	0.88 (0.72-0.95)	0.79(0.68-0.94)	0.311
Albumin, g/dL	4.27 (3.94-4.57)	4.19 (3.91-4.44)	4.42 (4.11-4.68)	0.044
Alanine aminotransferase, IU/L	22 (15-35)	23 (16-37)	19 (13-33)	0.315
Aspartate aminotransferase, IU/L	23 (18-32)	23 (18-33)	23 (17-28)	0.115
Sodium mg/L	139 (137-140)	139 (137-140)	139 (137-140)	0.346
Potassium mg/L	4.1 (3.7-4.4)	4.1 (3.7-4.4)	3.9 (3.7-4.3)	0.236
D-dimer, mg/L	82 (42-2613.8)	131.5 (52.5-3642.9)	57 (32.5-2089.35)	0.022
Troponin (cTnI), ng/mL	0.02 (0.01-0.05)	0.03 (0.01-0.06)	0.01 (0.01-0.03)	0.005
C-reactive protein, mg/L	0.3 (0.2-1.4)	0.4 (0.2-1.6)	0.2 (0.2-0.8)	0.039
Hematological test parameters				
White blood cell count	7.07±3.33	7.17±3.33	6.97±3.34	0.642
Neutrophil count	4.62±2.62	4.61±2.56	4.62±2.70	0.987
Lymphocyte count	1.88±1.16	1.78±1.17	2±1.14	0.132
Platelet count	234.74±64.28	233.91±64.58	235.61±64.23	0.835
Hemoglobin count	13.9 (12.6-15.3)	14.1 (12.8-15.3)	13.8 (12.3-15.3)	0.306
Hematocrit count	37.63±12.62	38.25±11.81	36.98±13.43	0.430
Mean platelet volume	9.5 (8.7-10.2)	9.4 (8.6-10.2)	9.5 (8.9- 10.1)	0.057
Mean corpuscular volume	85.5 (82.1-88.5)	85.5 (80.8- 88.6)	85.5 (82.4-88.5)	0.735
Neutrophil-to-lymphocyte ratio	2.23 (1.47-4.45)	2.44 (1.49-4.72)	2.02 (1.43-3.94)	0.321
Platelet-to-lymphocyte ratio	125.99 (93.51-187.85)	140.34 (97.27-193.06)	115.36 (89.46-170.59)	0.031

DISCUSSION

In this study, we examined the differences between the hematological parameters of COVID-19 patients presenting to ED with and without gastrointestinal symptoms. We found no significant difference between these two groups in terms of hematological parameters. To the best of our knowledge, this is the first study that investigated whether hematological parameters differed according to the presence or absence of gastrointestinal symptoms among COVID-19 cases.

In the literature, since SARS-CoV-2 RNA was first detected in the stool of a COVID-19 case with symptoms of nausea, vomiting, and diarrhea in the USA, more attention has been paid to the gastrointestinal system.[6] Digestive symptoms, such as anorexia, nausea, vomiting, and diarrhea are frequently reported in COVID-19 patients.[7] In addition, gastrointestinal symptoms, although rare, may be the only manifestation of the SARS-CoV-2 infection.[8] In support of this, the COVID-19 disease was reported in a patient with a positive stool test but negative pharyngeal and sputum viral tests.[9] In a multicenter study in China involving 1,099 patients of the same age, 55 (5%) of the COVID-19 patients were reported to have nausea or vomiting and 42 (3.8%) had diarrhea.[7] Diarrhea induced by SARS-CoV-2 was the initial symptom in a patient with COVID-19.[8] Diarrhea is also a common gastrointestinal symptom in patients with COVID-19, with an incidence ranging from 1.3% to 29.3% in the literature.[10] However, the frequency of gastrointestinal symptoms differs between studies,[6,7] which may be related to the different criteria used in the definition of diarrhea. Another plausible explanation may be clinicians' reluctance or disregard in relation to reporting gastrointestinal symptoms in COVID-19 patients.[11]

Hoffmann et al.[11] suggested that the gastrointestinal system infection mechanism of SARS-CoV was the angiotensin-converting enzyme-2 (ACE-2) cell receptor. SARS-CoV-2 uses ACE2 as a cell entry receptor.[12] Xiao et al.[13] showed that ACE-2 was rarely expressed in the esophageal epithelium but abundantly distributed in gastric, duodenal, and rectum glandular epithelial cells in the staining of viral nucleocapsid protein according to the analysis of endoscopic biopsy samples. That study showed that the gastrointestinal infection of SARS-CoV-2 and infectious virions could be secreted from virus-infected digestive tract cells.[13] Another study conducted by Liang et al.[10] reported that ACE-2 was highly expressed in the small intestine, especially in proximal and distal enterocytes. In their in vitro experimental study, Lamer et al.[14] successfully grew the virus in test tubes using the cell culture models of the human intestine. The authors showed how the virus replicated itself and damaged intestinal cells.[14] Lamer et al.[14] reported that the interaction between SARS-CoV-2 and ACE-2 could disrupt the function of ACE-2, resulting in diarrhea. Many researchers argue that fecal-oral transmission may be possible considering that SARS-CoV-2 RNA is detected in the stool and replicated in the gastrointestinal tract in some COVID-19 cases.[15]

Several mechanisms have been described in the literature for the occurrence of gastrointestinal symptoms. Firstly, viremia damages the gastrointestinal tract indirectly or directly through an inflammatory response. The chain

reaction of inflammatory factors and viremia can damage the gastrointestinal tract.[16] This systemic mechanism of action is considered to be especially effective in the patient group in which fecal viral replication cannot be demonstrated. [16] Secondly, enteropathic viruses can directly damage the intestinal mucosa and cause digestive symptoms.[14] This mechanism may be more effective in the patient group with known viral replication in the stool.[14] As a third mechanism, the gastrointestinal flora affected by the virus may be effective in the development of gastrointestinal symptoms; however, more evidence is needed to prove this idea.[17] It has been reported that mechanisms such as systemic hypoxia and gastrointestinal microthrombosis may also be additionally effective in critically ill COVID-19 patients. In our study, we hypothesized that hematological markers might be affected differently in this clinical entity, which has systemic and local effects. However, we found that hematological parameters were affected similarly in both COVID-19 groups with and without gastrointestinal symptoms. A logical explanation for this may be that systemic rather than local effects are predominant in patients with gastrointestinal symptoms.

Limitations

There are several limitations to our study, with the most important being the retrospective design and data being obtained from the hospital's computer-based information system. In addition, not all patients with COVID-19 were routinely tested for hematological parameters, and we had to exclude 602 COVID-19 cases due to the lack of data on hematological parameters. Furthermore, similar to other studies investigating gastrointestinal symptoms in COVID-19 patients, there may have been possible data loss or erroneous data because clinicians underestimated gastrointestinal symptoms. Finally, the single-center and limited cohort of our study limits the generalizability of our results; therefore, our data should be validated by further multicenter studies with larger cohorts.

CONCLUSION

According to our findings, there is no significant difference between the COVID-19 patients with and without gastrointestinal symptoms in terms of hematological parameters. The results of this study should be confirmed by further multicenter studies.

ETHICAL DECLARATIONS

Ethics Commite Approval: Ethical approval for the study was obtained from the Ethics Committee of University of Health Sciences Ümraniye Training and Research Hospital (approval number: 153, date: May 27, 2021).

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

Referee Evaluation Process: Externally peer-reviewed.

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

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

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Orjinal Araştırma / Original Article

The Evaluation of Postural Stability and Fall Risk in Morbidly Obese Preoperative Bariatric Patients: A Cross-Sectional Study

Morbid Obez Preoperatif Bariatrik Hastalarda Postural Stabilite ve Düşme Riskinin Değerlendirilmesi: Kesitsel Bir Çalışma

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Abstract

Aim: It is known that obese individuals show more postural instability and an increased fall risk than non-obese individuals. We aimed to evaluate the postural stability, fall risk and the contributing factors to stability in morbidly obese preoperative bariatric patients.

Material and Method: Thirty-eight morbidly obese preoperative bariatric patients (body mass index (BMI)≥40) and 52 non-obese (BMI <30) healthy individuals were included in our study. Postural stability indices (PSIs) and fall risk index (FRI) of the participants were evaluated by using the Biodex stability system. Fear of falling (FOF) was evaluated by questioning verbally as yes/no and by using the Falls Efficacy Scale-International (FES-I).

Results: In the study group, 18 patients (47.4%) were housewives and sedentary; 15 patients (39.5%) had Diabetes Mellitus Type 2 diagnosis. There was no statistically significant difference between the groups in terms of the presence of verbally questioned fear of falling, the presence of a history of falling, and the number of falls within the last year (p:0.831, p:0.558, p:0.596 respectively). However, FES-I and FRI scores were statistically significantly higher in the study group (p:0.006, p<0.001). A statistically significant positive correlation was found between FRI and weight, BMI, waist and hip circumferance (r:0.708, p<0.001; r:0.697, p<0.001; r:0.699, p<0.001; r:0.715, p<0.001 respectively).

Conclusion: Morbid obesity negatively affects FRI, which is an important dynamic stability indicator. We recommend the implementation of rehabilitation programs focused on dynamic tasks for postural balance training in morbidly obese patients before and after bariatric surgery.

Keywords: Obesity, body mass index, morbid obesity, postural stability, fall risk

Öz

Amaç: Obez bireylerin, obez olmayan bireylere göre daha fazla postural instabilite ve düşme riskinde artış gösterdiği bilinmektedir. Morbid obez preoperatif bariatrik hastalarda postural stabiliteyi, düşme riskini ve postural stabiliteye katkıda bulunan faktörleri değerlendirmeyi amaçladık.

Gereç ve **Yöntem**: Çalışmamıza bariatrik cerrahi öncesi değerlendirilen morbid obez 38 hasta (vücut kitle indeksi (VKİ)≥40) ve 52 obez olmayan (VKİ <30) sağlıklı birey dahil edildi. Katılımcıların postural stabilite indeksleri (PSİ) ve düşme riski indeksi (DRİ) Biodex stabilite sistemi kullanılarak değerlendirildi. Düşme korkusu (DK) sözel olarak düşme korkusu var/yok şeklinde sorularak ve Uluslararası Düşme Etkinlik Ölçeği (DEÖ-U) kullanılarak sorgulandı.

Bulgular: Çalışma grubundaki 18 hasta (%47,4) ev hanımı ve sedanterdi, 15 hastada (%39,5) Diabetes Mellitus Tip 2 tanısı mevcuttu. Gruplar arasında sözel olarak sorgulanan düşme korkusu varlığı, düşme öyküsü varlığı ve son bir yıl içinde düşme sayısı açısından istatistiksel olarak anlamlı fark yoktu (p:0,831, p:0,558, p:0,596 sırasıyla). Ancak DEÖ-U ve DRİ skorları çalışma grubunda istatistiksel olarak anlamlı derecede yüksekti (p:0,006, p<0,001). DRİ ile ağırlık, VKİ, bel ve kalça çevresi arasında istatistiksel olarak anlamlı pozitif korelasyon bulundu (r:0,708, p<0,001; r:0,697, p<0,001; r:0,699, p<0,001; r:0,715, p<0,001 sırasıyla).

Sonuç: Morbid obezite, önemli bir dinamik stabilite göstergesi olan DRİ 'yı olumsuz etkilemektedir. Morbid obez hastalarda bariatrik cerrahi öncesi ve sonrası postural denge eğitimi için dinamik görevlere odaklanan rehabilitasyon programlarının uygulanmasını önermekteyiz.

Anahtar Kelimeler: Obezite, vücut kitle indeksi, morbid obezite, postural stabilite, düşme riski

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INTRODUCTION

Postural stability is an adaptive process defined as the coordinated working process of the neuromuscular system, which involves maintaining the position of the center of gravity (COG) with continuous output from the visual, auditory and other neural senses.[1,2] It is the main component of many daily activities such as sitting, standing, walking and sportive motor skills.[3] Static postural stability is the skill that involves maintaining the position of the COG in very low activity situations. Dynamic postural stability can be thought of as maintaining postural stability in some different activities or on unstable surfaces.[1] Postural stability is associated with age, gender, anthropometric characteristics and support points.[4] There is a strong relationship between the impaired postural stability and falls. Decreasing the increased plantar pressure due to obesity through weight loss improves postural stability and may therefore reduce the fall risk.[5] However, there are limited number of studies investigating the relationship between obesity, postural stability and fall risk.[5-8]

Obesity is thought to be an obstacle in maintaining postural stability, especially after sudden loss of balance.[6] Because the fat accumulation in the body causes the COG to shift to the front in obese individuals compared to non-obese individuals.[9] In the treatment of obesity, which is an important problem of our age, bariatric surgery applications have come to the fore especially in morbidly obese patients, and successful results are observed in the literature. However, bariatric surgical applications are associated with various complications and the indications are currently being discussed.[10] To identify the factors contributing to instability in preoperative morbidly obese bariatric patients can enable to obtain patient-specific physical therapies and pre-operative measures to reduce instability to prevent comorbidities that may develop due to falls and monitor post-operative balance improvements. In addition, objective postural instability and increased fall risk in patients detected before bariatric surgery can motivate patients to lose weight and increase compliance with the diet and exercise program in the post-surgery period.

The main hypothesis of our study is that an increase in the risk of postural instability and fall risk may be detected in morbidly obese patients compared to healthy non-obese individuals. Based on this hypothesis, we aimed to determine postural stability disorders and fall risk in morbidly obese preopaerative bariatric patients using various clinical evaluations and BIODEX stability system (BSS).

MATERIAL AND METHOD

Study Design

Thirty-eight patients (24 females, 14 males; mean age 36.53±11.3) between the ages of 18-65 who applied to general surgery outpatient clinic between December 2018- December 2019 with the complaint of morbid obesity (body mass index (BMI)≥40) and planned bariatric surgery were included as study group. Fifty -two non-obese (BMI <30) healthy individuals (33 females, 19 males; mean age 34.12±9.63) between the ages of 18-65 were included as the control group. The patients were evaluated in the preoperative period. All individuals participating in our study were informed about the study and their verbal and written consents were obtained. Ethical approval was obtained from Tokat Gaziosmanpaşa University Faculty of Medicine Ethics Committee (approval number: 21.11.2018/18-KAEK-224) for our study. Throughout the study, the principles of the Declaration of Helsinki were adhered to.

Patients between the ages of 18-65, who were planned for bariatric surgery due to morbid obesity (BMI 40 kg/m2), who do not have alcohol and/or drug addiction and who do not have uncontrolled psychotic and depressive disorders were included in the study as study group, As the control group, healthy volunteers with a BMI of <30, without labyrinthite or any neurological disease that may affect balance were included. Volunteering was essential in the conditions of participation in the study. Patients with psychiatric and neurological diseases that may affect balance, additional orthopedic problems such as hip, knee, ankle osteoarthritis, lumbar or cervical spondylosis, a history of surgical intervention for lower extremity and spine, with a history of vertigo, scoliosis or kyphosis, or hearing/vision impairment, drug using that may affect balance, a shorter length of more than 2 cm between the lower extremities, and patients who described pain during evaluation or could not complete the evaluations were excluded from the study.

Data Collection

Fear of falling (FOF) was evaluated by questioning verbally as yes/no and by using the Falls Efficacy Scale-International (FES-I). FES-I is an internationally validated assessment questionnaire that consists of 16 simple questions evaluated by the individuals, which allows to assess the FOF during both easy and difficult physical and social activities. FES-I has been validated in Turkish.[11] The number of falls in the last year was also verbally questioned and recorded.

Body weight was measured with a standard beam scale and length, waist and hip circumference was taken according to Lohman et al.[12]

Postural stability indices (PSIs) and fall risk index (FRI) were evaluated by using BSS (Biodex Inc., Shirley, New York), which provides an objective evaluation. BSS consists of a platform which can move between 20º-360º and a LCD display connected to it with a computer software. When the postural stability analysis protocol (PSAP) (**Figure 1**) is applied with BSS; three different scores are obtained as PSIs. These are Mediolateral Stability Index (MLSI), Anteroposterior Stability Index (APSI), and Overall Stability Index (OSI). When the fall risk analysis protocol (FRAP) (**Figure 2**) is applied, the FRI score can be obtained. The MLSI and APSI shows the displacement of the platform center in the frontal and sagittal planes respectively. The OSI indicates the total variance of the movement of the platform center by using MLSI and APSI. These indices are

standard deviations that show the oscillations around the center of the platform, while high scores indicate an increased fall risk for FRAP, worse postural stability for PSAP.[13] In the PSAP protocol, the platform was static in the MLSI and APSI axes. In the FRAP, the platform was unstable, so it could be possible to predict FRI. FRAP consists of 12 dynamic stability levels. The level "12" was the most stable and the level "1" was the most unstable. In this study, platform level " 8 " was used for fall risk analysis and all patients were tested on the same platform level. Patients stood on the platform, with knees flexed slightly (10-15º), barefoot and in the most comfortable position where the patient could balance, foot coordinates were determined on both feet and eyes open (**Figure 1, 2**). Each participant was informed about the tests and the rules that they should follow. The tests were repeated 3 times to improve reliability and obtain the best results. OSI, APSI, MLSI and FRI scores obtained with BSS were recorded. High values obtained in these scores indicate deterioration in balance and increased fall risk. Participants' age, gender, education level and occupational status, height, weight, BMI, waist and hip circumference (in centimeters), presence of verbally questioned FOF, history of falling in the last year and, if any, number of falls in the last year were also recorded.

Statistical analysis

Data are expressed as mean±standard deviation or frequency and percent. Independent sample t test was used to compare the continuous normal data between groups. Mann Whitney U test was used to compare the continuous non-normal data between groups. Chi-Square test was used to compare the categorical data between/among groups. Categorical variables were presented as a count and percentage. Pearson correlation coefficient was used for correlation between variables. A p-value <0.05 was considered significant. Analyses were performed using The SPSS 22.0 (Chicago, IL, USA). G * Power program was used for power analysis. Our study was planned as 38 patients and 52 controls with 80% power, 5% margin of error and 0.35 effect size.

Figure 1. Postural stability analysis protocol

Figure 2. Fall risk analysis protocol

RESULTS

Thirty-eight morbidly obese patients and 52 non-obese healthy volunteers participated in our study. The anthropometric characteristics of the participants are in **Table 1.** Eighteen patients (47.4%) in the study group were housewives and had a sedentary life. In addition, 15 patients (39.5%) in the study group had Diabetes Mellitus Type 2 diagnosis. There was no statistically significant difference between the groups in terms of verbally questioned FOF and a history of falling within the last year (p: 0.831, p: 0.558). The sociodemographic characteristics of the participants in our study are in **Table 2**.

When evaluated in terms of falls number in the last year, no statistically significant difference was found between both groups (p: 0.596), but FES-I and FRI were statistically significantly higher in the study group (p: 0.006, p <0.001). Postural parameters of the participants are in **Table 3**.

In the correlation analyzes performed for all participants, a statistically significant positive correlation was found between FRI and weight, BMI, waist and hip circumferance (r: 0.708, p <0.001; r: 0.697, p <0.001; r: 0.699, p <0.001; r 0.715, p <0.001).

In the correlation analysis performed for the study group, no statistically significant correlation was found between FRI and age, height, weight, BMI, waist and hip circumference, the number of falls in the last 1 year, FES I and PSI. Only a statistically significant positive correlation was found between the number of falls in the last year and BMI, waist circumferance (r: 0.528, p: 0.001; r: 0.331, p: 0.042). In the correlation analyzes performed for the control group, a statistically significant positive correlation was found between FRI and age, weight, BMI, waist and hip circumferance (r:0.311, p:0.025; r: 0.389, p: 0.004; r: 0.413, p: 0.002; r: 0.363, p: 0.008; r: 0.365, p: 0.008).

DISCUSSION

In this study, the effects of morbid obesity on postural stability and fall risk were evaluated. While there was no statistically significant difference in PSIs compared to the control group, it was remarkable that FES-I was statistically significantly higher in the study group.

FOF is a common and serious health problem. Due to FOF, older people may restrict their activities, causing muscle weakness and impaired balance.[14,15] In different patient groups such as diabetes mellitus, hemiplegia, rheumatoid arthritis, hip osteoarthritis;[15] FES-I has been used to evaluate patients' FOF. There was no significant difference between the groups in the verbally questioned FOF in our study. The fact that FES-I was statistically significantly higher in the study group indicates that FES-I is an important and sensitive scale in revealing theFOF that the person has veiled.

In many previous studies, the effects of different nervous system pathologies, vision and hearing loss, and different musculoskeletal system diseases on postural stability and fall risk were investigated, and some studies emphasized that obesity impairs postural stability and causes an increase

Table 1. The anthropometric characteristics of the participants

	Group		p
	Obese	Control	
Age	36.53±11.3	34.12±9.63	0.279
Weight	123.47±22.71	66.48±10.98	<0.001
Length	166.11±10.66	164.81±8.55	0.524
BMI	44.77±7.19	24.44±3.29	<0.001
Waist circumference	126.03±12.68	82.69±11.07	<0.001
Hip circumference	136.89±12.57	98.37±7.08	<0.001

Data are shown as mean±standard deviation. Independent samples t test was used. BMI: Body Mass Index

Table 2. The sociodemographic characteristics of the participants

	Group		p
	Obese n (%)	Control n (%)	
Gender			
Female	24 (63.2)	33 (63.5)	0.976
Male	14 (36.8)	19 (36.5)	
Education			
Primary school	11 (28.9)	6 (11.5)	
Secondary school	20 (52.6)	30 (57.7)	0.085
Undergraduate and above	7 (18.4)	16 (30.8)	
Occupation			
Housewife	18 (47.4)	11 (21.2)	
Student	6 (15.8)	10 (19.2)	0.028
Retired	1 (2.6)	0 (0)	
Officer	13 (34.2)	31 (59.6)	
Smoking			
Present	14 (36.8)	21 (40.4)	0.733
Absent	24 (63.2)	31 (59.6)	
Alcohol using			
Present	9 (23.7)	5 (9.6)	0.069
Absent	29 (76.3)	47 (90.4)	
Accompanying disease			
Diabetes Mellitus	15 (39.5)	2 (3.8)	
Hypertension	6 (15.8)	7 (13.5)	
Hypothyroidism	0 (0)	0 (0)	
Hyperthyroidism	0 (0)	0 (0)	<0.001
Absent	11 (28.9)	43 (82.7)	
Diabetes Mellitus+ Hypertension	5 (13.2)	0 (0)	
Obstructive Sleep Apnea Syndrome	1 (2.6)	0 (0)	
Fear of falling			
Present	8 (21.1)	10 (19.2)	0.831
Absent	30 (78.9)	42 (80.8)	
History of falling			
Present	6 (15.8)	6 (11.5)	0.558
Absent	32 (84.2)	46 (88.5)	

Data are shown as frequency and percentage. Chi-square test was used.

Table 3. Postural parameters of the participants

	Group		p
	Obese	Control	
The number of falls	0.16±0.44	0.12±0.32	0.596
FES-I	21.29±5.06	18.79±3.43	0.006
Overall Stability Index	0.7±0.88	0.47±0.24	0.509*
Antero-Posterior Stability Index	0.52±0.52	0.36±0.2	0.119*
Medio-Lateral Stability Index	0.32±0.7	0.19±0.14	0.717*
Fall Risk Index	4.47±1.91	1.55±0.88	<0.001*

Data are shown as mean±standard deviation. *:Mann Whitney U test was used. Independent samples t test was used for the other ones. FES-I:The Falls Efficacy Scale-international

in fall risk.[16-24] In addition, it is known that obesity increases the fall risk in the elderly in relation to the decrease in the proprioceptive data control capacity of the elderly.[25] In their study with 45 elderly female patients, Mainenti et al.[26] emphasized that increased BMI was associated with impaired postural stability as patients had to balance a greater body mass volume on their support surfaces. However, the mean age of the patients participating in our study was relatively low, so the fact that the postural stability parameters of the patients in the study group were not different from the control group may be related to the low mean age of both groups and similar to each other.

Alonso et al.[27] evaluated the effects of anthropometric characteristics and gender on postural balance with a total of 100 patients, 50 male and 50 female, aged 20-40 years. They found that as the BMI increased, the postural stability in the unstable platform was disturbed and this was associated with an increased fall risk during movement.[27]

Błaszczyk et al.[8] stated that the increase in BMI causes a biomechanical limitation that may adversely affect the adaptation in maintaining upright posture, and this situation causes impaired postural stability and decreased dynamic stability in patients with a BMI of 40 and above. In our study; the high FES-I and FRI scores we detected in the study group, are consistent with the literature.

Owusu et al.[28] reported that hip and wrist fractures among 43 053 men aged 40–75 years increased in relation to waist circumference and waist-to hip ratio. In our study, when all patients including the control group were evaluated, a statistically significant positive correlation was found between FRI and waist, hip circumference measurements. When only the patient group was evaluated, there was a statistically significant positive correlation between the number of falls in the last 1 year and waist circumference. These are consistent with the results of Owusu et al.[28]

CONCLUSION

Postural stability is an essential prerequisite for many physical activities in daily life. Obesity is a disease that causes many complications by disrupting the biopsychosocial well-being of a person. The main result of our study is that morbid obesity negatively affects FRI, which is an important dynamic stability indicator. We recommend the implementation of rehabilitation programs focused on dynamic tasks for postural balance training in obese patients.

ETHICAL DECLARATIONS

Ethics Commite Approval: Ethical approval was obtained from Tokat Gaziosmanpaşa University Faculty of Medicine Ethics Committee (approval number: 21.11.2018/18-KAEK-224) for our study.

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

Referee Evaluation Process: Externally peer-reviewed.

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

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

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Orjinal Araştırma / Original Article

The Evaluation of Patients Admitted due to Minor Head Trauma with Clinical Decision Rules

Minör Kafa Travması Nedeniyle Başvuran Hastaların Klinik Karar Verme Kuralları Eşliğinde Değerlendirilmesi

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Abstract

Aim: We aimed to identify patients admitted to pediatric emergency service due to head trauma using clinical decision-making rules.

Material and Method: This is a prospective cohort study involving who referred to a tertiary university hospital pediatric emergency service due to minor head trauma. Evaluations were made with PECARN, CATCH and CHALICE clinical decision rules.

Results: 326 cases were included in the study. 63.5% (207) of the cases were male, and their ages were 52±52 months (min: 1 day - max: 214 months). 61.9% (202) of the cases were admitted due to a fall. 15.3% (49) cases presenting with minor head trauma had a (computed tomography) CT performed. In cases under the age of three months the CT scan rate was 66.6%, while it was 11% in cases over three months. 50% of the cases who had a CT scan satisfied the clinical decision rules. However, two cases who had traumatic brain injury(TBI) in the CT could not be determined with clinical decision rules. There was a statistically significant correlation between the presence of severe mechanism of injury and TBI findings in the CT($p<0,05$).

Conclusions: In the CT decision for patients who were admitted with minor head trauma, the role of clinical decision rules is note worthy. In addition, physician experience, the physicians' knowledge of clinical decision rules, the awareness of/raising awareness to the families about the harms of CT and the necessary conditions being provided by hospital observation units for the patients are also essential.

Keywords: Minor head trauma, child, CT, PECARN

Öz

Amaç: Minör kafa travması nedeniyle çocuk acil servise başvuran hastaları klinik karar verme kurallarını kullanarak tespit etmeyi amaçladık.

Gereç ve Yöntem: Minör kafa travması nedeniyle üçüncü basamak bir üniversite hastanesi çocuk acil servisine başvuran hastaları içeren, Prospektif kohort çalışmadır. PECARN, CATCH ve CHALICE klinik karar verme kurallarıyla hastalar değerlendirildi.

Bulgular: Çalışmaya 326 Olgu dahil edildi. Olguların %63,5 (207)'i erkek olup, yaşları 52±52 ay (min: 1 gün-maks: 214 ay) idi. Olguların %61,9 (202)'u düşme nedeniyle başvurdu. Tüm Bilgisayarlı tomografi(BT) çekilenler, toplam kafa travmalı hastaların %15,3 (49)'üydü. 3 ay altındaki olgularda BT çekilme oranı %66,6 iken, üç ay üstünde %11 idi. BT çekilen olguların %50'si klinik karar verme kurallarını karşılamaktaydı. Ancak BT'de travmatik beyin hasarı(TBH) olan iki olgu klinik karar verme kurallarıyla saptanamadı. Yüksek enerjili travma varlığı ile BT de TBH bulguları arasında istatistiksel olarak anlamlılık vardı ($p<0,05$).

Sonuç: Minör kafa travmasıyla başvuran hastalarda BT kararında, klinik karar verme kurallarının yeri büyüktür ancak hekim deneyimi, hekimlerin klinik karar verme kurallarını bilmesi, ailelerin BT'nin zararları konusunda bilinçli olması/bilinçlendirilmesi ve hastane gözlem ünitelerinin de bu hastaları gözlemede yeterli koşullara sahip olması gerekmektedir.

Anahtar Kelimeler: Çocuk, minör kafa travması, BT, PECARN

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INTRODUCTION

Injuries related to trauma are the most frequent cause of mortality in childrenandadolescents worldwide, especially in developed countries. Approximately 40% of deaths associated with trauma are related to head traumas, and TBI is an important reason formortality and disabilities.[1]

Computed tomography (CT) plays a key role in the management of patients with head trauma. However, it is difficult to determine indication in patients with minor head trauma.[2] Minor head trauma is a patient group with a Glasgow Coma Score (GCS) between the 13-15 interval. "Clinically important traumatic brain injury" is seen in %1 of patients with minor head trauma, and it is important not to skip over this group during the diagnosis. It is also important to determine patients requiring CT because of the risk of cancer due to radiation.[3]

Clinical decision rules help physicians for the decision ofthe requirement of a CT scan in patients with minor head trauma. Of these rules, the most frequently used is the USA based PECARN (The Pediatric Emergency Care Applied Research Network), while the England based CHALICE (The children's head injury algorithm for the prediction of important clinical eventsrule) and Canada based CATCH(Canadian Assessment of Tomography for Childhood Head injury rule) are other frequently used clinical decision rules.[4-7]

Our aim was to prospectively review patients who referred to our clinic with minor head trauma in light of clinical decision rules, determine patients with missed traumatic brain injuries by conducting their post-discharge follow-ups and identify our rate of CT use.

MATERIAL AND METHOD

The study, which was designed as a prospective cohort study, was carried out between the dates 1.6.2017 and 1.6.2018 in a tertiary university hospital in Ankara having an average of 49.000 annual patient admissions to the pediatric emergency service. The ethics committee approval for the study was obtained from the local ethics committee of the Medical Faculty of Gazi University (Decision no: BD2531547422).

Cases with GCS 13-15 who referred to the pediatric emergency service throughout the study due to head trauma were evaluated with the PECARN, CATCH, CHALICE clinical decision rules. The tomography of the cases were evaluated in terms of TBI. Patients who had missed traumatic brain injuries after their discharge were determined.

A study data form was created to record post-discharge monitoring information of the cases such as demographic information, vital signs, GCS, physical examination (PE), clinical states, hospitalization/discharge etc. before the study.

The data form was filled out by the physician evaluating the patient. The physician evaluating the patient made the decision of whether the patient would have a CT scan according to the "clinical decision rules". The decision of the physician was not interfered.

The history and PE findings of the patients required to have a CT scan according to the clinical decision rulesare presented in **Table 1**. These findings could also be found in our forms.

Traumatic brain injury (TBI) findings in the CT were defined as; skull fracture, pneumocephalus, intracranial hemorrhage or contusion, epidural–subdural hemorrhage, sigmoid sinus thrombosis, traumatic infarction, diffuse axonal injury, herniation findings.[8]

Table 1. Decision rules for CT acquisition in children with minor head injury

	PECARN <2 years	PECARN ≥2 years	CHALICE	CATCH
Historical Variables				
Loss of consciousness	5 sec≤	≥5 sec	>5 min	-
Vomiting	-	+	≥3	-
Headache	-	severe	-	worsening
Acting abnormally to parents	+	-	-	-
Amnesia	-	-	>5 min	-
Seizure	-	-	+	-
Suspicion of non-accidental injury	-	-	+	-
Severe mechanism of injury *	+	+	+	+
Physical Exam Variables				
Altered mental status	+	+	-	-
Skull fracture	+	basilar drowsy penetrating, Irritable Open, depressed,basilar depressed or basilar		
GCS	<15	<15	<14**	at 2 hours <15
Neurologic deficit	-	-	+	-
Scalp hematoma	nonfrontal	-	5 cm<	if 1year >Large, Boggy bruises or lacerations

Abbreviations: NAT= non-accidental trauma; GCS= Glasgow Coma Scale; sec= seconds; min= minutes
*Severe mechanism defined: (1) for PECARN as motor vehicle collision with patient ejection, death of passenger, or rollover, pedestrian or cyclist without helmet struck by vehicle, fall >0.9 meters if <2 years and >1.5 meters if >2 years, or head struck by high speed projectile; (2) for CHALICE as motor vehicle collision as occupant, pedestrian or cyclist >40 miles/hour, fall >3 meters, or head struck by high speed projectile; and (3) for CATCH as motor vehicle collision, fall >0.9 meters or 5 stairs, or unhelmeted bicycle fall. ** 1year> 15>

According tothe "clinical decision rules", the decision was made to discharge or monitoring/hospitalization of the patient. The clinical states of patients who were discharged after the monitoring processwere evaluated by calling them via telephone in the first month and first year of their discharge. Patients were asked if they referred to another hospital after the initial referral, if they had a CT taken, if they developed clinically TBI symptoms (death, staying for at least 2 days in the hospital or requiring intubation for more than 24 hours, brain surgery operation) or traumatic brain injury findings in the CT.

Inclusion Criteria

All cases under the age of 18 with minor head trauma(who had GCS 13-15), who referred to the pediatric emergency service within the first 24 hours of the incident were included in the study;

Exclusion Criteria

Cases who had a CT taken in another center before their referral, with an underlying neurological disorder and bleeding disorders,and could not be reached at the 1. and 12. months of follow-up after their emergency service discharge were not included in the study.

Statistical Analysis

The data were analyzed with IBM SPSS V23. The conformity to normal distribution was assessed with the Shapiro-Wilk test. The independent and dependent samples t-tests were used in the comparison of independent data with normal distribution and dependent data, respectively. The data conforming to normal distribution are presented as mean ± standard deviation. For the categorical data comparisons chi-square test and one-way ANOVA testwere used when comparing more than two variables. As for the age comparisons the t-test was used. Analysis results were presented as frequency (percentage) for categorical data, and as averages and standard deviations for numerical data. The significance level was accepted as $p<0.05$.

RESULTS

The number of cases evaluated as minor head trauma throughout the study period was 382 (7.8% of allcases), and 326 cases were included in the study (**Figure 1**). 63.5% (207) of the cases forming the study group were male, and their ages were 52±52 months (min: 1 day - max: 214 months). The average time of referral to the emergency service of the cases after the incident was 2.02 ± 0.42 hours. 49.1% (160) of the casesreferred to the emergency service between 08:00-16:00; and 47.9% (156) of them referred to the emergency service between 16:00-24:00. The GCS of all cases was 15 at the time of referral. 61.9% (202) of the cases were admitted due to a fall. There were no signs at the time of referral in 87.8% (286) of them. The demographic features of all cases with minor head trauma are presented in **Table 2**.

While 97.8% (319) of the caseswere discharged from the emergency service, 2.1% (7) of them were hospitalized inpediatric wards. No surgical interventions were performed on any patient included in the study, none of them were admitted to the pediatric intensive care unit and no mortalities were observed in any of the patients.

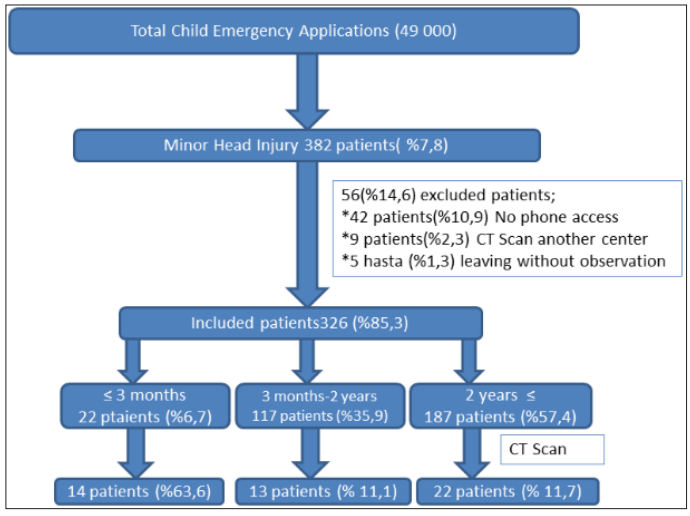

Figure 1. Study flow diagram.

Table 2. Demographic Data of the Cases

		n (%)
Sex	Male	207 (63.5)
	Female	119 (36.5)
Injury mechanizm	Fall	202 (61.9)
	Fall of stairs	16 (4.9)
	in-car traffic accident	7 (2.1)
	non-vehicle traffic accident	6 (1.8)
	motorcycle accident	0 (0)
	falling of the bike/crashing	11 (3.4)
	assault	2 (0.6)
	head struck by high speed projectile	9 (2.8)
	others	73 (22.4)
The form of trauma	Isolated head injury	81 (24.8)
	Without isolated head injury	245 (75.2)
Severe mechanism of injury *	Yes	44 (13.4)
	No	282 (86.5)
Symptoms	No symptom	286 (87.8)
	Vomiting	22 (6.7)
	Severe headache	9 (2.8)
	Loss of consciousness	5 (1.5)
	Amnesia	3 (0.9)
	Seizure	1 (0.3)
Physical Exam	Palpable skull fracture	-
	Temporal hematoma	7 (2.1)
	Occipital hematoma	2 (0.6)
	Parietal hematoma	5 (1.5)
	Frontal hematoma	20 (6.1)
Observation time n (%)	0-4 hour	153 (46.9)
	4-8 hour	155 (47.5)
	8-12 hour	4 (1.2)
	12-24 hour	4 (1.2)
	24-48 hour	2 (0.6)

*Severe mechanism defined: (1) for PECARN as motor vehicle collision with patient ejection, death of passenger, or rollover, pedestrian or cyclist without helmet struck by vehicle, fall >0.9 meters if <2 years and >1.5 meters if >2 years, or head struck by high speed projectile; (2) for CHALICE as motor vehicle collision as occupant, pedestrian or cyclist >40 miles/hour, fall >3 meters, or head struck by high speed projectile; and (3) for CATCH as motor vehicle collision, fall >0.9 meters or 5 stairs, or helmetless bicycle fall.

The characteristics according to the age group of the cases who did not have a CT taken are shown in **Table 3**. When the symptoms and clinical findings that affected the physicians' decision to take aCTwere evaluated, it was observed that physicians decided to take a CT in cases witha history of amnesia (%100;3 patients) andseizures (%100;1 patient), symptoms ofloss of consciousness (%60;3 patients) andvomiting; who had a temporal, parietal and frontal hematoma.

Table 3. Features of patients without CT, according to their age ranges

	0-3 months	4-24 months	24 months<
Number of case n (%)	8 (2.9)	104 (37.5)	165 (59.5)
Sex			
male	5	72	100
female	3	52	165
Mechanism of injury n (%)			
fall	5 (62.5)	81 (77.8)	82 (49.6)
fall of stairs	-	3 (3.9)	10 (6.1)
in-car traffic accident	1 (12.5)	-	5 (3)
non-vehicle traffic accident	-	-	3 (1.8)
motorcycle accident	-	-	-
falling of the bike/crashing	-	-	10 (6.1)
assault	-	1 (1)	-
head struck by high speed projectile	1 (12.5)	-	6 (3.6)
others	1 (12.5)	19 (18.3)	48 (29.1)
Severe mechanism of injury	2 (25)	6 (5.7)	26 (15.7)
Falling height:			
<91cm	4	68	-
91-150cm	-	5	-
>151cm	-	-	2
Number of stairs:			
<6	-	2	6
6-15	-	1	4
>15	-	-	0
Loss of consciousness	-	1	1
Basilar skull fracture	-	-	-
Severe headache	-	1	4
Vomiting:	-	9	6
<3	-	9	6
>3	-	-	-
Amnesia	-	-	-
Seizure	-	-	-
Palpable skull fracture	-	-	-
Temporal Hematoma	-	-	4
Occipital Hematoma	1	-	1
Parietal Hematoma	-	-	4
Frontal Hematoma	-	7	11
Lesion size:			
<3cm	1	4	15
3-5cm	-	3	4
>5cm	-	-	1
Observation time n (%)			
0-4 hour	3 (37.5)	48 (46.1)	91 (57)
4-8 hour	4 (50)	54 (52)	71 (43)
8-12 hour	-	2 (2)	-
12-24 hour	-	-	-
24-48 hour	-	-	-
48<hour	-	-	-
Emergency discharge n (%)	7	104 (100)	162 (98)
Hospitalization n (%)	-	-	3 (2)

The relationship between the demographic features of cases who were decided to have a CT scan after the first evaluation and TBI findings in the CT is presented in **Table 4**. All cases who had a CT taken were 15.3% (49) of the total cases with head trauma. When the age distribution of the cases having a CT taken was reviewed, it was seen that 44.9% (22) of the cases were over the age of two.A repeated CT was required only for 1(0.3%) child. TBI was seen in 2.1%(7), of the patients and clinically important TBI findings were not observed in any of the patients.

Patients who had a CT scan according to the clinical decision rules and the presence of findings in their CT is presented in **Table 5**.

Patients missed by clinical decision rules are presented in **Table 6**.

Table 4. The characteristics of CT cases according to their age ranges and their relationship with the presence of TBI in CT

	0-3 months	4-24 months	24 months<	p
Number of case n (%)	14 (28.5)	13 (26.5)	22 (44.8)	
Sex				
Male	11 (78.6)	7 (53.8)	12 (54.5)	0.813
Female	3 (21.4)	6 (46.2)	10 (45.5)	
Mechanism of injury n (%)				
fall	14 (100)	9 (69.2)	10 (63.6)	
fall of stairs	-	2 (15.3)	1 (4.5)	
in-car traffic accident	-	-	1 (4.5)	
non-vehicle traffic accident	-	-	3 (13.6)	
motorcycle accident	-	-	-	0.412
falling of the bike/crashing	-	-	1 (4.5)	
assault	-	-	1 (4.5)	
head struck by high speed projectile	-	1 (7.7)	1 (4.5)	
others	-	1 (7.7)	4 (18.2)	
Severe mechanism of injury	1 (7.1)	4 (30.7)	7 (31.8)	0.002*
Falling height:				
<91cm	13 (92.9)	5 (38.5)	-	0.042*
91-150cm	1 (7.1)	1 (7.7)	-	0.074
>151cm	-	1 (7.7)	4 (18.2)	0.008*
Number of stairs:				
<6	-	-	-	**
6-15	-	2 (15.4)	1 (4.5)	
>15	-	-	-	
Loss of consciousness	-	1 (7.7)	2 (9.1)	**
Basilar skull fracture	-	-	-	**
Severe headache	-	-	4 (18.2)	**
Vomiting:	0 (0)	4 (30.7)	2 (9.1)	
<3	0 (0)	1 (7.7)	1 (4.5)	0.498
>3	0 (0)	3 (23)	1 (4.5)	
Amnesia	-	-	3 (13.6)	0.309
Seizure	-	-	1 (4.5)	0.565
Palpabl skull fracture	-	-	-	**
Temporal Hematoma	1 (7.1)	1 (7.7)	1 (4.5)	0.713
Occipital Hematoma	-	-	-	**
Parietal Hematoma	-	1 (7.7)	-	0.565
Frontal Hematoma	-	1 (7.7)	1 (4.5)	0.411
Lesion size:				
<3cm	-	1 (7.7)	1 (4.5)	0.231
3-5cm	1 (7.1)	1 (7.7)	1 (4.5)	0.525
>5cm	-	1 (7.7)	-	**

* p <0.05 statistically significant, ** no variable

Table 5. Patients who undergo CT according to clinical decision rules and presence of findings in CT

Patients	Age (month)/sex	CT imaging reason	Finding in CT
1.	1/M	*/**	+
2.	8/M	*/**/***	-
3.	15/F	*/**	-
4.	19/M	***	-
5.	9/M	*/**	+
6.	13/F	***	-
7.	22/M	***	-
8.	3,5/F	*	-
9.	22/F	**	-
10.	13/M	**	-
11.	29/M	*	-
12.	51/M	*/**	-
13.	51/M	*/***	-
14.	61/M	*/**/***	+
15.	66/F	*/**	+
16.	69/F	*	-
17.	78/M	**/***	-
18.	98/F	*/**	-
19.	17/M	**/***	-
20.	179/M	*/***	-
21.	179/M	*/***	-
22.	197/F	*/**/***	+
23.	194/F	***	-
24.	41/M	**	-
25.	46/F	**/***	-

* PECARN, **CATCH, ***CHALICE

Table 6. Patients who fled according to clinical decision rules

Patients Mechanism of injury	Age (month)/ sex	CT imaging reason	Finding in CT
Patient fall of <90cm	66/M	Amnesia <5min	+
Patient falling from your own height	150/F	Temporal hematoma <3cm	+

Abbreviation: min: minutes

There was a statistically positive relationship between the cases who had an observation duration of 4 hours and more, and the CT rates (p<0.001).

In patients who had a CT scan, the rate of TBI was 14.2%. The TBI finding in all of these patients was a skull fracture. Most of these were seen in24 months≤.

In patients who had a CT scan, 28.5% (14) of the patients were under 3 months. All of these patients referred to the hospital due to a fall. 26.5% (13) of the patients who had a CT taken consisted of 3-24-month old'sand 69.2% (9) of these patients referred to the hospital due to a fall. 44.8% (22) of the patients who had a CT taken consisted of ≥24 months, and 63,6% (10) of these patients referred to the hospital due to a fall (**Table 2**).

A statistically significant relationship was found between the presence of Severe mechanism of injury and TBI findings in the CTscan (p<0.05) (**Table 2**). There was a statistically significant relationship between the increase of the falling distance and the presence of findings in the CT (p<0.05) (**Table 3**). There was not a statistically significant relationship between trauma mechanisms and the presence of findings in the CT scan (**Table 3**).

The criteria the patients who had a CT taken met in the clinical decision rules are presented in **Table 4**.

It was learned that none of the patients who were reached via telephone in the first month and the first year after their discharge referred to another hospital due to the same trauma, had a serious TBI and had a CT scan.

DISCUSSION

Minor head trauma is the most common reason of referral to the pediatric emergency services.[7] In our prospective cohort study where we reviewed patients who referred to our clinic due to minor head trauma, the rate of CT use was 15%. However, when we examined our CT rate according to our patients'age groups, this rate was 63.6% in the group of under three months and below and %11 in the group of 4 months and above. We have considered the reasons as to be the difficulty of neurological examination in three-month old patients and insufficient space to admit and observe the patients. As for our overall high CT rate, we assessed that the reasons for this can be physician experience and foresight, opinion differences among consulting physicians, the request of the families and once again, our observation unit not being adequate for a 24-hour monitoring of these patients.

When the literature was reviewed, in a study in which the multicenter PECARN rules were applied, this rate was 7%,[8] and in a study in which a pediatric hospital in the United States of America and Italy was compared, the CT rates of patients admitted due tominorhead traumawere 17.3% and 6.6%, respectively.[9] In another study, the CT rate of patients admitted to a pediatric trauma center due to minor head trauma was %94.6.[10] As seen in the literature, CT ratescan notably vary according to countries, clinics, and that the clinical decision rules are not used sufficiently. In our study, half of our cases who had a CT scan had a CT indication according to the clinical decision rules as well. The main reason was to be the presence of physicians working in different seniorities in our pediatric emergency service,having different consulting physicians, the requests of the families and the fear of head trauma in minor age groups. Additionally, the clinical decision rules should be clearer for the 3-month-old and younger patient group, where the CT rates were high in our study.

TBI İs the leading cause of mortality and disability in the world. When the literature was reviewed, clinically important TBI rates were given as 1.1%, 5.9% and 3% in different studies, respectively.[8,11,12] In our study, being consistent with the

literature, the TBI rate was 2.1%. All of these were skull fractures and they were mostly 2-year-old or older patients. Clinically important traumatic brain injuries were not observed in any patients. As seen in the literature, while TBI, especially clinically important traumatic brain inquiry is seen quite rarely in patients admitted with minor head trauma, using clinical decision rules in order to not miss these patientsis quite beneficial. Nevertheless, in our study clinical decision rules, 2 patients with TBI were missed. We should apply the rules, but we should not neglect conducting multifaceted evaluations for the patients.

According to the trauma mechanism, the most frequent referral was falling. In a study by Ortega et al., it was found that 53.3% of the patients who referred to the hospital with head trauma, referred due to high falls as well.[13] In another study, 93% of children under the age of 3 who presented with minor head trauma presented with a fall.[14]

In our study, a significant relationship was determined between referrals with severe mechanism of injurythe presence of findings in the CT scan. In the study conducted with 2-year-old and younger children, a statistically significant relationship was found between the height of the fall, TBI and clinically important TBI.[15] In another study conducted with patients who referred with minorhead trauma, a statistically significant relationship was found between falling from a height >1m and findings inthe CT scan.[16] In our study, being consistent with the literature, a significant relationship was identified between the increase in the distance of the fall and findings in the CT scan as well. A CT scan was taken in most of the patients who were two years old and older and fell from a height over 1.5 meters.

In our study, the most frequent symptom in the history was evaluated as vomiting (6.7%), followed by severe headaches, loss of consciousness, amnesia, and seizures, respectively. Although, a significant relationship was not found between these symptoms and findings in the CT scan. In a multicentric study, a significant relationship between vomiting and the presence of amnesia, and TBI was found, while a statistically significant relationship with headacheswas not found.[17] In another study vomiting (56.6%) was the most frequent symptom, followed up by headaches, and a statistically significant relationship was found between headaches and the duration of hospital stay.[18] In another study, a relationship was not be found between the vomiting symptom and TBI findings in the CT.[19] In a study conducted with patients who referred with head trauma, vomiting and headaches were the most frequent symptoms, while a significant relationship was only found between headaches and TBI.[20] As seen in the literature, vomiting is the most frequently seen symptom but the presence of the accompanying symptom, the duration of vomiting, the number of vomiting, its continuation during monitoring should be evaluated entirely. In our study, a significant relationship was not found between the number of vomiting and the presence of CT findings as well.

In a study in the literature, TBI was identified in 9 of 28 patients with temporal hematoma, 2 of the 15 patients with parietal hematoma, 2 of the 22 patients with occipital hematoma. In our study, a CT scan was taken in 42.8% of the patients with temporal hematoma, 20% of the patients with parietal hematoma, 10% of the patients with frontal hematoma. However, a significant relationship was not found between the presence of findings in the CT and the presence of hematoma. Although hematomas except for the ones in the frontal area are frightening, their existence alone should not be an indication for CT. They should be evaluated with their size and accompanying findings. In our study, a CT scan was taken mostly in patients who were accompanied by severe mechanism of injury or when their lesion size was more than 3 cm.

In a study in the literature, 94% of the patients were discharged from the pediatric emergency service.[3] In our study, 90% of the patients were monitored up to about 8 hours, and 97% of them weredischarged from thepediatricemergency service. We can explain one of the reasons for our high CT rate to be the shortness of our monitoring period.

In our study, the guardians of the patients were called in the 1. month and 12. month, and we determined that they have not referred to a hospital again due to the same trauma, did not have a CTscan taken and did not have a missed TBI. In another study where minor head trauma patients were reviewed,the guardians of the patients were called in the first and third month and have not determined a CT scan due to the same trauma or a missed clinically important TBI.[21]

The major limitations of our study were being a single-centered study, and the patients being evaluated by physicians of different seniorities.

CONCLUSION

In conclusion, clinical decision rules in the decision of CT scan in patients admissing with minor head trauma are important in the use of CT scan with the correct indication. However, the physicians' knowledge of the clinical decision rules, the awareness of/raising awareness to the families about the harms of CT and the necessary conditions being provided by hospital observation units for monitoring the patients are also essential. Also, for patients who are three months old and younger, clinical decision rules should be clearer and they must be evaluated in a separate category.

ETHICAL DECLARATIONS

Ethics Commite Approval: The ethics committee approval for the study was obtained from the local ethics committee of the Medical Faculty of Gazi University (Decision no: BD2531547422).

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

Referee Evaluation Process: Externally peer-reviewed.

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

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

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Orjinal Araştırma / Original Article

Evaluation of The Predictability of Platelet Mass Index for Short-Term Mortality in Patients with COVID-19: A Retrospective Cohort Study

COVID-19 Hastalarında Kısa Süreli Mortalite İçin Trombosit Kitle İndeksinin Öngörülebilirliğinin Değerlendirilmesi: Retrospektif Bir Grup Çalışması

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Abstract

Objective: This study aimed to determine the predictability of platelet mass index (PMI) for short-term mortality in patients with COVID-19.

Material and Method: This retrospective, observational, cohort study included corrected COVID-19 patients. Demographics, clinical characteristics, biochemical and hematological parameters and the data of all-cause mortality within 30 days after admission were noted. The receiver operating characteristic curve analysis and odds ratio were performed to determine the discriminative ability of the scores.

Results: Of the 1564 patients, with mean of age of 44±16 years included in the study. A total of 57 (3.6%) patients died within 30 days of emergency department presentation. There was a statistically significant difference between the survivor and non-survivor groups in terms of the platelet count, mean platelet volume (MPV) and PMI. According to the best Youden's index, the cut-off value for the platelet count was determined as 146 (sensitivity: 91.8%, specificity: 87.2%), and the area under curve (AUC) value was 0.593 (95% confidence interval 56.7-61.9). According to the best Youden's index, the cut-off value for the MPV was determined as 11 (sensitivity: 24.6%, specificity: 91%), and the AUC value was 0.579 (95% confidence interval 55.2-60.5). According to the best Youden's index, the cut-off value for the PMI was determined as 1513 (sensitivity: 28.1%, specificity: 87.2%), and the AUC value was 0.555 (95% confidence interval 52.8-58.2).

Conclusion: Platelet count, MPV and PMI were not predictor of 30-day mortality in patients with confirmed COVID-19 in emergency department.

Keywords: COVID-19, SARS-Cov-2, blood tests, coronavirus, platelet, laboratory

Öz

Amaç: Çalışmamızda, COVID-19 hastalarında trombosit kitle indeksinin (PMI) kısa dönem mortalite için öngörülebilirliğini belirlemeyi amaçladık.

Gereç ve Yöntem: Retrospektif, gözlemsel kohort çalışmamıza, doğrulanmış COVID-19 hastaları dahil edildi. Demografik, klinik özellikler, biyokimyasal ve hematolojik parametreler ve başvurudan sonraki 30 gün içinde tüm nedenlere bağlı ölüm verileri kaydedildi. Parametrelerin öngörebilirliklerini tespit edebilmek için alıcı işletim karakteristik eğrisi analizi ve olasılık oranı yapıldı.

Bulgular: Yaş ortalaması 44±16 yıl olan 1564 hasta çalışmaya dahil edildi. Acil servise başvurduktan sonraki 30 gün içinde toplam 57 (%3,6) hasta öldü. Trombosit sayısı, ortalama trombosit hacmi (MPV) ve PMI açısından yaşayan ve yaşamayan gruplar arasında istatistiksel olarak anlamlı bir fark vardı. En iyi Youden indeksine göre trombosit sayısı için cut-off değeri 146 (duyarlılık: %91,8, özgüllük: %87,2) ve eğri altındaki alan (EAA) değeri 0,593 (%95 güven aralığı 56,7-%) olarak belirlendi. 61,9). En iyi Youden indeksine göre MPV için cut-off değeri 11 (duyarlılık: %24,6, özgüllük: %91) ve EAA değeri 0,579 (%95 güven aralığı 55,2-60,5) olarak belirlendi. En iyi Youden indeksine göre PMI için kesme değeri 1513 (duyarlılık: %28,1, özgüllük: %87,2) ve EAA değeri 0,555 (%95 güven aralığı 52,8-58,2) olarak belirlendi.

Sonuç: Acil serviste doğrulanmış COVID-19 olan hastalarda trombosit sayısı, MPV ve PMI 30 günlük mortalitenin öngörücüsü değildir.

Anahtar Kelimeler: COVID-19, SARS-CoV-2, kan testleri, korona virüs, trombosit, laboratuvar

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INTRODUCTION

The coronavirus, a respiratory RNA virus, caused an epidemic in Wuhan, China at the end of 2019, causing severe acute respiratory failure. For this reason, this epidemic, which forces the social lives, economies, and health systems of countries, was called COVID-19.[1] From March 2020, when it was declared a pandemic, to June 2021, it infected more than 180 million people and caused the deaths of more than 3.5 million people.

With the spread of the disease around the world, many researchers studied the course of the disease and prognostic factors to use resources effectively.[2-4] It has been shown that an increase in inflammatory markers such as C-reactive protein (CRP), interleukin 6, leukocyte count, and erythrocyte sedimentation rate can be a marker of critical illness and mortality.[2,3,5] On the other hand, it has been shown that the decrease in markers such as lymphocyte count and albumin can also be used in the detection of critical patients and predicting mortality. Researchers constantly tried to find better markers.[4,5] In order to achieve better predictability, hematological ratios such as neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-CRP ratio, lymphocyte-to-monocyte ratio and platelet-to-lymphocyte ratio (PLR) were studied. [4-6] The predictability of mortality and critical illness of platelet count and platelet-related parameters was studied on COVID-19 patients. It has been reported that platelet count and mean platelet volume (MPV) may be a predictor of mortality for COVID-19. Thus, we hypothesized that the platelet mass index (PMI), which is formed by multiplying platelet count and MPV, may be a predictor in COVID-19. To the best of our knowledge, there is no research in the literature evaluating the predictability of PMI for short-term mortality in patients with COVID-19. In this study, we aimed to determine the predictability of PMI for short-term mortality in patients with COVID-19 in emergency department (ED).

MATERIALS AND METHOD

Study Design

This retrospective cohort study was conducted at University of Health Sciences, Ümraniye Training and Research Hospital a 695-bed tertiary education hospital with 1110 patient admissions per day (annual average) to ED. Data of the patients who admitted our pandemic clinics between June 15, 2021 and July 15, 2021 collected retrospectively.

Study Population

Our study population was patients who admitted to pandemic clinic for COVID-19 between June 15, 2021 and July 15, 2021. All patients with a positive test result for SARS-CoV-2, who were tested for platelet count and MPV, were included in the study. Hospitalization and intensive care admission decision of the patients was made by the emergency medicine specialist. The follow-up of hospitalized patients was done by a pulmonologist or an infectious disease specialist or an internist. Hospitalization decisions and treatment planning were made in accordance with the COVID-19 Outbreak Management and Working Guideline of Ministry of Health.

Data Collection

Demographics, clinical characteristics (included comorbidities, and symptoms), vital parameters on admission laboratory findings, and emergency department outcomes of each patient were obtained from the hospital computer-based patient data system and analyzed by researchers. Emergency department outcomes were noted as discharged, hospitalized to inpatient clinics, and admitted to intensive care unit. Comorbidities were recorded as coronary artery disease, diabetes mellitus, chronic obstructive pulmonary diseases, hypertension, congestive heart failure, chronic renal failure, active malignancy, and immunodeficiency. Symptoms of disease were recorded as fever, cough, sputum, dyspnea, weakness, myalgia, smell or taste defects, sore throat, headache, vomiting or nausea, and diarrhea. Systolic blood pressure, diastolic blood pressure, body temperature, pulse pressure, and peripheral oxygen saturation were recorded as vital parameters. The documented laboratory parameters were BUN, creatinine, CRP, albumin, white blood cell count, neutrophil count, lymphocyte count, platelet count, MPV, and mean corpuscular volume. NLR, PLR, and PMI were calculated by researcher.

To confirm COVID-19, ORF1ab and N gene of SARS-CoV-2 were embattled and Biorad CFX 96 platform were used. Twenty-nine and above Ct values were considered positive. Tests that were positive for both genes of ORFlab and N were reported as SARS-CoV-2 positive.

Statistical Analysis

IBM SPSS Statistics for Mac, Version 27.0. Armonk, NY, IBM Corp was used to perform statistical analyses. To assess the conformance of variables to normal distribution the Kolmogorov-Smirnov test was conducted. The data that matched normal distribution were presented with mean and standard deviation and values, and the remaining data were expressed as interquartile range and median values. Categorical data were presented with percentages and the number of cases. For the comparison of qualitative and quantitative data between two groups, the Mann-Whitney U and chi-square tests were used. The Bonferroni correction was used a method to counteract the problem of multiple comparisons of laboratory parameters. We also formed a receiver-operating characteristic curve (ROC) for short-term mortality and obtained the area under the curve (AUC) for individual variables by using MedCalc software (MedCalc Software Ltd, Ostend, Belgium). A p value lower than 0.05 was statistically significant in all analyses.

Ethics

The ethical committee approval of our study was obtained from the Ethical Committee of University of Health Sciences, Ümraniye Training and Research Hospital (approval number: B.10. 1.TKH.4.34 .H.GP.0.01/235). We retrospectively reviewed

the secondary data recorded from the computer-based patient data system of hospital. However, the recorded data didn't include any personal identifiable data; it included clinical information solely. Therefore, the necessity for informed consent was wild.

RESULTS

Patient Characteristics

Of the 1564 patients included in the study, 801(53.2%) were male. The mean of age of the 1564 patients was 44±16 years. A total of 57 patients died within 30 days of ED presentation. The rate of 30-day mortality was 3.6% for the study cohort. The demographic characteristics, clinical outcomes for the first 24 hours, comorbid diseases, symptoms, vital parameters at presentation, and mortality data comparison of them between the survivor and non-survivor groups are shown in **Table 1**. Initial laboratory findings comparison of them between the survivor and non-survivor groups are presented in **Table 2**. Nine hundred ninety-one of all patients were discharged, 550 were hospitalized to inpatient clinics, 23 were admitted to intensive care unit. Nine hundred eighty-nine of the patients who survived were discharged, 516 of them were hospitalized to inpatient clinics, and two of them were admitted to intensive care unit. Thirty-four of the patients who non-survived were hospitalized to inpatient clinics, 21 of them were admitted to intensive care unit. There was a statistically significant difference between the survivor and non-survivor groups in terms of the ED outcomes (p<0.001, Mann-Whitney U test).

Laboratory Values and Outcomes

Significant differences were observed between the survivor and non-survivor groups in laboratory parameters: Blood urea nitrogen [25.68 (21.4- 32.1) versus 47.08 (34.24-70.62) mg/dL, p=<0.001], creatinine [0.83 (0.73-0.98) versus 1.2 (0.92-1.53) mg/dL, p=<0.001], albumin [42.6±4.1 versus 36.1±5.2 mg/dL, p=<0.001], CRP [2 (1-5) versus 11.5 (8-16) mg/L, p= 0.003], hemoglobin [13.8±1.7 versus 12.7±2.2 g/dL, p=0.001], neutrophil count [3.63 (2.71-4.89) versus 6.25 (4.55-8.75), p=<0.001], and NLR [2.17 (1.48-356) versus 6.1 (3.59-8.84) p=<0.001].

The analysis of the ROC curve was performed to determine the discriminative ability of the laboratory parameters in 30-day mortality. **Table 3** and **Figure 1** present according to the best Youden's index the cut-off values of NLR, PLR, platelet count, MPV, and PMI and their sensitivity, specificity, AUC, positive and negative predictive values, likelihood ratios, accuracy and

Table 1. Baseline characteristics of the enrolled patients and comparison of the characteristics between the survivor and non-survivor groups

Variables	Total n=1564 (%, Standard deviation)	Survivor n=1507 (96.4%) (%, Standard deviation)	Non-survivor n=57 (3.6%) (%, Standard deviation)	p values
Age, years	44±16	43±16	71±13	<0.001
Gender				0.137
Male	837 (53.5%)	801(53.2%)	36 (63.2%)	
Female	727 (46.5%)	706 (46.8%)	21 (36.8)	
Comorbidities				
Chronic obstructive pulmonary diseases	35 (2.2%)	30 (2%)	5 (8.8%)	0.008
Hypertension	201 (12.9%)	178 (11.8%)	23 (40.4%)	<0.001
Diabetes mellitus	153 (9.8%)	143 (9.5%)	10 (17.5%)	0.044
Coronary artery disease	47 (3%)	38 (2.5%)	9 (15.8%)	<0.001
Congestive heart failure	15 (1%)	9 (0.6%)	6 (10.5%)	<0.001
Chronic renal failure	8 (0.5%)	4 (0.3%)	4 (7%)	<0.001
Active malignancy	16 (1%)	12 (0.8%)	4 (7%)	0.002
Immunodeficiency	3 (0.2)	2 (0.1%)	1 (1.8%)	0.105
Frequency of symptoms				
Fever	522 (33.4%)	499 (33.1%)	23 (40.4%)	0.255
Cough	889 (56.8%)	865 (57.4%)	24 (42.1%)	0.022
Sputum	44 (2.8%)	41 (2.7%)	3 (5.3%)	0.214
Shortness of breath	377 (24.1%)	351 (23.3%)	26 (45.6%)	<0.001
Weakness	285 (18.2%)	280 (18.6%)	5 (8.8%)	0.060
Myalgia	237 (15.2%)	632 (15.4%)	5 (8.8%)	0.171
Smell or taste defects	111 (7.1%)	111 (7.4%)	0	0.030
Headache	130 (8.3%)	129 (8.6%)	1 (1.8%)	0.083
Sore throat	158 (10.1%)	154 (10.2%)	4 (7%)	0.469
Nausea-vomiting	64 (4.1%)	57 (3.8%)	7 (12.3%)	0.007
Diarrhea	74 (4.7%)	71 (4.7%)	3 (5.3%)	0.749
Vital parameters				
Systolic blood pressure	124±18	123±17	138±26	0.001
Diastolic blood pressure	73±10	73±10	74±11	0.628
Pulse pressure	86±20	85±19	97±25	0.009
Body temperature	38.8±0.7	38.9±0.6	37.1±0.8	0.700
Oxygen saturation	96±7	96±5	87±11	<0.001

Table 2. Laboratory parameters of the enrolled patients and comparison of them between the survivor and non-survivor groups

Variables	Total Median/Mean (25th-75th percentiles/ Standard deviation)	Survivor Median/Mean (25th-75th percentiles/ Standard deviation)	Non-survivor Median/Mean (25th-75th percentiles/ Standard deviation)	p values
Blood urea nitrogen, mg/dL	27.89 (21.40-34.24)	25.68 (21.4- 32.1)	47.08 (34.24-70.62)	<0.001
Creatinine, mg/dL	0.84 (0.74-0.99)	0.83 (0.73-0.98)	1.2 (0.92-1.53)	<0.001
C-Reactive Protein, mg/L	2 (1-6)	2 (1-5)	11.5 (8-16)	0.003
Albumin, mg/dL	42.2±4.5	42.6±4.1	36.1±5.2	<0.001
White blood cell count	7.8 (5.3-8.1)	6.1 (5.1-7.8)	23.1 (12.8-26.8)	0.100
Neutrophil count	3.69 (2.73-4.99)	3.63 (2.71-4.89)	6.25 (4.55-8.75)	<0.001
Lymphocyte count	1.70±0.77	1.71±0.74	1.41±1.35	0.096
Hemoglobin, g/dL	13.7±1.7	13.8±1.7	12.7±2.2	0.001
Hematocrit	40.9±4.5	41±4.3	38.4±6.3	0.004
Platelet count	219±60	220±58	202±87	0.143
Mean corpuscular volume	85.4±5.7	85.4±5.5	87.1±7.7	0.100
Mean platelet volume, fL	9.7±1	9.6±1	10.1±1.3	0.021
Neutrophil-to-lymphocyte ratio	2.25 (1.5-3.74)	2.17 (1.48-356)	6.1 (3.59-8.84)	<0.001
Platelet-to-lymphocyte ratio	155±88.58	153.12±87.15	198.35±108.98	0.003
Platelet mass index	2091.30±524.63	2095.35±513.17	1998.04±741.06	0.331

* The Bonferroni-corrected p-value is 0.0033.

Table 3. Ability of the investigated laboratory parameters to predict 30-day all-cause mortality following ED admission

	AUC	Cut-off	Sensitivity	Specificity	PPV	NPV	LR+	LR-	Accuracy	95% CI	p-value
NLR	0.807	3.58	75.4	75.6	11.8	98.6	3.09	0.32	51.03	78.5-82.8	<0.001
PLR	0.642	>158.33	57.9	67.4	7.2	97.4	1.77	0.63	25.25	61.6-66.8	<0.001
Platelet	0.593	≤146	91.8	87.8	12.9	96.7	3.41	0.78	19.83	56.7-61.9	0.035
MPV	0.579	>11	24.6	91	10.6	96.5	2.73	0.83	15.56	55.2-60.5	0.057
PMI	0.555	≤1513	28.1	89.2	10.2	96.6	2.61	0.81	17.32	52.8-58.2	0.219

AUC: Area under curve; PPV: positive predictive value; CI: confidence interval; NPV: Negative predictive value; LR: likelihood ratio; MPV: mean platelet volume; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; PMI: platelet mass index

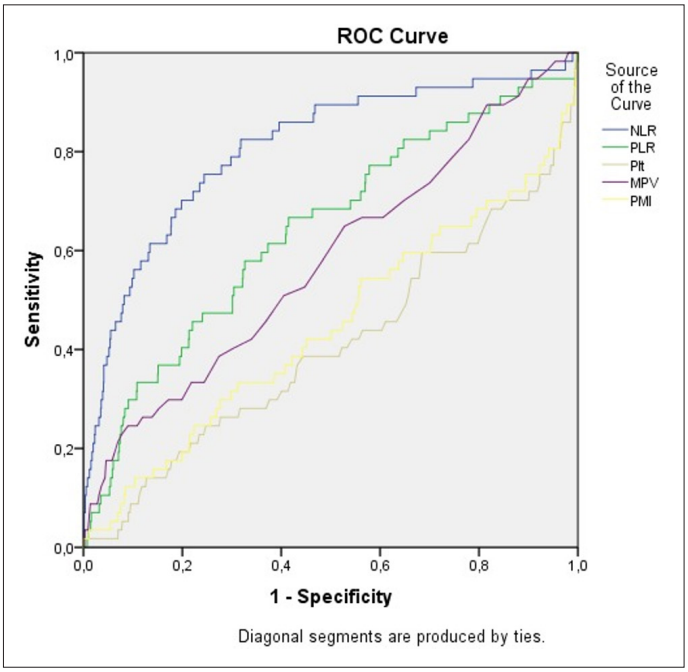

Figure 1. Receiver operating characteristic curves for the mean platelet volume (MPV), neutrophil-to-lymphocyte ratio (NLR) platelet-to-lymphocyte ratio (PLR) platelet mass index (PMI) and platelet count (Plt) for the prediction of 30-day mortality in patients with COVID-19

95% confidence interval values for the patients.

DISCUSSION

In this study, we investigated predictability of PMI for 30-day mortality. However, PMI was not useful in predicting 30-day mortality in patients with COVID-19 in ED. To the best of our knowledge, this is the first study that investigates predictability of PMI for 30-day mortality in patients with COVID-19.

In our analysis, parametric comparison tests were used to determine the significant difference between the survivors and the non-survivors in terms of platelet count, MPV and PMI values firstly. No significant relationship was found between them and the mortality. On the other hand, another analysis was performed based on the ROC curve to control the three parameters' ability of 30-day mortality. AUC values <0.5 were evaluated as close to random, while those close to one were considered close to the optimum predictor.[7,8] It has been reported that the AUC value should be >0.8 for a model to distinguish whether a patient survived or died.[7,8] In the discriminatory power analysis, we found the AUC value of platelet count, MPV and PMI as 0.593, 0.579, and 0.555, respectively which was unacceptable. Thus, according to ROC

analysis, this retrospective study with over 1500 patients, was verified that platelet count, MPV and PMI were not predictor of 30-day mortality in patients with confirmed COVID-19.

Platelet count has been investigated in infection, sepsis, septic shock and viral pneumonia and has been shown to predict mortality.[9] In their study with over 1400 patients, Yang et al.[10] found that thrombocytopenia was associated with in-hospital mortality. Liu et al.[11] showed that initial platelet count and changes in platelet count may be associated with mortality in their study in the early period of the pandemic and suggested that platelet count should be followed during hospitalization. Abnormal hematopoiesis due to infection of the bone marrow, immune-thrombocytopenia due to immune complexes and autoimmunity, and consumption thrombocytopenia due to microembolism and thrombosis have been held for thrombocytopenia.[12] However, some studies in the literature have shown that platelet count is not associated with mortality.[13,14] Bozan et al.[13] showed that there was no difference between survivors and non-survivors in terms of platelet count. Güçlü et al.[14] reported that there was no difference in platelet count between moderate and severe COVID-19 patients in their study.

In the current literature MPV has been found to be associated with mortality and poor outcome in malignancy, sepsis, and inflammation-related diseases.[15] Abnormal hematopoiesis due to infection of the bone marrow or immune complexes cause immature synthesis of platelets and abnormal volumes of platelets.[15] Based on this mechanism, the researchers investigated the relationship between MPV and COVID-19.[16-18] Sertbaş et al.[16], in their study with over 9000 patients, reported that MPV is a powerful predictor of mortality in hospitalized patients with COVID-19. Ouyang et al.[17] showed initial MPV and follow-up MPV higher on non-survivor group than survivors. Aktaş et al.[18] found that MPV had no prognostic value in geriatric COVID-19 patients in their study named "Is Mean Platelet Volume Useful for Predicting the Prognosis of COVID-19 Diagnosed Patients?".

There are limited publications in the literature about PMI, which is formed by multiplying platelet count and MPV.[19,20] Girgin et al.[19] reported in their study that low PMI levels are associated with poor prognosis. Okur et al.[20] showed that premature infants with bronchopulmonary dysplasia, necrotizing enterocolitis, retinopathy of prematurity, intraventricular hemorrhage and sepsis had lower PMI levels in early postnatal life than infants without these diseases.[20] They speculated that their results may be caused from inflammatory process. Our study was carried out with a similar hypothesis. Our results showed PMI is not predictor of 30-day mortality in patients with COVID-19. A logical explanation for this might be that platelet count and MPV were not predictors in our cohort.

Limitations

The main limitation of our study was its retrospective nature. Secondly, we could not include patients with corrected COVID-19 who hadn't been tested for platelet count and MPV. This was the most important limiting factor for our study population. Thirdly we did not exclude the chronic diseases that can affect the platelets as diabetes, renal diseases, and hypoxemia. Another limitation of our study was that the patients discharged from the hospitalized patients during the 30-day follow-up period and the length of hospital stay could not be recorded. Lastly, our study had single-center study, and therefore the results cannot be generalized to other healthcare institutions. We recommend multicenter studies in large populations to increase the generalizability of the results and to confirm them.

CONCLUSION

According to our results, platelet count, MPV and PMI were not predictor of 30-day mortality in patients with confirmed COVID-19 in ED. We recommend multicenter studies in large populations to increase the generalizability of the results and to confirm them.

ETHICAL DECLARATIONS

Ethics Commite Approval: The ethical committee approval of our study was obtained from the Ethical Committee of University of Health Sciences, Ümraniye Training and Research Hospital (approval number: B.10. 1.TKH.4.34 .H.GP.0.01/235).

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

Referee Evaluation Process: Externally peer-reviewed.

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

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

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Orjinal Araştırma / Original Article

Evaluation of Choroidal Thickness, Retinal Nerve Fiber Layer Thickness, Macular Thickness and Retinal Vessel Diameter by Optical Coherence Tomography in Patients with Peripheral Arterial Disease

Periferik Arter Hastalığı Olan Olgularda Optik Koherens Tomografi ile Koroid Kalınlığı, Retina Sinir Lifi Tabakası Kalınlığı Maküla Kalınlığı ve Retina Damar Çapı Ölçümlerinin Değerlendirilmesi

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Abstract

Aim: To evaluate retinal nerve fiber layer thickness, macular thickness and retinal vessel diameter by optical coherence tomography in patients with peripheral artery disease.

Material and Method: 35 patients with a diagnosis of peripheral arterial disease (PAD) and 32 healthy individuals (control group) were included in the study. Retinal thickness (RT), choroidal thickness (CT) in enhanced depth imaging (EDI) mode, retinal nerve fiber layer (RNFL) thickness, retinal artery and vein diameters were measured with optical coherence tomography (OCT) device.

Results: The mean age of the PAH group included in the study was 59.4±11.9 and the mean age of the control group was 55.5±5.3 years. A statistically significant difference was observed between the two groups in the values obtained from the CT in the subfoveal region of the EDI measured from three different regions and the nasal quadrant of the RNFL measured from 7 quadrants (p=0.03 and p=0.03, respectively). On the contrary, no statistically significant difference was observed in EDI and other measurements of RNFL, RT values, artery and vein diameters (p values were between 0.08-1.00).

Conclusion: In patients with PAD, it is important to determine the RNFL and CT to be thinner. It can be a guide in more comprehensive studies in the future.

Keywords: Choroidal thickness, optical coherence tomography, peripheral artery disease, retinal nerve fiber layer thickness, retinal thickness.

Öz

Amaç: Periferik arter hastalığı olan olgularda optik koherens tomografi ile koroid kalınlığı, retina sinir lifi tabakası kalınlığı, maküla kalınlığı ve retina damar çapı ölçümlerini değerlendirmek.

Gereç ve Yöntem: Çalışmaya 35 periferik arter hastalığı (PAH) tanılı hasta ve 32 sağlıklı birey (kontrol grubu) dahil edildi. Tüm bireylerin optik koherens tomografi (OKT) cihazıyla retina kalınlığı (RK), artırılmış derinlik görüntüleme (EDI) modunda koroid kalınlığı (KK), retina sinir lifi tabakası (RSLT) kalınlığı, retina arter ve ven çapı ölçümleri yapıldı.

Bulgular: Çalışmaya dahil edilen PAH grubunun yaş ortalaması 59.4±11.9 ve kontrol grubunun yaş ortalaması 55.5±5.3 yıl idi. Üç farklı bölgeden ölçülen EDI'nin subfoveal bölgedeki KK'da ve 7 kadrandan ölçülen RSLT'nin nazal kadranından elde edilen değerler iki grup arasında istatistiksel olarak anlamlı farklılık gözlendi (sırasıyla, p=0,03 ve p=0,03). Aksine EDI ile RSLT'nin diğer ölçümleri, RK değerleri, arter ve ven çapları ölçümlerinde istatistiksel olarak anlamlı bir farklılık gözlenmedi (p değerleri 0,08-1,00 arasında idi).

Sonuç: PAH hastalarında RSLT ve koroid tabakası kalınlığının daha ince olarak saptanması önemlidir. İleride yapılacak daha kapsamlı çalışmalarda yol gösterici olabilir.

Anahtar Kelimeler: Koroid kalınlığı, optik koherens tomografi, periferik arter hastalığı, retina kalınlığı, retina sinir lifi tabakası kalınlığı

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INTRODUCTION

Peripheral arterial disease (PAD) is a systemic progressive atherosclerotic disease usually manifested by obstruction or occlusion of the lower extremity arteries. Subclinical inflammation, oxidative stress and endothelial dysfunction play a role in the atherosclerotic process. The development of atherosclerosis is a multifactorial and very complex process that affects various genetic and environmental factors.[1] Atherosclerotic PAD, which affects all body arteries can also cause blockages in the retinal arteries and arterioles.

The veins of the retina are the only areas in the body where the circulation can be viewed directly by non-invasive methods. Digital imaging techniques developed in recent years have enabled better visualization of microvascular changes of the retina such as arteriolar narrowing of the retina and venular dilatation. Examination of retinal vessels is a valuable non-invasive option for the investigation of microvascular diseases.[2] The diameter of the retinal vessels is affected by oxygenation of the retina, and it has been suggested that dilatation of retinal venules may indicate retinal hypoxia.[3] It has been reported that arteriole and venule diameters should be evaluated separately since the ratio of arteriole/venule diameter provides limited information.[4]

The optical coherence tomography (OCT) device is commonly used in retinal imaging today. By performing segmentation analysis with different acquisition modes of the OCT device, it is possible to measure the thickness of the retina layers separately, as well as the thickness of the choroidal layer manually.

We think that the choroid, retina and retinal nerve fiber layer (RNFL) are affected in PAD due to the dense vascular and neuronal structure of the eye and its sensitivity to systemic changes. Therefore, in this study, we planned to investigate the effect of PAD on retinal thickness, choroidal thickness, and retinal vessel diameters.

MATERIALS AND METHODS

The present study was carried out in accordance with the principles of the Declaration of Helsinki, after the approval of the Scientific Research Ethics Committee of Bolu Abant İzzet Baysal University (No: 2020/252, Date:27.10.2020). Participants were informed about the study and their written consent was obtained.

The study was carried out prospectively between January 2020 and April 2020 at Bolu Abant İzzet Baysal University Eye Disease Clinic. Patients diagnosed with PAD in the cardiovascular surgery clinic were referred to the ophthalmology clinic. Thirty five patients with PAD (study group) and 32 healthy volunteers without PAD (control group) were included in the study. The ages of the individuals ranged between 42-80 years. Basic clinical and demographic characteristics of all participants were recorded, and afterward, a detailed eye examination was performed, and measurements were taken by OCT. All data obtained were evaluated by comparing between groups.

OCT Measurements

Retinal thickness (RT), choroidal thickness (CT) in enhanced depth imaging (EDI) mode and RNFL thickness were measured with the Spectralis® OCT device (Heidelberg Engineering, Heidelberg, Germany) (**Figure 1**). The OCT device automatically measures RT and RNFL (**Figure 1A**). However, CT measurements were manually measured in EDI mode from the foveal center, 1500 µm temporal, and 1500 µm nasal of the fovea (**Figure 1B**). Retinal artery and vein diameters were manually calculated in RNFL mode from the artery and vein that originated from the optic disc and extended towards the superior temporal, 1800 µm away from the center of the optic disc. In order to make precise measurements, the areas where the vessels do not bifurcate with 2X magnification were selected (**Figure 1C**).

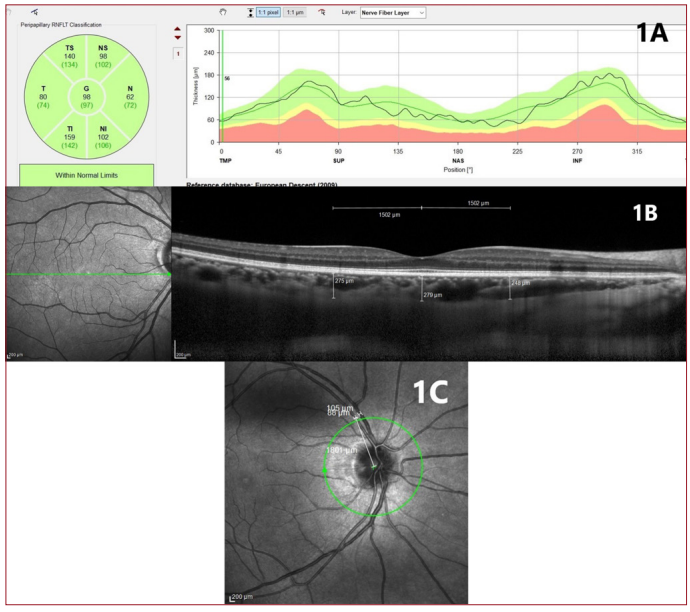

Figure 1. OCT measurements of the cases. **1A:** Printout of RNFL measurements. **1B:** Choroidal measurement in EDI mode. **1C:** Retinal vessel diameter measurement (measured at 2X magnification).

Statistical Analysis

The statistical analysis of the results was made with the "SPSS for Windows 25.0" program. Results were evaluated as mean±standard deviation. If the obtained data met the criteria of normal distribution (by Shapiro-Wilk test) and homogeneity (by KMO and Barlett sphericity test), it was evaluated with an independent sample t-test. P value less than 0.05 was considered statistically significant.

RESULTS

A total of 67 cases were included in the study. The demographic characteristics and ophthalmological measurements of the cases are given in **Table 1**. There was no statistically significant difference in age, gender, spherical equivalent, visual acuity, central corneal thickness (CCT), and intraocular pressure (IOP) between the groups (p value was between 0.08-0.78).

Table 1. Demographic characteristics and ophthalmological measurements of the cases

	PAD group (n=35)	Control group (n=32)	P value*
Gender (Male/Female, n)	30/5	26/6	0.65
Age (years)	59.4±11.9	55.5±5.3	0.08
Smoking rates (%)	26/35 (74%)	9/32 (28%)	<0.01
Visual acuity (decimal)	0.90±0.13	0.94±0.09	0.17
Spherical equivalent (Diopter)	0.24±1.08	0.40±0.99	0.56
IOP (mmHg)	14.97±4.08	14.72±3.01	0.78
CCT (µm)	547.65±31.887	542.71±25.589	0.53
RTc (µm)	221.78±25.284	221.14±16.842	0.90
RTn (µm)	349.72±17.982	352.69±18.013	0.50
RTt (µm)	326.28±17.456	326.29±18.764	1.00
CTs (µm)	274.16±69.189	315.00±80.123	0.03
CTn (µm)	231.00±71.589	248.03±72.210	0.34
CTt (µm)	253.47±68.334	276.26±68.032	0.18
RNFL Global (µm)	99.38±13.495	101.40±7.468	0.47
RNFL Temporal superior (µm)	135.03±21.390	138.37±16.044	0.49
RNFL Temporal (µm)	71.00±10.429	70.00±8.039	0.67
RNFL Temporal inferior (µm)	149.47±21.834	149.53±15.598	0.99
RNFL Nasal superior (µm)	107.91±23.726	108.87±18.131	0.86
RNFL Nasal (µm)	71.56±16.078	79.40±11.846	0.03
RNFL Nasal inferior (µm)	117.28±27.270	117.17±18.596	0.98
Arterial diameter (µm)	88.33±9.215	87.90±11.597	0.88
Vein diameter (µm)	120.00±21.582	117.90±17.685	0.68

* Independent sample t-test.
CCT: Central corneal thickness, CTn: Nasal choroidal thickness, CTs: Subfoveal choroidal thickness, CTt: Temporal choroidal thickness, IOP: Intraocular pressure; PAD: Peripheral artery disease; RNFL: Retinal nerve fiber layer, RTc: Central retinal thickness, RTn: Nasal retinal thickness, RTt: Temporal retinal thickness.

When the RT measured from the central, nasal, and temporal areas and the CT measured from the temporal and nasal areas were compared, no statistically significant difference was found between the groups (p value was between 0.18-1.00). On the contrary, CT measured from the subfoveal was found to be statistically significantly lower in the PAD group (p=0.03). Likewise, RNFL thickness was found to be significantly lower only in the nasal quadrant in the PAD group (p=0.03). Apart from this, no statistically significant difference was found between the groups in arterial and vein diameters (p=0.88, p=0.68, respectively).

DISCUSSION

The most important findings we obtained in our study; subfoveal CT, and RNFL values in the nasal quadrant were found to be significantly lower in patients with PAD compared to the control group. The fact that the thickness of the choroidal layer measured from the subfoveal was significantly lower in the PAD group suggests that choroidal blood supply decreased in this group. However, no significant difference was found between the values of CT measured in the nasal and temporal quadrants. On the other hand, the fact that the RNFL value measured from the nasal quadrant was significantly lower in the PAD group compared to the control group may indicate that optic nerve blood supply was also impaired in these patients and retinal nerve fibers were damaged.

PAD is an important atherosclerotic disease that often involves the lower extremity arteries and is associated with high cardiovascular mortality and morbidity.[5] The prevalence of PAD increases with age and reaches up to 20% in patients older than 70 years.[6] The most important risk factors include smoking, advanced age, hypertension, diabetes mellitus, hyperhomocysteinemia and hyperlipidemia.[7,8] Despite recent advances and new treatment options, PAD still causes limb ischemia, amputation or death.[9] Atherosclerotic risk factors play an important role in the progression and development of PAD. Presence of PAD that seriously affects the retinal arterial bed is a clinical condition that can lead to blindness.

RNFL is formed by astrocytes, retinal vessels, and extensions of Müller cells, with approximately 1-1.2 million axons of retinal ganglion cells. Retinal nerve fiber bundles pass through openings called pores in the scleral canal. This part is the area where the retinal nerve fiber bundle is most susceptible to glaucomatous damage, and in severe damage, these holes appear as slits, causing the optic dimple to appear wide.[10] The early sign of glaucomatous damage on OCT is a decrease in RNFL thickness. It has been suggested that various systemic factors such as advanced age, male gender, dyslipidemia, and hyperglycemia have an effect on RNFL thickness.[11] Higher arterial blood pressure and higher concentration of low-density lipoproteins have been associated with localized RNFL defects.[11] Considering that most patients with PAD have problems such as advanced age, male gender, hypertension and dyslipidemia, low RNFL thickness may be associated with this. In our study, the low RNFL thickness in the nasal segment that we observed in patients with PAD may be significant in more segments when adapted to large patient groups.

In addition to ocular problems, it is known that RNFL thickness may decrease due to many non-ocular reasons. When we look at studies examining RNFL thickness changes in some systemic diseases, it has been shown that RNFL thickness is lower in iron deficiency anemia, migraine without aura, obstructive sleep apnea syndrome and Alzheimer's disease.[12,13]

The choroid is a thin dense network of vessels that supply nutrients and oxygen to the outer retina, foveal avascular region, retinal pigment epithelium, and optic nerve between the retina and sclera. CT does not only change with pathological and pharmacological factors, age, the axial length of the eye, refractive changes, diurnal rhythm and perfusion pressure also affect CT changes. The root cause of these changes is still unknown. In a study by Ulaş et al.[14], it was reported that there was a significant increase in choroidal thickness 5 minutes after smoking in adolescents and returning to the basal level at 60 minutes. There are also studies showing that CT is significantly lower in patients between the ages of 60 and 80 who smoke chronically compared to non-smokers.[15-17] It is hypothesized

that chronic smoking causes chronic vasoconstriction and direct oxidative damage to the endothelium, resulting in vascular thinning in some individuals and a thinner choroid as a result. There are many studies in which subfoveal CT is lower in patients with heart-related perfusion impairment, such as chronic heart failure and carotid artery disease.[17-20] Choroidal hypoperfusion, choroidal ischemia and infarction may lead to multiple occlusions, leading to a reduction in CT, since chronic smoking and cardiac diseases are often seen together in patients with PAD.

It is known that some ocular and systemic diseases, drugs used, and genetic factors cause changes in retinal arteriole and venule diameters.[21-23] It has been found that the response of retinal venules to hemodynamic changes is reduced, vascular functions are impaired in smokers, and it has been suggested that the negative effects of smoking may occur without changes in the vessel diameter.[24] Ulaş et al.[25] also reported that there was no significant difference in retinal arteriole and venule diameters between smoking and non-smoking groups. Similarly, in our study, no significant difference was found in the arteriole and venule diameters in the PAD group compared to the control group.

The main limitations of our study are the relatively small number of patients and the fact that other systemic characteristics of the patients were not recorded and could not be associated with OCT results. In addition, the inability to include different ages and groups reduces the impact of the study. However, the positive findings obtained despite all limitations increase the importance of the study.

CONCLUSION

As a result, in our study, RNFL and thinning of the choroidal layer thickness were detected in PAD patients. Additional studies examining more parameters in larger populations are needed to better understand the mechanism and clinical significance of this thinning.

ETHICAL DECLARATIONS

Ethics Commite Approval: The study has ethical approval from Bolu Abant İzzet Baysal University Ethics Committee(No: 2020/252, Date:27.10.2020).

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

Referee Evaluation Process: Externally peer-reviewed.

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

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

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Orjinal Araştırma / Original Article

Stroke Awareness of Physicians Working in a Tertiary Healthcare Institution

Üçüncü Basamak Bir Sağlık Kuruluşunda Çalışan Hekimlerde İnme Farkındalığı

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Abstract

Aim: To investigate the knowledge and awareness of physicians working in tertiary healthcare institutions concerning stroke and treatment approaches for ischemic stroke.

Material and Method: Fifty-nine physicians with a mean age of 35.4 years were included in the study. A survey consisting of 12 questions taking less than 5 minutes to complete was delivered to the specialist and research assistant physicians who were actively employed in Adıyaman University Faculty of Medicine Training and Research Hospital and signed the voluntary informed consent form.

Results: Of the physicians participating in the study, 66.1% (n=39) were working as specialists and 33.9% (n=20) as research assistant physicians. More than half the physicians (57.6%, n=34) had not previously attended an informative meeting on stroke. The average rate of correct answers given to all survey questions was 37.8%. The research assistant physicians correctly answered the questions concerning the first intervention in a stroke patient, prevalence of stroke, and thrombolytic treatment agent at a higher rate than the specialist physicians. The physicians who had previously attended an informative meeting on stroke provided more correct answers to the questions on stroke preventability and thrombolytic treatment agent.

Conclusion: Undoubtedly, since time is one of the most important factors affecting mortality and morbidity in case of an ischemic stroke, it is vital that both society and healthcare professionals become aware of this health condition. We believe that the awareness of all physicians concerning stroke and its treatment should be increased through effective training and informative meetings.

Keywords: Ischemic stroke, thrombolytics, awareness, thrombectomy, physician

Öz

Amaç: Çalışmamızın amacı 3. basamak sağlık kuruluşunda çalışan hekimlerin inme farkındalığı ve iskemik inme tedavi yaklaşımları hakkındaki bilgi birikimlerinin araştırılmasıdır.

Gereç ve Yöntem: Çalışmaya yaş ortalaması 35,4 olan 59 hekim dahil edilmiştir. Çalışmada Adıyaman Üniversitesi Tıp Fakültesi eğitim araştırma hastanesinde aktif olarak görev yapan, bigilendirilmiş gönüllü onam formunu imzalayan uzman ve araştırma görevlisi hekimlere toplam 12 sorudan oluşan ve cevaplanması 5 dakikadan daha kısa süren anket formu ulaştırılmıştır.

Bulgular: Çalışmaya katılan hekimlerin %66,1'i (n=39) uzman hekim, %33,9'u (n=20) araştırma görevlisi olarak görev yapmaktaydı. Katılımcıların %57,6'sı (n=34) daha önce inme ile alakalı bir bilgilendirme toplantısına katılmamıştı. Tüm sorulara verilen ortalama doğru cevap oranı %37,8 olarak ölçüldü. İnmeli hastanın ilk müdahalesi, inme prevalansı ve trombolitik tedavi ajanı ile ilgili sorulara, araştırma görevlisi hekimlerin uzman hekimlere oranla daha yüksek oranda doğru cevap verdiği gözlenmiştir. İnme ile ilgili bilgilendirme toplantısına katılan hekimlerin, inmenin önlenebilirliği ve trombolitik tedavi ajanı ile ilişkili sorulara, daha yüksek oranda doğru cevap verdiği gözlenmiştir.

Sonuç: İskemik inmede hastaların mortalite ve morbiditesini etkileyen en önemli faktörlerden biri kuşkusuz ki zamandır. Gerek toplumun gerekse sağlık çalışanlarının bu konuda bilinçlenmesi hayati öneme sahiptir. Tüm hekimlerin etkin eğitimler ve bilgilendirme toplantılarıyla inme ve inme tedavisi konusunda farkındalıklarının arttırılmasına ihtiyaç olduğu kanaatindeyiz.

Anahtar Kelimeler: İskemik inme, trombolitik, farkındalık, trombektomi, hekim.

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INTRODUCTION

Stroke refers to a sudden-onset, focal neurological condition that develops due to cerebrovascular disease. Of all stroke cases, 80-85% are ischemic and 15-20% are hemorrhagic. Stroke constitutes a major economic, medical and social problem that causes severe disability and ranks third among the global causes of death following cancer and cardiac diseases.[1,2] The incidence of stroke can also vary between countries and even between people living in the same country, depending on race and geographical area. Studies have reported that the incidence of stroke is 1-3/1,000, and its prevalence is 6/1,000.[3]

Effective treatment of stroke cases can be undertaken with the administration of an intravenous thrombolytic agent and endovascular mechanical thrombectomy treatment. According to the acute ischemic stroke guidelines of the American Stroke Association, in order to apply intravenous thrombolytics for the treatment of stroke, the time from the onset of the patient's symptoms to admission to a healthcare institution should be less than 4.5 hours. This time has been determined as 6 hours for endovascular mechanical thrombectomy treatment, but it has been reported that this treatment can be applied to selected patients within a period of 24 hours from the onset of symptoms.[4]

All healthcare professionals should know the symptomatology of a stroke patient. For this reason, the FAST (Face, Arm, Speech, Time) test has been developed to quickly screen the symptoms of stroke. This test includes variables such as facial asymmetry, unilateral loss of strength in the arm, impaired speech and pronunciation, and rapid transfer of the patient to a healthcare facility.[5] Stroke diagnosis and treatment is fixed in a narrow time frame that can be measured in hours. The slightest disruption in diagnosis and treatment can lead to very unfavorable consequences, considering that an average of 1.9 million neuronal cells dies per minute in an ischemic brain.[6] The most decisive way to decrease morbidity and mortality rates in stroke patients is to use this limited time effectively as much as possible. The current study aimed to investigate the knowledge and awareness of physicians working in tertiary healthcare institutions concerning stroke and treatment approaches for ischemic stroke.

MATERIAL AND METHOD

In this study, a survey consisting of 12 questions that took less than 5 minutes to complete was delivered to the specialist and research assistant physicians who were actively working at Adıyaman University Faculty of Medicine Training and Research Hospital and signed the informed consent form. The questions in the survey were prepared in a multiple choice format and related to the subjects of stroke symptomatology, first intervention in stroke patients, and stroke treatment. Physicians working in neurology clinics, emergency medicine clinics and intensive care units where stroke patients are followed up were not included in the study. It was also recorded whether the participants had previously attended an informative meeting on acute ischemic stroke and its treatment and whether they had previously intervened in a case with a stroke.

The survey comprised the following questions:

Is stroke a preventable disease?

Yes No

Is stroke a treatable disease?

Yes No

What is the unexpected clinical or examination finding in a patient diagnosed with a stroke?

A) Speech disorder

B) Imbalance in walking

C) Visual impairment

D) Chest pain

4. Which of the following should not be undertaken in the first intervention of a patient with a stroke?

A) Blood glucose measurement

B) Insertion of a urinary catheter

C) Lowering blood pressure if it is high

D) Insertion of a vascular catheter

5. Globally, what is the approximate percentage of hemorrhagic stroke among all stroke cases?

A)15 B) 30 C) 45 D) 50 E) 60

6. Which intravenous thrombolytic treatment agent is widely used in the treatment of acute ischemic stroke in the world and in Turkey?

A) Tenecteplase

B) Urokinase

C) Streptokinase

D) Alteplase

7. Up to how many hours after the onset of stroke symptoms can thrombolytic therapy be administered?

A) 3 B) 4.5 C) 6 D) 8 E)12

8. Up to how many hours after the onset of stroke symptoms can mechanical thrombectomy treatment be administered?

A) 3 B) 4.5 C) 6 D) 8 E) 12

9. What is the absolute must-have imaging method that should be performed in a patient with a stroke before intravenous thrombolytic therapy?

A) Brain magnetic resonance imaging

B) Brain computed tomography

C) Carotid doopler ultrasonography

D) Brain magnetic resonance angiography

E) Brain magnetic resonance venography

10. What is the approximate risk of developing symptomatic intracranial hemorrhage after intravenous thrombolytic therapy?

A) 1 B) 5 C) 10 D) 15 E) 20

11. Which of the following is not one of the modifiable risk factors for stroke?

A) Hypertension
B) Diabetes
C) History of previous stroke and transient ischemic attack
D) Atrial fibrillation
E) Obesity

12. Which of the following agents has no place in the secondary prevention of stroke patients?

A) Warfarin
B) Piracetam
C) Clopidogrel
D) Statin
E) Rivoraxaban

Approval for the study was obtained from the Non-Interventional Clinical Research Ethics Committee of Adıyaman University (date: 16/03/2021, protocol number: 2021/3-29).

Statistical Analysis

Statistical analyses were carried out using SPSS version 22.0. The compliance of the variables to normal distribution was examined using histogram graphics and the Kolmogorov-Smirnov test. Categorical variables were compared using the Pearson's chi-square test. The Mann-Whitney U test was used when comparing non-parametric variables between the two groups. Results with a p value of less than 0.05 were evaluated as statistically significant.

RESULTS

With the survey, a total of 82 physicians were reached. After excluding 15 physicians who did not want to participate in the study and eight physicians who did not answer all the questions in the survey, the remaining 59 physicians were included in the study. Of the participants, 43 were male and 16 were female, with 66.1% (n=39) being specialists and 33.9% (n=20 research assistant physicians. The mean age of the participants was 35.4 years, and the mean professional experience was 10.4 years. Of the participants, 57.6% (n=34) had not previously attended an informative meeting on stroke. The rate of the participants who had previously intervened in a stroke case was 64.4% (n=38). The average rate of correct answers given to all questions was 37.8%. The rates of those who provided correct answers to the questions related to the treatability and preventability of stroke were 96.9% and 89.7%, respectively. The rates of those who gave correct answers to the questions on stroke symptoms and the first intervention in a stroke patient were 84.5% and 63.7%, respectively. The questions concerning the latest times to apply thrombolytic and endovascular mechanical thrombectomy treatments from the onset of symptoms were correctly answered by 29.3% and 51.7% of the participants, respectively, and the rate of those answering both questions correctly was 18.6%. While the question on which intravenous thrombolytic treatment agent is commonly used in the treatment of acute ischemic stroke was answered correctly by 37.9% of the participants, the rate of those that were aware of the risk of symptomatic intracranial hemorrhage development after thrombolytic therapy was 20.7%. Of the participants, 31% correctly selected the imaging method that should be performed before thrombolytic therapy. The distribution of correct answers given to all questions is summarized in **Figure 1.** The rates of correct answers in the survey were compared between the specialist and research assistant physicians. According to the results, the rate of correct answers to the fourth, fifth and sixth questions was higher among the research assistant physicians (p=0.049, 0.035, and 0.044, respectively). Fifty-five percent of the research assistant physicians and 35.6% of the specialist physicians had previously attended an informative meeting on stroke, but the difference between the two groups was not statistically significant (p=0.160). However, it was observed that the research assistant physicians had intervened in a stroke case at a higher rate compared to the specialist physicians (p<0.001). The rates of correct answers given to the survey questions were also compared between the physicians who had previously attended an informative meeting on stroke and those who had not. Accordingly, the rate of correct answers to the first and fifth questions was higher among the physicians who had attended such a meeting (p=0.030 and 0.033, respectively). When the rates of correct answers to the survey questions were compared between the physicians who had previously treated a patient with a stroke and those who had not, the former was found to have a higher rate of correct answers for the fifth and 10th questions (p=0.009 and 0.025, respectively). Concerning the relationship between professional experience and the rate of correct answers, the mean time in the profession was significantly lower for those that correctly answered the fourth question compared to those that provided an incorrect answer for the same question (p=0.018). Examining the relationship between the age of the physicians and the rate of correct answers to the survey questions, it was determined that the mean age of those that gave correct answers to the sixth question was significantly lower than those that answered it incorrectly (p=0.025).

Table 1. Comparison of the correct answers given by the specialist and research assistant physicians

	Specialist physician (%)	Research assistant physician (%)	p
Question 1	92.3	85	0.325
Question 2	97.4	95	0.567
Question 3	87.2	80	0.357
Question 4	53.8	80	0.049
Question 5	46.2	75	0.035
Question 6	28.2	55	0.044
Question 7	28.2	30	0.885
Question 8	56.4	40	0.233
Question 9	25.6	40	0.257
Question 10	20.5	20	0.623
Question 11	79.6	80	0.623
Question 12	89.7	85	0.446
Previous attendance in informative meetings on stroke	35.9	55	0.160
Previous intervention in a stroke case	48.7	95	<0.001

Pearson's chi-square test

Table 2. Comparison of the correct answer rates according to previous attendance ininformative meetings on stroke, previous intervention in a stroke case, age, and professional experience

	Previous attendance in informative meetings on stroke p	Previous intervention in a stroke case p	Age p	Professional experience p
Question 1	0.0301	0.295	0.706	0.633
Question 2	0.328	0.411	0.753	0.900
Question 3	0.415	0.163	0.688	0.783
Question 4	0.471	0.511	0.061	0.0182
Question 5	0.0331	0.0091	0.444	0.366
Question 6	0.361	0.303	0.0252	0.064
Question 7	0.906	0.218	0.893	0.644
Question 8	0.708	0.472	0.438	0.976
Question 9	0.432	0.155	0.178	0.306
Question 10	0.056	0.0251	0.473	0.940
Question 11	0.549	0.431	0.439	0.515
Question 12	0.328	0.196	0.906	0.787

[1] Pearson's chi-square test, 2Mann-Whitney U test

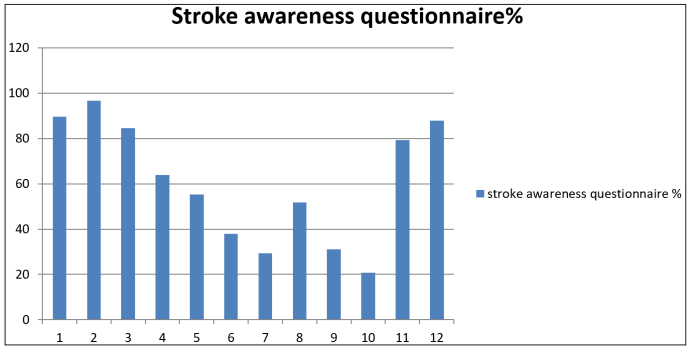

Figure 1. Distribution of correct answers to survey questions

DISCUSSION

Ischemic stroke is an emergency situation in which there is a race against time for the correct diagnosis, treatment and intervention. It is vital for physicians, who first come into contact with the patient and perform neurological and clinical evaluations, to know the symptoms, diagnosis and treatment algorithms to minimize mortality and morbidity. Our study showed that the physicians working in a tertiary healthcare facility did not have sufficient awareness of stroke and its treatment.

When a patient with stroke symptoms is encountered, the standard approach is to promptly perform clinical and neurological evaluations and transfer the patient to the nearest healthcare institution. The same sensitivity should be adopted in the approach to patients hospitalized for a different reason. For example, patients hospitalized for a non-neurological reason (diabetes, acute coronary syndrome, hypertension, surgery indication, etc.) are potential candidates for developing a stroke. It is very important that relevant relevant department physicians that follow up these patients and will make the first evaluation when an unexpected clinical finding occurs have sufficient awareness of stroke and its treatment. In these hospitalized patients, diagnosing stroke through a rapid evaluation will eliminate the time spent outside the hospital and shorten the time to reach treatment. Considering the high efficacy and low complication rate of early stroke treatment, the sensitivity of physicians who first evaluate these patients can significantly reduce the mortality and morbidity rates.

In the literature, there are population-based studies investigating stroke awareness.[7-9] However, research measuring the stroke awareness of healthcare workers, especially physicians, remains limited. In a study conducted in the USA on nursing staff, it was observed that 85% of the participants had sufficient knowledge of the signs and symptoms of stroke.[10] In a study conducted in Turkey in which family physicians' awareness of ischemic stroke was investigated, and it was found that the rate of correct answers to survey questions ranged between 20 and 30%.[11] This is in agreement with the results obtained from the current study revealing that the rate of correct answers to all questions was 37.8%.

Multinational studies with a large number of patients have shown the functional positive effect of thrombolytic therapy and mechanical thrombectomy applied early in patients presenting with an ischemic stroke.[12,13] Alteplase, an intravenous tissue plasminogen activator (iv-tPA) with thrombolytic function in ischemic stroke, is the only medical agent that offers disability-free survival and positively affects the prognosis when applied at an appropriate time.[14] Today, the most important parameter that will positively affect the success of iv-tPA and the prognosis of ischemic stroke is the application time of thrombolytic therapy. Following the onset of stroke symptoms, the early administration of iv-tPA

increases efficacy and reduces the risk of complications.[15] In our study, it was observed that the rate of correct answers to the questions related to the timing of both iv-tPA and mechanical thrombectomy was extremely low. More than 80% of the participants were not able to correctly answer both questions at the same time. The potential side effect of iv-tPA is undoubtedly a bleeding complication. Intracerebral bleeding and related clinical deterioration are rare but they are the most critical and feared side effects of iv-tPA.[16] In the early period following the use of iv-tPA, the rate of intracranial bleeding has been reported as 6%.[17] Similar to the treatment question, approximately 80% of the physicians participating in our study did not give a correct answer to the question related to the bleeding complication of iv-tPA. It is a cause for concern that ischemic stroke treatment, which has been widely used in Turkey for a decade, as well as its major complications are so under-recognized among physicians. Increasing the knowledge of physicians on this subject must be a primary goal.

In this study, we observed that the research assistant physicians correctly responded to the questions about the first intervention in a stroke patient, prevalence of stroke, and thrombolytic treatment agent at a higher rate than the specialist physicians. Similarly, we determined that the physicians with less professional experience correctly answered the question concerning the first intervention in a stroke patient at a higher rate, and those with a lower mean age correctly answered the question about the thrombolytic treatment agent at a higher rate. In addition, a higher rate of research assistant physicians were found to have previously intervened in a patient with a stroke. The physicians who had previously intervened in a stroke case also accurately responded to the questions related to the thrombolytic treatment agent and its complications at a higher rate. These results may be related to the young research assistant physicians spending more time in hospital and working more frequent shifts, which increases their possibility to encounter patients with a stroke. In addition, the physicians with a higher mean age that have specialized in their departments over many years may be providing outpatient services more frequently and they may have certain deficiencies in following the current advances in the field and fail to meet the requirements of dynamic medicine, which may have also contributed to our results. Our data revealed that the physicians who had previously attended an informative meeting on stroke gave more correct answers to the questions on the preventability of stroke and the thrombolytic treatment agent to be used. Although there was no significant difference in the rate of correct answers given to the remaining survey questions, the results generally indicated the necessity of organizing informative meetings on stroke for physicians.

This study has some limitations. First of all, the study population consists of a small group. In addition, since the study was conducted in a single center, the results may not reflect the generality.

CONCLUSION

Undoubtedly, since time is one of the most important factors affecting mortality and morbidity in patients with an ischemic stroke, it is vital that both society and healthcare professionals become aware of this health problem. We believe that the awareness of all physicians about stroke and its treatment should be increased through effective training and informative meetings.

ETHICAL DECLARATIONS

Ethics Committee Approval: Approval for the study was obtained from the Non-Interventional Clinical Research Ethics Committee of Adiyaman University (date: 16/03/2021, protocol number: 2021/3-29).

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

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Letter to the editor/ Editöre Mektup

Autism Spectrum Disorder with the Perspective of Etio-Pathogenesis; Enviremantal, Genetic, and Epigenetic Factors

Etiyo-Patogenez Perspektifi ile Otizm Spektrum Bozukluğu; Çevresel, Genetik ve Epigenetik Faktörler

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Dear Editor,

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder that is charecterized with deficits in social skills (communication and interaction), language skills and presence of steriotypical repetetive behaviours, and interests or activities that can persist throughout life.[1] ASD prevalance was recently reported with an increase at 1 in 59 children by Center for Disease Control and Prevention (CDC) USA.[2]

Although definite etiology of the ASD is still unclear; different evidences were determined from many conclusions of the studies suggesting and supporting etiologic and causative associaton of three factors (enviremental, genetic and epigenetic factors) with ASD. Each factor has two or three sided interaction with each other. Intestinal microbiota homeostasis is one of the most important element of environmental factors.[3,4]

Human gut microbiota consisting of more than three thousand of different bacterial species belonging to six different phyla and ten fold higher than cell numbers of human body. Human gut microbiota has bidirectional commnuciation (cross-talk) with the human brain called as microbiota gut brain axis (MGBA) via determined four different pathways; 1. Metabolic pathway 2. Neural (neuronal) pathway 3. Neuro-endocrin pathway 4. Immunologic pathway.[4] Perinatal maternal microbiota composition changes (density and diversity) resulting with maternal dysbiosis altering expression of the genes related with autism etiology (*CC2D1A, SHANK1-3, CASPR2, CNTNAP2, BRSK2*) and also epigenetic mechanisms. Maternal dysbiosis also results in regression of fetal neuerodevelopment and maturation of neuronal and brain cell of the fetus at intrauterin period. Maternal dysbiosis at perinatal period may also triggers maternal immun activation that may also have a negative affect on fetal neural development. Neuronal connectivity and signal transmisison impaired as a result of the explained neuro-immuno pathologies triggered with perinatal maternal dysbiosis. Accession of toxic and harmful molecules to brain is blocked by two major barriers: Bowel Brain Barrier (BBB) and Blood Brain Barrier (BBB).[5] Integrity of the two barriers are maintained by functions of tight junction proteins. Barrier functions are obtained and protected by eubiosis of intestinal microbiota. Dysbiosis leads to impairment of barrier functions and results in increased intestinal permability. Short chain fatty acids (propionate, acetate, butyrate) are components of the cellular membrane of especially two anaerobic species (*Bacteroides spp.*, and *Clostridium spp.*) and they can also be derived from fermentation of complex carbohydtrate molecules such as inulin in the intestine. Propionic acid (PPA) is a potent activator of pro enflammatory cytokines (IL1β, TNFα, IL6) synthesis, and can reach to the brain and initiates neuroenflammation. Overgrowth of Bacterodies

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and Clostiridum strains in the intestinal microbiota results in excessive production of PPA and initiates the neuroimmunopathologic changes that is one of the known mechanisms of autistic brain.[4,5]

Etio-pathogenesis of the neuro-immunopathologic changes in the autistic fetal brain can be explained with perinatal maternal dysbiosis, which causes alterations in maternal and fetal gen expressions, epigenetic mechanisms, maturation of neuronal cells and fetal neurodevelopment, concluding with abnormal neural signal transmisison, and maternal immune activation.

ETHICAL DECLARATIONS

Referee Evaluation Process: Externally peer-reviewed.

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Letter to the editor/ Editöre Mektup

Compound Heterozygous Niemann-Pick Type C Disease in The Neonatal Period

Yenidoğan Döneminde Birleşik Heterozigot Niemann-Pick Tip C Hastalığı

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Dear Editor,

Niemann-Pick C Disease (NPC; OMIM #257220 and OMIM #607625) is a rare lysosomal lipid storage disorder. NPC is characterized by accumulation of unesterified cholesterol and glycosphingolipids in the lysosome and endosome. Disease is inherited in an autosomal recessive and caused by NPC1 or NPC2 genes.[1] The wide clinical spectrum range from newborn to adulthood periods posses special problems for diagnosis Herein, we report a compound heterozygous NPC disease in the neonatal period.

A 34-year-old, gravida 3 mother delivered a male baby at 30 4/7 of weeks gestation by cesarean section, with a birth weight of 2100 g (>90 percentile) and an Apgar score of 7/9 in the 1st and 5th minute, respectively. Parents were not consanguineous. A detailed prenatal ultrasonography showed hyperechogenic fetal bowel. Although first trimester combined screening test was high, parents did not accept amniocentesis.

His brother was born 34 2/7 weeks gestation and birth weight was 3070 g.[2] He had nonimmunhydrops fetalis and diagnosed NPC. He died on postnatal 52nd day because of respiratory distress and progressive liver failure. The patient was born and followed up outside of our center.

He developed respiratory distress in the delivery room and was admitted to the neonatal intensive care unıt. On admission, he had tachypnea, skin edema, hepatosplenomegaly, hypotonic and weak neonatal reflexes. At 1 hour of life he was intubated and mechanically ventilated due to respiratory failure. The patient's respiratory problems were due to prematurity. Initial laboratory findings were as follows: complete blood count, coagulation parameters and TORCH screen were normal. The blood and urinary levels of amino acids, organic acids and serum chitotriosidase activity were normal. The measurement of lysosomal sphingomyelinase activity was below in our case which was 4.06 nmol/17h/mg protein (Normal: mean±SD: 7.73±3.08). Echocardiography showed a only patent foramen ovale. Results of abdominal ultrasonography showed hepatosplenomegaly and increased echogenicity. Thrombocytopenia (platelet count: 66×10^9/L) and direct hyperbilirubinemia (total/direct bilirubin: 15.8/3.1 mg/dL) appeared on the 5th day of life. Placentomegaly (weight: 672 g) and vacuolized cells (foamy macrophages in the stroma of terminal villi) were detected in the pathological examination of the placenta. The patient was discharged 40 days after the admission. We learned that the patient died at the age of 5 months due to sepsis.

The infant and our patient molecular genetic analysis were same: compound heterozygous for the deletion of c.1831_1836delGATGAA in exon 12 and c.3734_3735delCT in exon 24 of the NPC1 gene. The mother and father genetic analysis were respectively heterozygous for the deletion of c.1831_1836delGATGAA in exon 12 and c.3734_3735delCT in exon 24 of the NPC1 gene. Written informed consent was obtained from parents.

Presentation of NPC disease in the perinatal period is considerably limited. The prenatal clinical findings of NPC consisted of in utero hepatosplenomegaly, ascites,

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oligohydramnios and intrauterine growth restriction.[3] Our patient was born with hepatosplenomegaly and preterm delivery. The most important factors in neonatal mortality are respiratory failure and progressive liver disease.

The pathologic examination of the placenta may be a key to the diagnosis. The presence of abnormal vacuolized cells in the placenta is highly suspicious for GM1 gangliosidosis or lysosomal storage disorder.

Knowing the genetic abnormality of the index case is important for the chance of prenatal genetic diagnosis and to have a healthy baby.

Keywords: Niemann-Pick Type C, NPC1, newborn

ETHICAL DECLARATIONS

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