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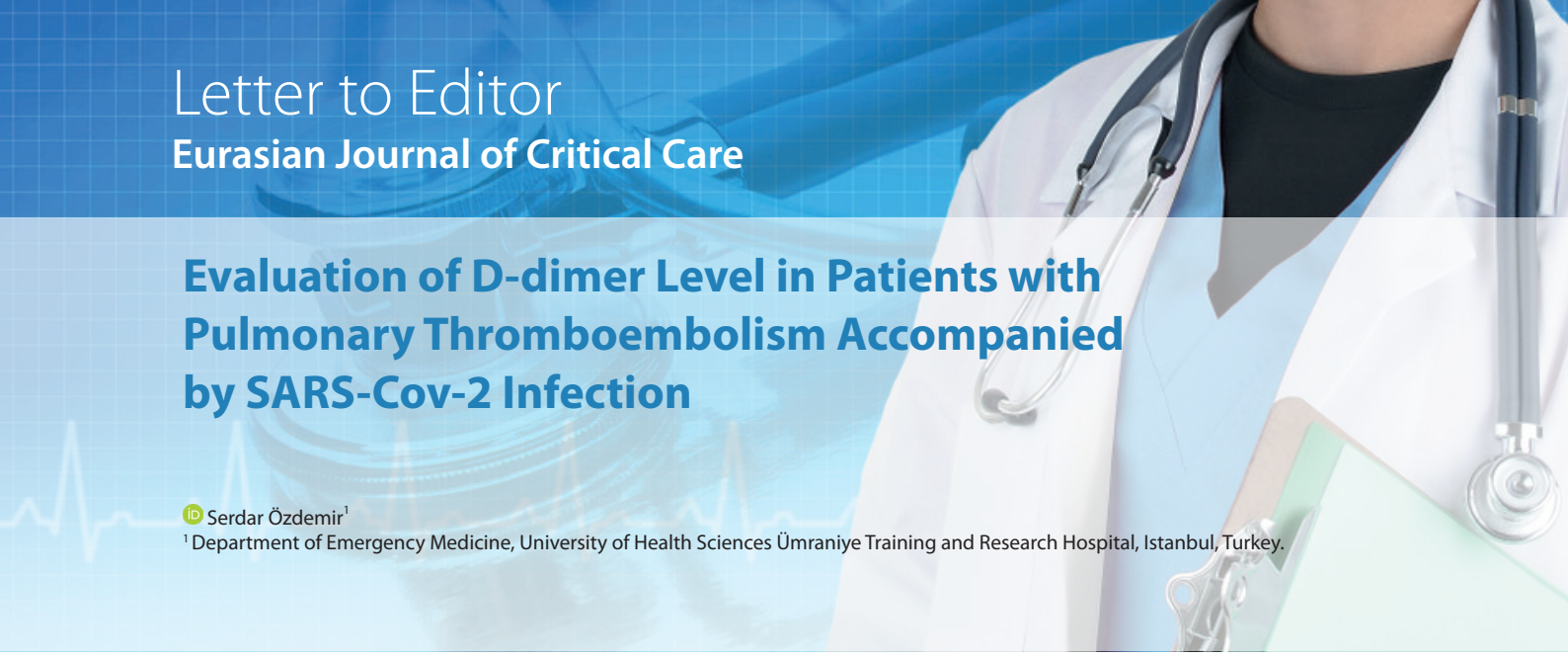

Evaluation of D-dimer Level in Patients with Pulmonary Thromboembolism Accompanied by SARS-Cov-2 Infection

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Dear Editor;

We read with interest your articles in the first issue of 2022 of the dear editor's journal, in which the experiences of patients with pulmonary embolism in the emergency department were shared. We would like to thank Bilir et al. and Örün et al. for these interesting articles (1,2). On the other hand, we would like to point out a few points about the evaluation of D-dimer level in patients with pulmonary thromboembolism accompanied by SARS-CoV-2 infection, which may be useful in the post-pandemic period.

In cases of pulmonary thromboembolism, leukocytosis, increase in serum lactate dehydrogenase and aspartate transaminase levels, increase in C-reactive protein and sedimentation rate can be detected. However, these findings are not specific for pulmonary thromboembolism. D-Dimer level can increase up to 8 times in pulmonary thromboembolism cases. The sensitivity of D-Dimer level in detecting pulmonary thromboembolism is reported to be 97-100% above 500 ng/ml. D-Dimer tests have a low sensitivity rate of 35-45% (3). Surgical intervention, trauma, kidney diseases, malignancies, severe infections, systemic lupus erythematosus, pregnancy, etc. In some cases, the test may be positive. D-dimer negativity is used to exclude pulmonary thromboembolism, especially in outpatients with low and moderate clinical probability without comorbidities (4).

Patients with SARS-CoV-2 infection have increased inflammatory markers such as lymphopenia, elevated lactate dehydrogenase, elevated C-reactive protein, D-dimer, ferritin, and interleukin-6 (IL-6). It has been stated that high IL-6 level is significant in terms of disease severity and procoagulation (5). Thrombocytopenia and D-dimer elevation were found to be significant in terms of intensive care admission, mechanical ventilator requirement and mortality (6). Elderly patients with comorbidities were associated with higher D-dimer values and severe SARS-CoV-2 infection(5). In a retrospective study, Okşaşoğlu grouped the sample of hospitalized patients with SARs-CoV-2 infection into groups with and without pulmonary thromboembolism. The mean D-Dimer level was 530±46 mcg/L in the patients with SARs-CoV-2 infection without pulmonary thromboembolism and 2880±2710 mcg/L in the patients with SARs-CoV-2 infection with pulmonary thromboembolism (7). In a cohort study of 974 patients by Ooi et al., a D-dimer value of 2247 mcg/L was found to provide a sensitivity and specificity of 72% and 74%, respectively, for the development of pulmonary thromboembolism in SARS-CoV-2 infected patients (8). Leonard-Lorant et al. showed the cut-off value of D-dimer levels to be 2660 mcg/L to predict pulmonary thromboembolism in SARS-CoV-2 infected patients (9).

As a conclusion, D-dimer values above 500 mcg/L are used by many clinics in patients with suspected pulmonary thromboembolism at moderate risk of management. In the management of SARS-CoV-2 infected patients, higher cut-off values for D-dimer should be used in the presence of clinical suspicion of pulmonary thromboembolism.

References

1. Bilir Ö, Ünlü A, Taşçı F, Ersunan G, Ataş İ. Evaluation of Systemic Thrombolytic Treatment in the Emergency Service in Unstable and Resuscitated Patients Due to Massive Pulmonary Embolism. Eurasian Journal of Critical Care. 2022; 4(1): 3-7.
2. Örün S, Bol O, Aköz A. Determination of Demographic Changes of Acute Pulmonary Embolism Patients Applied to Emergency Service: Retrospective Analysis of 60 Cases. Eurasian Journal of Critical Care. 2022; 4(1): 8-11.
3. Akça HŞ, Koylu R, Akıllı NB. Effect of Ionized Calcium Level on the Prognosis and Mortality of Patients with Pulmonary Embolism. American Journal of Internal Medicine. 2018;1:20-24.

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4. Akça HŞ, Özdemir S, Algın A, Altunok İ. Comparison of geriatric pulmonary embolism severity index (G-PESI) with PESI and s-PESI in predicting prognosis and mortality. J Health Sci Med / JHSM. 2022; 5(2): 676-681.

5. Özdemir S, Eroğlu SE, Algın A, Akca HS, Ozkan A, Pala E, et al. Analysis of laboratory parameters in patients with COVID-19: Experiences from a pandemic hospital. Ann Clin Anal Med. 2021;12 (Supp 4):518-23.

6. Algın A, Özdemir S. Evaluation of The Predictability of Platelet Mass Index for Short-Term Mortality in Patients with COVID 19: A Retrospective Cohort Study. J Contemp Med. 2021; 11(5): 728-733.

7. Okşaşoğlu M. COVID-19 Enfeksiyonu Sonrasi Pulmoner Emboli Gelişen Hastalarda C-Reaktif Protein ve D-dimer Yüksekliğinin Pulmoner Emboli Tanısına Katkısı. (Tez). İstanbul:Sağlık Bilimleri Üniversitesi. 2022.

8. Ooi MWX, Rajai A, Patel R, Gerova N, Godhamgaonkar V, Liong SY. Pulmonary thromboembolic disease in COVID-19 patients on CT pulmonary angiography - Prevalence, pattern of disease and relationship to D-dimer. Eur J Radiol. 2020 Nov;132:109336.

9. Léonard-Lorant I, Delabranche X, Séverac F, Helms J, Pauzet C, Collange O, et al. Acute Pulmonary Embolism in Patients with COVID-19 at CT Angiography and Relationship to d-Dimer Levels. Radiology. 2020 Sep;296(3):E189-E191.

Original Article
Eurasian Journal of Critical Care

Causes and Outcomes of Childhood Trauma with GCS Below 9

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Abstract

Background: Trauma, as one of the major public health challenges, was the leading cause of death and disability in most countries. Trauma was considered as the most common reason for emergency department admission. Children are the most susceptible group of society to trauma, so we designed a study to investigate the epidemiologic feature and outcomes of trauma in children under 18 years old. In light of these findings, we might be able to prevent trauma in children.

Materials and methods: We conducted a retrospective cross-sectional study during the spring season of 2019 (for 3 months). The study population was all children under eighteen years old with GCS below 9 (1814cases), referring to the emergency department of Tabriz Emam-Reza Hospital. Among 1814 patients, 1786 patients were included. For each included patient, the outcomes of the 24-hour follow-up have been recorded.

Result: In this study, 62.1% percent (n=1109) were males. The mean age of patients was 5.47 ± 3.1. There were 1271 (71.1%) head and neck trauma, 276 (15.5%) extremities trauma. Abdominal trauma (n=66, 3.7%) and spinal trauma (n=57, 3.2%) were the rarest types of mechanism. It was revealed that falling had the most incidence frequency (40.4%). Eventually, out of the entire study population, 1361 patients were discharged from the emergency department (75%), 5 patients transferred to the trauma ward (0.2%), 1 patient hospitalized in the intensive care unit (0.05%), 250 patients left the hospital against physician permission (14%), 110 patients referred to another center (6%), 59 patients escaped from the hospital (3%) and zero deaths.

Conclusion: Our study suggests that the head and neck were the most injured anatomic locations in children. Males were more susceptible to being exposed to trauma. Falling and traffic accidents were the most frequent mechanism of trauma that occurred in under eighteen-year-old children. Awareness of patterns of pediatric trauma may help the adoption of safety policies and develop prevention strategies. In this regard, training prevention strategies for parents and improving playground safety will be effective.

Keywords: Trauma, pediatric, children, injury, accident, epidemiology

Introduction

Trauma, as one of the major public health challenges, was the leading cause of death and disability in most countries(1). Trauma was considered as the most common reason for emergency department admission (2, 3). Children are the most susceptible group of society to trauma. Moreover, trauma is among the most common cause of their referral to the emergency department and the most common cause of child morbidity and mortality (4). It is estimated that trauma causes more than half of all child deaths in developed countries, which can have a profound socioeconomic burden on individuals, families, and societies (5, 6).

The literature revealed that one of every four children will sustain an unintentional trauma that warrants medical care each year (7). Iran Forensics Medicine Organization reported that trauma is recognized as the second leading cause of child death in Iran (8). In a study performed in Rafsanjan, trauma was characterized as the most frequent cause of child mortality at the age of 1 to 14 years (9). The leading causes of pediatric trauma are falls from heights, accidents, pedestrians, and sports injuries (5, 6). Furthermore, certain factors can affect increasing or decreasing childhood trauma. Nabian et al. found that the rate of childhood trauma during the covid-19 pandemic in 2020 has significantly decreased (10).

Although the general principles of trauma care in children and adults are the same, there are fundamental differences in the pattern and mechanism of injury in different age groups (11). Pediatric trauma requires special consideration based on specific injury patterns and trauma mechanism, diagnosis, and treatment due to different physiology, anatomy, and cognitive variability in children. In this regard, understanding the pattern of pediatric trauma and the epidemiology of trauma could provide helpful information to apply appropriate preventive

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measures (12). Moreover, Identification of risk factors and appropriate prior measures, e.g., training and enforcing driving rules, securing playgrounds, use of safety devices during driving, etc., could be useful to reduce the occurrence and mortality in children (13). This study aimed to investigate the epidemiologic feature and outcomes of trauma in children under 18 years old, referred to the emergency department of Tabriz Emam-Reza Hospital during the spring season of 2019 (for 3 months). In light of these findings, we might be able to prevent trauma in children.

Materials and Methods

We conducted a retrospective cross-sectional study during the spring season of 2019 (for 3 months). The study population was all children under eighteen years old with GCS below 9 (1814 cases), referring to the emergency department of Tabriz Emam-Reza Hospital. Among 1814 patients, 1786 patients were included. We excluded patients without a triage card and with incomplete documents.

For each included patient, a checklist including demographic information, kind of trauma, transfer system of the patient to the emergency department, injury mechanism (based on observations, examinations, and Forensic physician's report), anatomical location of the injury, and the organ involved, including the internal organs or bone involved (based on clinical examination findings and radiological findings), and the outcomes of the 24-hour follow-up of the patients have been recorded. The outcomes were considered as one of the seven states; discharge from the emergency department, hospitalization in a ward, hospitalization in the intensive care unit, leaving the hospital against physicians' permission, referring to another center, escaping from the hospital, and death.

The data were analyzed by descriptive statistical methods (frequency and mean ± standard deviation) using SPSS 22.0.0. Pearson / Spearman correlation coefficient was used to determine the correlation between quantitative/ qualitative variables. In this study, $P < 0.05$ was considered statistically significant. This research was approved by regional committee of research of Tabriz University of medical sciences with no.: IR.TBZMED.REC.1398.049.

Results

After applying inclusion and exclusion criteria, a total of 1786 traumatic children were included. Most (n=1109, 62.1%) were male. The mean age of patients was 5.47 ± 3.1. Demographic characteristics and detailed data regarding the mechanism of trauma, the injured body parts, and the outcomes are summarized in Table1.

There were 1271 (71.1%) head and neck trauma, 276 (15.5%) extremities trauma. Abdominal trauma (n=66, 3.7%) and spinal trauma (n=57, 3.2%) were the rarest types of mechanism. It was revealed that falling had the most incidence frequency (40.4%). Eighty-eight percent of patients were transferred to the hospital emergency department by EMS, and twelve percent were transferred by their family members. The injuries occurred most often between 7 P.M and 12 P.M.

Eventually, out of the entire study population, 1361 patients were discharged from the emergency department (75%), 5 patients transferred to the trauma ward (0.2%), 1 patient hospitalized in the intensive care unit (0.05%),

Table 1: Demographics characteristics of traumatic children

Variable		No.	Percent
Gender	Male	1109	62.1
	Female	677	37.9
	0-4	657	36.8
Age	4-8	544	30.5
	8-12	357	20
	12-18	228	12.7
	Falling	721	40.4
	Traffic Accidents	626	35.1
Mechanism of trauma	Sport injury	44	2.5
	Fight	48	2.7
	Others	347	19.3
	Head and neck trauma	1271	71.1
	Chest Trauma	73	4.1
Diagnosis	Abdominal trauma	66	3.7
	Spinal trauma	57	3.2
	Extremities trauma	276	15.5
	Others	43	2.4
	Discharge from emergency department	1361	76
	Hospitalization in ward	5	0.2
	Hospitalization in ICU	1	0.05
Outcome	Leaving the hospital against physicians' permission	250	14
	Referring to another center	110	6
	Escaping from hospital	59	3
	Death	0	0

Table 2: Frequency distribution of trauma in different anatomical parts of the body.

Anatomic area	Percent
Bone injuries	
Skull	54%
Femur	12%
Tibia	8%
Humerus	10%
Radius	5%
Others	11%
Organ injuries	
Brain	34%
Liver	17%
Spleen	5%
Spinal cord	13%
Skeletal injuries	%31

250 patients left the hospital against physician permission (14%), 110 patients referred to another center (6%), 59 patients escaped from the hospital (3%) and zero deaths.

Based on the results, 20.9% of head and neck trauma cases were treated by non-surgical methods. Also, 29% of extremities cases required surgical intervention. It was revealed that the most injured bone was the skull (54%). Brain (34%) damage was injury with the highest frequency among organ injuries. Table 2 shows the frequency distribution of trauma in different anatomical parts of the body. The most severe injury was chest and abdominal trauma.

Discussion

This present study assessed the epidemiology of pediatric trauma cases admitted to the emergency department of the trauma center in Tabriz, Iran during the spring season of 2019 (for 3 months). The results showed that falling (40.4%) and traffic accidents (35.1%) were the most frequent mechanism of trauma that occurred in under eighteen-year-old children, referring to the Emam-Reza Hospital. Discharge in the emergency department was the most frequent consequence of accidents. The head and neck were the most injured anatomic locations in children. Moreover, time of injury distribution revealed that most accidents occurred between 7 P.M and 12 P.M. Emergency medical services were the most common transfer method for patients.

Based on our results, most trauma injuries were related to males, which is consistent with the results of previous studies (14-17). This could be due to their greater tendency toward more risky activities (18).

This study suggests that falling was the most frequent mechanism of trauma, followed by traffic accidents, which is consistent with the results of previous studies in Iran (19, 20). Nevertheless,

Dolatabadi et al. (14) reported that the most common mechanism of trauma were traffic accidents and then falling. Child abuse, vehicle accidents, and drowning were reported by Peclet et al. (21), as the highest-evident trauma mechanism. In the study by Mobasheri et al. (15), stroke and falling were reported as the most frequent mechanism of trauma in children under six years old. Though it is difficult to sort out these inconsistent results, the differences in the incidence frequency of trauma mechanism may in part be explained by considering differences in the mean age of the study population (19).

In this study, the most injured anatomic locations were the head and neck, which is consistent with the results of previous studies (13, 14, 20). However, in another study by Khodayari Zarnaq et al. (19) the forearm and arm were observed with the highest frequency. The differences in the injured anatomic sites reported in this study could be caused by differences in the prevalence of trauma in the study population (19).

Based on our findings, The most severe injury was chest and abdominal trauma. In line with our results, Coulthard et al. (22) suggest that the high mortality rate was associated with thorax, abdomen, and spine trauma. Although, Inconsistent with this finding, Aoki et al. (23) reported that Head injury was the leading reason for death.

According to the results of the present study, the injuries occurred most often between 7 P.M and 12 P.M., which could be due to more children being on the playground during those hours (14). Similar results were reported in the previous studies (14, 24).

Our study showed that the most frequent transfer method was EMS. In this regard, Peclet et al. (21) reported that 42.5%, 37.8%, and 19.4% of their patients were transferred by ambulance, private vehicles, and helicopter, respectively. Moreover, Rahmani et al. (25) reported that most transfers during the morning were done by ambulance; however, the most common transfer method during the evening was the private vehicles of the patients' families. The difference between the transfer method in the mentioned studies could be due to cultural differences and facilities among the different populations (25).

To the best of our knowledge, the effect of the COVID-19 outbreak on pediatric trauma rates is poorly understood. In this regard, Nabian et al. (10) assessed the impact of the COVID-19 pandemic on the number of the pediatric trauma in Taleghani tertiary trauma center in Iran. They found that the rate of childhood trauma during the covid-19 pandemic in 2020 has significantly decreased, which could be due to lifestyle changes, quarantine, and School closures. This observation was also confirmed in the study by Sheridan et al. (26).

We found the following limitations of this study. The first one is the retrospective study design. The retrospective nature of the data collection restricted the ability to report detailed data due to missing some data and incomplete documentation and should be addressed in future prospective research aiming to evaluate the cause and outcome of pediatric trauma. The relatively small sample size and the lack of follow-up of patients after discharge were among the limi-

tations. Another limitation of this study was the uni-center study design. Future multi-center studies could shed more light on the epidemiology of pediatric trauma and develop prevention strategies.

Conclusion

In summary, our study suggests that the head and neck were the most injured anatomic locations in children. Emergency medical services were the most common transfer method for patients. Males were more susceptible to being exposed to trauma. Falling and traffic accidents were the most frequent mechanism of trauma that occurred in under eighteen-year-old children. Moreover, this study shows the warrant for attention to pediatric age group and pediatric vulnerability against trauma. Awareness of patterns of pediatric trauma may help the adoption of safety policies and develop prevention strategies. In this regard, training prevention strategies for parents and improving playground safety will be effective.

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References

1. Kyu HH, Pinho C, Wagner JA, Brown JC, Bertozzi-Villa A, Charlson FJ, et al. Global and National Burden of Diseases and Injuries Among Children and Adolescents Between 1990 and 2013: Findings From the Global Burden of Disease 2013 Study. JAMA pediatrics. 2016;170(3):267-87.
2. Jones S, Tyson S, Young M, Gittins M, Davis N. Patterns of moderate and severe injury in children after the introduction of major trauma networks. Archives of disease in childhood. 2019;104(4):366-71.
3. Naranje SM, Erali RA, Warner WC, Jr., Sawyer JR, Kelly DM. Epidemiology of Pediatric Fractures Presenting to Emergency Departments in the United States. Journal of pediatric orthopedics. 2016;36(4):e45-8.
4. Sridharan L, Crandall MJJoT, Surgery AC. Injury and health among children in vulnerable families. 2011;70(6):1539-45.
5. Chaitanya K, Addanki A, Karambelkar R, Ranjan R. Traumatic brain injury in Indian children. Child's nervous system: ChNS: official journal of the International Society for Pediatric Neurosurgery. 2018;34(6):1119-23.
6. Stephens S, Campbell R, Chaseling R, Ma N. Traumatic brain injuries in a paediatric neurosurgical unit: A Queensland experience. Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia. 2019;70:27-32.
7. Osterman MJ, Kochanek KD, MacDorman MF, Strobino DM, Guyer B. Annual summary of vital statistics: 2012-2013. Pediatrics. 2015;135(6):1115-25.
8. Esmaeili Z, Vaez Zadeh NJJoMUoMS. To study the accidents patterns in children under 15 years of age met with an accident in mazandaran province in 78-79. 2000;10(29):1-7.
9. Khodadadi H, Asadpoor M, Zohrehkermani S, Ravari AJJ-RUMS. Frequency of injuries in children under 15 years admitted to the emergency Hospital of Imam Ali Ibn Abi Talib (AS) in Rafsanjan 19992000. 2007;5(3):201-8.
10. Nabian MH, Vosoughi F, Najafi F, Khabiri SS, Nafisi M, Veisi J, et al. Epidemiological pattern of pediatric trauma in COVID-19 outbreak: Data from a tertiary trauma center in Iran. Injury. 2020;51(12):2811-5.
11. Allen CJ, Wagenaar AE, Horkan DB, Baldor DJ, Hannay WM, Tashiro J, et al. Predictors of mortality in pediatric trauma: experiences of a level 1 trauma center and an assessment of the International Classification Injury Severity Score (ICISS). 2016;32(7):657-63.
12. Pediatrics CoPEMJ. Management of pediatric trauma. 2016;138(2):e20161569.
13. Memarzadeh M, Hoseinpour M, Sanjary N, Karimi ZJKJ. A study on trauma epidemiology in children referred to Isfahan Alzahra Hospital during 2004-7. 2011;14(5):488-93.
14. Dolatabadi AA, Mohseninia N, Amiri M, Motamed H, Asl AH-JIjoem. Pediatric trauma patients in Imam Hossein emergency department; an epidemiologic study. 2016;3(1):4-8.
15. Mobasheri F, Azizi H, Rastbaf FJJoFUoMS. The epidemiological pattern of injuries among children under 15 years of age in Fasa in 2013. 2016;6(1):69-78.
16. Schwebel DC, Gaines JJJoD, Pediatrics B. Pediatric unintentional injury: Behavioral risk factors and implications for prevention. 2007;28(3):245-54.
17. Fatmi Z, Kazi A, Hadden WC, Bhutta ZA, Razzak JA, Pappas GJP, et al. Incidence and pattern of unintentional injuries and resulting disability among children under 5 years of age: results of the National Health Survey of Pakistan. 2009;23(3):229-38.
18. Hillier LM, Morrongiello BAJJopp. Age and gender differences in school-age children's appraisals of injury risk. 1998;23(4):229-38.
19. Zarnaq RK, Saadati M, Rezapour R, Baghaie HJJCP. Epidemiology of Injuries in Children Younger Than Five Years Old-Tabriz. 2018;9(4):e62092.
20. Asadi P, Asadi K, Rimaz S, Monsef-Kasmaie V, Zohrevandi B, Mohtasham-Amiri ZJJoGUoMS. Epidemiology of trauma in children admitted to Poursina teaching hospital. 2015;23(92):9-15.
21. Peclet MH, Newman KD, Eichelberger MR, Gotschall CS, Guzzetta PC, Anderson KD, et al. Patterns of injury in children. 1990;25(1):85-91.
22. Coulthard MG, Varghese V, Harvey LP, Gillen TC, Kimble RM, Ware RS. A review of children with severe trauma admitted

to pediatric intensive care in Queensland, Australia. PloS one. 2019;14(2):e0211530.

23. Aoki M, Abe T, Saitoh D, Oshima K. Epidemiology, Patterns of treatment, and Mortality of Pediatric Trauma Patients in Japan. Scientific reports. 2019;9(1):917.

24. Bernardo LM, Gardner MJ, Seibel K. Playground injuries in children: a review and Pennsylvania Trauma Center experience. Journal of the Society of Pediatric Nurses : JSPN. 2001;6(1):11-20.

25. Rahmani F, Parsian Z, Bakhtavar HE, Salmasi S, Hashemi TJJoRiCM. Epidemiologic Feature and Diagnostic Outcome of Traumatic PediatricPatients Referred to Emergency Department of Imam-Reza Hospital, Tabriz, Iran in 2016-2017. 2020;8(1):10-.

26. Sheridan GA, Nagle M, Russell S, Varghese S, O'Loughlin PF, Boran S, et al. Pediatric Trauma and the COVID-19 Pandemic: A 12-Year Comparison in a Level-1 Trauma Center. HSS journal : the musculoskeletal journal of Hospital for Special Surgery. 2020;16(Suppl 1):92-6.

Original Article
Eurasian Journal of Critical Care

The Significance of the Red Cell Distribution Width to Serum Calcium Ratio in Predicting the Severity of Acute Pancreatitis Patients

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Abstract

Background: Although serum calcium (Ca) and red cell distribution width (RDW) can be used to predict the severity of acute pancreatitis (AP), their sensitivity and specificity are limited. The goal of this study is to see how well the serum calcium ratio of RDW, which may be measured at presentation, predicts the severity of AP in patients with AP.

Materials and methods: AP patients admitted to a tertiary hospital's emergency department between 14 February 2021 and 14 February 2022 were screened retrospectively. According to the 2012 Atlanta classification guidelines, AP severity was classified as mild acute pancreatitis (MAP), moderate acute pancreatitis (MSAP), and severe acute pancreatitis (SAP). During admittance to the emergency department, vital signs, laboratory exams, and imaging findings were gathered from the database.

Results: This study comprised 384 AP patients, including 166 males (56.8%), 239 patients with MAP, and 145 patients with MSAP or SAP. The mean RDW/Ca changes considerably according to pancreatitis severity ($p<0.05$). Pancreatitis severity rises considerably when RDW/Ca value increases (odds ratio: 2.27; lower(95 % CI):1.07; upper(95 % CI):4.83; $p<0.05$).

Conclusion: RDW/Ca can be a valuable indicator to predict the severity of patients with AP.

Keywords: Acute pancreatitis, red cell distribution width, serum calcium, disease severity

Introduction

Acute pancreatitis (AP) is parenchyma inflammation of the pancreas that can cause local and systemic complications[1,2]. Revised Atlanta Classification in 2012 defined mild acute pancreatitis (MAP) as the absence of organ failure and the absence of local or systemic complications. Moderate acute pancreatitis (MSAP) was defined as the presence of local or systemic complications and/or organ failure with no indication of chronic organ failure, whereas severe acute pancreatitis (SAP) was defined as persistent organ failure lasting more than 48 hours[3]. Although the majority of patients have a modest illness, around 20% of AP patients develop a clinical picture linked with mortality and morbidity[4]. Early diagnosis and rapid medical or endoscopic therapy can improve the prognosis in people with fatal or clinically severe AP[5]. As a result, the best marker/prognostic score for diagnosing clinically severe AP should be simple, inexpensive, noninvasive, easily accessible, accurate, and quantitative[5,6]. Many prognostic grading methods and biomarkers have been developed to identify patients with severe and fatal AP in the early stages [4]. However, the majority of them are difficult and cannot be efficiently applied early on. Ranson and Bedside Index severity in AP (BISAP) are the most often utilized grading systems due to their availability within the first 24 hours and ease of evaluation[6].

RDW, a common parameter in the complete blood count test, is a simple, affordable, and widely accessible parameter that evaluates the variance in the size of peripheral red blood cells (RBC)[7]. RDW is linked to elevated inflammatory markers such as interleukin-6, fibrinogen, and C-reactive protein (CRP)[8]. RDW has been demonstrated to be an accurate predictor of death in the elderly and in individuals suffering from a systemic illness[9-11]. It has also been demonstrated that RDW predicts death in AP patients[12]. Low calcium levels have been found to be a significant signal for diagnosing patients with severe AP, risk of mortality, and an indicator of severity[13]. However, several studies revealed contradictory results when evaluating the association between RDW, total serum calcium (TSC),

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and AP-specific prognostic ratings in patients with AP[14,15]. Although RDW and Ca can be used to predict AP severity and death on their own, their sensitivity and specificity are limited.

The purpose of this study was to determine the predictive usefulness of the red blood cell distribution width to serum calcium (RDW/Ca) ratio in determining the severity of acute pancreatitis patients.

Materials and Methods

Study design and settings: This clinical study is a retrospective cohort study conducted in the emergency department of a tertiary hospital. The study was approved by the Local Ethics Commission (protocol code: 29, decision no: 29, issue: E-48670771-514.99 date: 29 February 2022). The institutional review board waived informed consent to conduct this retrospective study. The current study was carried out in accordance with the Helsinki Declaration.

Selection of participants:

Inclusion criteria;

- Age ≥ 18 years;
- Meeting the diagnostic criteria for AP in the 2012 revised international consensus on the classification and definition of Atlanta pancreatitis. According to the revised Atlanta Classification for AP, at least two of the three characteristics are required for diagnosis: persistent abdominal pain and a threefold increase in serum levels of amylase and/or lipase or characteristic findings on abdominal imaging[3,16].

Exclusion criteria;

- Age < 18 years;
- Time from onset of abdominal pain to admission to hospital ≥ 72 hours
- Chronic pancreatitis;
- History of malignant tumor;
- AP resulting from poisoning, surgery, and trauma;
- Postoperative pancreatic lesions;
- Women during pregnancy or perinatal period
- Diseases affecting the hematological system (lymphoma, leukemia, and bone marrow malignancies) or other chronic inflammatory diseases (including tuberculosis, Henoch-Schönlein purpura)
- Chronic use of erythropoietin
- recent history of transfusion
- Complicated with chronic essential liver diseases and kidney failure;
- Missing clinical data and follow-up.

Study protocol

AP patients admitted to a tertiary hospital's emergency department between February 14, 2021, and February 14, 2022 were screened retrospectively. The severity of AP was divided into 3 groups as MAP, MSAP, and SAP using Atlanta classification standards[3]. During admittance to the emergency department, vital signs, laboratory exams, and imaging findings were gathered from the database.

Out-come

The value of RDW's serum calcium ratio (RDW/Ca) in predicting AP severity

Statistical analysis

Parametric tests were used without the normality test due to the Central Limit Theorem compatibility[17]. In the analysis of the data, the mean and standard deviation were used while the continuous data statistics were made in the scales, and the frequency and percentage values were used when defining the categorical variables. The student's t-test statistic is given to compare the means of two independent groups. Chi-square test statistics were used to evaluate the relationship between categorical variables. Risk factors associated with pancreatitis severity were evaluated with an odds ratio and 95% confidence interval. The statistical significance level of the data was taken as $p<0.05$. In the evaluation of the data, www.e-picos.com New York software and MedCalc statistical package program were used.

Results

This study comprised 384 AP patients, including 166 males (56.8 %), 239 patients with MAP, and 145 patients with MSAP or SAP. Table 1 shows the baseline and clinical characteristics of the groups.

The mean RDW/Ca changes considerably depending on the severity of the pancreatitis ($p<0.05$). While RDW/Ca was 1.56±0.22 in patients with mild pancreatitis and 11.63±0.34 in patients with moderate-to-high severity, those with moderate-to-high severity had a higher mean RDW/Ca. The factors affecting the severity of pancreatitis are evaluated in table 2.

It is statistically significant that it is 1.74 times more likely to be male in those with moderate-to-high pancreatitis severity than in those with low pancreatitis severity. (odds ratio:1.74; lower(%95 CI):1.15;upper(%95 CI):2.65; $p<0.05$).

Age, SpO2, HCT, HGB, LYM, MCV, MONO, MPV, NEU, PLT, WBC, GLUCOSE, ALT, AST, ALP, CRP, CA, and RDW factors were found to have no effect on estimating the severity of pancreatitis ($p>0.05$).

As the systolic blood pressure value increases, the severity of pancreatitis decreases significantly. (odds ratio:0.64; lower(%95 CI):0.56;upper(%95 CI):0.71;$p<0.05$).

As the diastolic blood pressure value increases, the severity of Pancreatitis decreases significantly. (odds ratio:0.75; lower(%95 CI):0.71;upper(%95 CI):0.8;$p<0.05$).

Table 1: Difference and Relationship Evaluation of Pancreatitis Severity and Characteristics

		Total (n=384)	MAP (n=239)	MSAP + SAP (n=145)	
Features		x̄±SD	x̄±SD	x̄±SD	**p-value**
Age		62,5±17,8	61,7±17,8	63,8±17,9	0,27
Systolic Blood Pressure(mmHg)		131,25±19	142,68±8,84	112,41±16,95	**<0,0001**
DiastolicBloodPressure (mmHg)		79,63±11,2	86,41±5,48	68,48±9,25	**<0,0001**
Heart Rate(Pulse/min)		95,16±16,04	84,94±8,09	112±10,84	**<0,0001**
Respiratory Rate /min / min(Respiratory/min)		20,2±1,7	19,7±1,8	21,1±1,1	**<0,0001**
Fever(°C)		36,55±0,32	36,47±0,13	36,68±0,47	**<0,0001**
SpO_2(%)		96,04±1,03	95,99±0,62	96,11±1,46	0,27
HCT(%)		40,02±5,53	40,08±5,17	39,94±6,11	0,81
HGB(g/L)		13,31±2,04	13,32±1,91	13,28±2,24	0,85
LYM(10^3mcL)		1,46±0,95	1,51±0,93	1,39±0,98	0,23
MCV(fL)		87,62±6,32	87,36±6,88	88,04±5,27	0,31
MONO(10^3mcL)		0,57±0,31	0,56±0,26	0,61±0,37	0,09
MPV(fL)		10,59±1,32	10,58±1,35	10,61±1,27	0,82
NEU(10^3mcL)		9,52±4,06	9,34±3,79	9,82±4,46	0,25
PLT(10^3mcL)		248,67±83,49	249,28±82,51	247,69±85,37	0,86
WBC(10^3mcL)		11,69±4,11	11,53±3,84	11,96±4,51	0,32
Glucose(mg/dL)		145,78±69,61	142,3±57,88	151,51±85,43	0,21
ALT(U/L)		178,28±148,08	195,13±165,48	150,97±120,29	**0,04**
AST(U/L)		186,59±180,89	198,13±154,48	167,73±135,24	0,17
Albumin(g/dL)		40.18±5.81	40.76±5.48	39.23±6.23	**0,01**
ALP(U/L)		190,02±138,25	178,92±131,59	208,33±148,56	0,24
Creatinine(mg/dL)		1,23±1,02	1,04±0,83	1,54±1,32	**<0,0001**
Na(mmol/L)		137,49±4,78	138,02±3,91	136,64±5,85	**0,006**
Ure (mg/dL)		46,81±35,84	40,92±23,25	56,56± 38,68	**0,001**
CRP(mg/L)		38,35±29,99	35,94±30,21	42,27±40,56	0,32
CA(mg/dL)		9,04±0,73	9,09±0,62	8,98±0,87	0,13
RDW(fL)		14,23±1,73	14,13±1,41	14,41±2,14	0,12
RDW/Ca		1,59±0,28	1,56±0,22	1,63±0,34	**0,03**
		n(%)	n(%)	n(%)	
Gender (famela/male)	Famela Male	218(56,8) 166(43,2)	148(61,9) 91(38,1)	70(48,3) 75(51,7)	**0,009**
Mortality (No/Yes)	No Yes	361(94) 23(6)	239(100) -	122(84,1) 23(15,9)	**<0,0001**

Student's t / Chi-square p<0.05 significance
SpO_2: Blood oxygen saturation, **HCT:** Hematocrit, HGB: Hemoglobin, **LYM:** lymphocyte, **MCV:** Mean cellular volume, **MONO:** monocyte, MPV: mean platelet volume, **NEU:** Neutrophil, **PLT:** Platelets, **WBC:** White blood cells**, ALT: Alanine** aminotransferase, **AST:**Aspartate aminotransferase, **ALP:** Alkaline phosphatase, **Na:** sodium, **CRP:** C reactive protein, **CA:** Calcium, **RDW:** Red Cell Distribution Width)

As the heart rate value increases, the severity of pancreatitis increases significantly (odds ratio:1.33; lower(%95 CI):1.26;upper(%95 CI):1.42;p<0.05).

As the respiratory rate value increases, the severity of pancreatitis increases significantly. (odds ratio:1.76; lower(%95 CI):1.52;upper(%95 CI):2.04;p<0.05).

As the fever measurement value increases, the severity of pancreatitis increases significantly. (odds ratio:17.11; lower(%95 CI):5.03;upper(%95 CI):58.16;p<0.05). In other words, it can be said that a 1 unit increase in the fever measurement value increases the severity of pancreatitis 17.11 times.

As the albumin value increases, the severity of pancreatitis decreases significantly. (odds ratio:0.96; lower(%95 CI):0.92;upper(%95 CI):0.99;p<0.05).

As the creatinine value increases, the severity of pancreatitis increases significantly. (odds ratio:1.39; lower(%95 CI):1.14;upper(%95 CI):1.69;p<0.05).

As the Na value increases, the severity of pancreatitis decreases significantly. (odds ratio:0.94; lower(%95 CI):0.89;upper(%95 CI):0.98;p<0.05).

As the urea value increases, the severity of pancreatitis increases significantly. (odds ratio:1.02; lower(%95

Table 2: Relationship between baseline variables and Pancreatitis Severity (n = 384)

Variable	Odds Ratio	Lower (%95 CI)	Upper (%95 CI)	p-value
Age	1,01	0,99	1,02	0,26
Gender	1,74	1,15	2,65	**0,009**
Systolic Blood Pressure(mmHg)	0,64	0,56	0,71	**<0,0001**
Diastolic Blood Pressure (mmHg)	0,75	0,71	0,8	**<0,0001**
Heart Rate(Pulse/min)	1,33	1,26	1,42	**<0,0001**
Number of Breaths(Respiratory/min)	1,76	1,52	2,04	**<0,0001**
Fever (°C)	17,11	5,03	58,16	**<0,0001**
SpO2(%)	1,12	0,92	1,37	0,27
HCT(%)	0,99	0,96	1,03	0,81
HGB(g/L)	0,99	0,89	1,09	0,85
LYM(10^3mcL)	0,87	0,69	1,09	0,23
MCV(fL)	1,02	0,98	1,05	0,31
MONO(10^3mcL)	1,76	0,9	3,46	0,09
MPV(fL)	1,02	0,87	1,19	0,82
NEU(10^3mcL)	1,03	0,98	1,08	0,25
PLT(10^3mcL)	1,01	0,99	1,02	0,86
WBC(10^3mcL)	1,03	0,98	1,08	0,32
Glukose (mg/dL)	1,02	0,99	1,03	0,21
ALT(U/L)	0,98	0,97	1,01	0,06
AST(U/L)	0,99	0,98	1,02	0,17
Albumin (g/dL)	0,96	0,92	0,99	**0,01**
ALP(U/L)	0,99	0,98	1,01	0,25
Creatinine(mg/dL)	1,39	1,14	1,69	**0,001**
NA(mmol/L)	0,94	0,89	0,98	**0,008**
URE(mg/dL)	1,02	1,01	1,03	**0,004**
CRP(mg/L)	1,01	0,99	1,02	0,32
Ca(mg/dL)	0,8	0,6	1,07	0,12
RDW(fL)	1,1	0,97	1,24	0,13
RDW/Ca	2,27	1,07	4,83	**0,03**

** It is significant at the p<0.05 level. (Odds ratio)*
SpO_2: blood oxygen saturation, **HCT**: Hematocrit, **HGB**: Hemoglobin, **LYM**: lymphocyte, **MCV**: average volume, **MONO**: monocyte, **MPV**: mean platelet volume, **NEU**: Neutrophil, **PLT**: Platelets, **WBC**: White blood cells, **ALT**: Alanine aminotransferase, **AST**: Aspartate aminotransferase, **ALP**: Alkaline fosfataz, **Na**: sodium, **CRP**: C reactive protein, **CA**: Calcium, **RDW**: Red Cell Distribution Width)

CI):1.01;upper(%95 CI):1.03;p<0.05).

As the RDW/Ca value increases, the severity of pancreatitis increases significantly. (odds ratio:2.27; lower(%95 CI):1.07;upper(%95 CI):4.83;p<0.05). In other words, it can be said that a 1 unit increase in the RDW/Ca value increases the severity of pancreatitis 2.27 times.

Discussion

AP has an important place in gastrointestinal system emergencies. Although the majority of AP patients have a modest and favorable prognosis, people with a severe clinical course who suffer organ failure (OF) account for around 20-30%

of all AP patients[18]. The development of OF in individuals with AP has a significant impact on their clinical course and death[5,19-22]. As a result, it demonstrates the critical need of identifying predictors of illness severity and mortality in AP. Several grading methods have been developed to define individuals with AP who are at high risk of morbidity and death[6]. Ranson and BISAP are two commonly used scoring systems[6,23].

The accuracy of Ranson and BISAP scores was determined to be 0.69 and 0.74, respectively[6]. At presentation, the prognosis of severe AP (e.g. MSAP and SAP) is still difficult to predict. Because major AP problems develop as a consequence of a worsening of pre-existing morbidity upon hospitalization[24]. As a result, serum indicators such as RDW, hematocrit, creatinine, BUN, TSC, lactate, and CRP have been intensively researched for early detection of severe AP (ie MSAP and SAP) and improved prognosis[5,25-28].

RDW, which has been linked to high levels of inflammatory markers such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and interleukin (IL), has been recognized as a significant prognostic factor for AP mortality risk[8,29-31]. AP may raise RDW levels by boosting inflammatory cytokines, which limit erythrocyte maturation and hasten the entrance of immature erythrocytes into the peripheral blood circulation[32]. RDW was shown to be independently linked with AP mortality in a comprehensive study[33].

The majority of AP-related mortality occurs in patients with severe AP, implying that, in addition to predicting mortality in AP, finding predictors of AP severity is critical[5,21]. In our study, all 23 patients who died had MSAP-SAP. Another research indicated that RDW, unlike TSC, was not a predictor of AP severity, while being a more helpful sign of AP severity than serum glucose or serum calcium[14,15]. In our study, no significant difference was found in terms of RDW, calcium and glucose averages, and pancreatitis severity. ($p>0.05$). However, the RDW/Ca mean differed significantly according to the severity of Pancreatitis. ($p<0.05$).

Hypocalcemia in AP patients frequently means the development of pancreatic parenchymal tissue necrosis, indicating the probability of SAP. According to one study, there is a link between the severity of AP and the degree of calcium clearance[34].

Serum calcium levels are often low during pancreatitis, and the presence of hypocalcemia is factored into the AP prognostic score system[35]. Hypocalcemia in AP patients frequently implies pancreatic necrosis, which is a significant predictor of the potential of SAP. A study found that the blood calcium level in MSAP and SAP patients was significantly lower than in MAP patients[36]. In our study, there was no significant relationship between mean serum calcium and pancreatitis severity ($p>0.05$). Research demonstrated a substantial and independent connection between RDW/TSC ratio and AP mortality, with a 0.820 AUROC[37]. Furthermore, in determining AP mortality, this research was shown to be superior to the RDW/TSC ratio and RDW conventional prognostic ratings at admission[37]. A study evaluating the usefulness of RDW/Ca within 24 hours for predicting MSAP and SAP found that RDW/Ca (AUC = 0.912) had better predictive power than single factors in predicting MSAP and SAP in acute pancreatitis[37]. RDW (AUC = 0.768, $P < 0.05$) and Ca (AUC = 0.875, $P < 0.05$)[24]. In addition, this study demonstrated that RDW/Ca is an independent risk factor for clinical worsening in AP. APACHE-II scoring system, Ranson scoring system, etc. Compared with RDW/Ca, there was a significant advantage in the early prediction of clinical worsening[36]. In our study, the severity of pancreatitis increases significantly as the RDW/Ca ratio increases (odds ratio:2.27; lower(%95 CI):1.07;upper(%95 CI):4.83;$p<0.05$). In other words, a 1 unit increase in RDW/Ca value increased the severity of pancreatitis 2.27 times.

The severity of pancreatitis increases dramatically as the fever measurement value rises. (odds ratio:17.11; lower(%95 CI):5.03;upper(%95 CI):58.16;$p<0.05$). With the increase in the severity of pancreatitis, fever occurs secondary to the increased inflammation. Therefore, fever is an important parameter as an indicator of severity.

Limitations

There are some limitations to our study. Some patients were not included in the study because of the patients whose data could not be accessed in the registry system and the patients who were referred to other hospitals. In addition, RDW samples were collected from a single center and therefore there may have been minor differences in RDW levels in other populations studied. Future prospective and multicenter studies are needed for more reliable results.

Conclusion

RDW and TSC are simple, inexpensive, non-invasive, and quantitative serum indicators that are included in complete blood count and biochemistry tests and are therefore easily accessible at the time of admission. In conclusion, RDW/Ca be a valuable indicator to predict the severity of patients with AP.

Ethics Committee Approval: *The study was approved by Prof.Dr.Cemil Taşcıoğlu City Hospital Ethics Committee and the requirement for informed consent was abandoned (protocol code: 29, decision no: 29, issue: E-48670771-514.99 date: 29 February 2022). The present study was conducted in line with the Declaration of Helsinki.*

References

1. Vege SS, DiMagno MJ, Forsmark CE, Martel M, Barkun AN. Initial Medical Treatment of Acute Pancreatitis: American Gastroenterological Association Institute Technical Review. *Gastroenterology*. 2018;154(4):1103-1139.
2. Lee PJ, Papachristou GI. New insights into acute pancreatitis. *Nat Rev Gastroenterol Hepatol*. 2019;16(8):479-496.
3. Sarr MG. 2012 revision of the Atlanta classification of acute pancreatitis. *Pol Arch Med Wewn*. 2013;123(3):118-124.
4. Wang X, Cui Z, Zhang J, Li H, Zhang D, Miao B, Cui Y, et al. Early predictive factors of in hospital mortality in patients with severe acute pancreatitis. Pancreas. 2010 Jan;39(1):114-5.
5. Almeida N, Fernandes A, Casela A. Predictors of Severity and In-Hospital Mortality for Acute Pancreatitis: Is There Any Role for C-Reactive Protein Determination in the First 24 Hours? GE Port J Gastroenterol. 2015 Jul 3;22(5):187-189.
6. Cho JH, Kim TN, Chung HH, Kim KH. Comparison of scoring systems in predicting the severity of acute pancreatitis. World J Gastroenterol. 2015 Feb 28;21(8):2387-94.
7. Miyamoto K, Inai K, Takeuchi D, Shinohara T, Nakanishi T. Relationships among red cell distribution width, anemia, and interleukin-6 in adult congenital heart disease. Circ J. 2015;79(5):1100-6.
8. Perlstein TS, Weuve J, Pfeffer MA, Beckman JA. Red blood cell distribution width and mortality risk in a community-based prospective cohort. Arch Intern Med. 2009 Mar 23;169(6):588-94.
9. Parizadeh SM, Jafarzadeh-Esfehani R, Bahreyni A, Ghandehari M, Shafiee M, Rahmani F, et al. The diagnostic and prognostic value of red cell distribution width in cardiovascular disease; current status and prospective. Biofactors. 2019 Jul;45(4):507-516.
10. Wang B, Gong Y, Ying B, Cheng B. Relation between Red Cell Distribution Width and Mortality in Critically Ill Patients with Acute Respiratory Distress Syndrome. Biomed Res Int. 2019 Mar 21;2019:1942078.
11. Hu ZD, Lippi G, Montagnana M. Diagnostic and prognostic value of red blood cell distribution width in sepsis: A narrative review. Clin Biochem. 2020 Mar;77:1-6.
12. Goyal H, Awad H, Hu ZD. Prognostic value of admission red blood cell distribution width in acute pancreatitis: a systematic review. Ann Transl Med. 2017 Sep;5(17):342.
13. Feng S, Wei Q, Hu Q, Huang X, Zhou X, Luo G, et al. Research Progress on the Relationship Between Acute Pancreatitis and Calcium Overload in Acinar Cells. Dig Dis Sci. 2019 Jan;64(1):25-38.
14. Ye JF, Zhao YX, Ju J, Wang W. Building and verifying a severity prediction model of acute pancreatitis (AP) based on BISAP, MEWS and routine test indexes. Clin Res Hepatol Gastroenterol. 2017 Oct;41(5):585-591.
15. Wang QM, Luo MW, Xiao B. [Value of red blood cell distribution width in assessing the severity of acute pancreatitis]. Nan Fang Yi Ke Da Xue Xue Bao. 2017 Jul 20;37(7):993-996. Chinese.
16. Zhou H, Mei X, He X, Lan T, Guo S. Severity stratification and prognostic prediction of patients with acute pancreatitis at early phase: A retrospective study. Medicine (Baltimore). 2019 Apr;98(16):e15275.
17. Norman, G. (2010). Likertscales, levels of measurementandthe "laws" of statistics. Advances in HealthSciencesEducation, 15 (5), 625-632. DOI 10.1007/s10459-010-9222-y
18. Liu G, Tao J, Zhu Z, Wang W. The early prognostic value of inflammatory markers in patients with acute pancreatitis. Clin Res Hepatol Gastroenterol. 2019 Jun;43(3):330-337.
19. Garg PK, Singh VP. Organ Failure Due to Systemic Injury in Acute Pancreatitis. Gastroenterology. 2019 May;156(7):2008-2023.
20. Yadav D, Lowenfels AB. The epidemiology of pancreatitis and pancreatic cancer. Gastroenterology. 2013 Jun;144(6):1252-61.
21. Wang X, Cui Z, Zhang J, Li H, Zhang D, Miao B, et al. Early predictive factors of in hospital mortality in patients with severe acute pancreatitis. Pancreas. 2010 Jan;39(1):114-5.
22. Gülen B, Sonmez E, Yaylaci S, Serinken M, Eken C, Dur A, et al. Effect of harmless acute pancreatitis score, red cell distribution width and neutrophil/lymphocyte ratio on the mortality of patients with nontraumatic acute pancreatitis at the emergency department. World J Emerg Med. 2015;6(1):29-33.
23. Park JY, Jeon TJ, Ha TH, Hwang JT, Sinn DH, Oh TH, et al. Bedside index for severity in acute pancreatitis: comparison with other scoring systems in predicting severity and organ failure. Hepatobiliary Pancreat Dis Int. 2013 Dec;12(6):645-50.
24. He F, Zhu HM, Li BY, Li XC, Yang S, Wang Z, et al. Factors predicting the severity of acute pancreatitis in elderly patients. Aging Clin Exp Res. 2021 Jan;33(1):183-192.
25. Cardoso FS, Ricardo LB, Oliveira AM, Canena JM, Horta DV, Papoila AL, et al. C-reactive protein prognostic accuracy in acute pancreatitis: timing of measurement and cutoff points. Eur J Gastroenterol Hepatol. 2013 Jul;25(7):784-9
26. Gutiérrez-Jiménez AA, Castro-Jiménez E, Lagunes-Córdoba R. Calcio sérico total y calcio corregido como predictores de severidad en pancreatitis aguda [Total serum calcium and corrected calcium as severity predictors in acute pancreatitis]. Rev Gastroenterol Mex. 2014 Jan-Mar;79(1):13-21. Spanish
27. Kılıç MÖ, Çelik C, Yüksel C, Yıldız BD, Tez M. Correlation between Ranson score and red cell distribution width in acute pancreatitis. Ulus Travma Acil Cerrahi Derg. 2017 Mar;23(2):112-116.
28. Valverde-López F, Matas-Cobos AM, Alegría-Motte C, Jiménez-Rosales R, Úbeda-Muñoz M, Redondo-Cerezo E. BISAP, RANSON, lactate and others biomarkers in prediction of severe acute pancreatitis in a European cohort. J Gastroenterol Hepatol. 2017 Sep;32(9):1649-1656.
29. Hu ZD, Chen Y, Zhang L, Sun Y, Huang YL, Wang QQ, et al. Red blood cell distribution width is a potential index to assess the disease activity of systemic lupus erythematosus. Clin Chim Acta. 2013 Oct 21;425:202-5.
30. Şenol K, Saylam B, Kocaay F, Tez M. Red cell distribution width as a predictor of mortality in acute pancreatitis. Am J Emerg Med. 2013 Apr;31(4):687-9.
31. Wang D, Yang J, Zhang J, Zhang S, Wang B, Wang R, et al. Red cell distribution width predicts deaths in patients with acute pancreatitis. J Res Med Sci. 2015 May;20(5):424-8. doi: 10.4103/1735-1995.163951.
32. Sharma D, Jakkampudi A, Reddy R, Reddy PB, Patil A, Murthy HVV, et al. Association of Systemic Inflammatory and Anti-inflammatory Responses with Adverse Outcomes in Acute

Pancreatitis: Preliminary Results of an Ongoing Study. Dig Dis Sci. 2017 Dec;62(12):3468-3478.

33. Gravito-Soares M, Gravito-Soares E, Gomes D, Almeida N, Tomé L. Red cell distribution width and red cell distribution width to total serum calcium ratio as major predictors of severity and mortality in acute pancreatitis. BMC Gastroenterol. 2018 Jul 5;18(1):108.

34. Komolafe O, Pereira SP, Davidson BR, Gurusamy KS. Serum C-reactive protein, procalcitonin, and lactate dehydrogenase for the diagnosis of pancreatic necrosis. Cochrane Database Syst Rev. 2017 Apr 21;4(4):CD012645.

35. Rajput R, Mittal A, Singh J, Dalal S, Vohra S. Recurrent diabetic ketoacidosis: a rare presenting manifestation of primary hyperparathyroidism. Clin Cases Miner Bone Metab. 2016 Sep-Dec;13(3):262-264.

36. Han T, Cheng T, Liao Y, He Y, Liu B, Lai Q, et al. The ratio of red blood cell distribution width to serum calcium predicts severity of patients with acute pancreatitis. Am J Emerg Med. 2022 Mar;53:190-195.

37. Gravito-Soares M, Gravito-Soares E, Gomes D, Almeida N, Tomé L. Red cell distribution width and red cell distribution width to total serum calcium ratio as major predictors of severity and mortality in acute pancreatitis. BMC Gastroenterol. 2018 Jul 5;18(1):108.

Original Article
Eurasian Journal of Critical Care

What are the Alternatives to the LRINEC Score in Identifying Necrotizing Soft Tissue Infections in the Emergency Department?

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Abstract

Background: The emergency department (ED) is an dynamically high-risk setting. Our aim is to determine the blood parameters associated with necrotizing soft tissue infections (NSTI) to strengthen the LRINEC score.

Materials and methods: We analyzed 109 patients who were diagnosed with necrotizing soft tissue infection in the Urology, Dermatology, Plastic surgery and General Surgery clinics of Atatürk University between 2013 and 2016. In the same period, we matched 624 patients diagnosed with cellulitis as a control group.

Results: Of four defined clinic's records to Atatürk University Hospital in 2013 to 2016, 109 matched and 624 matched control records were abstracted. Diagnoses associated with the NSTIs were: gangrene (n=47), gas gangrene (n=7), Fournier's gangrene (n=44) and necrotizing fasciitis (n=11). In patients with Necrotizing Soft Tissue Infection, BUN (p=0,00), K (0,011), Neutrofil (p=0,013), Lenfosit (p=0,003), Htc (p=0,00), RDW (p=0,002), Plt (p=0,042), AST (p=0,00), ALT (p=0,00) and INR (p=0,003) values were found to be statistically significant in making the diagnosis.

Conclusion: BUN, K, Neutrofil, Lenfosit, Htc, RDW, Plt, AST, ALT and INR values measured from blood tests of patients diagnosed with NSTI can be used in distinctive diagnosis of Soft Tissue Infection (STI). Increased awareness of these values may improve Emergency Department (ED) decision making and prevent miss diagnose.

Keywords: Cellulitis, gas gangrene, laboratory risk indicator for necrotizing fasciitis, LRINEC, necrotising fasciitis.

Introduction

Necrotizing soft tissue infections (NSTI) are bacterial infections caused by necrotic lesions in any layer of soft tissue.[1] NSTIs; Includes Necrotizing Fasciitis, Fournier's Gangrene, Necrotizing Myositis and other necrotizing infections. Identification is made according to the depth of the necrotized tissue and the anatomically involved area. However, this classification is insufficient to guide the treatment. In the diagnosis of emergency department, the surgical layers cannot be differentiated and microbiological factors cannot be determined. Considering the diagnostic possibilities of the clinics and the limitations of intervention, the diagnosis can be made by evaluating the underlying factors and the findings of the patients.

Etiology includes trauma, chronic skin infections, dental infections, postoperative infections, animal and parasite bites, herpes infections and burns.[1] Infection is most common in the extremities and perineum. The most common complaint of patients is pain with erythema and swelling, which can be seen with many diseases and is uncharacteristic for any disease. Within 24-72 hours, redness and gangrene formation associated with septic shock may occur. It has been shown that mortality is affected when the time from the onset of symptoms to surgical intervention is over 24 hours.[2]

The Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score has been developed to make the right decision in differentiating it from other serious soft tissue infections that should be considered in the diagnosis.[3] LRINEC score is calculated by hemoglobin, glucose, c-reactive protein, creatinine, sodium and leukocyte count measured from blood tests taken from patients (Table 1). It has been used since 2004. Using routine laboratory blood values, 89.9% sensitivity and 92% positive predictive value make this score an effective diagnostic tool.[3]

The LRINEC score was defined primarily by studying far eastern communities, and studies were conducted on its adequacy in identifying NSTI patients in different ethnic groups. The microorganisms that each society is exposed to differ due to the living conditions of the social environment, the nutritional habits of the people, the percentage of comorbid diseases, and the presence of substance addiction

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Table 1: LRINEC Score

Parameter	Unit	Score
CRP	mg/dL	
<15		0
≥15		4
WBC	Per mm^3	
<15000		0
15000-25000		1
>25000		2
Hemoglobin	g/dL	
>13,5		0
11.0-13.5		1
<11		2
Na	mmol/L	
≥135		0
<135		2
Creatine	mg/dl	
≤1.6		0
>1.6		2
Glucose	mg/dL	
≤180		0
>180		1

<5 low risk(<50% NF probability), 6-7 medium risk (50-75% NF probability), >8 high risk (>75% NF probability)

and immunodeficiency syndromes that have effects on the immune system. Because of these differences, it was shown in a study conducted in England that the sensitivity of the LRINEC score decreased to 43%.[4] The suspicion that the individual differences of the patients may affect the LRINEC score has led to the development of new diagnostic methods.

NSTI is typically caused by toxin-producing bacteria and the inflammatory response to them. This may cause tissue pathology, systemic toxicity, septic shock, and multiple organ failure.[5] The most common agents in the literature are anaerobes, including gram (+) cocci, gram (-) rod and clostridium species.

Diagnosing whether an infection is necrotizing or not is very important for its treatment and patient prognosis. The diagnosis of NSTI should be made early and quickly, and the need for broad-spectrum antibiotics should be determined with recurrent surgical debridements. Hemodynamic support therapy and iv immunoglobulin and hyperbaric oxygen therapy are among the other treatment options that can be evaluated in intensive care units.[6,7]

In our study, we searched an alternative diagnostic method to the LRINEC score in differentiating patients diagnosed with NSTI from other soft tissue infections. We searched for parameters that would increase the sensitivity of the LRINEC score in differential diagnosis. Thus, we wanted to prevent misdiagnosis or missed diagnosis in emergency departments with high patient density and circulation.

Materials and Methods

Study design

We conducted a matched retrospective case-control study of patients older than 18 years who had diagnosed with selulitis or necrotising soft tissue infection like gangrene, gas gangrene, necrotising fasciitis and Fournier gangrene. Study approval was obtained from the coordinating center's Institutional Review Board with waiver of informed consent (Meeting Number: 1 Desicion Number: 24 Date: 04.01.2018).

Settings

Patients were selected from the dermatology, urology, general surgery and plastic surgery clinics between 01.01.2013 and 31.12.2016. The diagnosis of the selected patients was made by residents and specialist doctors who provided patient care in the relevant clinics. The diagnosis of the patients was determined by the examination, lab tests and biopsy materials taken.

Selection of Participants

After marking the ICD codes (L03, N 49.3, A48.0, M72.5, L08.8) suitable for the diagnoses, the cases and control group were reached from the hospital data processing center. Patients with gangrene (n=47), gas gangrene (n=7), necrotizing fasciitis (n=11) and Fournier's gangrene (n=44) constituted our case group with necrotizing soft tissue infections. Patients diagnosed with cellulitis (n=624) constituted the control group, which was chosen to represent soft tissue infection. The blood tests in the electronic file record were examined to see the results of the current status of the cases and the control group on blood values.

We examined standard complete blood count, biochemistry, C-Reactive Protein (CRP) and Sedimentation (ESR) values from laboratory tests applied to case and control groups.

Among the sample, 400 patients were excluded because of missing data (CRP, WBC, Sedim, AST, ALT, INR) and 14 patients were under 18 years of age. As a result, 733 patients were included in the study (Figure 1).

Our sample size was determined by the total number of patients diagnosed with gangrene, gas gangrene, Fournier's gangrene, and Necrotizing fasciitis in the Urology, General surgery, Plastic surgery, and Dermatology clinics and obtained through electronic medical review during a 36-month enrollment period. According to historical data, a total of 733 patients were encountered during this time, with 624 case-control designs.

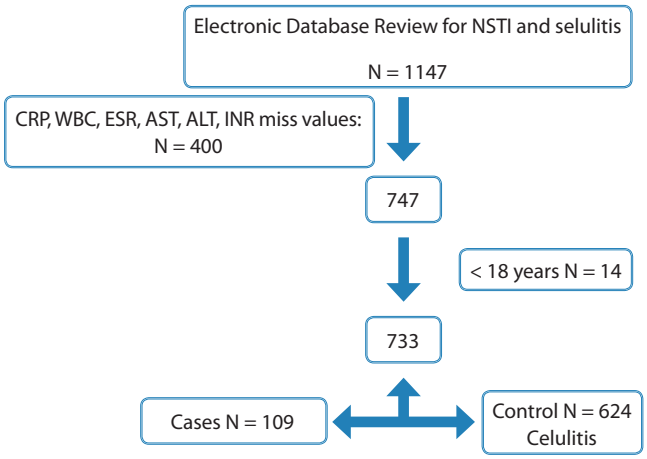

Figure 1: Summary diagram for case-control enrollment.

Methods of Measurement

The LRINEC score is calculated from hemoglobin, glucose, c-reactive protein, creatinine, sodium, and leukocyte counts measured from blood tests from patients. As it is known, it is used to distinguish necrotizing fasciitis from other soft tissue infections.

Fournier's gangrene severity index (FGSI) was first defined in 1995.[8] It is calculated using some clinical and laboratory parameters. These are: body temperature, pulse, respiratory rate, serum sodium-potassium-creatinine levels, hematocrit (%) level, white blood cell count (total/mm3 × 1000) and serum venous bicarbonate level (mmol/l).

In a retrospective study conducted by Ozan Bozkurt et al., the capacity to determine mortality and morbidity was evaluated with three different scoring systems such as FGSI, LRINEC and neutrophile–lym-phocyte ratio (NLR).[9]

Studies have shown that liver and kidney functions are impaired due to multi-organ failure and sepsis in necrotizing soft tissue infections. Accordingly, an increase in coagulopathy values, especially AST, ALT values and serum creatine kinase values was observed.

In the light of all these studies, we compared the blood parameters, kidney function values, liver enzymes and infection markers measured from the complete blood count of the patients in our study. Chronic disease diagnoses, x-ray, ultrasound, computed tomography or magnetic resonance images of the patients could not be accessed due to the loss of data in patients files.

Statistical Analysis

Statistical analysis of the study was performed with SPSS Version 21.0 program (SPSS Inc, Chicago, Illinois, USA). Percentage frequency analysis was performed for demographic characteristics such as gender. For numerical data, CBC parameters, biochemical tests, PT INR, Sedim and LRINEC Score mean ± standard deviation minimum and maximum were calculated (Table 2).

The diagnosis order and number of patients participating in the study were as follows: cellulitis: 624, gangrene: 47, gas gangrene: 7, necrotizing fasciitis: 11, Fournier's gangrene: 44 patients. We collected four diagnoses of necrotizing soft tissue infection in one group. These 109 patients diagnosed with NSTI formed the case group of our study. The control group consists of 624 patients with the diagnosis of cellulitis.

Kolmogorov-Smirnov test was performed to determine the distribution of analyzed blood parameters. Independent t-test (Table 2), which is one of the parametric tests, was used for the analysis of normally distributed parameters, and Mann Whitney U Test was used for those with non-normal distribution (Table 2). p-values less than 0.05 were considered as statistically significant.

Results

During the three-year period determined for the study, 1147 patients diagnosed with cellulite, gangrene, gas gangrene, necrotizing fasciitis and Fournier's gangrene were reached. Of these, 400 were excluded because of missing data (CRP, WBC, Sedim, AST, ALT, INR) and 14 because they were under the age of 18. As a result, 733 patients were included in the study. The diagnosis order and number of patients participating in the study were as follows: cellulitis: 624, gangrene: 47, gas gangrene: 7, necrotizing fasciitis: 11, Fournier's gangrene: 44 patients.

BUN (p=0.00), K (p=0.011), Neutrophil (p=0.013), Lymphocyte (p=0.003), Htc (p=0.00), RDW (p=0.002), Plt (p=0.042), AST (p=0.00), ALT (p=0.00) and INR (p=0.003) values which are not parameters of the LRINEC score were found to be statistically significant in diagnosing (Table 2). Glucose (p=0.013), Na (p=0.00), Creatine (p=0.023), WBC (p=0.001), Hb (p=0.000) and CRP (p=0.012) values, which are among the LRINEC score parameters, were also statistically significant (Table 2).

In our study, increases in AST and ALT values were observed in a total of 109 patients with necrotizing soft tissue infections. This increase was 64.18±28.64U/L for ALT with the highest mean. It was observed that this ALT value lagged behind the AST measurement with a mean value of 114.98±66.99U/L.

The mean BUN value for the NSTI was 25.28±2.25 mg/dl. In patients with cellulitis, the mean was 20.40±1.49 mg/dl.

In our study, CRP values were >360 mg/dl for both groups, and the mean was 415.80 mg/dl in the Case group (p=0.012).

While the mean value of the LRINEC test used in differential diagnosis was 1.84±0.22 in the control group, it was 3.01±0.27 in the case group.

Table 2: Mean, SD, 95%CI for mean of the labaratory results of patients with NSTI (Necrotising Soft Tissue Infection) and control patients with cellulitis at admission, t-z-p values

Parametre	Normal Values	Unit	Cellulitis		%95 CI			NSTI		%95 CI			
			N	Mean±SD	Lower	Upper	t,Z	N	Mean±SD	Lower	Upper	t, Z	P value
Na	135-145	mmol/L	627	136,9±3,76	-0,87	,75000	-,151	109	136,96±5,13	-1,07000	0,95	-,122	,000
Cr	0,66-1,09	mg/dl	627	0,98±0,08	-,27074	,07000	-1,120	109	1,08±0,09	-,28000	,08000	-1,047	,023
BUN	17-43	mg/dl	624	20,40±1,49	-7,80446	-1,95000	-3,272	109	25,28±2,25	-9,34000	-,40000	-2,161	,000
AST	15-35	U/L	622	29,37±28,01	-140,60199	-30,60000	-3,056	109	114,98±66,99	-218,39532	######	-1,278	,000
Glc	74-110	mg/dl	627	129,07±7,75	-28,77908	1,66000	-1,748	109	142,63±9,21	-31,78000	4,66000	-1,471	,013
ALT	7,0-35	U/L	618	28,30±12,34	-60,11978	-11,64000	-2,906	109	64,18±28,64	-92,66000	######	-1,252	,000
LRINEC	0		627	1,84±0,22	-1,621	-,730	-5,216	109	3,01±0,27	-1,710	-,640	-4,336	,000
WBC	4,4-10,9	10^3cells/uL	627	357,93			-3,234	109	429,29				,010
Hb	11,9-14,6	g/dL	627	386,13			-5,398	109	267,06				,000
CRP	0-5	Mg/L	627	360,28			-2,516	109	415,80				,012
K	3.5-5.5	mmol/L	627	376,84			-2,554	109	320,50				,011
Neu	2,1-8,8	10^3cells/uL	281	151,81			-2,478	30	194,67				0,013
Leu	4,0-11	10^3cells/uL	595	361,05			-2,976	105	297,20				,030
Htc	36,3-44	%	627	385,83			-5,302	109	268,84				,000
RDW	%11.6-%14.6	%	627	358,50			-3,060	109	426,00				,002
Plt	150-400	10^3cells/uL	627	361,86			-2,031	109	406,68				,042
INR	0.8-1.1		331	202,6			-3,001	92	245,82				0,003

(Na, sodium; K, potassium; BUN, Blood Urea Nitrogen; BUN; AST, Aspartat Aminotransferaz; ALT, Alanin aminotransferaz; Cr, creatine; Glc,glucose; WBC, White blood cell; Ne, neutrofile; Leu, Leucosite; Plt, Platelet Count Test; Hb, hemoglobine; Htc, hemotocrite; RDW, red cell distribution width; ESR, eritrosite sedimentation rate; CRP, C-reactive proteine; LRINEC, laboratory risk indicator for necrotising fasciitis; CI, confidence interval)

Discussion

In this case-control study, in which laboratory tests that can be used to differentiate necrotizing soft tissue infections from other soft tissue infections were sought, we determined that Neutrophil, Lymphocyte, Htc, RDW, Plt, BUN, K, AST, ALT and INR values were statistically significant in the diagnosis in addition to the LRINEC score parameters. Our study was repeated with statistics that Na, Creatine, Glucose, WBC, Hb and CRP values were differential in the diagnosis of cases in parallel with the LRINEC score.

If sepsis and MODS develop in necrotizing soft tissue infections, liver and kidney functions will be affected. The expected increase in laboratory values from these markers was observed in our study in parallel with other studies. In some studies, ALT value increased more than AST value, while in our study, the increase in AST values was higher. While the mean BUN value was >18 mg/dl in other studies[10], it was above 19 mg/dl in our cases. In the studies scanned in the literature to date, no data has been found that BUN value measurements can be diagnostic for NSTI. Our study is the first study to contribute to the literature in this context.

An increase in WBC value in all groups as an indicator of infection was an expected result. The increase in Neutrophile and Leucosite values with Wbc may be due to the effect of multifactorial agents.

One of the important results of our study is that Htc, RDW, Plt, Neutrophile, Leucosite values obtained from complete blood count can be used to differentiate NSTI cases from the control group. In our study, it has been shown that the Htc value is valuable in diagnosing, as in the study of FGSI and Ozan Bozkurt et al. Although there is no study about the prognostic Plt value when the literature is scanned, there are data showing that high Plt values are associated with mortality.[11]

CRP value, one of the evaluated parameters, can give an idea about the follow-up and progression of NSTIs. In a retrospective study by Moore et al. on 134 patients, CRP levels were shown to be highly correlated with mortality.[12] In a study by Kincius et al., it was shown that the basal CRP level of 41 patients with Fournier's gangrene was higher in those who did not survive.[13] In some studies, it has been stated that increased serum creatinine, sodium and lactate levels are proportional to the increase in mortality, but the same relationship cannot be said for CRP.[14,15] In our study, the mean CRP value was measured as 415.80 Mg/L in the case group. This study does not contribute to the effect of CRP value, which is expected to increase proportionally with infection, on prognosis.

When the studies carried out to date are examined, no data has been found that AST, ALT, RDW, Plt and INR values can be used to differentiate NSTI and cellulitis cases. Our study is the first with its contribution to this evaluation.

Other methods that can be used for early diagnosis of NSTI are radiological imaging methods. It is important to observe gas in the tissue on direct radiographs, and the presence of bullae and crepitation on examination. Computed tomography (CT), which is available in many emergency departments and is easily accessible, is more useful than plain radiographs. On CT, an increase in adipose tissue and thinning of the fascia can be seen in the affected area. It shows edema in soft tissue better than direct radiographs. The sensitivity of magnetic resonance (MR) imaging is high in terms of necrotizing fasciitis (93-100%).[16] Tissue necrosis and inflammatory edema cause abnormal signal increase on T2-weighted images. On T1-weighted images, edema and necrosis create variable signal intensity throughout the weakened deep fascia tissue.[17] The gold standard diagnosis is made with amputated tissue in surgery.

As a conclusion the most important step in the diagnosis of NSTI patients is awareness. Patients' histories, predisposing factors, clinical symptoms and diagnostic parameters are red flags that guide treatment. In clinics where patient density and circulation are fast, it is necessary to minimize the risk of missing these diagnoses, which have a serious impact on prognosis and mortality. Effective diagnostic methods should be used in emergency department in order to speed up the diagnosis process of patients and shorten the access time to treatment. BUN, K, Neutrophil, Lymphocyte, Htc, RDW, Plt, AST, ALT and INR values were observed to be statistically significant in line with the data we obtained in our study. It should be remembered that these parameters can be used in addition to the LRINEC score parameters. In this patient group, where delayed treatment and intervention increase mortality, evaluations with high diagnostic value should be kept in mind.

Limitations

Our study has limitations. First of all, as in every retrospective study, the deficiencies in the data scanned backwards decreased the number of cases in our study. Second, Incomplete blood tests from the cases prevented some cases from being included in the study. Third, the fact that the groups were evaluated with blood values and biopsy results caused the patients to be taken from clinics other than the emergency department. For the same reason, necrotizing soft tissue infection patients and cellulitis patients diagnosed in the emergency department were not included in the study. Fourth, the absence of vital signs in the electronic files of the case and control groups prevented us from interpreting according to FGSI. Fifth, since the discharge status and short-term (1 week) follow-up of the patients included in the study could not be performed, so that no comment could be made regarding the contribution of the evaluation to the prognosis.

References

1. Çalbay A. (2019). Ortopedik Aciller pp 341-349, Ankara: Akademisyen Kitapevi ISBN: 978-605-258-394-4.
2. Liu Y-M, Chi C-Y, Ho M-W et al. Microbiology and factors affecting mortality in necrotizing fasciitis. J Microbiol Immunol Infect. 2005 Dec;38(6):430–5.
3. Wong C-H, Khin L-W, Heng K-S, Tan K-C, Low C-O. The LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score: a tool for distinguishing necrotizing fasciitis from other soft tissue infections. Crit Care Med. 2004 Jul;32(7):1535–41.
4. Al-Hindawi A1, McGhee J2, Lockey J1, Vizcaychipi M1.Validation of the laboratory risk indicator for necrotising fasciitis scoring system (LRINEC) in a Northern European population. J Plast Reconstr Aesthet Surg. 2017 Jan;70(1):141-143.
5. Morgan MS. Diagnosis and management of necrotising fasciitis: a multiparametric approach. J Hosp Infect. 2010 Aug;75(4):249–57.
6. Hakkarainen TW, Kopari NM, Pham TN, Evans HL. Necrotizing soft tissue infections: review and current concepts in treatment, systems of care, and outcomes. Curr Probl Surg. 2014 Aug;51(8):344–62.
7. Hussein QA, Anaya DA. Necrotizing soft tissue infections. Crit Care Clin. 2013 Oct;29(4):795–806.
8. Laor E, Palmer LS, Tolia BM, Reid RE, Winter HI (1995) Outcome prediction in patients with Fournier's gangrene. J Urol 154(1):89–92.
9. Bozkurt O, Sen V, Demir O, Esen A.Evaluation of the utility of different scoring systems (FGSI, LRINEC and NLR) in the management of Fournier's gangrene. Int Urol Nephrol. 2015 Feb;47(2):243-8.
10. Taro Shimizu 1, Yasuharu Tokuda. Necrotizing fasciitis. Intern Med. 2010;49(12):1051-7.
11. Sung Jin Park, Dong Heon Kim , Chang In Choi , Sung Pil Yun , Jae Hun Kim , Hyung Il Seo. Necrotizing soft tissue infection: analysis of the factors related to mortality in 30 cases of a single institution for 5 years. Ann Surg Treat Res. 2016 Jul;91(1):45-50.
12. Moore SA, Levy BH, Prematilake C, Dissanaike S. The Prediction Predicament: Rethinking Necrotizing Soft Tissue Infections Mortality. Surg Infect (Larchmt). 2015 Aug 10;10.1089/sur.2015.002 [Epub ahead of print].
13. Kincius M, Telksnys T, Trumbeckas D, Jievaltas M, Milonas D. Evaluation of LRINEC Scale Feasibility for Predicting Outcomes of Fournier Gangrene. Surg Infect (Larchmt). 2016 Mar 29.
14. Krieg A, Dizdar L, Verde PE, Knoefel WT. Predictors of mortality for necrotizing soft-tissue infections: a retrospective analysis of 64 cases. Langenbecks Arch Surg.2014 Mar;399(3):333–41.
15. Keeley J, Kaji A, Kim D, et al. Predictors of mortality in necrotizing soft tissue infection.Am Surg. 2014 Oct;80(10):989–93.
16. Young MH, Aronoff DM, Engleberg NC. Necrotizing fasciitis: pathogenesis and treatment. Expert Rev Anti Infect Ther. 2005 Apr;3(2):279–94.
17. Fugitt JB, Puckett ML, Quigley MM, Kerr SM. Necrotizing fasiitis, Radiographics 2004; 24: 1472-1476.

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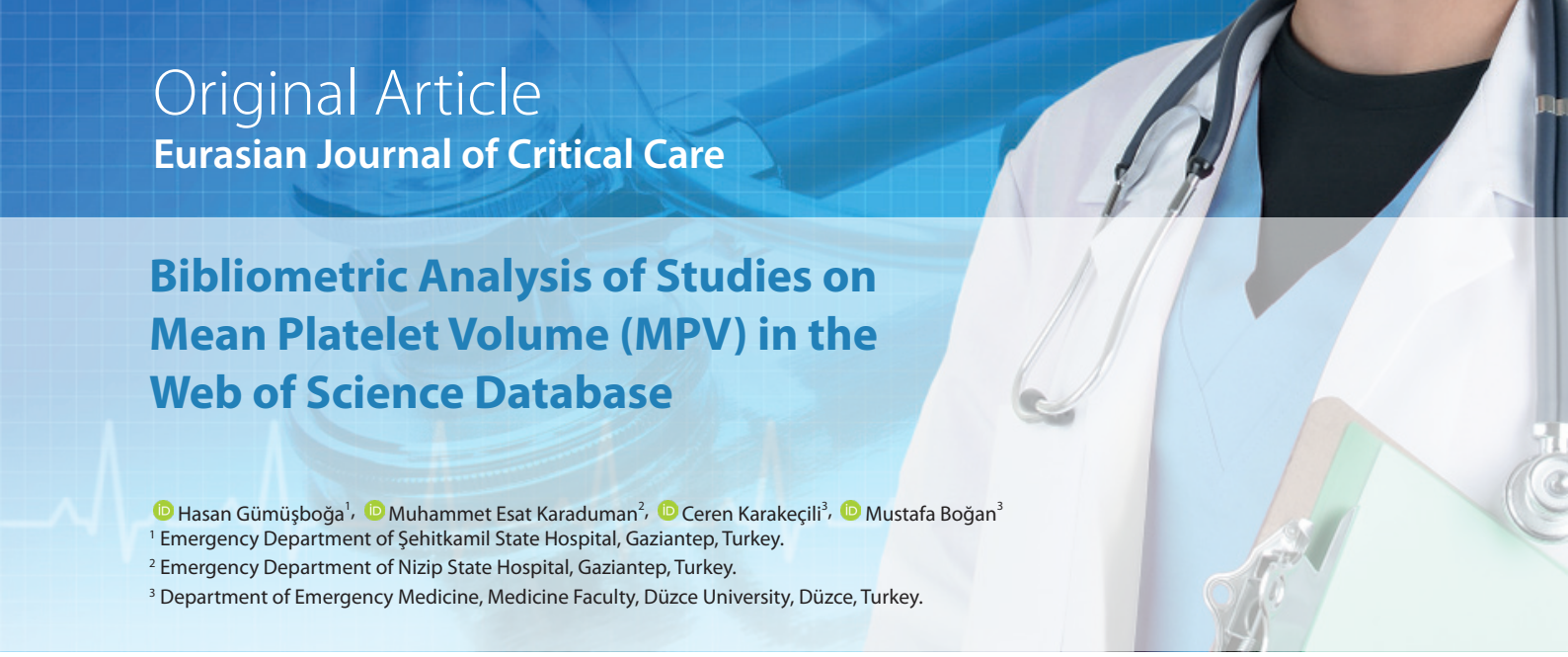

Bibliometric Analysis of Studies on Mean Platelet Volume (MPV) in the Web of Science Database

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Abstract

Background: Mean platelet volume (MPV) was investigated by many medical disciplines for different disease groups. But, the use of MPV values in clinical practice is limited. In this study, it is aimed to make a bibliometric analysis of studies on MPV over the Web of Science database and also to reveal Turkey's contribution to this issue.

Materials and methods: This bibliometric analysis was performed in June 2021 as a result of a search for mean platelet volume (MPV) in all indexes in the Web of Science (WOS) database.

Results: The most of the MPV studies in the world were conducted on hematology (1256, 18.9%), general internal medicine (746, 11.2%), peripheral vascular diseases (579, 8.7%), cardiology/cardiovascular system diseases (537, 8%), experimental medicine research departments (376, 5.6%), and surgical sciences (342, 5.1%) in the fields of science/subject. The rank of emergency medicine is 64 (0.9%) in the world and 41 (2.1%) in Turkey. 17 of the 25 authors who published the most were Turkish.

Conclusion: In many studies, when the standard deviations are taken into account, the difference between the groups cannot be seen mathematically, even if they are statistically different. Therefore, the use of MPV values in clinical practice is limited. However, these studies suggest that academic promotion is aimed rather than contributing to the scientific literature.

Keywords: Mean Platelet volume, emergency medicine, Turkey, academic promotion

Introduction

Mean platelet volume (MPV) is a simple and cheap test that is calculated as part of a complete blood count and measures the mean size of platelets. High MPV levels indicates increased platelet activation, the number of large platelet and platelet hyperaggregability. Also high level of MPV indicates that larger and younger platelets are released into the circulation, as it increases when there is rapid platelet consumption. When level of MPV is low, platelets are usually smaller. [1]

MPV is a value similar to Mean corpuscular volume (MCV) for red blood cells and is expressed as femtoliter (fL).[1, 2] MPV measurements are made in two ways. First one, with the measurement of platelet volume using optical technology, second one, it is determined by the geometric mean of the converted logarithmic normal platelet volume data in impedance technology systems. Therefore, the MPV value is an indicator that can change according to the type of instrument used and the measurement technique and does not have international standardization.[2] For example, while the normal MPV value was determined as 6-13.2 (fL) in an adult with a normal platelet count by impedance technology; 5.6-12.1 (fL) range may be normal when measured by optical methods. Therefore, the reference range of the laboratory that uses a specific hematological device should be checked.[2]

The bibliometric analysis method is carried out in order to present a scientific road map to all researchers who are interested in any subject, and thus to gain a macroscopic and holistic perspective on the subject.[3] Web of Science (formerly Web of Knowledge) is a website that provides subscription access to multiple databases that provide comprehensive citation data for many different academic disciplines.[4] When this database was searched, it was seen that the relationship of MPV was investigated by many medical disciplines for different disease groups. In this study, it is aimed to make a bibliometric analysis of studies on MPV over the Web of Science database and also to reveal Turkey's contribution to this issue.

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Materials and Methods

Study Design:

The study was a retrospective observational study that did not include human subjects and therefore ethics committee approval was not required.

Process:

This bibliometric analysis was performed in June 2021 as a result of a search for mean platelet volume (MPV) in all indexes in the Web of Science (WOS) database accessed. 'Mean platelet volume' was written in the topic section and a search was made in the WOS. "Web of Science Categories: (All); Document Types: (All); Languages: (English); Timespan: (All); Indexes: (All)". A total of 6638 studies belonging to before and after 1997 were detected. As a result of this search, the number of publications (according to science/subject area, years, types and countries), WOS indexes (SCIE, SSCI, ESCI, Other), "H Index" of subjects, universities that contribute the most in Turkey and analysis of the data of top 25 authors who published extensively was performed.

Statistical Analysis:

Data are presented as the number and/or percentage of publications.

Results

As a result of the analysis, the total number of publications, WOS index distribution and H Index numbers are given in Table 1.

Table 1: Descriptive Data

PARAMETER	All World (n)	Turkey (n)
Total Number of Publications	6638	1880
WOS Index		
SCIE	5978	1595
SSCI	88	27
ESCI	620	279
Other	338	66
Subject H Index	123	52

The most of the MPV studies in the world were conducted on hematology (1256, 18.9%), general internal medicine (746, 11.2%), peripheral vascular diseases (579, 8.7%), cardiology/cardiovascular system diseases (537, 8%), experimental medicine research departments (376, 5.6%), and surgical sciences (342, 5.1%) in the fields of science/subject. In Turkey, the most of the MPV studies were conducted on internal medicine (393, 20.9%), cardiology/cardiovascular diseases (350, 18.6%), hematology (215, 11.4%), experimental medicine research department (120, 6.3%), pediatrics (97, 5.1%), and surgical sciences (83, 4.4%) in science/subject areas. The rank of emergency medicine is 64 (0.9%) in the world and 41 (2.1%) in Turkey. Distribution of the number of publications by Science/Subject fields is given in Figure 1.

When we look at the distribution of the number of publications by years, there were no publications on MPV in Turkey before 1997. From 1997 to 2021, the number of publications related to MPV is gradually increasing. (The data were obtained in June 2021, because of that the data for 2021 do not show the whole year.) It was seen the highest number of publication in 2020 (661, 9.9%) in the world, and

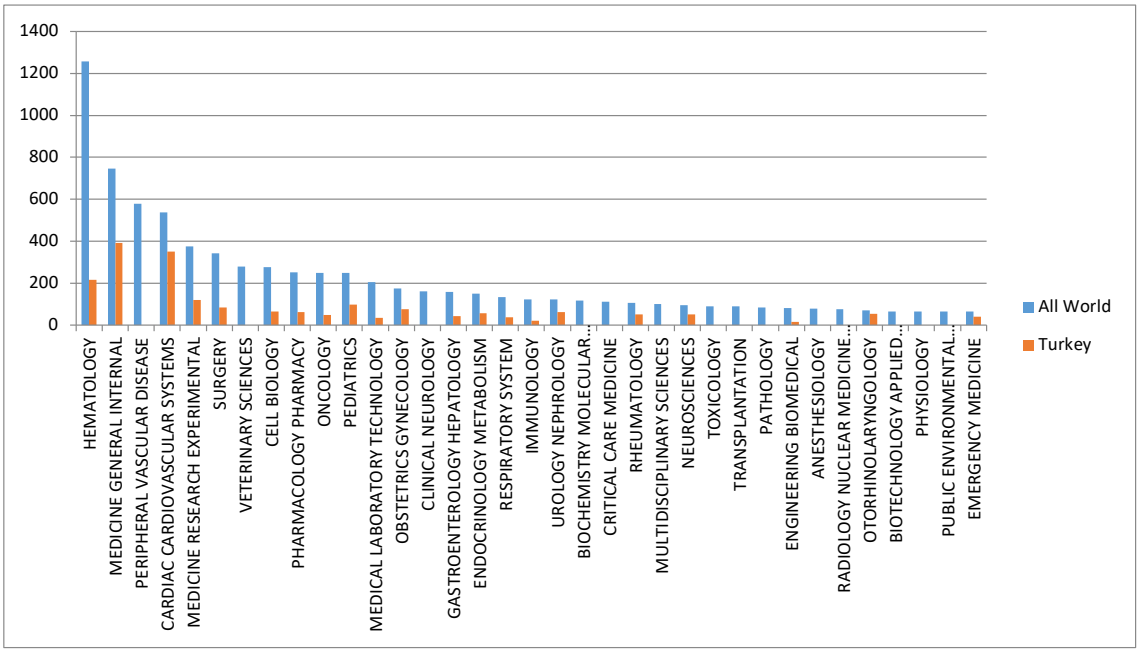

Figure 1: Distribution of MPV publications by Science/Subject areas

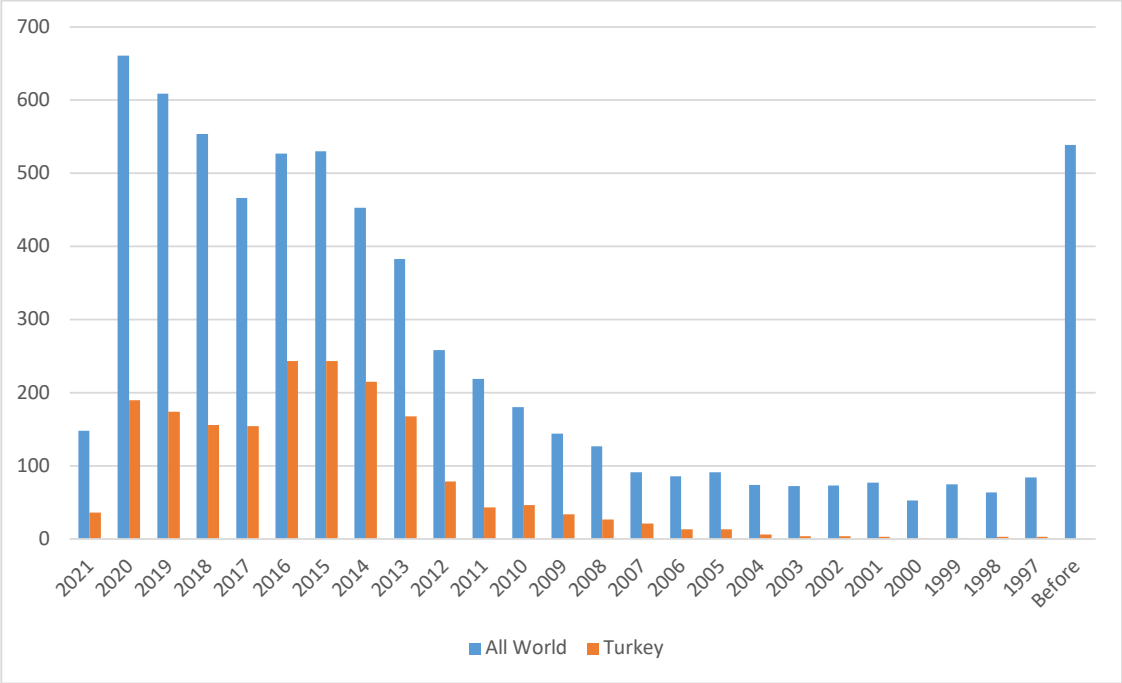

Figure 2: Distribution of MPV publications by years

in Turkey in 2015 and 2016 (243, 12.9%). Distribution of MPV publications by years is given in Figure 2.

When the types of MPV studies are examined, it has been determined that the most of publications were original articles, letters to the editor and meeting summary presentations are made both in the world and in Turkey. The number and percentages of publications by type are given in Table 2.

Looking at the distribution of MPV studies by country, the highest numbers were observed for Turkey (1880, 28.3%), USA (1033, 15.5%), China (644, 9.7%), Italy (346, 5.2%) and England (306, 4.6%). The number of MPV studies by country is given in Figure 3.

Looking at the top 25 authors who make the most publications in the world about MPV; the first six authors were Turkish. At the same time, it was determined that 17 of the 25 authors who published the most were Turkish. The other authors of the top 25 were from Italy, China, South Korea and England. MPV studies in Turkey were mostly performed at Süleyman Demirel University (109, 5.7%), Gülhane Medicine Academy (91, 4.8%), Health Sciences University (87, 4.6%), Dicle University (63, 3.3%) and Erciyes University (54, 2.8%) (Table 3).

Table 2: Number and percentage of MPV publications

	All World		Turkey	
	n	%	n	%
ARTICLE	5521	83.17	1492	79.3
LETTER	413	6.22	269	14.30
MEETING ABSTRACT	350	5.27	98	5.21
REVIEW	249	3.75	27	1.43
PROCEEDINGS PAPER	143	2.15	12	0.63
EARLY ACCESS	64	0.96	9	0.47
EDITORIAL MATERIAL	45	0.67	6	0.31
NOTE	27	0.40	1	0.05
BOOK CHAPTER	10	0.15	1	0.05
CORRECTION	10	0.15	-	-
DATA PAPER	3	0.04	-	-
RETRACTED PUBLICATION	3	0.04	-	-
RETRACTION	2	0.03	-	-

Discussion

Mean platelet volume, a measure of platelet size and activation, has been associated with various diseases in recent studies.[5,6] It has been found that MPV increases in some of these diseases and decreases in some cases.[5] Bone marrow failure, severe anemia, cancers, splenomegaly, inflammatory and autoimmune diseases can cause low MPV levels. However, high MPV levels can be seen in conditions such as heart diseases, diabetes, thrombocytopenia, myeloproliferative diseases, and preeclampsia.[7]

Increased MPV was observed in many clinical conditions. It is an independent high risk factor for death in patients after an acute ischemic cardiac event[8], it is associated with a higher risk of death for a long time after

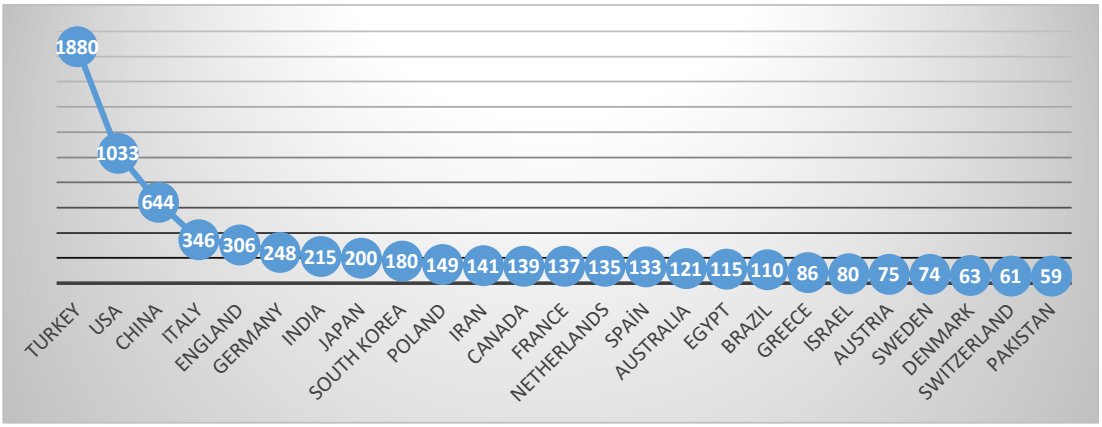

Figure 3: Number of MPV publications by country

Table 3: The top 25 authors in the world

Name	Number of Publications (n)	(%)	H Index	Department	Country
VAROL E	81	1.22	22	Cardiology	Turkey
BEYAN C	62	0.93	11	Hematology	Turkey
BEYAN E	54	0.81	8	Internal Medicine	Turkey
BALTA S	41	0.61	26	Cardiology	Turkey
OZAYDIN M	38	0.57	27	Cardiology	Turkey
DEMIRKOL S	36	0.54	26	Cardiology	Turkey
LIPPI G	32	0.48	70	Biochemistry	Italy
DOGAN A	31	0.46	22	Cardiovascular surgery	Turkey
CELIK T	28	0.42	31	Cardiology	Turkey
WANG RT	28	0.42	26	Internal Medicine	China
SAHIN M	27	0.40	16	Endocrinology	Turkey
KAYA MG	25	0.37	28	Cardiology	Turkey
CHO SY	23	0.34	21	Infectious diseases	China
LI Y	22	0.33	14	Public Health	China
AKSOY F	21	0.31	13	Cardiology	Turkey
DEMIR M	21	0.31	13	Gastroenterology	Turkey
ZHANG Y	21	0.31	21	Gastroenterology	China
AKTAS G	20	0.30	13	Internal Medicine	Turkey
LEE HJ	20	0.30	16	Laboratory Medicine	China
MIKHAILIDIS DP	20	0.30	85	Biochemistry	England
UNLU M	20	0.30	21	Cardiology	Turkey
ZHANG J	20	0.30	18	Dermatology	China
COBAN E	19	0.28	18	Internal Medicine	Turkey
ICLI A	19	0.28	15	Cardiology	Turkey
CAYLI M	18	0.27	21	Cardiology	Turkey

transdermal cardiac intervention[9], it is associated with the risk of acute stroke[10], it is associated with the intensity of inflammation in tuberculosis[11], it is useful in determining the activity of Crohn's disease and distinguishing these patients from healthy individuals[12,13], it is responsible for the increased risk of diabetes and poor outcomes[14], the preoperative level is quite high in primary gastric cancer patients compared to healthy subjects.[15] Also, it is associated with tumor growth in patients with papillary thyroid cancer.[6] Decreased MPV was observed in increased activity of ulcerative colitis[17], active SLE in adult patients[18]. It is as an independent prognostic factor of survival of patients after intestinal tumor resection[19], as a useful marker in differentiating patients with neuroendocrine tumor of the pancreas from pancreatic adenocarcinoma.[20] In lung cancer, there are studies showing that low preoperative level is an independent negative prognostic factor in patients after total cancer resection[21], and that it is independently associated with the presence of cervical cancer.[22]

MPV, a routine and cheap test performed during complete blood counting, can provide important information about the course and prognosis of many inflammatory conditions. However, for the practical use of MPV, clinical laboratories should strive for standardization of both the preanalytical and analytical phases.[5] Although many studies are published every year that it is associated with many diseases, the measurement of MPV is still not well standardized. The standard technique that needs to be defined should include all the details of MPV to be measured at which optimal temperature, which anticoagulants should be used, how long after blood collection and with which technique.[23,24] For now, MPV should not be used to show active or severe states of diseases or as a mortality predictor until measurement techniques are standardized.[23]

In our study, it has been observed that thousands of MPV studies have been conducted in different diseases and medical disciplines, most of which are original articles and SCIE, especially in the last 10 years. MPV studies were performed on the fields of hematology and general internal medicine in the world, and general internal medicine and cardiology in Turkey. It has been determined that most of the MPV studies are from Turkey (n=1880) and the first 6 of the 25 authors (17 of whom are Turkish) who publish the most are Turkish researchers.

Limitation

Studies that were not indexed in the Web of Science database were not included in the study.

Conclusion

Although studies have been conducted in many medical disciplines and diseases related to MPV, it has been determined that it is not used as a definitive diagnostic criterion in clinical practice, but creates supportive predictions. In many studies, when the standard deviations are taken into account, the difference between the groups cannot be seen mathematically, even if they are statistically different. Therefore, the use of MPV values in clinical practice is limited. In addition, it will be interesting to determine the 'MPV threshold', which indicates the intensity of the inflammatory process, the presence of the disease, the increased risk of developing the disease, the increased risk of thrombotic complications, the increased risk of death and the presence of the disease, and more studies are needed on this subject.

References

1. Çiler Erdağ G, Coşkun FT, Biçer S, Uğraş M, Giray T, Kaspar Ç, et al. Can Mean Platelet Volume be Used as a Marker in Children with Acute Appendicitis? Cocuk Acil ve Yogun Bakım, 2017;4(1):17-21.
2. Hoffmann JJML. Reference range of mean platelet volume. Thromb Res. 2012; 129(4):534-5.
3. Köse G, Kurutkan MN, Orhan F. Kalp yetmezliği konusunda en çok atıf alan ilk 100 makalenin bibliyometrik analizi. Sağlık Akademisyenleri Dergisi, 2020;7(2):13.
4. Wikipedia. Web of Science, https://tr.wikipedia.org/w/index.php?title=Web_of_Science&oldid=24457252. [accessed 07 Jan 2022].
5. Korniluk A, Koper-Lenkiewicz OM, Kamińska J, Kemona H, Dymicka-Piekarska V. Mean Platelet Volume (MPV): New Perspectives for an Old Marker in the Course and Prognosis of Inflammatory Conditions. Mediators Inflamm. 2019:9213074.
6. Ball S, Arevalo M, Wongsaengsak S, Dennis JA, Nugent K. Implications of mean platelet volume in health and disease: A large population study on data from National Health and Nutrition Examination Survey. Thromb Res. 2019;175:90-4.
7. Medlineplus. MPV Blood Test: MedlinePlus Medical Test, https://medlineplus.gov/lab-tests/mpv-blood-test/ [accessed 14 May 2022].
8. Slavka G, Perkmann T, Haslacher H, Greisenegger S, Marsik C, Wagner OF, et al. Mean platelet volume may represent a predictive parameter for overall vascular mortality and ischemic heart disease. Arterioscler Thromb Vasc Biol. 2011;31(5):1215-8.
9. Shah B, Oberweis B, Tummala L, Amoroso NS, Lobach I, Sedlis SP, et al. Mean platelet volume and long-term mortality in patients undergoing percutaneous coronary intervention. Am J Cardiol. 2013;111(2):185-9.
10. Greisenegger S, Endler G, Hsieh K, Tentschert S, Mannhalter C, Lalouschek W. Is elevated mean platelet volume associated with a worse outcome in patients with acute ischemic cerebrovascular events? Stroke. 2004;35(7):1688-91.
11. Feng Y, Yin H, Mai G, Mao L, Yue J, Xiao H, et al. Elevated serum levels of CCL17 correlate with increased peripheral blood platelet count in patients with active tuberculosis in China. Clin Vaccine Immunol. 2011;18(4):629-32.
12. Gasparyan AY, Sandoo A, Stavropoulos-Kalinoglou A, Kitas GD. Mean platelet volume in patients with rheumatoid arthritis: the effect of anti-TNF-α therapy. Rheumatol Int. 2010;30(8):1125-9.
13. Liu S, Ren J, Han G, Wang G, Gu G, Xia Q, vd. Mean platelet volume: a controversial marker of disease activity in Crohn's disease. Eur J Med Res. 2012;17:27.
14. Rollini F, Franchi F, Muñiz-Lozano A, Angiolillo DJ. Platelet function profiles in patients with diabetes mellitus. J Cardiovasc Transl Res. 2013;6(3):329-45.
15. Kılınçalp S, Ekiz F, Başar O, Ayte MR, Coban S, Yılmaz B, et al. Mean platelet volume could be possible biomarker in early diagnosis and monitoring of gastric cancer. Platelets. 2014;25(8):592-4.
16. Carlioglu A, Simsek E, Durmaz SA, Ozmen HK. Increased mean platelet volume in papillary thyroid cancer. Endocrine Abstracts [Internet]. https://www.endocrine-abstracts.org/ea/0035/ea0035p1114 17 Nisan 2014 [accessed 01 May 2022]
17. Yüksel O, Helvaci K, Başar O, Köklü S, Caner S, Helvaci N, et al. An overlooked indicator of disease activity in ulcerative colitis: mean platelet volume. Platelets. 2009;20(4):277-81.
18. Delgado-García G, Galarza-Delgado DÁ, Colunga-Pedraza I, Borjas-Almaguer OD, Mandujano-Cruz I, Benavides-Salgado D, et al. Mean platelet volume is decreased in adults with active lupus disease. Rev Bras Reumatol Engl Ed. 2016;56(6):504-8.
19. Li N, Yu Z, Zhang X, Liu T, Sun YX, Wang RT, et al. Elevated mean platelet volume predicts poor prognosis in colorectal cancer. Sci Rep. 2017;7(1):10261.
20. Karaman K, Bostanci EB, Aksoy E, Kurt M, Celep B, Ulas M, et al. The predictive value of mean platelet volume in differential diagnosis of non-functional pancreatic neuroendocrine tumors from pancreatic adenocarcinomas. Eur J Intern Med. 2011;22(6):e95-98.
21. Kumagai S, Tokuno J, Ueda Y, Marumo S, Shoji T, Nishimura T, et al. Prognostic significance of preoperative mean platelet volume in resected non-small-cell lung cancer. Mol Clin Oncol. 2015;3(1):197-201.
22. Shen WJ, Fu S, Li N, Li LL, Cao ZG, Li C, et al. Decreased Mean Platelet Volume is Associated with Cervical Cancer Development. Asian Pac J Cancer Prev. 2017;18(7):1769-72.
23. Beyan C, Beyan E. Letter to the editor: The mean platelet volume should not be used in prediction of mortality. Turk J Bioch. 2015;4(1):79-79.
24. Lancé MD, Sloep M, Henskens YMC, Marcus MAE. Mean platelet volume as a diagnostic marker for cardiovascular disease: drawbacks of preanalytical conditions and measuring techniques. Clin Appl Thromb Hemost. 2012;18(6):561-8.

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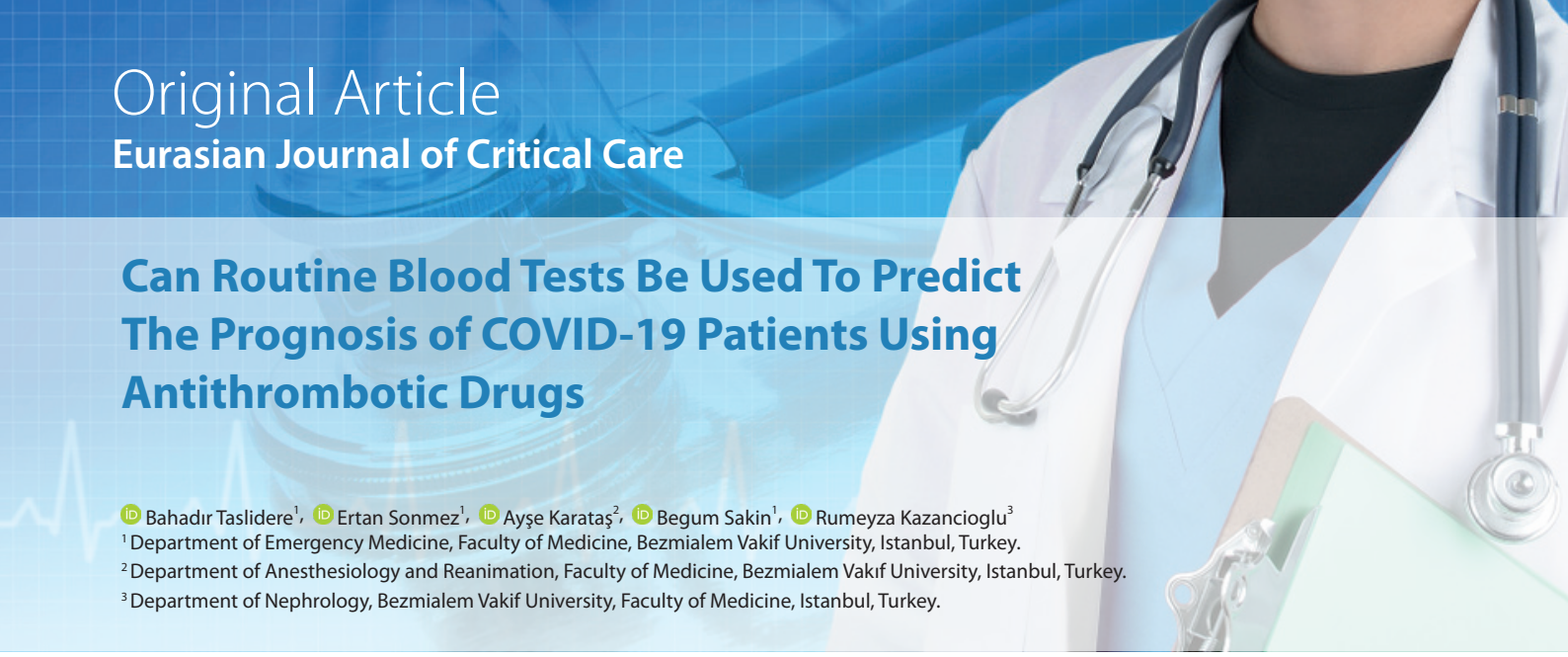

Can Routine Blood Tests Be Used To Predict The Prognosis of COVID-19 Patients Using Antithrombotic Drugs

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Abstract

Background: COVID-19 may predispose to thromboembolism due to excessive inflammation, hypoxia, and immobilization. We investigated whether these antithrombotic drugs are useful or harmful to tackle COVID-19 and which laboratory parameters are more usable for this purpose.

Materials and methods: In our study, patients diagnosed with COVID-19 while using antithrombotic drugs and COVID-19 patients who did not use antithrombotic drugs were compared. Demographic data, laboratory values, clinical results, duration of hospital stay, and mortality were noted and compared.

Results: The study was conducted on 236 patients admitted to the emergency department. The mean value of creatine, LDH, PT, NLR, troponin, and ferritin were higher in the drug-using group. Home quarantine and hospitalization rate was 68.8% (n = 33) in antiplatelet users, and 46.2% (n = 6) in the anticoagulant group.

Conclusion: The difference between the groups may have been caused by the number of chronic diseases and polypharmacy. The interaction of drugs used for the treatment of COVID-19 with antithrombotic agents is unknown. In addition, as the correlation between COVID-19 and thrombosis is not exactly known, adding antithrombotic drugs to the treatment of the disease is controversial. In our study, the biomarkers used to predict prognosis were worse in COVID-19 patients who continued antithrombotic therapy at the therapeutic dose. In the case of antithrombotic agents, the risks that may arise should always be considered. We recommend monitoring routine blood parameters, especially NLR, LDH, PT, APTT, troponin, and ferritin levels, for the prognosis monitoring of COVID-19 patients who will continue their current antithrombotic therapy

Keywords: COVID-19, antithrombotic, prognosis, biomarkers

Introduction

Thromboembolism is a serious, life-threatening clinical problem. Common risk factors include advanced age, immobility, inflammation, infections, and deep vein thrombosis. However, age-related comorbidities, complex polypharmacy, and drug–drug interactions cause increased risk. [1] Although venous stasis, endothelial damage, and hypercoagulation are among the mechanisms that play a role in the pathophysiology of the disease, there is another point to be considered. One rare virus that increases the predisposition to thrombosis is SARS-CoV 2. [2] Thromboembolic events are among the causes of increased morbidity and mortality in COVID-19. The incidence of thromboembolic complications in COVID-19 is between 8–27%. [3,4] The pulmonary thromboembolism rate detected in patients with COVID-19 in the intensive care unit is around 20%. [5] Therefore, The International Society on Thrombosis and Hemostasis (ISTH) recommends the use of antithrombotic drugs in COVID-19 patients. [6] There is currently no accepted approach to recommend the use of prophylactic anti-thrombolytics in COVID-19 patients, even if there are reasonable grounds for providing antithrombotic treatment. In addition, there is no evidence that it is beneficial for non-critical patients. [7,8] However, if anticoagulant therapy is required for patients diagnosed with COVID-19, coagulopathy symptoms should be followed closely. It is important to find suitable parameters for patient follow-up. In our study, COVID-19 patients who were already using antithrombotic agents due to chronic disease were compared with those who did not use the drugs. We investigated whether these antithrombotic drugs are useful or harmful in tackling COVID-19. For this purpose, we used routine blood test data—a potential diagnostic tool for COVID-19.

Materials and Methods

Our study, conducted between 03.11.2020 and 04.30.2020, included patients over the age of 18 who were admitted to the emergency department and diagnosed with COVID-19. Approval was obtained from the Ethics Committee of

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Bezmialem Vakıf University with the decision number 06/110, dated 05.05.2020. The data were retrospectively scanned with the International Classification of Diseases (ICD)- 10 code U07.3 (COVID-19) in the hospital registry. Patients with positive COVID-19 PCR tests or those who were compatible with COVID-19 pneumonia on thoracic tomography were included in the study. These patients were divided into two groups: those who used antithrombotic drugs and those who did not. The reported drugs used by patients were reached through the online prescription provision system. Demographic data, laboratory values, clinical results, and hospital stay duration were recorded. Those using antithrombotic drugs were divided into two groups (antiplatelet (AP) and anticoagulant (AC)) according to the pharmacological type of drugs. Blood samples obtained from the patients were analyzed, and complete blood count, lymphocyte count, neutrophil/lymphocyte ratio (NLR), C-reactive protein (CRP), kidney and liver parameters, cardiac enzymes, lactate dehydrogenase (LDH), coagulation parameters, D-dimer, ferritin, and electrolyte results were evaluated comparatively. Duration of hospital stay, clinical prognosis, and mortality of patients were noted. Ethics committee approval of the relevant institution and university was obtained for this retrospective study.

Consent to Participate: The informed consent process was waived (study conducted retrospectively, permission was obtained from the relevant institution)

Statistical analysis

The compliance of continuous variables to normal distribution was tested by Shapiro Wilk test. Descriptive statistics (mean, standard deviation (SD), minimum (Min.), median (Med.), maximum (Max.)) were used to define continuous variables. Comparison of more than two independent and non-normally distributed variables was made with the Kruskal Wallis test, while two independent, non-normally distributed variables were compared with the Mann-Whitney U test. Chi-Square (Fisher Exact test where appropriate) was used to examine the relationship between categorical variables. The statistical significance level was set at 0.05. The analyses were performed using the MedCalc Statistical Software version 12.7.7 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2013) Program.

Results

The study was conducted on 236 patients admitted to the emergency department, with a mean age of 57.56 ± 15.16 years (range: 19–93 years). There were 107 females (45.3%) and 129 males (54.7%) (Table 1). Eighty-two patients (34.7%) had no history of chronic disease, while 154 patients (65%) did. Among them, 84 patients (5.6%) had one chronic disease, and 70 patients (29.7%) had two or more. Sixty-one patients (25.8%) were using antithrombotic drugs, with 48 (78.6%) using antiplatelet agents; 13 (21.4%) were using anticoagulants, and 175 (74.2%) were not. Common chronic diseases among patients in the study; hypertension 68 patient (28.8%), diabetes mellitus 55 patient (23.3%), coronary artery disease 38 patient (16.1%), chronic lung diseases 34 patient (14.4 %), cerebrovascular diseases 11 patient (4.7 %), chronic kidney diseases 9 patient (3.8%), liver diseases 7 patient (3.0%) and malignancy 15 patient (6.4%) (Table 2). Among those using and not using antithrombotic medication, dyspnea (n=29, 47.5%) and dry cough (n=61, 34.9%) were the most common complaints, respectively, with significant differences between the groups (p=0.001). Desaturation was remarkable among the patients' vital signs using antithrombotic drugs (SO2: 89.97 ± 8.82) (p=0.012). NLR was significantly higher in patients using antithrombotic drugs (p <0.001). LDH was measured as 316 u/L in antithrombotic users and 291 u/L in non-users (p=0.002) (reference range (r.r.) 125–220). In patients using antithrombotic medication and non-users, PT was 18.19 ± 4.52 seconds and 14.8 ± 3.03 seconds, respectively, (r.r.=13.0–14.3) (p <0.001), PTT was 36.35 ± 15.25 sec and 31.86 ± 9.55, respectively, (r.r.=23–35) (p=0.028),

Table 1: Participant Demographics Table

		Mean (Std. dev.)	Range
Age in years		57,56±15,16	19-93
		Number	%
Gender	Female	107	45,3
	Male	129	54,7

Table 2: Drugs, Chronic Diseases and Outcome

		Number	%
Antithrombotic (AT) Drug	Non-users	175	74,2
	Users	61	25,8
Anticoagulant (AC) Drug	Non-users	223	94,5
	Users	13	5,5
Antiplatelet (AP) Drug	Non-users	188	79,7
	Users	48	20,3
Number of Comorbid Diseases	No history of chronic disease	82	34,7
	One chronic disease	84	35,6
	Two or more chronic diseases	70	29,7
Outcome	Discharged/ Home Quarantine	41	17,4
	Hospitalization (Services)	142	60,2
	Intensive Care Hospitalization	26	11,0
	Death	27	11,4

troponin was 72.5 pg/mL and 17.3 pg/mL (p <0.001), respectively, (r.r.=0–31), ferritin was 536 ng/mL and 352 ng/mL, respectively (r.r. 4.63–204) (p=0.043) (Table 3). There were no statistically significant differences in hospital stay duration regarding antithrombotic drug use (p=0.926). The rate of exitus and hospitalization were significantly higher in patients using antithrombotic drugs (p=0.002, p=0.011, respectively) (Table 4). We evaluated the results by grouping antithrombotic agents by type. The first group consisted of 48 people who used antiplatelet drugs (Acetylsalicylic acid 37.7%, Clopidogrel 36.1%, Ticagrelor 4.9%, Dipyridamole 1.6%). There were 13 people in the other group who were using anticoagulant drugs (Apixaban 6.6%, Dabigatran 4.9%, Rivaroxaban 4.9%, Warfarin 4.9%). Home quarantine and hospitalization rate was 68.8% (n = 33) in antiplatelet (AP) users, and 46.2% (n = 6) in the anticoagulant (AC) group. The intensive care and death rates were 31.3% (n = 15) in the AP group and 53.9% (n = 7) in the AC group (p = 0.040). According to the post-hoc pairwise comparison results, the systolic blood pressure, BUN, creatine, LDH, NLO, troponin average of AC users were high, and mean heart rate was low (p <0.05) (Table 5,6)

Table 3: Comparison of Laboratory Parameters According to Antithrombotic Drug Use

	Non-users	Users	P-value
	Mean (Std. dev.) Range	Mean (Std. dev.)W Range	
Body Temperature	37,09±1,08 37 (35-40)	36,88±1,08 36,7 (35-39)	0,236
Systolic Blood Pressure	129,47±25,54 127 (58-229)	140,48±29,95 136 (58-226)	0,004
Heart Rate	100,91±26,19 98 (40-260)	91,75±18,43 91 (43-136)	0,011
Pulse Oximetry (SpO2)	92,7±5,89 94 (62-100)	89,97±8,42 93 (60-99)	0,012
Blood Urea Nitrogen (BUN)	16,81±11,62 13 (5-92)	27,11±16,65 21 (7,48-69)	<0,001
Creatinine	1,03±0,86 0,81 (0,16-7)	1,48±1,54 0,95 (0,6-11)	0,001
Aspartate Transaminase	37,49±38,19 27 (9-445)	31,77±17,46 25 (9-74)	0,352
Alanine Transaminase	37,06±35,54 27 (7-326)	29,98±16,51 25 (9-82)	0,433
Potasyum	4,12±0,52 4 (2,46-6,89)	4,3±0,49 4,23 (3,5-5,5)	0,017
Lactate Dehydrogenase	291,51±223,35 246 (97-1825)	316,18±128,97 280 (56-686)	0,002
Prothrombin Time	14,82±3,03 15 (11-29)	18,19±4,52 17 (13,7-33)	<0,001
Partial Thromboplastin Time	31,86±9,55 33 (11-100)	36,35±15,25 34 (16-120)	0,028
International Normalized Ratio (INR)	1,27±0,2 1,23 (0,66-2,3)	1,36±0,39 1,24 (0,94-2,71)	0,907
White Blood Cell	6,96±3,24 6,1 (1,5-24)	8,4±4,06 7,98 (3,12-24)	0,011
Neutrophil-To-Lymphocyte Ratio (NLR)	3,47±2,06 2,7 (1,1-12)	6,04±5,34 4,4 (0,7-26)	<0,001
Platelet Count (PLT)	228,86±95,56 210 (66-651)	235,67±89,62 213 (102-482)	0,554
Platelet-To-Lymphocyte Ratio (PLR)	174,03±116,06 140 (20-806)	194,63±125,72 157 (50,1-586)	0,276
Mean Platelet Volume	7,71±1,59 7,5 (3,5-11,66)	7,8±1,51 7,68 (4,76-11,44)	0,631
Troponin	17,3±66,93 3,7 (0,2-746,8)	72,58±153,23 14 (1,1-800)	<0,001
D-dimer	468,94±727,09 246 (76-4111)	538,21±747,24 278 (138-3895)	0,056
Creatine Kinase	108,56±148,42 57 (0,1-1053)	83,74±98,01 56 (2-400)	0,464
C-reactive protein (CRP)	57,64±64,22 27,54 (0-295)	76,66±84,34 41 (0,44-304,2)	0,121
Ferritin	351,2±543,38 188 (19,5-4392)	536±834,4 256 (9,9-4800)	0,043

Mann-Whitney U test

Table 4: Outcomes According to Antithrombotic Drug Use

	Antithrombotic Drugs	Non-users		Users		p-value
		Number	%	Number	%	
Outcome	Discharged/ Home Quarantine	32	18,3	9	14,8	0,011
	Hospitalization (Services)	112	64,0	30	49,2	
	Intensive Care Hospitalization	18	10,3	8	13,1	
	Death	13	7,4	14	23,0	

Fisher's Exact test

Table 5: Comparison of Antiplatelet and Anticoagulant Drug Users

		Antiplatelet		Anticoagulant		p
		N	%	N	%	
Outcome	Discharged/ Home Quarantine	8	16,7	1	7,7	0,040
	Hospitalization (Services)	25	52,1	5	38,5	
	Intensive Care Hospitalization	3	6,3	5	38,5	
	Death	12	25,0	2	15,4	

Fisher's Exact test

Discussion

Patients with COVID-19 are at increased risk of thromboembolic events, especially concerning the critical situation and inactivity caused by this disease. Due to the difficulties in diagnosis, the reported incidence of these complications has a wide range of 8–20%. [3,9] Age, gender,

Table 6: Comparison of Laboratory Parameters According to Antiplatalet and Anticoagulant Usage

	Antiplatelet	Antıkoagülan	p-value
	Mean (Std. dev.) Range	Mean (Std. dev.) Range	
Body Temperature	36,93±1 36,75 (35-39)	36,72±1,34 36,1 (35-39)	0,412
Systolic Blood Pressure	144,69±27,91 140 (90-226)	124,92±33,18 130 (58-176)	0,103
Heart Rate	91,44±16,09 90,5 (63-136)	92,92±26,11 100 (43-136)	0,537
Pulse Oximetry (SpO2)	90,29±8,01 93 (60-99)	88,77±10,05 93 (60-96)	0,621
Blood Urea Nitrogen (BUN)	26,7±16,77 20,56 (7,48-69)	28,61±16,81 21,17 (10-68,22)	0,408
Creatinine	1,56±1,69 1,03 (0,6-11)	1,17±0,75 0,95 (0,66-3,45)	0,514
Lactate Dehydrogenase	314,81±133,3 276 (56-686)	321,23±116,35 297 (219-641)	0,731
Prothrombin Time	17,32±3,3 16,2 (13,7-27)	21,39±6,73 20 (13,7-33)	0,047

and the presence of chronic diseases stand out as risk factors. Comorbid diseases are more common in males than in females. [10] In our study, the patients' mean age was 57.56 ± 15.16 years, and 54.7% were male. About 25.8% (n=61) of 236 evaluated patients used antithrombotic agents due to their underlying medical conditions. Patients receiving antithrombotic therapy for underlying conditions are advised to continue these medications (at the same dose) if they are diagnosed with COVID-19. Similarly, all guidelines agree that other hospitalized patients with COVID-19 should receive prophylactic dose antithrombotic. Recent statements by the International Society on Thrombosis and Hemostasis (ISTH) recommend that all patients hospitalized with COVID-19 receive thromboprophylaxis or full-dose therapeutic anticoagulation. [11] A meta-analysis compared patients with COVID-19 treated with a prophylactic dose of anticoagulation with those treated with a therapeutic dose of anticoagulation. The results showed no difference between the two groups in terms of thromboembolism and mortality, [12,13] antithrombotic use at therapeutic doses is discussed in many similar studies. Until now, no joint decision has been identified that determines prophylactic and therapeutic antithrombotic use strategies. Studies showing the safety and efficacy of therapeutic anticoagulant doses in patients with COVID-19 are limited. Our research is valuable in this respect because we compared the prognosis of patients who used antithrombotic and those who did not, using routine blood tests for COVID-19 patients. Thus, we wanted to find out what laboratory values could guide patient management. Moreover, using routine blood tests is advantageous in terms of time and cost. COVID-19 patients are routinely tested for coagulopathy markers, such as D-dimer level, prothrombin time, neutrophil count, LDH, troponin, and platelet count. Laboratory parameters are used to monitor the course and prognosis of the disease. Predictors of disease outcomes in these patients need to be assessed to decrease morbidity and societal burden. For example, the American Society of Hematology should anticipate the need for intensive care; D-Dimer recommends monitoring PT, PTT, and platelet count. [14] Among the parameters examined in our study, the mean BUN, creatine, LDH, PT, PTT, WBC, NLR, Troponin, and Ferritin values were higher among the antithrombotic users. For example, studies have shown that the mortality rate increases when LDH is higher than 255 u/l. In our study, mean LDH was measured as 316 u/l. [15] Data in COVID-19 patients has suggested significant differences in LDH levels between antithrombotic users and non-drug users (p: 0,002). LDH is known to be found in lung tissue; severe infections can cause cytokine-mediated tissue damage and increase LDH release. Therefore, the severity of the disease in COVID-19 patients correlates with the increase in LDH. [16] COVID-19 patients using antithrombotic medication had significantly higher levels of PT, PTT than those without the thrombotic disease. There were no significant differences in levels of INR, D-DIMER, and PLT. PT and PTT are coagulating system factors that can be used for early diagnosis of DIC and had great value in disease prognosis. PT duration is an important finding in terms of coagulopathy, and in our study, it was longer than three seconds. In this case, it can be considered that patients transition from a high coagulation state to a fibrinolytic state due to excessive consumption of coagulation factors. [17] The neutrophil–lymphocyte ratio can help clinicians identify severe cases early, triage early, and initiate effective management. While NLR was 3.47 in those who do not use antithrombotic, it increased to 6.04 in those who did. [18] NLR has been shown to be an independent risk factor for severe disease. Another indicator of poor prognosis is troponin. Elevated troponin levels are common in patients with COVID-19 and are associated with fatal outcomes; [19] while it was 72.58 pg/ml in users, it was 17.3 pg/ml in the other group. The normal value of ferritin varies according to age and gender, so it should be in the range of 20–500 ml/ng. In our study, its mean value was 536 ng/ml among antithrombotic users. [20] The mortality rate was 11.4% (27 people) in the group using antithrombotic drugs and 7.4% in the other group. The patients in the antithrombotic drug user group had a higher case–fatality rate than the non-thrombotic disease group (p=0,011). This difference between mortalities may have been caused by the chronic diseases and polypharmacy because more than one drug is used to treat COVID-19 and the degree of interaction of these drugs with antithrombotic agents is unknown. However, it is known that antivirals used in treatment have such an interaction; [21,22] that is, drug–drug interactions can cause negative outcomes in patients. Hydroxychloroquine, azithromycin, oseltamivir, lopinavir, ritonavir, and favipiravir are frequently used

to treat COVID-19 patients in our country. As is known, lopinavir and ritonavir are potent cytochrome P450 3A4 inhibitors; therefore, they may increase the concentrations of direct-acting oral anticoagulants. [23] The rate of those with two or more chronic diseases was 65.3%. In our study, like various other studies, it was observed that the disease was more severe as the number of chronic diseases increased. [24] Even if the presence of chronic disease is important in the prognosis, it has been observed that it is more important to have two or more chronic diseases. Chronic diseases observed in our patients were hypertension (59%), diabetes mellitus (42.6%), heart diseases (32.8%), chronic lung diseases (24.6%), cerebrovascular diseases (13.1%), kidney diseases (11.5%), liver diseases (4.9%), and malignancy (4.9%). The incidence of diseases with high prevalence in the population was also high in our study. The high number of chronic diseases and drug–drug interactions due to the antivirals may worsen the prognosis. Since the mechanism between COVID-19 and thrombosis has not been fully explained, adding antithrombotic drugs to the treatment is controversial. In our study, the biomarkers used to predict prognosis were worse in COVID-19 patients who continued antithrombotic therapy at the therapeutic dose. We also evaluated the results by grouping antithrombotic agents by type. According to the results, the requirement for intensive care was higher in those using anticoagulant drugs. While the rate of intensive care admission and exitus was 31.3% in those using antiplatelet agents, this rate was 53.9% in those using anticoagulants. The mortality rate was higher in those using antithrombotic drugs compared to non-users. The mean value of BUN, creatine, LDH, PT, PTT, WBC, NLR, troponin, and ferritin were higher in the drug-using group. This difference between the groups may have been caused by the number of chronic diseases and polypharmacy.

Limitations

In the study, a single ICD code was scanned. Therefore, it is certain that it will miss COVID-19 cases that may be classified under different codes.

Conclusion

Antithrombotics should not be used in therapeutic doses for COVID-19. We recommend monitoring routine blood parameters, especially NLR, LDH, PT, PTT, troponin, and ferritin levels, for the prognosis monitoring of COVID-19 patients who will continue their current antithrombotic therapy.

References

1. Raskob GE, Angchaisuksiri P, Blanco AN, et al. Thrombosis: a major contributor to global disease burden. *Arterioscler Thromb Vasc Biol.* 2014; 34(11): 2363-71. doi: 10.1161/ATVBAHA.114.304488.
2. Goeijenbier M, van Wissen M, van de Weg C, et al. Review: viral infections and mechanisms of thrombosis and bleeding. *J Med Virol.* 2012; 84(10): 1680-96. doi: 10.1002/jmv.23354.
3. Lodigiani C, Iapichino G, Carenzo L, et al. Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy. *Thromb Res.* 2020; 191: 9-14. doi: 10.1016/j.thromres.2020.04.024
4. Klok FA, Kruip MJHA, van der Meer NJM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID 19. *Thromb Res.* 2020; 191: 145-7. doi: 10.1016/j.thromres.2020
5. Lim W, Meade M, Lauzier F, et al. Failure of anticoagulant thromboprophylaxis: risk factors in medical-surgical critically ill patients. *Crit Care Med.* 2015; 43(2): 401-10. doi: 10.1097/CCM.0000000000000713
6. Thachil J, Tang N, Gando S, et al. ISTH interim guidance on recognition and management of coagulopathy in COVID-19. *J Thromb Haemost.* 2020; 18(5): 1023-6. doi: 10.1111/jth.14810
7. Iba T, Nisio MD, Levy JH, et al. New criteria for sepsis-induced coagulopathy (SIC) following the revised sepsis definition: a retrospective analysis of a nationwide survey. *BMJ Open.* 2017; 27; 7(9): 017046. doi:10.1136/bmjopen-2017-017046
8. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet.* 2020; 28; 395(10229): 1054-62. doi:10.1016/S0140-6736(20)30566-3
9. Middeldorp S, Coppens M, van Haaps TF, et al. Incidence of venous thromboembolism in hospitalized patients with COVID-19. Comparative Study. J *Thromb Haemost.* 2020; 18(8): 1995-2002. doi: 10.1111/jth.14888.
10. Murray MK, Bode K, Whittaker P. Gender-specifc associations between coronary heart disease and other chronic diseases: crosssectional evaluation of national survey data from adult residents of Germany. *J Geriatr Cardiol.* 2019; 16(9): 663–70. doi: 10.11909/j.issn.1671-5411.2019.09.004.
11. Flaczyk A, Rosovsky RP, Reed CT, et al. Comparison of published guidelines for management of coagulopathy and thrombosis in critically ill patients with COVID 19: implications for clinical practice and future investigations. *Crit Care*. 2020; 16; 24(1): 559. doi: 10.1186/s13054-020-03273-y
12. Paranjpe I, Fuster V, Lala A, et al. Association of treatment dose anticoagulation with in-hospital survival among hospitalized patients with COVID-19. *J Am Coll Cardiol.* 2020; 7; 76(1): 122-4. doi: 10.1016/j.jacc.2020.05.001.
13. Siegal DM, Barnes GD, Langlois NJ, et al. A toolkit for the collection of thrombosis-related data elements in COVID-19 clinical studies. *Blood Adv.* 2020; 22; 4(24): 6259-73. doi: 10.1182/bloodadvances.2020003269.
14. Al-Samkari H, Karp Leaf RS, Dzik WH, et al. COVID and coagulation: bleeding and thrombotic manifestations of SARS-CoV2 infection. *Blood.* 2020; 23; 136(4): 489-500. doi: 10.1182/blood.2020006520.
15. Henry BM, Aggarwal G, Wong J, et al. Lactate dehydrogenase levels predict coronavirus disease 2019 (COVID-19) severity and mortality: A pooled analysis. *Am J Emerg Med*. 2020; 38(9): 1722–6. doi: 10.1016/j.ajem.2020.05.073.
16. Zhang ZL, Hou YL, Li DT, Li FZ. Laboratory findings of COVID-19: a systematic review and meta-analysis.

Scand. *J Clin Lab Invest.* 2020; 80(6): 441-7. doi: 10.1080/00365513.2020.1768587.

17. Long H, Nie L, Xiang X, et al. D-Dimer and Prothrombin Time Are the Significant Indicators of Severe COVID-19 and Poor Prognosis. *Biomed Res Int.* 2020: 6159720. doi: 10.1155/2020/6159720.

18. Yang AP, Liu JP, Tao WQ, Li HM. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. *Int Immunopharmacol*. 2020; 84: 106504. doi: 10.1016/j.intimp.2020.106504.

19. Lippi G, Lavie CJ, Sanchis-Gomar F. Cardiac troponin I in patients with coronavirus disease 2019 (COVID-19): evidence from a meta-analysis. *Prog Cardiovasc Dis.* 2020; 63(3): 390-391. doi: 10.1016/j.pcad.2020.03.001.

20. Velavan TP, Meyer CG. Mild versus severe COVID-19: laboratory markers. *Int J Infect Dis.* 2020; 95: 304-7. doi: 10.1016/j.ijid.2020.04.061.

21. Sivaloganathan H, Ladikou EE, Chevassut T. COVID-19 mortality in patients on anticoagulants and antiplatelet agents. *Br J Haematol.* 2020; 190(4): 192-5. doi: 10.1111/bjh.16968.

22. Egan G, Hughes CA, Ackman ML. Drug interactions between antiplatelet or novel oral anticoagulant medications and antiretroviral medications. *Ann Pharmacother*. 2014; 48(6): 734-40. doi: 10.1177/1060028014523115.

23. Agarwal S, Agarwal SK. Lopinavir-Ritonavir in SARS-CoV-2 Infection and Drug-Drug Interactions with Cardioactive Medications. *Cardiovasc Drugs Ther*. 2020; 12; 1-14. doi: 10.1007/s10557-020-07070-1.

24. Guan WJ, Liang WH, Zhao Y, et al. Comorbidity and its impact on 1590 patients with Covid-19 in China: a nationwide analysis. *Eur Respir J.* 2020; 55(5): 2000547. doi: 10.1183/13993003.00547-2020

Original Article
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D-Dimer Levels and Prognostic Features in Pulmonary Embolism

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Abstract

Background: The aim of our study is to investigate the efficacy of D-dimer marker in patients who applied to the emergency department with a preliminary diagnosis of pulmonary embolism. Study Design: Retrospective study.

Materials and methods: This study was conducted retrospectively at Bursa Uludağ University Faculty of Medicine Hospital between January 2018 and December 2018. Patients whose D-dimer levels were checked considering the preliminary diagnosis of pulmonary embolism were included in the study.

Results: A total of 3411 patients were included in the study. In all patients, the diagnosis of PE was made by computed tomography pulmonary angiography. Examination of 1968 patients with (+) D-dimer revealed new diagnosis in 702 patients (35.67%). Pulmonary embolism was diagnosed in a total of 74 patients (10.54%) whereas the most common alternative diagnoses was 33.62% (n=236) pneumonia. On examination of 1443 patients with negative D-dimer levels, pulmonary embolism was diagnosed in 7 (3.14%) patients whereas the most common other diagnoses was 44.84% (n=100) Acute Coronary Syndrome. However, in the D-dimer positive patient group, the rate of newly diagnosed patients requiring clinical and intensive care hospitalization was found to be significantly higher.

Conclusion: In conclusion, even if pulmonary embolism is not detected in D-dimer positive cases, it is thought that these patients need further investigation, considering the frequency of serious conditions requiring clinical and intensive care unit admission.

Keywords: Emergency medicine, pulmonary embolism, D-Dimer

Introduction

D-dimer is a fibrin degradation end product and plasma D-dimer levels increases as a result of thrombosis and fibrin breakdown. Balance exists between fibrin formation and degradation under physiological conditions. Hence, plasma D-dimer level may be a biological indicator of hemostatic abnormalities and thrombosis[1].

D-dimer levels may be elevated in thrombotic diseases such as Pulmonary Embolism (PE) and Venous Thromboembolism (VTE). D-dimer is one of the diagnostic parameters in PE and Deep Vein Thrombosis (DVT)[2]. A high D-dimer level alone is not sufficient to diagnose PE. However, it can be used to exclude PE in patients with a low or moderate probability of PE[3]. The specificity of D-dimer in confirming the diagnosis of PE and DVT is low[2].

Comorbidities such as cancer, inflammatory diseases, infection, aortic dissection, pneumonia, and renal failure are pathological causes that affect D-dimer levels. Pregnancy and age are non-pathological causes affecting D-dimer levels[4].

A D-dimer concentration of ≥500 ng/mL is considered positive and <500 ng/mL is considered negative[5]. D-dimer levels increase with age. Therefore, the specificity of the D-dimer test is reduced in elderly patients (> 50 years). Many studies recommends the formula; Age x 10 = ng/mL, for threshold value in patients over 50 years of age[6]. For patients considered to be at low risk of PE, a normal D-dimer (<500 ng/mL) effectively excludes PE and typically no further testing is required[3].

The aim of our study is to determine the relationship between the prognostic features and existing comorbidities of patients who admit to the emergency department with preliminary diagnosis of PE, and thus to investigate the effectiveness of D-dimer marker.

Materials and Methods:

This study, which was conducted retrospectively with the approval of Bursa Uludag University Faculty of Medicine Clinical Research Ethics Committee, dated 16 June 2021,

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number 2021-8/25 (Annex-1), within the scope of specialization thesis. A total of 3411 patients over the age of 18 years, who appiled to Uludag University Faculty of Medicine Emergency Service between January 2018 and December 2018 with a pre-diagnosis of PE and D-dimer levels examined, were included.

The list of patients whose D-dimer levels were investigated within the specified date was obtained from the electronic medical record system. Patient information was obtained from Uludağ University electronic medical record system and calculated according to age, gender, plasma D-dimer concentration and pregnancy status. The D-dimer cut-off value, was determined according to patients' new diagnosis, ongoing diseases and hospitalization-discharge information.

500 ng/ml plasma D-dimer concentration was accepted in young patients whereas the corrected formula (Age x 10 = ng/mL) was used in elderly (≥ 50 years) patients.

These values and above were considered D-dimer positive, while those below these values were considered D-dimer negative. D-dimer threshold value in pregnant women was accepted as 1000 ng/ml. In all patients, the diagnosis of PE was made by computed tomography pulmonary angiography.

Patients under the age of 18, patients whose D-dimer examination was requested with diagnoses other than PE, patients whose D-dimer value could not be determined due to coagulation of the sample or low amount, and repeated admissions of the same patient were not included in the study.

In calculating the sample size of the study, Power was determined by taking at least 80% and Type-1 error 5% for each variable. Descriptive statistics for the categorical variables in the study were expressed as mean, standard deviation, numbers (n) and percentages (%). Chi-square test was calculated to determine the relationships between D-Dimer level and other categorical variables. Statistical significance level (a) was taken as 5% in the calculations and SPSS (IBM SPSS for Windows, ver.25) statistical package program was used for analysis.

Results

A total of 3411 patients; 1963 male (57.5%) and 1448 female (42.5%), were included in the study. The mean age was calculated as 59.74 (+/-18.08).

Examination of 1968 patients with (+) D-dimer revealed new diagnosis in 702 patients (35.67%), whose distribution is shown in Table-1.

As seen in the table, PE was diagnosed in a total of 74 patients (10.54%) and the most common other diagnoses were 33.61% (n=236) pneumonia and 13.96% (n=98) ACS, respectively. Other less common diseases are arterial embolism, intracranial hemorrhage, gastrointestinal bleeding, urinary tract infection, bone fracture, aortic dissection and sepsis. Out of 925 newly diagnosed patients in the emergency department, 315 (34.05%) were admitted to the Intensive Care Unit (ICU), 410 (44.32%) hospitalized, while 188 (20.32%) patients were discharged.

Table 1: Distribution of new diagnoses in D-dimer positive patients.

		(+) D-Dimer		*p.
		N	%	
Primary New Diagnosis	PN	236	33,61%	,001
	ACS	98	13,96%	
	PE	74	10,54%	
	DVT	32	4,55%	
	ARI	31	4,41%	
	PLE	27	3,84%	
	CVD	22	3,13%	
	CEL	21	2,99%	
	ML	18	2,56%	
	PX	8	1,13%	
	ELT	5	0,71%	
	AP	3	0,42%	
	OTHER	127	18,09%	
	TOTAL	702	100%	

** Significance level according to Pearson Chi-square test results*
PN: Pneumonia
ACS: Acute Coronary Syndrome
PE: Pulmonary Embolism
ARI: Acute Renal Insufficiency
DVT: Deep Vein Thrombosis
PLE: Pleural Effusion
CVD: Cerebrovascular Disease
CEL:Celult
ML: Malignant
PX: Pneumothorax
ELT: Electrolyte Disorder
AP: Acute Appendicitis

In 1522 (77.34%) of the D-dimer positive patients, additional problems developed on the basis of existing diseases were detected and treated. The distribution of these diseases is shown in Table-2.

As seen in the table, the most common accompanying diseases were malignancy in 24.57% (n=374), Coronary Artery Disease (CAD) in 14.38% (n=219) and hypertension in 12.68% (n=193) respectively. Other less common diseases are previous history of CVD, previous history of PE, cirrhosis, heart valve replacement and Alzheimer's.

No emergency pathology was detected in 1146 (58.23%) patients with positive D-dimer and they were discharged with recommendations after their initial evaluation.

Examination of 1443 patients with negative D-dimer revealed new diagnoses in 223 patients (15.45%) and their distribution is shown in Table 3.

As seen in the table, PE was diagnosed in 7 (3.13%) patients, while the frequency of most common other diagnoses was 44.84% (n=100) ACS and 24.21% (n=54) pneumonia, respectively. Other less common diseases were arterial em-

Table 2: Comorbidities in D-dimer positive patients

		(+) D-Dimer		*p.
		N	%	
Eski tanı	ML	374	24,57%	,001
	CAD	219	14,38%	
	HT	193	12,68%	
	COPD	139	9,13%	
	DM	115	7,55%	
	HF	98	6,43%	
	CRF	97	6,37%	
	RM	51	3,35%	
	AST	26	1,70%	
	DVT	15	0,98%	
	EPL	5	0,32%	
	OTHER	190	12,48%	
	TOTAL	1522	100%	

** Significance level according to Pearson Chi-square test results*
ML: Malignant
CAD: Coronary Artery Disease
HT: Hypertension
COPD: Chronic Obstructive Pulmonary Disease
DM: Diabetes Mellitus
HF: Heart Failure
CRF: Chronic Renal Failure
RM: Rheumatological Disease
AST: Asthma
DVT: Deep Vein Thrombosis
EPL: Epilepsy

Table 3: Distribution of new diagnoses in patients with negative D-dimer.

		D-Dimer (-)		*p.
		N	%	
Primary New Diagnosis	ACS	100	44,84%	,001
	PN	54	24,21%	
	PX	8	3,58%	
	PE	7	3,13%	
	CEL	7	3,13%	
	AP	5	2,24%	
	ML	4	1,79%	
	CVD	3	1,34%	
	ELT	3	1,34%	
	ARI	2	0,89%	
	DVT	2	0,89%	
	OTHER	25	11,21%	
	TOTAL	223	100%	

** Significance level according to Pearson Chi-square test results.*
ACS: Acute Coronary Syndrome
PN: pneumonia
PX: Pneumothorax
PE: Pulmonary Embolism
CEL: Cellulite
AP: Acute Appendicitis
ML: Malignant
CVD: Cerebrovascular Disease
ELT: Electrolyte Disorder
ARI: Acute Renal Failure
DVT: Deep Vein Thrombosis

bolism, pleural effusion, atrial fibrillation, gastrointestinal bleeding, intracranial hemorrhage. Out of 223 newly diagnosed patients in the emergency department, 95 (42.6%) were admitted to the ICU, 70 (31.4%) to relevant clinics, while 54 (24.2%) patients were discharged.

In 806 (55.85%) of negative D-dimer patients, additional problems developing on the basis of existing diseases were detected and treated. Their distribution is shown in Table-4.

As seen in the table, the most common accompanying diseases were CAD in 19.35% (n=156), hypertension in 16.50% (n=133), malignancy in 12.90% (n=104) and COPD in 12.28% (n=99). Other less common diseases are previous history of PE, atrial fibrillation, previous history of CVD and valve replacement. When 806 cases with previously diagnosed diseases were evaluated; 92 patients (11.4%) were treated in ICU whereas 81 patients (10.0%) were hospitalized in relevant clinics. While 5 (0.6%) patients refused treatment and left the emergency department, a total of 628 (77.9%) patients were discharged. No pathology was detected 1207 (83.64%) patients with negative D-dimer and they were discharged with recommendations after their initial evaluation.

A comparison of the results of D-dimer positive and D-dimer negative patients is shown in Table 5 and Figure 1.

As seen in the Table 5 and Figure 1, 17.17% (n=338) of D-dimer positive patients were admitted to the ICU, while 23.53% (n=463) were hospitalized. 8.80% (n=127) of patients with negative D-dimer were admitted to the intensive

Table 4: Comorbidities in D-dimer negative patients.

		D-Dimer (-)		*p.
		N	%	
Eski Tanı	CAD	156	19,35%	,001
	HT	133	16,50%	
	ML	104	12,90%	
	COPD	99	12,28%	
	DM	76	9,42%	
	RD	34	4,21%	
	HF	33	4,09%	
	CRF	24	2,97%	
	AST	22	2,72%	
	DVT	15	1,86%	
	EPL	11	1,36%	
	OTHER	99	12,28%	
	TOTAL	806	100%	

** Significance level according to Pearson Chi-square test results.*
CAD: Coronary Artery Disease
HT: Hypertension
ML: Malignant
COPD: Chronic Obstructive Pulmonary Disease
DM: Diabetes Mellitus
RD: Rheumatological Disease
HF: Heart Failure
CRF: Chronic Renal Failure
AST: Asthma
DVT: Deep Vein Thrombosis
EPL: Epilepsy

Table 5: Comparison of the results of D-dimer positive and D-dimer negative patients

		(-) D-Dimer		(+) D-Dimer		*p.
		N	%	N	%	
Result	DS	1207	83,65%	1146	58,23%	,001
	ICU	127	8,80%	338	17,17%	
	CLN	101	7,00%	463	23,53%	
	TR	8	0,55%	14	0,71%	
	EX	0	0,00%	5	0,25%	
	UA	0	0,00%	2	0,10%	
	TOTAL	1443	100%	1968	100%	

** Significance level according to Pearson Chi-square test results.*
DS: Discharge
ICU: Intensive care unit
CLN: Clinic
TR: Treatment rejection
EX: Exitus
UA: Unauthorized abandonment

care unit, while 7.00% (n=101) were hospitalized. D-dimer was positive in 13 out of 28 pregnats patients without any additional pathology.

In this study, the sensitivity of D-dimer was 91.36%, specificity 43.12%, positive predictive value 3.76%, and negative predictive value 99.51%, respectively.

Discussion

The D-dimer test is best used in conjunction with clinical probability assessment in the diagnosis of PE. The negative predictive value of the D-dimer test, studied with quantitative methods, is high and a normal D-dimer level excludes acute PTE or DVT with a sensitivity of >95%, especially in outpatients, patients without comorbidities, and with low and moderate clinical probability[7,8].

The specificity of plasma D-dimer level is low[9]. In our study, PE was diagnosed in only 74 of 1968 D-dimer positive cases. However, for patients considered to be at low risk of PE, a normal D-dimer (<500 ng/mL) effectively excludes PE and usually no further testing is required in this regard[8]. In our study, PE was diagnosed in 7 out of 1443 negative D-dimer cases. In this study, the sensitivity of D-dimer was 91.36%, specificity 43.12%, positive predictive value 3.76%, and negative predictive value 99.51%.

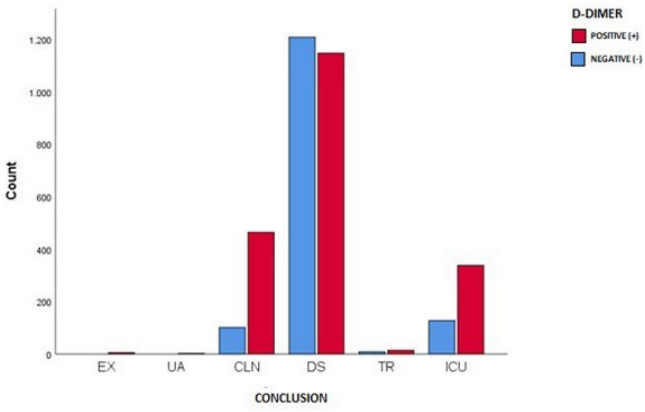

Figure 1: D-dimer positive patients

D-dimer levels increases in advanced ages (>50 years)[9]. In a multinational prospective study, the proportion of patients in whom PTE could be excluded without false-negative findings was reduced from 6.4% to 30% by adding 10 mg/L to age, instead of the standard 500 mg/L D-dimer level in patients aged> 50 years[10]. In our study, we used the age-adjusted formula when determining the threshold value for old patients.

Acute diseases increases D-dimer levels[9]. In a study by Giuseppe Lippi et al. including 1647 patients who admitted to the emergency department and D-dimer levels checked with a preliminary diagnosis of VTE, the most common diagnoses were 15.6% infection, 12.1% VTE, 9.4% syncope, 8.9% cardiac failure, 8.2% trauma and 5.8% malignancy respectively[11]. In the study of Halide Akbaş et al. involving 671 patients, the most common diagnoses in patients with high D-dimer levels who admitted to the emergency department were 19% infection, 15.9% heart and circulatory diseases, 12.9% non-specific diseases, 12% atypical chest pain, 10.7% malignancy and 7.6% PE respectively[12]. Likewise, in our study, PE was diagnosed only in 74 patients (10.54%), while the most common diagnoses were 33.61% (n=236) pneumonia and 13.96% (n=3). 98) ACS.

Cancer is an important cause of venous thrombosis[13]. Levitan et al., in their study, reported a high incidence of VTE in cancer patients[14]. Elderly patients with lung cancer complicated with PE have dyspnea, chest pain, and/or hemoptysis[15]. These findings are similar to the clinical presentation of PE[16]. As a matter of fact, in our study, malignancy was detected in 18 patients (2.56%) in the newly diagnosed positive D-dimer group, while the most common accompanying disease was malignancy with a rate of 24.57% (n=374) out of 1522 patients with a previous diagnosis.

Studies have concluded that there is a positive correlation between plasma D-dimer levels and stroke[17]. Joan Montaner et al., in their study to elucidate the etiology of stroke, showed that D-dimer levels are high in acute, subacute, and chronic periods[18]. Folsom et al. found that high serum basal D-dimer levels are associated with ischemic and cardioembolic stroke[19]. In our study, obstructive CVD was found in 3.13% (n=22) of the newly diagnosed patients.

D-Dimer level increases in renal dysfunction[9]. Gregor Linder et al., in their study on 1305 patients, found that D-dimer levels increased in patients with eGFR<60 mL/min[20]. In our study, chronic renal failure was found in 6.37% (n=97) of D-dimer positive cases.

D-dimer levels increase during normal pregnancy[21]. In a study conducted on healthy pregnant women by measuring

D-dimer levels during the three trimesters, D-dimer levels increased progressively during pregnancy and reached the highest level in the third trimester[22]. In our study, 13 out of 28 pregnant patients were found to have positive D-dimer with no additional pathology.

The specificity of plasma D-dimer levels in the diagnosis of PE is low[9]. Halide Akbaş et al., in their study that D-dimer levels were not effective in predicting hospitalization[12]. However, in our study, although the diagnosis of PE was low in D-dimer positive cases, other diseases requiring hospitalization were found to be significantly higher ($p<0.05$). While the rate of hospitalization to ICU was 17.2% in D-dimer positive patients, this rate was 8.8% in D-dimer negative patients. The clinical hospitalization rate was 23.5% in D-dimer positive patients whreas this rate was 7% in D-dimer negative patients.

Limitations

Since our study is retrospective, the lack of some data, such as risk scoring, is the limiting factor for our study.

Conclusion

D-dimer has a low specifity in the diagnosis of PE. However, other than PE, the rate of patients requiring clinical and especially ICU hospitalization is high in D-dimer positive cases. Therefore, even if PE is not detected in D-dimer positive cases, it is thought that further investigation should be considered having in mind the probability of serious conditions such as malignancy that may not be detected during emergency examination and investigations. There is need for new studies on this subject.

References

1. Weitz JI, Fredenburgh JC, Eikelboom JW. A Test in context: D-Dimer. J Am Coll Cardiol 2017;70:2411-2420.
2. Keller K, Beule J, Balzer JO, Dippold W. D-Dimer and thrombus burden in acute pulmonary embolism. Am J Emerg Med 2018 ;36:1613-1618.
3. Bass AR, Fields KG, Goto R, Turissini G, Dey S, Russell LA. Clinical decision rules for pulmonary embolism in hospitalized patients: a systematic literature review and meta-analysis. Thromb Haemost 2017;117:2176-2185.
4. Wakai A, Gleeson A, Winter D. Role of fibrin D-dimer testing in emergency medicine. Emerg Med J 2003;20:319–325.
5. Geersing GJ, Janssen KJ, Oudega R, et al. Excluding venous thromboembolism using point of care D-dimer tests in outpatients: a diagnostic meta-analysis. BMJ 2009;339:b2990.
6. Farm M, Siddiqui AJ, Onelöv L, et al. Age-adjusted D-dimer cut-off leads to more efficient diagnosis of venous thromboembolism in the emergency department: a comparison of four assays. J Thromb Haemost 2018;16:866-875.
7. Carrier M, Righini M, Djurabi RK, et al. VIDAS D-dimer in combination with clinical pre-test probability to rule out pulmonary embolism. A systematic review of management outcome studies. Thromb Haemost 2009;101:886-892.
8. den Exter PL, van Es J, Klok FA, et al. Risk profile and clinical outcome of symptomatic subsegmental acute pulmonary embolism. Blood 2013;122:1144-1149.
9. Kabrhel C, Mark Courtney D, Camargo CA Jr, et al. Factors associated with positive D-dimer results in patients evaluated for pulmonary embolism. Acad Emerg Med 2010;17:589-597.
10. Righini M, Van Es J, Den Exter PL, et al. Age-adjusted D-dimer cutoff levels to rule out pulmonary embolism: the ADJUST-PE study. JAMA 2014;311:1117-1124.
11. Lippi G, Bonfanti L, Saccenti C, Cervellin G. Causes of elevated D-dimer in patients admitted to a large urban emergency department. Eur J Intern Med 2014;25:45-48.
12. Akbaş SH, Can M, Kılıçarslan I, Özdem S, Çete Y, Gültekin M. Acil Servise Başvuran Yüksek D-dimer Düzeyli Hastalarda Tanı Dağılımı ve D-dimer Düzeylerinin Hastaneye Yatış ve Ölüm Oranları ile İlişkisi. Turk J Emerg Med 2004;4:149-154.
13. Falanga A, Russo L, Milesi V, Vignoli A. Mechanisms and risk factors of thrombosis in cancer. Crit Rev Oncol Hematol. 2017;118:79-83.
14. Levitan N, Dowlati A, Remick SC, et al. Rates of initial and recurrent thromboembolic disease among patients with malignancy versus those without malignancy. Risk analysis using Medicare claims data. Medicine 1999;78:285-291.
15. Wang S, Zimmermann S, Parikh K, Mansfield AS, Adjei AA. Current Diagnosis and Management of Small-Cell Lung Cancer. Mayo Clin Proc 2019 ;94:1599-1622.
16. Stein PD, Gottschalk A, Saltzman HA, Terrin ML. Diagnosis of acute pulmonary embolism in the elderly. J Am Coll Cardiol 1991 ;18:1452-1457.
17. Hamatani Y, Nagai T, Nakai M, et al. Elevated plasma d-dimer level is associated with short-term risk of ischemic stroke in patients with acute heart failure. Stroke 2018; 49:1737-1740.
18. Montaner J, Perea-Gainza M, Delgado P et al. Etiologic diagnosis of ischemic stroke subtypes with plasma biomarkers. Stroke 2008;39:2280-2287.
19. Folsom AR, Gottesman RF, Appiah D, Shahar E, Mosley TH. Plasma d-dimer and incident ischemic stroke and coronary heart disease: the atherosclerosis risk in communities study. Stroke 2016;47:18-23.
20. Lindner G, Funk GC, Pfortmueller CA, et al. D-dimer to rule out pulmonary embolism in renal insufficiency. Am J Med 2014 ;127:343-347.
21. Kovac M, Mikovic Z, Rakicevic L, et al. The use of d-dimer with new cutoff can be useful in diagnosis of venous thromboembolism in pregnancy. Eur J Obstet Gynecol Reprod Biol. 2010;148:27-30.
22. Gutiérrez García I, Pérez Cañadas P, Martínez Uriarte J, et al. D-dimer during pregnancy: establishing trimester-specific reference intervals. Scand J Clin Lab Invest 2018;78:439-442.

Original Article
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Evaluation of Nursing Home Residents Applying to The Emergency Service

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Abstract

Background: Emergency deparment (ED) has an important role at the care of nursing home residents and acts facilitator role at the acute care, admission to the hospital, unexpected injuries and hospitals. Our research is aiming the evaluation of the demographic and clinical features of the nursing home patients applying to ED.

Materials and methods: The nursing home residents who are aged 18 and over 18 applying to ED at the date between 15.04.2014-15.05.2015 are included to this respective study. In the study, demographic information of the patients and diagnosis and treatment information in the emergency room were evaluated.

Results: 51 (52%) of the patients are male. The average age of them is 73. The most frequent disease observed in their medical history is Alzheimer's disease. The physical examinations of the patients resulted that they have cachexia and dehydration. The oftenest diagnosises detected are lung disease (23.5%), infection (22.4%) and malnutrition (22.4%). It has been also detected that 45% of them admitted to hospital and 3.1% of them are to die. The rate of intensive care admission is 64% while the service admission rate is 36%.

Conclusion: The rate of the admission of the nursing home residents to ER and especially to intensive care units is quite high. To ameliorate this condition, training and supervision of the nursing home workers should be made more carefully and often. Since we do not have sociodemographic and clinical data about the nursing home residents applying to ED, more study must be made about this area.

Keywords: Emergency Service, Nursing home resident, geriatric patient.

Introduction

The elderly population is increasing all over the world. People over the age of 65 made up 7.5% of the population in our country in 2012. This rate is expected to increase to 10.2% in 2023, 20.8% in 2050 and 27.7% in 2075(1). According to TurkStat data, life expectancy at birth is estimated to be 74.6 years for 2010 and 78.5 years for 2050 for both sexes; life expectancy at birth for 2013 is 74.7 years for men and 79.2 years for women, and it is estimated that this ratio will be 75.8 years for men and 80.2 years for women in 2023(2). In the United States of America (USA), the elderly population constitutes 13% of the population but accounts for more than 1/3 of hospitalizations and total health expenditures. (3). Various factors such as changes in family structure, economic conditions, and women working outside the home contribute to the decline in the care of the elderly in the home(4).

The emergency department plays an important role in the care of nursing home residents, facilitating the management of unexpected illness and injury, acute care and hospitalization(5). Long-term care patients are a very small proportion of ED patients, but their health needs require a large share of resources(6). Older adults may often have multiple comorbidities, complex medical histories, cognitive impairment and dementia, and have limited abilities and physiological capacities to compensate for critical illness. Their limitations in vision, hearing and cognitive function may alter their ability to express symptoms, tell their medical history and even give personal information(5). Many of these patients have a progressive neurological disease such as Alzheimer's or vascular dementia. When elderly nursing home residents are ill, they are often brought to the emergency department with current symptoms and little documentation about their illness(3). All these factors take up a significant amount of time of the physicians and other health personnel in the emergency department, as well as increasing the length of stay of these patients in the emergency department and increasing the number of examinations and consultations.

The World Health Organization (WHO) takes into account the ¬chronological definition of old age and considers

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this period as¬ "65 years and older". The older population is also divided into subgroups. The age group of 65-74 years is defined as young age or early age, the age group of 74-84 years as old age or middle age, and the age group of 85 years and older as oldest age or advanced age(7). However, the WHO definition is used as a basis in national and international studies of aging.

Old age is considered a physiological event and is defined as the loss of physical and mental powers in such a way that they cannot be restored, the decrease of the organism's potential to establish a balance between internal and external factors, and the physical and mental deterioration of the person(8). The physical, mental and social changes that occur with age lead to a decrease in the functional capacity of older people and increase their need for assistance(9).

The problems that occur in old age are not only due to chronological aging. In addition to rapid population growth, urbanization, conversion to nuclear family due to internal and external migration, decrease in the number of extended families, economic problems, women's participation in the labor force, lack of suitable and sufficient space for the elderly due to downsizing of houses as a result of conversion to nuclear family, young people's view of old age, intergenerational communication problems, deterioration of health in old age, and addiction have made home care for the elderly more difficult. Although the traditional approach in our country has been to house the elderly in the family, for the above reasons, the elderly in our country are now being housed in facilities that are different from the family environment, and the need for services for the elderly in our major cities is increasing(10).

Despite the importance of emergency services in the care of nursing home patients, there have been few studies of the use of emergency services by these patients in the United States. The aging of society is leading to increasingly frequent problems with health care services for the elderly. It is known that the geriatric age group accounts for approximately 15% of all emergency department admissions, and this is expected to increase to 25% in the 2020s(11).

Most emergency physicians are not specifically trained in geriatric care, and many report that they are not comfortable managing these patients(12). Knowledge of the characteristics of geriatric conditions presenting to the emergency department can be helpful in making the correct diagnosis and providing emergency treatment. Older patients have been reported to present to the ED more frequently and with more complex problems than younger patients, to require more intensive care, to undergo more radiologic and laboratory procedures, to stay longer in the ED, and to be admitted to hospitals and intensive care units more frequently than other age groups(13).

Of the elderly patients discharged after admission to the ED, 27% return to the ED, are admitted as inpatients, or die within 3 months(10).

In our literature search, we found that there are few studies worldwide on the assessment of nursing home admissions to the emergency department. The purpose of our study is to examine the demographic and clinical characteristics of nursing home patients admitted to the emergency department who cause high rates of hospitalization and intensive care unit admissions.

Materials and Methods

This retrospective descriptive epidemiological study was initiated with the decision of the Education Planning Committee of Kayseri Training and Research Hospital dated 12/11/2015 under number 47. Patients aged 18 years and older who presented to the emergency department of our hospital between 15.04.2014 and 15.05.2015 and were accommodated in nursing homes and private care facilities were included in the study. The parameters to be studied were printed on a form. The information about the patients was entered into the forms by the physicians in the respective departments. The information used and analyzed in our study came from scanning these forms and records.

The research data were entered into the IBM SPSS 20.0 statistical program and reviewed after data entry was completed.

Descriptive statistics (frequency, percentage distribution), chi-square test for comparison of categorical variables between two groups, one-way analysis of variance (Anova, F-test) for comparison of more than two group averages, t-test for students between different groups of social variables, and paired samples t-test for different variables of the same groups were used as statistical analysis in the analysis of the data obtained from the study evaluation forms. Results are expressed in terms of mean±SD or frequency (percentage); $p < 0.05$ was considered statistically significant at 95% confidence interval.

The emergency department of our hospital consists of 4 departments. It consists of the examination unit, which usually treats patients in the green zone (sore throat, urinary symptoms, abdominal pain, etc.); the trauma unit, which treats trauma patients with low trauma score; the monitored observation unit, which treats patients with chest pain, unconsciousness, severe respiratory distress, melena, etc. or patients with poor general condition are treated; and the resuscitation unit, where unconscious patients, patients with cardiac arrest, patients with high trauma score, patients with poor general condition, ventricular tachycardia (VT), ventricular fibrillation (VF), or patients requiring isolation are treated.

Results

The study included 98 nursing home and elderly home patients over 18 years of age who presented to the emergency

Table 1: Sociodemographic characteristics

Gender	Number (n)	Percentage (%)
Male	51	52
Female	47	48
Age groups		
18-64	21	21
65-74	25	26
75-84	30	31
85 and above	22	22
Social security		
Social Security Administration	57	58
Green card	20	20
No social security	21	22
Form of transfer		
Outpatient clinic	73	75
Nursing home vehicle	24	24
Private vehicle	1	1
Application unit		
Resuscitation	60	61
Trauma	15	16
Supervised observation	12	12
Examination	11	11
Admission time range		
08:00-16:00	56	57
16:00-24:00	28	29
00:00-08:00	14	14

Table 2: Main complaints at admission

Main complaint	Number (n)	Percentage (%)
Neurological problem	18	18.4
Problem with respiratory tract	18	18.4
Swallowing disorder	14	14.3
Falling	13	13.3
Fire	9	9.2
Gastrointestinal System (GIS) symptoms	8	8.2
Chest pain	2	2
Abnormal laboratory findings	2	2
Other	14	14.3
Total	98	100,0

Table 3: Number and percentage of blood and other tests ordered.

Blood and other tests requested	Number (n)	Percentage (%)
Complete blood count	80	81.6
Emergency biochemistry	78	79.6
Coagulation tests	73	74.5
Cardiac enzymes	53	54.1
Blood gas	41	41.8
Complete urinalysis	37	37.8
Fasting blood glucose	30	30.8
Other examinations	20	20,4

department between 04/15/2014 and 04/15/2015. Fifty-one (52%) of the patients were male and forty-seven (48%) were female. The average age was 73 years. The most common age group was 75-84 years, followed by 65-74 years. The demographic data of the patients are shown in Table 1.

Analysis of the patients' vital signs at the time of admission revealed that the measured temperature was above 37.5 in 9.2% of the patients. In addition, in 12.2% of these patients, the mean arterial pressure (MAP) was less than 65 mmHg.

When analyzing the presenting complaints, it was found that the most common reasons for admission were neurological and respiratory problems, each accounting for 18%. All the main reasons for admission are shown in Table 2 in number and percentage. 32.7% of patients had more than one complaint.

The most common disease was Alzheimer's disease. Hypertension and diabetes mellitus were the second and third most common diseases. The rates of requested examinations are shown in Table 2. The most frequently requested imaging modality was direct radiography, at 54%. computed tomography (CT) of the brain was requested in 34% of cases.

On physical examination, the general outlook of the patients was rated as 20.4% poor, 40.8% fair, and 38.8% good. Cachexia and dehydration were noted in 24% of patients. Absence of swallowing reflex in 14.3% of patients, presence of positive thoracic interrogation findings in 34.7% and positive abdominal examination findings in only 7.1% of patients. It was found that 6.1% of patients already had a urinary catheter and 14.3% of patients did not have an electrocardiography (ECG) in sinus rhythm. In 29.6% of patients, the glaskow coma scale (GCS) score was 14 and below, whereas in the other patients, a GCS score of 15 was obtained.

In a systematic analysis of the patients' diagnoses, the most common diagnosis was pulmonary disease (23.5%), followed by infections and malnutrition (22.4%). Mental status disorder and acute renal failure (ARF), chronic renal failure (CRF), or abnormal electrolyte findings were found in 21.4% of diagnoses. These diagnoses were followed by cerebrovascular events. The systemic diagnoses of the patients are listed in Table 4.

Table 4: Systemic group-specific diagnoses received by patients.

Diagnoses	Number (n)	Percentage (%)
Diseases of the lungs	23	23,5
Infectious diseases	22	22,4
Malnutrition	22	22,4
Mental state disorder	21	21.4
ARF, CRF, or abnormal electrolyte findings	21	21.4
Cerebrovascular incident	17	17.3
Heart disease	10	10.2
GIS diseases	7	7.2
Non-cardiac chest pain	3	3.1
Drug intoxication or side effect	3	3.1
Diseases of the urogenital system	2	2
Injury of limbs	3	3.1
Trauma to chest, abdomen, or pelvis	5	5.1
Miscellaneous trauma	7	7.1

When interventional procedures were analyzed, urinary catheter insertion was the most common procedure. When patients were analyzed by outcome, it was found that 52% of patients were discharged and 35% were hospitalized. It was noted that 9 patients were referred to the intensive care unit. Adding this figure, it was found that 45% of patients were hospitalized and 3.1% died. No statistically significant difference was found when the outcome of patients was compared with age groups (p=0.418).

When patients were analyzed by place of hospitalization, it was found that 64% were admitted to the intensive care unit (ICU) and 36% to the infirmary.

When comparing the place of admission and length of stay in the ED, it was found that the length of stay in the ED was significantly different and longer for patients admitted to the resuscitation unit than for patients admitted to other units (f=6.61, p<0.001). It was found that the majority of trauma patients were discharged within one hour, while the majority of monitored observation patients were discharged within 60-120 minutes. In the resuscitation unit, where the majority of patients were evaluated, it was found that the evaluation of 46.7% of the patients was completed between 2-4 hours. The resuscitation unit was the 2nd unit where patients stayed the longest (41.7%; >4 hours).

32.7% of the patients had more than one presenting complaint. However, there was no significant difference between the presence of more than one presenting complaint and the length of stay in the emergency department (p=0.26). However, in the presence of more than one complaint, the outcome of the patients was different even if not statistically significant. While the discharge rate was 60.6% in patients without multiple complaints, it was 34.4% in patients with multiple complaints. In addition, the hospitalization rate of patients with more than one complaint increased significantly. While the hospitalization rate was 28.8% in patients without more than one complaint, it was 50% in those with more than one complaint. Statistically significant results were obtained when the presence or absence of more than one complaint was compared with the general appearance of the patients (p<0.05). Only 10.6% of the patients without more than one complaint had a poor general condition while 40.6% of the patients with more than one complaint had a fair and poor general condition.

Although statistically significant results were not found when the time of admission and the units in which the patients were evaluated in the emergency department were compared, patients were most frequently admitted to the emergency department by 112 ambulance and then most frequently by nursing home vehicle in all time periods.

Patients with a history of Alzheimer's disease were more likely to be diagnosed with malnutrition (p<0.005), but the presence of a history of Alzheimer's disease was not significant in terms of ARF, CRF and electrolyte disorders (p=0.05). Nephrology and neurology consultations were requested at similar rates in patients with and without a history of Alzheimer's disease.

Significant results were obtained when the patients were analyzed in terms of outcome and hospitalization according to GCS (p<0.05, f:15,616). Of the patients with GCS≤14, 51.7% were hospitalized and 20.7% were referred for intensive care. However, 66.7% of patients with a GCS of 15 were discharged.

A statistically significant difference was found when patients were compared according to GCS according to the diagnoses of ARF, CRF, abnormal electrolyte findings, which was similar to the result obtained in the GCS-nephrology consultation comparison (p<0.01). While 48.3% of patients with GCS≤14 had ARF, CRF or electrolyte disturbance in their diagnosis, 44.8% of these patients were asked for nephrology consultation. These rates were 10.1% and 7.2% in patients with a GCS of 15.

Although there was no statistically significant difference between the GCS and the request for neurological consultation and the diagnosis of cerebrovascular disease, it was notable that 76% of patients with a GCS≤14 were not diagnosed with a cerebrovascular event and 83% of these patients were not asked for a neurological consultation (p=0.32). However, when comparing GCS diagnosis to mental status disorder diagnosis, 45% of patients with a GCS≤14 were diagnosed with a mental status disorder (p<0.001).

The comparison of patients with a fever of 37.5 and above with patients with a current clinical diagnosis of infection was also significant (p<0.01). However, it was noted that 13 patients had normal fever despite a diagnosis of infection.

Patients who had dehydration on physical examination were more likely to be diagnosed with ARF, CRF, abnormal electrolyte findings, and malnutrition (p<0.01).

Patients diagnosed with ARF, CRF, and electrolyte disturbances were more likely to have a nephrology consultation requested than other patients ($p<0.01$). Half of the patients diagnosed with ARF, CRF and abnormal electrolyte findings remained in the emergency department for more than 2 hours.

When patients were analyzed by length of stay in the ED, 71.4% of patients stayed longer than 2 hours in the ED. The highest rate was found between 120 and 240 minutes (39.4%).

When patient outcomes and hospitalizations were analyzed according to mean arterial pressure (MAP) at the time of admission, only 16.7% of patients with an MAP<65 mmHg were discharged, and more than 80% were admitted or referred as inpatients. 4/5 of hospitalized patients were admitted to the intensive care unit. Of the patients with MAP≥65 mmHg, 57% were discharged. Similarly, 57.5% of these patients were treated in the intensive care unit**.**

When the length of stay of patients in the emergency department was analyzed according to the time of admission, no significant difference was found.

Only 2% of patients were readmitted to the ED within the last 72 hours.

Finally, no significant difference was found between age groups in terms of patient outcome and length of stay in the ED.

Discussion

Of the patients included in the study, 51 (52%) were male and 47 (48%) were female. In studies conducted abroad, the proportion of female patients ranged from 63 to 72%(3,5,6,14). The reason for this difference could be the small total number of patients in our study and the sociocultural differences between our country and other countries. In our study, the mean age was 73 years and 4/5 of the patients were geriatric patients. In the study by Ackermann R. et al, the percentage of geriatric patients was 84%, which was similar to our study(3).

Sixty-one percent of the patients were examined in the resuscitation department of our emergency department, which was determined to be the red area. Although there was no similar classification in the studies, in a study conducted in Canada, 35.3% of patients were classified as very urgent (emergent) in a narrow classification (nonurgent, urgent, emergent(6)). The reason for the significant difference could be that most patients in nursing homes in our country have advanced illnesses that can no longer be cared for by their relatives and need to be treated, and these patients have to be waited on by their caregivers in desperation until their consciousness changes and are then taken to the emergency room.

¾ of patients were admitted to the hospital by ambulance. In a study conducted abroad, the rate of admission by ambulance was 80%(4). This rate is similar to that in our study. The reasons for the high rate of admission to the ambulance may be that the care centers do not have a sufficient number and equipment of vehicles, the general condition of the patients is poor, and the patients do not have the possibility of outpatient admission.

More than half of the patients were admitted during working hours. This rate was reported as 44% in the study by Wang H. et al, 42.9% in the study by Ackermann R. et al, and 56.8% in the study by Iwata M. et al(3,5,14). This difference may be due to the fact that nursing home staff, who provide continuous care to patients, work during the day and sufficient staff are available during working hours.

When patients were analyzed by admission complaints, the most common reasons for admission were neurological (18%) and respiratory (18%) conditions. In a study by Ackermann R. et al, which is similar to our study, respiratory problems were the most common reason for admission and the second most common reason for admission was mental status change(3). In a meta-analysis of twenty-seven studies, the most common prior diagnosis when patients were referred to the emergency department was pneumonia (11%), and the second and third most common diagnoses were soft tissue injuries and fractures, each with 10%(15). The fact that alzheimer's disease (AD) is the most common chronic disease in our study and that these patients often present with neurologic and respiratory problems due to acute alterations in consciousness may be the reason for the high rate of patients with respiratory and neurologic complaints in our study.

The most common diagnostic blood count and emergency biochemistry values were requested from the patients. The third most frequently requested blood test was the measurement of cardiac enzyme levels. Because nursing home patients are usually frail, have limited information about their background and illnesses, and do not have adequate awareness at the time of admission, blood tests and imaging are requested for diagnostic purposes. In addition, the majority of patients included in our study were elderly, and some diseases in elderly patients have atypical findings and presentations.

Although direct radiography was requested in 55% of our patients, CT in 47%, ultrasonography (USG) in 7.1%, and magnetic resonance imaging (MRI) in 6.1%, these rates were 85.4% direct radiography, 35% CT, 2.8% USG, and 0.7% MRI(6) in a similar study. The small number of trauma patients in our study may have caused this difference. We think that the fact that there was a period of approximately 8 years between the date of the similar study and our study is responsible for the higher rates of computed tomography and MRI orders in our study. New imaging modalities can be used frequently to prevent malpractice and misdiagnosis. We believe that the number of USG orders has increased because of the widespread use of USG by emergency physicians and the ease of access to the radiology specialist on

daily duty in the emergency department of our hospital.

Physical examination of our patients revealed cachexia in ¼, dehydration in ¼, and impaired oral hygiene in 41%. The high rate of cachexia and dehydration in nursing home patients suggests that the nutritional needs of patients are not being adequately met. To ensure that these patients are fed according to their caloric needs and adequate hydration, the necessary staff, especially the dietitian, should be available with adequate equipment. It is believed that the necessary care to provide adequate and balanced nutrition to these patients is not shown and is more likely to be neglected than financial concerns. The fact that patients' oral hygiene is also compromised indicates that their personal care is inadequate.

The most common diagnoses are pulmonary disease, infection, malnutrition, mental status disorders, ARF-CRF, or abnormal electrolyte findings. In a study by Sahryn L. et al, the most common diagnoses were falls, abnormal laboratory findings, and respiratory system problems(16). In another study, the most common diagnoses were sepsis and infectious diseases 23.7%, cardiac disease 20.9%, trauma 18%, respiratory disease 15.5%, and genitourinary system disease 14.9%(5). In a similar study, the most common diagnoses were musculoskeletal system problems (24%), cardiovascular system diseases (16%), and respiratory system diseases (13%)17).

Mental status disorder in patients can have many causes; it can occur secondary to events such as infections, abnormal electrolyte findings, cerebrovascular disease (SVD), or primary causes such as Alzheimer's disease. The reason for the low number of cardiac system diagnoses in our study is that patients in nursing homes in our city are usually end-stage patients, and these patients usually come to the emergency department with diagnoses such as poor general condition, mental status disorders, oral intake disorders, and respiratory distress.

The most common procedure was the insertion of a urinary catheter. This procedure is now widely used as diagnostic urine test (UA) in patients with impaired mental status and inability to urinate, and urinary catheterization in critically ill patients (sepsis, etc.) with ARF-CRF and electrolyte disturbances who need to undergo fluid intake follow-up during follow-up.

When patients were analyzed by the outcome, it was found that 52% were discharged and 45% were hospitalized. Three percent of patients had their tumor removed. Our hospitalization rates are similar to those reported in the literature(3,5). 2/3 of hospitalized patients were admitted to the intensive care unit. However, in a study by Wang H. et al.(5), this rate was 19.5%. The lack of clear criteria for intensive care unit admission leads to a higher rate of hospitalization of nursing home patients with multiple diseases who need close follow-up and special care.

When the patients are analyzed according to the length of stay on the basis of their place of admission, the patients who wait the longest in the emergency department are the patients admitted to the resuscitation unit. On the other hand, patients admitted to the trauma unit wait the least. The reasons for waiting longer for patients admitted to the resuscitation unit are that the general condition of the patients is worse and more tests are needed for diagnosis, the patients usually have more problems combined together and therefore more consultations are requested, and the time until the intensive care unit is found and the referral process is realized is prolonged in intensive care unit bed occupancy. The reasons for the low waiting time of patients admitted for trauma may be that the traumas in the patients are mostly local and low energy, the patients can usually be diagnosed quickly with x-ray and blood tests that would prolong the length of stay of the patients are not requested.

When the outcome of the patients according to the place of admission is analyzed, it is seen that the highest rates of hospitalization and referral are from the resuscitation and examination unit. The reason for this high rate of hospitalization and referral in the examination unit, which is normally considered to be the green area, is that patients who are evaluated here after being brought by outpatient or nursing home vehicle are then transferred to the yellow area. During this period, the duration of examination and evaluation in this area, where the highest patient density is experienced in the emergency department, is prolonged in parallel with this.

Hospitalization rate and deterioration in general appearance increase in patients with multiple complaints. Since these patients with multiple complaints are complicated patients, the consultation rate and hospitalization rate increase in parallel.

Malnutrition and cachexia are more common in patients with Alzheimer's disease. On the other hand, ARF, CRF and electrolyte disorders, nephrology and neurology consultations were found equally in patients with and without a history of Alzheimer's disease. The reason for this is that these patients receive sufficient fluid intake but do not receive adequate and balanced nutrition and remain malnourished. Even with adequate fluid intake, patients are not diagnosed with ABI, CRF and electrolyte disorders and nephrology consultation is not requested. Neurology consultation is not requested as there is no significant change in the level of consciousness of these patients.

When the outcome and hospitalization of patients according to GCS were analyzed, it was found that patients with GCS<15 had a higher rate of hospitalization and were also hospitalized in the intensive care unit at a higher rate. Among patients with GCS<15, 48.3% were diagnosed with ARF, CRF or electrolyte disturbance, and 44.8% of these patients were asked for nephrology consultation. These patients living in the nursing home with a borderline level of consciousness are monitored by caregivers who do not have adequate training, while partial changes in their consciousness and oral intake are not taken into account and they are followed for a long time in this way. Patients are usually

brought to the emergency room when acute symptoms such as fever, seizures, etc. develop. Therefore, these patients are diagnosed with ARF and abnormal electrolyte disorders when they are brought to the emergency department.

It was found that the patients' GCS score did not affect the request for a neurological consultation. In patients with a history of dementia, no neurological consultation is requested if there is no difference between patients with dementia in the past, if the neurological examination is normal, or if a metabolic disorder explains the change in consciousness. However, about half of the patients with GCS<15 have mental status disorder, and most of the patients' mental status disorders are thought to be due to dementia and metabolic causes in the past.

Physical examination of the patients revealed that nutritional problems were associated with cachexia, dehydration, and impaired oral hygiene. Although the presence of cachexia in patients may be associated with dementia, dehydration and impaired oral hygiene suggest that patients are not adequately nourished or properly cared for.

The average length of stay in the emergency department was 4 hours. This duration was calculated to be approximately 5 hours (289 min) in the study by Wang et al.(5) After a clinical diagnosis is made, patients are rapidly transferred to the wards for further investigations, necessary treatments are initiated in the wards, and consultations that are considered less urgent should also be requested in the appropriate departments after hospitalization. It was found that the waiting time in the emergency department did not affect the outcome of patients.

Patients with a mean arterial pressure <65 mmHg were usually admitted as inpatients. These patients were admitted to the ICU at a high rate of 4/5. Because these patients had poorer general health and required positive inotropic support, they were more likely to be admitted to the ICU.

Only 2 (2%) patients were admitted to the ED within the last 72 hours. A similar rate (3%) was found in the study by Wang et al.(5)

Limitations

The main limitations of the study are the small number of nursing homes and patients in our country and the retrospective nature of the study. Another important limitation is the small number of patients with sufficient data. Another limitation of the study is that the examination results of patients admitted to the emergency department were subject to the interpretation of the examining physician.

Conclusion

Our study was important in evaluating the admissions of nursing home patients to the emergency department and ensuring that the necessary precautions are taken. Our study demonstrated the importance of having the necessary history information and care from trained staff to avoid wasting time with these complicated patients who come to the ED with very little information. Again, thanks to the special units to be set up for these patients, unnecessary visits to the emergency room and requests for examinations can be avoided. Although important because it is one of the rare hospice studies conducted in our nation's emergency departments, it is obvious that many more studies should be conducted.

References

1. Türkiye Halk Sağlığı Kurumu. Türkiye Sağlıklı Yaşlanma Eylem Planı ve Uygulama Programı. Ankara: Anıl Reklam Matbaa; 2015.
2. TÜİKAdrese Dayalı Nüfus Kayıt Sistemi 2010 Yılı Sonuçları. http://www.tuik.gov.tr/PreHaberBultenleri.do?id=15. Erişim Tarihi:12/01/2016
3. Ackermann RJ, Kemle K a, Vogel RL, Griffin RC. Emergency department use by nursing home residents. Ann Emerg Med. 1998;31(6):749–57.
4. Özçakar N, Kartal M, Dirik G, Tekin N,Güldal D. Burnout And Relevant Factors In Nursıng Staff : What Affects The Staff Working In An Elderly Nursing Home? Turkish J Geriatr. 2012;15(3):266–72.
5. Wang HE, Shah MN, Allman RM, Kilgore M. Emergency department visits by nursing home residents in the United States. J Am Geriatr Soc. 2011;59:1864–72.
6. Gruneir A, Bell CM, Bronskill SE, Schull M, Anderson GM, Rochon PA. Frequency and pattern of emergency department visits by long-term care residents--a population-based study. J Am Geriatr Soc. 2010;58:510–7.
7. Özşaker E, Demir-Korkmaz F, Dölek M. Acil Servise Başvuran Yaşlı Hastaların Bireysel Özelliklerinin ve Başvuru Nedenlerinin İncelenmesi. Turkish J Geriatr. 2011;14(2):128–34.
8. Külahçı H, Emiroğlu ON. The Usability of the Omaha System in Identifying the Health Needs , Nursing Interventions and Outcomes. Sağlık Bilimleri Fakültesi Hemşirelik Derg. 2012;1:36–50.
9. Ardahan M. Yaşlılık ve Huzurevi. Aile ve Toplum Dergisi. 2010;20:25–32.
10. Karadağ B. Acil polikliniğine başvuran ve gözleme alınan hasta profili: Üç yıllık inceleme. Akad Geriatr kongresi. 2009;
11. Hwang U, Morrison RS. The geriatric emergency department. J Am Geriatr Soc. 2007;55:1873–6.
12. Samaras N, Chevalley T, Samaras D, Gold G. Older Patients in the Emergency Department: A Review. Ann Emerg Med; 2010;56:261–9.
13. Logoglu A, Ayrik C, Kose A, Bozkurt S, Demir F, Narci H, et al. Examination of Demographic Characteristics of Nontraumatic Elderly Cases Admitted to the Emergency Department. Turkish J Emerg Med. 2013;13:171–9.

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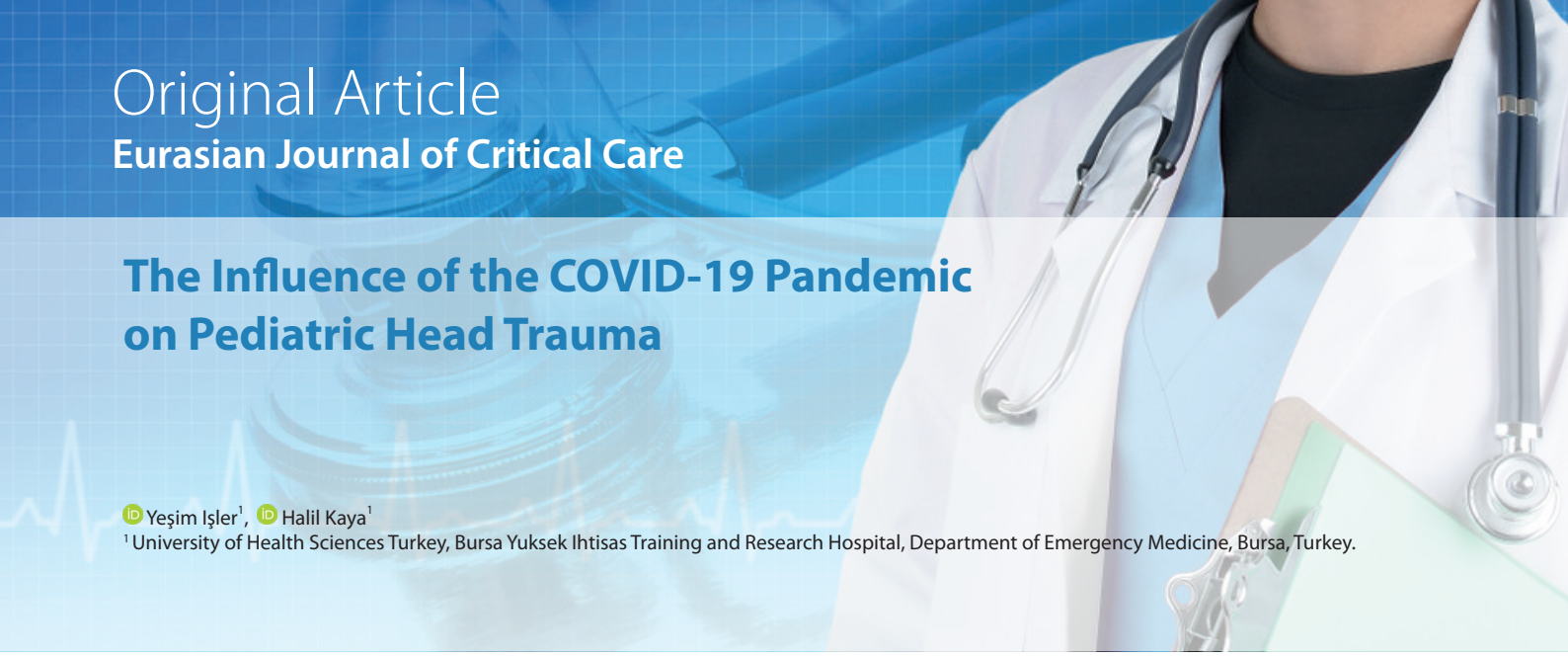

The Influence of the COVID-19 Pandemic on Pediatric Head Trauma

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Abstract

Background: We compared the pre-COVID-19 (2019–2020) and COVID-19 (2020–2021) periods in terms of the incidence of pediatric head trauma (PHT) cases. The incidence of PHT during the pre- COVID-19 pandemic (PCP) and COVID-19 pandemic (CP) periods was investigated.

Materials and Methods: A total of 6,158 patients with PHT seen in a tertiary emergency department between March 15, 2019 and March 15, 2021 were retrospectively reviewed. 1,198 patients for whom were included in the study. The age, gender, type of trauma, Glasgow Coma Scale score, computerized brain tomography findings, and consultation results of the patients were recorded.

Results: The records of 729 and 469 PHT cases in the PCP and CP periods were analyzed, respectively. The number of patients with PHT was significantly lower in the CP period ($p < 0.001$). While the incidence rates of falls, traffic accidents, and bicycle accidents were higher in the PCP period ($p > 0.05$), trauma rates were lower in the CP period ($p < 0.001$). The incidence of falling from a height was highest in the 7–12 years age group ($p < 0.05$). Cranial fracture, and epidural, subdural, and intracranial bleeding rates, were higher ($p > 0.05$) in the PCP period. While the mortality rate was higher in the PCP period, the treatment refusal rate was higher in the CP period ($p < 0.001$).

Conclusion: The rate of PHT decreased, while treatment refusal rates increased during the CP period. However, mortality rates due to PHTs were higher before the CP.

Key words: COVID-19, emergency department, pediatric head trauma, pre-pandemic, pandemic

Introduction

Coronavirus disease 2019 (COVID-19), a novel disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in China in December 2019 and quickly spread worldwide[1]. Various restrictions have been implemented by governments, including a national curfew in many countries[2]. To reduce the spread of the virus, businesses, schools, and childcare facilities closed worldwide. Social distancing measures were helpful and necessary for slowing down the transmission of the virus[3]. Similarly, social restrictions were imposed in many countries. The effect of those regulations on rates of hospitalization for head trauma (HT) injuries, especially pediatric HT (PHT), is still unknown.

PHT is one of the most important medical problems worldwide, and one of the most common causes of morbidity and mortality in the pediatric population[4].Studies have shown that more than 500,000 children present to emergency rooms due to HT; 60,000 receive inpatient treatment and 7,000 die each year in the United States[5]. Many of the injuries that cause PHTs are preventable, and with appropriate precautions the number of injuries and adverse consequences could be reduced[6].

This study evaluated PHT cases presenting to a tertiary emergency department during the pre-COVID-19 pandemic (PCP) and COVID-19 pandemic (CP) periods. We also obtained demographic and injury profiles of PHT cases and compared them between the two periods. To the best of our knowledge, this is the first study to focus on PHT during the CP.

Materials and Methods

In total, 6,158 patients with HT under the age of 18 years, who presented to the emergency department of the tertiary-level University of Health Sciences, Bursa Yüksek Ihtisas

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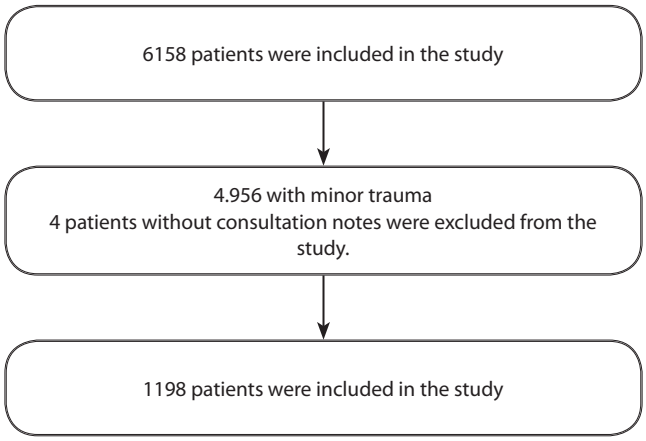

Figure 1: Flowchart on the study

Training & Research Hospital (Bursa, Turkey) between 15 March 2019 and 15 March 2021, were retrospectively reviewed. In total, 4,956 patients who had minor HT (Patients without loss of consciousness, amnesia, vomiting, diffuse headache) but did not require a consultation, and 4 who did not have a consultation note, were excluded from the study. Ultimately 1,198 patients for whom a neurosurgery consultation was requested and information was available were included (Figure 1). Written approval was obtained from the ethics committee of the hospital during the planning phase of our study (2011-KAEK-25 2021/04-15).

Patient data were obtained from patient cards and epicrisis reports, obtained from the hospital's patient information management system. The age, gender, type of trauma, Glasgow Coma Scale (GCS) score, computerized brain tomography (CBT) findings, and consultation results were recorded. On CBT scans, intracranial hemorrhage, skull fractures, epidural hematomas, and subdural hematomas were considered as severe traumatic brain injury. Patients under the age of 18 without HT were excluded. The patients were divided into two groups as PCP and CP period.

The chi-square test was performed to compare the PCP and CP periods in terms of patient gender, GCS severity, trauma type, injury type, and outcome; only outcome showed significance ($p < 0.001$).

Statistical Analysis

IBM SPSS Statistics for Windows (version 21.0; IBM Corp., Armonk, NY, USA) was used for the statistical analyses. As descriptive statistics, continuous variables are expressed as median (interquartile range, IQR), while categorical variables are expressed as number (%). The Kolmogorov-Smirnov test was used to test the normality of the data distribution. Chi-squared and Fisher's exact tests were used to analyze categorical variables. P-values < 0.05 were considered statistically significant.

Results

A total of 1,198 patients were included in this study. The median age of the patients was 5 (IQR: 3–9) years; 759 (63.4%) were in the 0–6 age group and 779 (65%) were male. In total, 709 patients (60.9%) presented to the emergency department during the PCP period. The GCS classifies traumatic brain injuries as mild (score of 14–15), moderate (score of 9–13), or severe (score of 3–8). The classifies traumatic brain injuries as mild grade 1, moderate grade 2 and severe grade 3. The GCS grade of 1,163 patients (97.1%) was 1. Falling from a height was the most common cause of trauma (n = 1,060; 88.5%); 503 (42.0%) of these patients were hospitalized (Table 1).

Table 1: Clinical and Demographic data

		n	%
		Frequency	Percent
Age group	0-6	759	63.4
	7-12	288	24.0
	13-17	151	12.6
Gender	Female	419	35.0
	Male	779	65.0
Period	Pre-Covid-19	729	60.9
	Covid-19	469	39.1
GCS	Grade 1	1163	97.1
	Grade 2	13	1.1
	Grade 3	22	1.8
Trauma type	Falling from height	1060	88.5
	Traffic accident	92	7.7
	Bicycle accident	46	3.8
	ICB	12	1.0
Injury type	Fracture	321	26.8
	Epidural	36	3.0
	Subdural	63	5.3
	Fracture + Bleeding	34	2.8
	No	732	61.1
Other traumas	No	1115	93.1
	Extremity	30	2.5
	Chest	14	1.2
	Abdomen	14	1.2
	Vertebra	25	2.1
Outcome	Hospitalized	503	42.0
	Discharged	675	56.3
	Ex	6	.5
	Treatment refusal	11	.9
	Referral	3	.3
	Total	1198	100.0

The GCS classifies traumatic brain injuries as mild (score of 14–15) (grade 1), moderate (score of 9–13), (grade 2) or severe (score of 3–8) (grade 3).

During the PCP period, the mortality rate in the emergency department was higher than in the CP period, while the treatment refusal rate was higher in the latter period (Table 2).

Table 2: Analysis of pre-Covid 19 and Covid 19 periods and some variables

			Period		Total	Chi-square Test
			Pre-Covid	Covid		
Gender	Female	n	262	157	419	χ^2=0.762, p>0.05
		%	62.5%	37.5%	100.0%	
	Male	n	467	312	779	
		%	59.9%	40.1%	100.0%	
GCS	Grade 1	n	709	454	1163	χ^2=0.303, p>0.05
		%	61.0%	39.0%	100.0%	
	Grade 2	n	7	6	13	
		%	53.8%	46.2%	100.0%	
	Grade 3	n	13	9	22	
		%	59.1%	40.9%	100.0%	
Trauma type	Falling from height	n	653	407	1060	χ^2=3.416, p>0.05
		%	61.6%	38.4%	100.0%	
	Traffic accident	n	52	40	92	
		%	56.5%	43.5%	100.0%	
	Bicycle accident	n	24	22	46	
		%	64.8%	59.5%	100.0%	
Injury type	ICB	n	8	4	12	χ^2=3.734, p>0.05
		%	66.7%	33.3%	100.0%	
	Fractures	n	203	118	321	
		%	63.2%	36.8%	100.0%	
	Epidural	n	21	15	36	
		%	58.3%	41.7%	100.0%	
	Subdural	n	32	31	63	
		%	50.8%	49.2%	100.0%	
	Fracture + Bleeding	n	21	13	34	
		%	61.8%	38.2%	100.0%	
Outcome	No	n	444	288	732	χ^2=24.151, p<0.001
		%	60.7%	39.3%	100.0%	
	Hospitalization	n	276	227	503	
		%	54.9%	45.1%	100.0%	
	Discharge	n	444	231	675	
		%	65.8%	34.2%	100.0%	
	Ex	n	5	1	6	
		%	83.3%	16.7%	100.0%	
	Treatment refusal	n	2	9	11	
		%	18.2%	81.8%	100.0%	
	Referral	n	2	1	3	
		%	66.7%	33.3%	100.0%	
Total		n	729	469	1198	
%			60.9%	39.1%	100.0%	

Incidence of falling from a height was highest in the PCP than CP period in the 7–12 years age group (Table 3).

Table 3: Analysis of pre- Covid-19 and Covid-19 periods and age

	Variable	n	median (IQR: 25-75)	p value
Age	Pre-Covid	729	5(3-10)	<0.001
	Covid	469	4(2-8)	
	Total	1198	5(3-9)	

In our study neurosurgery consultation was requested for 729 patients during the PCP period and 469 during the CP period. In the former period, the frequency of consultations, number of patients hospitalized in the neurosurgery department, and mortality rate of patients with HT due to falling from a height, being involved in a traffic accident, or falling off a bicycle all decreased. However, the rate of treatment refusal increased during the CP period.

Discussion

In this study, we retrospectively compared the incidence of PHTs between the PCP and CP periods. To the best of our knowledge, this is the first retrospective study to evaluate the impact of the CP on the incidence of PHTs in a tertiary hospital setting.

The literature indicates that the number of admissions to the emergency department decreased during the CP[7]. Similarly, the number of patients presenting to the emergency department decreased during the SARS epidemic[8]. Oseran *et al*. reported a 33.7% decrease in emergency department admissions in 2020 compared to 2019[9]. There have also been some reports of a decrease in emergency department admissions for life-threatening myocardial infarctions, hyperglycemic crisis, surgical emergencies, and acute orthopedic trauma during the CP[10-12]. In our study, the number of patients who presented to the emergency department with PHT during the CP period decreased by 44.8% compared to the PCP period. This may be related to a decrease in falls in children due to quarantine restrictions.

HT is an important cause of morbidity and mortality in the pediatric population. Sanford *et al*. reported a change in pediatric injury and trauma types during the CP period[13]. Many authors have reported an overall decrease in blunt injuries due to the severe restrictions imposed in various countries[14]. Similarly, we found that the rate of HT, which was 60.9% in the PCP period, significantly decreased to 39.1% in the CP period. GCS is frequently used to measure the extent of brain damage in patients with head injury[15]. The GCS classifies traumatic brain injuries as mild (score of 14–15), moderate (score of 9–13), or severe (score of 3–8). In our study, 97.1% of patients had a grade of 1, 1.1% a

Table 1: Analysis of pre- Covid-19 and Covid-19 periods and age group and trauma type

Age group				Period		Total	Chi-square Test
				Pre-Covid	Covid		
0-6	Trauma type	Falling from height	n	418	303	721	χ^2=0.827, p>0.05
			%	58.0%	42.0%	100.0%	
		Traffic accident	n	15	15	30	
			%	50.0%	50.0%	100.0%	
		Bicycle accident	n	5	3	8	
			%	62.5%	37.5%	100.0%	
	Total		n	438	321	759	
			%	57.7%	42.3%	100.0%	
7-12	Trauma type	Falling from height	n	163	63	226	χ^2=6.715, p<0.05
			%	72.1%	27.9%	100.0%	
		Traffic accident	n	25	16	41	
			%	61.0%	39.0%	100.0%	
		Bicycle accident	n	10	11	21	
			%	47.6%	52.4%	100.0%	
	Total		n	198	90	288	
			%	68.8%	31.3%	100.0%	
13-17	Trauma type	Falling from height	n	72	41	113	χ^2=0.929, p>0.05
			%	63.7%	36.3%	100.0%	
		Traffic accident	n	12	9	21	
			%	57.1%	42.9%	100.0%	
		Bicycle accident	n	9	8	17	
			%	52.9%	47.1%	100.0%	
	Total		n	93	58	151	
			%	61.6%	38.4%	100.0%	

grade of 2, and 1.8% a grade of 3. The rate of grade 1 cases, which was 61% in the PCP period, decreased to 39% in the CP period; the incidence of grade 2 cases changed from 53.8% to 46.2% and the incidence of grade 3 cases decreased to 40.9% from 59.1%. The number of admissions to the emergency department due to PHT decreased during the CP period, especially cases with a GCS grade of 1. Parents may have been more likely to ignore mild traumas during the CP. Males suffer more PHTs than females[16,17]. In our study, the trauma rates during both the PCP and CP periods were higher in boys than girls. Boys are more active than girls, and play "harder", such that PHTs are more common than in girls; this would not have changed during the pandemic.

Falls were the most common etiology of the PHTs in this study, especially in the 0–6 years age group. Other studies also showed that falls in childhood were the most common cause of HT[18]. In our study, falls accounted for 61.6% of the PHTs among all age groups. During the CP period, this rate decreased to 38.4%. Falling from a height during the PCP period was most common in the 7–12 years age group. We speculate that the closure of community playgrounds and traffic restrictions during the CP may have reduced the rate of such falls, along with closer supervision and control by families.

Traffic accident was the second most common etiology of PHT during the PCP period[2-4]. In our study, traffic accident was the second most common cause of PHT, accounting for 56.5% of cases during the CP period. Bicycles are widely used for transportation and recreation in many countries, and studies have been published on associated traumatic accidents. The literature shows a male predominance in bicycle accidents, and 33–70% of traumatic accidents involve HTs[17,19]. In our study, the proportion of patients who had a PHT due to a bicycle accident was 52.2% in the PCP period and 47.8% in the CP period. The fact that children can ride bicycles alone may have increased the rate of bicycle accidents during the pandemic period, given that community playgrounds were closed.

In one studies, epidural hematoma was the most common type of intraparenchymal lesion[20]. However, Klevian *et al*.

reported that subdural hematoma was the most common type, accounting for 46% of all intraparenchymal lesions[21]. In our study, computed tomography (CT) was performed in all patients; the CT results of 732 patients were normal (60.7% in the PCP period and 39.3% in the CP period). Parents may have been hesitant to being their child to the emergency department for mild traumas due to a fear of COVID-19 infection.

While 285 (61.1%) patients had a pathology during the PCP period, 181 (38.8%) had one during the CP period. The most common pathology detected in both periods was skull fracture (PCP: n = 203 (63.2%), CP: n = 118 (36.8%)). The most common type of intraparenchymal lesion was subdural hematoma, which was detected in 32 cases (50.8%) in the PCP period and 31 (49.2%) in the CP period. This was followed by epidural hematoma, fracture with hemorrhage, and intracranial hemorrhage. Güzel *et al*. detected intracranial hemorrhage in 34.7% of patients with skull fractures, and reported that all of them were epidural hematomas[20]. In their study on 193 pediatric fall cases, Park *et al*. found the rate of intracranial hemorrhage was 75% among cases with skull fractures[22]. In our study, intracranial hemorrhage was found in 21 (61.8%) of the patients in the PCP period and 13 (38.2%) in the CP period. Additionally, we observed epidural hematoma in 21 (58.3%) patients during the PCP period and 15 (41.7%) during the CP period; these rates are lower than those in the literature.

Of the patients included in this study, 276 (54.9%) were hospitalized during the PCP period and 227 (45.1%) during the CP period. Güzel *et al*. reported a hospitalization rate of 18.6% in their study of patients who presented due to falls[20]. In a US study, the rate was 28%[23]. The lower hospitalization rates in our study compared to the literature may be due to the fact that most of our patients suffered from mild head traumas.

Conclusion

We found an increase in the treatment refusal rate during the CP period due to social distancing and self-isolation rules. This may have been because, due to the restrictions, parents were always with their children while working from home. In addition, we found that 83.3% of the mortalities occurred during the PCP period. This suggests that the number and severity of traumas, and the mortality rate, decrease when children are constantly under the supervision of their parents.

During the CP period, there was a significant decrease in pediatric head injuries, which we infer was due to the national quarantine regulations. Also, parents were likely hesitant to visit healthcare facilities. This study provides information that could inform future public health policies pertaining to the CP, and also provides a basis for research into alternative strategies to address non-emergency pediatric traumas and relieve the burden on emergency departments.

Limitations

Our study had several limitations. A large number of patients with minor head trauma who did not want consultation were excluded from the study. We could not evaluate the effect of factors such as family structure, socioeconomic status, access to and use of health services. It was also a single-center and retrospective analysis; We think that multinational studies are needed.

References

1. Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak of global health concern. Lancet. 2020;395(10223): 470–3. doi: 10.1016/S0140-6736(20)30185-9.
2. Moreland A, Herlihy C, Tynan M.A, Sunshine G, McCord R.F, Hilton C, et al. Timing of State and Territorial COVID-19 Stay-at-Home Orders and Changes in Population Movement-United States, March 1–May 31, 2020. MMWR Morb. Mortal. Wkly. Rep. 2020;69(35):1198-1203. doi: 10.15585/mmwr.mm6935a2.
3. Lewnard JA, Lo NC. Scientific and ethical basis for social-distancing interventions against COVID-19. The Lancet Infectious Diseases, 2020;20(6):631-633. doi: 10.1016/S1473-3099(20)30190-0.
4. Yanagawa Y, Sakamoto T. Characteristics of pediatric trauma in an urban city in Japan. Pediatr Emerg Care 2009;25:572-4. DOI:10.1097/PEC.0b013e3181b4f60e
5. Bowman SM, Bird TM, Aitken ME, Tilford JM. Trends in hospitalizations associated with pediatric traumatic brain injuries. Pediatrics 2008;122(5):988-93.doi: 10.1542/peds.2007-3511.
6. Diamond IR, Parkin PC, Wales PW, Bohn D, Kreller MA, Dykes EH et al. Preventable pediatric trauma deaths in Ontario: a comparative population-based study. J Trauma 2009;66:1189-95. DOI:10.1097/ta.0b013e31819adbb3
7. Boserup B, McKenney M, Elkbuli A. The impact of the COVID-19 pandemic on emergency department visits and patient safety in the United States. Am J Emerg Med 2020; 38(9):1732–36 doi: 10.1016/j.ajem.2020.06.007
8. Man CY, Yeung RS, Chung JY, Cameron PA Impact of SARS on an emergency department in Hong Kong. Emerg Med (Fremantle) 2003;15(5–6):418–22 doi: 10.1046/j.1442-2026.2003.00495.x.
9. Oseran AS, Nash D, Kim C, Moisuk S, Lai PY, Pyhtila J, et al. Changes in hospital admissions for urgent conditions during COVID-19 pandemic. Am J Manag Care 2020;26(8):327–28 DOI: 10.37765/ajmc.2020.43837
10. Rodriguez-Leor O, Cid-Álvarez B, Ojeda S Martín-Moreiras J, Rumoroso JR, López-Palop J et al. Impact of the COVID-19 pandemic on interventional cardiology activity in Spain. REC Interv Cardiol 2020;2(2):82-9 https://doi.org/10.24875/RECICE.M20000123
11. Lange SJ, Ritchey MD, Goodman AB, Twentyman E, Fuld J, Schieve LA et al. Potential Indirect Effects of the COVID-19 pandemic on use of emergency departments for acute life-threatening conditions–United States, January-May 2020.

MMWR Morb Mortal Wkly Rep 2020;26;69(25):795-800. doi: 10.15585/mmwr.mm6925e2.

12. Park C, Sugand K, Nathwani D, Bhattacharya R, Sarraf KM. Impact of the COVID-19 pandemic on orthopedic trauma workload in a London level 1 trauma center: the "golden month." Acta Orthop 2020; 91:1–6 DOI: 10.1080/17453674.2020.1783621

13. Sanford EL, Zagory J, Blackwell JM, Szmuk P, Ryan M, Ambardekar A. Changes in Pediatric Trauma during COVID-19 Stay-at-Home Epoch at a Tertiary Pediatric Hospital. J. Pediatr. Surg. 2021;56(5):918-22. doi:10.1016/j.jpedsurg.2021.01.020

14. Sherman WF, Khadra HS, Kale NN, Wu VJ, Gladden PB, Lee OC. How Did the Number and Type of Injuries in Patients Presenting to a Regional Level I Trauma Center Change During the COVID-19 Pandemic with a Stay-at-Home Order? Clin. Orthop. Relat. Res. 2021;479(2):266-75. DOI: 10.1097/CORR.0000000000001484

15. Carroll LJ, Cassidy JD, Holm L, Kraus J, Coronado VG. Methodological issues and research recommendations for mild traumatic brain injury: the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. J Rehabil Med. 2004;(43 Suppl):113-25. DOI: 10.1080/16501960410023877

16. Schneier AJ, Shields BJ, Hostetler SG, Xiang H, Smith GA. Incidence of pediatric traumatic brain injury and associated hospital resource utilization in the United States. Pediatrics 2006;118:483-92. doi: 10.1542/peds.2005-2588.

17. Klin B, Rosenfeld-Yehoshua N, Abu-Kishk I, Efrati Y, Kozer E, Jeroukhimov I et al. Bicycle-related injuries in children: disturbing profile of a growing problem. Injury 2009;40:1011-3. DOI: 10.1016/j.injury.2009.01.135

18. Melo JR, Di Rocco F, Lemos-Júnior LP, Roujeau T, Thélot B, Sainte-Rose C, et al. Defenestration in children younger than 6 years old: mortality predictors in severe head trauma. Childs Nerv Syst 2009;25:1077-83. DOI: 10.1007/s00381-009-0924-5

19. Yeung JHH, Leung CSM, Poon WS, Cheung NK, Graham CA, Rainer TH. Bicycle related injuries presenting to a trauma center in Hong Kong. Injury, Int. J. Care Injured 2009;40; 555-9. doi: 10.1016/j.injury.2008.08.015

20. Güzel A, Karasalihoğlu S, Küçükuğurluoğlu Y. Evaluation of the fall-related trauma cases applied to our pediatric emergency department. Ulus Travma Acil Cerrahi Derg 2007;13(3):211-6.

21. Kleiven S, Peloso PM, von Holst H. The epidemiology of head injuries in Sweden from 1987 to 2000. Inj Control Saf Promot 2003; 10: 173-80. doi: 10.1076/icsp.10.3.173.14552.

22. Park SH, Cho BM, Oh SM. Head injuries from falls in preschool children. Yonsei Med J 2004; 45: 229-32. DOI: 10.3349/ymj.2004.45.2.229

23. Committee on Injury and Poison Prevention. American Academy of Pediatrics: Falls from heights: windows, roofs, and balconies. Pediatrics 2001; 107: 1188-91.

Case Report
Eurasian Journal of Critical Care

Central Pontine Myelinolysis as a Result of Ideally Corrected Hyponatremia in a Post-Covid Patient

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Abstract

Central pontine myelinosis (CPM) has a broad prognostic spectrum ranging from asymptomatic cases to mortality. CPM is a non-inflammatory neurological condition with various clinical features and onset patterns. In this case report, we aim to present the first case of central pontine myelinolysis because of an optimally corrected hyponatremia in a post-COVID-19 patient our knowledge while assessing the clinical and radiological findings. This case showed us that hyponatremia developed in a patient without comorbidity in the days following the COVID-19 infection and that ODS might occur later, despite the slow recovery of hyponatremia. For patients with symptomatic recovery from hospitalized COVİD-19 disease, care should be taken in terms of fluid and electrolyte disorders that may develop later.

Keywords: Hyponatremia, central pontine myelinolysis, COVID-19

Introduction

Hundreds of case reports about osmotic demyelination syndrome have been published since its first report in 1959. The term was coined because it not only indicates the pathologic character of the disease but also points to the specific anatomical location. Central pontine myelinolysis (CPM) is an essential subset of a group of disorders called osmotic demyelination syndrome (ODS), which involves damage in different parts of the brain, mainly in the pontine white matter pathways[1]. Hyponatremia causes a decrease in the serum tonicity which makes it easier for water to move from the extracellular field toward brain cells. This will cause water to move towards the extracellular area, and brain cells will undergo apoptosis. This phenomenon is known as osmotic demyelination syndrome (ODS).

Post covid syndrome is diagnosed if the symptoms and signs after COVİD-19 infection last longer than twelve weeks and other reasons to explain this situation are excluded[2]. Hyponatremia is one of the most common electrolyte disturbances in the acute phase of COVİD-19 infection. Hyponatremia can be seen both at the time of diagnosis and during treatment. In the literature, the presence of hyponatremia has been reported at a rate of 30% in COVİD-19 patients[3].

In this case report, we aim to present the first case of central pontine myelinolysis because of an optimally corrected hyponatremia in a post-COVID-19 patient our knowledge while assessing the clinical and radiological findings.

Case Report

A 54-year-old male patient presented with complaints of increasing speech and walking difficulties for one month. He did not have any chronic disease in his history. He had a history of hospitalization due to COVİD-19 infection 38 days before his admission. It was learned that complaints of muscle pain, weakness, difficulty in walking, seizures, speech disorder and, agitation continued approximately ten days after discharge. The serum sodium level at discharge was 136 mmol/l, decreasing to 122 mmol/l within ten days. During this period, the patient had applied to psychiatry and internal medicine outpatient clinics many times. Finally, the patient was hospitalized in the same clinic for hyponatremia and treated for four days. No pathology was detected in cranial computed tomography (CT) or magnetic resonance (MR) imaging. According to the neurologist, electroencephalography results were typical. Looking back, serum sodium decreased to 122 mEq/L in electrolyte follow-ups and increased to 136 mEq/L in the following four days.

When she applied to the emergency department, her blood pressure was: 161/86 mmHg, heart rate: 90 beats/min, respiratory rate: was 20/min, SpO2: 97, and body

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temperature was 36.6. His Glasgow coma scale (GCS) score was 15, he was in a normal state of consciousness, and he was oriented and cooperative but agitated. His neuromuscular examination revealed heavy dysarthria. He had ptosis in the right eye. He had bilateral intentional tremors during his cerebellar examination. He had truncal ataxia and hyperreflexia of deep tendons. His finger-to-nose test was mildly impaired in the right limb. No pathology was detected in other system examinations. In the laboratory values of the patient, leukocyte 12.9 10^3/ul, hemoglobin 13.6 g/dl, hematocrit 40.6%, platelet 548 10^3/ul, C-reactive protein: 1.21 mg/l, INR: 1.23, blood urea 59 mg/dL, glucose 110 mg/dL, sodium 139 mEq/L, potassium 4.08 mEq/L, aspartate aminotransferase 24 U/L, alanine aminotransferase 41 U/L, , troponin-I 2.3 ng/L were found. The patient's electrocardiogram was normal.

In the non-contrast brain CT scan done in our emergency department, there was a hypodensity in the pons. His cranial diffusion MR scan results were concordant with central pontine myelinolysis. The patient was administered intravenous steroids and then hospitalized in the neurology ward. In our case, pontine demyelination was detected after the examinations, as the complaints did not resolve approximately one month after the COVİD-19 infection.

Discussion

Hyponatremia is discussed as the most common electrolyte disorder in COVID-19 infection, as well as a poor prognostic factor. Inflammation, increased IL-6 secretion, and other inflammatory cytokines can be shown as the cause of hyponatremia developing during Covid-19 infection. Our case was treated by being hospitalized due to COVİD-19 infection. Days after she was discharged from the hospital, complaints of speech disorder, gait disturbance, and seizures emerged. Later, hyponatremia was detected. For patients with symptomatic recovery from hospitalized COVİD-19 infection, care should be taken in terms of fluid and electrolyte disorders that may develop later. A study mentions that COVID coinfection could also be a risk factor for the manifestation of extrapontine myelinolysis[4]. CPM was also reported to be not as rare as formerly known and to be responsible for most of the neurologic damage in patients with chronic hyponatremia[5]. The exact mechanism leading to osmotic demyelination syndrome is not fully understood, and there is no specific treatment. After the diagnosis, the treatment is supportive, and the main goal is to prevent complications. Ayus et al.[6] reported that a rapid correction of hyponatremia into mild hyponatremia is not dangerous and they recommend the serum sodium level be adjusted so it would not exceed 126 mM/l in the first 48 hours of treatment. They reported that a slow correction of hyponatremia (slower than 0.6 Mm/l) has higher mortality than a rapid correction of hyponatremia (faster than 2 mM/l). McKee et al.[7] showed that in the pathogenesis of CPM, rather than a fast or excessive correction of hyponatremia, a very high serum hyperosmolarity and chronicity of hyponatremia are also important factors. The American Expert Panel Recommendations endorse a serum sodium (Na) correction limit of 10–12 mEq/L in any 24-hour and 18 mEq/L in any 48-hour period for patients at average risk of ODS, and eight mEq/L in any 24-hour period for patients at high risk of ODS[8].

Conclusion

This case showed us that hyponatremia developed in a patient without comorbidity in the days following the COVID-19 infection, and that ODS may occur later, despite the slow recovery of hyponatremia. For patients with symptomatic recovery from hospitalized COVİD-19 infection, care should be taken in terms of fluid and electrolyte disorders that may develop later.

Figure 1: Hypodense, non-enhancing lesion in sagittal sequence, CT image of CPM (white arrow)

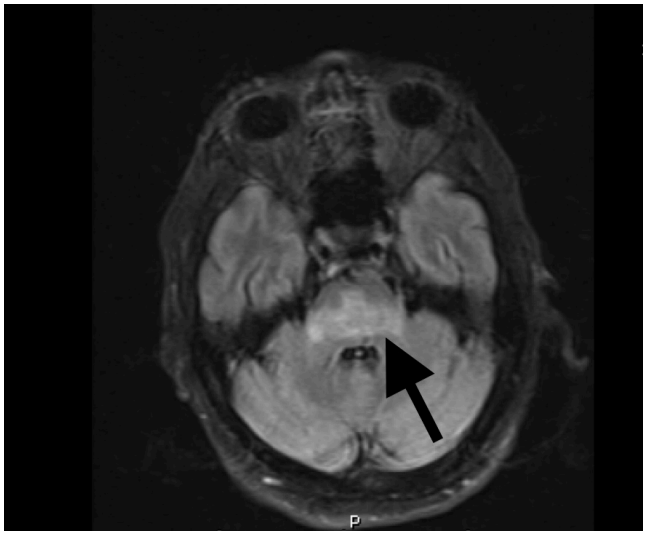

Figure 2: Hyperintense lesions in FLAIR MRI (white arrow)

References

1. Danyalian A, Heller D. Central Pontine Myelinolysis. 2020 Aug 10. In: StatPearls [https://pubmed.ncbi.nlm.nih.gov/31869161/]. Treasure Island (FL): StatPearls Publishing; 2021 Jan
2. COVID-19 rapid guideline: managing the longterm effects of COVID-19. NICE guideline, 2020. https://www.nice.org.uk/guidance/ng188.
3. Butt I., Sawlani V., Geberhiwot T. Prolonged confusional state as first manifestation of COVID-19. Ann Clin Transl Neurol. 2020;7:1450-52
4. Abd Ur Rehman M, Abdulrahman AF, Zainab A, Paksoy Y, Kharma N: Hyponatremia and extrapontine myelinolysis in a patient with COVID-19: a case report. Clin Case Rep. 2021;9(7):e04463. doi: 10.1002/ccr3.4463.
5. Gankam Kengne F, Decaux G: Hyponatremia and the brain. Kidney Int Rep 2017; 3:24–35.
6. Ayus JC, Krothapalli RK, Arieff Al :Changing concepts in treatment of severe symptomatic hyponatremia. Rapid correction and possible relation to central pontine myelinolysis. Am J Med. 1985;78:897-902. doi: 10.1016/0002-9343(85)90209-8.
7. Mc Kee AC, Winkelman MD, Banker BQ: Central pontine myelinolysis in severely burned patients:Relationship to serum hyperosmolality.Neurology1988; 38:1211-7
8. Verbalis JG, Goldsmith SR, Greenberg A, Korzelius C, Schrier RW, Sterns RH, Thompson CJ: Diagnosis, evaluation, and treatment of hyponatremia: Expert panel recommendations. Am J Med. 2013;126:1–42. doi: 10.1016/j.amjmed.2013.07.006