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e-mail: oktayemergency@gmail.com
ORCID ID: orcid.org/0000-0002-1643-6007

Publisher Contact
Address: Molla Gürani Mah. Kaçamak Sk. No: 21/1 34093 İstanbul, Turkey
Phone: +90 (530) 177 30 97
E-mail: info@galenos.com.tr/yayin@galenos.com.tr
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ORIGINAL RESEARCH

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Relationship Between Hematological Parameters and Mortality in Patients with Acute PTE

Adem Melekoğlu[1], Seda Özkan[2], Derya Öztürk[1]

[1]University of Health Sciences Turkey, Şişli Hamidiye Etfal Training and Research Hospital, Clinic of Emergency Medicine, İstanbul, Turkey
[2]İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Department of Emergency Medicine, İstanbul, Turkey

Abstract

Objective: Acute pulmonary thromboembolism (APE) is one of the cardiopulmonary diseases that are frequently seen in emergency departments and have a high mortality rate. In this study, we investigated the relationship between hematological parameters, risk scores, clinical-radiological findings, and mortality with a definite diagnosis of APE in our emergency department.

Materials and Methods: Patients who were diagnosed with definitive PE by computed tomography pulmonary angiography in the emergency department of our hospital between May 2016 and May 2021 were analyzed retrospectively. The relationship between hematological parameters and mortality in these patients was investigated. SPSS 22.0 for the Windows program was used for statistical analysis.

Results: Two hundred and fifty nine patients were included in the study. Thirty-day mortality occurred in 20% of 259 patients. The mean age of the patients was 66.8. Female patients (54%) were more than the number of males. The most common risk factor was venous thromboembolism in the lower extremities, which was detected in 38.6% of the patients. Neutrophil-to-lymphocyte ratio (NLR) and red blood cell distribution width levels, which are among the hematological parameters of the patients, were associated with mortality (p=0.001). Receiver operating characteristic analysis of NLR for mortality revealed a cut-off value of >4.

Conclusion: NLR is associated with mortality in APE. We also determined that NLR, which is an inexpensive and easy test, is a predictive parameter for mortality. It may be useful to use hematological parameters together with other scorings in determining the prognosis in APE.

Keywords: Acute pulmonary thromboembolism, neutrophil to lymphocyte ratio, pulmonary embolism severity index

Introduction

Acute pulmonary embolism (APE) is a serious cardiovascular disease with high morbidity and mortality rates. It has been reported that APE is one of the most common causes of sudden death in hospital, and the annual incidence rates of PE are 39-115 cases per 100,000 people [1].

The prognostic importance of several clinical and laboratory variables has been established in patients with APE [2,3]. Additionally, elevated levels of biochemical markers such as troponin, brain natriuretic peptide (BNP), N-terminal pro-B type BNP (NT-proBNP), heart type fatty acid binding protein (H-FABP), myoglobin, and white blood cell (WBC) count predict adverse events in APE [4]. Immediate initiation of anticoagulation and/or thrombolytic therapy is vital to decreasing patient mortality and morbidity rates. Laboratory parameters may be used to guide the therapy, particularly in relatively stable patients [5].

Inflammation plays an important role in venous thromboembolism, and in a meta-analysis, it was observed that monocyte chemotactic proteins were involved in the disease's pathogenesis. Recently, neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have been proposed as better inflammatory indicators than WBC count [6]. NLR and PLR are inflammatory and immunologic-based ratios identified as prognostic indicators of cancer or cardiac -related mortality

Address for Correspondence: Derya Öztürk, University of Health Sciences Turkey, Şişli Hamidiye Etfal Training and Research Hospital, Clinic of Emergency Medicine, İstanbul, Turkey
Phone: +90 212 373 50 00 **E-mail:** drderyaozturk@yahoo.com **ORCID-ID:** orcid.org/0000-0001-7318-0725
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[6]. Recent studies have shown the potential prognostic role of NLR and PLR in patients with APE [6]. However, the current view on the prognostic role of NLR and PLR in PE is still controversial due to the different results between studies [6].

In the latest European Respiratory Society APE Guideline (2019), high laboratory values (such as lactate, urea, creatinine) have been reported to be associated with mortality [7]. Recent studies have shown that red cell distribution width (RDW) is associated with the prediction, severity, and prognosis of pulmonary embolism [8]. RDW is an indicator of variability in red blood cell size and is routinely reported as part of a patient's completea blood count. The biomolecular mechanism underlying the association between RDW and APE is largely unknown, but is thought to result from the association of RDW with acute inflammatory markers and variations in blood viscosity [8].

In this study, we investigated the relationship between hematological parameters (NLR, PLR, and RDW), risk scores, clinical-radiological findings, right ventricular (RV) failure, and mortality in 259 patients with a definite diagnosis of APE in our emergency department.

Materials and Methods

This study was planned in accordance the Declaration of Helsinki and the recommendations of our hospital Ethics Committee. After obtaining approval from the Ethics Committee of Dışkapı Yıldırım Beyazıt Training and Research Hospital (date: 26.10.2015, decision no: 26/04), our patients began to be recruited retrospectively. Patient data were obtained from the electronic files of the patients. Patients with missing data were excluded from the study.

Our hospital is a busy hospital that provides tertiary healthcare services and has approximately 270,000 admissions to the emergency department annually. A total of 259 patients who were diagnosed with PE by only computed tomography (CT) pulmonary angiography were included in the study to create a homogeneous universe among the patients who were admitted to the emergency department of our hospital between May 2016 and May 2021.

Patients with suspected APE are classified in the emergency department using the Wells' and Geneva risk classification [9]. Pulmonary CT angiography screening is promptly performed in patients with low clinical risk, patients with D-dimer levels >500 µg/L, and patients with high-risk scores. The original pulmonary embolism severity index (PESI) is calculated (age, male gender, cancer, chronic heart failure, chronic lung disease, pulse rate, systolic blood pressure, respiratory rate, temperature, altered mental status, arterial oxyhemoglobin saturation), as well as the risk classification of patients diagnosed with PTE, and classified as class I-V [10]. Electrocardiograms (ECG) of the patients were evaluated by an emergency specialist and cardiologist. The data obtained were recorded by us in the electronic file of the patients.

Venous blood was collected from the antecubital region of the patients and transferred to the laboratory for evaluation of hematological parameters. WBC, hemoglobin (Hgb), hematocrit, Plt, mean platelet volume, RDW, NLR, PLR, D-dimer, troponin-I, CK-MB, and lactate levels were determined and recorded.

The patients were evaluated with echocardiogram (ECHO) measurements by an experienced cardiologist. In ECHO, RV dimensions were measured at diastole from the apical four -chamber view at diastole at the level of the middle of the ventricle. RV enlargement was defined as a RV size bigger than 3.3 cm. Systolic pulmonary artery pressure was calculated by adding the trans tricuspid pressure gradient to the mean right atrial pressure calculated from the diameter of the inferior vena cava and movement during breathing [11].

In the radiology clinic, we performed multislice spiral pulmonary tomography using the pulmonary embolism protocol (field of view: 35 cm, section thickness: 4 mm, contrast material volume: 100 mL with contrast medium (injection rate: 4 mL/sec) using Siemens brand tomography device. APE was diagnosed in case of complete or partial lumen filling defect in the main pulmonary artery or its distal branches. The diagnosis of deep vein thrombosis was made by an experienced radiologist after performing lower extremity venous Doppler ultrasonography.

Patients diagnosed with APE were administered with 1 mg/kg enoxaparin, and 47 patients (19%) who were at clinically high risk were administered with 100 mg/2 h infusion of alteplase (recombinant tissue-type plasminogen activator) treatment. Patients who were admitted to the service or intensive care unit (ICU) according to their clinical status were scanned 30 days later in terms of early mortality from the hospital electronic data registry system and their data were recorded.

Exclusion criteria:

- Patients with active malignancy, history of use of immunosuppressive agents, and anemia (Hgb <10.5),
- Patients were diagnosed with acute coronary artery disease in the last month,
- Patients with septic disease at the time of diagnosis of embolism and other inflammatory diseases that may cause inflammation,
- Patients under the age of 18 and pregnant patients,
- Patients were referred to other hospitals for different reasons,

Statistical analysis was performed by including 259 patients who did not meet the exclusion criteria and had filling defects observed in CT pulmonary angiography.

Statistical Analysis

The SPSS 22.0 for Windows (IBM, USA) program was used for statistical analysis. Descriptive statistics of the results were indicated as numbers and ratio for categorical variables, and mean, standard deviation, and minimum, and maximum for numerical variables. Comparisons of numerical variables between the two independent groups were compared with the Student's t-test in case the data were normally distributed, or using the Mann-Whitney U test. The relationships between numerical variables in the groups were examined by Pearson's correlation coefficient when the parametric test condition was met, or else, by Spearman's correlation coefficient. The comparison of the ratios in the groups was evaluated by chi-square test. In the comparison of three or more independent groups, the One-Way ANOVA test in the cases of parametric test conditions were met, or else, Kruskal-Wallis test was used. Variables that were statistically significant were evaluated with multivariate logistic regression analysis. MedCalc (version 20.009) was used in the receiver operating characteristic (ROC) analysis of the variables related to mortality. A p value lower than 0.05 was considered as statistically significant.

Results

Patients who were admitted to the emergency department between May 2016 and May 2021 and were diagnosed with APE on pulmonary CT angiography were included in the study. The data of 259 (female: 54%-male: 46%) patients who were followed-up after hospitalization in the ward or ICU were analyzed in terms of mortality within 30 days (20%) and survival (80%).

The mean age of all patients was 66.8 years, and in the patients with mortality, the mean age was 75.8 years (p=0.001; Table 1). The most common complaints of patients presenting to the emergency department were dyspnea and chest pain, followed by the unilateral increase in diameter in the lower extremity, pain, and tachycardia. Among the vital signs of the patients, systolic and diastolic blood pressures were lower in the patients with mortality, whereas heart rate and respiratory rate were higher (Table 2).

When the risk factors for APE were examined, venous thromboembolism in the lower extremities was detected in 38.6% of the patients. This risk factor was followed by immobilization, which was present in 73 patients. Among the risk factors, only malignancy (18.9%) was significantly associated with mortality (p=0.008). The most common chronic disease detected in both groups was hypertension, which was significantly associated with mortality (p=0.036). The history of coronary artery disease (21.6%) was the second most common chronic disease in all the groups (Table 1).

When the ECGs of the patients were analyzed, sinus tachycardia was the most common pattern (40.9%) in all patients. Sinus tachycardia was followed by T-wave inversion and atrial fibrillation in V1-3, respectively, were other common rhythms and they were not significantly associated with mortality.

ECHO findings showed enlargement of the right atrium and ventricle in 152 (58.7%) patients. Findings of RV failure in ECHO were associated with mortality (p=0.042). The mean pulmonary artery systolic pressure of all patients was measured as 50.3 mmHg and was higher in patients with mortality (56.73 mm/hg) (p=0.001). Considering the indications and contraindications of the patients, thrombolytic therapy was given to 47 of them. Early mortality developed in eight patients who received thrombolytic therapy.

When the laboratory findings of the patients were examined, NLR was higher in patients with mortality and those who survived (p=0.001). Similarly, blood urea, WBC, and RDW were higher in patients with mortality (p=0.001). High lactate level was associated with mortality (p=0.001).

Patients were grouped according to the PESI classification. In the analysis performed with Kruskal-Wallis test, more mortality was seen in the group with a high PESI class (p=0.001). While no mortality was observed in the class I patient group, 39 died patients (75%) were in class V (Table 3).

NLR and other risk factors, which differed significantly for mortality in univariate analysis, were also analyzed by multivariate logistic regression analysis. Among all variables, we found that only NLR was significantly associated with mortality [p=0.023, odds ratio: 0.245, 95% confidence interval (CI): 1.034-1.577] (Table 4).

ROC curve analysis revealed that NLR is a moderate-to-high predictor of mortality [area under the curve (AUC): 0.718; 95% CI:0.659-0.772; p=0.001; Figure 1]. Cut-off value in ROC analysis of NLR for mortality >4.

Discussion

In addition to aggravating conditions, comorbidities, clinical, and imaging, laboratory findings must assess the overall risk of mortality and early outcomes of a patient directly related to the severity of APE and premature death associated with APE. RV overload due to the APE is associated with increased myocardial tension releasing BNP, NT-pro BNP, and cardiac troponins and premature death [12].

In addition to these laboratory parameters, the measurement of NLR is an inexpensive and simple test, and NLR has been reported to be an independent variable associated with mortality in inflammatory diseases [13]. In the recent studies,

NLR, whose relationship with mortality has been investigated in many inflammatory diseases recently, has been suggested to be associated with mortality in APE [6]. Our primary finding in this study was that in the patients with or without comorbidity, inflammation markers such as NLR, PLR, RDW, impaired vital signs, and high PESI score were associated with mortality. We also determined that NLR, which is an inexpensive and easy test, is a predictive parameter for mortality.

In the study by Celik et al. [14], they determined that NLR, PLR, and RDW could be diagnostic markers in APE. In our study, NLR, PLR, and RDW values, which are associated with increased inflammation from hematological parameters, were associated with mortality in univariate analysis, similar to the results obtained in a study involving 203 patients [15]. These studies showed the prognostic importance of inflammatory markers in terms of diagnosis and mortality. APE is already a life-threatening cardiopulmonary disease. Additionally, if inflammatory markers are high, even in stable patients, treatment may be more aggressive.

Among these hematological parameters that increased due to inflammation, which were significantly associated with mortality in univariate analysis, only NLR showed a significant difference in mortality in multivariate regression analysis. This makes NLR more prominent than other inflammation markers in APE.

ROC analysis revealed that NLR is a moderate-to-high predictor of mortality with a cut-off value of >4. We found the sensitivity

Table 1. Comparison of demographic characteristics and risk factors in study groups

	Dead (52) n (%)	**Survive (207) n (%)**	**Total (259) n (%)**	**p**
Age (mean ± SD)	75.85±11.66	64.54±16.3	66.8±16.1	**0.001***
Sex (female)	24 (46.2)	117 (56.5)	141 (54.4)	0.180$^{\chi 2}$
Complaints**				
Dyspnea	47 (90.4)	176 (85)	223 (86.1)	0.438$^{\chi 2}$
Chest pain	18 (34.6)	94 (45.4)	112 (43.2)	0.212$^{\chi 2}$
Syncope	8 (15.4)	27 (13)	35 (13.5)	0.830$^{\chi 2}$
Palpitation	13 (25)	28 (13.5)	41 (15.8)	0.070$^{\chi 2}$
Pain-swelling in the leg	6 (11.5)	39 (18.8)	45 (17.4)	0.299$^{\chi 2}$
Risk factors**				
Active DVT	14 (26.9)	86 (41.5)	100 (38.6)	0.076$^{\chi 2}$
Prior surgery	4 (7.7)	38 (18.4)	42 (16.2)	0.09$^{\chi 2}$
Malignancy	17 (32.7)	32 (15.5)	49 (18.9)	**0.008$^{\chi 2}$**
Immobilization	16 (30.8)	57 (27.5)	73 (27.2)	0.771$^{\chi 2}$
Comorbidity**				
CVD	5 (9.6)	9 (4.3)	14 (5.4)	0.247$^{\chi 2}$
HT	30 (57.7)	86 (41.5)	116 (44.8)	**0.036$^{\chi 2}$**
DM	9 (17.3)	39 (18.8)	48 (18.5)	0.956$^{\chi 2}$
CAD	15 (28.8)	41 (19.8)	56 (21.6)	0.220$^{\chi 2}$
ECG**				
Sinus tachycardia	24 (46.2)	82 (39.6)	106 (40.9)	0.391$^{\chi 2}$
S1Q3T3	0	10 (4.8)	10 (3.9)	0.102$^{\chi 2}$
T wave inversion in V1-V3	10 (19.2)	42 (20.3)	52 (20.1)	0.865$^{\chi 2}$
Right bundle branch block	10 (19.2)	32 (15.5)	42 (16.2)	0.653$^{\chi 2}$
Atrial fibrillation	14 (26.9)	30 (14.5)	44 (17)	0.054$^{\chi 2}$
Thrombolytic areas	8 (15.4)	39 (18.8)	47 (18.1)	0.706$^{\chi 2}$
Right insufficiency	37 (71.2)	115 (55.6)	152 (58.7)	**0.042$^{\chi 2}$**
sPAP (mean ± SD)	56.73±16.4	48.72±17.83	50.33±17.81	**0.001***
Wells score (mean ± SD)	4.19±2.12	4.44±4.87	4.39±2.19	0.442*
Genova points (mean ± SD)	7.35±3.34	7.05±3.78	7.11±3.69	0.322*

*Mann-Whitney U test, **There may be more than one finding in the same patient, DVT: Deep vein thrombosis, CVD: Cerebrovascular disease, HT: Hypertension, DM: Diabetes mellitus, CAD: Coronary artery disease, sPAP: Systolic pulmonary artery pressure, SD: Standard deviation

Table 2. Comparison of laboratory parameters and vital signs of study groups

	Dead (mean ± SD)	Survive (mean ± SD)	Total (mean ± SD)	p
Vital signs				
Systolic BP	106±21.63	118.17±22.69	115.74±22.96	**0.001***
Diastolic BP	64.60±12.99	72.85±12.52	71.19±13.02	**0.001***
Pulse	111.54±20.86	102.72±19.89	104.5±21.23	**0.007***
Respiratory rate	23.94±5.99	19.94±3.93	20.7±4.81	**0.001***
Fire	36.82±0.47	36.82±0.49	36.82±0.49	0.872*
Hematological parameters				
NLR	8.09±5.28	5.46±5.47	5.99±5.52	**0.001***
PLR	216±169.7	183.2±275.23	189.8±257.59	**0.019***
Neutrophil	10.87±5.63	7.41±3.57	8.1±4.29	**0.001***
Lymphocyte	1.54±0.61	1.88±0.91	1.81±0.87	**0.011***
Platelet	274±169	250±110	255±124	0.750*
RDW	16.52±2.1	15.55±2.37	15.74±2.35	**0.001***
WBC	13591±4944	11059±3729	11567±41119	**0.001***
Troponin I	0.22±0.28	0.28±0.66	0.27±0.6	0.110*
Lactate	2.92±2.01	2.21±1.22	2.35±1.44	**0.005***
Urea	63.8±36.75	45.91±21.3	49.5±26.09	**0.001***
Creatinine	1.08±0.43 (0.39-2.3)	0.99±0.3 (0.43-2.2)	1.01±0.33 (0.39-2.3)	0.292*
pH	7.39±0.098	7.41±0.067	7.41±0.075	0.154*
SO_2	85.18±9.11	88.69±10.71	87.99±10.49	**0.001***
HCO	22.26±4.51	23.16±3.37	22.98±3.64	**0.031***
BE	-1.92±4.47	-0.89±3.3	-0.76±3.45	**0.011***
D-dimer	8650±10963	8146±7693	7438±8394	0.649*

*Mann-Whitney U test, NLR: Neutrophil lymphocyte ratio, PLR: Platelet lymphocyte ratio, RDW: Red cell distribution width, MPV: Mean platelet volume, WBC: White blood cell, SD: Standard deviation

Table 3. Statistical analysis of PESI for mortality

	Dead	Survive	Total	p
PESI	**n (%)**	**n (%)**	**n (%)**	
Class I	0	31 (15)	31 (12)	
Class II	1 (1.9)	36 (17.4)	37 (14.3)	
Class III	2 (3.8)	56 (27.1)	58 (22.4)	**0.001#**
Class IV	10 (19.2)	37 (17.9)	47 (18.1)	
Class V	39 (75)	47 (22.9)	86 (33.2)	

#Kruskal-Wallis test, PESI: Pulmonary embolism severity index

and specificity of the it to be 86.5% and 56%, respectively. In the study conducted to determine the normal NLR level in 413 normal healthy adults, the upper limit of NLR was found to be 3.53 [16]. In a study by Kasapoğlu et al. [17], they found NLR as a moderate predictor of mortality with an AUC value of 0.604. They found the sensitivity and specificity to be 69% and 48%, respectively (cut-off >7.3). In another study conducted on APE patients, the cut-off value was found as 5.99 and the AUC value was found to be 0.792. Studies showed that NLR

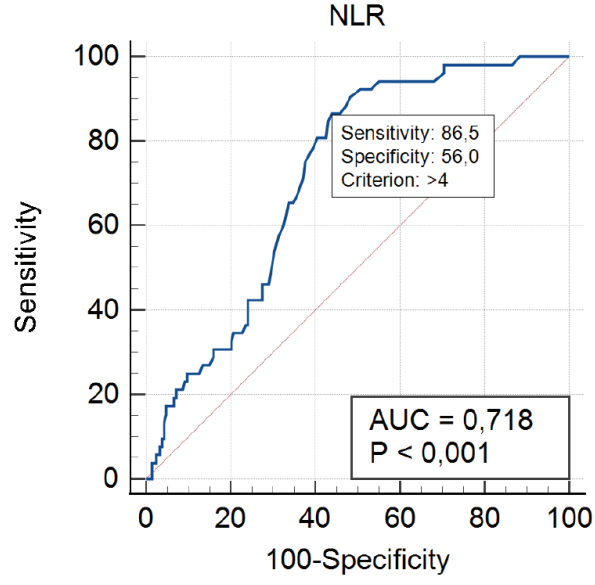

Figure 1. ROC analysis for NLR to detect mortality

ROC: Receiver operating characteristic, NLR: Neutrophil lymphocyte ratio, AUC: Area under the curve

Table 4. Multivariate regression analysis for mortality

	Odds ratio	95% confidence interval Lover-upper	p
sPAP	0.011	0.968-1.011	0.331
Pulse	0.012	0.971-1.006	0.195
Malignancy	2.201	0.919-5.268	0.077
NLR	0.245	1.034-1.577	**0.023**
PLR	0.0001	0.999-1.001	0.435
RDW	0.105	0.764-1.060	0.208
Lactate	0.100	0.683-1.199	0.487
WBC	0.001	1.000-1.000	0.722
Urea	0.015	0.971-1.000	0.044
SO_2	0.033	0.996-1.072	0.079
PCO_2	0.011	0.949-1.029	0.579
HCO_3	0.002	0.920-1.091	0.967
BE	0.064	0.938-1.212	0.329

sPAP: Systolic pulmonary artery pressure, NLR: Neutrophil lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, RDW: Red cell distribution width, WBC: White blood cell

is a moderate-to-high predictor of mortality with moderate-to-high AUC value [18]. When we compared the cut-off value of our study with these studies, we attributed the low cut-off value in our study was because the mean NLR value in the patient group with mortality and discharged groups was lower than the average the above studies.

Cardiac damage marker troponin I was higher in mortality and survivor groups, but we could not find any difference between them. One study found that mean troponin I levels in APE were higher in the deceased and surviving groups [15]. Troponin I level was higher in the group with RV failure in APE than in the normal group. We also found that RV failure is associated with mortality in APE.

In studies, RDW was found to be high in patients with APE with mortality [19]. In our study, we found the RDW value to be significantly higher in the mortality group. The biomolecular mechanism underlying the association between RDW and APE is largely unknown, but is thought to result from the association of RDW with acute inflammation and changes in blood viscosity [8].

The PESI, consisting of 11 different clinical scorings combining clinical and comorbidity in determining severity in APE, is the most extensively validated classification system to date. The main strength of PESI lies in the reliable identification of patients at low risk for 30-day mortality (PESI classes I and II). In PESI class V, the risk of death rises up to 25% [20,21]. In our study, mortality was observed in one case in PESI classes I and II. In our study, we found that the mean age of the cases with mortality to be higher than the group who survived. The age factor used in PESI scoring explains the higher number of elderly patients and mortality rate in the class IV-V group compared to other studies.

High mortality due to the APE in emergency services led to the generation of different combinations of clinical, laboratory, and imaging in determining prognosis [22,23]. This is associated with increased cost, labor, and time loss. Because of these, cheap, simple, and easy tests are being researched in determining the prognosis in APE. Because it is cost -effective and easy, it may be beneficial to use hematological parameters with other scoring for the determination of prognosis in APE.

Study Limitations

We had some limitations in our study. First, our study was single-centered and the number of cases was limited. Because of the high bed occupancy rate of our hospital, patients diagnosed in the emergency department and referred to other centers were excluded from the study. Additionally, we had to exclude patients whose lower extremity venous Doppler ultrasound could not be performed since we did not have a radiologist in the evenings and on weekends. Moreover, since NT-proBNP and H-FABP were not routinely analyzed in our biochemistry laboratory, we did not have the opportunity to compare these biomarkers with other variables in RV failure.

Conclusion

NLR is a determined hematological parameter associated with mortality in inflammatory diseases. In our study, we found that NLR was a predictive of mortality in patients with APE patients. We believe that the use of NLR, which is easy and inexpensive to measure, by emergency clinicians for the prognosis determination of patients diagnosed with APE in the emergency department will be beneficial.

Ethics

Ethics Committee Approval: Ethics Committee of Dışkapı Yıldırım Beyazıt Training and Research Hospital (date: 26.10.2015, decision no: 26/04).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.M., S.Ö., D.Ö., Concept: A.M., S.Ö., D.Ö., Design: A.M., S.Ö., Data Collection or Processing: S.Ö., D.Ö., Analysis or Interpretation: A.M., S.Ö., Literature Search: A.M., S.Ö., D.Ö., Writing: A.M., S.Ö., D.Ö.

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References

1. Wendelboe AM, Raskob GE. Global burden of thrombosis: epidemiologic aspects. Circ Res. 2016;118:1340-7.
2. Kucher N, Goldhaber SZ. Cardiac biomarkers for risk stratification of patients with acute pulmonary embolism. Circulation. 2003;108:2191-4.
3. Agnelli G, Becattini C. Acute pulmonary embolism. N Engl J Med. 2010;363:266-74.
4. Konstantinides SV, Torbicki A, Agnelli G, Danchin N, Fitzmaurice D, Galiè N, et al. 2014 ESC guidelines on the diagnosis and management of acute pulmonary embolism. Eur Heart J. 2014;35:3033-69.
5. Donzé J, Le Gal G, Fine MJ, Roy PM, Sanchez O, Verschuren F, et al. Prospective validation of the Pulmonary Embolism Severity Index. A clinical prognostic model for pulmonary embolism. Thromb Haemost. 2008;100:943-8.
6. Wang Q, Ma J, Jiang Z, Ming L. Prognostic value of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in acute pulmonary embolism: a systematic review and meta-analysis. Int Angiol. 2018;37:4-11.
7. Kostrubiec M, Pływaczewska M, Jiménez D, Lankeit M, Ciurzynski M, Konstantinides S, et al. The prognostic value of renal function in acute pulmonary embolism-a multi-centre cohort study. Thromb Haemost. 2019;119:140-8.
8. Hammons L, Filopei J, Steiger D, Bondarsky E. A narrative review of red blood cell distribution width as a marker for pulmonary embolism. J Thromb Thrombolysis. 2019;48:638-47.
9. Shen JH, Chen HL, Chen JR, Xing JL, Gu P, Zhu BF. Comparison of the Wells score with the revised Geneva score for assessing suspected pulmonary embolism: a systematic review and meta-analysis. J Thromb Thrombolysis. 2016;41:482-92.
10. Jiménez D, Aujesky D, Moores L, Gómez V, Lobo JL, Uresandi F, et al. Simplification of the pulmonary embolism severity index for prognostication in patients with acute symptomatic pulmonary embolism. Arch Intern Med. 2010;170:1383-9.
11. Jae KOH, James BS, A. Jamil T. Appendix 6 In: The Echo Manual 2009; 3th ed.: 401-15.
12. Konstantinides SV, Meyer G, Becattini C, Bueno H, Geersing GJ, Harjola VP, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J. 2020;41:543-603.
13. Azab B, Chainani V, Shah N, McGinn JT. Neutrophil-lymphocyte ratio as a predictor of major adverse cardiac events among diabetic population: a 4-year follow-up study. Angiology. 2013;64:456-65.
14. Celik A, Ozcan IT, Gündes A, Topuz M, Pektas I, Yesil Eet al. Usefulness of admission hematologic parameters as diagnostic tools in acute pulmonary embolism. Kaohsiung J Med Sci. 2015;31:145-9.
15. Karataş MB, İpek G, Onuk T, Güngör B, Durmuş G, Çanga Y, et al. Assessment of prognostic value of neutrophil to lymphocyte ratio and platelet to lymphocyte ratio in patients with pulmonary embolism. Acta Cardiol Sin. 2016;32:313-20.
16. Forget P, Khalifa C, Defour JP, Latinne D, Van Pel MC, De Kock M. What is the normal value of the neutrophil-to-lymphocyte ratio? BMC Res Notes. 2017;10:12.
17. Kasapoğlu US, Olgun Yıldızeli Ş, Arıkan H, Erer A, Kabadayı F, Yalçınkaya E, et al. Comparison of neutrophil to lymphocyte ratio with other prognostic markers affecting 30 day mortality in acute pulmonary embolism. Tuberk Toraks. 2019;67:179-89.
18. Ma Y, Mao Y, He X, Sun Y, Huang S, Qiu J. The values of neutrophil to lymphocyte ratio and platelet to lymphocyte ratio in predicting 30 day mortality in patients with acute pulmonary embolism. BMC Cardiovasc Disord. 2016;16:123.
19. Cha MJ, Lee HS, Kim HM, Jung JH, Choi EK, Oh S. Association between red cell distribution width and thromboembolic events in patients with atrial fibrillation. Eur J Intern Med. 2017;46:41-6.
20. Donzé J, Le Gal G, Fine MJ, Roy PM, Sanchez O, Verschuren F, et al. Prospective validation of the Pulmonary Embolism Severity Index. A clinical prognostic model for pulmonary embolism. Thromb Haemost. 2008;100:943-8.
21. Elias A, Mallett S, Daoud-Elias M, Poggi JN, Clarke M. Prognostic models in acute pulmonary embolism: a systematic review and meta-analysis. BMJ Open. 2016;6:e010324.
22. Hobohm L, Hellenkamp K, Hasenfuß G, Münzel T, Konstantinides S, Lankeit M. Comparison of risk assessment strategies for not-high-risk pulmonary embolism. Eur Respir J. 2016;47:1170-8.
23. Dellas C, Tschepe M, Seeber V, Zwiener I, Kuhnert K, Schäfer K, et al. A novel H-FABP assay and a fast prognostic score for risk assessment of normotensive pulmonary embolism. Thromb Haemost. 2014;111:996-1003.

ORIGINAL RESEARCH

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Evaluation of Laboratory Findings for Treating Acute Ischemic Stroke

Dilara Keskinbalta[1], Derya Öztürk[2], Adem Melekoğlu[2], Ender Uysal[3], Ertuğrul Altınbilek[2]

[1]Bayrampaşa State Hospital, Clinic of Emergency Medicine, İstanbul, Turkey
[2]University of Health Sciences Turkey, Şişli Hamidiye Etfal Training and Research Hospital, Clinic of Emergency Medicine, İstanbul, Turkey
[3]Akdeniz University Faculty of Medicine, Department of Radiology, Antalya, Turkey

Abstract

Objective: Acute ischemic stroke is an emergency clinical condition resulting from occlusion of intracranial arteries leading to neural tissue destruction. In this study, we evaluated whether lactate levels and monocyte/high-density lipoprotein (HDL) ratio can be used as a marker in predicting treatment outcomes in patients who underwent intravenous thrombolysis (IVT) or mechanical thrombectomy (MT) after IVT.

Materials and Methods: In this retrospective study, demographic data, clinical status, radiological results, laboratory data, the National Institutes of Health Stroke Scale (NIHSS) scores on admission and after treatment, and clinical data of patients who were diagnosed with acute ischemic stroke and underwent IVT or IVT + MT between January 01, 2019 and December 31, 2019 in the Emergency Medicine Clinic of University of Health Sciences Turkey, Şişli Hamidiye Etfal Training and Research Hospital were evaluated. The vessels of the patients causing ischemic pathology were evaluated and divided into three groups as middle cerebral artery (MCA), posterior cerebral artery (PCA), and anterior cerebral artery (ACA). The distribution of quantitative data was evaluated using the Kolmogorov-Smirnov test. The Kruskal-Wallis and Mann-Whitney U tests was used to compare independent quantitative data between groups.

Results: A total of 189 cases (male: 57.7%) with a mean age of 69.5±12.9 years were included in our study. Monocytes/HDL and lactate levels were similar between the MCA, PCA, and ACA groups. The total cholesterol/HDL ratio was found to be significantly higher in the PCA group than in the MCA group ($p<0.05$). There was a significant decrease in the NIHSS scores of the patients after treatment compared with the scores at the time of admission ($p<0.05$). No significant differences between the groups were observed with regard to the changes in NIHSS scores.

Conclusion: It was shown that monocyte/HDL ratio and lactate levels were not significant in predicting the success of treatment and neurological improvement in patients with acute ischemic stroke.

Keywords: Monocyte/HDL ratio, lactate, ischemic stroke

Introduction

Stroke is defined as regardless of a cause other than a vascular cause, a sudden onset clinical condition that causes focal or global cerebral dysfunction, lasting 24 h or longer, and may cause death. It is the second most common cause of mortality after cardiovascular diseases and the primary cause of disability and loss of job. Its etiology consists of two types of strokes as ischemic (85%) and hemorrhagic (15%) [1-3]. Risk factors that cannot be altered for stroke are age, gender and genetic factors, while hypertension, diabetes, atherosclerosis, obesity, smoking, and alcohol use are among modifiable risk factors. Prevention and reduction of modifiable risk factors are critical in alleviating the stroke incidence [4-6].

Monocytes and lipid-laden macrophages formed by monocyte activation play an important role in the synthesis and release of proinflammatory and prooxidant cytokines. Monocytes, constituting 3-8% of leukocytes in peripheral blood, have important roles in controlling inflammatory processes [4-7]. High-density lipoprotein (HDL) cholesterol is been shown to be antithrombotic, anti-inflammatory, antioxidant, and inhibit the oxidation of low-density lipoprotein (LDL) cholesterol. Recent studies have suggested that the monocyte/HDL ratio (MHR)

Address for Correspondence: Ertuğrul Altınbilek, University of Health Sciences Turkey, Şişli Hamidiye Etfal Training and Research Hospital, Clinic of Emergency Medicine, İstanbul, Turkey
Phone: +90 212 373 50 00 **E-mail:** dr_ertugrul@yahoo.com **ORCID-ID:** orcid.org/0000-0003-4201-8850
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may be a unique marker of inflammation and oxidative stress. With this aspect, it can be used as a criterion that is calculated easily showing the presence and prognosis of inflammatory and inflammation-related diseases. Studies have shown that increased lactate, which is a marker of tissue hypoperfusion, may also have a role in stroke prognosis [7-10]. Therefore, in our study, we investigated the effects of lactate levels and MHR on mortality and stroke treatment.

Materials and Methods

Patients and Study Design

This retrospective study was conducted in the University of Health Sciences Turkey, Şişli Hamidiye Etfal Training and Research Hospital Emergency Medicine Clinic between January 01, 2019 and December 31, 2019 (University of Health Sciences Turkey, Şişli Hamidiye Etfal Training and Research Hospital Ethic Committee approval date: 30.06.2020, no: 1560). Patients who were treated with intravenous thrombolytic administration or thrombolytic + thrombectomy treatment in the emergency department with the diagnosis of acute cerebrovascular disease were included in the study. Demographic data, clinical features, radiological results, laboratory data, and National Institutes of Health Stroke Scale (NIHSS) scores of the patients were recorded at admission and after treatment. The patients who were admitted to the emergency department due to ischemic cerebrovascular disease without thrombolytic indication, patients who underwent thrombectomy only, those with hemorrhagic cerebrovascular disease, patients referred to an external center, patients who do not accept thrombolytic therapy, and patients who died after treatment were excluded from the study. All patients between the ages of 18-99 who were not excluded with the above reasons and who underwent thrombectomy and thrombolytic therapy together were included. NIHSS scores at admission to the emergency department and NIHSS scores after treatment were calculated and recorded.

Statistical Analysis

In the statistical analysis, IBM SPSS 22.0 (Armonk, New York) software was used. Mean, standard deviation, median, maximum, minimum, frequency, and ratio values were used in descriptive statistics of the numeric data. The distribution of numeric variables was evaluated using the Kolmogorov-Smirnov test. Kruskal-Wallis and Mann-Whitney U tests was used to compare the independent quantitative data between the groups. For the analysis of independent qualitative data, the chi-square test was used. Fischer's exact test was used when chi-square test conditions were not met. In cases where the p value was less than 0.05 in a 95% confidence interval, the results of statistical analysis were considered as significant.

Results

Our study included 189 patients with a mean age of 69.5±12.9 years and 57.7% of them were male. Of all patients, 88.4% of them had comorbidities. Lactate levels were 1.75±1.18 and MHR was 0.02±0.01 at the time of admission to the emergency department. The NIHSS scores at admission were 11.4±5.3, and post-treatment NIHSS scores were 7.52±5.03 (Table 1).

The patients were divided into groups according to the occluded intracranial artery causing ischemia. There was no

Table 1. Demographic data and laboratory findings of the patients

		Minimum-maximum	Median	Mean ± SD/n-%
Age (years)		30-96	70	69.5±12.9
Gender	Female			80-42.3
	Male			109-57.7
Comorbidity	(-)			22-11.6
	(+)			167-88.4
Monocyte/HDL		0.00-0.16	0.01	0.02±0.01
Lactate		0.60-9.70	1.40	1.75±1.18
NLR		0.60-23.00	2.53	3.54±3.05
Cholesterol		101.0-352.0	200.0	202.7±48.8
Non-HDL cholesterol		45.0-303.0	159.0	160.7±46.4
Total cholesterol/HDL		1.80-9.07	4.82	4.95±1.23
NIHSS at admission		1.0-22.0	11.0	11.4±5.3
NIHSS after treatment		0.00-22.00	7.00	7.52±5.03
NIHSS change		-18.0-12.0	-3.0	3.9±4.5

Statistical analysis: chi-square test, HDL: High-density lipoprotein, NIHSS: National Institutes of Health Stroke Scale, SD: Standard deviation, NLR: Neutrophil-to-lymphocyte ratio

significant difference between the anterior cerebral artery (ACA), middle cerebral artery (MCA), and posterior cerebral artery (PCA) groups in terms of patients' age, gender, and the distribution of comorbidities (p>0.05). Cholesterol, triglyceride, LDL, HDL, non-HDL, lactate and monocyte levels and neutrophil-to-lymphocyte ratio (NLR) and MHR did not differ significantly between the MCA, ACA, and PCA groups (p>0.05). The total cholesterol/HDL ratio was significantly higher in the PCA group than the MCA group (p<0.05). The total cholesterol/HDL ratio in the ACA group did not differ significantly from the MCA and PCA groups (p>0.05) (Table 2).

NIHSS scores at admission and after treatment differed significantly between the MCA, ACA, and PCA groups (p<0.05). However, there was no significant difference between the groups in terms of changes in the NIHSS scores at admission and after treatment (p>0.05) (Table 3).

There were no significant associations in terms of NIHSS score at admission, after treatment, change in NIHSS scores, and laboratory parameters (Table 4).

Discussion

Increased age is among the risk factors that cannot be change in stroke etiopathogenesis, and the stroke incidence increases with age. The annual incidence of stroke was 1.3-3.6/1.000 in the 55-64 age group, 4.9-8.9/1.000 in the 65-74 age group, and

Table 2. Demographic data and laboratory findings according to the occluded cerebral artery

			MCA	ACA	PCA	p
Age	Mean ± SD		70.7±12.5	68.3±12.2	65.3±15.1	0.128[A]
	Median		70.5	68.0	70.0	
Gender	Female	n%	60-46.2	11-33.3	9-34.6	0.286[X²]
	Male	n%	70-53.8	22-66.7	17-65.4	
Comorbidity	(-)	n%	13-10.0	3-9.1	6-23.1	0.146[X²]
	(+)	n%	117-90.0	30-90.9	20-76.9	
Monocyte/HDL	Mean ± SD		0.0±0.0	0.0±0.0	0.0±0.0	0.466[K]
	Median		0.0	0.0	0.0	
Lactate	Mean ± SD		1.7±1.0	1.8±0.8	2.0±2.2	0.318[K]
	Median		1.4	1.6	1.4	
NLR	Mean ± SD		3.7±3.3	3.3±2.6	2.9±1.8	0.082[K]
	Median		2.5	2.7	2.1	
Cholesterol	Mean ± SD		199.2±48.4	208.7±47.7	212.5±51.8	0.217[A]
	Median		195.2	212.0	225.5	
Non-HDL cholesterol	Mean ± SD		156.6±46.6	166.4±43.3	173.7±47.7	0.125
	Median		152.5	165.0	180.0	
Total cholesterol/HDL	Mean ± SD		4.8±1.3	5.0±1.0	5.5±1.0	**0.039**[A]
	Median		4.7	4.9	5.4	

[A]: One-Way ANOVA, [K]: Kruskal-Wallis test (Mann-Whitney U test), [X²]: Chi-square test, MCA: Middle cerebral artery, ACA: Anterior cerebral artery, PCA: Posterior cerebral artery, HDL: High-density lipoprotein, NLR: Neutrophil-to-lymphocyte ratio, SD: Standard deviation

Table 3. Evaluation of the NIHSS score according to the occluded cerebral artery

		MCA	ACA	PCA	p
NIHSS at admission	Mean ± SD	11.3±5.3	11.9±6.0	11.0±4.9	0.854[K]
	Median	10.0	11.0	10.5	
NIHSS after treatment	Mean ± SD	7.4±5.0	8.1±5.0	7.2±5.5	0.574[K]
	Median	7.0	7.0	5.0	
NIHSS change	Mean ± SD	-3.9±4.6	-3.8±4.5	-3.7±3.7	0.898[K]
	Median	-3.0	-3.0	-3.5	
Intragroup change p		**0.000**[W]	**0.000**[W]	**0.000**[W]	

[K]: Kruskal-Wallis test, [W]: Wilcoxon test, MCA: Middle cerebral artery, ACA: Anterior cerebral artery, PCA: Posterior cerebral artery, NIHSS: National Institutes of Health Stroke Scale, SD: Standard deviation

Table 4. Evaluation of laboratory findings according to the NIHSS

	NIHSS at admission		NIHSS after treatment		NIHSS change	
	r	p	r	p	r	p
Monocyte/HDL	0.009	0.903	0.042	0.565	0.007	0.922
Lactate	0.091	0.214	0.124	0.089	-0.020	0.780
NLR	0.037	0.613	0.014	0.853	-0.033	0.650
Cholesterol	-0.037	0.610	-0.053	0.469	-0.014	0.850
Non-HDL cholesterol	-0.042	0.566	-0.056	0.447	-0.013	0.856
Total cholesterol/HDL	-0.053	0.466	-0.054	0.461	-0.004	0.961

Spearman correlation, NIHSS: National Institutes of Health Stroke Scale, HDL: High-density lipoprotein, NLR: Neutrophil-to-lymphocyte ratio

13.5-17.9/1.000 in the >75 age group. It has been reported that approximately 70% of stroke patients are over the age of 65 [11]. Boğdaycıoğlu [12] reported the mean age of stroke patients as 71.5±12 years. In our study, the mean age of the patients was found to be 69.5±12.9, which is consistent with other studies.

Gender is one of the important factors in the etiology of stroke, and the rate of male stroke patients is higher than female patients in the literature [13,14]. Gender, which is one of the unchangeable risk factors, was higher in males in our study, in line with the literature.

Stroke patients are often elderly patients, and the rate of comorbidity increases with age. In our study, the most common comorbidities were hypertension, diabetes mellitus, and ischemic heart disease, respectively. There was no significant difference between the ischemic vessel in terms of comorbidity. In the study by Boğdaycıoğlu [12], the rate of comorbidity was found to be 76.3%. In our study, the rate of comorbid disease was 88.4%, consistent with the literature. In our study, different than the literature, MHR values were low and there was no significant difference between the groups, whereas the MHR was 0.67±0.59 in stroke patients. In addition, when we evaluated the NLR values, there was no significant difference in terms of ischemic vessels.

In the study of Jo et al. [15], increased lactate levels were reported as an independent risk factor for poor clinical outcome and are associated with increased mortality. There are various studies in which lactate levels are associated with mortality. In our study, it was shown that lactate levels were not different in terms of vascular pathologies and were not associated with poor outcome. In the study by Boğdaycıoğlu [12], the total cholesterol/HDL ratio was found to be 5.22±1.59, and it was concluded that the total cholesterol/HDL-C ratio in females was associated with ischemic stroke. In the study of Zhang et al. [16], low HDL and high total cholesterol/HDL ratio were associated with the risk of ischemic stroke. In our study, where we focused on the effect of occluded artery on ischemia, the total cholesterol/HDL ratio in the PCA group was significantly higher than that in the MCA group, but the total cholesterol/HDL ratio was not in the ACA group. It is different from the MCA and PCA groups.

It was concluded that high cholesterol ratios were associated with ischemic stroke, but cholesterol/HDL ratio was not significantly associated with vessels with ischemic pathology. When cholesterol, non-HDL cholesterol, and triglyceride levels were evaluated in terms of vessels causing ischemic pathology, no significant difference was found.

In the study by Ülker et al. [17], it was shown that the NIHSS score at admission to hospital is an important marker in determining the early prognosis. In our study, when the NIHSS scores at hospitalization were compared with the NIHSS scores after treatment, a significant decrease was observed on discharge. The efficacy of thrombolytic therapy was demonstrated in accordance with the literature. No relationships between NIHSS scores on admission and post-treatment scores and monocyte levels, HDL levels, monocyte/HDL levels, lactate levels, neutrophil levels, lymphocyte levels, NLR value, cholesterol levels, non-HDL cholesterol levels, total cholesterol/ HDL value, triglyceride levels, and LDL levels. It can be concluded that laboratory parameters do not affect the outcome of the treatment applied

Conclusion

Monocyte/HDL ratio and lactate levels have no effect on prognosis in patients with ischemic stroke patients.

Ethics

Ethics Committee Approval: University of Health Sciences Turkey, Şişli Hamidiye Etfal Training and Research Hospital Ethic Committee approval date: 30.06.2020, no: 1560.

Informed Consent: Retrospective study.

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Authorship Contributions

Surgical and Medical Practices: D.K., D.Ö., E.A., Concept: D.K., D.Ö., A.M., E.A., Design: D.K., A.M., E.U., E.A., Data Collection or Processing: D.K., A.M., E.U., E.A., Analysis or Interpretation: D.K., A.M., E.U., E.A., Literature Search: D.K., E.U., E.A., Writing: D.K., D.Ö., E.A.

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References

1. Rowland LP, Pedley TA. Serebrovasküler hastalığın patogenezi, sınıflandırılması ve epidemiyolojisi. 12th ed. Merritt's Neurology Türkçe, İstanbul: Güneş Tıp Kitabevleri; 2012. p.250-63.
2. Efstathiou SP, Tsioulos DI, Zacharos ID, Tsiakou AG, Mitromaras AG, Mastorantonakis SE, et al. A new classification tool for clinical differentiation between haemorrhagic and ischaemic stroke. J Intern Med. 2002;252:121-9.
3. Roger VL, Go AS, Lloyd-Jones DM, Adams RJ, Berry JD, Brown TM, et al. Heart disease and stroke statistics--2011 update: a report from the American Heart Association. Circulation. 2011;123:e18-e209.
4. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. 2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2018;49:e46-e110.
5. Rist PM, Buring JE, Ridker PM, Kase CS, Kurth T, Rexrode KM. Lipid levels and the risk of hemorrhagic stroke among women. Neurology. 2019;92:e2286-94.
6. Yaghi S, Elkind MS. Lipids and cerebrovascular disease: research and practice. Stroke. 2015;46:3322-8.
7. Barter PJ, Nicholls S, Rye KA, Anantharamaiah GM, Navab M, Fogelman AM. Antiinflammatory properties of HDL. Circ Res. 2004;95:764-72.
8. Ancuta P, Wang J, Gabuzda D. CD16+ monocytes produce IL-6, CCL2, and matrix metalloproteinase-9 upon interaction with CX3CL1-expressing endothelial cells. J Leukoc Biol. 2006;80:1156-64.
9. Canpolat U, Çetin EH, Cetin S, Aydin S, Akboga MK, Yayla C, et al. Association of monocyte-to-HDL cholesterol ratio with slow coronary flow is linked to systemic inflammation. Clin Appl Thromb Hemost. 2016;22:476-82.
10. Koçak HE, Acipayam H, Elbistanlı MS, Yiğider AP, Alakhras W, Kıral MN, et al. Is the monocyte/HDL ratio a prognostic marker of idiopathic sudden hearing loss? Otolaryngol Pol. 2016;70:26-30.
11. Neurological Disorders; A Public Health Approach. In Neurological disorders A Public Health Challenge. WHO 2006, WHO Press Switzerland. 3, p.151-63. https://apps.who.int/iris/handle/10665/43605
12. Boğdaycıoğlu N. Akut iskemik inmeli hastalarda non-HDL, Total Kolesterol, HDL kolesterol ve LDL-kolesterol düzeyleri Ş.E.E.A.H. Tıp Bülteni 2013;47:187-92.
13. Efstathiou SP, Tsioulos DI, Zacharos ID, Tsiakou AG, Mitromaras AG, Mastorantonakis SE, et al. A new classification tool for clinical differentiation between haemorrhagic and ischaemic stroke. J Intern Med. 2002;252:121-9.
14. Fatema K, Bailey KR, Petty GW, Meissner I, Osranek M, Alsaileek AA, et al. Increased left atrial volume index: potent biomarker for first-ever ischemic stroke. Mayo Clin Proc. 2008;83:1107-15.
15. Jo S, Jeong T, Lee JB, Jin YH, Yoon J, Jun YK, et al. Initial hyperlactatemia in the ED is associated with poor outcome in patients with ischemic stroke. Am J Emerg Med. 2012;30:449-55.
16. Zhang Y, Tuomilehto J, Jousilahti P, Wang Y, Antikainen R, Hu G. Total and high-density lipoprotein cholesterol and stroke risk. Stroke. 2012;43:1768-74.
17. Ülker M, Dayan C, Hoşver Y, Dirican A, Günaydın S, Arpacı B. İskemik inmede başlangıç National Institute of Health (NIH) Skorunun erken dönem prognozu belirlemedeki değeri: Geniş hasta gruplu retrospektif bir çalışma. Düşünen Adam 2004;17:154-7.

ORIGINAL RESEARCH

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Comparison of Ambulance Patients and Outpatients Presented to the Pandemia Area of a University Hospital Emergency Department

Derviş Yıldız[1], Durdu Mehmet Uzucek[2], Ahmet Burak Urfalıoğlu[3], Satuk Buğra Yapıcı[4], Kemal Şener[5], Akkan Avci[6], Sadiye Yolcu[6]

[1]*İskenderun State Hospital, Clinic of Emergency Medicine, Hatay, Turkey*
[2]*Necip Fazıl City Hospital, Clinic of Emergency Medicine, Kahramanmaraş, Turkey*
[3]*Kırıkhan State Hospital, Clinic of Emergency Medicine, Hatay, Turkey*
[4]*Mehmet Akif İnan Training and Research Hospital, Department of Emergency Medicine, Şanlıurfa, Turkey*
[5]*University of Health Sciences Turkey, Başakşehir Çam and Sakura City Hospital, Clinic of Emergency Medicine, İstanbul, Turkey*
[6]*University of Health Sciences Turkey, Adana City Training and Research Hospital, Clinic of Emergency Medicine, Adana, Turkey*

Abstract

Objective: In this study, we compared the coronavirus disease-2019 (COVID-19)+/suspected patients who presented to the pandemia area (outpatient enterance/ambulance enterance) of our emergency department (ED) and to determine whether the ambulance system is used appropriately or not during this pandemia process.

Materials and Methods: Patients were divided into two groups as outpatients and ambulance patients. Demographic data, sampling ratio of polymerase chain reaction (PCR) swab, PCR positivity, thorax computed tomography (CT), CT positivity, hospitalization ratio and hospitalization day, length of stay in the ED, and the outcome of the groups were compared.

Results: The mean age of ambulance patients was 53.8±20.2 (min: 18, max: 93), and the ambulance patients were 41.4±16.04 (min: 18, max: 96) and this value was significantly higher in ambulance patients. Length of stay in the ED of the ambulance patients was 6.1 h and this value was 2.9 h for the other group. Hospitalization length of discharged patients from the intensive care unit (ICU) was 20.6 days for ambulance patients and 16.9 days for outpatients. Three of the outpatients and 22 of the ambulance patients died during hospitalization and 18 of these were males.

Conclusion: The mean age, CT positivity, and PCR test positivity were significantly higher in ambulance patients. Similarly, ambulance patients' length of stay in the ED was higher who were discharged from the ED. ICU hospitalization, hospitalization length, and mortality ratio were higher in ambulance patients. Considering these results, it is important to develop appropriate strategies for ambulance and outpatients, to prevent already crowded EDs squeezing under the COVID-19 burden.

Keywords: COVID-19, ambulance, emergency department, outpatients, intensive care unit

Introduction

Emergency departments (ED) are units that provide 24 h healthcare service. This situation leads the EDs easy-reacheable and inappropriate use of these units and so over-crowdedness ocur. Other reasons for this crowdedness are disasters and contagions, so the patients present to the EDs first when these situations ocur [1-3].

Coronavirus disease-2019 (COVID-19) had first started in China and spread to most of the countries on earth. And global pandemia was announced on March 11, 2020. ED has become the first presentation unit and served as a tampon during this COVID-19 pandemia. Prehospital emergency medical services and EDs become unsufficient since the pandemia has started [4].

Address for Correspondence: Akkan Avci, University of Health Sciences Turkey, Adana City Training and Research Hospital, Clinic of Emergency Medicine, Adana, Turkey
Phone: +90 533 423 03 69 **E-mail:** drakkanavci@gmail.com **ORCID-ID:** orcid.org/0000-0002-4627-0909
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In this study, we compared the COVID-19 +/suspected patients who were presented to the pandemia area (outpatient enterance/ambulance enterance) of our ED and to determine whether the ambulance system is used appropriately or not during this pandemia process. According to our knowledge, there is a lack of data for the emergency service observation, prognosis, and outcome of COVID-19 +/suspected patients according to the presentation method. This study may contribute to the literature.

Materials and Methods

After the ethics committee approval (AUniversity of Health Sciences Turkey, Adana City Training and Research Hospital Ethics Committee -22 April 2020-827), we researched the data of outpatients ambulance patients who presented to the pandemia area of our ED and 15 March-15 May 2020 via the hospital's automation system. Patients were divided into two groups as outpatients and ambulance patients. Demographic data, sampling swab for polymerase chain reaction (PCR)-if yes the test result, chest computed tomography (CT) screening-if yes the imaging result, length of stay in the ED (hour), hospitalization length (day), hospitalization unit [inpatient clinic (IPC)/intensive care unit (ICU)], and the outcome were recorded on the study forms. These parameters were compared between the two groups. Patients under 18 years old, patients with missing data, patients who were referred to another hospital because of ICU bed, and patients become ex in the ED were excluded from the study.

Statistical Analysis

Statistical comparisons were performed using the statistical software package SPSS 25.0 (SPSS Inc., Chicago, IL, USA). The Shapiro-Wilk test was used to control for the normal distribution. The normally distributed variables were evaluated parametric, and non-normally distributed parameters were evaluated with non-parametric tests. The mean values of the independent groups were compared with t-test and Mann-Whitney U test. A chi-square test was used for comparing the ratios of two independent groups. The Kruskal-Wallis test was used to compare the grous more than two and Mann-Whitney U test was used as the post-hoc test. Benferoni correction was used for p value. The spearman correlation was used for independent parameters. The categorical variables are expressed in frequencies and percentages. Definitive statistics were expressed as a mean ± standard deviation and median (interquartile range). A p value <0.05 was considered significant.

Results

We included 436 (46.5%) ambulance and 501 (53.5%) outpatients, and totally 937 patients in this study. The mean age of the ambulance patients was 53.8±20.2 (min: 18, max: 93), and 41.4±16.04 (min: 18, max: 96) fort he outpatients. The mean age of the ambulance group was significantly higher (p=0.000).

The chest CT imaging ratio was significantly higher in the ambulance patients (91.7% vs. 72.9%) (p=0.000). The compatible CT result ratios of the ambulance and outpatient groups were 34.5% and 29.5% consecutevly (p=0.143).

The PCR test was ratio was significantly higher in the ambulance patients (98.2% vs. 91%) (p=0.000). PCR positivity ratio in the ambulance patients was 28.5% and this value was 30.5% in the outpatient group, but this difference was not statistically significant (p=0.508).

Fifty-six (12.8%) of the ambulance patients, and 16 (3.19%) outpatients were hospitalized in the ICU.

When we considered the patients who were discharged from the ED, the mean waiting time of the ambulance patients was 6.1±5.8 hours and this value was 2.9±4.63 hours for outpatients. Fifty-six (12.8%) of the ambulance patients and 12 (3.19%) outpatients were hospitalized in the ICU. The mean hospitalisation length of the patints who were discharged from the ICU was compared. Ambulance patients were hospitalized 20.6 days, and the outpatients were hospitalized 16.9 days (p=0.00). And this difference was statistically significant. Three of the outpatients and 22 of the ambulance patients died. Eighteen of these 25 patients were males. Length of stay in the ED and hospitalization length in the ICU/IPC of the groups are summarized in Table 1.

We found much more COVID-19 compatibility in males' chest CTs in the ambulance patient group (66.9% vs. 33.1%) (p=0.019).

In the outpatient group, the elder age was significantly correlated with the waiting time duration in the ED (p=0.000, r=0.333). Similarly, this correlation was determined in the ambulance group too (p=0.000, r=0.424). And hospitalization length was significantly correlated with age in the ambulance patients (p=0.00, r=0.187).

Discussion

Patients present to the EDs via ambulance or as an outpatient. Crowdedness of EDs has still been an important problem for most of the countries. This crowdedness has several causes, and solution suggestions are being discussed. Unnecessary presentations (both for outpatients and ambulances) constitute are the major problem and followed by a long waiting time of complicated patients in the ED for hospitalization [5,6].

ED presentations have been arose for 15 years in the UK. Treatment and dischargement within 24 and 48 h in the ED observation rooms made EDs much more attractive for people. And the circulation has become much more rapid [7].

Table 1. The time spent in the ED, hospitalisation length in the ICU/IPC of the groups

Outcome	Groups	Time					p
		n	Mean	Minninum	Maximum	SD	
Discharged from the ED (hour)	Ambulance	156	6.17	1	36	5,78001	**0.000**
	Outpatient	337	2.94	0	72	4,63900	
Discharged from the ICU (hour)	Ambulance	35	20.60	1	54	12,80900	0.416
	Outpatient	13	16.92	1	62	16,45935	
Ex in the ICU (day)	Ambulance	21	16.76	1	85	20,67101	0.254
	Outpatient	3	12.00	8	17	4,58258	
Discharged from the IPC (day)	Ambulance	201	8.09	1	60	7,32366	**0.001**
	Outpatient	150	6.85	1	34	4,90362	
Ex in th IPC (day)	Ambulance	1	6.00	-	-	-	-
	Outpatients	0	0	-	-	-	-

ED: Emergency department, ICU: Intensive care unit, IPC: Inpatient clinic, SD: Standard deviation

EDs are easy reachable units and the capacities of the EDs are being developed and enlarged each day to prevent the crowdedness, this enlargement causes new crowded masses and much more patients waiting in the ED. Determining the primary necessity of the patients and providing the priority of the critically ill patients are the most important keypoints in managing the circulation of an ED. An effective triage may help in these situations. Comprehensive and modern hospitals have separated entrances for ambulances and outpatients. This is a kind of triage because we know that critically ill patients almostly brought by ambulances, although it may have some inaproppriate use. Therefore, the ambulance patients can be accepted as red according to the triage systems and evaluated immediately [5].

COVID-19 infection started in China in December 2019 and spread worldwide in 2020 and called pandemia [7,8]. ED s have been the fisrt admission unit of COVID-19 +/suspected patients. Besides, admissions of patiens with mild symptoms made the situation unsolvable for emergency healthcare workers [9]. Recently, precautions and knowing more about the disease made it easier to struggle. But nowadays, the second wave has started and it looks much more destructive than the previous. Therefore, it is going to be an important keypoint to differentiate critically ill-moderate-mild patients for a better ED circulation.

In our study, 46.5% patients were ambulance patients. And 58.3% of the total presentations to the pandemia area were males. The mean age of the ambulance patients was 53.8, and 41.4 for the outpatients in an Australia emergency -based study, 55% of the suspected COVID-19 patients were male and the mean age was 60. In the same study 59% patients were presented with an ambulance. This study was based on the complaints and findings of the suspected patients [4]. In the same study, 29% of the patients were hospitalized in the ICU, and 13% of the patients who were hospitalized into the IPC were referred to another hospital. We are a third -degree hospital so we did not refer any patients to the other hospitals' ICU or IPCs. According to Spanish data, 74.6% of the COVID-19 suspected patients were hospitalized. 5.9% of those were to the ICU, and 14.6% of the hospitalized patients died [9].

The mean age of the ambulance patients was higher than the outpatients in our study. Because older people have many comorbidity and their COVID-19 process is progresses mugh more severe and they cannot present as an outpatient. Similarly COVID-19 mortality ratio is higher in elder patients. In some studies, mortality is related especially to ischemic heart diseas, pneumonia, demans, and chronic obstructive pulmonary disease [10-12].

The thorax CT rate was higher in ambulance patients in our study compared with the outpatients. The conformity ratio of CT with COVID-19 was 34.5% and 29.5% in outpatients. When its thought that elder patients present with an ambulance and with significant breathing problems usage of CT imaging doesnot seem confusing.

According to these results, emergency room areas can be re-planned during the evaluation process of COVID-19 patients in emergency services. A separate area can be created for ambulance and ambulatory entrances of patients. This area to be created can be in the emergency room or in another hospital area. In these areas, patients can be managed with a multidisciplinary approach.

Conclusion

While a many uncertainty of COVID-19 infection continue, prehospital emergency medical systems and emergency services are exposed to a high weight, especially this second wave, emergency clinicians must prepare themselves and the

plan of for EDs for COVID-19 suspected/+ ambulance and outpatients. We should predict the fort he clinical situations we will meet, which diagnostic tests we should see, which hospitalization clinic is the best fort he patients and the outcome. If we can not dope out, there is no way to plan the circulation of the department. This predictable study may be a light for EDs for not to squeeze under the COVID-19 burden, which are overcrowdening day by day.

Ethics

Ethics Committee Approval: University of Health Sciences Turkey, Adana City Training and Research Hospital Ethics Committee, date: 22.04.2020, decision no: 827.

Informed Consent: Since the data were obtained from the hospital automation system and our study was a retrospective cross-sectional study, informed consent forms were not obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: D.Y., D.M.U., A.B.U., S.B.Y., A.A., S.Y., Concept: D.Y., A.B.U., S.B.Y., K.Ş., A.A., S.Y., Design: D.Y., A.B.U., S.B.Y., K.Ş., A.A., S.Y., Data Collection or Processing: D.Y., D.M.U., A.B.U., S.B.Y., Analysis or Interpretation: D.Y., D.M.U., S.B.Y., K.Ş., A.A., S.Y., Literature Search: D.M.U., A.B.U., K.Ş., A.A., S.Y., Writing: D.Y., A.A., S.Y.

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References

1. Di Somma S, Paladino L, Vaughan L, Lalle I, Magrini L, Magnanti M. Overcrowding in emergency department: an international issue. Intern Emerg Med. 2015;10:171-5.
2. Alyasin A, Douglas C. Reasons for non-urgent presentations to the emergency department in Saudi Arabia. Int Emerg Nurs. 2014;22:220-5.
3. Moskop JC, Sklar DP, Geiderman JM, Schears RM, Bookman KJ. Emergency department crowding, part 1--concept, causes, and moral consequences. Ann Emerg Med. 2009;53:605-11.
4. O'Reilly GM, Mitchell RD, Rajiv P, Wu J, Brennecke H, Brichko L, et al. Epidemiology and clinical features of emergency department patients with suspected COVID-19: Initial results from the COVID-19 Emergency Department Quality Improvement Project (COVED-1). Emerg Med Australas. 2020;32:638-45.
5. Çalis M, Sener K, Kaya A, Sari S, Polat M, Yolcu S. The prediction levels of emergency clinicians about the outcome of the ambulance patients and outpatients. Am J Emerg Med. 2020;38:1463-5.
6. Olshaker JS, Rathlev NK. Emergency Department overcrowding and ambulance diversion: the impact and potential solutions of extended boarding of admitted patients in the Emergency Department. J Emerg Med. 2006;30:351-6.
7. Pope I, Ismail S, Bloom B, Jansen G, Burn H, McCoy D, et al. Short-stay admissions at an inner city hospital: a cross-sectional analysis. Emerg Med J. 2018;35:238-46.
8. Burki TK. Coronavirus in China. Lancet Respir Med. 2020;8:238.
9. Martín-Sánchez FJ, Del Toro E, Cardassay E, Valls Carbó A, Cuesta F, Vigara M, et al. Clinical presentation and outcome across age categories among patients with COVID-19 admitted to a Spanish Emergency Department. Eur Geriatr Med. 2020;11:829-41.
10. Möckel M, Bachmann U, Behringer W, Pfäfflin F, Stegemann MS. How emergency departments prepare for virus disease outbreaks like COVID-19. Eur J Emerg Med. 2020;27:161-2.
11. Singer AJ, Morley EJ, Meyers K, Fernandes R, Rowe AL, Viccellio P, et al. Cohort of four thousand four hundred four persons under investigation for COVID-19 in a New York Hospital and Predictors of ICU Care and Ventilation. Ann Emerg Med. 2020;76:394-404.
12. Flynn D, Moloney E, Bhattarai N, Scott J, Breckons M, Avery L, et al. COVID-19 pandemic in the United Kingdom. Health Policy Technol. 2020;9:673-91.

ORIGINAL RESEARCH

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Comprehensive Evaluation of Blood Product Transfusions Administered in the Emergency Department

Savaş Seçkin[1], Abuzer Coşkun[2], Burak Demirci [2], Betül Çam[3]

[1]Elazığ State Hospital, Clinic of Emergency Medicine, Elazığ, Turkey
[2]University of Health Sciences Turkey, İstanbul Bağcılar Training and Research Hospital, Clinic of Emergency Medicine, İstanbul, Turkey
[3]University of Health Sciences Turkey, Başakşehir Çam and Sakura City Hospital, Clinic of Emergency Medicine, İstanbul, Turkey

Abstract

Objective: It was aimed to evaluate the clinical and laboratory findings, the frequency and distribution of post-transfusion complications of patients who presented to the emergency department with a transfusion indication.

Materials and Methods: In our study, patients aged 18 years and over who applied to the emergency medicine clinic between January 01, 2019 and March 31, 2019, who had blood and blood product transfusions, were retrospectively analyzed. The demographic and clinical characteristics of the patients, the reason for transfusion, the number of transfused blood products, the presence and type of complications were analyzed.

Results: Three hundred and sixty-eight patients who received blood and blood product transfusions were included in the study. The mean age of the patients was 62.5±19.3 years (range 18-96 years), 193 (52.4%) were female and 175 (47.6%) were male. The most common causes of transfusion were symptomatic anemia in 110 patients (29.9%), oncological diseases in 71 patients (19.3%), gastrointestinal bleeding in 65 patients (17.7%), and chronic renal failure patients in 59 (16%) patients. No post-transfusion complication was observed in 358 (97.3%) patients for all blood products. Multiple erythrocyte suspension (ES) data revealed significant variation in hemoglobin and hematocrit levels among patients (p=0.001). Additionally, a significant difference was found in the international normalized ratio because of administering more than one unit of fresh frozen plasma (FFP) (p=0.002). Complications were observed in 2.9% of patients given ES and 1.9% of patients given FFP, whereas none of the patients given thrombocyte suspension developed.

Conclusion: The appropriate use of blood and blood products in the emergency department plays a critical role in preventing patient morbidity and mortality. Performing the transfusion procedure in the correct indication is important in preventing the risk of infection in the emergency department.

Keywords: Blood transfusion, red blood cells, blood product, hemoglobin, emergency department

Introduction

Blood and blood product transfusions, which play an important role in critical patient care, are used in the emergency department as a treatment option for trauma and acute blood loss. On the basis of symptoms and clinical examination, the correct identification of patients with a high priority for blood transfusion and estimation of blood volume for transfusion are often performed. However, giving each blood unit incurs costs for the healthcare system, and these products must be transfused quickly. Hence, accurate prognosis and identification of patients' blood transfusion requirements must be considered as well [1]. Blood and blood products are living tissues made up of various structures, each serving a different purposes. Blood transfusion is a life-saving procedure that is similar to tissue transplantation and carries some risks [2].

Blood and blood product transfusions are frequently performed in emergency departments where many patients come for treatment and diagnosis [2]. Approximately 15 million units

Address for Correspondence: Savaş Seçkin, Elazığ State Hospital, Clinic of Emergency Medicine, Elazığ, Turkey
Phone: +90 553 532 89 19 **E-mail:** drsavasseckin@hotmail.com **ORCID-ID:** orcid.org/0000-0002-5893-8929
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of erythrocyte suspension (ES) are transfused annually in the United States, and this figure is 85 million units worldwide [3]. In line with the recommendations in the guidelines for blood transfusion, lower values for ES transfusion were determined for critically ill patients in conditions such as intensive care and onco-hematology [4]. While a threshold of 7 g/dL is given for the hemoglobin (Hb) value, especially for patients with acute gastrointestinal (GI) bleeding, the lower limit of Hb value is 10 g/dL in cases of acute coronary syndrome or heart failure or in a patient with symptomatic anemia describing tachycardia, mental status change, hypotension, and dyspnea. recommended as dL [5,6]. Apart from these conditions, the threshold value may vary according to the tolerance status of the patient in patients who receive chemotherapy, are anemic due to chronic conditions, or have hematological malignancies [7].

Transfusion of blood and blood products is a transplantation process for living tissues that might result in life-threatening problems such as allergic reaction and volume overload [8]. There is a need in the literature for research on the outcomes of transfusions and the frequency of complications. Research focusing on the transfusion of blood and blood products, particularly in emergency services, is crucial for developing acute transfusion requirement algorithms.

This study aimed to increase awareness in the operation of the emergency service by examining the clinical circumstances and laboratory findings of patients in the emergency department, which form the transfusion indication. Therefore, it will be possible to evaluate the correct indication for blood transfusion in the emergency room and to provide the appropriate intervention by anticipating potential complications.

Materials and Methods

Study Design and Population

The study sample comprises 368 patients 18 years and older who received blood and blood product transfusions in the emergency department of our hospital between January 1, 2019 and March 31, 2019. The patient information was extracted from the computerized recording system. It is a hospital for tertiary education and research with comprehensive computer data security. Participants with missing data in the electronic registration system were excluded from the study, whereas patients who underwent transfusions of blood and blood products were included.

Before starting the study, permission was obtained from the Clinical Research Ethics Committee of University of Health Sciences Turkey, İstanbul Bağcılar Training and Research Hospital (date: 15.01.2021, number: 2021.01.1.1.09.208. r1.009). In the conduct of the study, the Declaration of Helsinki and the principles of Good Clinical Practice were followed. The data of the patients included in the study were not used other than for scientific purposes. No financial support was received from any person or organization at any stage of the research, including design, data collection, data analysis, and writing.

Patient data were obtained by retrospectively scanning patient files. During the screening, a case report form was used. The case report form includes 16 variables of patients' demographic and clinical characteristics and transfusion-related characteristics. These variables are age, gender, triage level (yellow, green, and red areas), blood group, reason for transfusion, pre-transfusion and post-transfusion Hb, hematocrit (Hct), international normalized ratio (INR) values and platelet count, transfused blood product ES, fresh frozen plasma (FFP), thrombocyte suspension (TS), and whole blood, number of blood products [unit (U)], the presence of complications, type of complication, and outcome of patients (outpatient treatment, hospitalization, intensive care admission, emergency surgical operation, exitus).

Statistical Analysis

SPSS version 22.0 statistical software was used in the analysis of the data. The socio-demographic characteristics, clinical characteristics, and descriptive statistics of the transfusion-related characteristics of the patients included in the study are given. The descriptive statistics of the study are shown using mean ± standard deviation and median, minimum, and maximum values for numerical variables, and numbers (n) and percentage (%) for categorical variables. For continuous numerical variables that did not show a normal distribution, the Mann-Whitney U test was used for comparisons of two groups, and the Kruskal-Wallis test was used for comparisons of more than two groups. Dunn's post-hoc test was used for post-hoc pairwise comparisons. Fisher's exact test was used to compare categorical variables. The statistical significance limit was accepted as $p<0.05$.

Results

The mean age of the patients was 62.5±19.3 years (range 18-96 years), 193 (52.4%) were female and 175 (47.6%) were male. When the triage levels were examined, 138 patients (37.5%) were observed in the green area, 140 patients (38.0%) were in the yellow area, and 90 patients (24.5%) were in the red area. According to the blood groups, the blood group of 20 (5.4%) patients were 0 Rh (-), 110 (29.9%) 0 Rh (+), 24 (6.5%) A Rh (-), 134 (36.4% A Rh (+), 10 (2.7%) B Rh (-), 54 (14.7%) B Rh (+), and 16 (4.3%) AB Rh (+) were determined (Table 1).

Common causes of blood transfusion were symptomatic anemia in 29.9%, oncological disease in 19.3%, GI hemorrhage in 17.7%, and chronic renal failure (CRF) in 16.0%. Other causes included warfarin overuse, non-traumatic hemorrhage, traumatic hemorrhage, and hematological diseases. The mean

Hb value before transfusion of the patients participating in the study was 6.98±1.95 g/dL, the mean Hct value was 22.78±5.74 (%), the mean platelet count was 268635±163300 cells/μL, and the mean INR was 1.89±2.50. Post-transfusion complications were not observed in 358 (97.3%) patients, whereas 5 (1.4%) had fever, 4 (1.1%) urticaria, and 1 (0.3%) volume overload. Of the patients, 204 (55.4%) were followed-up outpatients, 134 (36.4%) were hospitalized, 18 (4.9%) were hospitalized in the intensive care unit, 10 (2.7%) had emergency surgery, and 2 (0.5%) resulted in mortality (Table 1).

Table 1. Demographic and clinical characteristics of patients transfused with blood and blood products

Demographic and clinical characteristics		n (%)
Gender	Female	193 (52.4)
	Male	175 (47.6)
Age (year)	<40	55 (14.9)
	40-59	88 (23.9)
	60-79	145 (39.4)
	>80	80 (21.7)
Mean ± SD (age/year)	62.5±19.3	
Application area	Green	138 (37.5)
	Yellow	140 (38.0)
	Red	90 (24.5)
Blood group	0 Rh (-)	20 (5.4)
	0 Rh (+)	110 (29.9)
	A Rh (-)	24 (6.5)
	A Rh (+)	134 (36.4)
	B Rh (-)	10 (2.7)
	B Rh (+)	54 (14.7)
	AB Rh (+)	16 (4.3)
Transfusion reason	Symptomatic anemia	110 (29.9)
	Oncological disease	71 (19.3)
	Gastrointestinal hemorrhage	65 (17.7)
	Chronic renal disease	59 (16.0)
	Warfarin overuse	23 (6.3)
	Non-traumatic hemorrhage	17 (4.6)
	Traumatic hemorrhage	12(3.3)
	Hematological disease*	11 (3.0)
Post-transfusion complication	None	358 (97.3)
	Fever	5 (1.4)
	Urticaria	4 (1.1)
	Volume load	1 (0.3)
Clinical outcome	Outpatient treatment	204 (55.4)
	Inpatient service	134 (36.4)
	Intensive care unit	18 (4.9)
	Emergency surgery	10 (2.7)
	Mortality	2 (0.5)
Total		368 (100)

Distribution of variables as n (%), *Thrombotic thrombocytopenic purpura, immune thrombocytopenic purpura, myelodiplastic syndrome, thalassemia etc. includes diseases, SD: Standard deviation

When the distribution of ES transfusion was analyzed according to the triage level and transfusion reasons, the mean ES given to the patients admitted to the green area was 1.56±0.77 U, 1.71±0.96 U in the yellow area, and 1.83±0.89 U in the red area. This difference between the groups was not statistically significant (p=0.070). Among the causes of transfusion, GI hemorrhage was the most common cause of ES transfusion, whereas hematological diseases, oncological diseases, traumatic hemorrhages, and warfarin overuse were other causes. There was a significant difference between the reasons for ES transfusion administration (p=0.001). Considering the distribution of FFP in transfusion rates, the mean FFP given to patients admitted to the green area was 0.14±0.49 U, 0.20±0.53 U in the yellow area, and 0.36±0.74U in the red area (p=0.016). Warfarin overuse was found to be the most common cause of 1.87±0.55 U among the causes of FFP transfusion (p=0.001). When the TS transfusion distribution of the patients was examined, the mean TS given to the patients applied in the green area was 0.03±0.21 U, 0.07±0.33 U in the yellow area, and it was found that no TS was given to the patients who applied to the red area. This difference between the groups was not statistically significant (p=0.066). Among the causes of TS transfusion, hematological diseases were the most common cause (p=0.001, Table 2).

Hb changes after transfusion in patients who received ES transfusion mean Hb change in patients who received 1U ES was 1.16±0.64 g/dL, 2.20±0.93 g/dL in patients who received 2U, 2.99±1.23 g/dL in patients who received 3U. It was determined as 3.08±1.34 g/dL in those given 4U, and 5.80 g/dL in those given 5U. (p=0.001). In post-hoc pairwise comparisons of post-transfusion Hb changes in patients who received ES transfusion, there was a statistically significant difference between patients given 1U ES and patients given 2U (p=0.001) and between patients given 2U of ES and patients given 3U (p=0.014) in terms of Hb exchange levels. However, there was no statistically significant difference in Hb change between patients given 3U and patients given 4U, and between patients given 4U and patient given 5U (Figure 1).

When the post-transfusion Hct changes according to the number of transfusions were examined, the mean Hct change was 3.81±2.69% in patients given 1U ES, 6.50±3.41% in patients given 2U, 8.71±3.81% in patients given 3U. While it was 8.53±4.19% in those given 4U, the change in Hct was found to be 17.30% in 1 patient who was given 5U (p=0.001). Post-Hoc paired comparisons of Hct changes after transfusion in patients who received ES transfusion found a statistically significant difference in terms of Hct change levels between

patients given 1U ES and patients given 2U (p=0.001), and patients given 2U ES and patients given 3U (p=0.016). However, there was no statistically significant difference between the patients given 3U and the patients given 4U, and between the patients given 4U and the patient given 5U in terms of Hct change (Figure 2).

Discussion

Changes in environmental conditions in modern life, an increase in the number of patients in emergency services, and the appearance of new types of diseases increase the demand for blood, for which there is no substitute [9]. Blood and its derivatives derived from humans are expensive and difficult to obtain; therefore, it is vital to handle these products with more care and avoid their unnecessary use [10,11]. In this study, we studied the indications, therapeutic applications, and problems of blood and its products, which are commonly used by emergency services.

Because of several clinical investigations, blood and its products are used differently based on gender. 61% of the 507 patients who received blood transfusions in the study by Waiswa et al. [12] were male, whereas 39% were female. In the study by Okello et al. [13] on patients aged 28 to 54 years, 55% of the transfused patients in 2012 were female. According to the literature, 175 (46.6%) of 368 patients in our study were male.

When the blood group distributions of the transfused patients were examined, the blood groups of the transfused patients were examined and it was found that 41.4% were group A, 36% were group O, 15.4% were group B, and 7.2% were group AB [14]. In the blood transfusion study by Azizi et al. [15], it was determined that 28.6% group A, 34.3% group O, 14.3% group B,

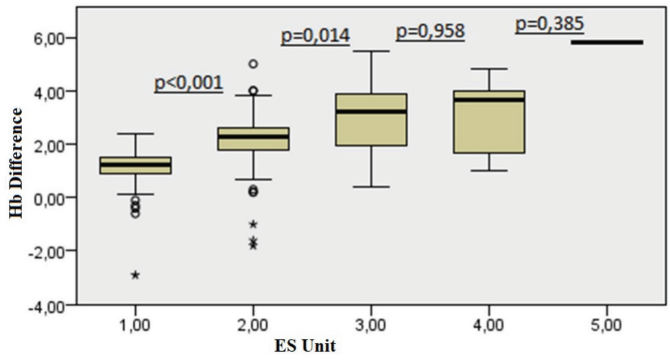

Figure 1. Post-transfusion Hb changes according to the number of transfusions in patients who received ES transfusion

HB: Hemoglobin, ES: Erythrocyte suspension

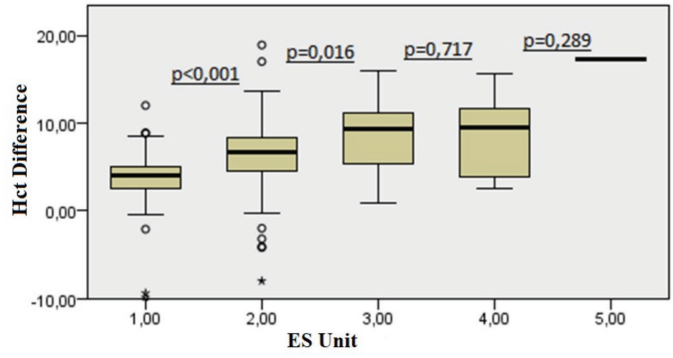

Figure 2. Post-transfusion Hct changes according to the number of transfusions in ES transfused patients

HCT: Hematocrit, ES: Erythrocyte suspension

Table 2. Distribution of ES, FFP and TS transfusions according to patients' application area and transfusion reasons

		Erythrocyte suspension unit		Fresh frozen plasma unit		Thrombocyte suspension unit	
		Mean ± SD	p value	Mean ± SD	p value	Mean ± SD	p value
Triage level	Green	1.56±0.77	0.070	0.14±0.49	**0.016**	0.03±0.21	0.066
	Yellow	1.71±0.96		0.20±0.53		0.07±0.33	
	Red	1.83±0.89		0.36±0.74		0	
Transfusion reason	Symptomatic anemia	1.65±0.60	**0.001**	0.04±0.19	**0.001**	0.00±0.00	**0.001**
	Oncological disease	1.70±0.72		0.11±0.32		0.08±0.33	
	Gastrointestinal hemorrhage	2.20±1.02		0.12±0.38		0.02±0.12	
	Chronic renal disease	1.64±0.76		0.03±0.18		0	
	Warfarin overuse	0.57±1.12		1.87±0.55		0	
	Non-traumatic hemorrhage	1.41±0.71		0.59±0.87		0	
	Traumatic hemorrhage	1.67±0.49		0.33±0.89		0	
	Hematological disease*	1.82±1.47		0		0.64±0.92	
Total		1.68±0.88		0.21±0.58		0.04±0.24	

Chi-square test was used (p<0.05 significance level), *Thrombotic thrombocytopenic purpura, immune thrombocytopenic purpura, myelodiplastic syndrome, thalassemia etc. includes diseases. ES: Erythrocyte suspension, FFP: Fresh frozen plasma, TS: Thrombocyte suspension, SD: Standard deviation

and 14.3% group AB patient. In 8.6 percent of the patients, the blood group was not determined. In our study, we think that the patients with excess blood groups 0 and A are the patient group that receives the most transfusions because it is the most common blood group in the community.

The most prevalent reasons for transfusion were symptomatic anemia, cancer, GI bleeding, and CRF. In comparable research, gastroenterological (34%), oncological (19%), and hematooncological (13%) causes have been identified [16-18].

The transfusion of blood and its products is inevitably fraught with difficulties. During the transfusion of blood components, allergic responses are prevalent, and the clinical severity of these reactions varies [18]. In the study by Hatayama et al. [19], the incidence of blood transfusion reactions was determined to be 2.6% throughout 11,423 infusions. In the study by Sarkodee-Adoo et al. [20] examining the association between the development of transfusion responses and platelet storage time, 0.26% of patients who received TS transfusions exhibited an allergic reaction. The study by Heddle et al. [21] also revealed that 4.8% of patients receiving TS transfusions experienced an adverse reaction. In our study, problems were not seen in 97.3% of patients, whereas 1.4% of patients experienced fever, 1.1% urticaria, and 0.3% volume overload. We believe that, despite the similarity of the conditions, our hospital's expertise and experience allow us to observe complications at an acceptable rate.

Studies have also found that severe organ failure and high mortality rates were observed in patients who underwent transfusion [22]. In a study by Rao et al. [23] on patients who received multiple transfusions in intensive care units, they showed that the frequency of mortality increased with transfusion. In the study by Leal-Noval et al. [24] with patients with similar age, Acute Physiology and Chronic Health Evaluation-II and Sequential Organ Failure Assessment scores, diagnosis, and Hb values, and patients who did not receive transfusion and those who received transfusion. found higher mortality rates in patients who were treated. In a randomized pilot study by Walsh et al. [25], free and restrictive transfusion strategies were compared in patients aged 55 years and older and receiving mechanical ventilation for more than four days. In a comparison of mortality and length of stay in the intensive care unit between patients who received free transfusion Hb below 9 g/dL and those who received restrictive transfusion Hb below 7 g/dL, those who received free transfusion had higher death rates [25]. Two (0.5%) of the 368 patients who received blood and blood products died in our study. Patients with mortality had Hb below 7g/dL and had active bleeding. We believe that mortality is mostly related to the serious clinical condition of the patients and not due to transfusion.

In research including 61 cancer patients, Mercadante et al. [26] reported that the median Hb value before the transfusion was 8 g/dL. In our investigation, this value was shown to be more than the usual Hb value. In this study, we assessed the degree of change in Hb, Hct, platelet count, and INR values before and after transfusion. The average pre-transfusion Hb level of the patients in our study was 6.98±1.95 g/dL, and the Hct level was 22.78±5.74%. The low mean values of Hb and Hct observed in our study are due to active bleeding. The values in the service and intensive care units were found to be somewhat higher due to the intervention of active bleeding by emergency services personnel and the transfusion of blood and blood products.

When the Hb value of patients falls below 8 g/dL in general, ES transfusion is frequently performed at higher levels in surgical patients [13,16]. In the CRIT study, it was shown that 45% of the patients received 5U or more ES transfusions, an average of 4.6±4.9U ES was given, and the amount of blood transfused and clinical survival were independent factors [27]. In the study by Fuller et al. [28], they included 93 patients diagnosed with septic shock and divided the patients into two groups as non-transfused and administered, and it was found that an average of 4.56U blood transfusion was administered to 43 patients who received blood transfusion. In the study by Shapiro et al. [18], it was shown that an average of 5.8±5.5 units of ES was given to trauma patients followed in the intensive care unit and that a large amount of transfusion was needed. In our study, it was observed that 342 patients were given ES in a 90-day follow-up. In our hospital, blood transfusion is targeted for patients with an average Hb value below 7 g/dL. When the effect of ES and the number of units given to the patients on the increase in Hb and Hct were examined, a significant change was detected up to the first 3U. However, no significant change was detected in patients who received ES transfusion over 3U. Additionally, the risk of complications was found to be the same among ES transfusions given more than once.

Patients who are followed-up by emergency services and whose blood and products are transfused various rates of hospitalization, referral to a better-equipped hospital, and discharge. In some studies, 1.6% of patients who underwent blood and product transfusions in the emergency department were referred to another health institution, discharged, or died in the emergency department [29,30]. In our study, 204 patients (55.4%) were discharged, 134 (36.4%) were transferred to the service, 18 to the intensive care unit, and 10 (2.7%) underwent emergency surgery. We did not refer any of our patients to an external center. Again, we attribute this to the fact that our hospital has a professional, tertiary-level transfusion program.

Study Limitations

Our study has some limitations. The most important of these is that it is applied in a single center and on a limited patient

population, and it is retrospective. Additionally, additional diseases of the patients, the drugs they used, and the short follow-up period are other important reasons for restriction.

Conclusion

It is obvious that blood transfusions have a life-saving effect, but it is clear that there are also risks of transfusion-related complications. Additionally, we believe that clinical decision-makers for blood and blood product transfusions will benefit patients by determining the volume of transfusion and blood product to be supplied, as well as assessing the possibility of complications. There is a need for prospective, randomized, and controlled multicenter trials in a broader population.

Ethics

Ethics Committee Approval: Clinical Research Ethics Committee of University of Health Sciences Turkey, İstanbul Bağcılar Training and Research Hospital (date: 15.01.2021, number: 2021.01.1.1.09.208.r1.009).

Informed Consent: Required informed consent was provided.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: S.S., A.C., B.D., B.Ç., Design: S.S., A.C., B.D., B.Ç., Data Collection or Processing: S.S., A.C., B.D., B.Ç., Analysis or Interpretation: S.S., A.C., B.D., B.Ç., Literature Search: S.S., A.C., B.D., B.Ç., Writing: S.S., A.C., B.D., B.Ç.

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

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References

1. Alimohammadi H, Kianian Y, Zerepoosh FB, Derakhshanfar H, Alavi-Moghadam M, Hatamabadi HR, et al. Accuracy of emergency transfusion score in prediction need for blood transfusion among multiple trauma patients: A cross-sectional study from Iran. Int J Crit Illn Inj Sci. 2017;7:248-51.
2. Long B, Koyfman A. Red blood cell transfusion in the emergency department. J Emerg Med. 2016;51:120-30.
3. Dhesi AS, Moss R, Deelen R, O'Reilly C, Bielby L. A survey of transfusion practitioners in international society of blood transfusion member countries. Vox Sang. 2020;115:200-10.
4. MacLennan S. Guidelines for the Blood Transfusion Services. 8th ed. Redbook; 2013.
5. Oldham J, Sinclair L, Hendry C. Right patient, right blood, right care: safe transfusion practice. Br J Nurs. 2009;18:316-20.
6. Long B, Koyfman A. Emergency medicine evaluation and management of anemia. Emerg Med Clin North Am. 2018;36:609-30.
7. Deveau SR. Blood products and their use in traumatic major haemorrhage. Emerg Nurse. 2016;23:31-7.
8. Walker RH. Special report: transfusion risks. Am J Clin Pathol. 1987;88:374-8.
9. Cap AP, Beckett A, Benov A, Borgman M, Chen J, Corley JB, et al. Whole blood transfusion. Mil Med. 2018;183:44-51.
10. McQuilten ZK, Crighton G, Brunskill S, Morison JK, Richter TH, Waters N, et al. Optimal dose, timing and ratio of blood products in massive transfusion: results from a systematic review. Transfus Med Rev. 2018;32:6-15.
11. Perelman I, Khair S, Dermer E, Tinmouth A, Saidenberg E, Fergusson D. The epidemiology of multicomponent blood transfusion: a systematic review. Transfus Med. 2019;29:80-94.
12. Waiswa MK, Moses A, Seremba E, Ddungu H, Hume HA. Acute transfusion reactions at a national referral hospital in Uganda: a prospective study. Transfusion. 2014;54:2804-10.
13. Okello CD, Shih AW, Angucia B, Kiwanuka N, Heddle N, Orem J, et al. Mortality and its associated factors in transfused patients at a tertiary hospital in Uganda. PLoS One. 2022;17:e0275126.
14. Ning S, Heddle NM, Acker JP. Exploring donor and product factors and their impact on red cell post-transfusion outcomes. Transfus Med Rev. 2018;32:28-35.
15. Azizi S, Tabary SZ, Soleimani A. Prevalence of acute blood transfusion reactions in Mazandaran Heart Center, Sari, Iran, 2010-2012. Med Arch. 2014;68:137-9.
16. Saheb S, Gallo A. Urgent therapeutic plasma exchange. Transfus Apher Sci. 2020;59:102991.
17. Fernández-Zarzoso M, Gómez-Seguí I, de la Rubia J. Therapeutic plasma exchange: review of current indications. Transfus Apher Sci. 201958:247-53.
18. Shapiro MJ, Gettinger A, Corwin HL, Napolitano L, Levy M, Abraham E, et al. Anemia and blood transfusion in trauma patients admitted to the intensive care unit. J Trauma. 2003;55:269-73.
19. Hatayama Y, Matsumoto S, Hamada E, Kojima N, Hara A, Hino N, et al. Analysis of acute transfusion reactions and their occurrence times. Yonago Acta Med. 2018;61:87-90.
20. Sarkodee-Adoo CB, Kendall JM, Sridhara R, Lee EJ, Schiffer CA. The relationship between the duration of platelet storage and the development of transfusion reactions. Transfusion. 1998;38:229-35.
21. Heddle NM, Klama LN, Griffith L, Roberts R, Shukla G, Kelton JG. A prospective study to identify the risk factors associated with acute reactions to platelet and red cell transfusions. Transfusion. 1993;33:794-7.
22. Corwin HL, Surgenor SD, Gettinger A. Transfusion practice in the critically ill. Crit Care Med. 2003;31:S668-71.
23. Rao SV, Jollis JG, Harrington RA, Granger CB, Newby LK, Armstrong PW, et al. Relationship of blood transfusion and clinical outcomes in patients with acute coronary syndromes. JAMA. 2004;292:1555-62.
24. Leal-Noval SR, Muñoz-Gómez M, Jiménez-Sánchez M, Cayuela A, Leal-Romero M, Puppo-Moreno A, et al. Red blood cell transfusion in non-bleeding critically ill patients with moderate anemia: is there a benefit? Intensive Care Med. 2013;39:445-53.
25. Walsh TS, Boyd JA, Watson D, Hope D, Lewis S, Krishan A, et al. Restrictive versus liberal transfusion strategies for older mechanically ventilated critically ill patients: a randomized pilot trial. Crit Care Med. 2013;41:2354-63.
26. Mercadante S, Ferrera P, Villari P, David F, Giarratano A, Riina S. Effects of red blood cell transfusion on anemia-related symptoms in patients with cancer. J Palliat Med. 2009;12:60-3.
27. Meyer DE, Cotton BA, Fox EE, Stein D, Holcomb JB, Cohen M, et al. A comparison of resuscitation intensity and critical administration threshold in predicting early mortality among bleeding patients: a multicenter validation in 680 major transfusion patients. J Trauma Acute Care Surg. 2018;85:691-6.

28. Fuller BM, Gajera M, Schorr C, Gerber D, Dellinger RP, Parrillo J, et al. Transfusion of packed red blood cells is not associated with improved central venous oxygen saturation or organ function in patients with septic shock. J Emerg Med. 2012;43:593-8.

29. Sazama K, DeChristopher PJ, Dodd R, Harrison CR, Shulman IA, Cooper ES, et al. Practice parameter for the recognition, management, and prevention of adverse consequences of blood transfusion. College of American Pathologists. Arch Pathol Lab Med. 2000;124:61-70.

30. Oakley FD, Woods M, Arnold S, Young PP. Transfusion reactions in pediatric compared with adult patients: a look at rate, reaction type, and associated products. Transfusion. 2015;55:563-70.

CASE REPORT

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Pericardial Tamponade Due to Methotrexate Toxicity: A Case Report

Mustafa Ahmet Afacan[1], İsmail Tayfur[2], Burcu Genç Yavuz[1], Özlem Tataroğlu[3]

[1]*University of Health Sciences Turkey, Haydarpaşa Numune Training and Research Hospital, Clinic of Emergency Medicine, İstanbul, Turkey*
[2]*University of Health Sciences Turkey, Sancaktepe Prof. Dr. İlhan Varank Training and Research Hospital, Clinic of Emergency Medicine, İstanbul, Turkey*
[3]*University of Health Sciences Turkey, Kartal Dr. Lütfi Kırdar Training and Research Hospital, Clinic of Emergency Medicine, İstanbul, Turkey*

Abstract

Methotrexate (MTX) is a folic acid analog that inhibits the growth of rapidly proliferating cells, such as bone marrow or cancer cells, through its anti-inflammatory and anti-proliferative properties. With these characteristics, using MTX for treating moderate or severe psoriatic arthritis results in a significant improvement in the health of patients with this condition. Although MTX has many side effects, pericardial tamponade is a very rare complication. Rapidly progressing tamponade is associated with high morbidity and mortality. Here, we present a case of pericardial tamponade in a 69-year-old female patient due to MTX use and its possible facilitating effect.

Keywords: Methotrexate, psoriatic arthritis, pericardial tamponade

Introduction

Psoriatic arthritis (PsA), a chronic inflammatory disease of the joints, develops in approximately 30% of psoriasis cases and can be accompanied by an extra-articular involvement [1]. Today, despite the availability of the development of new therapeutic agents, MTX remains the main treatment option for PsA due to its strong immunosuppression efficacy and tolerability [2,3]. As an immunosuppressant, weekly, low-dose MTX (7.5 to 25 mg) administered orally or subcutaneously shows great efficacy in PsA [4]. Recent studies have also highlighted the advantages of using methotrexate (MTX) alone or in combination therapy with a TNF-alpha inhibitor or cyclosporine A, resulting in better treatment outcomes and fewer side effects [5]. Although complications associated with MTX treatment have been frequently reported in the literature, pericarditis and pericardial effusion, which are also serositis complications, are quite uncommon ones [6]. Pulmonary toxicity has been well-described and may take various forms. Pulmonary infiltrates are the most commonly encountered form of MTX pulmonary toxicity, and these infiltrates resemble hypersensitivity lung disease.

Case Report

A 69-year-old female presented to the emergency department with dyspnea and syncope. Her anamnesis revealed that the patient had a diagnosis of PsA and had been receiving a single dose of 17.5 mg/week MTX for the last four months due to the lack of symptoms being uncontrolled by steroid treatment. It was also determined that the patient, who had not previously experienced respiratory problems, had complaints of dyspnea and cough for the last 10 days.

During the patient's physical examination in the emergency department, the Glasgow Coma scale remained at 13/15, she was tachycardic with a heart rate of 115 beats/min (sinus rhythm), and her initial blood pressure was 80/65 mmHg. At 72% SaO_2 in room air, she had a temperature of 36.7°C. The patient was observed to have jugular venous fullness, and her respiratory system examination revealed bilateral lung sounds that were more prominent on the right side, reduced breathing sounds, and fine crepitant rales. Additionally, there was 3+ pretibial pitting edema. The patient appeared cachectic and had lost 10 kg within the last two months.

Address for Correspondence: Mustafa Ahmet Afacan, University of Health Sciences Turkey, Haydarpaşa Numune Training and Research Hospital, Clinic of Emergency Medicine, İstanbul, Turkey
Phone: +90 216 336 05 65 **E-mail:** drmustafaahmet@hotmail.com **ORCID-ID:** orcid.org/0000-0003-1045-0681
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The results of laboratory parameters were as follows: pH 7.52, $PaCO_2$ 25.2 mmHg and PaO_2 56 mmHg in blood gas, D-dimer 3,143 ng/mL, total protein 3.7 g/dL, albumin 2.31 g/dL, C-reactive protein 11.2 g/dL, and white blood cell count 14,500 Ul, while the remaining blood parameters were within the normal ranges. An electrocardiogram was performed and showed sinus tachycardia with ST segment depression, best seen in V3-V6 leads. The patient was thought to have had a pulmonary embolism due to hypoxic, hypocarbic respiratory alkalosis, and syncope, but the contrast-enhanced thoracic computed tomography (CT) showed no pulmonary embolism. However, the sagittal and axial plane CT images showed a large pericardial effusion with a compressed small heart. A moderate-sized bilateral pleural effusion was also observed. The patient had clinical and hemodynamic findings consistent with pericardial tamponade (Figures 1, 2). Resuscitation was initiated with intravenous crystalloid and noradrenaline infusion with a target of 65 mmHg mean arterial blood pressure. With a preliminary diagnosis of tamponade, the patient was referred to the cardiology and cardiovascular surgery department where urgent left anterior thoracoscopic pericardiocentesis was performed and a 310 mL effusion was drained. The analysis of the patient's pericardial fluid showed an exudate with 3.2 g/dL total protein, 108 mg/dL glucose, 720 IU/L lactate dehydrogenase, and 1020 density. No pathogen was detected in the culture of the fluid and no malignant cells were detected in the cytological examination. Medical treatment was started, and the patient was discharged as healthy after 11 days of hospitalization.

Discussion

MTX can cause serious or life-threatening side effects, such as muscle weakness, shortness of breath, upper stomach pain, mouth sores, pneumonitis, and MTX-related liver disease, confusion, or seizures [6]. Acute pneumonitis is the most common pulmonary toxicity associated with MTX, although its pathogenesis has not yet been fully elucidated [7]. Apart from lung pathologies, the most feared complications of MTX therapy are chronic liver injury, cirrhosis, and portal hypertension [8]. However, pericardial tamponade due to MTX use that is described in the current case is a very rare complication and has only been reported in two cases in the literature.

Conditions that cause cardiac tamponade include malignancies, acute myocardial infarction, cardiac catheterization procedures, collagen tissue diseases, bacterial or viral infections, tuberculosis, and hypothyroidism [9]. No malignancy, infection, or thyroid dysfunction were detected in the current case. The normal findings of the patient in the control chest X-ray before medical treatment indicate that a clinical change occurred secondary to MTX treatment.

The mechanisms by which low-dose MTX exhibits its therapeutic effect have not yet been fully elucidated. However, renal excretion constitutes the main elimination pathway of MTX [8]. The drug is filtered by glomeruli and undergoes active tubular secretion and reabsorption [10]. Fifty percent of circulating MTX is bound to albumin and excreted by the urinary system at a rate of 65-80% within 12 h of ingestion [11]. The low albumin level of 2.31 g/dL in our patient may have changed the pharmacokinetics of MTX, resulting in a decrease in the excretion of the substance and leading to toxicity in the blood, despite the dose taken. The cachectic appearance of the patient may have been associated with hypoalbuminemia,

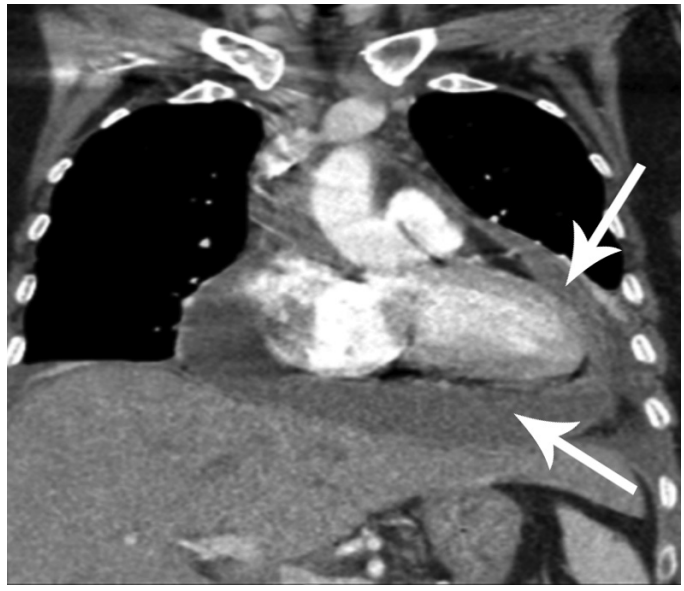

Figure 1. Thoracic computed tomography image in the sagittal plane showing pericardial effusion (arrows)

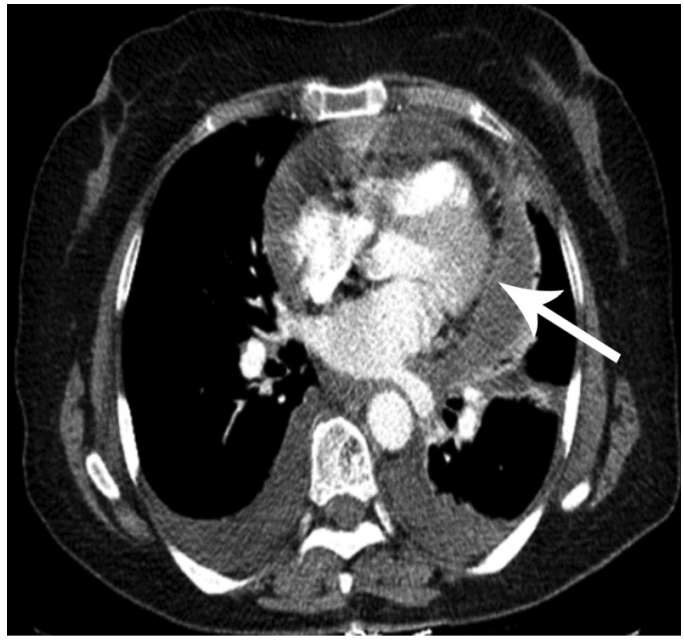

Figure 2. Thoracic computed tomography image in the axial plane showing pericardial and pleural effusion (arrow)

as well as a factor in facilitating MTX toxicity. We consider 17.5 mg/week MTX to be within the treatment dose limits and postulate that a low albumin level of 2.31 g/dL resulted in toxicity, leading to the development of pericardial tamponade.

Conclusion

The treatment of patients with PsA should be designed by taking into account the severity of the disease, response to previous treatments, and the presence of co-morbidities. The routine use of MTX in patients with hypoalbuminemia and cachexia may facilitate end-organ toxicity. We suggest that in this patient group, hypoalbuminemia should be resolved and the MTX dose should be reduced or included in a combination therapy to reduce the risk of unwanted end-organ toxicity, such as tamponade.

Ethics

Informed Consent: Patient consent was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.A.A., Concept: M.A.A., İ.T., Design: M.A.A., İ.T., B.G.Y., Ö.T., Data Collection or Processing: M.A.A., B.G.Y., Ö.T., Analysis or Interpretation: M.A.A., B.G.Y., Literature Search: M.A.A., B.G.Y., Writing: M.A.A., Ö.T.

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

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References

1. Gladman DD. Recent advances in understanding and managing psoriatic arthritis. F1000Res. 2016;5:2670.
2. Brown PM, Pratt AG, Isaacs JD. Mechanism of action of methotrexate in rheumatoid arthritis, and the search for biomarkers. Nat Rev Rheumatol. 2016;12:731-42.
3. Kaushik SB, Lebwohl MG. Psoriasis: Which therapy for which patient: psoriasis comorbidities and preferred systemic agents. J Am Acad Dermatol. 2019;80:27-40.
4. Mease PJ, Armstrong AW. Managing patients with psoriatic disease: the diagnosis and pharmacologic treatment of psoriatic arthritis in patients with psoriasis. Drugs. 2014;74:423-41.
5. Ruhoff JT, Horn HC, Ellingsen T. Efficacy of methotrexate in management of peripheral psoriatic arthritis - a systematic review. Dan Med J. 2019;66:A5570.
6. Dündar B, Karalök A, Ureyen I, Gündoğdu B, Oçalan R, Turan T, et al. Case report: methotrexate-induced pericardial effusion. J Turk Ger Gynecol Assoc. 2013;14:48-9.
7. Conway R, Carey JJ. Risk of liver disease in methotrexate treated patients. World J Hepatol. 2017;9:1092-100.
8. Lateef O, Shakoor N, Balk RA. Methotrexate pulmonary toxicity. Expert Opin Drug Saf. 2005;4:723-30.
9. Bedoui Y, Guillot X, Sélambarom J, Guiraud P, Giry C, Jaffar-Bandjee MC, et al. Methotrexate an old drug with new tricks. Int J Mol Sci. 2019;20:5023.
10. Skipina TM, Sane DC, Cui C, Song S, Phillips SG, Jarrett RW. A plasma cell-based pericardial effusion leading to tamponade in a patient with multiple myeloma - a case report and review of the literature. Cardiovasc Pathol. 2019;40:41-6.
11. Inoue K, Yuasa H. Molecular basis for pharmacokinetics and pharmacodynamics of methotrexate in rheumatoid arthritis therapy. Drug Metab Pharmacokinet. 2014;29:12-9.

CASE REPORT

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Unmasking the Rare Culprit: A Case Report of Hypertriglyceridemia-induced Pancreatitis

Hany A. Zaki

Hamad Medical Corporation, Department of Emergency Medicine, Doha, Qatar

Abstract

Hypertriglyceridemia-induced pancreatitis is a rare but serious form of acute pancreatitis caused by elevated levels of triglycerides in the blood. Early diagnosis and management are essential to prevent disease progression and improve outcomes. We present a case of a 27-year-old male who presented to the emergency department with diffuse abdominal pain and associated symptoms. Laboratory tests and imaging studies revealed evidence of acute pancreatitis with tissue necrosis and reactive inflammation involving the duodenum. The patient was diagnosed with hypertriglyceridemia-induced pancreatitis and treated with aggressive fluid resuscitation, pain management, nutritional support, and insulin infusion. The patient had an uneventful medical intensive care unit follow-up and was discharged with full recovery. The case report highlights the importance of considering hypertriglyceridemia as a potential cause of acute pancreatitis and the utility of ultrasound and computed tomography scans in early diagnosis and management. Early intervention, including identification and treatment of the underlying cause of hypertriglyceridemia, aggressive fluid resuscitation, pain management, and nutritional support, is essential in preventing disease progression and improving outcomes.

Keywords: Hypertriglyceridemia, pancreatitis, triglyceride, case report

Introduction

Hypertriglyceridemic pancreatitis is a medical emergency that often requires urgent attention in the emergency department. It is a condition where high levels of triglycerides in the blood cause inflammation of the pancreas, leading to severe abdominal pain, nausea, vomiting, and elevated pancreatic enzymes.

The exact mechanism by which hypertriglyceridemia causes pancreatitis is not fully understood. However, it is believed that the accumulation of triglycerides in the pancreas leads to tissue injuryand inflammation, which can result in the development of acute pancreatitis [1].

The initial management of hypertriglyceridemic pancreatitis in the emergency department involves closely monitoring the patient's vital signs, managing pain, and initiating intravenous fluids to prevent dehydration and maintain an electrolyte balance. The patient is also typically fasted to rest the pancreas, and close monitoring for signs of complications, such as respiratory distress or shock, is essential [2].

In severe cases, plasmapheresis or lipid-lowering medication may be necessary to rapidly reducetriglyceride levels. Surgical intervention may also be required in some cases to remove damagedpancreatic tissue or drain fluid collection [3,4].

Prevention of hypertriglyceridemic pancreatitis in the emergency department involves recognizing patients with a history of hypertriglyceridemia or pancreatitis and initiating early treatment to prevent complications. Patients with a history of hypertriglyceridemia should be counseled on dietary modifications and medication compliance to prevent the development of acute pancreatitis [5].

Here, we present a young patient with hypertriglyceridemic pancreatitis. Our aim is to show the importance of early recognition and treatment for these patients.

Address for Correspondence: Hany A. Zaki, Hamad Medical Corporation, Department of Emergency Medicine, Doha, Qatar
Phone: +0396996 **E-mail:** hanyzaki1976@gmail.com **ORCID-ID:** orcid.org/0000-0002-3994-7088
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Case Report

A 27-year-old male with no past medical history presented to the emergency department with constant, diffuse abdominal pain surrounding the umbilicus for the last 4 h. He had associatedwith nausea but denied vomiting. On examination, the patient appeared not in severe pain or distress, and was oriented and cooperative. Chest sounds were clear, and the abdomen was soft and lax. The vital signs at admission were: blood pressure 111/58 mmHg, respiratory rate 20/minute, heart rate 115 beats per minute, oxygen saturation 96%, and body temperature 37°C. Laboratory tests showed elevated white blood cell count (12.3 10^3/uL), hemoglobin (20 g/dL), creatinine (119 umol/L) , and C-reactive protein (CRP) (90 mg/L) levels. The patient also had elevated alanine aminotransferase (67 U/L), aspartate transaminase (48 U/L), and lipase (738 U/L) levels. An abdominal ultrasound revealed a bulky pancreas with mild peripancreatic fluid and mild ascites. A subsequent abdominal computed tomography (CT) scan showed edematous pancreatitis with non-enhancing parts involving the distal body and tail representing tissue necrosis less than 30%. The CT scan also showed severe reactive inflammation involving all parts of the duodenum with a thickened wall and surrounding inflammation. Following the CT scan, the patient became more painful, tachycardic, and tachypneic, and was admitted to the medical intensive care unit (MICU). Repeat blood tests after 12 h showed improved hemoglobin and creatinine levels after intravenous fluid replacement, but CRP levels were dramatically increased. A lipid panel ordered for possible hypertriglyceridemic pancreatitis showed a triglyceride level of 39.6 mmol/L. The insulin infusion was started, and the patient had an uneventful MICU follow-up. The patient was later discharged with full recovery.

Discussion

In this case report, we discuss the importance of the early diagnosis of hypertriglyceridemia-induced pancreatitis and its management. Hypertriglyceridemia-induced pancreatitis is a rare but serious form of acute pancreatitis that is caused by elevated levels of triglycerides in the blood. Early diagnosis and management of hypertriglyceridemia are essential to prevent disease progression and improve outcomes [6].

In our case, the patient presented with diffuse abdominal pain and associated symptoms. Laboratory tests showed elevated levels of leukocytes, hemoglobin, creatinine, CRP, and pancreatic enzymes, including lipase. An abdominal ultrasound and subsequent CT scan revealedevidence of acute pancreatitis with tissue necrosis and reactive inflammation involving theduodenum.

Ultrasound is a commonly used imaging modality for the diagnosis of acute pancreatitis, and it can be used for many purposes including evaluation of the pancreatic edema, fluid, intraabdominal collection, and gastric content, etc. [7,8].

In the case presented, an abdominal ultrasound was performed, which revealed a bulky pancreas with mild peripancreatic fluid and mild ascites. These findings were consistent with acute pancreatitis and provided important diagnostic information to guide further management.

In addition to its diagnostic utility, ultrasound can also be useful for monitoring disease progressionand response to treatment. For example; serial ultrasound examinations can be used to track changes in the size and location of fluid collections, which can help guide decisions regarding theneed for drainage procedures or other interventions [7].

It is worth noting that while ultrasound is a valuable tool in the diagnosis and management of acute pancreatitis, it is not always sufficient on its own. In some cases, additional imaging studies such as CT or magnetic resonance imaging may be necessary to providea more detailed assessment of the extent of disease and any associated complications [7].

In the case presented, a subsequent abdominal CT scan was performed, which provided additional information about the extent of pancreatic involvement and the presence of duodenal inflammation.

Early intervention is crucial for managing hypertriglyceridemia-induced pancreatitis. The first stepin management is to identify and treat the underlying cause of hypertriglyceridemia, such as uncontrolled diabetes or certain medications. Additionally, aggressive fluid resuscitation, pain management, and nutritional support are essential in the management of acute pancreatitis [6].

Here, the patient's triglyceride levels were very high, and an insulin infusion was started to control hypertriglyceridemia. Insulin lowers triglyceride levels by increasing lipoprotein lipase activity, which hydrolyzes triglycerides in the bloodstream. This resulted in a significant reductionin triglyceride levels, which helped prevent disease progression and improve outcomes.

Conclusion

In conclusion, hypertriglyceridemia-induced pancreatitis is a rare but serious form of acute pancreatitis that requires early diagnosis and management. Early intervention, including identification and treatment of the underlying cause of hypertriglyceridemia, aggressive fluid resuscitation, pain management, and nutritional support, is essential in preventing disease progression and improving outcomes. The use of insulin to control hypertriglyceridemia may also be a useful adjunctive therapy for hypertriglyceridemia-induced pancreatitis.

Ethics

Informed Consent: Written consent was taken from the patient.

Peer-review: Externally peer-reviewed.

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References

1. Yadav D, Pitchumoni CS. Issues in hyperlipidemic pancreatitis. J Clin Gastroenterol. 2003;36:54-62.
2. Mosztbacher D, Hanák L, Farkas N, Szentesi A, Mikó A, Bajor J, et al. Hypertriglyceridemia-induced acute pancreatitis: A prospective, multicenter, international cohort analysis of 716 acute pancreatitis cases. Pancreatology. 2020;20:608-16.
3. Talukdar R, Vege SS. Acute pancreatitis. Curr Opin Gastroenterol. 2015;31:374-9.
4. Navina S, Acharya C, DeLany JP, Orlichenko LS, Baty CJ, Shiva SS, et al. Lipotoxicity causes multisystem organ failure and exacerbates acute pancreatitis in obesity. Sci Transl Med. 2011;3:107ra110.
5. Working Group IAP/APA Acute Pancreatitis Guidelines. IAP/APA evidence-based guidelines for the management of acute pancreatitis. Pancreatology. 2013;13:e1-15.
6. Stefanutti C, Labbadia G, Morozzi C. Severe hypertriglyceridemia-related acute pancreatitis. Ther Apher Dial. 2013;17:130-7.
7. Burrowes DP, Choi HH, Rodgers SK, Fetzer DT, Kamaya A. Utility of ultrasound in acute pancreatitis. Abdom Radiol (NY). 2020;45:1253-64.
8. Mackenzie DC, Azad AM, Noble VE, Liteplo AS. Test performance of point-of-care ultrasound for gastric content. Am J Emerg Med. 2019;37:123-6.

CASE REPORT

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Managing Hemiballismus Hemichorea Caused by Hyperglycemia in an Emergency Department

Sarper Yılmaz[1], Süleyman Alpar[2]

[1]University of Health Sciences, Kartal Dr. Lütfi Kırdar City Hospital, Department of Emergency Medicine, İstanbul, Turkey
[2]Beykent University Faculty of Medicine, Department of Emergency Medicine, İstanbul, Turkey

Abstract

Chorea, which is a common kind of uncontrollable movement disease, chorea is caused by dysfunctional neural networks that connect the basal ganglia with the frontal cortex. If a patient complains of chorea, a complete medical history is required to rule out other possible causes, including infection with group A beta-hemolytic streptococcus, a history of drug use, as well as the patient's age at start and course (acute or insidious). Static chorea may be caused by structural or chemical injury to the basal ganglia or by benign hereditary chorea, both of which are associated with neurodegenerative illnesses. It is also necessary to conduct a neurological examination that includes an evaluation of the distribution and features of chorea. Non-ketotic hyperglycemia is a common cause of acute chorea. In addition to hemichorea, hyperglycemia may also produce chorea that is widespread. Patients with hyperglycemia that fit the normal description have been shown to have an unusual symptom of uncontrolled high hyperglycemia: hyperglycemia-induced hemiballismus hemichorea (HIHH). Even if all patients present with abnormal, hyperglycemic non-ketotic chorea, the differential diagnosis should be considered. Dopamine blockers, tetrabenazine, and topiramate are used to treat HIHH patients who do not respond to hyperglycemia treatment.

Keywords: Hemiballismus hemichorea, movement disorders, hyperglycemic states

Introduction

Chorea is a prominent involuntary movement disorder that is caused by malfunctioning neural networks linking the basal ganglia and frontal cortical motor regions. The condition is defined by a continuous stream of random, short, involuntary muscular contractions that may be caused by a number of factors. Chorea is produced by the caudate nucleus, putamen, subthalamic nucleus, and thalamus, as well as their interconnected connections [1]. According to Piccolo et al. [2] the most common etiologies of sporadic chorea admitted to different neurology departments during a five-year period were vascular (40%), drug-induced (14%), Huntington's disease (10%), and acquired immunodeficiency syndrome (10%), with the diagnosis remaining uncertain in 6%. Hereditary choreas often improve gradually and are symmetrical; but acquired choreas are more likely to be acute or subacute in nature and might be asymmetrical or unilateral.

Chorea often affects the distal limbs and face, but it may also impair breathing and phonation, resulting in slurred speech or involuntary vocalizations. Patients may conceal chorea by blending it into voluntary motions (parakinesia). Patients are often oblivious of their strange motions, which family members can often see. Chorea is often present during rest and may be exacerbated by distracting motions, although it vanishes during sleep [3].

Neurologic examination is also critical and must include an assessment of chorea distribution and related characteristics. Acute chorea is often attributed to non-ketotic hyperglycemia. Hyperglycemia may also cause hemichorea or widespread chorea [4]. On T1-weighted images of afflicted patients, an

Address for Correspondence: Assoc. Prof. Sarper Yılmaz MD, University of Health Sciences, Kartal Dr. Lütfi Kırdar City Hospital, Department of Emergency Medicine; Health Management in Emergencies and Disasters, Yeditepe University, İstanbul, Turkey
Phone: +90 507 280 11 64 **E-mail:** sarperyilmaz08@gmail.com **ORCID-ID:** orcid.org/0000-0001-8166-659X
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magnetic resonance imaging often reveals a high signal intensity in the contralateral striatum. Once glycemic control is attained, chorea should gradually resolve itself, although aberrant movements may continue for more than a year.

The doctor should make every effort to rule out a secondary etiology during therapy. A simple laboratory workup may aid in elucidating the triggering event. Secondary chorea often improves or resolves when the primary cause is appropriately treated or the offending drug is withdrawn. Regrettably, no medication has been shown to significantly reduce or stop the course of inherited choreas, with the exception of copper-reducing therapy in Wilson disease.

Hemichorea/hemiballism associated with non-ketotic hyperglycemia is a well-recognized syndrome in the emergency department (ED), but few case series have been reported in the literature.

Case Report

A 58-year-old woman was taken to an ED a week ago with a left upper-limb movement that she could not control. Her heart failure was complicated by a history of high blood pressure, coronary artery disease, and type 2 diabetes mellitus (DM). While awake, the subject participated in these activities, which ceased after the individual fell asleep. The five-year anniversary of her diagnosis with type 2 DM had not helped her regulate her blood sugar levels.

When the patient was hospitalized, the following were her vital signs and blood glucose levels: body temperature: 37.3 degrees Celsius; pulse rate: 90 beats per minute; breathing rate: 15 beats per minute; and heart rate: 140/72 mmHg.

According to the findings of a neurological evaluation, the patient had normal verbal capacity and showed involuntary atetoid motions of her left upper limb (Figure 1).

It is normal for her to have hypotonia and weak muscles at her age. A basic medical assessment found nothing further concerning. A random blood sugar reading of 515 mg/dL was likewise within the normal range, and the results of inflammatory markers, thyroid function tests, and an electrocardiogram were all normal. Blood and urine tests showed no signs of acidity or ketones. An abnormally dense putamen was seen on computarized tomography images of the brain without contrast (Figure 2).

Ballistic or choreiform movements in the setting of high blood sugar and the absence of ketoacidosis are typical clinical and radiological signs that aid to establish the diagnosis. Low doses of insulin and olanzapine were administered to the patient. Three days later, glycemic control was attained. After two days, the chorea had disappeared.

Discussion

To characterize hyperglycemia-induced hemiballismus hemichorea (HIHH), as HIHH was initially described by Bedwell, groundbreaking in 1960. Many women in their fifties to eighties (mean age seventy-one years) report having

Figure 1. Involuntary atetoid motions of left upper limb

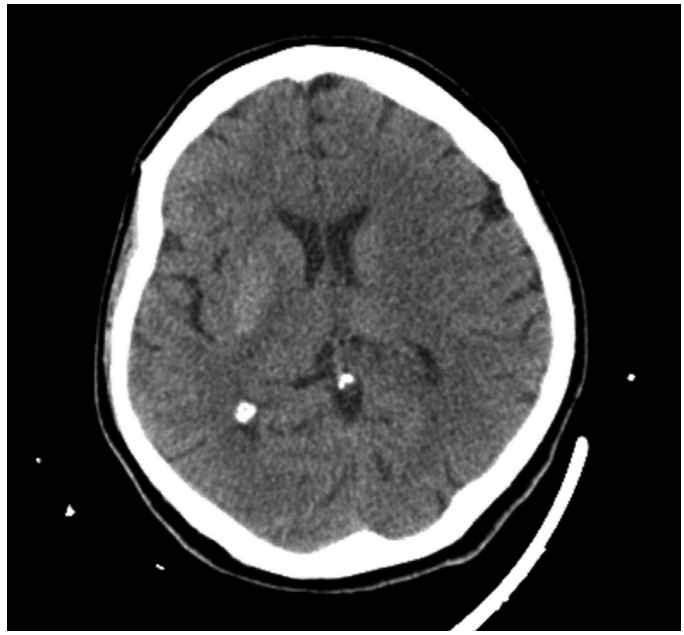

Figure 2. Non-contrast computed tomography demonstrates putaminal hyperdensity on the right hemisphere

choreic and ballistic motions on one side of their bodies. These women do not have a history of DM, but the symptoms arise over a few hours and resolve after 24-48 hours of achieving normal blood sugar levels. The vulnerability of Asian women is unexplained [4]. Many popular drugs, including Hormone Replacement therapy, L-dopa, and others, should be checked out as potential causes. In individuals under the age of fifty, Wilson's disease or Huntington's chorea may be genetic. Human immunodeficiency virus (HIV), hyperthyroidism, the antiphospholipid syndrome, and carbon monoxide poisoning are all possible causes of post-streptococcal Sydenham's chorea.

The pathophysiology of HIHH is shrouded in mystery. The following are a number of the options that have been discussed [5].

1- Blood-brain-barrier disruption may lead to intracellular acidosis and localized metabolic dysfunction.

2- There have been reported instances of petechial hemorrhages, while others have been associated with striatal infarction.

3- It is possible that postmenopausal women's dopamine receptors are more sensitive, which may contribute to hyperkinesis.

4- Non-ketotic individuals lack acetoacetate, a component required for the conversion of gamma-aminobutyric acid (GABA) into dopamine.

This type of hemiballismus is characterized by irregular, involuntary, and unbalanced movement patterns. GABA ergic neurons in the contralateral striatum may be affected by hyperglycemia and ischemia excitotoxicity. Overactivation of the subthalamic nuclei resulting in an increase in excitatory cortical output is a consequence [5]. The disorder is accompanied by hyperintensities in the striatum and globus pallidus, as well as apparent diffusion coefficient mapping without contrast enhancement. Striatal infarction is a rather uncommon occurrence. N-acetylaspartate: creatine ratio and N-acetylaspartate: cholinate ratio may be related with a higher lactate peak [4].

A great majority of these abnormalities vanish after treating hyperglycemia. Anti-nuclear antibody, anti-streptolysin antibodies, and HIV enzyme-linked immunosorbent assays may be required in the correct environment, along with thyroid and liver function testing. Dopamine-blocking medicines, tetrabenazine, or topiramate have been utilized in circumstances when hyperglycemia therapy is inadequate. Dopamine receptor blockers have traditionally been regarded as being the most effective medication for alleviating the intensity of choreic movements, regardless of their etiology. Although first-generation antipsychotic drugs (typical neuroleptics) have a long history of being used to treat chorea, there is less evidence to support their effectiveness, and they are increasingly avoided owing to their increased risk of adverse effects. Second-generation anti-psychotic medications (atypical neuroleptics), such as olanzapine, risperidone, and aripiprazole, have been shown to help alleviate chorea and may have a more favorable side effect profile.

Conclusion

This type of hyperglycemia may show up as an indicator of uncontrolled and severe hyperglycemia: HIHH. Any patient with abnormal glucose levels should have hyperglycemic non-ketotic chorea included in the differential diagnosis, as indicated in this case report. Non-ketotic hyperglycemia, although rare, is an essential differential diagnosis for individuals with hemichorea-hemiballismus because of its positive prognosis when detected and treated early.

Ethics

Informed Consent: Informed consent was obtained from the patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.Y., S.A., Concept: S.Y., S.A., Design: S.Y., S.A., Analysis or Interpretation: S.Y., S.A., Literature Search: S.Y., Writing: S.Y.

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

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References

1. Lee MS, Marsden CD. Movement disorders following lesions of the thalamus or subthalamic region. Mov Disord. 1994;9:493-507.
2. Piccolo I, Defanti CA, Soliveri P, Volontè MA, Cislaghi G, Girotti F. Cause and course in a series of patients with sporadic chorea. J Neurol. 2003;250:429-35.
3. Phillips W, Shannon KM, Barker RA. The current clinical management of Huntington's disease. Mov Disord. 2008;23:1491-504.
4. Chang CV, Felicio AC, Godeiro Cde O Jr, Matsubara LS, Duarte DR, Ferraz HB, et al. Chorea-ballism as a manifestation of decompensated type 2 diabetes mellitus. Am J Med Sci. 2007;333:175-7.
5. Lin JJ, Chang MK. Hemiballism-hemichorea and non-ketotic hyperglycaemia. J Neurol Neurosurg Psychiatry. 1994;57:748-50.