Original Article

HEALTH SCIENCES
MEDICINE

DOI: 10.32322/jhsm.1160392
J Health Sci Med 2022; 5(6): 1512-1517

Platelet-to-lymphocyte ratio and mean platelet volume-to-platelet count ratio for predicting mortality in critical COVID-19 patients

Hayriye Cankar Dal[1], Kudret Yasemin Yalnız[2], Damla Tosun[2], Bilge Gözükara[1], Hülya Şirin[3], Cihangir Doğu[1], Dilek Öztürk Kazancı[1], Sema Turan[1]

[1]University of Health Sciences, Ankara City Hospital, Department of Intensive Care Unit, Ankara, Turkey
[2]University of Health Sciences, Ankara City Hospital, Department of Anesthesiology and Reanimation, Ankara, Turkey
[3]University of Health Sciences, Gulhane School of Medicine, Department of Public Health, Ankara, Turkey

Cite this article as: Cankar Dal H, Yalnız KY, Tosun D, et al. Platelet-to-lymphocyte ratio and mean platelet volume-to-platelet count ratio for predicting mortality in critical COVID-19 patients. J Health Sci Med 2022; 5(6): 1512-1517.

ABSTRACT

Introduction: Defining the markers that can be used in clinical practice for predicting the mortality of critical patients will be cautionary for taking necessary measures in high-risk cases. Although there are a large number of studies conducted during the pandemic, no mortality marker to predict the prognosis of intensive care unit (ICU) patients with COVID-19 has yet been defined. Platelet indices can be easily evaluated with a complete blood count (CBC) analysis, one of the most accessible tests worldwide. This study aimed to evaluate the role of platelet indices such as mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), platelet-to-lymphocyte ratio (PLR), and MPV-to-platelet count ratio (MPV/PLT) in predicting the mortality of ICU patients with COVID-19.

Material and Method: This single-center, retrospective, cross-sectional study included 201 critical COVID-19 patients over 18 years of age who were hospitalized in ICU between August 2020 and February 2021. Patients were divided into two groups as survivors and non-survivors. The relationship of MPV, PDW, PCT, PLR, and MPV/PLT parameters evaluated at ICU admission with mortality was investigated.

Results: There was no significant difference between the survivor and non-survivor groups in terms of platelet count, MPV, PCT, and PDW. The comparison of the platelet ratios revealed higher PLR and MPV/PLT ratio in the non-survivor group than in the survivor group ($p<0.05$). The cut-off value of PLR for predicting mortality was found to be 292.20 (AUC: 0.601 [95% CI 0.522-0.681]) ($p<0.05$), while the cut-off of MPV/PLT was found to be 0.0289 (AUC: 0.590 [95% CI 0.510-0.671]) ($p<0.05$).

Conclusion: The results of this study demonstrated PLR and MPV/PLT ratio were associated with mortality. The use of ratios such as MPV/PLT and PLR as an early prognostic indicator instead of platelet indices alone, like MPV in ICU patients with COVID-19, may help identify high-risk patients early.

Keywords: COVID-19, mortality, PLR, MPV/PLT, intensive care

INTRODUCTION

The COVID-19 pandemic, which started in February 2020, has been affecting the world for more than two years. Although the number of cases has decreased with the measures and vaccination studies, the effects of the pandemic still continue today (1). During this period, a large numbers of severe COVID-19 cases were followed in intensive care units (ICU) around the world.

Numerous studies have been conducted to identify severe cases, determine hospitalization criteria, predict prognosis, and investigate various laboratory examinations (2,3). These studies have mainly evaluated patients treated in emergency departments and outpatient clinics with high patient density. Studies on ICU patients have focused on determining the criteria for admission to the ICU. Although many parameters have been studied, a specific mortality marker to predict the prognosis of critically ill ICU patients with COVID-19 has not yet been defined. While studies have emphasized inflammatory markers since the disease causes systemic inflammation, there are studies conducted with various markers such as pro-inflammatory cytokines, C-reactive protein (CRP) and ferritin (4-6). Even though the relationship of the

Corresponding Author: Hayriye Cankar Dal, hayriyecankar@hotmail.com
Received: 10.08.2022 **Accepted:** 22.08.2022

studied markers with the disease is significant with high specificity and sensitivity, the tests to be used in pandemics affecting the whole world must be easily accessible and cost-effective in clinical practice. Complete blood count (CBC) is an inexpensive test that produces rapid results and can be easily accessed in all hospitals. It is known that viral diseases such as COVID-19 lead to changes in hematological parameters. Lymphopenia is common in viral infections, and studies have shown the relationship between disease severity and depth of lymphopenia. Many parameters can be evaluated in a single CBC analysis; however, studies using CBC in cases of COVID-19 have generally focused on lymphocyte levels (7).

Although platelets are mainly responsible for hemostasis, they affect the immunomodulatory system. There are studies investigating platelet count and platelet indices to predict prognosis, especially in viral infections and non-COVID-19 critically ill patients with sepsis (8). Studies evaluating the role of platelet count and platelet indices in predicting the prognosis of COVID-19 cases have generally investigated outpatients or patients hospitalized in the ward (9). It has been reported that platelet indices, including mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), platelet-to-lymphocyte ratio (PLR), and MPV-to-platelet count ratio (MPV/PLT) are more sensitive than platelet count for predicting prognosis in critically ill patients (10,11). Although studies have been conducted to evaluate platelet count in adult ICU patients with COVID-19, there are no ICU studies with large series investigating the relationship between platelet indices, the ratios of these parameters, and ICU mortality.

The effects of the recognition of the disease with numerous studies and the experience of health professionals on the reduced impact of the pandemic and the decreased mortality compared to the initial stage of in the fight against COVID-19 cannot be denied. Therefore, studies on COVID-19 are critical in benefiting from the experience gained during the COVID-19 pandemic in the fight against viral infections in future epidemics.

There are clinical scoring systems that predict mortality in ICU patients. However, a scoring system or mortality marker that has been specifically developed for COVID-19 and is used in clinical practice has not yet been defined. The use of cost effective, easy-to-evaluate markers that can be accessed everywhere for predicting mortality risk and prognosis of critically ill patients will be beneficial in terms of early recognition of these patients and taking necessary measures in clinical practice. This study aimed to evaluate the role of platelet indices MPV, PDW, PCT, PLR, and MPV/PLT, which can be evaluated with CBC, in predicting the mortality of ICU patients with COVID-19.

MATERIAL AND METHOD

This is a single-center, retrospective, cross-sectional study conducted in a tertiary pandemic hospital, in Ankara, Turkey. After obtaining ethics committee approval, all patient data were collected from electronic medical records and patient files (Approval Date: 07.04.2021; Approval Number: 2021/E2-21-358). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The study included patients over 18 years of age who were hospitalized in the COVID-19 ICU between 1 August, 2020 and 1 February, 2021 and who had a positive real-time reverse transcriptase-polymerase chain reaction (RT-PCR) test result for COVID-19. Patients with comorbidities that could affect platelet indices such as immunodeficiency and hematological disorders, patients on chronic therapies that could affect platelet indices, pregnant womens, and those hospitalized in the ICU for less than 24 hours were excluded from the study. Throughout the study period, 382 patients with COVID-19 were followed up in the ICU. Eighty-eight patients were excluded from the study due to testing negative in RT-PCR, 49 patients due to comorbidities or drug use that could affect platelet indices and 44 patients due to mortality in the first 24 hours of admission. The study included 201 patients who met the inclusion criteria and had complete data. The diagnosis of COVID-19 was made by RT-PCR. In our hospital, the intensive care specialists determine the indication for ICU admission of patients.

Patients' demographic data, comorbidities, Acute Physiology and Chronic Health Evaluation II (APACHE-II) scores, Sequential Organ Failure Assessment (SOFA) scores, and Glasgow Coma Scale (GCS) scores at ICU admission were reviewed. Platelet, lymphocyte, white blood cell and neutrophil counts, MPV, PDW, PCT, neutrophil-to-lymphocyte ratio (NLR), haemoglobin, D-dimer, CRP, procalcitonin, ferritin, interleukin-6 (IL-6), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) measured on the day of ICU admission were recorded. Eventually, the PLR and MPV/PLT ratio were calculated. CBC was performed using the ADVIA 2120 Hematology System (Siemens Healthcare). Mortality rates, invasive mechanical ventilation (MV) requirement, MV duration and ICU length of stay (LOS) were analyzed. Patients were divided into two groups: survivors and non-survivors.

Statistical Analysis: Statistical Package for the Social Science (SPSS) version 25.0 software package was used to analyze the study data. In the study, the continuous variables were presented as median (minimum-maximum) values, while categorical variables were presented as frequency and relative percentage values. Student's t-test or Mann-Whitney U test was used

depending on normality distribution in the inter-group comparison of continuous variables. The chi-square test or Fisher's exact test were used to compare categorical variables. A "Receiver Operating Characteristic (ROC)" analysis was carried out to predict mortality. The area under the curve (AUC), cut-off points, and the sensitivity and selectivity values of these cut-off points were calculated. A p-value <0.05 was considered statistically significant in all analyses.

RESULTS

The study included 201 critically ill ICU patients with COVID-19, with a mean age of 70.00±14.49 years. Of the patients, 72 (35.8%) were female, and 129 (64.2%) were male. The survivor and non-survivor groups were similar in terms of gender distribution. The mean age of the survivor group (62.61±16.23 years) was lower than that of the non-survivor group (71.92±11.48 years) (p<0.05). The most frequent comorbidity in the entire population was hypertension (51.7%). The non-survivor group had higher APACHE-II and SOFA scores and lower GCS scores compared to the survivor group (p<0.05). The median ICU LOS of all patients was 9 (range, 1-56) days. The ICU LOS was 10 (range, 1-56) days in the non-survivor group and 7 (range, 2-39) days in the survivor group, with a significant difference between the two groups (p<0.05). The MV duration was 4 (range, 0-55) days in the non-survivor group, which was longer (p<0.05) compared to the survivor group (**Table 1**). The ICU mortality rate of the entire population was 56.2%.

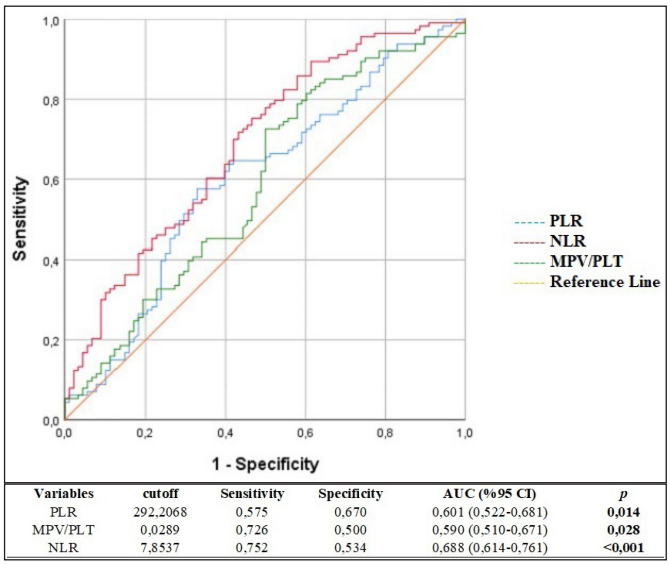
Table 1. Demographic and clinical characteristics of the patients

Variables	All patients (n=201)	Survivors (n=88, 43.8%)	Non-survivors (n=113, 56.2%)	P
Age, y (mean±SD)	70.00±14.49	62.61±16.23	71.92±11.48	<0.001*
Gender n (%)				
Female	129 (64.2%)	60 (68.2%)	69 (61.1%)	0.296
Male	72 (35.8%)	28 (31.8%)	44 (38.9%)	
Comorbidities n (%)				
Hypertension	104 (51.7%)	40 (45.5%)	64 (46.6%)	0.115
Diabetes Mellitus	67 (33.3%)	23 (26.1%)	44 (38.9%)	0.056
COPD	34 (16.9%)	9 (10.2%)	25 (22.1%)	0.041*
Asthma	10 (5.0%)	4 (4.5%)	6 (5.3%)	1.000
CV Disease	72 (35.8%)	26 (29.5%)	46 (40.7%)	0.102
CKD	15 (7.5%)	7 (8.0%)	8 (7.1%)	1.000
CVD	17 (8.5%)	4 (4.5%)	13 (11.5%)	0.133
APACHE II	18 (3-50)	11 (3-42)	25 (9-50)	<0.001*
GCS	15 (3-15)	15 (4-15)	12 (3-15)	<0.001*
SOFA	4 (0-15)	3 (0-10)	8 (3-15)	<0.001*
ICU LOS, days	9 (1-56)	7 (2-39)	10 (1-56)	0.013*
MV duruation, days	1 (0-55)	0 (0-32)	4 (0-55)	<0.001*

* Significant difference at p < 0.05 p-values were calculated by Student's t-test, chi-squared test, Fisher's exact test or Mann–Whiney U test. Data were described as numbers of cases (%) for qualitative variables and as means (±SD) or medians (min-max) for quantitative variables.
Abbreviations: n: number, SD: standard deviation, y: years, COPD: Chronic obstructive pulmonary disease, CV: cardiovascular, CKD: chronic kidney disease, CVD: Cerebrovascular disease, APACHE II: acute physiology and chronic health evaluation-II scores, GCS: Glasgow Coma Scale, MV: mechanical ventilation, LOS: length of stay, ICU: intensive care unit.

The survivor and non-survivor groups were compared in terms of laboratory parameters. There was a significant difference between the two groups in terms of markers showing inflammation, including absolute lymphocyte and neutrophil count, CRP, procalcitonin, ferritin, and IL-6 measured on the day of ICU admission (p<0.05). The median absolute lymphocyte count of all patients hospitalized in the COVID-19 ICU was 0.83 (range, 0.53-3.32), with lymphocyte count being significantly lower in the non-survivor group (0.78 [range, 0.53-2.02]) compared to the survivor group (0.97 [range, 0.72-3.32]) (p<0.05) (**Table 2**). The cut-off value of lymphocyte for predicting mortality was 0.920 (AUC: 0.832 [95% CI 0.776-0.888]) (p<0.05). The median NLR of the entire population was 10.22 (range, 0.65-74.60); the median NLR of the non-survivor group (12.06 [range, 0.65-74.60]) was higher than that of the survivor group (7.21 [range, 0.97-37.69]) (p<0.05). The cut-off value of NLR for predicting mortality was 7.853 (AUC: 0.688 [95% CI 0.614-0.761]) (p<0.05).

The analysis of platelet count, MPV, PCT and PDW revealed no significant difference between the two groups. The comparison of the two groups in terms of platelet ratios showed higher PLR (321.79 [range, 51.16-1250.75] / 244.64 [range, 29.82-661.84]) and MPV/PLT ratio (0.035 [range, 0.010-0.230] / 0.030 [range, 0.010-0.130]) in the non-survivor group compared to the survivor group (p<0.05). The evaluation with ROC curve for predicting mortality revealed a cut-off value of 292.20 for PLR (AUC: 0.601 [95% CI 0.522-0.681]) (p<0.05) and a cut-off value of 0.0289 for MPV/PLT (AUC: 0.590 [95% CI 0.510-0.671]) (p<0.05) (**Figure 1**).



Variables	cutoff	Sensitivity	Specificity	AUC (%95 CI)	p
PLR	292,2068	0,575	0,670	0,601 (0,522-0,681)	**0,014**
MPV/PLT	0,0289	0,726	0,500	0,590 (0,510-0,671)	**0,028**
NLR	7,8537	0,752	0,534	0,688 (0,614-0,761)	**<0,001**

Figure 1. The Receiver Operating Characteristic (ROC) curve analysis for PLR, MPV/PLT, NLR for predicting ICU mortality
Abbreviations: ROC: Receiver Operating Characteristic, ICU: intensive care unit, AUC: area under the curve, CI: confidence interval, PLR: platelet-to-lymphocyte ratio, MPV/PLT: mean platelet volume-to-platelet count, NLR: neutrophil-to-lymphocyte ratio.

Table 2. Laboratory parameters of survivor and non-survivor patients

Variables	All Patients (n=201)	Survivors (n=88, 43.8%)	Non-survivors (n=113, 56.2%)	p
Hemoglobin (gr/dL)	12.50±2.14	12.55±2.15	12.47±2.15	0.783
WBC (×10^9/L)	10.49 (0.59-59.00)	9.63 (2.04-35.13)	11.20 (0.59-59.00)	0.156
Lymphocyte (×10^9/L)	0.83 (0.53-3.32)	0.97 (0.72-3.32)	0.78 (0.53-2.02)	<0.001*
Neutrophile (×10^9/L)	9.29 (0.44-54.46)	7.91 (1.76-30.53)	10.10 (0.44-54.46)	0.042*
Platelet (×10^9/L)	268 (38-838)	292 (81-662)	260 (38-838)	0.055
MPV (f/l)	8.9 (7.1-14.2)	8.7 (7.1-14.2)	9.0 (7.4-14.1)	0.083
PCT (%)	0.24 (0.05-0.74)	0.27 (0.08-0.60)	0.23 (0.05-0.74)	0.055
PDW (%)	55.70 (15.40-83.60)	55.25 (31.60-78.80)	57.00 (15.40 (83.60)	0.621
PLR	283.87 (29.82-1250.75)	244.64 (29.82-661.84)	321.79 (51.16-1250.75)	0.014*
NLR	10.22 (0.65-74.60)	7.21 (0.97-37.69)	12.06 (0.65-74.60)	<0.001*
MPV/PLT	0.034 (0.010-0.230)	0.030 (0.010-0.130)	0.035 (0.010-0.230)	0.028*
CRP (g/L)	0.100 (0.002-0.630)	0.081 (0.003-0.311)	0.131 (0.002-0.630)	<0.001*
Procalcitonin (µg/L)	0.18 (0.02-178.80)	0.12 (0.02-178.80)	0.23 (0.02-37.60)	<0.001*
Ferritin (µg/L)	713 (9-19000)	429 (14-19000)	815 (9-14273)	0.003*
IL-6 (pg/ml)	46.3 (4.7-1000.0)	31.9 (4.7-1000.0)	58.9 (5.0-1000.0)	<0.001*
AST (U/L)	49 (4-2900)	42 (4-382)	53 (12-2900)	0.006*
ALT (U/L)	37 (6-1605)	39 (6-383)	35 (7-1605)	0.996
D-dimer (mg/L)	2.0 (0.3-35.2)	1.45 (0.3-35.2)	2.2 (0.3-35.2)	0.018*

* Significant difference at $p < 0.05$. p-values were calculated by Student's t-test or Mann–Whiney U test. Data were described as means (±SD) or medians (min-max) for quantitative variables. **Abbreviations:** n: number, WBC: white blood cells, CRP: C-reactive protein, MPV: mean platelet volume, PDW: Platelet distribution width, PCT: Plateletcrit, PLR: Platelet-to-lymphocyte ratio, PLT: platelet, MPV/PLT: mean platelet volume-to-platelet count, NLR: neutrophil-to lymphocyte ratio, IL-6: Interleukin-6, AST: aspartate aminotransferase, ALT: alanine aminotransferase.

DISCUSSION

Despite the decrease in the number of cases compared to two years ago, it cannot be anticipated when the pandemic will end. Since the beginning of the pandemic, the vast majority of patients with severe COVID-19 have been followed in ICUs. Especially in the periods when the number of cases peaked, the number of ICU beds was insufficient to meet the need, leading to high mortality rates worldwide. In critical cases, it is valuable to determine the risk factors at the time of admission and to have inexpensive, easily accessible parameters for predicting the prognosis in order to prevent negative outcomes. Although there are many studies on COVID-19 in the literature, a mortality marker that can be easily accessed and used in clinical practice to predict the prognosis of critically ill ICU patients with COVID-19 has not yet been defined.

Platelets are mainly responsible for hemostasis and are known to affect the immune system. Platelet count and platelet indices have been reported to be associated with inflammation and, effective in predicting the prognosis of patients with sepsis, with feasibility as a mortality marker in non-COVID-19 critically ill patients (8,11). Studies have shown higher mortality rates in patients with low platelet count among adult COVID-19 patients (12). However, although low platelet counts are associated with mortality in COVID-19 patients, thrombocytopenia is usually seen in very severe cases, with a low incidence of overt thrombocytopenia (13,14). In ICU patients, thrombocytopenia can have different causes, such as hemodilution, bacterial septicaemia, and bone marrow suppression (15). So, it would not be reasonable to use platelet counts alone as an indicator of mortality. Although the results of our study showed a lower platelet count in non-survivors compared to survivors, there was no statistically significant difference between the two groups. Therefore, the role of platelet indices in predicting mortality was evaluated in our study since these parameters have been reported to be more sensitive for predicting prognosis compared to platelet count in non-COVID-19 critically ill patients but have not been studied in large series to demonstrate the mortality relationship in ICU patients with COVID-19.

In the literature, there are various studies examining platelet indices in different patient groups with non-critical COVID-19. A paper comparing COVID-19 outpatients with non-COVID-19 patients reported higher MPV and PDW and lower PCT in the COVID-19 group than in the control group, suggesting that these parameters may be a warning for the suspicion of COVID-19 at the diagnosis stage (16). Guclu et al. (9) compared moderate and severe COVID-19 cases found no difference between the survivor and non-survivor groups in terms of admission MPV values and reported an association with a 1.76-fold increase in mortality for every 1 unit increase in the follow-up MPV measured on day 3. Our study evaluating ICU patients with COVID-19 showed no difference in MPV, PCT, and PDW parameters evaluated at ICU admission. PLR and MPV/PLT ratio were higher in the non-survivor group and were associated with mortality. Studies suggest the use of MPV/PLT and PLR as a prognostic indicator instead

of MPV or platelet indices alone in non-COVID-19 ICU patients (17). A small-series study evaluating the admission parameters of 96 ICU patients in the COVID-19 patient group found no difference between non-survivors and survivors in terms of the admission MPV value but reported the significance of the MPV/PLT ratio in demonstrating mortality (18). The study of Yardimci et al. (19) evaluating 722 patients hospitalized in COVID-19 wards reported that 44 patients were transferred to ICU and the MPV/PLT ratio of severely ill patients who required ICU were higher compared to those treated in wards. However, the study did not mention the relationship between MPV/PLT ratio and mortality. We believe that our study, which demonstrated a significant difference in MPV/PLT ratios between the non-survivor and survivor groups, will come to the fore both because it included patient population consisting entirely of ICU patients and it primarily evaluated ICU mortality.

PLR, which is associated with systemic inflammation, is a parameter that has been used as a new generation inflammation marker in recent studies in various infection case groups such as septicemia and pneumonia. The study of Shen et al. (20) on non-COVID-19 critically ill patients evaluating 5537 ICU patients with sepsis reported a strong association between PLR >200 and mortality. A COVID-19 study evaluating 306 patients reported higher PLR in patients who developed pneumonia compared to those who did not, stating that a PLR cut-off value of 139 could be used for predicting the development of pneumonia (21). A review evaluating PLR in COVID-19 cases explained the more significant association of high admission PLR with mortality compared to other platelet parameters by the increase in PLR as a result of deeper lymphopenia compared to thrombocytopenia in baseline examinations (22). It is known that a cytokine storm can develop in ICU patients with COVID-19, leading to high mortality rates. Evaluation of PLR, as a systemic inflammation indicator, at the time of ICU admission may be a guide in identifying the progression to septicemia or cytokine storm in this patient group, thus preventing mortality. In our study, PLR was higher in the non-survivor group, and the cut-off value of PLR for predicting mortality was found to be 292.20.

COVID-19 infection causes an increase in infection parameters due to rapid viral replication and the uncontrolled release of pro-inflammatory cytokines and chemokines. Numerous studies have been conducted with inflammation markers to evaluate the prognosis and mortality of COVID-19 patients during the pandemic (23). There are studies evaluating leukocyte subsets and pro-inflammatory cytokine levels such as IL-6, IL-1, IL-10, and TNF in COVID-19 which is known to cause hyper-inflammation and cytokine storm (24). However, the parameters to predict the prognosis in epidemic situations that affect the whole world and cause pandemics should be cost-effective tests that can be performed anywhere. CBC is an inexpensive and easily accessible test. Lymphopenia is known to be common in viral infections. Therefore, one of the parameters frequently investigated in patients with COVID-19 has been the lymphocyte count. A study by Wang et al. (7) reported that a lymphocyte count of less than 0.95 × 109/L was associated with higher mortality compared to a lymphocyte count of > 0.95 × 109/L. The ROC analysis performed in our study revealed a cut-off value of 0.920 × 109/L for the lymphocyte count to predict mortality.

NLR is another CBC parameter reported to be associated with the severity of COVID-19. As a result of studies conducted with non-COVID-19 patients in the literature, it is known that NLR shows mortality more sensitively than isolated neutrophil and lymphocyte levels in viral and bacterial pneumonia (25). A retrospective study of 151 COVID-19 patients reported a median NLR value of 1.95 (1.43–2.58) in survivors and 13.87 (7.50–24.82) in non-survivors. However, the study did not indicate the number of patients who required ICU (26). In our study, the cut-off of NLR value for predicting mortality was 7.85. The results of our study evaluating critically ill patients with COVID-19 showed significantly higher median NLR in the non-survivor group compared to the survivor group. It is believed that this rate increases with the severity of the disease. A meta-analysis of 38 articles evaluating admission NLR levels of patients with COVID-19 reported higher NLR in severe COVID-19 cases and in the non-survivor group (27). These studies evaluating CBC parameters in COVID-19 generally include the outpatient groups, while our study, the entire population of which consisted of ICU patients with COVID-19, differs from the published studies in the literature in this regard. The limitation of our study is its retrospective and single-center design. We believe that prospective multicenter studies will support these results.

CONCLUSION

The results of our study evaluating platelet indices for predicting mortality of ICU patients during the pandemic demonstrated an association between PLR, MPV/PLT ratio, and mortality. Using ratios such as MPV/PLT and PLR as an early prognostic indicator instead of platelet indices alone, like MPV in ICU patients with COVID-19, may help identify high-risk patients early. We believe that our study will shed light on future studies in terms of using these easily accessible and cost-effective CBC parameters in clinical practice to identify high-risk patients early at the time of admission and prevent poor outcomes.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee (Approval Number: 2021/E2-21-358 and Approval Date: 07.04.2021) for studies involving humans.

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

Referee Evaluation Process: Externally peer-reviewed.

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

Financial Disclosure: The authors declared that this study has received no financial support.

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

REFERENCES

1. World Health Organization. WHO Coronavirus (COVID-19) Dashboard. https //covid19.who.int/ (accessed date: 19 April 2022).
2. Marin BG, Aghagoli G, Lavine K, et al. Predictors of COVID-19 severity: A literature review. Rev Med Virol 2021; 31:1-10.
3. Qi J, He D, Yang D, et al. Severity-associated markers and assessment model for predicting the severity of COVID-19: a retrospective study in Hangzhou, China. BMC Infect Dis 2021; 21: 774.
4. Hou H, Zhang B, Huang H, et al. Using IL-2R/lymphocytes for predicting the clinical progression of patients with COVID-19. Clin Exp Immunol 2020; 201: 76-84.
5. Smilowitz NR, Kunichoff D, Garshick M, et al. C-reactive protein and clinical outcomes in patients with COVID-19. Eur Heart J 2021; 42: 2270-9.
6. Henry BM, de Oliveira MHS, Benoit S, Plebani M, Lippi G. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis. Clin Chem Lab Med 2020; 58: 1021-8.
7. Wang S, Sheng Y, Tu J, Zhang L. Association between peripheral lymphocyte count and the mortality risk of COVID-19 inpatients. BMC Pulm Med 2021; 21: 55.
8. Vardon-Bounes F, Gratacap MP, Groyer S, et al. Kinetics of mean platelet volume predicts mortality in patients with septic shock. PLoS One 2019; 14: e0223553.
9. Güçlü E, Kocayiğit H, Okan HD, et al. Effect of COVID-19 on platelet count and its indices. Rev Assoc Med Bras (1992) 2020; 66: 1122-7.
10. Vélez-Páez JL, Legua P, Vélez-Páez P, et al. Mean platelet volume and mean platelet volume to platelet count ratio as predictors of severity and mortality in sepsis. PLoS One 2022; 17: e0262356.
11. Zhang Z, Xu X, Ni H, Deng H. Platelet indices are novel predictors of hospital mortality in intensive care unit patients. J Crit Care 2014; 29: 885.
12. Liu Y, Sun W, Guo Y, et al. Association between platelet parameters and mortality in coronavirus disease 2019: Retrospective cohort study. Platelets 2020; 31: 490-6.
13. Larsen JB, Pasalic L, Hvas AM. Platelets in coronavirus disease 2019. Semin Thromb Hemost 2020; 46: 823-5.
14. Pujani M, Raychaudhuri S, Verma N, et al. Association of Hematologic biomarkers and their combinations with disease severity and mortality in COVID-19- an Indian perspective. Am J Blood Res 2021; 11: 180-90.
15. Ostadi Z, Shadvar K, Sanaie S, Mahmoodpoor A, Saghaleini SH: Thrombocytopenia in the intensive care unit. Pak J Med Sci 2019; 35: 282-7.
16. Shankaralingappa A, Tummidi S, Arun Babu T. Diagnostic value of platelet indices in COVID 19 infection: a case-control study from a single tertiary care center. Egypt J Intern Med 2022; 34: 35.
17. Golwala ZM, Shah H, Gupta N, Sreenivas V, Puliyel JM. Mean platelet volume (MPV), platelet distribution width (PDW), platelet count and plateletcrit (PCT) as predictors of in-hospital paediatric mortality: a case-control Study. Afr Health Sci 2016; 16: 356-62.
18. Mobarki AA, Dobie G, Saboor M, et al. MPR and NLR as prognostic markers in ICU-admitted patients with COVID-19 in Jazan, Saudi Arabia. Infect Drug Resist 2021; 14: 4859-64.
19. Yardımcı AC, Yıldız S, Ergen E, et al. Association between platelet indices and the severity of the disease and mortality in patients with COVID-19. Eur Rev Med Pharmacol Sci 2021; 25: 6731-40.
20. Shen Y, Huang X, Zhang W. Platelet-to-lymphocyte ratio as a prognostic predictor of mortality for sepsis: interaction effect with disease severity-a retrospective study. BMJ Open 2019; 9: e022896.
21. Damar Çakırca T, Torun A, Çakırca G, Portakal RD. Role of NLR, PLR, ELR and CLR in differentiating COVID-19 patients with and without pneumonia. Int J Clin Pract 2021; 75: e14781.
22. Sarkar S, Kannan S, Khanna P, Singh AK. Role of platelet-to-lymphocyte count ratio (PLR), as a prognostic indicator in COVID-19: a systematic review and meta-analysis. J Med Virol 2022; 94: 211-21.
23. Gao YD, Ding M, Dong X, et al. Risk factors for severe and critically ill COVID-19 patients: a review. Allergy 2021; 76: 428-55.
24. Wang J, Jiang M, Chen X, Montaner LJ. Cytokine storm and leukocyte changes in mild versus severe SARS-CoV-2 infection: review of 3939 COVID-19 patients in China and emerging pathogenesis and therapy concepts. J Leukoc Biol 2020; 108: 17-41.
25. Han Q, Wen X, Wang L, et al. Role of hematological parameters in the diagnosis of influenza virus infection in patients with respiratory tract infection symptoms. J Clin Lab Anal 2020; 34: e23191.
26. Wang X, Li X, Shang Y, et al. Ratios of neutrophil-to-lymphocyte and platelet-to-lymphocyte predict all-cause mortality in inpatients with coronavirus disease 2019 (COVID-19): a retrospective cohort study in a single medical centre. Epidemiol Infect 2020; 148: e211.
27. Simadibrata DM, Calvin J, Wijaya AD, Ibrahim NAA. Neutrophil-to-lymphocyte ratio on admission to predict the severity and mortality of COVID-19 patients: A meta-analysis. Am J Emerg Med 2021; 42: 60-9.