Cerrahpaşa Med J 2022; 46(2): 151-155 ORIGINAL ARTICLE

The Relationship of Platelet Parameters with Duration of Hospitalization and Fatality in COVID-19 Patients

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Abstract

Objective: In coronavirus disease 2019 infection, indicators are needed to predict survival and length of hospital stay. Our aim is to determine the relationship between thrombocyte parameters, duration of hospitalization, and mortality.

Methods: After the ethics committee approval, patients hospitalized with coronavirus disease 2019 with PCR positivity between March and September 2020 were retrospectively screened. Patients were divided into two groups survivors and non-survivors. Intergroup data was evaluated using Kolmogorov–Smirnov, Student's *t*-test, Mann Whitney U, chi-square, and Pearson and Spearman's rho tests by SPSS version 22.

Results: Totally 3914 patients were included in the study, of which 1766 (45%) were female and 2148 (55%) were male. The mean age was 59. The mean hospital stay was 10 days. Five hundred and sixty-four (14%) of our patients died. When the survivors and non-survivors are compared, platelet lymphocyte ratio, platelet distribution width,and platelet large cell ratio were higher in the non-survivors. The death in patients with thrombocytopenia was higher than in the group without thrombocytopenia. Patients with higher platelet large cell ratio (PLCR) and those with lower mean platelet volume were hospitalized for longer.

Conclusion: Platelet lymphocyte ratio, platelet distribution width, and platelet large cell ratio are the parameters that can be used to predict coronavirus disease 2019 infection mortality, and platelet lymphocyte ratio and mean platelet volume are the parameters to predict hospitalization durations.

Keywords: COVID-19, hospital stay, mortality, predictors

Introduction

In December 2019, cases of pneumonia, known as new coronavirus pneumonia, began to appear for the first time in Wuhan, China's Hubei province. In 2019, The World Health Organization (WHO) officially named this disease the coronavirus disease 2019 (COVID-19). The following month, the disease spread rapidly from Wuhan to other cities and then to other countries. Until May 2021, internationally 162,492,769 cases were confirmed and 3,482,907 deaths have been reported.[1]

While complaints such as fever, cough, and shortness of breath are more common in patients, symptoms of other body systems other than the respiratory system may also be seen. Among the laboratory examinations of the patients, normal or decreased leukocyte count, lymphopenia, and thrombocytopenia are remarkable.[2,3]

Till now, there is no effective specific treatment for COVID-19. However, it is tried to prevent the epidemic with vaccination. Due to the lack of a specific treatment and high mortality and morbidity, starting treatment in the early period still maintains its importance despite all passing time. There is a need for predictive indicators to predict mortality and hospital stay from clinical and laboratory values obtained when patients visit the hospital. Platelets play an important role in the inflammation and coagulation procedure. Activated platelets secrete a large number of substances belonging to the main factors of inflammation. The number of studies including platelet parameters and platelet lymphocyte ratio (PLR) is very few and the number of cases is quite insufficient in order to find an indicator with a high prediction regarding mortality and duration of hospital stay in COVID-19 infection. Therefore, the aim of this study was to examine the relationship between the platelet parameters such as mean platelet volume (MPV), platelet distribution width (PDW), platelet large cell ratio (PLCR), and PLR with the hospital stay and mortality.

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Methods

Data Collection

For this single-centered retrospective study, the approval dated September 22, 2020, and numbered 373 was obtained from the ethics committee of Prof. Dr. Cemil Taşçıoğlu City Hospital. Informed consent was not required due to the retrospective use of de-identified administrative data. By scanning the database with the help of our hospital's data processing service, 4836 patients over the age of 18 who were hospitalized in our third step hospital between March 20, 2020, and November 10, 2020, and whose diagnosis of COVID-19 was confirmed by PCR were included in this study. The data of 3914 patients were detailed, excluding cases whose hemogram, fibrinogen, D-dimer, ferritin, interleukin 6 (IL-6), C-reactive protein (CRP), albumin, lactic dehydrogenase

(LDH), urea, creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and calcium values were not checked on the first day of hospitalization.

Biochemical analyzes were done with the colorimetric method and with the autoanalyzer Beckman Coulter Brand AU5800 (US device), and the hemogram was done with the autoanalyzer Mindray Brand BC6800 (China device). Gender, age, duration of hospital stay, and survival of all patients were noted. All patients were divided into two groups survivors and non-survivors, and it was examined whether there was a difference between the two groups in terms of platelet parameters, PDW, PLCR, MPV, and PLR. In addition, it was evaluated whether there was a correlation between these parameters and the duration of hospitalization of the patients who were discharged from the hospital.

Statistical Analysis

While evaluating the findings obtained in the study, IBM SPSS Statistics 22 (IBM SPSS, Turkey) program was used for statistical analysis. The suitability of the parameters to the normal distribution was evaluated with the Kolmogorov-Smirnov test. While evaluating the study data, in addition to descriptive statistical methods (e.g., mean, standard deviation, and frequency), student's *t*-test was used for the comparison of normally distributed parameters between two groups, and Mann Whitney U test was used for the comparison of non-normally distributed parameters between two groups. A chi-square test was used to compare qualitative data. Pearson correlation analysis was used to analyze the relationships between parameters conforming to the normal distribution, and Spearman's rho correlation analysis was used to examine the relationships between the parameters not conforming to the normal distribution. Statistically $P < .05$ was considered significant.

Results

The study was conducted with a total of 3914 patients, of which 1766 (45.1%) were female and 2148 (54.9%) were male, with ages ranging from 18 to 102. The mean age was 59.94 ± 17.14 years, and the median age was 61. The duration of stay ranged from 1 to 137 days, with a mean of 12.65 ± 9.87 days with a median duration of 10 days. While 3350 (85.6%) of the patients were discharged with recovery, 564 (14.4%) died. The mean age and duration of stay of the people who lost their lives were statistically significantly higher than those who were discharged with recovery ($P = .000$; $P < .05$). The male gender ratio of the people who lost their lives (59.8%) was statistically significantly higher than those who were discharged with recovery (54.1%) ($P = .012$; $P < .05$). There was not any statistically significant difference between the thrombocyte number, the non-survivors, and the survivors. Age and gender evaluation according to the way of discharge from the hospital are shown in Table 1. The levels of WBC, neutrophil, PLR, CRP, D-dimer, ferritin, IL-6, LDH, urea, creatinine, and AST of the patients who lost their lives are statistically significantly higher than those who were discharged after recovery ($P < .05$). The PDW levels of the patients who lost their lives were statistically significantly higher than those who were discharged with recovery ($P = .001$). The PLCR levels of the patients who lost their lives were statistically significantly higher than those who were discharged with recovery ($P = .024$). Lymphocyte and hemoglobin levels of the patients who lost their lives were statistically significantly lower than those who were discharged with cure ($P < .05$). There was no statistically significant difference between platelet, MPV, and ALT levels between the two groups ($P > .05$). Evaluations according to the way out of the hospital are shown in Table 2.

Table 1. Age and Gender Evaluation According to the Way Out of the Hospital

	Non-Survivors		Survivors		
	Mean ± SD		Mean ± SD		*P*-Value
Age (year)	69.97 ± 13.65 (71)		58.25 ± 17.09 (59)		[1].000*
Duration of Hospital Stay (day)	18.22 ± 15.22 (16)		11.72 ± 8.28 (10)		[1].000*
	n	%	n	%	
Sex					
Female	227	40.2	1539	45.9	[2].012*
Male	337	59.8	1811	54.1	
Platelet Count (/mm^3)					
<150,000	171	30.3	715	21.3	[2].000*
>150,000	293	69.7	2635	78.7	–

[1]Mann Whitney U Test, [2]chi-square test, *$P < .05$ was considered significant.

There was a negative, weak, but statistically significant relationship between the duration of hospital stay and lymphocyte number ($P < .05$). There was a negative, very weak, but statistically significant relationship between the duration of hospital stay, hemoglobin, and MPV ($P < .05$).

There is a positive, weak, but statistically significant relationship between duration of hospital stay and neutrophil–lymphocyte ratio, D-dimer, ferritin, LDH, urea, creatinine, and CRP levels ($P < .05$). There was a positive, very weak, but statistically significant correlation between duration of hospital stay and AST, PLR, and neutrophil levels ($P < .05$). There was no statistically significant relationship between the duration of hospital stay and PDW, PLCR, fibrinogen, IL-6, and ALT ($P > .05$). Correlations related to duration of hospital stay have been shown in Table 3.

Discussion

The COVID-19 pandemic is a global public health problem with a very high mortality rate for which a complete cure has not yet been found.

The treatment of infected patients is as important as the importance of the work done to avoid getting infected with COVID-19. In this respect, it is important to predict which patient has an increased risk of mortality and which patient will need to be hospitalized for longer in this disease for which a definitive treatment has not been found yet.

With the help of this foresight, step-by-step treatment schemes of patients can be shaped more easily and more intensive treatment can be started earlier, thus reducing mortality and improving hospital resource allocation.

Previous studies have shown that older age is associated with an increased risk of death in COVID-19 infection. As a result of our study, it was seen that in addition to older age, male gender and long-term hospitalization are associated with increased mortality. Mertoglu et al.[3,4] in accordance with our study, reported a poor prognosis for older age and male gender.

Table 2. Evaluations According to the Way Out of the Hospital

	Non-Survivors	Survivors	
	Mean ± SD (median)	**Mean ± SD (median)**	***P*-Value**
WBC (10^3/uL)	10.65 ± 7.5 (8.75)	7.86 ± 4.36 (6.86)	[1]**.000***
Thrombocyte (/mm^3)	209.920 ± 102.013 (192.000)	217.102 ± 89.836 (202.000)	[2].116
Hemoglobin (g/dL)	11.97 ± 23.9 (121)	12.79 ± 20.2 (130)	[2]**.000***
PDW (fL)	16.28 ± 0.49 (16.3)	16.21 ± 0.45 (16.2)	[2]**.001***
PLCR (%)	27.39 ± 9.36 (26.6)	26.44 ± 8.51 (25.5)	[2]**.024***
MPV (fL)	10.01 ± 1.43 (9.9)	9.92 ± 1.28 (9.8)	[2].146
Lymhocyte(10^3/μL)	1.32 ± 3.31 (0.89)	1.41 ± 1.36 (1.22)	[1]**.000***
Notrofil (10^3/μL)	8.76 ± 6.43 (7.02)	5.89 ± 3.9 (4.89)	[1]**.000***
Neutrophil/Lymphocyte	11.79 ± 14.32 (7.62)	5.7 ± 6.47 (3.96)	[1]**.000***
Platelet/Lymphocyte	289.39 ± 325.65 (201.37)	200.14 ± 160.63 (160.24)	[1]**.000***
Fibrinogen (mg/dL)	216.59 ± 322.64 (4.96)	255.55 ± 307.3 (5.33)	[1].266
D-Dimer (ng/m	3501.27 ± 9842.75 (1120)	1074.82 ± 2926.68 (488)	[1]**.000***
Ferritin (mL/ng)	1222.93 ± 3246.91 (618.2)	463.11 ± 637.69 (268.8)	[1]**.000***
IL-6 (pg/mL)	420.55 ± 1029.54 (91.7)	150.3 ± 555.81 (26.85)	**.000***
LDH (U/L)	553.29 ± 748.4 (407)	327.19 ± 177.09 (289)	[1]**.000***
Urea (mg/dL)	78.68 ± 56.91 (60)	41.66 ± 31.03 (33)	[1]**.000***
Creatinin (mg/dL)	1.71 ± 1.79 (1.15)	1.1 ± 1.26 (0.84)	[1]**.000***
AST (IU/L)	78.69 ± 327.53 (40)	44.56 ± 93.76 (31)	[1]**.000***
ALT (IU/L)	42.24 ± 125.89 (21)	34.26 ± 61.04 (22)	[1].710
CRP (mg/L)	144.24 ± 100.41 (129.7)	75.85 ± 74.68 (56)	[1]**.000***

[1]Mann Whitney U Test, [2]student *t*-test, *: $P < .05$ was considered significant. WBC, White Blood Cell; PDW, Platelet Distribution Width; PLCR, Platelet Large Cell Ratio; MPW, Mean Platelet Volume; IL-6, interleukin 6; LDH, lactic dehydrogenase; AST, Aspartate Aminotransferase; ALT, Alanine aminotransferase; CRP, C-Reactive Protein.

We saw that the number of patients with a thrombocyte value less than 150 000 was higher in the group with high mortality. In addition, we determined that, the increases in the other thrombocyte parameters PLR, PDW, and PLCR were higher in the non-survivors. In the literature review, while there are studies that found a relationship between the increased severity and mortality of COVID-19 disease and low platelet count, there are studies reporting the opposite.[2,5-7] In a study of 30 patients by Qu et al.[8] they found that platelets first increased at the beginning of the disease and then decreased in the following days. Indeed, in the case of initial inflammation, increased IL-6 and thrombopoietin (THPO)-mediated megakaryocyte production may increase, but with the progression of the disease, multiple factors such as bone marrow suppression secondary to an infection, platelet activation due to endothelial damage, and cytokine storm cause a decrease in platelet count.[8] The difference in the results of studies examining the relationship between the severity and mortality of COVID-19 infection and the platelet count may be due to the fact that platelet values are high at the beginning of the disease and low in the later stages. In our study, however, no relationship could be found between the platelet count and survival. When we divided the patients into two groups, those with thrombocytopenia defined as those below 150.000 and those above, according to the platelet count, we see that death was more in patients with a platelet count below 150.000 than the other group.

As another result of our study, increased PLR was found to be associated with increased mortality and prolonged hospital stay. When we look at the literature, the role of PLR in the evaluation of inflammatory processes has been examined, and, similar to our study, increased PLR has been reported as a poor prognosis marker in COVID -19 infection.[9-15]

In a study conducted in patients with sepsis in the years before COVID-19, high MPV and increased PDW were defined as poor prognostic criteria in sepsis.[16] In studies on MPV and mortality in the COVID-19 patient group, increased MPV was found to be associated with increased mortality.[7,17] However, MPV was not found to be associated with mortality in our study. This may be due to the early stage of infection at the time of hospitalization. Although the negative relationship between the length of hospital stay and MPV is statistically significant, it is very weak.

In two studies examining PDW in a small number of patients with COVID-19 patients, increased PDW was associated with increased mortality.[17,18] PDW reflects the change in platelet size.

Table 3. Correlations Related to the Durations of Hospital Stay

	Duration of Hospital Stay	
	r	*P*
[1]WBC (10^3/uL)	0.014	.389
[2]Thrombocyte (/mm^3)	−0.029	.07
[2]Hemoglobin (g/dL)	−0.071	**.000***
[2]PDW (fL)	−0.018	.248
[2]PLCR (%)	−0.028	.077
[2]MPV (fL)	−0.037	**.019***
[1]Lymphocyte (10^3/uL)	−0.128	**.000***
[1]Neutrophil (10^3/uL)	0.046	**.004***
[1]Neutrophil/Lymphocyte	0.11	**.000***
[1]Platelet/Lymphocyte	0.051	**.001***
[1]Fibrinogen (mg/dL)	0.012	.567
[1]D-dimer (ng/mL)	0.113	**.000***
[1]Ferritin (mL/ng)	0.19	**.000***
[1]IL-6 (pg/mL)	−0.008	.845
[1]LDH (U/L)	0.135	**.000***
[1]Urea (mg/dL)	0.182	**.000***
[1]Creatinin (mg/dL)	0.129	**.000***
[1]AST(IU/L)	0.084	**.000***
[1]ALT(IU/L)	−0.008	.631
[1]CRP (mg/L)	0.165	**.000***

[1]Spearman's rho correlation test, [2]Pearson correlation analysis, *$P < .05$ was considered significant. WBC, White Blood Cell; PDW, Platelet Distribution Width; PLCR, Platelet Large Cell Ratio; MPW, mean platelet volume; IL-6, interleukin 6; LDH, lactic dehydrogenase; AST, Aspartate Aminotransferase; ALT, Alanine aminotransferase; CRP, C-Reactive Protein.

PDW increases with increased platelet destruction and the inclusion of newly formed immature platelets into the circulation.[19] In COVID-19 patients, increased PDW pathogenesis may be due to direct platelet activation, bone marrow infection, increased inflammation, and cytokine storm of COVID-19.[20] In our study, a relationship between increased PDW and increased mortality was observed. However, no relationship was found between the duration of hospital stay and PDW.

There is no study in the literature on PLCR in COVID-19 patients yet. Our study is first in this respect.

PLCR expresses an increase in new platelets, larger in size, and is sensitive to changes in platelet size. In a study conducted in a group of patients with sepsis before the COVID-19 pandemic, increased PLCR was associated with poor prognosis.[21] In our study, there is a relationship between increased PLCR and mortality. However, no relationship was found between the duration of hospital stay and PLCR. The limitations of our study are that it is a single-center and retrospective study.

In conclusion, increased PLR, PDW, and PLCR can be safely used as mortality predictor parameters in COVID-19 infection. Increased PLR can be used as an indicator to predict the duration of hospital stay. Identification and awareness of early biomarkers of mortality and duration of hospital stay can facilitate early aggressive treatment, reduce mortality, and improve hospitalization costs.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Prof. Dr. Cemil Taşçıoğlu City Hospital (Date: September 22, 2020 No: 373).

Informed Consent: Informed consent was not required due to the retrospective use of de-identified administrative data.

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