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RESEARCH ARTICLE

Clinical and diagnostic utility of platelet count and its parameters in COVID-19

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Abstract

The majority of the published studies have described the alterations in platelet count and platelet indices in both severe and non-severe Coronavirus Disease 2019 (COVID-19). However, their association with COVID-19 mortality remains unclear. In the present study, our aim is to determine the temporal evolution of platelet count and its parameters between survivors and non-survivors, as well as their potential association with clinical outcomes. This cross-sectional study included 1118 inpatients (≥18 years old) diagnosed as SARS-CoV-2 positive by a Real-Time Polymerase Chain Reaction (RT-PCR) and hospitalized between May 1st, 2020 and November 1st, 2020. Data of complete blood count (CBC) parameters evaluated on different days after admission was gathered and the median value of each CBC parameter was considered for assessing the difference between survivors and non-survivors. There was statistically significant variation between survivors and non-survivors for platelet count [p<0.001, mean difference-80 x 10^9/L], mean platelet volume [p<0.001, mean difference- 0.7 fL], platelet distribution width [p<0.001, mean difference-2.5%] and platelet-lymphocyte ratio [p<0.001, mean difference-123.8]. Thrombocytopenia occurred more commonly in deceased patients compared to survivors. Platelet count, Mean Platelet Volume (MPV) and Platelet Distribution Width (PDW) differed significantly between survivors and non-survivors, revealing distinct trends indicating their importance in the management of COVID-19 patients. These cost-effective parameters can be easily obtained from a CBC.

1. INTRODUCTION

In December 2019, an outbreak of COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) occurred in Wuhan, China, and swiftly spread across the world (1). The first confirmed case of COVID-19 in India was reported on 27th, January 2020, when the patient presented with a one-day history of dry cough and a sore throat (2).

The most common hematological findings in COVID-19 patients include lymphopenia, neutrophilia, and eosinopenia. Mild thrombocytopenia, and less frequently, thrombocytosis are also observed. Additionally, abnormal coagulation parameters and elevated D-dimer levels have been identified in this disease (3-5). Leukocytosis, lymphopenia, and thrombocytopenia are associated with greater severity (6). In a study by Liu et al. (7), COVID-19 patients with thrombocytopenia exhibited a statistically significantly higher mean platelet volume

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(MPV) compared to COVID-19 patients with retained platelet counts. Furthermore, COVID-19 patients were found to have a significantly higher MPV than critically ill non-COVID-19 patients matched for platelet count. The platelet size showed a positive correlation with surface receptor number and ATP content (8). Larger platelets possess a high number of ribosomes and an increased potential for protein synthesis due to their ability to incorporate more amino acids. In comparison to smaller platelets, larger platelets demonstrate an increased hemostatic potential, tend to bind more fibrinogen and exhibit greater phosphorylation levels following thrombin stimulation (9). Another study indicated that in addition to the lung capacity of patients, MPV may serve as an auxiliary test in predicting mortality in COVID-19 patients. While mortality was 8.4 times higher in patients with oxygen saturation under 90% at hospital admission, a 1 unit increase in MPV raised mortality by 1.76 times (10). Lanini et al. (11) demonstrated that increased neutrophil counts, decreased lymphocyte counts, elevated MPV, and anemia with anisocytosis were associated with poor prognosis in COVID-19 patients. An Indian study comparing COVID-19 cases and non-COVID-19 controls found that platelet indices such as platelet count, plateletcrit, MPV, platelet distribution width (PDW), and platelet–large cell ratio (P-LCR) were significantly altered in COVID-19 infection (12). Although many studies have shown that thrombocytopenia occurs more commonly in severe disease, it remains unclear whether platelet count and its parameters are independent predictors of COVID-19 mortality. In the present study, we aimed to determine the temporal evolution of platelet count and its parameters in survivors and non-survivors, and their potential association with patient clinical outcomes. This will enhance our understanding of disease pathogenesis and clinical management, and aid in the development of more precise therapeutic strategies for COVID-19 patients.

2. MATERIALS AND METHODS

2.1. Study Design and Data Collection

In this cross-sectional study, 1118 inpatients (≥18 years old) who tested positive for SARS-CoV-2 nucleic acid by a real-time polymerase chain reaction and were hospitalized at Pondicherry Institute of Medical Sciences, Puducherry, South India, between May 1, 2020 and November 1, 2020 were included. Demographic details, clinical information, and laboratory findings were gathered from medical records and the Hospital Information Software (HIS). Clinical variables included age, gender, medical co-morbidities, COVID-19 severity, length of hospital stay in isolation ward/ICU, and survival status. Complete blood counts and differential count values were recorded from the automated hematology analyzers and the medical records. Results of other pertinent investigations such as C-reactive Protein (CRP) and D-dimer were also collected from medical records and the HIS. Automated hematology analyzers Horiba Pentra DF Nexus / DX Nexus (Horiba Medical, Montpellier, France) were utilized for Complete Blood Count (CBC) during the study period. Coagulation parameters and D-dimer testing were performed using a CS-2400 coagulation analyzer (Sysmex Corporation, Kobe, Japan). Quantitative D–dimer determination was performed using a latex-enhanced immunoturbidimetric assay (Siemens, Marburg, Germany).

The data on CBC parameters, evaluated on different days after hospital admission, was collected. This data included hemoglobin, hematocrit, platelet count, mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit, white blood cell (WBC) count, differential count, absolute basophil count, absolute neutrophil count, absolute lymphocyte count, absolute eosinophil count and absolute monocyte count. Neutrophil-Lymphocyte Ratio (NLR) and Platelet-Lymphocyte Ratio (PLR) were also calculated. For patients with multiple CBC values during their hospital stays, the median value of each CBC parameter was considered for assessing the difference between survivors and non-survivors. The nadir value was utilized for platelet count. Tables 1 and 2 present the disparities between survivors and non-survivors.

2.2. Exclusion Criteria

Patients who were discharged against medical advice during the study period were excluded.

2.3. Statistical Analysis

The clinical and laboratory data were entered into a Microsoft Excel file. Patients were categorized into groups based on the department of hospitalization (ward/ICU) and survival status. Mann-Whitney's test was utilized for statistical analysis of continuous variables that were not normally distributed. Chi-square/Fisher's exact test was conducted to assess the relationship between categorical variables. Univariate and multivariate binary logistic regression analyses were employed to identify the association of platelet parameters with mortality. Variables that were significant at ≤0.1 in simple regression were considered for multiple logistic

regression analysis. A p-value <0.05 was considered statistically significant for all tests. Statistical analysis was carried out using IBM SPSS Statistics for Windows, version 20.0 (IBM Corp., Armonk, NY, USA).

2.4. Trend Analysis

Trend analysis was conducted based on the CBC data obtained throughout the hospital stay for both survivors and non-survivors. The frequency of testing for each individual case depended on the physician's decision. The daily CBC counts of all survivors and non-survivors were included for analysis. Median values of all CBC parameters obtained on various days of admission for all patients (see Figure 1) were calculated and plotted to illustrate the trendline.

2.5. Ethical Considerations

This study was conducted after receiving approval from the Institute Ethics Committee (IEC: RC/2020/82). A waiver of informed consent was granted for the study. Confidentiality of the patient's details was strictly maintained.

3. RESULTS AND DISCUSSION

3.1. Study Characteristics

Of a total of 1118 patients, 781 (69.9%) were males. The median age of all hospitalized COVID-19 patients was 53 years. Among them, 730 (65.3%) had co-morbidities such as hypertension, diabetes, chronic kidney disease, coronary artery disease, cancer, congestive cardiac failure, COPD, tuberculosis and others. Out of the hospitalized patients, 134 patients required ICU admission, and 57 patients died. Among the 134 patients admitted to the ICU, 55 patients did not survive. Additionally, two patients died in the isolation wards. The baseline characteristics are presented in Table 1.

Table 1. The baseline characteristics of COVID-19 patients based on clinical outcomes (deceased vs. survived) and ICU admission status.

Characteristics	All patients (1118)	Clinical Outcome			Admitted to ICU		
		Deceased (57)	Survived (1061)	p-value	No (984)	Yes (134)	p-value
Age (Median, years)	53 42-63	66 59-73	52 42-62	<0.001	52 41-61	65 54-74	<0.001
Male Sex (%)	781	47 (82.5%)	734 (69.2%)	0.033	679 (69.0%)	102 (76.1%)	0.092
Presence of co-morbidities (%)	730	51 (89.5%)	679 (64.0%)	<0.001	609 (61.9%)	121 (90.3%)	<0.001
Diabetes mellitus (%)	563	43 (75.4%)	520 (49.0%)	<0.001	462 (47.0%)	101 (75.4%)	<0.001
Hypertension (%)	437	36 (63.2%)	401 (37.8%)	<0.001	345 (35.1%)	92 (68.7%)	<0.001
Coronary artery disease (%)	88	7 (12.3%)	81 (7.6%)	0.204	60 (6.1%)	28 (20.9%)	<0.001
Chronic kidney disease (%)	29	5 (8.8%)	24 (2.3%)	0.013	15 (1.5%)	14 (10.4%)	<0.001

Platelet count, MPV, plateletcrit, WBC count, NLR, and PLR values were accessible for all hospitalized patients. PDW values were obtainable for 1025 (96.6%) survivors and 56 (98.2%) non-survivors. D-dimer values were available for 896 (84.4%) survivors and 55 (96.5%) non-survivors and CRP for 945 (89.1%) survivors and 54 (94.7%) non-survivors. Similarly, PDW values were obtainable for 132 (98.5%) ICU patients and 949 (96.4%) isolation ward patients. Quantitative D-dimer was evaluated in 122 (91.0%) ICU patients and 829 (84.2%) ward patients. CRP values were accessible for 123 (91.8%) ICU patients and 876 (89.0%) ward patients.

The MPV, plateletcrit, PDW, WBC count, NLR, PLR, D-dimer and CRP values exhibited significant variations between survivors and deceased patients, as depicted in Table 2. The nadir platelet count was categorized as ≤50 x 10^9/L, 51-100 x 10^9/L, 101-150 x 10^9/L and ≥151 x 10^9/L in both survivors and non-survivors (refer to Table 3). The observed variation was statistically significant (p-value <0.001), with thrombocytopenia being more prevalent in deceased patients compared to survivors.

The association between platelet parameters and mortality was estimated by binary logistic regression. In comparison to males, female patients had a relative risk (RR) of 0.47 [95% confidence interval (CI) of 0.15-1.44]. Platelet counts of 101-150 x 10^9/L and ≤100 x 10^9/L, relative to platelet counts of ≥151 x 10^9/L (used as the reference), demonstrated RRs of 2.88 (95% CI of 0.87-9.55) and 31.91 (95% CI of 7.45-136.62), respectively. Table 4 presented the RR and 95% CI of MPV, PDW, WBC count, NLR, and PLR.

Table 2. Laboratory parameters of COVID-19 patients based on clinical outcomes (survivors vs. deceased) and ICU admission status (non-ICU vs. ICU patients)

Parameter	Clinical Outcome			Non-ICU Patients (n = 984)	ICU Patients (n = 134)	p-value
	Survivors (n = 1061)	Deceased (n = 57)	p-value			
Platelet count (x 10^9/L)	236 191-300	156 89-248	<0.001	237 192-301	192 133-274	<0.001
Mean Platelet Volume (fL)	8.3 7.7-8.8	9.0 8.3-9.6	<0.001	8.2 7.7-8.8	8.8 8.1-9.5	<0.001
Plateletcrit (L/L)	0.204 0.167-0.250	0.199 0.158-0.272	0.928	0.203 0.166-0.247	0.220 0.170-0.293	0.005
Platelet distribution width (%)	14.4 13.0-16.3	16.9 15.0-19.0	<0.001	14.3 13.0-16.0	16.1 14.0-18.0	<0.001
WBC count (x 10^9/L)	5.9 4.7-7.8	12.9 10.4-17.3	<0.001	5.8 4.6-7.5	10.9 8.2-14.0	<0.001
Neutrophil-lymphocyte ratio	2.7 1.7-4.6	15.7 10.3-21.0	<0.001	2.5 1.7-4.1	9.4 6.6-15.5	<0.001
Platelet-lymphocyte ratio	178.7 132.4-259.2	302.5 212.4-462.3	<0.001	173.8 129.7-244.5	292.6 217.7-410.9	<0.001
D-Dimer (µg/L)	0.40 0.24-0.75	1.98 1.00-6.55	<0.001	0.38 0.24-0.65	1.62 0.79-3.79	<0.001
C-reactive protein (mg/L)	12.0 6.0-27.5	48.0 24.0-96.0	<0.001	10.3 6.0-24.0	36.0 21.5-74.0	<0.001

Abbreviations: WBC, white blood cell. Note: Data expressed as Median (Interquartile range)

Table 3. Nadir platelet counts in survivors and deceased patients

Nadir Platelet Count (x 10^9/L)	Survivors (n = 1061)	Deceased (n = 57)	All patients (n = 1118)
≥151	961 90.6%	29 50.9%	990 88.6%
101-150	83 7.8%	11 19.3%	94 8.4%
51-100	13 1.2%	10 17.5%	23 2.1%
≤50	4 0.4%	7 12.3%	11 1.0%

Table 4. The association between various platelet parameters and mortality (estimated by binary logistic regression) among COVID-19 patients

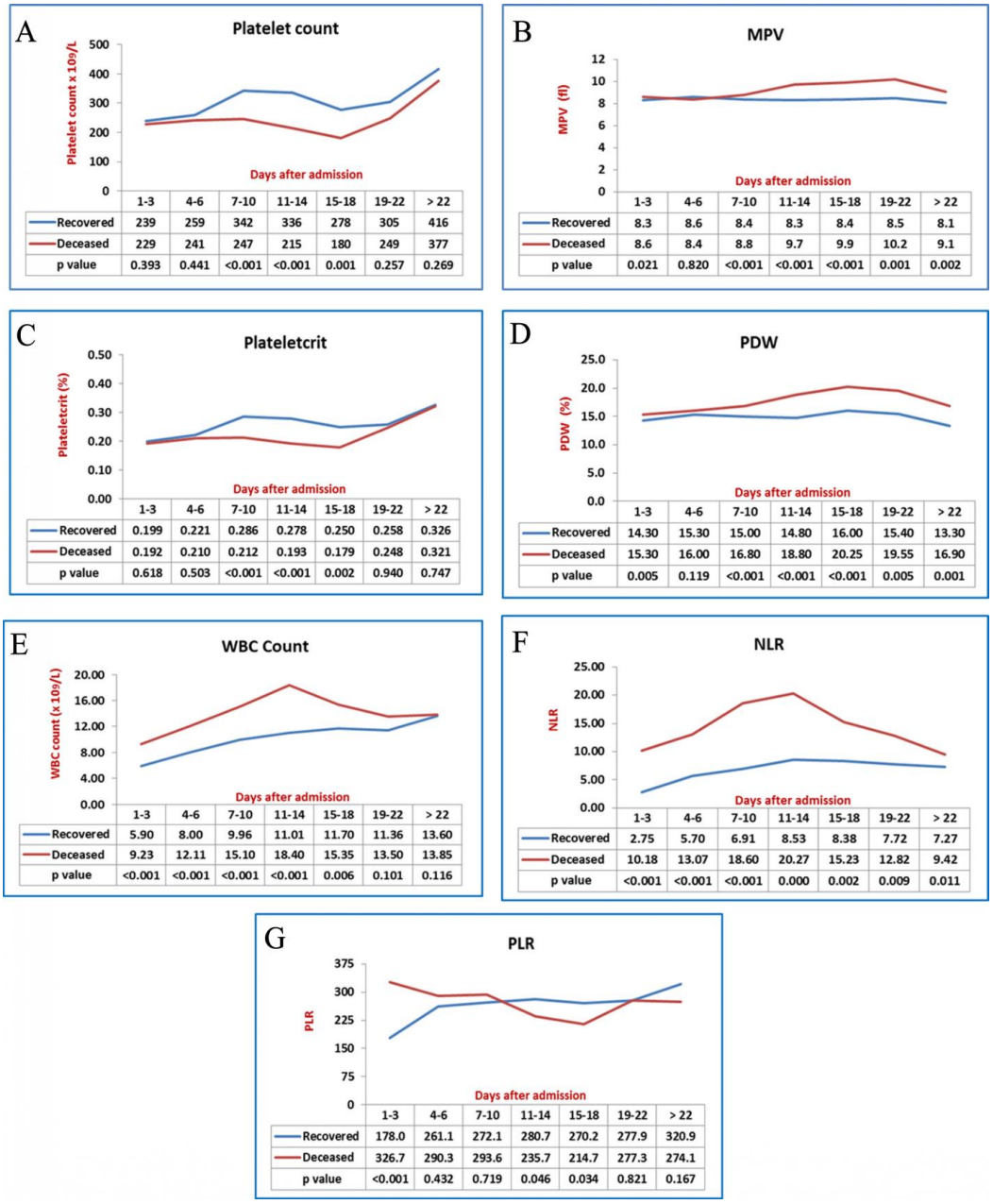
Variable	Univariate			Multivariate		
	RR	95% CI	p-value	RR	95% CI	p-value
Age	1.08	1.05-1.10	< 0.001	1.02	0.98-1.06	0.303
Sex (Female)	0.48	0.24-0.96	0.037	0.47	0.15-1.44	0.185
Comorbidities	4.78	2.03-11.25	< 0.001	4.40	0.83-23.39	0.082
Platelet count ≥151 x 10^9/L	1.00			1.00		
Platelet count 101-150 x 10^9/L	4.39	2.12-9.11	< 0.001	2.88	0.87-9.55	0.084
Platelet count ≤100 x 10^9/L	33.14	15.39-71.36	< 0.001	31.91	7.45-136.62	< 0.001
MPV > 8.8 fL	2.55	1.48-4.38	0.001	1.09	0.33-3.64	0.888
PDW > 15%	5.11	2.76-9.49	< 0.001	0.77	0.20-2.94	0.705
WBC count x 10^9/L	1.49	1.38-1.60	< 0.001	1.14	1.00-1.29	0.043
Neutrophil-Lymphocyte ratio	1.42	1.34-1.51	< 0.001	1.35	1.18-1.55	< 0.001
Platelet-Lymphocyte ratio	1.00	1.00-1.01	< 0.001	1.00	0.99-1.00	0.337

Abbreviations: RR, Relative Risk; CI, Confidence Interval; MPV, Mean Platelet Volume; PDW, Platelet Distribution Width; WBC, White Blood Cell.

3.2. Analysis of Changes In Platelet and Hematological Parameters Over A Period of Several Days After Admission

The data of CBC parameters evaluated on different days after hospital admission was analyzed to understand the trend (refer to Figure 1). Median values of the CBC parameters were calculated for both survivors and non-survivors. Graphs were plotted with median values of the hematological parameters of each group on the vertical axis and days after admission on the horizontal axis.

For the first three days of admission, there were 1206 CBCs available for survivors and 91 CBCs available for non-survivors. The median values of platelet parameters, WBC, PLR, and NLR of all the 1206 CBCs for survivors and 91 CBCs for non-survivors were calculated and plotted for the 1-3-day period post-admission. The number of CBCs included in subsequent time periods were as follows: the 4-6 days, 7-10 days, 11-14 days, 15-18 days, 19-22 days, and > 22 days time periods were 206, 184, 80, 42, 30, and 59 for survivors and 58, 77, 67, 46, 14 and 12 for non-survivors respectively.



A	1-3	4-6	7-10	11-14	15-18	19-22	> 22
Recovered	239	259	342	336	278	305	416
Deceased	229	241	247	215	180	249	377
p value	0.393	0.441	<0.001	<0.001	0.001	0.257	0.269

B	1-3	4-6	7-10	11-14	15-18	19-22	> 22
Recovered	8.3	8.6	8.4	8.3	8.4	8.5	8.1
Deceased	8.6	8.4	8.8	9.7	9.9	10.2	9.1
p value	0.021	0.820	<0.001	<0.001	<0.001	0.001	0.002

C	1-3	4-6	7-10	11-14	15-18	19-22	> 22
Recovered	0.199	0.221	0.286	0.278	0.250	0.258	0.326
Deceased	0.192	0.210	0.212	0.193	0.179	0.248	0.321
p value	0.618	0.503	<0.001	<0.001	0.002	0.940	0.747

D	1-3	4-6	7-10	11-14	15-18	19-22	> 22
Recovered	14.30	15.30	15.00	14.80	16.00	15.40	13.30
Deceased	15.30	16.00	16.80	18.80	20.25	19.55	16.90
p value	0.005	0.119	<0.001	<0.001	<0.001	0.005	0.001

E	1-3	4-6	7-10	11-14	15-18	19-22	> 22
Recovered	5.90	8.00	9.96	11.01	11.70	11.36	13.60
Deceased	9.23	12.11	15.10	18.40	15.35	13.50	13.85
p value	<0.001	<0.001	<0.001	<0.001	0.006	0.101	0.116

F	1-3	4-6	7-10	11-14	15-18	19-22	> 22
Recovered	2.75	5.70	6.91	8.53	8.38	7.72	7.27
Deceased	10.18	13.07	18.60	20.27	15.23	12.82	9.42
p value	<0.001	<0.001	<0.001	0.000	0.002	0.009	0.011

G	1-3	4-6	7-10	11-14	15-18	19-22	> 22
Recovered	178.0	261.1	272.1	280.7	270.2	277.9	320.9
Deceased	326.7	290.3	293.6	235.7	214.7	277.3	274.1
p value	<0.001	0.432	0.719	0.046	0.034	0.821	0.167

Figure 1. The sequential changes in platelet indices among 1118 COVID-19 patients after admission. The median count of platelet count (A), mean platelet volume (B), plateletcrit (C), platelet distribution width (D), white blood cell count (E), neutrophil-lymphocyte ratio (F) and platelet-lymphocyte ratio (G) in a period of time were used for tabulation.

In the first 6 days, the platelet counts among non-survivors were slightly lower than those of survivors. However, as time progressed, the platelet counts of the deceased patients decreased significantly compared to those of the survivors. During the initial 6 days of admission, MPV values were similar in both survivors and non-survivors. However, after this period, MPV progressively increased and notably surpassed levels observed in survivors. PDW followed a similar trend to MPV. The trend in the plateletcrit values also mirrored that of platelet count.

Non-survivors exhibited higher WBC counts compared to survivors, with the WBC counts of survivors remaining within the reference interval, while those of the non-survivors were substantially elevated. NLR also followed a similar trend. Initially, PLR was higher in deceased patients compared to the survivors, but it showed a progressive decline after 10 days.

Automated hematology analyzers can rapidly measure platelet count and its indices in blood as part of a CBC. Platelet indices such as MPV, plateletcrit, platelet large cell ratio, and PDW are markers of platelet activation. They are also associated with platelet morphology and proliferation kinetics. Systematic reviews have highlighted that platelet indices offer clinical and practical advantages in emergency settings (13). Additionally, platelet indices have been found to be elevated in patients with conditions such as diabetes mellitus, myocardial infarction, malignancies, and surgical conditions including acute appendicitis, cholecystitis, and acute mesenteric ischemia (14).

The median value of platelet count (nadir platelet count) amongst survivors and non-survivors in our study was 236 x 10^9/L and 156 x 10^9/L respectively, which is comparable to findings in other similar studies (10,15,16). Platelet count below 100 x 10^9/L was observed in 29.8% of non-survivors, while among survivors, it was only 1.6%. Yang et al. (17) also demonstrated that thrombocytopenia was more likely to occur in non-survivors than in survivors. Similarly, Liu et al. (7) observed an increasing trend in platelet count among survivors.

Temporal analysis revealed that platelet counts at the time of admission were slightly lower amongst non-survivors compared to survivors. A progressive decrease in platelet count was observed after 6 days among non-survivors. The lowest platelet count in non-survivors was observed between days 15 to 18 since admission. In survivors, the lowest platelet counts were also observed at the time of admission, followed by a subsequent increasing trend. However, a dip was noted between days 15 to 18 since admission. Thereafter, an increasing trend was observed until discharge. Yang et al. (17) also demonstrated an increasing trend in platelet count among survivors and a progressive decrease in platelet count for non-survivors, with the nadir platelet count occurring between days 15 to 20 since admission. Interestingly, the timeline charts revealed a dip in the platelet count between 16-18 days in survivors, following which the platelet levels increased.

The study by Lanini et al. (11) demonstrated that platelet counts irreversibly declined during the second week of the disease in non-survivors. Among survivors, platelet counts peaked on day 19 and eventually remained steady.

In the study conducted by Yang et al. (17), it was shown that mortality decreased with increasing platelet counts. Using >150 x 10^9/L as the reference, the RR for patients with nadir platelet counts of 100 - 150 x 10^9/L, 50 - 100 x 10^9/L and 0 - 50 x 10^9/L were 3.42, 9.99 and 13.68 respectively. In our study, the RR for patients with nadir platelet counts of 101 - 150 x 10^9/L and 0 - 100 x 10^9/L was 2.88 and 31.91, respectively, compared to the reference platelet count of ≥151 x 10^9/L.

Platelet count emerges as an independent risk factor for mortality, with its dynamic changes closely intertwined with mortality rate (7). Our data also further supports the notion that platelet count serves as an independent risk factor for COVID-19 mortality, emphasizing the significance of monitoring declining platelet counts (18).

In our study, MPV was notably higher in non-survivors and those requiring ICU admission (Table 1). These findings align with similar studies (15,16). Timeline charts depict a progressive elevation in MPV among non-survivors compared to survivors. The study by Lanini et al. (11) also disclosed a steady rise in MPV among non-survivors, contrasting with a tendency toward normalization over time in survivors. In a study by Ouyang et al. (16) focusing on COVID-19 non-survivors, the MPV measured 10.01 fL in the initial test and 11.11 fL in the final test. The elevated MPV possibly stems from the heightened circulation of immature platelets, representing a response by megakaryocytes to platelet consumption (8).

PDW showed a significant difference between non-survivors (16.9%) and survivors (14.4%). In the study conducted by Güçlü et al. (10), the mean PDW was higher in non-survivors (18.63 ± 1.56%) compared to survivors (17.89 ± 1.55%). Similarly, Bommenahalli et al. (19) also observed higher mean PDW in non-survivors. PDW serves as a measure of platelet anisocytosis, with increased PDW attributed to elevated circulation of immature platelets following platelet destruction.

However, in our analysis, MPV, PDW, and plateletcrit were not independently associated with COVID-19 mortality, as indicated in Table 4. Contrary to this, the retrospective cohort study by Liu et al. (7) identified platelet count and plateletcrit as independent risk factors for mortality in COVID-19 patients. MPV and PDW were not found to be independently associated with COVID-19 mortality in their study (7), consistent with our study.

It is intriguing to observe the temporal changes in platelet count and its indices, as these changes may aid in identifying patients requiring ICU admission and those at high risk of mortality (20). Platelets serve a vital role in both physiological hemostasis and pathological thrombosis. Alterations in platelet levels could reflect underlying pathological changes in the lung. Notably, lung involvement becomes more extensive in the later phases of the disease. As the disease progresses, the frequencies of consolidation and crazy paving patterns tend to rise, whereas the frequencies of ground-glass opacifications and ground-glass opacifications with consolidations decrease (20).

Platelets continuously circulate through the lungs, contributing to pulmonary vascular reactivity, repair, and remodeling. They also play a key role in maintaining pulmonary defenses and integrity and act as effectors of injury in lung diseases. Evidence suggests that the lungs serve as sites of thrombopoiesis and act as reservoirs for platelets (21). Therefore, a progressive decrease in platelet counts may indicate a worsening thrombotic state, warranting close clinical attention.

The mechanism by which SARS-CoV-2 induces thrombocytopenia is not fully elucidated. However, it is known that SARS-CoV-2 can trigger a low-grade disseminated intravascular coagulopathy (DIC) state, leading to increased platelet consumption within the damaged lungs. Moreover, normal hematopoiesis may be impaired by SARS-CoV-2 through its binding to CD13 and/or CD66a of hematopoietic cells and bone marrow stromal cells, resulting in immune-mediated stem cell damage (7). Additionally, megakaryocyte suppression can occur due to systemic inflammation or cytokine storm associated with COVID-19. Furthermore, the formation of platelet autoantibodies followed by platelet clearance may also contribute to thrombocytopenia (8).

Platelet changes may indeed be influenced by medical co-morbidities such as hypertension and diabetes, particularly in individuals prone to microvascular and macrovascular complications (9,14). However, the multivariate analysis conducted in our study reveals that platelet changes serve as independent predictors of mortality, even after adjusting for age, sex and comorbidities.

The WBC count was significantly higher in non-survivors compared to survivors; a trend that was also observed among COVID-19 patients admitted to ICU. Our statistical analysis indicated that the elevated WBC count is primarily due to an increase in neutrophils and their precursors. Consistently, a previous study found that WBC counts in both the initial and final tests were higher in non-survivors compared to the survivors (16). Similarly, Güçlü et al. (10) reported a higher mean WBC count in non-survivors.

Studies have consistently demonstrated that a higher NLR is associated with severe COVID-19 cases compared to milder ones (22-24). In our study, non-survivors exhibited markedly elevated NLR compared to survivors, with patients requiring ICU admission also presenting with a higher median NLR. These findings align with similar studies conducted in China, where higher NLR values were reported in non-survivors (25,26). Therefore, NLR emerged as an easily accessible and cost-effective biomarker for assessing prognosis in COVID-19 patients.

The elevated NLR results from an increase in neutrophils and a decrease in lymphocyte counts, signifying an imbalanced inflammatory response. Inflammatory factors can stimulate neutrophil production and accelerate the apoptosis of lymphocytes, ultimately leading to lowered cellular immunity (27). Throughout the follow-up period in our study, NLR remained consistently higher in non-survivors compared to survivors.

Temporal analysis conducted by Lanini et al. (11) revealed that survivors and non-survivors initially presented with similar neutrophil counts at the onset of symptoms. However, in survivors, neutrophil count remained within the normal range throughout the follow-up period, whereas, in non-survivors, there was a sharp increase in neutrophil counts, significantly differing from those of survivors by day 6 after symptom onset. Additionally, average lymphocyte counts were significantly lower in non-survivors compared to survivors since the first day of symptom onset (11).

Indeed, PLR serves as another cost-effective independent prognostic biomarker that aids in distinguishing between severe and non-severe COVID-19 patients (24). In a study by Yang AP et al. (27), the binary logistic analysis revealed that elevated NLR (hazard risk 2.46, 95% CI 1.98–4.57) emerged as an independent factor for poor clinical outcomes of COVID-19. NLR retained significance even after adjusted for age and gender. However, PLR did not emerge as an independent risk factor, consistent with the findings of our study. While PLR could predict disease severity, it was not able to predict mortality in the study by Wang et al. (28).

Nevertheless, it is important to acknowledge the limitations of this study. It is a single-center study, and further research is warranted to validate our findings in larger, multicenter cohorts. Additionally, the pathophysiological mechanisms underlying these hematological alterations remain incompletely understood, highlighting the need for continued investigation in this area.

4. CONCLUSIONS

The monitoring of platelet count and other platelet parameters is crucial in the management of COVID-19 patients. Our study found significant differences in platelet count, MPV, and PDW between survivors and non-survivors, with distinct trends observed throughout the course of admission. These cost-effective parameters can be easily obtained from a CBC. The temporal evolution of platelet count and its indices holds promise in predicting the clinical course and mortality in COVID-19 patients. Importantly, our findings highlight thrombocytopenia as an independent risk factor for COVID-19 mortality. However, further research is imperative to fully understand the relationship between platelet alterations and COVID-19 complications.

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