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Understanding the Significance of Thrombocytopenia in COVID-19 Patients: A Comparative Analysis with Normal Platelet Counts

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A B S T R A C T

Background: Thrombocytopenia, characterized by abnormally low platelet counts, has emerged as a significant hematological manifestation in COVID-19 patients, raising concerns due to its potential implications on disease severity and prognosis.

Objective: The aim of the study is to study thrombocytopenia as a prognostic factor in positively detected COVID-19 patients and to investigate its relationship with the patient's hospital length of stay and the prognosis.

Methodology: About 50 patients were involved in this study from January 2022 to June 2022. Complete blood count was done, on the intervals of Day 8, 16 and 24. Follow-up was done regarding the mortality and their stay in the hospital. Ten patients were detected to be thrombocytopenic; their hospital stay duration was significantly higher. A high statistically significant difference was found among the thrombocytopenic patient's group and the group with the normal values of platelet counts. It was concluded that there is an association between the hospital stay duration of patients, poor prognosis with thrombocytopenia, in Covid-19 patients.

Results: In this study of 50 patients (mean age 45.13 ± 16.78), 48.0% were male and 52.0% were female. Total leukocyte count (TLC) dropped significantly over time (P=0.001): 6.93 ± 3.99 upon admission, 6.39 ± 3.43 on day 8, 6.21 ± 3.003 on day 16, and 4.211 ± 1.4123 on day 24. Hemoglobin levels also dropped significantly (P=0.001): 11.89 ± 1.99 upon admission, 10.96 ± 1.79 on day 8, 10.86 ± 1.57 on day 16, and 9.624 ± 0.7456 on day 24. A significant difference (P<0.001) was observed between groups with normal platelet counts and thrombocytopenic counts regarding outcomes.

Conclusion: Platelet count measurements on days 8, 16, and 24 after admission are valuable predictors of severity in moderate COVID-19 cases. Thrombocytopenia in moderate cases is associated with longer hospital stays (all thrombocytopenic patients waited 26 days for a measurement).

Keywords: Platelet Counts; COVID-19; Thrombocytopenia

Introduction

The outbreak of the novel coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has led to a global health crisis with far-reaching implications across medical disciplines. While respiratory complications dominate the clinical landscape of COVID-19, accumulating evidence has highlighted the intricate interplay between the virus and the hematological system, particularly concerning thrombocytopenia, a condition characterized by abnormally low platelet counts. Thrombocytopenia, often observed in critically ill patients, has emerged as a significant hematological manifestation in COVID-19, prompting intensive investigation into its clinical implications, underlying mechanisms, and prognostic significance.[1,2] COVID-19 is expected to incubate for up to 14 days.[3] Runny nose, cough, headaches, dyspnea, sore throat, exhaustion, and new loss of taste or smell are all symptoms of the COVID-19 virus.[2] Some COVID-19 individuals may have and lower respiratory tract symptoms, gastrointestinal symptoms such vomiting, nausea, or diarrhea before to developing a fever.[4]

The pathophysiology of thrombocytopenia in the context of COVID-19 remains multifactorial and com-plex, reflecting the intricate interplay between viral infection, host immune response, and systemic inflammation. Several hypotheses have been proposed to elucidate the mechanisms underlying thrombocyt-openia in COVID-19, including direct viral-induced bone marrow suppression, immune-mediated destruction of platelets, endothelial dysfunction, and dysregulation of the coagulation cascade. However, the precise etiology of thrombocytopenia in COVID-19 is still under investigation, underscoring the need for further research to unravel the intricate molecular pathways involved.

Thrombocytopenia is associated with worse COVID-19 outcomes, with a prevalence of 5–41%.[2] When it comes to COVID-19 patients, thrombocytopenia is less common than lymphopenia. Less than 5% to roughly 53.6% of cases of thrombocytopenia were recorded.[5] It is possible that monitoring platelets during a patient's hospital stay can aid in prognosis prediction due to the correlation observed between a rise in platelet count and a reduction in mortality.[6] Thrombocytopenia is assoc-iated with a higher risk of serious illness and death and may serve as a marker for the onset of the disease in COVID-19 patients.[7]

Despite the evolving understanding of thrombocytopenia in COVID-19, its clinical significance and implications on disease severity and prognosis remain a subject of debate and ongoing investigation. Emerging evidence suggests that thrombocytopenia may serve as a biomarker of disease severity and mortality risk in COVID-19 patients, with several studies reporting an association between lower platelet counts and adverse clinical outcomes, including increased risk of thrombotic events, acute respiratory distress syndrome (ARDS), multi-organ failure, and death. Furthermore, thromboc-ytopenia in COVID-19 has been linked to a dysregulated immune response, cytokine storm, and endothelial dysfunction, contributing to the systemic inflammatory cascade and microvascular thrombosis observed in severe cases.[8]

Given the potential implications of thrombocytopenia on disease progression and clinical outcomes, comprehensive hematological monitoring and early identification of thrombocytopenia in COVID-19 patients are paramount for risk stratification, prognostication, and timely intervention. However, the optimal management strategies for thrombocytopenia in COVID-19 remain a subject of ongoing investigation, with limited consensus on the efficacy of specific therapeutic interventions, including platelet transfusions, immunomodulatory agents, and anticoagulant therapy.

So, the present study was planned with the aims to contribute to the growing body of knowledge surrounding hematological complications in COVID-19 and pave the way for future research endeavors aimed at improving clinical outcomes and mitigating the burden of disease.

Objective

The aim of the study is to study thrombocytopenia as a prognostic factor in positively detected COVID-19 patients and to investigate its relationship with the patient's hospital length of stay and the prognosis.

Methodology

A prospective observational study was conducted at Department of Medicine, Lady Reading Hospital, Peshawar, Pakistan from January 2022 to June 2022 participated in this study. All COVID positive cases verified by positive SARSCoV-2 PCR results, radiological features, and clinical histories were included in this study. Strong exclusive criteria were also followed for this study which told that any such patient in which any congenital or acquired cause of thrombocytopenia (e.g., drug-induced immune thrombocytopenic purpura), cirrhosis of the liver and any previous affection in the bone marrow were found were not enrolled in this study. Following these inclusive and exclusive criteria, a total of Fifty patients were included in this study.

All study cases after initial screening were also screened for Complete blood counts (CBCs) (require ward admission, SpO2 ≥ 92%) at time of admission. At the time of admission, all patients had normal platelet counts (above 150); individuals with abnormal counts were excluded. A complete blood count (CBC) was done on

Table 1. Finding of Laboratory in Covid-19 patients

Parameters	On admission	After 8 days	At 16 days	At 24 days	P-value
TLC (mean ± SD)	6.93 ± 3.99	6.39 ± 3.43	6.21 ± 3.003	4.211 ± 1.4123	<0.001
Hb (mean ± SD)	11.89 ± 1.99	10.96 ± 1.79	10.86 ± 1.57	9.624 ± 0.7456	<0.001
Platelets (mean ± SD)	236.69 ± 89.27	227.57 ± 98.12	220.67 ± 119.45	167.43 ± 89.78	<0.001

patients who left the hospital before the 14 or 21-day mark, and on days 7, 14, and 21 after admission. Divided into four groups based on platelet counts: 0–50, 50–100, 100–150, and more than 150.

The duration of hospital stay and the death rate were noted. We kept track of how many patients recovered (no longer requiring hospital admission) and being sent home, deteriorated, needing to be sent to the intensive care unit and died.

All data were entered into the specialized designed excel sheet, and after completion were transferred into SPSS version 25.0 for analysis purposes. The mean, standard deviation, and range were used for numerical data (parametric distribution); the median and interquartile range are used for nonparametric data. Percentage and frequency of non-numerical data was determined.

Prior to the commencement of this study, approval was obtained from the Institutional Ethical Committee (IEC), Lady Reading Hospital Peshawar in accordance with ethical guidelines and regulations governing research involving human participants.

Results

A total of 50 patients were included in this study with the age range of 22 - 80 years (mean ± SD = 45.13 ± 16.78). Among the study cases 48.0% were male and 52.0% were female patients. Table 1 shows that the hospital stay ranged from 14 to 24 days, with a mean ± SD of 16.13 ± 2.10 days.

With a P value of 0.001, that the level of total leukocyte count (TLC) had dropped statistically considerably. The mean concentration (SD) was 6.93 ± 3.99 upon admission, 6.39 ± 3.43 on day 8, 6.21 ± 3.003 on day 16, and 4.211 ± 1.4123 on day 24. The level of hemoglobin dropped statistically considerably (P-value = 0.001). The mean concentration (SD) was 11.89 ± 1.99 upon admission, 10.96 ± 1.79 on day 8, 10.86 ± 1.57 on day 16, and 9.624 ± 0.7456 on day 24.

Furthermore, a statistically significant decrease in platelet counts (P<0.001) was found. Table 2 shows the mean platelet concentration ± SD upon admission (236.69 ± 89.27), on day 8, 227.57 ± 98.12 on day 16, and on day 24 was 167.43 ± 89.78.

On the day of admission, all patients had normal platelet counts (above 150); those with abnormal counts were not included.

On day 8, 11 (22%) of the individuals had lower platelet levels. Three (6%) of them had moderate thrombocytopenia, two (4%) had severe thrombocytopenia, and six (12%) had mild thrombocytopenia. Fourteen individuals, or seventy percent, had lower platelet counts on day sixteen. Of these, four patients (8%), seven patients (14%), and four patients (8%), all had mild thrombocytopenia, moderate thrombocytopenia, and severe thrombocytopenia. Five (10%) of the individuals had lower platelet counts at day 24. Two (4%) of them had moderate thrombocytopenia, two (4%) had severe thrombocytopenia, and one (2%) had mild thrombocytopenia.

Table 3 indicates that 29 patients (or 72% of the normal platelets group) had full recovery, meaning they could be discharged home or stay in the hospital no longer.

Three of the patients passed away, while eight of them had deterioration and required ICU hospitalization. Among thrombocytopenic patients, two patients passed away, six showed worsening, and two showed full recovery. Regarding the outcome, a significant statistical difference (P<0.001) was found between the groups with normal values of platelet counts and those with thrombocytopenic counts.

Table 4 displays the progression of six patients with moderate thrombocytopenia, the death of two patients with thrombocytopenia (severe), and the complete recovery of two patients with mild thrombocytopenia.

Tables 5 and 6 demonstrate that the thrombocytopenic group had a considerably longer hospital stay (P<0.001) than the normal platelets group.

Nineteen patients were anemic, fourteen were leukopenic, and eighteen were thrombocytopenic on day 18.

Discussion

The coronavirus 2 (SARS-CoV-2) discovery has caused grave worries worldwide. On February 11, 2020, the WHO had recognized formally SARS-CoV2-induced illnesses as COVID-19.[9] A common side effect of viral diseases is thrombocytopenia. It was observed that Thrombo-

Table 2. Platelet counts in among study cases

Days	N (%)
At Day 8	
Normal Platelets	9 (78.0)
Thrombocytopenia	
Mild (100-150)	6 (12.0)
Moderate (50-100	3 (6.0)
Severe (<50)	2 (4.0)
At Day 16	
Normal Platelets	35 (70.0)
Thrombocytopenia	
Mild (100-150)	4 (8.0)
Moderate (50-100	7 (14.0)
Severe (<50)	4 (8.0)
At Day 24	
Normal Platelets	45 (90.0)
Thrombocytopenia	
Mild (100-150)	1 (2.0)
Moderate (50-100	2 (4.0)
Severe (<50)	2 (4.0)

cytopenia was experienced in 41% of COVID-19 patients.[2] Possible mechanisms of coronavirus-induced thrombocytopenia include aberrant bone marrow microenvironment, attacks on hematopoietic stem cells and cellular immunity and cytokine storm, decreased thrombopoietin production, increased platelet consumption lung damage, and drug-induced thrombocytopenia.[8]

The present study was in line with some other studies which were presented the same results like the present study. According to a study conducted by Zhao and colleagues on 532 patients (246 men and 286 women), poor vision in COVID-19 patients was associated with a decrease in the early calculated platelet count (mean ± SD = 51.19 ± 15.68). The mean age of the death group was 64.7 ± 13.1 years, which was older than the mean age of the survival group (48.2 ± 14.4 years, P = 0.001). The diagnosis of covid-19 was confirmed based on medical history, radiological findings and positive COVID-19 PCR. All patients had CBC within normal limits at admission and at baseline, 16 days, and 24 days later. The age of the patients in this study ranged from 22 to 80 years and the sex ratio was 1.[10] Whereas in the present study, 50 patients participated (mean ± SD = 45.13 ± 16.78), the mean ± SD platelet count of the participants decreased on the intervals of day 8; 227.57 ± 98.12, day 16; 220.67 ± 119.45 and day 24; 167.43 ± 89.78 (P <0.001). Among the ten participants, with thrombocy-

Table 3. Disparity in the results between the thrombocytopenic and normal platelet count groups

Outcome	Platelet Count		P-value
	Normal platelet count (N = 40)	Thrombocytopenia (N = 10)	
Complete recovery	29	2	<0.001
Deterioration (need ICU admission)	8	6	<0.001
Death	3	2	<0.001

topenia, two participants passed away and three participants passed away with normal platelet count.

In another study on COVID patients, Bao et al. discovered that COVID-19-induced thrombocytopenia was a critical biomarker associated with reduced capability of coagulation, increased incidence of blood clots and mortality.[11] Similarly, Yang and colleagues recruited 1476 individuals with confirmed COVID-19, 0f which 776 men and 700 were women. This study revealed that the non-survivors were older and more likely to be male (65.5 vs. 50.0%, P<0.001) than the survivors, with a median age of 57 (47–67) years.[12]

Kaur et al.[13] studied the morphologic alterations in the circulating platelets of COVID patients. Twenty hospitalized patients, 13 of whom were male and 7 of whom were female, with an average age of 65, were included in the study. According to a recent study by Qu and colleagues, partners, the proportion of platelet to lymphocyte is associated with the patient's visualization that are detected positive with COVID illness. Thirteen individuals total—sixteen men and fourteen women—age arranging from 36–65 years, participated in the study. Researchers discovered that patients in the severe group were older, with the average age difference between the two groups being 60 versus 49 years.[14] In our case, a significantly statistical difference was found between the groups with the platelet normal count group and the thrombocytopenia group. The patients suffering with severe thrombocytopenia were more prone to death than the mild ones (P = <0.001).

According to Castro et al.,[15] conducted a study involving laboratory findings and mortality among individuals hospitalized and positive with COVID-19 in the region of eastern Massachusetts, the retrospective cohort analysis included 2511 hospitalized patients, of whom 50.9% were male and 53.9% were female. Guçlu et al. investigated the impact of COVID-19 on platelet count and related indicators in 215 COVID-19 patients, whose mean age was 64.32 ± 16.07 years. The review population consisted of 125 males and 95 females, with a greater age difference between the non-survivor and survivor patients.[16]

32.6% of patients in Bao et al.[11] People in this study had high blood pressure, 17.4% were diabetic, 5.6% found to have heart disease, patients with hepatitis B 3.4%, 6.2% with chronic lung disease, 1.7% had cerebrovascular disease, renal disease about 1.7% and 1.1% had chronic kidney disease. There is cancer. According to the results

Table 4. Disparity in the outcome between groups with normal platelet counts and those with severe thrombocytopenic groupings

Outcome	Platelet Count				P-value
	Normal platelet count (N = 40)	Thrombocytopenia (N = 10)			
		Mild	Moderate	Severe	
Complete recovery	29	2	0	0	<0.001
Deterioration (need ICU admission)	8	0	6	0	<0.001
Death	3	0	0	2	<0.001

Table 5. Relationship between hospital stay length and platelet count

Hospital Stay	Platelet Count		P-value
	Normal platelet count (N = 40)	Thrombocytopenia (N = 10)	
Mean	15.67	23.00	<0.001
Standard Deviation	3.12	0.0	<0.001

of the study, on the 18th day after admission, anemia developed in five patients, leukopenia in 14 patients, and thrombocytopenia in 18 patients. Twenty patients were enrolled, 13 of whom required intensive care unit admission. When they compared their results with those of Kaur and colleagues, they found that 65% of patients had diabetes, the most common hematological abnormality, followed by neutrophilia and lymphopenia (no indication of date of occurrence). The platelet count is also normal in most patients. Compared with this study, the sample size is large there times as with our study, so the results are inconsistent.[13] According to our study, 19 patients were anemic, eighteen were thrombocytopenic on day 18 and fourteen were leukopenic.

According to Qu et al.,[14] the mean peak platelet value of severe patients over the entire course of treatment was 386 x 109/l, which was 301 x 109/l higher than that of non-severe patients. Guclu et al.[16] reported that 54 patients had thrombocytopenia on the admission day and 52 patients had thrombocytopenia on the observation third day (2020), which is compatible with the results of our study. According to Zhu et al.,[17] 126 patients did not have thrombocytopenia and 41 patients had thrombocytopenia on the day of admission. All patients in our study had normal platelet counts (below 150) on the admission day at the hospital, and those with values that are not normal, were excluded from the study.

The results of our study showed that the length of stay for each patient was 16.13 ± 2.10 days for patients with normal counts of platelets to 24 days for patients with low counts of platelets. This is consistent with a study by Zhao and colleagues that found that platelet counts on days 5 and 6 and days 14 and 15 for the first stage of platelet count loss were associated with death in a cohort of COVID-19 patients. Similar to our findings, Bao and colleagues found that the counts of platelets were lower in patients with severe disease than those having comparatively less severe disease. These results confirmed those of Yang and colleagues, who found that thrombocytopenia was less common in non-survivors. Qu and colleagues reported that platelets in critically ill patients increased significantly during treatment, initially increasing and then decreasing. This result is consistent with the research result.

According to research by Guçlu and colleagues, thrombocytopenia to be common in 31 survivors and 22 non-survivors (P=0.003). According to our study, the likelihood of thrombocytopenia was not correlated with the severity of the disease, but it was higher in non-survivors than in survivors. Non-survivors had lower platelet counts than survivors on the admission day and the third follow-up day, but this difference was not statistically significant.[16]

According to Zhu et al.,[17] the risk of death was more than twice as high (47.62%) and nearly three times higher (56.10%) in the group of thrombocytopenic patients compared to the nonthrombocytopenic one, in the duration of 28 days. Whether patient's death and thrombocytopenia were inherently related, however, was unclear. Significant differences were seen in the 28-day mortality (56.10 vs. 27.78%, P=0.01) and 180-day mortality (65.85 vs. 47.62%, P=0.04) between individuals with and without thrombocytopenia. Thirteen thrombocytopenic patients and sixty-six people without thrombo-

Table 6. Laboratory findings at day 18

Parameters	Study Group at 18 days
Anemia	5
Leukopenia	14
Thrombocytopenia	18

cytopenia made it out alive.[17]

Conclusion

In moderate cases of COVID-19 individuals, a platelet count measurement performed on days 8, 16, and 24 after admission is a valuable predictive and severity predictor. In moderate cases of COVID-19 patients, thrombocy-topenia is linked to an extended hospital stay (all thrombocytopenic patients waited 26 days for a measurement). In mild cases of COVID-19 patients, thrombocytopenia is linked to a higher death rate on day 26 of hospital admission.

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