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Association of Baseline Hematological Parameters with Thromboembolic Events in Hospitalized COVID-19 Patients

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ABSTRACT

Background: COVID-19 carries an increased risk of blood clot complications because of its effects on the body's inflammation and clotting processes. Identifying patients who are at risk as early as possible is crucial for healthcare providers. Regular blood tests can provide useful information to predict these risks.

Objective: To determine the frequency of in-hospital thromboembolic events among COVID-19 patients and assess the influence of blood parameters, measured at the time of admission, on the occurrence of these events.

Methodology: This retrospective study included 364 hospitalized COVID-19 patients. Demographic, clinical, and laboratory data at admission were collected from medical records. Thromboembolic events were documented and confirmed through clinical and imaging findings. Logistic regression analysis was used to identify independent predictors.

Results: Thromboembolic events occurred in 6.6% of hospitalized COVID-19 patients, with myocardial infarction being the most common. Patients with such events had significantly lower hemoglobin, higher MPV, and elevated D-dimer levels. Age, low hemoglobin, and high MPV were identified as independent predictors. No significant differences were observed in C-reactive protein, LDH, or total WBC count.

Conclusion: Age, low hemoglobin, and high MPV are independent predictors of thromboembolic events in hospitalized COVID-19 patients. These common blood parameters may help identify risk early. Including them in clinical assessments can improve prevention measures. More prospective studies are necessary to confirm these findings.

Keyword: COVID-19; Thromboembolic Events; D-Dimer; MPV

Introduction

Coronavirus Disease 2019 (COVID-19) is caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) and has quickly become a global pandemic. It shows a wide range of clinical symptoms. Initially, it was seen mainly as a respiratory infection; however, it is now clear that COVID-19 impacts several organ systems, such as the cardiovascular, hematologic, renal, and neurological systems.[1,2] The disease's pathophysiology is complex and includes immune system issues, damage to blood vessel linings, the release of cytokines, and a tendency to form blood clots. All these factors influence the severity of the disease and its complications.[3,4]

Among the extrapulmonary manifestations, thromboembolic events have raised significant concerns. These events include both venous and arterial thromboses and can result in serious illness and death in hospitalized patients. Thrombotic complications can happen even with standard blood clot prevention measures, which shows the severe nature of COVID-19-related coagulopathy.[5,6] The hypercoagulable state seen in COVID-19 is linked to problems with blood vessel lining, widespread inflammation, platelet activation, and blood flow stagnation, which are the key elements of Virchow's triad.[7]

Hematological and inflammatory biomarkers have become more important as possible predictors of disease progression and negative events in COVID-19. Basic blood parameters, which are cheap and widely available, may show underlying health issues and can help with clinical risk assessment.[8] Parameters like hemoglobin concentration, platelet indices, white blood cell count, and mean platelet volume (MPV) are commonly measured upon hospital admission. They have been studied for their diagnostic and prognostic value in infectious and thrombotic conditions.[9,10]

MPV is a measure of platelet size and activity. It has shown potential as an indicator of thrombotic risk in various diseases. Larger platelets are more reactive, producing more thromboxane A2 and showing greater levels of procoagulant surface molecules.[11] In the case of COVID-19, high MPV may indicate increased platelet activation and aggregation, which can lead to the formation of clots. Similarly, low hemoglobin levels can worsen hypoxia and damage blood vessel lining, creating a more thrombotic environment.[12]

Despite increasing evidence about COVID-19-related thromboinflammation, there is still no agreement on how well routine blood tests can predict thromboembolic complications. Most studies have taken place in high-resource settings where advanced diagnostic tools and imaging technologies are available. In contrast, resource-limited settings often depend on basic lab tests to guide clinical decisions. This makes it essential to find accessible and reliable biomarkers.[13]

Understanding the link between initial blood parameters and thromboembolic events could aid in identifying risks early, allowing for timely interventions and better thromboprophylaxis strategies. It could also improve patient care by guiding decisions on how much anticoagulation to use and how often to monitor patients during hospitalization.

In this setting, the current study aims to assess how often thromboembolic events occur in hospitalized COVID-19 patients. It will also look into the possible role of baseline blood parameters, especially hemoglobin and mean platelet volume, in predicting these complications.

Objective

To determine the frequency of in-hospital thromboembolic events among COVID-19 patients and assess the influence of blood parameters, measured at the time of admission, on the occurrence of these events.

Methodology

This retrospective observational study took place at Benazir Bhutto Hospital, Rawalpindi. It included adult patients hospitalized with a COVID-19 diagnosis during the study period from January 2021 to December. The study aimed to evaluate how often in-hospital thromboembolic events occurred and to assess the relationship between baseline blood parameters, particularly hemoglobin and mean platelet volume (MPV), and the development of these events in COVID-19 patients.

Patients were eligible if they were 18 years or older and had a confirmed COVID-19 diagnosis by reverse transcription polymerase chain reaction (RT-PCR). They could also qualify with a highly probable diagnosis based on clinical symptoms and typical chest imaging findings, such as bilateral ground-glass opacities. To be classified as highly probable cases, patients needed at least two negative RT-PCR tests taken 24 to 48 hours apart. A total of 364 patients who met these criteria and had complete laboratory and clinical data were included in the final analysis.

Exclusion criteria included patients referred from outside facilities with incomplete medical records, those discharged within 24 hours of admission, patients who left against medical advice, and individuals with a known thromboembolic disease diagnosis before admission.

The study received approval (Ref. 201/BBH/2021) from the institutional ethical review board of Benazir Bhutto Hospital, Rawalpindi, and the requirement for informed consent was waived due to the retrospective nature of the data collection. All patient data were anonymized and handled following the Declaration of Helsinki.

Demographic and clinical characteristics were collected from the hospital's electronic health records. This included age, gender, comorbidities (such as hypertension,

diabetes mellitus, chronic kidney disease, heart failure, malignancy, and chronic obstructive pulmonary disease), and outcomes (intensive care unit admission, oxygen therapy requirement, and in-hospital mortality). The primary outcome was the occurrence of any thromboembolic event during hospitalization. These events included myocardial infarction, cerebrovascular accident, deep vein thrombosis, pulmonary embolism, and peripheral arterial thrombosis, all diagnosed using standard imaging, laboratory, or electrocardiographic criteria noted in patient records.

Laboratory parameters measured within the first 24 hours of admission were collected. These included hemoglobin, white blood cell count, lymphocyte count, platelet count, MPV, red cell distribution width (RDW), D-dimer, fibrinogen, C-reactive protein (CRP), lactate dehydrogenase (LDH), ferritin, procalcitonin, and serum albumin. When multiple values were recorded during this time, the earliest value was used for analysis to reflect the baseline status.

All data were entered into a standardized spreadsheet and checked by two independent researchers to ensure accuracy and consistency. Any discrepancies were resolved by consensus or consultation with a third investigator.

Statistical analysis was performed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were reported as medians with interquartile ranges, while categorical variables were presented as frequencies and percentages. Comparisons between groups (patients with and without thromboembolic events) used the Mann-Whitney U test for continuous variables and the Chi-square or Fisher's exact test for categorical variables, as appropriate. Variables with a p-value less than 0.1 in univariate analysis went into a binary logistic regression model to identify independent predictors of thromboembolic events. Adjusted odds ratios with 95% confidence intervals were reported. The model's fitness was assessed using the Hosmer-Lemeshow test, and a two-tailed p-value of less than 0.05 was considered statistically significant.

Results

A total of 364 hospitalized patients diagnosed with COVID-19 were included in the study. Among them, 192 (52.7%) were male and 172 (47.3%) were female, with a median age of 60 years (IQR: 48 to 71). The overall frequency of thromboembolic events was 6.6% (n=24) during hospitalization.

Thromboembolic complications were more common in male patients (n=14, 58.3%) than in females (n=10, 41.7%), though this difference was not statistically significant (p>0.05). Comorbidities were present in 248 patients (68.1%), with the most common being hypertension (35.7%), diabetes mellitus (29.1%), and chronic kidney disease (10.4%). Among patients who experienced thromboembolic events, the presence of hypertension (58.3% vs. 33.5%, p=0.018), heart failure (20.8% vs. 4.3%, p=0.006), and chronic kidney disease (25% vs. 8.2%, p=0.011) was significantly higher compared to those without these events (Table 1).

Among the 24 thromboembolic events, the most common was myocardial infarction (n=14, 3.8%). Next was cerebrovascular accident (n=5, 1.4%), followed by deep vein thrombosis (n=3, 0.8%), peripheral arterial thrombosis (n=1, 0.3%), and pulmonary embolism (n=1, 0.3%). Figure 1 shows the distribution of these events. This pie chart illustrates the distribution of thromboembolic events observed among 24 hospitalized COVID-19 patients who developed complications (total study sample: n=364). The most frequent complication was myocardial infarction (58%), followed by deep vein thrombosis (21%), cerebrovascular accident (12%), pulmonary embolism (4%), and peripheral arterial thrombosis (3%). The figure emphasizes how arterial thrombotic events, particularly myocardial infarction, are important thromboembolic issues in this group.

On admission, we noticed clear differences in lab results between patients who developed thromboembolic events and those who did not. Patients with thromboembolic complications had much lower hemoglobin levels, with a median value of 11.2 g/dL compared to 12.9 g/dL in those without events (p=0.003). Moreover, mean platelet volume (MPV) was higher in patients who experienced thromboembolic events, with a median of 10.1 fL versus 9.2 fL for those who did not. This suggests a potential role of platelet activation in thrombotic risk (p=0.009). Additionally, D-dimer levels were higher among patients with thromboembolic events. Their median level was 1.32 µg/mL compared to 0.76 µg/mL in those without, which was statistically significant (p=0.021). However, there were no significant differences in total white blood cell (WBC) count, lymphocyte count, C-reactive protein (CRP), or lactate dehydrogenase (LDH) levels between the two groups (Table 2).

To identify independent predictors of thromboembolic events, we included variables with a p-value less than 0.1 from the univariate analysis in a multivariate logistic regression model. The final analysis showed that age, hemoglobin, and mean platelet volume (MPV) were significant independent risk factors. Older age was linked to a higher risk of thromboembolic events, with an odds ratio (OR) of 1.036 (95% confidence interval [CI]: 1.008, 1.066; p=0.012). Lower hemoglobin levels were connected with a reduced risk of thrombosis (OR: 0.822; 95% CI: 0.710, 0.951; p=0.008), meaning that patients with anemia had a higher chance of developing complications. Moreover, higher MPV was associated with thromboembolic events (OR: 1.329; 95% CI: 1.071, 1.648; p=0.010), highlighting the role of platelet activation

Table 1. Demographic and Clinical Characteristics of Study Population (n = 364)

Variable	Total (n=364)	Thrombosis (+) (n=24)	Thrombosis (–) (n=340)	p-value
Age, median (IQR)	60 (48–71)	66 (55–78)	58 (46–70)	0.014
Male sex, n (%)	192 (52.7%)	14 (58.3%)	178 (52.4%)	0.54
Hypertension	130 (35.7%)	14 (58.3%)	114 (33.5%)	0.018
Diabetes Mellitus	106 (29.1%)	10 (41.7%)	96 (28.2%)	0.17
Heart Failure	22 (6%)	5 (20.8%)	17 (5%)	0.006
Chronic Kidney Disease	38 (10.4%)	6 (25%)	32 (8.2%)	0.011

in the development of thrombosis in COVID-19 patients (Table 3).

This forest plot shows the odds ratios (OR) and 95% confidence intervals (CI) for the independent predictors of thromboembolic events in hospitalized COVID-19 patients. The data comes from a multivariate logistic regression analysis. Age was positively linked to risk (OR: 1.036; 95% CI: 1.008, 1.066; p=0.012). In contrast, hemoglobin had an inverse relationship (OR: 0.822; 95% CI: 0.710, 0.951; p=0.008). Mean Platelet Volume (MPV) was a significant positive predictor (OR: 1.329; 95% CI: 1.071, 1.648; p=0.010). The x-axis is plotted on a logarithmic scale centered at OR=1, showing no effect (Figure 2).

Discussion

In this study of 364 hospitalized patients with COVID-19, we found a thromboembolic event rate of 6.6%. Myocardial infarction was the most common type of complication. Our findings show that age, hemoglobin levels, and mean platelet volume (MPV) are independent predictors of thromboembolic events. These results align with the increasing evidence that points to a complex thromboinflammatory process in COVID-19 patients.

The overall rate of thromboembolic events in our group was similar to the 4.4 to 10% range found in various international studies of hospitalized patients. A study from France by Degrave et al. reported a thromboembolic rate of 10% among non-ICU COVID-19 patients who were receiving oxygen therapy.[14] Likewise, Lalor et al. noted major arterial and venous events in 4.4% of their COVID-19 group.[15] In a registry from a tertiary center in Croatia, Jurin et al. discovered a thrombotic event rate of 8.3%, highlighting the variable yet significant occurrence of thromboembolic complications in hospitalized settings.[16]

One of the key findings of our study was that older age independently predicts thromboembolic events. Older patients had a much higher risk. This aligns with previous studies that show age-related problems with blood vessels, immune responses, and lower levels of fibrinolysis that contribute to thrombosis. A nationwide study in the U.S. showed a clear increase in thrombotic complications with age in COVID-19 patients.[17] Radkhah et al. also pointed out that age is a major risk factor for pulmonary embolism in Iranian COVID-19 patients.[18] Zuin

Table 2. Comparison of Admission Laboratory Parameters by Thromboembolic Event Status

Parameter	Thrombosis (+)	Thrombosis (–)	p-value
Hemoglobin (g/dL)	11.2 (10.1–12.4)	12.9 (11.6–13.8)	0.003
MPV (fL)	10.1 (9.4–10.8)	9.2 (8.5–10.1)	0.009
D-dimer (µg/mL)	1.32 (0.86–2.14)	0.76 (0.43–1.23)	0.021
CRP (mg/L)	42.8 (18.6–120)	36.3 (12.4–88.5)	0.32
LDH (U/L)	310 (258–410)	290 (230–380)	0.12

Table 3. Multivariate Logistic Regression for Predictors of Thromboembolic Events

Variable	OR	95% CI	p-value
Age (per year)	1.036	1.008–1.066	0.012
Hemoglobin (per g/dL)	0.822	0.710–0.951	0.008
MPV (per fL)	1.329	1.071–1.648	0.010

et al. concluded from a systematic review that being over 60 is strongly linked to venous thromboembolism in ICU patients.[19]

We also found that low hemoglobin levels at admission were linked to a higher chance of thromboembolic complications. Anemia may worsen tissue hypoxia, increase platelet-vessel wall interactions, and raise vascular resistance. These factors can promote thrombosis. Sadeghi et al. support these findings, showing that hemoglobin was inversely related to thrombotic risk in COVID-19 pneumonia.[13] Martinot et al. noted that patients with lower hemoglobin levels faced worse clinical outcomes and a higher risk of extrapulmonary complications, including thrombosis.[20] Similarly, Hultcrantz et al. studied Scandinavian blood donors and found that lower hemoglobin concentrations were connected to a greater risk of thromboembolic events, even among healthy individuals.[12]

Another important predictor we found in our analysis was elevated mean platelet volume (MPV). MPV indicates platelet activation and size. Larger platelets are more metabolically and enzymatically active, making them more likely to cause clots. The link between high MPV and thromboembolic complications in our group aligns with the findings of Duan et al. They noted that critically ill COVID-19 patients who developed VTE had higher MPV levels.[11] Zein et al. confirmed in their meta-analysis that patients with worse COVID-19 outcomes had significantly higher MPV compared to those with better outcomes.[10] Additionally, a study by Gozukucuk et al. found that non-surviving patients had significantly higher MPV levels, backing up its value as a prognostic marker.[21]

Interestingly, while inflammatory markers like CRP and LDH often rise in severe COVID-19, they were not linked to thromboembolic events in our group. This might show that COVID-19 coagulopathy has multiple causes, where

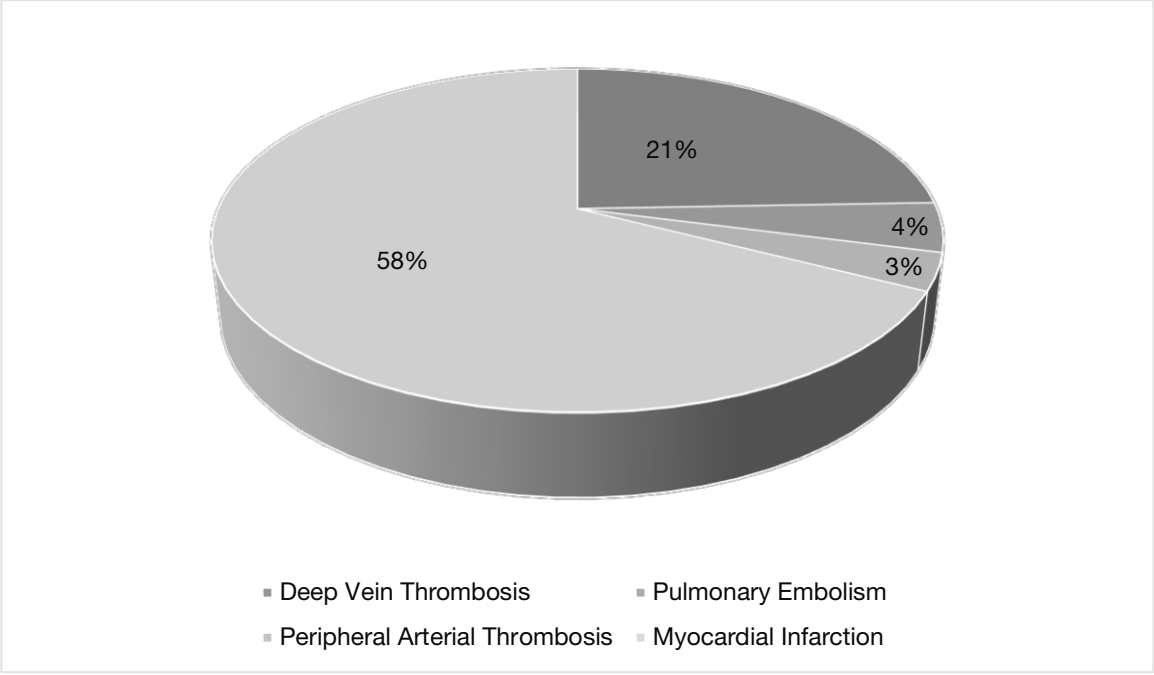

Figure 1. Distribution of thromboembolic complications among hospitalized COVID-19 patients

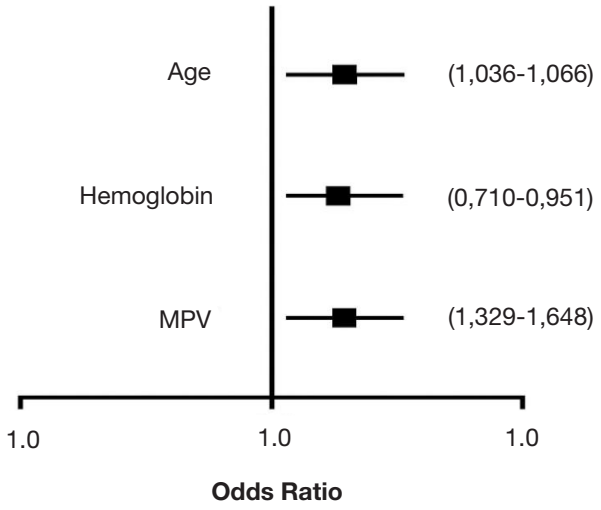

Figure 2. Forest plot showing odds ratios and confidence intervals for significant predictors of thromboembolic events

direct damage to blood vessel lining and platelet activation are more important than just systemic inflammation. Similar findings were noted by Alizad et al., who mentioned that CRP and LDH did not reliably predict blood clot complications, even though they connected with overall disease severity.[9]

Overall, our results support the idea that basic blood parameters—age, hemoglobin, and MPV—are useful and accessible markers for spotting patients at higher risk of thromboembolic events. These parameters can be included in clinical decision-making, especially in settings with limited resources where advanced coagulation tests or imaging may not be easily available.

Conclusion

In this study of hospitalized COVID-19 patients, we found that many experienced thromboembolic events, with myocardial infarction being the most common complication. Our results show that older age, low hemoglobin levels, and high mean platelet volume (MPV) at the time of hospital admission are linked to a greater risk of thromboembolic events. These commonly available blood test results could be useful for early risk assessment, particularly in settings with limited resources where advanced diagnostic tools are hard to come by. Including these predictors in clinical decision-making may help shape thromboprophylaxis strategies and improve patient outcomes. More prospective, multicenter studies are needed to confirm these findings and examine their use in clinical practice.

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