Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/cjmpyd69

COAGULATION ABNORMALITIES AND THROMBOTIC COMPLICATIONS IN COVID-19: A HEMATOLOGICAL PERSPECTIVE

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ABSTRACT

Background: COVID-19, caused by SARS-CoV-2, impacts the respiratory system and induces significant coagulation abnormalities and thrombotic complications, particularly in severe cases. This study evaluated these hematological changes and 'their association with disease severity and outcomes'.

Methods: 'A retrospective observational study was conducted at Khyber Medical University' from January 2023 to January 2024, involving 120 COVID-19 patients. Participants 'were categorized into mild/moderate (n=80) and severe/critical (n=40) groups'. Demographics, laboratory parameters, coagulation profiles, and clinical outcomes were analyzed, and statistical comparisons were made between the groups.

Results: Severe/critical cases showed significantly elevated D-dimer levels, prolonged PT and aPTT, increased fibrinogen levels, and reduced platelet counts compared to mild/moderate 'cases ($p < 0.001$)'. 'Inflammatory markers, including CRP, ferritin, and IL-6', were markedly higher in the severe group ($p < 0.001$). Thrombotic complications, such as DVT (25%) and PE (18%), were more frequent in severe cases, alongside higher mortality (40% vs. 2.5%, $p < 0.001$). Vaccination was associated with reduced disease severity, highlighting its protective role.

Conclusion: Coagulation abnormalities and thrombotic complications are strongly associated with COVID-19 severity. 'Elevated markers, D-dimer and inflammatory cytokines, underscore the hypercoagulable and inflammatory state in severe cases'. These findings highlight the importance of early detection, proactive monitoring, and individualized anticoagulation strategies to improve outcomes in high-risk patients.

Keywords: COVID-19, coagulation abnormalities, thrombotic complications, hypercoagulability, inflammation, hematology, D-dimer, cytokine storm, anticoagulation therapy.

Introduction

'Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has presented unprecedented challenges to global healthcare systems'(1). While the primary pathology of COVID-19 involves the respiratory system, increasing evidence has revealed a significant impact on the hematological and coagulation systems, particularly in severe cases. These disturbances, characterized by hypercoagulability and systemic inflammation, are often linked to adverse outcomes, including thrombotic complications and increased mortality(2).

Coagulation abnormalities in COVID-19 range from elevated D-dimer levels and prolonged coagulation times to severe complications such as disseminated intravascular coagulation (DIC). 'Thrombotic events, including deep vein thrombosis (DVT), pulmonary embolism (PE), and ischemic stroke, have been frequently observed, particularly in critically ill patients'(3). 'This hypercoagulable state is thought to result from a complex interplay of endothelial injury, inflammatory cytokine release, and immune system dysregulation, often called thromboinflammation'(4).

Identifying and managing coagulation abnormalities is critical for improving patient outcomes in COVID-19. Early recognition of these markers can guide therapeutic strategies, including anticoagulation therapy, and may prevent the progression of complications. Understanding the hematological changes associated with COVID-19 is essential to optimizing care and reducing mortality, particularly in severe cases(5).

This study evaluates the coagulation abnormalities 'and thrombotic complications observed in COVID-19 patients admitted to' Khyber Medical University. By analyzing laboratory 'parameters, thrombotic events, and clinical outcomes, the research provides valuable insights into the role of hematological markers in disease progression and severity'. The findings aim 'to contribute to a better understanding of COVID-19 pathophysiology and'''' to inform clinical management practices.

Methodology

'This retrospective observational study was conducted at Khyber Medical University' from January 2023 to January 2024. One hundred twenty patients diagnosed with COVID-19 confirmed via reverse transcription polymerase chain reaction (RT-PCR), were included. Patients were categorized based on disease severity 'into two groups: mild/moderate (n=80) and severe/critical (n=40), following the World Health Organization (WHO) classification criteria for COVID-19 severity'.

The study included patients aged 18 years or older admitted to the hospital during the study period. Individuals with pre-existing coagulopathies unrelated to COVID-19, active malignancies, or anticoagulant therapy before admission were excluded. Demographic details such as age, gender, BMI, smoking status, and comorbidities (e.g., hypertension, diabetes, cardiovascular disease) were documented. Clinical severity, vaccination status, and outcomes were also recorded.

Laboratory investigations included routine complete blood count (CBC), coagulation parameters (D-dimer, prothrombin time [PT], activated partial thromboplastin time [aPTT], fibrinogen levels, and platelet counts), and inflammatory markers (C-reactive protein [CRP], ferritin, and interleukin-6 [IL-6]). These tests were performed upon admission and during hospitalization to monitor disease progression. Thrombotic and bleeding events, including deep vein thrombosis (DVT), pulmonary embolism (PE), ischemic stroke, and disseminated intravascular coagulation (DIC), were recorded using clinical and diagnostic criteria.

Data collection was standardized using electronic medical records and laboratory information systems. Outcomes, including mortality, length of hospital stay, and recovery rates, were compared between the two severity groups. 'Statistical analysis was performed using SPSS version 25'. Continuous 'variables were expressed as mean ± standard deviation or median with interquartile range, while categorical variables were presented as frequencies and percentages'. 'Chi-square and independent t-tests were used to compare variables between groups, and a p-value of <0.05 was considered statistically significant'.

This study was approved by Khyber Medical University's institutional ethics committee. Due to the retrospective nature of the data collection, informed consent was waived. All patient data were anonymized to ensure confidentiality.

Results

'The study included 120 participants, of which' 60% were male. Participants with severe or critical COVID-19 were significantly older (mean age: 65.3 years) compared to those with mild or moderate disease (mean age: 54.1 years, **$p < 0.001$**). Obesity, represented by a higher BMI, was more prevalent in the severe/critical group (**$p = 0.012$**). Hypertension and diabetes were also significantly more common in the severe/critical group (65% and 50%, respectively) than in the mild/moderate group

(38% and 25%, respectively, **p < 0.01**). Vaccination was associated with less severe disease, with 62% of mild/moderate cases being vaccinated compared to only 25% of severe/critical cases (**p < 0.001**).

Table 1: Baseline Demographics and Clinical Characteristics of Participants

Variable	Total (n=120)	Mild/Moderate (n=80)	Severe/Critical (n=40)	p-value
Age (years)	58.2 ± 12.3	54.1 ± 10.8	65.3 ± 11.5	<0.001
Gender (Male, %)	72 (60%)	40 (50%)	32 (80%)	0.003
BMI (kg/m²)	27.5 ± 3.6	26.8 ± 3.2	28.9 ± 4.1	0.012
Smoking Status (%)	25 (21%)	15 (19%)	10 (25%)	0.47
Hypertension (%)	56 (47%)	30 (38%)	26 (65%)	0.009
Diabetes Mellitus (%)	40 (33%)	20 (25%)	20 (50%)	0.004
COVID-19 Severity	-	80 (67%)	40 (33%)	-
Vaccination (%)	60 (50%)	50 (62%)	10 (25%)	<0.001

Coagulation abnormalities were evident, with elevated D-dimer levels significantly associated with severe/critical cases '(median: 2,100 ng/mL) compared to mild/moderate cases (median: 850 ng/mL, **p < 0.001**)'. Prolonged PT and aPTT were also observed in the severe/critical group (15.9 ± 1.3 seconds and 37.1 ± 4.2 seconds, respectively, **p < 0.001**). Fibrinogen levels were notably higher in severe/critical cases (**p = 0.004**), while platelet counts were significantly lower in this group (160 ± 50 × 10⁹/L) compared to mild/moderate cases (240 ± 60 × 10⁹/L, **p < 0.001**).

Table 2: Coagulation Parameters in COVID-19 Patients

Parameter	'Total (n=120)'	'Mild/Moderate (n=80)'	'Severe/Critical (n=40)'	'p-value'
D-dimer (ng/mL)	1,200 (850–1,750)	850 (700–1,200)	2,100 (1,800–3,200)	<0.001
PT (seconds)	14.8 ± 1.2	14.2 ± 1.1	15.9 ± 1.3	<0.001
aPTT (seconds)	34.5 ± 3.4	33.2 ± 2.8	37.1 ± 4.2	<0.001
Fibrinogen (mg/dL)	490 ± 140	450 ± 130	550 ± 150	0.004
Platelet Count (×10⁹/L)	210 ± 65	240 ± 60	160 ± 50	<0.001

Inflammatory markers showed a clear correlation with disease severity. CRP levels were markedly higher in severe/critical cases (median: 150 mg/L) compared to mild/moderate cases (median: 30 mg/L, **p < 0.001**). 'Ferritin levels were also significantly elevated in severe/critical patients (median: 1,600 ng/mL) compared to mild/moderate patients (median: 600 ng/mL, **p < 0.001**)'. Similarly, IL-6 levels were dramatically higher in severe/critical cases '(median: 250 pg/mL) than in mild/moderate cases (median: 30 pg/mL, **p < 0.001**), highlighting the role of cytokine storm in disease progression.

Table 3: Inflammatory Markers in COVID-19 Patients

Marker	'Total (n=120)'	'Mild/Moderate (n=80)'	'Severe/Critical (n=40)'	'p-value'
C-reactive Protein (mg/L)	50 (20–120)	30 (15–60)	150 (80–300)	<0.001
Ferritin (ng/mL)	850 (400–1,500)	600 (350–1,000)	1,600 (1,000–2,800)	<0.001
IL-6 (pg/mL)	50 (15–200)	30 (10–50)	250 (100–800)	<0.001

CBC abnormalities were prominent in severe/critical COVID-19 cases. Hemoglobin levels were significantly lower in severe/critical patients (11.0 ± 2.0 g/dL) compared to mild/moderate patients (13.2 ± 1.5 g/dL, **p < 0.001**), indicating anemia. Severe/critical cases had higher WBC counts (11.0 ± 3.4 × 10⁹/L) and neutrophil percentages (85 ± 8%) than mild/moderate cases (8.5 ± 2.8 × 10⁹/L and 70 ± 10%, respectively, **p < 0.001**).

Conversely, lymphocyte percentages were significantly lower in severe/critical cases (10 ± 3%) than in mild/moderate cases (18 ± 4%, **p < 0.001**). Platelet counts were reduced in severe/critical cases, consistent with thrombocytopenia (**p < 0.001**). Increased RDW levels in severe/critical cases (17.0 ± 2.0%) also suggest a poor prognosis (**p < 0.001**).

Table 4: Complete Blood Count (CBC) Parameters

Parameter	'Total (n=120)'	'Mild/Moderate (n=80)'	'Severe/Critical (n=40)'	p-value
Hemoglobin (g/dL)	12.5 ± 1.8	13.2 ± 1.5	11.0 ± 2.0	<0.001
WBC Count (×10⁹/L)	9.2 ± 3.1	8.5 ± 2.8	11.0 ± 3.4	<0.001
Neutrophils (%)	75 ± 12	70 ± 10	85 ± 8	<0.001
Lymphocytes (%)	15 ± 5	18 ± 4	10 ± 3	<0.001
Platelet Count (×10⁹/L)	210 ± 65	240 ± 60	160 ± 50	<0.001
RDW (%)	15.2 ± 1.8	14.5 ± 1.2	17.0 ± 2.0	<0.001

Thrombotic ccomplications were more frequent in severe/critical cases. Deep vein thrombosis (DVT) occurred in 25% of severe/critical cases compared to 6% of mild/moderate cases (**p = 0.007**). Pulmonary embolism (PE) and ischemic stroke were significantly more common in severe/critical patients (18% and 10%, respectively) than in mild/moderate cases (4% and 1%, respectively, **p < 0.02**). Major bleeding events were also more frequent in severe/critical cases (15%) than mild/moderate cases (3%, **p = 0.01**), likely reflecting the interplay between coagulation abnormalities and anticoagulant therapy.

Table 5: Thrombotic and Bleeding Complications

Event	'Total (n=120)'	'Mild/Moderate (n=80)'	'Severe/Critical (n=40)'	'p-value'
Deep Vein Thrombosis (%)	15 (12.5%)	5 (6%)	10 (25%)	0.007
Pulmonary Embolism (%)	10 (8%)	3 (4%)	7 (18%)	0.012
Ischemic Stroke (%)	5 (4%)	1 (1%)	4 (10%)	0.019
Major Bleeding Events (%)	8 (7%)	2 (3%)	6 (15%)	0.010

Severe/critical COVID-19 cases 'were associated with significantly higher mortality (40%) compared' to mild/moderate cases (2.5%, **p < 0.001**). The length of hospital stay was significantly longer for severe/critical patients (18 ± 7 days) compared to mild/moderate patients (10 ± 3 days, **p < 0.001**). Recovery rates were higher in mild/moderate cases (97.5%) than in severe/critical cases (60%, **p < 0.001**), underscoring the impact of disease severity on patient outcomes.

Table 6: Outcomes of COVID-19 Patients

Outcome	'Total (n=120)'	'Mild/Moderate (n=80)'	'Severe/Critical (n=40)'	p-value
Mortality (%)	18 (15%)	2 (2.5%)	16 (40%)	<0.001
Length of Stay (days)	12 ± 5	10 ± 3	18 ± 7	<0.001
Recovery (%)	102 (85%)	78 (97.5%)	24 (60%)	<0.001

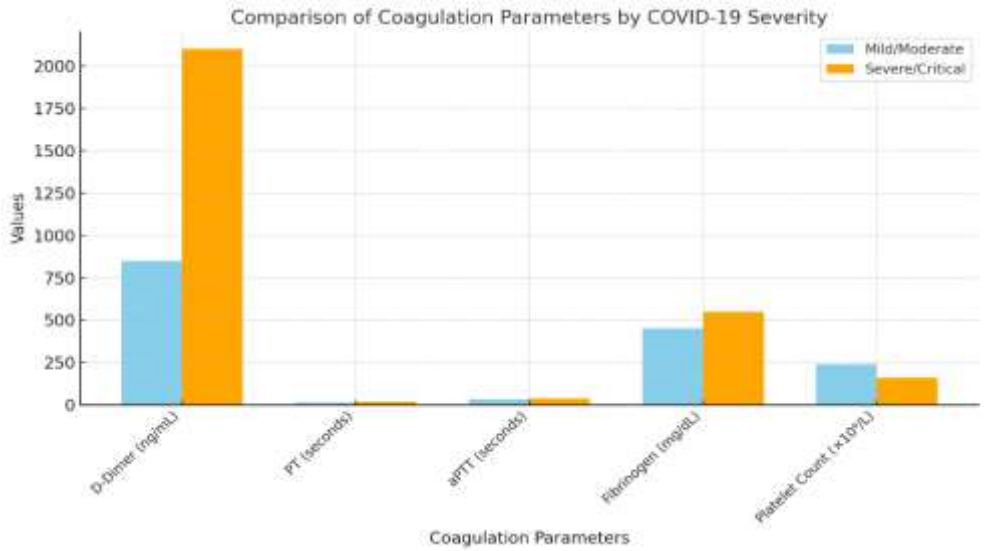

Figure 1: illustrates a comparison of coagulation parameters between patients with mild/moderate and severe/critical COVID-19. D-dimer levels were significantly elevated in the severe/critical group, indicating a heightened thrombotic risk. 'Prothrombin time (PT) and activated partial

thromboplastin time (aPTT) were also prolonged in this group', reflecting impaired coagulation. Fibrinogen levels were notably higher in severe cases, aligning with an inflammatory and hypercoagulable state. Conversely, platelet counts were lower in severe/critical cases, consistent with thrombocytopenia. These trends underscore the worsening coagulation abnormalities as disease severity increases, emphasizing the need for close monitoring of these parameters in critically ill patients.

Discussion

The findings of this study highlight significant coagulation abnormalities and thrombotic complications in COVID-19 patients, with these issues being more pronounced in those with severe or critical disease. Elevated D-dimer levels, prolonged prothrombin time (PT) and activated partial thromboplastin time (aPTT), increased fibrinogen levels, and reduced platelet counts were prominent in patients with severe illness. These results 'align with previous studies that have established the hypercoagulable state as a hallmark of severe COVID-19'.

Elevated D-dimer levels observed in this study corroborate findings that reported that increased D-dimer levels are strongly associated with disease severity and higher mortality rates (6-8). The significant prolongation of PT and aPTT observed in severe cases was consistent with earlier research indicating a dysregulated coagulation cascade in critically ill COVID-19 patients. This supports the hypothesis that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection induces a prothrombotic state via endothelial damage, cytokine release, and microvascular injury(9, 10).

Fibrinogen, an acute-phase reactant, was elevated in severe cases, reflecting heightened inflammation and its contribution to clot formation. Previous studies, highlighted fibrinogen's role in COVID-19-associated coagulopathy(11, 12). Conversely, thrombocytopenia was more common in severe cases in this study, aligning with reports suggesting that platelet consumption due to microthrombosis and immune-mediated destruction may underlie this reduction(13-15).

Inflammatory markers, including C-reactive protein (CRP), ferritin, and interleukin-6 (IL-6), were significantly elevated in patients with severe disease. These findings were consistent with prior studies, which emphasize the role of a cytokine storm in driving systemic inflammation and coagulation disturbances. The interplay between inflammation and thrombosis, commonly referred to as thromboinflammation, 'appears central to the pathophysiology of severe COVID-19' (16, 17).

Thrombotic complications, including deep vein thrombosis (DVT), pulmonary embolism (PE), and ischemic stroke, were significantly higher in severe cases. 'These complications align with the findings of studies that documented a high prevalence of thrombotic events in critically ill COVID-19 patients' (18, 19). The elevated risk of thrombosis underscores the importance of early anticoagulation therapy in managing these patients. However, 'the occurrence of bleeding events in severe cases' , as observed in this study, highlights the delicate balance required in anticoagulation management, consistent with findings(20).

Mortality and prolonged hospital stay in severe cases were expected outcomes, consistent with prior studies linking coagulopathy and inflammation to poor prognosis. Vaccination status played a protective role in reducing severity, emphasizing widespread vaccination's importance in mitigating severe outcomes.

The study confirms that COVID-19 severity is strongly associated with coagulation abnormalities, thrombotic complications, and adverse outcomes. These findings are consistent with existing literature, reinforcing the critical need for vigilant monitoring and tailored anticoagulation strategies in high-risk patients. Further research is warranted to refine therapeutic interventions and reduce the burden of thromboinflammatory complications in severe COVID-19.

Conclusion

This study highlights the significant association between coagulation abnormalities, 'thrombotic complications, and the severity of COVID-19'. Elevated D-dimer levels, prolonged coagulation times (PT and aPTT), increased fibrinogen levels, and reduced platelet counts were markedly evident in 'patients with severe and critical disease'. These findings underline the hypercoagulable and

inflammatory state characteristic of severe COVID-19, emphasizing the interplay between thromboinflammation and poor clinical outcomes.

'Thrombotic events such as deep vein thrombosis, pulmonary embolism, and ischemic stroke' were more prevalent in severe cases, underscoring the critical need for early detection and management of these complications. Simultaneously, the occurrence of bleeding events highlights the complexities of balancing anticoagulation therapy, particularly 'in critically ill patients'.

This study also reaffirms the protective role of vaccination in reducing disease severity, reinforcing its importance as a public health measure. By identifying key hematological and inflammatory markers associated with disease progression, this research contributes to a deeper understanding of COVID-19 pathophysiology. It highlights the need for proactive monitoring and individualized treatment approaches.

Further research is essential to optimize anticoagulation strategies and explore innovative therapies that address both thrombotic and inflammatory components of severe COVID-19, ultimately improving patient outcomes and reducing mortality.

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