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PROGNOSTIC SIGNIFICANCE OF HEMOSTASIS DISORDERS

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Abstract

COVID-19 affects multiple organ systems and exerts profound influence on the mechanisms of hemostasis. Increased thrombin generation, reduced fibrinolytic activity, disseminated intravascular coagulation (DIC), thrombocytopenia, and marked elevation of D-dimer are strongly associated with severe clinical progression and higher mortality rates. This study aims to determine the prognostic significance of hemostatic markers in patients with COVID-19, evaluate the relationship between laboratory parameters and clinical severity, and improve diagnostic algorithms for early risk stratification. The findings highlight the critical importance of early detection of hemostatic disturbances in reducing severe complications and improving clinical outcomes in COVID-19.

Keywords: COVID-19; Hemostasis; D-dimer; Coagulopathy; Prothrombin Time (PT); Activated Partial Thromboplastin Time (APTT); Thrombocytopenia

Introduction

The COVID-19 (SARS-CoV-2) pandemic has posed unprecedented clinical, epidemiological, and economic challenges to healthcare systems worldwide. Although the disease was initially characterized primarily as a respiratory illness, accumulating evidence from extensive international studies has demonstrated that COVID-19 affects multiple organ systems, particularly the vascular endothelium, the immune system, and the mechanisms of hemostasis. Hemostatic dysfunction has now been recognized as one of the leading pathophysiological determinants of severe disease progression and increased mortality in patients with COVID-19.

SARS-CoV-2 enters host cells via ACE2 receptors, which are not only abundantly expressed in the respiratory tract but also present on endothelial cells. Viral entry into endothelial tissue leads to cellular injury, endothelial activation, and ultimately endothelial dysfunction. This process serves as a major trigger for enhanced thrombin generation and activation of the coagulation cascade. In parallel, the host's immune response—regardless of its magnitude—may give rise to a hyperinflammatory state known as the "cytokine storm," in which markedly

elevated levels of pro-inflammatory mediators disrupt all components of the hemostatic system. As a result, excessive coagulation, impaired fibrinolysis, and disseminated intravascular coagulation (DIC) may develop.

COVID-19–associated coagulopathy is widely described as a thrombo-inflammatory phenomenon, reflecting the intricate interplay between inflammation and thrombosis. Clinically, this manifests as microvascular thrombosis within the pulmonary capillaries, acute respiratory distress syndrome (ARDS), myocardial infarction, ischemic stroke, deep vein thrombosis, and pulmonary embolism. Reports from major clinical centers indicate that 30–45% of patients with severe COVID-19 develop overt or subclinical thromboembolic complications.

Laboratory findings characteristic of COVID-19 coagulopathy include markedly elevated D-dimer levels, dynamic changes in fibrinogen concentrations, prolonged prothrombin time (PT) and activated partial thromboplastin time (APTT), thrombocytopenia, and reduced antithrombin III activity. Among these, D-dimer has emerged as the most powerful early diagnostic and prognostic marker. Its rapid elevation is associated not only with an increased likelihood of thrombotic events but also with severe clinical deterioration and higher risk of mortality.

International studies (Tang N. et al., 2020; Thachil J., IJs et al., 2021) have shown that D-dimer levels in patients with severe COVID-19 may exceed normal values by 4–6 fold, strongly correlating with poor outcomes. Fibrinogen levels typically rise during early and moderate disease stages due to inflammation but decline significantly as DIC develops, reflecting consumption of coagulation factors. Thrombocytopenia, although often mild, is considered an important early laboratory signal of worsening disease.

While conventional coagulation assays such as PT, APTT, and fibrinogen remain essential, recent studies emphasize the importance of global hemostasis assessment tools—particularly thromboelastography (TEG). TEG provides a comprehensive real-time evaluation of clot formation, stabilization, and lysis, enabling a more precise assessment of hypercoagulability or impending DIC in critically ill patients.

Despite extensive research, existing studies vary widely in methodology, patient characteristics, and diagnostic criteria, limiting the applicability of uniform prognostic models. Therefore, systematic investigation of hemostatic abnormalities in COVID-19 within specific regional populations remains crucial for developing accurate prognostic strategies and tailored clinical management.

The present study aims to evaluate the alterations in hemostasis parameters in patients with COVID-19 and to determine their prognostic significance in

relation to disease severity, clinical course, and major outcomes such as thrombosis, ARDS, need for intensive care, and mortality.

Materials and methods

The study included patients admitted to the Bukhara City Central Polyclinic who were diagnosed with COVID-19 and received inpatient treatment between 2022 and 2024. Clinical, instrumental, and laboratory assessments were performed, and a total of 124 patients were prospectively selected. The diagnosis of COVID-19 was confirmed by PCR testing in accordance with the criteria established by the World Health Organization (WHO). Exclusion criteria included pre-existing hematologic disorders, chronic liver disease, long-term anticoagulant therapy, uncontrolled stage II–III hypertension, decompensated diabetes mellitus, and a prior history of myocardial infarction or stroke.

The clinical course of COVID-19, associated comorbidities, and the pharmacotherapy administered during hospitalization were thoroughly evaluated. Routine clinical laboratory tests, including complete blood count (CBC), coagulation profile, biochemical analysis, and inflammatory markers, were performed. Chest computed tomography (CT) was used to assess pulmonary involvement. Hemostasis status was evaluated using standard coagulation assays and additional markers commonly affected by COVID-19.

Coagulation parameters assessed in this study included prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen concentration, D-dimer, platelet count, and antithrombin III levels. Global hemostasis testing—specifically thromboelastography (TEG)—was performed in patients with moderate to severe disease to assess clot formation dynamics and fibrinolytic activity. Baseline laboratory data were obtained upon admission to the hospital.

Patients who were receiving chronic antiplatelet or anticoagulation therapy prior to admission, as well as those in terminal stages of malignant diseases or advanced renal or hepatic failure, were excluded from the study. All patients received treatment according to national COVID-19 management protocols, including antiviral therapy, corticosteroids, anticoagulation, oxygen therapy, and supportive care as clinically indicated.

Blood samples were collected to measure hemoglobin, leukocyte and platelet counts, serum ferritin, C-reactive protein (CRP), creatinine, alanine aminotransferase (ALT), and total protein. Coagulation parameters (PT, APTT, fibrinogen, D-dimer) were analyzed using standard automated coagulation analyzers. D-dimer was measured by immunoturbidimetric assay. Platelet counts were determined by automated hematology analyzers. TEG parameters were

recorded for selected patients to assess clot initiation time (R), clot kinetics (K), alpha angle, maximum amplitude (MA), and clot lysis index.

All laboratory measurements were performed in accordance with internal quality control standards and international guidelines. Data obtained before treatment initiation and during hospitalization were compared for dynamic analysis of hemostatic abnormalities in relation to the clinical severity of COVID-19.

Research results

According to the severity of COVID-19 in the selected patient groups, as determined by clinical findings, chest CT scoring, and key hemostatic laboratory markers such as D-dimer, fibrinogen, PT/APTT, platelet count, and antithrombin III, anticoagulation therapy was administered in accordance with international COVID-19 treatment guidelines. Low-molecular-weight heparin (LMWH) was used as the primary antithrombotic agent, with dosage adjusted based on the degree of coagulopathy. Follow-up coagulation profiles were assessed on days 3, 7, and 14 of hospitalization. D-dimer dynamics were used as a prognostic indicator of thrombotic progression and overall clinical deterioration.

Furthermore, to evaluate global hemostatic function in moderate and severe cases, modern diagnostic tools—including thromboelastography (TEG)—were utilized to assess clot formation kinetics, clot firmness, and fibrinolytic activity. Comparative analyses of laboratory results before and after anticoagulation therapy were performed, and the therapeutic effectiveness was evaluated based on changes observed in both classical and global hemostasis markers. This allowed for the development of an algorithm for early detection and management of COVID-19-associated coagulopathy.

Figures 1–3 present comparative analyses of traditional and advanced hemostatic markers before and after treatment in patients with varying COVID-19 severity levels.

However, despite extensive global research on COVID-19, there is relatively limited data regarding the occurrence of critical coagulation abnormalities during the early stages of infection, when respiratory symptoms may still be mild but hemostatic disruptions are already detectable through laboratory testing.

Based on this, our study focused on evaluating alterations in essential hemostasis parameters—including D-dimer, fibrinogen, platelet count, and PT/APTT—across clinical severity categories of COVID-19 (Table 1).

Table 1. Frequency of Abnormal Hemostasis Markers in Patients With COVID-19 (n = 180)

Hemostasis Abnormality	Total (%)	Men (n=74)	Women (n=106)
Elevated D-dimer	62.4±1.1	59.3±0.9	64.7±0.8
Hyperfibrinogenemia	48.5±0.8	45.2±0.7	50.9±0.6
Prolonged PT/APTT	27.1±1.5	29.5±1.3	25.4±1.1
Thrombocytopenia	31.3±1.4	33.8±1.2	29.2±1.0
Combined Abnormalities	41.8±0.9	44.1±0.9	40.1±0.7

The analysis of the research results enabled the formation of practical principles for early detection and effective anticoagulation-based therapy in patients with COVID-19-associated coagulopathy.

In the next stage of the study, we evaluated the effectiveness of early anticoagulant therapy (LMWH) combined with supportive treatment. Hemostasis markers were re-assessed after 14 days of therapy. Follow-up testing revealed measurable improvements in coagulation parameters, particularly in D-dimer levels, PT/APTT, and platelet counts.

After 14 days, D-dimer, fibrinogen, platelet count, and antithrombin III levels, as well as inflammatory markers such as ferritin, were evaluated and compared with baseline values. Statistically significant improvements were observed in most laboratory parameters following treatment ($p < 0.01$).

Table 2. Comparative Analysis of Hemostasis Markers Before and After Anticoagulation Therapy

Indicator	Mild COVID-19 (n=34)	Moderate COVID-19 (n=97)	Severe COVID-19 (n=49)
D-dimer (µg/ml)	0.68 → 0.42*	1.92 → 1.21*	3.87 → 2.41*
Fibrinogen (g/L)	4.1 → 3.6	5.8 → 4.7	6.2 → 4.8
Platelets (×10⁹/L)	186 → 208	159 → 174	134 → 152
PT (sec)	13.1 → 12.4	14.6 → 13.5	16.8 → 14.9
APTT (sec)	32.8 → 30.5	36.7 → 33.6	41.3 → 37.1

*Note: *$p < 0.001$

Additionally, clinical outcomes correlated strongly with laboratory improvements. Among patients with severe COVID-19, a 2-fold reduction in D-dimer levels was associated with decreased need for intensive care support and improved oxygenation parameters. Furthermore, normalization of fibrinogen and

PT/APTT values indicated better control of coagulation activation and reduced risk of progression to DIC.

TEG analysis demonstrated reductions in clot stiffness and hypercoagulability following anticoagulant therapy. Patients exhibiting improved TEG parameters showed faster clinical stabilization and shorter hospitalization duration.

The comparison of marker dynamics before and after treatment confirms that early and appropriately dosed anticoagulation plays a significant role in mitigating COVID-19-related coagulopathy, reducing thrombotic complications, and improving overall prognosis.

The figure shows that after 14 days of anticoagulation treatment, the frequency of hemostatic abnormalities—including elevated D-dimer, prolonged PT/APTT, and thrombocytopenia—decreased across all COVID-19 severity groups.

Conclusions

A comparative analysis of hemostatic parameters before and after anticoagulation therapy demonstrated a clear trend toward improvement, including reductions in D-dimer levels, normalization of PT/APTT, and partial recovery of platelet counts. Although some changes did not reach strict statistical significance ($p=0.05$), the overall dynamics strongly suggest that early therapeutic intervention plays a crucial role in controlling COVID-19–associated hypercoagulability. These findings highlight the clinical importance of timely identification and monitoring of hemostasis disorders, particularly in patients with heightened inflammatory responses and elevated thrombotic risk. The results also support the integration of routine coagulation profiling—along with global hemostasis testing such as TEG—into standard COVID-19 management protocols to guide individualized anticoagulation strategies. Ultimately, early detection and correction of coagulation abnormalities may significantly reduce the incidence of severe complications and improve patient outcomes in COVID-19.

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