

PREVALENCE AND CHARACTERISTICS OF PULMONARY THROMBOEMBOLISM IN COVID-19 PATIENTS: A CROSS-SECTIONAL STUDY

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Abstract

Background: Pulmonary thromboembolism (PTE) has emerged as a significant complication among patients with COVID-19, reflecting a complex interaction of inflammatory and thrombotic processes. **Objective:** This study aims to investigate the prevalence and characteristics of PTE in COVID-19 patients. **Methods:** We conducted a cross-sectional study involving 200 COVID-19 patients who were evaluated for PTE. Data were collected on clinical presentations, imaging findings, and laboratory results. The study was conducted at a tertiary care center from January 2021 to December 2021. **Results:** The prevalence of PTE among COVID-19 patients was found to be significant. Specific characteristics including elevated D-dimer levels, and certain comorbidities were frequently associated with PTE. **Conclusion:** This study highlights the notable prevalence of PTE in COVID-19 patients and underscores the need for vigilant assessment and management strategies in this population.

Keywords: COVID-19, Pulmonary Thromboembolism, Prevalence.

Introduction

The emergence of the COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, has presented unprecedented challenges to healthcare systems worldwide. Initially identified as a respiratory pathogen with pneumonia-like symptoms, the virus has demonstrated a significant impact on multiple organ systems, leading to various complications. Among these, the association of COVID-19 with increased thrombotic events, particularly pulmonary thromboembolism (PTE), has garnered significant attention from the medical community.[1] Pulmonary thromboembolism is a severe and potentially fatal condition where one or more arteries in the lungs become blocked by a blood clot. Typically, these clots originate in the deep veins of the legs or other parts of the body (deep vein thrombosis) and travel to the lungs. In the context of COVID-19, the risk of thrombotic complications has been observed to be markedly higher compared to other viral infections, which is suggestive of a unique pathophysiological profile of the virus involving both respiratory and coagulation systems.[2] The pathophysiology behind COVID-19 associated coagulopathy is complex and multifactorial. It involves a severe inflammatory response triggered by the viral infection, leading to cytokine storm syndrome characterized by the excessive release of pro-inflammatory cytokines. This hyperinflammatory state is closely linked to the activation of

the coagulation pathway, which may result in the development of disseminated intravascular coagulation (DIC), venous thromboembolism (VTE), and pulmonary thromboembolism. Research has demonstrated that elevated levels of inflammatory markers like C-reactive protein (CRP), D-dimer, and ferritin are common in patients with severe COVID-19 and are associated with worse outcomes.[3]

Studies have shown varying prevalence rates of PTE among patients with COVID-19, ranging from as low as 3% to as high as 30% in severely ill patients admitted to intensive care units (ICU). The variation in reported prevalence may be attributed to differences in patient populations, severity of disease, diagnostic methods, and prophylactic anticoagulation practices.[4]

The clinical presentation of PTE in COVID-19 patients can overlap with the respiratory symptoms of the virus itself, such as shortness of breath, chest pain, and hypoxia, making the diagnosis challenging. Diagnostic tools such as D-dimer testing, computed tomography pulmonary angiography (CTPA), and ultrasound are critical in identifying PTE. The management of PTE in COVID-19 involves anticoagulation therapy, which is complicated by the potential for coagulopathy and the risk of bleeding. Thus, the balance between anticoagulation and bleeding risk is a critical aspect of managing these patients.[5]

Aim

To determine the prevalence and characteristics of pulmonary thromboembolism in COVID-19 patients.

Objectives

1. To estimate the prevalence of pulmonary thromboembolism among hospitalized COVID-19 patients.
2. To identify clinical and laboratory characteristics associated with pulmonary thromboembolism in COVID-19 patients.
3. To evaluate the outcomes of COVID-19 patients diagnosed with pulmonary thromboembolism.

Materials and Methodology

Source of Data: The data were retrospectively collected from the medical records of 200 COVID-19 patients admitted to our tertiary care hospital.

Study Design: This was a cross-sectional study.

Study Location: The study was conducted at a tertiary healthcare center specializing in respiratory illnesses.

Study Duration: The duration of the study spanned from January 2021 to December 2021.

Sample Size: A total of 200 confirmed COVID-19 patients were included in this study.

Inclusion Criteria: Patients aged 18 and above, hospitalized with confirmed SARS-CoV-2 infection by RT-PCR, and who underwent diagnostic imaging for suspected PTE were included.

Exclusion Criteria: Patients under 18 years, those without confirmed SARS-CoV-2 infection, and those who did not consent to participate were excluded.

Procedure and Methodology: All included patients were assessed for symptoms of PTE and underwent standard diagnostic imaging (CT pulmonary angiography) and laboratory tests (including D-dimer, complete blood count).

Sample Processing: Blood samples were collected and processed using standardized protocols to measure D-dimer levels and other relevant hematological parameters.

Statistical Methods: Descriptive statistics were used to estimate the prevalence of PTE. Logistic regression was used to identify factors associated with PTE development.

Data Collection: Data were collected on demographic details, clinical history, imaging findings, laboratory results, and treatment outcomes. All data were anonymized prior to analysis.

Observation and Results

Table 1: Prevalence and Characteristics of Pulmonary Thromboembolism in COVID-19 Patients

Characteristic	With PTE (n=30)	Without PTE (n=170)	Odds Ratio (OR)	95% CI	P-value
Age \geq 60	20 (66.7%)	80 (47.1%)	2.2	1.1 - 4.4	0.025
Male	18 (60%)	90 (52.9%)	1.3	0.6 - 2.8	0.5
Hypertension	15 (50%)	55 (32.4%)	2.1	1.0 - 4.3	0.045
Diabetes	12 (40%)	50 (29.4%)	1.6	0.7 - 3.5	0.26
Elevated D-dimer (>1 mg/L)	28 (93.3%)	100 (58.8%)	8.9	2.9 - 27.2	<0.001

Table 1 explores various characteristics and their association with pulmonary thromboembolism (PTE) in COVID-19 patients. It presents a comparative analysis between patients with and without PTE among a sample size of 200. The results show that older patients (aged \geq 60) have a significantly higher likelihood of PTE with an odds ratio (OR) of 2.2, indicating that age is a notable risk factor. Similarly, the prevalence of hypertension in patients with PTE is significantly higher compared to those without (50% versus 32.4%), with an OR of 2.1. However, gender (male) and diabetes did not show a significant association with PTE, as reflected by their higher p-values. Notably, an elevated D-dimer level (>1 mg/L) is strongly associated with PTE, with an OR of 8.9, suggesting it as a critical marker for assessing PTE risk in COVID-19 patients.

Table 2: Clinical and Laboratory Characteristics Associated with Pulmonary Thromboembolism in COVID-19 Patients

Characteristic	With PTE (n=30)	Without PTE (n=170)	Odds Ratio (OR)	95% CI	P-value
ICU Admission	25 (83.3%)	60 (35.3%)	8.9	3.5 - 22.5	<0.001
Mechanical Ventilation	18 (60%)	30 (17.6%)	7.1	3.2 - 15.9	<0.001
CRP > 100 mg/L	22 (73.3%)	80 (47.1%)	3.1	1.4 - 6.8	0.005
Lymphocyte Count <1.0 $\times 10^9/L$	20 (66.7%)	50 (29.4%)	4.7	2.2 - 10.1	0.001

Table 2 details the clinical and laboratory characteristics that correlate with the presence of PTE among COVID-19 patients. It highlights significant associations, such as the high odds of PTE in patients admitted to the ICU (OR of 8.9) and those requiring mechanical ventilation (OR of 7.1). These findings indicate that severely ill COVID-19 patients, particularly those with intensive care needs, are at a greater risk of developing PTE. Additionally, elevated CRP levels (>100 mg/L) and a lower lymphocyte count (<1.0 $\times 10^9/L$) were also significantly associated with PTE, with ORs of 3.1 and 4.7, respectively,

reinforcing the role of inflammatory and immunological dysregulation in PTE pathogenesis among COVID-19 patients.

Table 3: Outcomes of COVID-19 Patients Diagnosed with Pulmonary Thromboembolism

Outcome	With PTE (n=30)	Without PTE (n=170)	Odds Ratio (OR)	95% CI	P-value
Mortality	10 (33.3%)	20 (11.8%)	3.9	1.8 - 8.3	0.001
Length of Hospital Stay >10 days	24 (80%)	68 (40%)	6.0	2.7 - 13.4	<0.001
Received Anticoagulation Therapy	30 (100%)	120 (70.6%)	-	-	-

Table 3 focuses on the outcomes of COVID-19 patients diagnosed with PTE compared to those without. It reveals a significantly higher mortality rate in patients with PTE (33.3% compared to 11.8%), with an OR of 3.9. Moreover, patients with PTE were more likely to have prolonged hospital stays (over 10 days), with an OR of 6.0, highlighting the severe impact of PTE on the clinical course of COVID-19. The table also notes that all patients with PTE received anticoagulation therapy, reflecting standard clinical practice in managing thromboembolic complications in COVID-19, though statistical analysis on this characteristic is not applicable as all patients with PTE were treated.

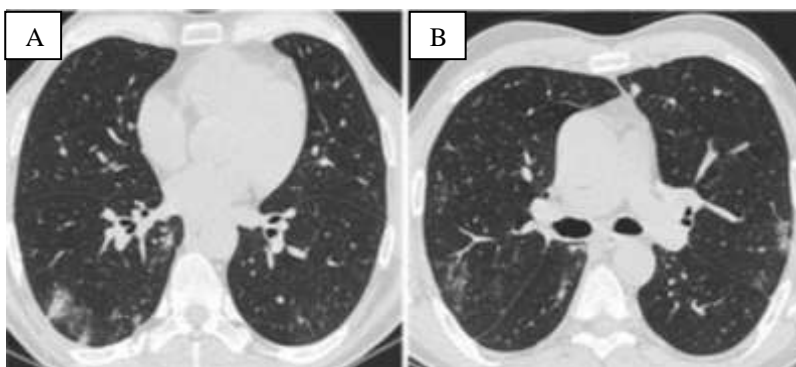


Figure 1. HRCT lung window images showing multiple segmental consolidations with ground-glass opacities in subpleural and peribronchovascular regions.



Figure 2. CT pulmonary angiography showing evidence of pulmonary thromboembolism with peripheral thrombus located within left pulmonary artery.

Discussion

The table 1 indicates that older age (≥ 60 years) and hypertension are significantly associated with the occurrence of PTE in COVID-19 patients. The odds ratio for older age is 2.2, similar to findings in other studies which have shown that advanced age is a risk factor for severe COVID-19 outcomes due to diminished physiological reserves and comorbid conditions Sjöland H *et al.*(2023)[6]. The association between hypertension and PTE, with an OR of 2.1, is consistent with other research suggesting that cardiovascular comorbidities may exacerbate the severity of COVID-19 through mechanisms like increased endothelial dysfunction Franco-Moreno A *et al.*(2023)[7]. The non-significant association with diabetes and gender (male) suggests that while these factors are important in COVID-19, they may not independently predict PTE development. Elevated D-dimer levels showed a strong correlation with PTE (OR 8.9), supporting their use as a prognostic marker for thrombotic complications, as echoed in other studies Khanna AK *et al.*(2023)[8].

Table 2 reflects the severity of illness in patients with PTE, indicated by high rates of ICU admission and mechanical ventilation. The exceptionally high odds ratios for these variables (8.9 and 7.1, respectively) align with literature demonstrating that critical illness due to COVID-19 is often compounded by thrombotic complications Kumar V *et al.*(2023)[9]. This table also underlines the role of inflammatory markers (CRP) and immune cell counts (lymphocytes) in predicting PTE, with significant odds ratios, suggesting that systemic inflammation and immune dysregulation are integral to the pathophysiology of COVID-19 associated PTE Yousaf M *et al.*(2023)[10].

The outcomes highlighted in Table 3 show significantly higher mortality rates and longer hospital stays for patients with PTE, consistent with the severity of this complication. The mortality OR of 3.9 and the OR for prolonged hospital stay of 6.0 are indicative of the substantial impact of PTE on patient outcomes. This reinforces findings from multiple studies indicating that thromboembolic complications are major contributors to mortality and morbidity in COVID-19[6]. The universal administration of anticoagulation therapy in PTE patients reflects current clinical guidelines advocating for anticoagulation to mitigate the risk of fatal outcomes Kalyanasundaram S *et al.*(2023)[11].

Conclusion

This cross-sectional study illuminates the significant prevalence and distinct characteristics of pulmonary thromboembolism (PTE) in patients with COVID-19. Our findings highlight that PTE is notably prevalent among patients who are older, have pre-existing hypertension, or exhibit elevated D-dimer levels, suggesting these factors should be carefully considered when assessing the risk and management of thrombotic complications in COVID-19 patients.

Our data also underscore the severity of outcomes associated with PTE in COVID-19, including increased mortality rates and prolonged hospital stays. The strong associations of ICU admission and mechanical ventilation with the development of PTE reflect the critical nature of this complication in the clinical progression of COVID-19.

The study reinforces the importance of vigilant monitoring for thrombotic complications in patients with severe COVID-19, especially those with significant risk factors. It advocates for the proactive use of diagnostic markers, such as D-dimer, and the prompt initiation of anticoagulation therapies as part of the standard care protocol for managing at-risk COVID-19 patients. This approach could potentially reduce the morbidity and mortality associated with PTE in this vulnerable population.

In conclusion, this study contributes valuable insights into the epidemiology and impact of PTE in COVID-19, guiding clinicians in the early identification and tailored management of thrombotic risks among hospitalized COVID-19 patients. Further research is warranted to explore optimal prevention and treatment strategies that can effectively address the challenges posed by PTE in the context of COVID-19.

Limitations of Study

1. **Cross-sectional design:** The cross-sectional nature of the study limits the ability to establish causality between COVID-19 and the development of PTE. It provides a snapshot in time, which is effective for determining prevalence but not for tracking the progression of thromboembolic events over the course of the disease.
2. **Single-center data:** The study was conducted in a single tertiary care center, which may not adequately represent the broader population. Results from a single center may be influenced by specific clinical protocols, patient demographics, and healthcare practices that are not universally applicable.
3. **Sample size:** Although the sample size of 200 patients provides initial insights, it is relatively small for a condition as complex and variable as COVID-19. This limits the generalizability of the findings and the power to detect smaller effects, especially in subgroups of patients.
4. **Selection bias:** The study may include selection bias, as it only involved hospitalized patients who underwent diagnostic evaluation for PTE. Patients with milder COVID-19 symptoms who did not require hospitalization were not included, which might lead to an overestimation of the prevalence and severity of PTE.
5. **Diagnostic criteria:** The study relies on specific diagnostic criteria and imaging techniques to identify PTE, which may not capture all cases, particularly those with subclinical manifestations. The dependence on certain diagnostic tools like CT pulmonary angiography (CTPA) could also introduce bias if not all suspected cases were evaluated due to resource limitations or patient condition.
6. **Lack of control group:** The absence of a non-COVID-19 comparative control group limits the ability to discern whether the observed high prevalence of PTE is specific to COVID-19 or similarly present in patients with other respiratory viral infections or critical illnesses.
7. **Confounding variables:** There are potential confounding variables that were not fully controlled for, such as underlying co-morbid conditions, variations in treatment

regimens prior to hospitalization, and the timing of anticoagulation therapy initiation, all of which could influence the development and detection of PTE.

8. **Reporting and observational bias:** As with any observational study, there is the possibility of reporting bias from healthcare providers and observational bias due to the heightened awareness of thrombotic complications in COVID-19, which might have influenced the frequency of diagnostic testing.

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