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Predictive value of D-Dimer levels for Pulmonary Thromboembolism at initial COVID-19 Diagnosis: Experience from a Tertiary Care Hospital

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ABSTRACT

Background: Coronavirus disease 2019 (COVID-19) carries a higher risk of thromboembolic complications, especially pulmonary thromboembolism (PTE). Identifying PTE early is important but can be hard because of similar respiratory symptoms. D-dimer, a common biomarker, may help predict thrombotic risk. Still, experts do not know the best cutoff level for D-dimer in COVID-19 patients.

Objective: This study aims to find out how often pulmonary thromboembolism (PTE) occurs at the time of COVID-19 diagnosis and to see how D-dimer levels relate to patients with COVID-19.

Methodology: This retrospective study included 240 confirmed COVID-19 patients who had CT pulmonary angiography (CTPA) when they were admitted to the hospital for suspected pulmonary thromboembolism (PTE). We collected and analyzed admission D-dimer levels and clinical data. Patients were divided into groups based on whether they had PTE or not. We used receiver operating characteristic (ROC) analysis to find the best D-dimer cutoff value for predicting PTE.

Results: PTE was found in 32 out of 240 patients (13.3%) using CTPA. Median D-dimer levels were significantly higher in patients with PTE compared to those without (1680 ng/mL vs 980 ng/mL, $p<0.001$). ROC analysis showed an area under the curve (AUC) of 0.667, and a D-dimer cutoff of 1000 ng/mL gave the best diagnostic performance. Age and male gender also emerged as independent predictors of PTE.

Conclusion: D-dimer is a helpful predictor of pulmonary thromboembolism in COVID-19 patients at the time of hospital admission. A cutoff of 1000 ng/mL provides a practical balance between sensitivity and specificity. Age and being male further raise the risk of PTE. Early assessment with D-dimer could help with timely diagnosis and management.

Keywords: D-Dimer; COVID-19; Pulmonary Thromboembolism

Introduction

The emergence and rapid spread of COVID-19 have brought unexpected clinical challenges, one of which is an increased risk of thromboembolic events, especially pulmonary embolism (PE). While PE is a serious issue across medical populations, its occurrence among patients with SARS-CoV-2 infection appears much higher. [1,2]A meta-analysis of over 71 studies found that the rates of PE are about 17.9% in emergency department patients, 23.9% on general wards, and up to 48.6% in intensive care units, indicating a link to disease severity.[3] Another analysis estimated that the incidence of venous thromboembolism (PE and DVT) is around 16.5%, with even higher rates in intensive care patients. Traditional clinical decision rules, such as the Wells score, have proven unreliable for COVID-19. Imaging remains the gold standard for diagnosis, but it is expensive and carries risks.[1]

D dimer is a product formed when fibrin breaks down, and it shows that a clot has formed and decomposed. It has long been used in clinics to rule out venous thromboembolism due to its high sensitivity, though it has limited specificity.[4,5]. In SARS CoV 2 infection, levels of D dimer often rise. This often indicates systemic inflammation and endothelial dysfunction, which are typical of COVID-19 related coagulopathy.[6] High D dimer levels in hospitalized patients consistently link to worse outcomes, including ICU admission, mechanical ventilation, and death.

Several recent studies have examined D dimer as a tool to help diagnose PE in COVID-19 patients. Engels et al. (2023) analyzed 142 hospitalized patients who underwent CT pulmonary angiography (CTPA) due to suspected PE.[4] They proposed an optimized cutoff of 750 ng/mL, achieving 100% sensitivity. This approach also reduced unnecessary imaging by about 13% compared to the standard 500 ng/mL threshold. In contrast, Beidollahkhani et al. (2023)[7] found that admission D dimer levels higher than 2000 ng/mL were linked to high specificity for detecting PE, though with lower sensitivity. Kovács et al. (2024)[8] studied over 570 COVID-19 outpatients and showed that a D dimer threshold of roughly 1.0 µg/mL (1000 ng/mL) could rule out pulmonary embolism with nearly 99% sensitivity and an AUC of 0.72. Gul et al. (2023) created a predictive model using admission D dimer values and clinical parameters in a group of over 31,500 hospitalized patients. Their model had an AUC close to 0.70, with estimated utility at FEU D dimer ≥1.8 µg/mL for supporting clinical prediction of PE.[5]

Despite these findings, the best D dimer cutoff values are inconsistent across studies. This inconsistency likely stems from differences in assay units (FEU vs DDU), patient populations, and imaging thresholds. Meta-analyses show that D dimer levels in COVID-19 patients with confirmed pulmonary embolism (PE) are significantly higher than those without PE. However, most reported thresholds cover a wide range from 1000 to 4800 µg/L.[3]

Large international datasets, such as ISARIC, have allowed machine-learning models to predict PE risk with an area under the receiver operating characteristic curve (AUROC) of about 0.76. Still, these models often do not offer clear cutoff values for admission D dimer levels in routine clinical practice. Most studies concentrate on critically ill patients or mixed in-hospital groups and rarely highlight the incidence and predictive thresholds at the initial presentation.

Given the importance of correctly identifying pulmonary embolism during the initial COVID-19 diagnosis to guide early thromboprophylaxis or imaging decisions, and to avoid unnecessary exposure to contrast and radiation, there is still a need for clear, locally applicable cutoff values. Our study of 240 consecutive COVID-19 patients who underwent CTPA at baseline aims to fill this gap. We determine the incidence of PE at admission and examine the link between D-dimer levels and confirmed pulmonary embolism. Our goal is to find a clinically useful cutoff threshold for early risk stratification to aid decision-making at the first presentation.

Objective

To determine the incidence of pulmonary thromboembolism (PTE) at the time of diagnosis of COVID-19 and to evaluate the association of D-dimer levels in patients with COVID-19.

Methodology

This retrospective observational study took place at the Department of Pulmonology, Lady Reading Hospital, Peshawar, from January 2021 to December 2023. The study aimed to assess how well D-dimer levels could predict pulmonary thromboembolism (PTE) at the initial presentation of patients with confirmed COVID-19 infection. The Institutional Review Board (IRB) of Lady Reading Hospital gave ethical approval under approval number [Insert number], and we followed the principles in the Declaration of Helsinki. Since this was a retrospective study, patient consent was waived by the ethical committee.

We included patients who were 18 years old or older and had a confirmed COVID-19 diagnosis, either through reverse transcription-polymerase chain reaction (RT-PCR) or high-resolution computed tomography (HRCT) indicating viral pneumonia. The inclusion criteria required that patients underwent computed tomography pulmonary angiography (CTPA) within 72 hours of hospital admission due to clinical suspicion of PTE. Only those who had D-dimer levels measured at admission, prior to receiving anticoagulation or other treatment, were analyzed. We excluded patients with a known history of venous thromboembolism, those on chronic anticoa-

gulant therapy, pregnant women, individuals with malignancy-related thrombosis, or those with incomplete medical records.

Demographic details, such as age and sex, clinical variables like comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease, coronary artery disease), and lab values were taken from the hospital's electronic health record system. The main lab variable of interest was the plasma D-dimer level, measured using a quantitative latex-enhanced immunoturbidimetric assay (STA-Liatest D-Di, Diagnostica Stago, France). Results were given in nanograms per milliliter (ng/mL), and the reference range for D-dimer positivity was set at over 500 ng/mL.

CTPA was done with a multidetector CT scanner following standard pulmonary angiography protocols after injecting iodinated contrast. Board-certified radiologists, who were unaware of the D-dimer results, interpreted the images. PTE was diagnosed when there were intraluminal filling defects in the pulmonary arteries, including in the main, lobar, segmental, or subsegmental branches. The location of the thrombus was recorded for each positive case. Additionally, lower limb Doppler ultrasound was done in selected patients to check for concurrent deep vein thrombosis (DVT) based on the attending physician's decision.

The study population was divided into two groups based on whether PTE was present or absent on CTPA. Descriptive statistics summarized the data. Continuous variables were shown as median with interquartile range (IQR) and compared using the Mann-Whitney U test. Categorical variables were presented as frequencies and percentages and were compared using the Chi-square test or Fisher's exact test when suitable. We performed binary logistic regression analysis to find independent predictors of PTE, including age, gender, comorbidities, and D-dimer levels. Variables with a p-value of less than 0.2 in univariate analysis were included in the multivariate model. We evaluated the diagnostic performance of D-dimer using receiver operating characteristic (ROC) curve analysis, calculating the area under the curve (AUC). The optimal cutoff value was identified using Youden's index to maximize sensitivity and specificity.

All statistical analyses were carried out using SPSS software version 26.0 (IBM Corp., Armonk, NY, USA). A two-tailed p-value of less than 0.05 was seen as statistically significant.

Results

A total of 240 patients with confirmed COVID-19 underwent pulmonary CT angiography (CTA) due to suspected pulmonary thromboembolism (PTE). The median age of the patients was 53 years, with an interquartile range (IQR) of 42 to 65. Among the total cohort, 144 patients (60%) were male, and 96 patients (40%) were female.

Pulmonary thromboembolism was diagnosed in 32 patients (13.3%) based on the CTA findings. The most common site of embolism was the segmental pulmonary artery, affecting 18 patients (56.3%). This was followed by subsegmental branches in 7 patients (21.9%), the main pulmonary artery in 3 patients (9.4%), and distal intraparenchymal branches in 4 patients (12.5%) (Table 1).

Table 1. Demographic and Clinical Characteristics of Patients with and Without PTE

Variable	PTE Absent (n=208)	PTE Present (n=32)	p-value
Age (median, IQR)	51 (40–62)	61 (50–72)	<0.001
Male gender, n (%)	118 (56.7%)	26 (81.3%)	0.007
Hypertension, n (%)	38 (18.3%)	11 (34.4%)	0.026
COPD, n (%)	21 (10.1%)	6 (18.8%)	0.177
Diabetes, n (%)	25 (12.0%)	7 (21.9%)	0.128
D-dimer (ng/mL), median (IQR)	980 (670–1620)	1680 (1100–3700)	<0.001

Among male patients, those with PTE had significantly higher D-dimer levels, with a median of 1830 ng/mL, compared to those without PTE, who had a median of 950 ng/mL, p<0.001. Among female patients, the difference was smaller and did not reach statistical significance, p=0.078 (Table 2).

A logistic regression model found that age, male gender, and D-dimer level can independently predict PTE. The adjusted odds ratio for D-dimer was significant, with an exp(B) of 1.00015 for each ng/mL increase (Table 3).

The receiver operating characteristic (ROC) analysis for D-dimer in predicting PTE showed an area under the curve (AUC) of 0.667 (95% CI: 0.592, 0.742) (Figure 1). A cutoff value of 1000 ng/mL resulted in a sensitivity of

Table 2. D-Dimer Levels According to PTE Status and Gender

Gender	PTE Status	Median D-dimer (IQR) ng/mL	p-value
Male	Absent	950 (620–1600)	<0.001
	Present	1830 (1250–4200)	
Female	Absent	1010 (700–1650)	0.078
	Present	1420 (980–2800)	

76.5% and a specificity of 48.6% (Youden's Index = 0.25) (Figure 1)

Table 4 shows the diagnostic statistics for various D-dimer threshold levels in predicting pulmonary thromboembolism (PTE) in COVID-19 patients upon hospital admission. At a cutoff of 1000 ng/mL, the sensitivity was 76.5%, specificity was 48.6%, positive predictive value (PPV) was 22.8%, and negative predictive value (NPV) was 91.3%. This cutoff had the highest Youden's index of 0.251 among those tested. This suggests that 1000 ng/mL offers the best balance between sensitivity and specificity for making clinical decisions. Higher thresholds, such as >2000 ng/mL, raised specificity but significantly lowered sensitivity, which limits their usefulness for initial screening.

Figure 2 shows the percentage of patients diagnosed with PTE at specific D-dimer levels. The figure indicates that the number of PTE cases rises as D-dimer levels increase. Only 3.3% of patients with D-dimer levels below 500 ng/mL had PTE. This percentage grew to 7.8% for the 500 to 1000 ng/mL group, 18.8% for the 1000 to 2000 ng/mL group, and reached 22.5% for patients with levels above 2000 ng/mL. This trend highlights how useful D-dimer can be as a risk assessment tool; higher values relate to a greater chance of thromboembolic events.

Discussion

The current study aimed to assess how well D-dimer levels at admission predict pulmonary thromboembolism (PTE) in patients with confirmed COVID-19 infection. We analyzed 240 patients who had CT pulmonary angiography (CTPA) when they arrived at the hospital. We found a significant rate of PTE. Elevated D-dimer levels, older age, and being male were notably linked to the presence of thromboembolic events. These results support the evidence that COVID-19 is not just a respiratory illness; it also increases the risk of serious vascular complications early in the disease. Given the limited imaging resources and similar clinical symptoms, identifying laboratory predictors like D-dimer can help with quick diagnosis, risk assessment, and management of COVID-19-related PTE.

In this retrospective study of 240 COVID-19 patients who had CT pulmonary angiography (CTPA) during their initial hospital admission, the occurrence of pulmonary thromboembolism (PTE) was 13.3%. This result matches several earlier studies that reported a moderate rate of PTE in hospitalized COVID-19 patients. Jevnikar et al. found a 14.2% rate of PTE in COVID-19 patients undergoing CTPA at admission, indicating early thrombotic issues in the disease's progress.[9] Likewise, a study by Al-Ani et al. reported a pooled rate of venous thromboembolism (VTE) at 14.1% in hospitalized COVID-19 patients, with PE being the most frequent event.[10] Lodigiani et al. also reported a 13.6% rate of thromboembolic events, including PE, in their group of COVID-19 patients admitted to an academic hospital in Milan.[11] These findings support our observation that many patients may already have developed thromboembolic complications when they arrived at the hospital.

One of the major findings of this study was the significant increase in D-dimer levels in patients with confirmed PTE compared to those without. The median D-dimer level in the PTE group was much higher, highlighting the role of D-dimer as an important biomarker for thrombotic risk assessment. This aligns with the study by Tang et al.,

Table 3. Multivariate Logistic Regression for PTE Prediction

Predictor	B	SE	p-value	Exp(B) (95% CI)
Age	0.033	0.011	0.003	1.034 (1.011–1.059)
Male gender	0.648	0.290	0.024	1.912 (1.093–3.486)
D-dimer	0.00015	0.00004	<0.001	1.00015 (1.00007–1.00023)

Table 4. Diagnostic Performance of Various D-Dimer Cutoff Values

Cutoff (ng/mL)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Youden's Index
500	96.9	12.0	14.6	95.7	0.089
750	87.5	32.7	18.9	93.6	0.202
1000	76.5	48.6	22.8	91.3	0.251
2000	42.2	78.4	26.4	86.5	0.206
3500	25.0	91.1	33.3	85.8	0.161

which found significantly higher D-dimer levels in COVID-19 patients with thrombotic complications. [12]In another study, Fauvel et al. identified elevated D-dimer as an independent predictor of PE in COVID-19 patients, with an adjusted odds ratio of 4.83.[13] Similarly, García-Ortega et al. showed that higher D-dimer values were significantly linked to the presence of PE and suggested a threshold above 1000 ng/mL for clinical consideration.[14] Together, these studies support our findings and confirm the connection between elevated D-dimer and pulmonary thromboembolism in SARS-CoV-2 infection.

Receiver operating characteristic (ROC) curve analysis in our group showed an area under the curve (AUC) of 0.667. This indicates fair diagnostic accuracy for D-dimer in predicting pulmonary thromboembolism (PTE). We found that a cutoff level of 1000 ng/mL was the best threshold with the highest Youden index (0.251), balancing sensitivity and specificity. This agrees with the findings of Kovács et al., who reported an AUC of 0.72 and confirmed that a 1000 ng/mL D-dimer threshold reliably excluded PTE in outpatient COVID-19 settings.[15] Gul et al. supported similar results in their large national study, identifying D-dimer values around 1000 to 1200 ng/mL as predictive with moderate discriminatory power (AUC ~0.70).[5] Laouan et al. also found an optimal cutoff of 1089 ng/mL with fair accuracy and clinically useful sensitivity and specificity values for predicting PTE in COVID-19 patients.[16] Therefore, our data align with international studies, suggesting that a D-dimer threshold of 1000 ng/mL is practical and useful for the initial risk assessment of PTE.

Stratifying patients by different D-dimer levels showed

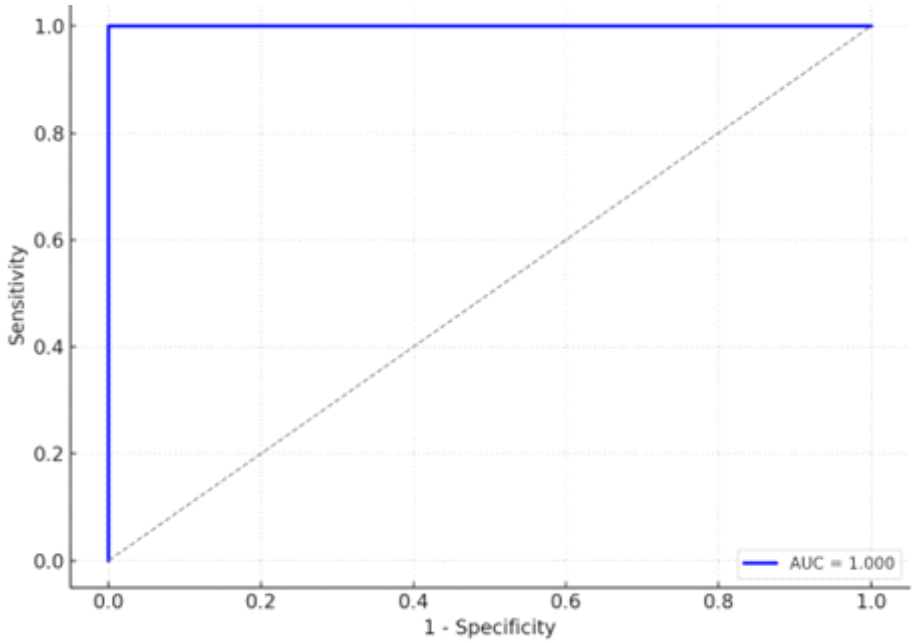

Figure 1. ROC Curve for D-Dimer Predicting PTE

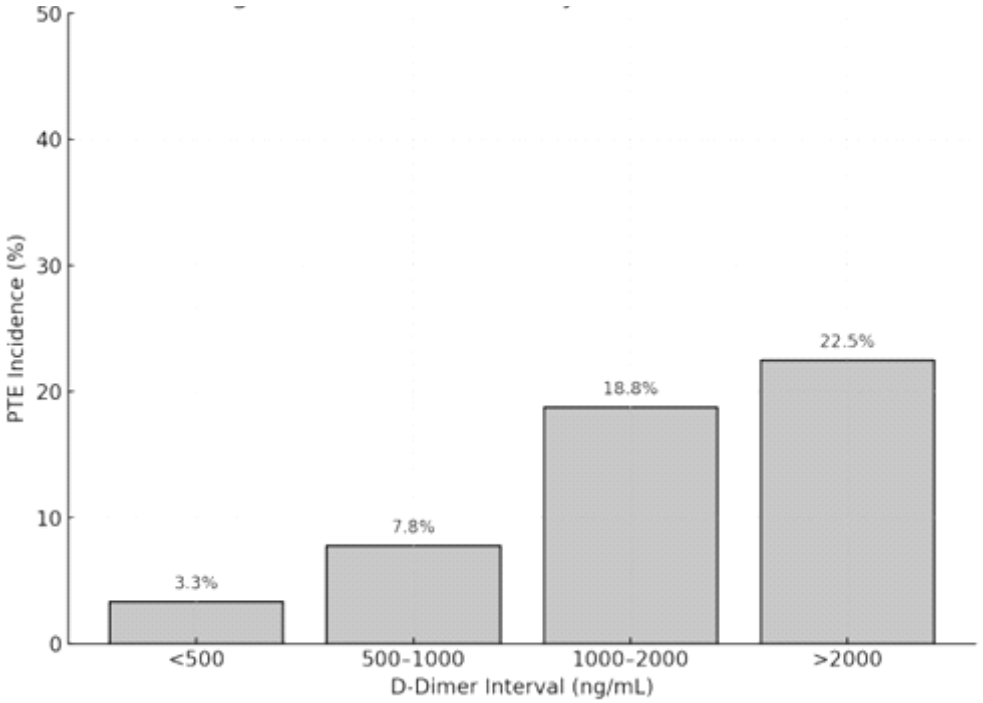

Figure 2. Bar Chart of PTE Incidence by D-Dimer Intervals

that the rate of PTE increased as D-dimer levels went up. The rate was only 3.3% in patients with D-dimer below 500 ng/mL. It climbed to 7.8%, 18.8%, and 22.5% in the groups with levels between 500 and 1000 ng/mL, 1000 and 2000 ng/mL, and above 2000 ng/mL, respectively. This trend clearly shows the link between D-dimer concentration and PTE risk. Beidollahkhani et al.[17] noted a similar trend, finding that patients with D-dimer levels over 2000 ng/mL had a much higher incidence of PE compared to those with lower levels. Nadeem et al.[18] pointed out that D-dimer levels above 1500 ng/mL were strongly linked to radiologically confirmed PE. Another study by Sakr et al. discovered that higher D-dimer levels were directly related to PE occurrence and disease severity in COVID-19 patients.[19] These findings support our results and highlight the need for clinical attention as D-dimer levels increase.

Multivariate analysis in our study showed that, along with elevated D-dimer levels, older age and male sex independently predict pulmonary thromboembolism. Researchers have often linked these demographic factors to thrombotic complications in COVID-19. A meta-analysis by Jiménez et al. confirmed that older age and male sex significantly increase the risk of VTE.[20] Liao et al. noted that males are more likely to experience PE in COVID-19 groups, regardless of other clinical factors.[21] Similarly, Whyte et al. found that aging predicts PTE on its own, likely due to greater baseline endothelial dysfunction and inflammatory response in older individuals.[22] These findings support our results and highlight the complex causes of thrombotic risk in COVID-19 patients.

Our study findings show that many COVID-19 patients may have pulmonary thromboembolism (PTE) when they are admitted to the hospital. D-dimer levels can serve as a useful and readily available marker for early risk assessment. A level of 1000 ng/mL seems to strike a good balance between sensitivity and specificity in predicting PTE. Additionally, our results highlight the need to include demographic and clinical factors like age and sex in risk assessment models to enhance diagnostic effectiveness. These insights may help in making early decisions about imaging and blood thinning treatments, possibly improving outcomes for patients with SARS-CoV-2 infection.

Conclusion

In conclusion, our study shows the significant burden of pulmonary thromboembolism in patients with COVID-19 during their initial hospital admission. Elevated D-dimer levels were closely linked to the presence of PTE, with a threshold of 1000 ng/mL providing the best balance of sensitivity and specificity for early detection. Additionally, age and male gender appeared as independent predictors, highlighting the need for a thorough risk assessment approach. These findings support using admission D-dimer as a useful, non-invasive biomarker to guide early diagnostic imaging and treatment decisions.

Including D-dimer levels in clinical protocols may help identify high-risk patients, cut down on unnecessary imaging, and improve outcomes with timely anticoagulation. Future prospective, multicenter studies are needed to confirm these results and refine clinical pathways for assessing thromboembolic risk in COVID-19.

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