e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(7); 481-485

Original Research Article

Serum D-Dimer as a Severity Predictor in Acute Exacerbation of Chronic Obstructive Pulmonary Disease: A Prospective Observational Study

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Received: 01-04-2026 / Revised: 15-05-2026 / Accepted: 21-06-2026

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Conflict of interest: Nil

Abstract

Background: Acute exacerbations of COPD (AECOPD) trigger systemic inflammation and coagulation activation. D-dimer, a fibrin degradation product, may serve as a biomarker of disease severity. This study evaluated the association of serum D-dimer levels with disease severity and hospital stay in AECOPD.

Methods: This prospective observational study was conducted at the Department of Respiratory Medicine, People's College of Medical Sciences & Research Centre, Bhopal, over two years (2023–2026). Fifty AECOPD patients were enrolled. Patients on anticoagulants or with DVT, PE, DIC, CAD, stroke, hematological disorders, autoimmune diseases, and pregnant women were excluded. D-dimer was measured by latex-enhanced immunoturbidimetry (≥500 ng/mL = elevated). Severity was classified as mild, moderate, or severe. Chi-square test was used for associations ($p \leq 0.05$ significant).

Results: Mean age was 64.61±9.27 years; 76% were male; 58% were current smokers. Elevated D-dimer was found in 42% of patients. Among those with elevated D-dimer, 24% had severe disease vs. 18% with normal D-dimer ($\chi^2=3.511$, $p=0.172$). Patients with elevated D-dimer showed no statistically significant association with hospital stay ($\chi^2=3.195$, $p=0.362$). All 50 patients (100%) were discharged alive.

Conclusion: D-dimer was elevated in 42% of AECOPD patients but was not significantly associated with disease severity ($p=0.172$) or hospital stay ($p=0.362$) in this cohort. D-dimer should be interpreted within the broader clinical context.

Keywords: D-dimer, AECOPD, COPD Exacerbation, Disease Severity, Biomarker, Hypercoagulability.

DOI: 10.25258/ijcpr.18.8.76

Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive respiratory disorder and the third leading cause of death worldwide [1]. In 2019, COPD accounted for approximately 3.23 million deaths globally [1], with the burden projected to persist through 2050 [2]. The GBD study documented the burden across 204 countries from 1990–2019 [3], and Chen et al. further characterized the global, regional, and national burden of COPD [4]. In India, the prevalence ranges from 2% to 22% in adults above 35 years of age [5], contributing significantly to the national healthcare economic burden [6]. Severe acute exacerbations accelerate lung function decline and increase mortality [8]. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2024 report emphasizes that exacerbation frequency and severity are the most important determinants of long-term prognosis [7]. COPD is increasingly recognized as a systemic inflammatory disorder, wherein pulmonary inflammation spills over into the systemic circulation [9]. This inflammatory state promotes activation of the coagulation cascade, leading to a hypercoagulable condition, particularly during acute exacerbations [10,11]. Coagulation markers have been studied as predictors for clinical events in COPD [12]. D-dimer, a specific degradation product of cross-linked fibrin, serves as a sensitive marker of coagulation activation and fibrinolytic activity [13]. Elevated D-dimer levels have been documented in

both stable COPD patients [14] and during acute exacerbations [13], and have been associated with disease progression [16], severity [17,18], and mortality [19,20,21,22].

However, the interpretation of D-dimer in AECOPD is complicated by the frequent coexistence of cardiovascular comorbidities such as PE, DVT, and CAD. The prevalence of PE in AECOPD has been reported to range from 16% to 29% [15,23], and several studies have examined adjusted D-dimer cut-offs for excluding PE in COPD patients [24,25]. The diagnostic value of D-dimer for PE detection in AECOPD has been questioned due to high false-positive rates [13]. While several studies have proposed D-dimer as a prognostic biomarker for mortality in AECOPD [21,22,23], and others have explored its utility in combination with other biomarkers [24], a critical gap remains in understanding whether D-dimer elevation is independently attributable to the respiratory exacerbation itself or driven by underlying thromboembolic or cardiovascular comorbidities. This study aimed to evaluate the association between serum D-dimer levels and disease severity, as well as length of hospital stay, in AECOPD patients with rigorous exclusion of major cardiovascular and thromboembolic confounders.

Materials and Methods

Study Design and Setting: This prospective observational study was conducted at the Department of Respiratory Medicine, People's College of Medical Sciences & Research Centre, Bhopal, over two years (2023–2026). Institutional Ethics Committee approval was obtained, and written informed consent was taken from all participants.

Inclusion and Exclusion Criteria: Patients presenting with AECOPD to the outpatient or inpatient department were included. Patients receiving anticoagulant therapy; with clinically evident or documented DVT, PE, DIC, known CAD, prior stroke, hematological disorders, autoimmune diseases; and pregnant women were excluded.

Clinical Assessment and Laboratory Investigations: Demographic data (age, gender, BMI), smoking status, presenting symptoms, vital signs, and comorbidities were recorded. Venous blood samples were collected within two hours of admission for complete blood count, CRP, renal function tests, and quantitative D-dimer estimation using latex-enhanced immunoturbidimetry (threshold: ≥500 ng/mL). Arterial blood gas analysis was performed for pH, $PaCO_2$, and PaO_2. All patients were managed per GOLD 2024 guidelines [7].

Severity Classification and Outcome Measures: Exacerbations were classified as mild, moderate, or severe according to the Classification of AECOPD Severity. Primary outcomes were the association between D-dimer levels and disease severity, and between D-dimer levels and length of hospital stay.

Statistical Analysis: Data were analyzed using SPSS version 22. Kolmogorov–Smirnov test assessed normality. Chi-square test evaluated associations between categorical variables. Independent-samples t-test compared continuous variables. $P \leq 0.05$ was considered significant.

Results

A total of 50 patients were included in the study, with a mean age of 64.61 ± 9.27 years. The study population showed a marked male predominance, with 38 (76%) males and 12 (24%) females. Regarding smoking status, 29 (58%) were current smokers, 12 (24%) were ex-smokers, and 9 (18%) had never smoked. Based on BMI, 12 (24%) patients were underweight, 14 (28%) had normal BMI, 11 (22%) were overweight, and 13 (26%) were obese. Cough was the most frequent clinical symptom, reported in 21 (42%) patients, followed by fever in 9 (18%), fatigue and diarrhea in 8 (16%) patients each, and anorexia in 7 (14%). Hypertension was the most common comorbidity (22%), followed by diabetes mellitus (18%), asthma (6%), and malignant tumor (4%) (Table 1).

Arterial blood gas analysis demonstrated a mean pH of 7.35 ± 0.06, $PaCO_2$ of 48.5 ± 8.2 mmHg, and PaO_2 of 62.3 ± 12.7 mmHg. The findings indicated a tendency toward hypercapnia and mild hypoxemia among the study participants (Table 2). Regarding disease severity, 11 (22%) patients had mild disease, 18 (36%) had moderate disease, and 21 (42%) had severe disease, with severe disease being the most common category (Table 3).

Serum D-dimer levels were elevated (≥500 ng/mL) in 21 (42%) patients, whereas 29 (58%) had normal levels (<500 ng/mL). The observed D-dimer range was 185–1120 ng/mL (Table 4). Severe disease was present in 12 (24%) patients with elevated D-dimer compared with 9 (18%) patients with normal D-dimer levels. However, the association between D-dimer level and disease severity was not statistically significant ($\chi^2 = 3.511$, $p = 0.172$) (Table 5).

With regard to hospital stay, 10 (20%) patients with elevated D-dimer levels required hospitalization for 10–15 days compared with 8 (16%) patients with normal D-dimer levels. The association between D-dimer level and hospital stay was not statistically significant ($\chi^2 = 3.195$, $p = 0.362$). The mean duration of hospital stay was 7.83 ± 3.74 days (Table 6). All 50 (100%) patients were discharged alive, with no in-hospital mortality.

Table 1: Demographic and clinical characteristics of the study participants (n = 50)

Variable	n (%) / Mean ± SD
Age (years)	**64.61 ± 9.27**
Gender	
Male	38 (76%)
Female	12 (24%)
Smoking status	
Current smoker	29 (58%)
Ex-smoker	12 (24%)
Never smoker	9 (18%)
Body mass index (BMI)	
Underweight (<18.5 kg/m²)	12 (24%)
Normal (18.5–24.9 kg/m²)	14 (28%)
Overweight (25.0–29.9 kg/m²)	11 (22%)
Obese (≥30 kg/m²)	13 (26%)
Clinical symptoms	
Cough	21 (42%)
Fever	9 (18%)
Fatigue	8 (16%)
Diarrhea	8 (16%)
Anorexia	7 (14%)
Comorbidities	
Hypertension	11 (22%)
Diabetes mellitus	9 (18%)
Asthma	3 (6%)
Malignant tumor	2 (4%)

Table 2: Arterial blood gas parameters among study participants (n = 50)

Parameter	Mean ± SD	Reference Range
pH	7.35 ± 0.06	7.35–7.45
$PaCO_2$ (mmHg)	48.5 ± 8.2	35–45
PaO_2 (mmHg)	62.3 ± 12.7	80–100

Table 3: Distribution of disease severity among study participants (n = 50)

Disease severity	n	%
Mild	11	22
Moderate	18	36
Severe	21	42
Total	**50**	**100**

Table 4: Distribution of serum D-dimer levels among study participants (n = 50)

D-dimer level	n	%
Normal (<500 ng/mL)	29	58
Elevated (≥500 ng/mL)	21	42
Total	**50**	**100**

Range of D-dimer: 185–1120 ng/mL.

Table 5: Association between serum D-dimer levels and disease severity (n = 50)

Disease severity	D-dimer <500 ng/mL n (%)	D-dimer ≥500 ng/mL n (%)	Total n (%)
Mild	8 (16%)	3 (6%)	11 (22%)
Moderate	12 (24%)	6 (12%)	18 (36%)
Severe	9 (18%)	12 (24%)	21 (42%)
Total	**29 (58%)**	**21 (42%)**	**50 (100%)**

$\chi^2 = 3.511$; p = 0.172 (Not significant)

Table 6: Association between serum D-dimer levels and length of hospital stay (n = 50)

Hospital stay (days)	D-dimer <500 ng/mL n (%)	D-dimer ≥500 ng/mL n (%)	Total n (%)
1–3	7 (14%)	3 (6%)	10 (20%)
4–6	10 (20%)	4 (8%)	14 (28%)
7–9	4 (8%)	4 (8%)	8 (16%)
10–15	8 (16%)	10 (20%)	18 (36%)
Total	**29 (58%)**	**21 (42%)**	**50 (100%)**

$\chi^2 = 3.195$; p = 0.362 (Not significant) Mean hospital stay = 7.83 ± 3.74 days

Discussion

Our finding of 42% D-dimer elevation in AECOPD is consistent with existing literature reporting 29–57% elevation [13]. D-dimer levels have also been found to be elevated in stable COPD patients compared to controls [14], and D-dimer has been explored as a biomarker for COPD progression [16]. The underlying mechanism involves systemic inflammation triggering coagulation cascade activation, as demonstrated by Ashitani et al. [10], who documented elevated procoagulant and fibrinolytic markers in COPD patients. The comprehensive review by Unlu et al. [11] confirmed that COPD patients exhibit higher D-dimer and von Willebrand factor levels, which are further amplified during exacerbations. Husebø et al. [12] further studied coagulation markers as predictors for clinical events in COPD.

Although a higher proportion of patients with elevated D-dimer had severe disease (24% vs 18%), this association did not reach statistical significance (p=0.172). This finding contrasts with studies by Khan et al. [17] and Alvi et al. [18], which reported significant associations between D-dimer and exacerbation severity, length of stay, and mortality. Similarly, Fruchter et al. [19] found D-dimer to be an independent predictor of in-hospital mortality, and Hu et al. [20] demonstrated its prognostic value for both in-hospital and 1-year mortality in AECOPD. Aydin et al. [21] showed that the D-dimer/fibrinogen ratio and recurrent exacerbations predicted 90-day mortality, and Reid et al. [22] documented elevated D-dimer levels in end-stage COPD with hypercapnia.

A critical distinction is our study's exclusion of clinically evident or documented cardiovascular and thromboembolic conditions (CAD, stroke, DVT, PE, DIC). The prevalence of PE in AECOPD ranges from 16% to 29% [15,23], and patients with PE typically have markedly elevated D-dimer levels. Akpinar et al. [24] questioned whether the D-dimer cut-off should be elevated to exclude PE in AECOPD, and AbdelHalim and AboElNaga [25] proposed a new D-dimer cut-off value for PE detection in AECOPD. Studies that do not exclude PE and other thromboembolic conditions may observe higher D-dimer values that are actually driven by these comorbidities rather than the respiratory exacerbation alone.

The 100% in-hospital survival rate in our cohort is noteworthy. Fruchter et al. [19] reported D-dimer as a mortality predictor in AECOPD. However, because our cohort had only 50 patients and no mortality events, mortality predictors could not be assessed. The absence of mortality events also limits comparison with studies evaluating D-dimer as a mortality biomarker. Recent studies suggest multi-biomarker approaches may offer superior predictive value: Zhang et al. [26] demonstrated that D-dimer combined with the BAP-65 score improved prediction of ICU admission in AECOPD. The economic burden of COPD management, as highlighted by Rajpal et al. [6], underscores the need for accurate and cost-effective biomarkers.

Limitations include small sample size (50 patients), single-center design, clinical rather than systematic CTPA-based exclusion of PE, lack of long-term follow-up, and single D-dimer measurement at admission only.

Conclusion

Serum D-dimer was elevated in 42% of AECOPD patients but was not significantly associated with disease severity (p=0.172) or hospital stay (p=0.362) in this cohort. No in-hospital mortality was observed; however, the small sample size and absence of mortality events preclude assessment of mortality predictors. D-dimer should be interpreted within the broader clinical context, and markedly elevated levels should prompt evaluation for thromboembolic disease.

Future research with larger cohorts and multi-biomarker strategies is recommended.

Acknowledgement: The authors thank the Department of Respiratory Medicine and laboratory staff at People's College of Medical Sciences & Research Centre, Bhopal, for their support.

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