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ORIGINAL ARTICLE

Prothrombotic State in Patients of Chronic Obstructive Pulmonary Disease with Acute Exacerbation

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Abstract

Background: Knowledge of COPD evolved towards growing recognition of a systemic component of the disease and the role of its comorbidities. Although chronic obstructive pulmonary disease (COPD) is not a high-risk factor for pulmonary embolism (PE), acute exacerbations of chronic obstructive pulmonary disease (AECOPD) complicated with PE occur in numerous patients. AECOPD is often complicated with respiratory failure. In the majority of patients, due to hypoxemia and carbon dioxide retention the blood is in a hypercoagulable or prothrombotic state. Venous thromboembolism (VTE) is also a common threat to hospitalized COPD patients. In a meta-analysis, pulmonary embolism prevalence was estimated to affect 20% of subjects with COPD exacerbation, whereas deep vein thrombosis was detected in 12.4% of those patients. In the present study, D-dimer, Fibrinogen, Mean Platelet Volume and Hematocrit were used as markers of the prothrombotic state in patients of COPD presenting with acute exacerbation. The evidence of thromboembolism was seen by imaging like CT-pulmonary angiography and ultrasound Doppler of lower limb. The study also analysed effect of Low Molecular Weight Heparin on preventing thromboembolism. **Methodology:** Forty-four (44) patients of acute exacerbation of COPD were prescribed a standardized treatment regimen. All patient's D dimer, fibrinogen, haematocrit and mean platelet volume were measured within 48 hours of admission. Every alternate patient was given LMWH, Enoxaparin for 6 days irrespective of their thrombotic state. All patients in the study were subjected to venous doppler bilateral lower limb on day 7 and after 3 months and CT pulmonary angiography at 3 months or during the time of development of symptoms of suspected Pulmonary Embolism. **Results:** The D Dimer level was elevated in 35 (79.5%) out of 44 patients with value above 250ng/ml. 10 patients (22.7%) had fibrinogen values greater than 500 mg/dL. The mean hematocrit value was 47% with 6 patients had haematocrit of >52%. The values of D-Dimer and fibrinogen decreased on the 7th day in both groups. The post-treatment means value of D-Dimer and fibrinogen decreased in both the groups; however, it was not significantly statistically. One patient was reported to have chronic PTE in CT pulmonary angiography done at 3rd month. He belonged to the control group, hence had not received LMWH as treatment. **Conclusions:** Among the prothrombotic markers, D-Dimer was significantly elevated in the majority. No significant change in prothrombotic markers was observed in patients of COPD with acute exacerbation receiving low molecular weight heparin in addition to conventional treatment. One patient witnessed a thromboembolic event in the form of pulmonary embolism and had elevated D-Dimer, Fibrinogen, and hematocrit levels and had received conventional treatment.

Key words: Acute exacerbations of chronic obstructive pulmonary disease, D-Dimer, Fibrinogen, Hematocrit, CT pulmonary angiography

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Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a disease of increasing public health importance around the world. COPD is currently the fourth leading cause of death in the world but is projected to be the 3rd leading cause of death by 2020 [1]. COPD is a leading cause of long-term illness and death globally, with numerous individuals enduring the disease for many years and ultimately dying prematurely due to the condition or its associated complications. Globally, the COPD burden is projected to increase in the coming decades because of continued exposure to COPD risk factors and aging of the population. It is well known that COPD is a syndrome of progressive airflow limitation caused by chronic inflammation of the airways and lung parenchyma, but it also produces significant systemic consequences. The role of systemic inflammation as evidenced by the rise in inflammatory markers is now being increasingly recognized to play an important role in systemic effects. The relationship between acute exacerbations of COPD (AECOPD) and pulmonary embolism (PE) has been an important subject of research. The pathophysiological changes in COPD are as follows: i) reconstruction of the pulmonary

vascular bed: extensive contraction and arterial hypertension caused by long-term hypoxia, vascular intimal hyperplasia, and vascular fibrosis and occlusion; and ii) blood hypercoagulability: blood stasis caused by increased erythrocyte formation due to long-term hypoxia, vascular endothelial cell dysfunction, pulmonary heart disease combined with right ventricular dysfunction, dependence on corticosteroids and increased concentrations of blood-clotting substances. These changes cause venous blood stasis, vein endothelial injury, and blood hypercoagulability (the three elements of Virchow's triad), leading to the formation of the prothrombotic state (PTS). AECOPD is often complicated with respiratory failure. In the majority of patients, due to hypoxemia and carbon dioxide retention [2-4] the blood is in a hypercoagulable or PTS state, with the formation of small pulmonary artery thrombi leading to a poor prognosis [5-6]. Fibrinogen is a glycoprotein synthesized by the liver. Agnelli et al [11] indicated that an increased fibrinogen level was an important risk factor for thrombosis and cardiovascular diseases. D dimer is the specific degradation product of cross linked fibrin and is used as a molecular marker of hypercoagulation and secondary increased fibrinolytic activity [7-8].

It is known that platelets play a major role in inflammation as in thrombosis. Mean platelet volume disturbances reflect changes in either the level of platelet stimulation or the rate of platelet production. Moreover, mean platelet volume has been used as an indicator of platelet function for inflammatory diseases, and because inflammation plays a crucial role in COPD, alterations in platelet activity and consequently in the mean platelet volume are expected [9-11].

Materials and Methods

Study Design

This was a randomized controlled study carried out over a period of one year in the Department of Medicine, Maulana Azad Medical College, and associated Lok Nayak Hospital, New Delhi, India, after obtaining clearance from the Institutional Ethics Committee.

Inclusion Criteria

Patients of COPD with acute exacerbation (as defined by GOLD criteria) (1), aged e" 35 years. Acute exacerbation of COPD is defined as an acute event characterized by worsening of the patient's respiratory symptoms that are beyond the normal day to day variations and requires a change in the medication of patients.

Exclusion Criteria

Known cases of hypercoagulable states, coronary artery disease, pregnant women, past history of myocardial infarction, a previously diagnosed case of other chronic respiratory diseases, chronic kidney disease, chronic liver disease.

Methodology

A total of 44 patients of COPD were enrolled in this study. Informed consent was obtained from all patients. These patients were subjected to complete history and physical examination and particulars of the patients such as name, age, sex, pack-years of smoking, pre-existing comorbidities, etc. were noted in a pre-structured proforma. Chest X-Ray and ECG were done. A series of hematological and biochemical investigations i.e. hemogram, liver function test, kidney function test, and arterial blood gas analysis were carried out. Also, D-Dimer, Fibrinogen, Mean Platelet Volume, and Haematocrit were observed in all 44 patients within 48 hours of admission.

Of the 44 patients, 22 patients were given low molecular weight heparin 0.4ml subcutaneous once a day for 6 days irrespective of the prothrombotic markers. Bilateral lower limb venous doppler for all patients was done on day 7 and at 3rd month and CT pulmonary angiography was done on 3rd month. Thus, the prothrombotic markers were studied for all 44 patients, and the role of anticoagulation in preventing any thromboembolic event was observed.

Statistical Analysis

The data was analyzed using IBM SPSS version 25.0 software. The analysis of quantitative variables was conducted using the mean, standard deviation (SD), median, and other relevant measures. The association between two qualitative variables was done using Chi-square test while that between two quantitative variables was done using the Pearson correlation test. A P- value of & lt; 0.05 was considered significant.

Observations and Results

Demographic Characteristics

The majority of the study population was in the age group of 50-70 years. The study population had an average age of 64.7 years. The mean of males was 65 years and that of females was 62 years. Approximately 84% of the patients in the study were males while 15% were females.

Smoking Habits

Out of 44 patients, 39 were either bidi or cigarette smoker's majority being bidi smokers. The remaining were exposed to chulha smoke, all of them being females.

Among bidi/cigarette smokers: Mean pack years 36.38 ± 4.95 years

Among chulha smoke exposure: Mean exposure 15.6 ± 3.7 years.

Comorbidities

14 Out of 44 patients had comorbidity. Out of 14, all of them either had Type2 DM or Hypertension and one among them had both.

Prothrombotic Markers

Since the values observed for D-dimer had a skewed distribution, the median value was also calculated which was 990ng/ml (Range:190-5340 ng/ml).

Thromboembolic Event

None of the study population had any evidence of DVT on the 7th day and 3rd month after admission. One patient had evidence of chronic PTE diagnosed at 3rd month by CT pulmonary angiography.

Discussion

This study was undertaken in the Department of Medicine of Lok Nayak hospital, Maulana Azad Medical College, New Delhi. A total of 44 patients of COPD in acute exacerbation were enrolled in the study after informed valid consent. Based on previous studies, the sample size was calculated to be 44 (22 in each group) using OpenEpi, Version 3.

Age Distribution

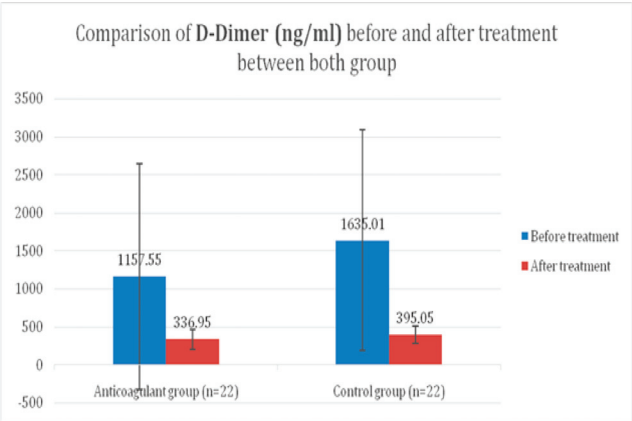
The mean age of males was 65.19 years with a standard deviation of 7.3 years. The mean age of females was 62.57 years with a standard deviation of 9.36 years. The age distribution found in this

Table 1: Blood coagulation profile of study subjects (44)

	D-DIMER (ng/ml)	FIBRINOGEN (mg/dl)	Haematocrit (%)	MPV (fL)
Mean	1396.27	422.93	47.002	8.56
SD	1469.656	126.839	4.2020	1.44

Table 2: Comparisons of blood coagulation state of the two groups of patients before and after treatment.

	Anticoagulant group (n=22)		Control group (n=22)		P-value between groups
	Mean	SD	Mean	SD	
MPV (fL)					
Before treatment	8.56	1.48	8.55	1.43	0.67
After treatment	8.31	0.93	8.54	0.94	0.57
P-value between before and after treatment within the group	0.07		0.97		
Haematocrit (%)					
Before treatment	46.09	3.37	47.91	4.80	0.27
After treatment	45.45	3.22	46.85	4.43	0.41
P value between before and after treatment	<0.001		<0.001		
	Anticoagulant group (n=22)		**Control group (n=22)**		**P-value between groups**
	Mean	**SD**	**Mean**	**SD**	
D-Dimer (ng/ml)					
Before treatment	1157.55	1484.97	1635.01	1448.46	0.12
After treatment	336.95	132.61	395.05	118.96	0.08
P value between before and after treatment within group	<0.001		<0.001		
Fibrinogen (mg/dl)					
Before treatment	413.64	146.27	432.23	106.60	0.48
After treatment	275.09	73.15	298.18	67.49	0.19
P value between before and after treatment	<0.001		<0.001		



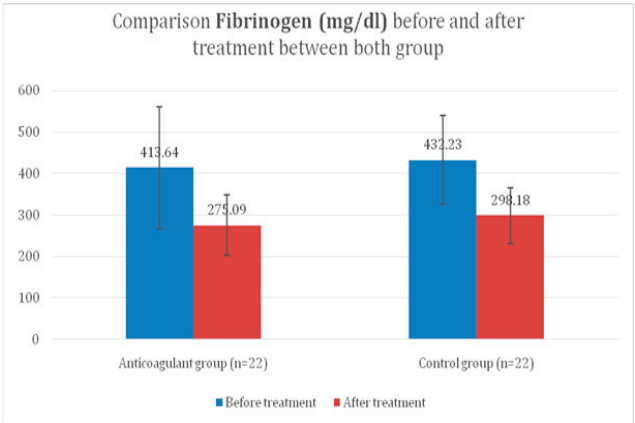


Table 3: Comparisons of arterial blood gas indicators of the two groups before and after treatment

	Anticoagulant group (n=22)		Control group (n=22)		P-value between groups
	Mean	SD	Mean	SD	
PaO_2					
Before treatment	64.42	29.75	65.05	19.85	0.61
After treatment	87.47	3.15	86.05	3.84	0.27
P value between before and after treatment	<0.01		<0.01		
$PaCO_2$					
Before treatment	59.68	15.51	68.80	19.79	0.10
After treatment	50.02	6.24	53.28	6.82	0.11
P value between before and after treatment	<0.001		<0.001		
$3SaO_2$					
Before treatment	88.73	11.57	87.73	7.47	0.24
After treatment	94.71	2.58	93.85	2.74	0.24
P value between before and after treatment	<0.001		<0.001		

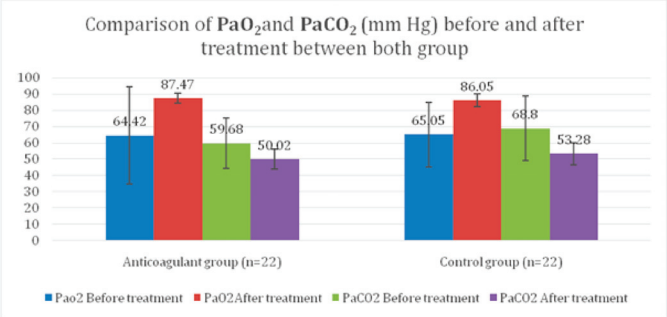


Table 4: Comparisons of blood coagulation state of the two groups of patients before and after treatment

	Intubated (n=9)	
	Mean	SD
D-Dimer (ng/ml)		
Before treatment	2751.22	1989.61
After treatment	455.56	121.13
Fibrinogen (mg/dl)		
Before treatment	467.56	116.47
After treatment	337.0	58.92
	Intubated (n=9)	
	Mean	**SD**
MPV (fL)		
Before treatment	8.48	1.29
After treatment	8.58	1.08
Haematocrit (%)		
Before treatment	49.36	5.80
After treatment	48.18	4.80

study group is similar to previous studies. A study conducted by Jain et al [12] among 702 patients of COPD, the mean age of the patients was 60.61 ± 10.36 years. Another study conducted by Ashitani et al [4] the mean age was found to be 72.6 ± 5.2 years. Mean age was found to be 68.3 ± 3.9 years and 62.3 ± 7.92 years in a study conducted by Cella et al [13] and Zhang et al [14]. Thus the age distribution observed in this study is unvarying with the previous studies.

Gender

The study population comprised predominantly of males. Around 84% were males and 15.9% were females in the study population. In a study conducted by Jain et al [12], 70.2% were males and 29.8% were females. As the smoking habit is more common in males, COPD is more prevalent among males. The prevalence of chronic obstructive pulmonary disease (COPD) in women is increasing, as is hospitalization for COPD. Increased tobacco use in women likely explains some of the increase in the prevalence of COPD in women, but evidence suggests that women might be more vulnerable to lung function impairment caused by smoking, experience more severe shortness of breath, and have a poorer overall health status compared to men with equivalent tobacco exposure. Non- smokers with COPD are also more likely to be female.

Smoking

Among 44 patients 88% were either bidi or cigarette smoker majority being males. Most of them were bidi smokers. The remaining 11.6% had chulha smoke exposure, all of them being female. Although smoking (tobacco consumption) is widely recognized as the most important risk factor for COPD, it is now also recognized that a substantial proportion of COPD cases (one quarter to one-third of all cases) cannot be explained only by smoking, and the disease also occurs in non-smokers. It has been suggested that the interaction of other risk factors, such as biomass exposure, with smoking, might further increase the risk of COPD. The PUMA study reported that individuals exposed to household biomass smoke are twice as likely to develop COPD than unexposed people [14]. In this study, among bidi/cigarette smokers, mean pack-years was found to be 36.38 ± 4.95 years and among chulha smoke exposure mean duration of exposure was 15.6 ± 3.7 years. In PUMA study, subjects with COPD had an average of 44 pack-years of tobacco smoking and 12 years of biomass exposure [15].

Comorbidities

Chronic obstructive pulmonary disease (COPD) is frequently associated with comorbid conditions such as cardiovascular diseases, diabetes, hypertension, osteoporosis, and mental health disorders. However, the prevalence of these comorbidities varies significantly across studies. In our study we excluded chronic kidney disease as inflammatory and prothrombotic markers are elevated in mild to moderate renal disease. We excluded chronic liver disease as they have baseline coagulation abnormalities hence giving false results. Patients with known coronary artery disease were excluded from the study due to their use of antiplatelet therapy, which could affect the results. Among the study group of 44 participants, approximately 68% did not have any comorbidities. Of the remaining individuals, the most common comorbid conditions were hypertension and Type 2 diabetes mellitus, observed in 15.9% and 13.6% of the group, respectively. Similarly, in a study involving 270 hospitalized COPD patients, Antonelli Incalzi and colleagues identified hypertension in 28%, diabetes in 14%, and ischemic heart disease in 10% [16].

Pulmonary embolism (PE) appears to be a more prevalent comorbidity in COPD than previously recognized, though current data remains limited and somewhat inconsistent. Diagnosing PE in COPD patients is challenging because the primary symptoms of PE often overlap with those of a COPD exacerbation. In one study of 211 consecutive patients admitted for severe COPD exacerbations of unknown origin, spiral CT or ultrasonography revealed PE in 25% of cases, as reported by Tillie-Leblond and colleagues [17]. Conversely, Rutschmann and collaborators found a low incidence of PE in a study of 123 consecutive patients admitted for acute COPD exacerbations. PE was identified in 6.2% of patients with clinical suspicion and only 1.3% of those with low suspicion [18].

ABG analysis:

The mean pO_2 in the study group was 64.73 mm Hg and mean pCO_2 was 64.24 mm Hg with a mean pH of 7.33 indicating type 2 respiratory failure with respiratory acidosis. Arterial blood gas findings in COPD are non-specific but are characterized by hypoxemia and hypercapnia, with elevated bicarbonate indicative of chronic metabolic correction of respiratory acidosis. In a case report of 3 patients with known COPD complicated by PE, Lipmann et al [19] suggested a drop in $PaCO_2$ of 10mmHg or more in otherwise previously hypercapnic COPD patients as indicative of thromboembolism. On the other hand, Lesser et al [20] reported 108 patients presenting with a history of COPD and newly diagnosed PE to have no difference in the reduction in $PaCO_2$, despite prior hypercapnia on arterial blood gas. But old ABG analysis of the study group could not be traced. The correction of hypoxemia with oxygen or positive pressure flow may support the diagnosis of COPD, while major pulmonary embolism with an intrapulmonary or intracardiac shunt may be resistant to correction. In our study group, post-treatment ABG revealed a correction of hypoxemia. Thus, ABG data alone or in combination with other clinical data are not useful in the assessment of suspected PE.

Prothrombotic State in COPD

Here we analyzed the blood coagulation profile of the patients which included D-Dimer, Fibrinogen, Haematocrit, and mean platelet volume.

D-Dimer

Out of 44 patients, 35 of them (79.5%) had a D-Dimer value above 250ng/ml which is the normal value. In our study group mean D-dimer value was 1396.27 ng/ml with a high standard deviation of 1469 ng/ml, due to a small sample size and skewed distribution. The median D-Dimer found in this group was 929ng/ml, with the lowest value being 190ng/ml and the highest being 5340ng/ml. In a similar study conducted by Song et al [21] on 30 patients presenting with acute exacerbation, the D-dimer mean value was 3600ng/ml. In another study conducted by Zhang et al [14], the median of D-dimer in the exacerbated COPD patients was 2839 ng/ml. Our study population had a large variation in D-Dimer values hence not consistent with similar studies. D-Dimer is a specific degradation product formed by the hydrolysis of cross-linked fibrin by plasmin and it is the smallest peptide generated by cross-linked fibrin degradation. Due to good stability, high sensitivity, and strong specificity in plasma, D-Dimer has been recognized as a mark of thrombosis. However, D-dimer is also an acute-phase reactant whose production stimulates high levels of cytokines, so D-dimer can be served as an inflammatory marker and COPD is a chronic inflammatory disease. Hence, the D-dimer levels in COPD patients are still conflicting.

Table 5: CT Pulmonary angiography finding in COPD subjects (n=44)

CT Pulmonary angiography finding	No. (%)
No PTE	43 (97.7)
Chronic PTE	1 (2.3)

Table 6: Parameters in patient with chronic PE

D-dimer (ng/ml)	Fibrinogen (mg/dL)	Haematocrit (%)	Mean Platelet Volume (fL)
3540	470	53.1	8.7

Fibrinogen

Out of 44, only 10 patients (22.7%) had values greater than 500 mg/dL. The mean of the observed fibrinogen values was 422.9 mg/dL with a standard deviation of 126 mg/dL. The median fibrinogen value was 446 mg/dL. This value was consistent with fibrinogen levels observed in a study conducted by Zhang et al [14] during the exacerbation phase of COPD, the mean value of fibrinogen was 352 ± 81.3 mg/dL. Elevation of the fibrinogen level is an important risk factor of thrombosis. It is an indicator of prothrombotic state, airway progressive inflammation, and lung tissue injury. Though the levels were not greater than 500mg/dL, the mean value is closer to the upper limit of the normal range and is consistent with similar studies.

Haematocrit

The mean hematocrit value was 47% in our study group, with 6 patients out of 44 who had a haematocrit of >52%. In a study conducted bySchwarcz et al [22] to evaluate thromboembolic events in smoker's polycythemia and non-smokers polycythemia, the mean hematocrit value was 59.0 ± 3.2 % in smokers polycythemia. Only 1 patient in smokers polycythemia had evidence of DVT/PTE as compared to 9 in the polycythemia group. In conclusion, it was found in that study that patients with smokers' polycythemia had significantly fewer thromboembolic events per patient and episodes of peripheral arterial thromboembolism than did individuals with Polycythemia vera, the results of this study demonstrated that smokers' polycythemia does not represent a hypercoagulable state equivalent to that of polycythemia vera. In another case-control study by Nadeem et al [22] compared the prevalence of VTE in age- and sex-matched patients with COPD with and without secondary polycythemia, which demonstrated that the frequency of VTE events was similar in patients with and without secondary polycythemia. These results indicate that secondary polycythemia itself is unlikely to be an independent risk factor for VTE. Hence hematocrit is not a useful parameter to assess the hypercoagulable state in COPD.

Mean Platelet Volume

The mean value of the mean platelet volume in the study group was 8.56±1.44 fL. In a study conducted by Agapakis et al [23], he studied different parameters in patients of COPD presenting in acute exacerbation and compared it with those of stable COPD. The mean platelet volume in the study population was 8.5±0.9 fL whereas in stable COPD it was 9.3±1.3 fL thus depicting a decrease in mean platelet volume during exacerbation. In a similar study done by Kocak et al [24], it was observed that mean MPV (fL) in COPD with acute exacerbation was 8.96 fL whereas in stable COPD it was 7.92 fL. Since we did not have a control group to study the difference, the mean platelet volume observed in this study does not convey if it is low or high. MPV is a simple and easy method of assessing platelet function and reûects the platelet production rate and stimulation. Larger platelets are both metabolically and enzymatically more active than smaller platelets and they have greater prothrombotic potential. Therefore, increased MPV can be accepted as a simple marker of platelet activation. In another study conducted by Talay et al [25] on patients presenting with pulmonary embolism, it was found that MPV in the PE group was significantly higher than in the control group (9.42±1.22 fl vs. 8.04±0.89 fl, p<0.0001). In another similar study conducted by Valor et al[26] to evaluate platelet indices in PE, MPV was signiûcantly higher among PE patients when compared with the control group (9.6 ± 1.0 vs. 8.1 ± 0.8 fL, respectively; p<0.001). Because MPV reflects thrombocyte activation and inflammation, it may also reflect the inflammatory burden of acute attack in COPD. However, the results of studies observed MPV in COPD are conflicting in literature.

Effect of Low Molecular Weight Heparin (enoxaparin)

Here we evaluated the role of LMWH in preventing any thromboembolic event. Every alternate patient was administered enoxaparin for 6 days irrespective of their prothrombotic state.

- The values of D-Dimer and fibrinogen decreased in both treatment and control groups on the 7th day. However, the post-treatment mean value of D-Dimer and fibrinogen was lower in the treatment group than the control group but it was not statistically significant.
- There was a fall in hematocrit in both the treatment and control group.
- There was no significant change in mean platelet volumes in both groups. However, the mean value of MPV was lower in the treatment group than the control group.
- In ABG analysis, pO2 in both the groups improved after treatment irrespective of whether they received enoxaparin or not. However, the mean pO2 value was higher in the anticoagulation group as compared to the control group. The pCO2 value also decreased in both group but the mean pCO2 was lower in the treatment group. However, the difference between the two groups was not statistically significant. No evidence of DVT in any of the patients.
- One patient was reported to have chronic PTE in CT pulmonary angiography done at 3rd month. He belonged to

the control group, hence not received enoxaparin as treatment.

No side effects of enoxaparin were observed in any of the patients.

In a similar study conducted by Shi et al [27] where 70 patients of COPD presenting with acute exacerbation were randomly divided into two groups (one receiving anticoagulation and the other group getting the routine treatment) and D-dimer and fibrinogen levels were observed in both the groups. Following the treatment, the D-Dimer level and blood coagulation indicators of the anticoagulation group were significantly improved compared with those before treatment, and the extents of the improvements were significantly greater than those in the control group. For the control group, there was no significant difference between the D-Dimer level and blood coagulation indicators before and following treatment.

In another study conducted by Song et al [21], the conditions of the patients in the LMWH and conventional treatment groups were noticeably improved following treatment. Compared with the conventional treatment group, the hematocrit, Fibrinogen, PaO2, and PaCO2 of the LMWH treatment group were improved. The differences were significant ($P<0.05$). The D dimer levels of the patients in the two groups were decreased following therapy. Compared with the conventional treatment group, the LMWH group was improved noticeably, but the difference between groups was not significant ($P>0.05$), similar to the results observed in our study. And in this study, in the conventional treatment group, one patient was complicated by cerebral infarction and another by lower limb vein embolism. In our study, one patient in the conventional treatment group developed chronic PTE. As we had evaluated the patients only for DVT and PE, no other thromboembolic events like cerebral infarction were studied. No obvious focal neurological deficit was observed in any of the patients, hence ruling out any major cerebrovascular events.

In our study, there was no significant difference in the changes in the prothrombotic markers in both the anticoagulation and conventional treatment group. D-dimer and fibrinogen. These are also markers of inflammation and COPD is a state of chronic inflammation. The drop in mean D-dimer and fibrinogen levels was seen in both the groups and the difference between the two groups was insignificant.

In a study conducted by Kampolis et al [28], 50 patients of COPD who presented with acute exacerbation were evaluated for PE despite low Well's score. PE was detected in 10 patients (20%). D-dimer levels of COPD patients with PE (median value: 7655 ng/ml) were significantly higher than those of the patients without PE (median value: 940 ng/ml) ($p<0.001$). The calculated area under the ROC curve for D-dimer was 0.89 with an optimal cut off value at 2190 ng/ml. It was observed that patients hospitalized for COPD exacerbation with low clinical probability for PE present D-dimer levels higher than normal, even without PE. The D-dimer cut off value used to exclude PE should be adjusted, thus reducing the unnecessary use of diagnostic procedures.

Thromboembolic Events

In our study, only one patient (i.e. 2.3%) out of 44 had evidence of chronic PTE. None of the patients had any evidence of DVT. In a study conducted by Akpinar et al [29] showed that PE was present in 29.1% of the patients who were hospitalized due to an exacerbation of COPD. The D-dimer value in this patient was 3540ng/ml which is above the cut off value of D-Dimer in COPD patients with pulmonary embolism observed in the study conducted by Kampolis et al [15]. Also fibrinogen level was 470mg/dL, hematocrit observed was 53.1% and mean platelet volume was 8.7 fL which were close to the observed mean values of the study group except for higher hematocrit. The precise prevalence of PE in patients experiencing an acute exacerbation of COPD, as well as the clinical characteristics of these patients, remains uncertain.

Conclusion and Recommendations

Chronic obstructive pulmonary disease was more prevalent in the age group of 50-70 years and more prevalent in males with smoking history. Among the prothrombotic markers, D-Dimer was significantly elevated in the majority. Most of them had mean platelet volume, fibrinogen, and hematocrit in the normal range. No significant change in prothrombotic markers was observed in patients of COPD with acute exacerbation who received low molecular weight heparin in addition to conventional treatment alone. One patient witnessed a thromboembolic event in the form of pulmonary embolism and had elevated D-Dimer, Fibrinogen, and hematocrit levels and had received conventional treatment. The prothrombotic markers D-Dimer and fibrinogen are also markers of inflammation and hence can be elevated in chronic inflammatory conditions like COPD who present in acute exacerbations. Smokers polycythemia can be considered as a risk for thromboembolism in patients of COPD. The role of mean platelet volume needs to be further studied. The benefits of anticoagulation treatment in patients of COPD with acute exacerbation in preventing thromboembolic events can be demonstrated by recruiting a larger study population.

Limitation of Study

The sample size was small therefore the statistical power of the study was low and the study duration was very short. We did not have baseline values of mean platelet volume of patients during a stable phase, availability of which would have helped in getting more elaborate results about mean platelet volume. We did not exclude patients with pneumonia where D-Dimer value could be raised due to sepsis as well. There was no uniformity in the severity of disease in the study population.

Declaration of patient consent

The all authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Data access statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request. The datasets shall be made available from the corresponding author on request.

Conflict of Interest:	Author declare no COI
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