



## PREVALENCE OF PULMONARY EMBOLISM IN PATIENTS SUFFERING FROM ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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### ABSTRACT

**Objective:** To determine the frequency of pulmonary embolism in patients presented with COPD exacerbations.

**Methodology:** This cross-sectional study was conducted in Indus Hospital, Karachi, Pakistan from July 2024 to December 2024. A total of 57 patients with COPD exacerbations were analyzed. COPD was defined as: if the ratio of FEV1/FVC was  $< 0.7$  on post-bronchodilator spirometry, then it was considered a case of COPD. Demographic characteristics, vital signs, arterial blood gas, and chest x-ray details were noted. A complete blood count and pulmonary angiography were done to assess the presence of pulmonary embolism.

**Results:** A total of 57 patients with COPD exacerbation were included and analyzed. The mean age, BMI, and duration of COPD were  $63.56 \pm 12.06$  years,  $23.45 \pm 23.45$  kg/m<sup>2</sup>, and  $17.72 \pm 10.31$  years. There were 53 (93.0%) male, and 4 (7.0%) females. There were 41 (71.9%) patients who belonged to rural areas. History of smoking was present in 55 (96.5%) patients. Seventeen (29.82%) patients were hypertensive, while 3 (5.26%) had diabetes mellitus. Frequency of PE in patient with COPD exacerbation was 8.8% (n=5/57). Relatively higher BMI was associated with the presence of PE (p=0.016).

**Conclusion:** The prevalence of pulmonary embolism was notable in patients with COPD exacerbations. Pulmonary embolism should be taken more seriously, especially when chest discomfort is present and no obvious infectious cause can be found.

**Keywords:** Chronic obstructive pulmonary disease, COPD exacerbation & pulmonary embolism.

### INTRODUCTION

The inflammatory lung condition known as chronic obstructive pulmonary disease (COPD) prevents air from entering the lungs by obstructing the airflow.<sup>1</sup> COPD symptoms comprise wheezing,

coughing up mucus and sputum, and trouble breathing.<sup>2</sup> Continuous, prolonged contact with noxious chemicals or particulate matter—most frequently from cigarette smoke—are usually the commonest causes behind COPD.<sup>3</sup>

The two main disorders that make up COPD are emphysema and chronic bronchitis, and they often coexist.<sup>4</sup> Following ischemic heart disease and stroke, COPD is the third most common cause of mortality worldwide. Due to COPD, roughly 210 million people throughout the world have been affected, and in around 11.3% of the population in Pakistan, it stands as the 3<sup>rd</sup> leading disease of the respiratory system after tuberculosis and asthma.<sup>5</sup> Acute exacerbations and a persistent loss in respiratory capacity are typical features of the diagnostic trajectory of COPD. A COPD exacerbation is described as “an acute event characterized by a worsening of the patient’s respiratory symptoms that is beyond normal day-to-day variations” by the Global Initiative for Chronic Obstructive Lung Disease (GOLD).<sup>6</sup> It has been estimated that 50-70% of COPD exacerbations are caused by an infection, with the remaining 10% resulting from environmental pollutants. Unknown causes account for as much as 30% of exacerbations, and in 18% of COPD patients admitted for an acute exacerbation, pulmonary embolism (PE) was determined.<sup>7</sup> Venous thromboembolism, which includes deep vein thrombosis and PE, is more common in patients with COPD. Patients who are bedridden, elderly, or have many diseases are more at risk of PE.<sup>8</sup> PE refers to a blood clot that forms in the vessels of the lung, which leads to a decreased blood oxygen level and affects the involved organ as well as other organs by damaging any of the lung parts due to obstruction.<sup>9</sup> A PE may pose a fatal risk as one-third of those who are undiagnosed or left untreated die as a result of it.<sup>10</sup> Deep vein thrombosis (DVT) is the most prevalent cause of PE because it results in blood clots forming in the veins of the legs. A number of underlying factors can result in DVT, especially injury or damage from bone fractures, muscle tears causing blood vessel damage, long-term inactivity, and some medical conditions that cause hypercoagulable states.<sup>11</sup>

According to the currently accessible data, not many studies are available in the database at the regional or national levels that focused solely on PE in patients experiencing COPD exacerbations. Therefore, we carried out the current study with the objective of determining the frequency of PE in patients presented with COPD exacerbations. The study also addressed the various differences among the local population, such as the demographic, cultural, and learning curve of the cure. The findings of this study would be able to fill the existing gap, open a new forum of discussion, and provide knowledge and information regarding the medical workup of patients with PE.

## Methodology

This cross-sectional study was executed at the Department of Pulmonology, Indus Hospital, Korangi Campus, Karachi, during July 2024 to December 2024. The study got prior approval from the institutional ethical committee. A sample size of 57 was calculated considering the frequency of PE as 16%<sup>12</sup> in COPD exacerbation patients, with a confidence level of 90%, and 8% margin of error. A non-probability, consecutive sampling technique was employed for sample selection. The inclusion criteria were patients of either gender aged between 18 and 85 years with COPD exacerbations for more than two years. The exclusion criteria were patients with impaired renal function ( $\text{CrCl} < 45 \text{ ml/min}$ ), heart, kidney, and liver problems, contrast allergy, or taking anticoagulant treatment within 3 months. Patients with hormonal changes or with the syndrome of inappropriate anti-diuretic hormone (SIADH) were also not included in the study. Those with chronic, severe vomiting or diarrhea and other causes of dehydration were excluded too.

COPD was defined as: if the ratio of FEV1/FVC was  $< 0.7$  on post-bronchodilator spirometry, then it was considered a case of COPD.<sup>13</sup> Exacerbation of COPD was labeled as the patients having exacerbation of COPD for more than 48 hours on treatment and have a history of diagnosis of COPD as shown by previous record of spirometry (FEV1 less than 80% predicted and FEV1 / FVC ratio  $< 70\%$ ), plus any two or more of i) dyspnea at rest (patients having  $> 25$  breaths per minute measured by counting the number of breaths in one minute using stopwatch); ii) sputum production (patients producing sputum  $> 30 \text{ ml}$  per 12 hours measured by collecting the sputum and measured

graduated glass beaker performed in the ward); iii) purulent sputum ( $> 25$  pus cells per low power field of sputum measured by sputum microscopy performed in a medical laboratory using a microscope at least for the last two days).<sup>14</sup>

After assuring patients or those next to them about objective, safety, and the secrecy of information, with the right to withdraw from study at any point in time without mentioning the reason, written informed consent was obtained. A brief history of demographic data (age, gender, weight, height, BMI, smoking status, hypertension, diabetes mellitus, and duration of symptoms were noted at the time of enrollment. Weight was measured on a standard weighing scale to the nearest of 0.1 kg, while the standing height of the subjects was measured with the standard method to the nearest of 0.1 cm. Smoker was marked as if an individual smoked  $> 10$  packs a year, either currently smoking for  $> 1$  year or quitting smoking since  $< 6$  months. Hypertension was defined as blood pressure 140/90 mmHg for non-diabetics and 130/80 mmHg for diabetics on two separate occasions or on anti-hypertensive medication for at least 6 months.<sup>15</sup> Diabetes mellitus was defined as any patient who was fasting plasma glucose  $> 7$  mmol/l (126 mg/dl), or 2 hours postprandial plasma glucose  $> 11$  mmol/l (200 mg/dl), or on anti-diabetes medication for at least 6 months.<sup>16</sup> Vital signs, arterial blood gas, and chest x-rays were obtained from all the patients. A complete blood count and pulmonary angiography were done to assess the outcome variable (PE). The presence of all of the following was deemed PE: i) D-dimer level  $\geq 500$  ng/ml; ii) on pulmonary angiography, vessels appear white and the embolus appears dark. Inclusion criteria were strictly followed to control the bias and explanatory variables. All of the necessary information was collected on a predesigned proforma.

The employment of "IBM-SPSS Statistics", version 26.0, made the data statistically analyzed. For quantitative characteristics such as age, height, weight, BMI, and length of COPD, mean and standard deviation (SD) were computed. Gender, residential status, smoking status, hypertension, diabetes mellitus, and PE were all shown as frequencies and percentages. To determine how effect modifiers affected the outcome variable, stratification based on age, gender, residence status, smoking status, BMI, and length of COPD was used to control the modifiers. Post-stratification, chi-square or Fisher's exact test (as per need) was applied, taking  $P \leq 0.05$  as the statistical criteria for significance.

## RESULTS

A total of 57 patients with COPD exacerbation were included and analyzed. The mean age, BMI, and duration of COPD were  $63.56 \pm 12.06$  years,  $23.45 \pm 23.45$  kg/m<sup>2</sup>, and  $17.72 \pm 10.31$  years. Table-1 is showing descriptive details of quantitative characteristics of patients.

**Table 1: Descriptive details of quantitative characteristics of patients (n=57)**

| Characteristics          | Mean $\pm$ SD     | Median | IQR |
|--------------------------|-------------------|--------|-----|
| Age (years)              | 63.56 $\pm$ 12.06 | 68     | 19  |
| Height (cm)              | 162.16 $\pm$ 8.70 | 162    | 11  |
| Weight (kg)              | 61.75 $\pm$ 15.41 | 62     | 22  |
| BMI (kg/m <sup>2</sup> ) | 23.45 $\pm$ 23.45 | 24.2   | 7   |
| Duration of COPD (years) | 17.72 $\pm$ 10.31 | 15     | 15  |

There were 53(93.0%) male, and 4 (7.0%) females. There were 41 (71.9%) patients who belonged to rural areas. History of smoking was present in 55 (96.5%) patients. Seventeen (29.82%) patients were hypertensive, while 3 (5.26%) had diabetes mellitus.

Frequency of PE in patient with COPD exacerbation was 8.8% (n=5/57). Relatively higher BMI was associated with the presence of PE (p=0.016). PE was not found to have any statistically significant association with age (p=0.283), gender (p=0.999), residential status (p=0.308), duration of COPD (p=0.462), smoking (p=0.999), hypertension (p=0.615), or diabetes mellitus (p=0.995), as shown in table-2

**Table 2: Descriptive details of quantitative characteristics of patients (n=57)**

| Study variables          |           | Pulmonary embolism (PE) |            | P-value |
|--------------------------|-----------|-------------------------|------------|---------|
|                          |           | Yes (n=5)               | No (n=52)  |         |
| Age (years)              | ≤60       | 3 (60.0%)               | 17 (32.7%) | 0.283   |
|                          | 61-70     | -                       | 16 (30.8%) |         |
|                          | >70       | 2 (40.0%)               | 19 (36.5%) |         |
| Gender                   | Male      | 5 (100%)                | 48 (92.3%) | 0.999   |
|                          | Female    | -                       | 4 (7.7%)   |         |
| Residential status       | Urban     | -                       | 16 (30.8%) | 0.308   |
|                          | Rural     | 5 (100%)                | 36 (69.2%) |         |
| Duration of COPD (years) | ≤10       | 3 (60.0%)               | 17 (32.7%) | 0.462   |
|                          | 11-20     | 1 (20.0%)               | 21 (40.4%) |         |
|                          | >20       | 1 (20.0%)               | 14 (26.9%) |         |
| BMI (kg/m <sup>2</sup> ) | <18       | -                       | 8 (15.4%)  | 0.016   |
|                          | 18.1-29.9 | 2 (40.0%)               | 38 (73.1%) |         |
|                          | ≥30       | 3 (60.0%)               | 6 (11.5%)  |         |
| Smoking                  | Yes       | -                       | 2 (3.8%)   | 0.999   |
|                          | No        | 5 (100%)                | 50 (96.2%) |         |
| Hypertension             | Yes       | 4 (80.0%)               | 36 (69.2%) | 0.615   |
|                          | No        | 1 (20.0%)               | 16 (30.8%) |         |
| Diabetes mellitus        | Yes       | 5 (100%)                | 49 (94.2%) | 0.995   |
|                          | No        | -                       | 3 (5.8%)   |         |

## DISCUSSION

The mean age of the patients in this study was 63.56±12.06 years. There were 93% males and 7.02% females. This is consistent with the published literature in which the mean age usually ranges between 60-75 years, with males in the vast majority.<sup>17-18</sup> Almost 96.5% of patients were smokers. Jindal et al<sup>19</sup> also detected smokers being in the majority in their study.

This study revealed that PE was present in 8.8% of patients presented with COPD exacerbation. Studies from various parts of the world have shown the prevalence of PE in patients with COPD exacerbations, from 7.35% to 36.11%.<sup>20-21</sup> Relatively higher proportions of PE in COPD exacerbation could be attributed to demographic and cultural diversity in some populations. Other reasons for disparities across the research may be partially explained by variations in the inclusion and exclusion criteria and the context in which different investigations have been executed. According to a 2017 comprehensive analysis that included research before 2015, PE was present in 16.1% of people with COPD exacerbations.<sup>22</sup> On the contrary, the research published after 2015 presented a higher prevalence of PE than the research conducted before 2015.<sup>22</sup> The sensitivity and accuracy of PE diagnosis have significantly increased as a result of recent developments in CT imaging.<sup>23</sup>

Because the clinical signs of acute exacerbation of COPD and PE overlap, early detection of PE is crucial yet challenging. Those who experienced dyspnea, pleuritic chest pain, elevated heart rate, lower limb asymmetry or edema, and prolonged hospital stays were more likely to develop PE in patients experiencing COPD exacerbations.<sup>24</sup>

In this study, age, gender, and residential status in patients experiencing exacerbations of COPD, cigarette smoking, and comorbidities (diabetes, hypertension) did not seem to significantly enhance the prevalence of PE. These findings are consistent with the systematic review conducted by Aleva et al,<sup>24</sup> and Fu et al.<sup>25</sup> Additional clinical factors that may possibly be related to PE in COPD patients like peripheral vascular disease, congestive heart failure, and impaired exercise capacity, even yet, most data suggests a link between PE and cancer and surgery.<sup>17,19</sup>

Due to the relatively small sample size, and single-center design, this study's ability to account for excellence was constrained. Furthermore, there was no venous lower limb ultrasonography examination done. COPD exacerbations of unidentified etiology were classified solely on the basis of the clinician's evaluation.

## Conclusion

The frequency of pulmonary embolism in patients with COPD exacerbations was notable. In patients with COPD exacerbations, pulmonary embolism should be taken more seriously, especially when chest discomfort is present and no obvious infectious cause can be found. Further prospective, large multicenter studies are needed to confirm our findings and evaluate the role of potential risk factors for PE in this setting.

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