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Clinical and Paraclinical Characteristics and Predictive Factors of Chronic Obstructive Pulmonary Exacerbation

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is a common global condition, yet real-world data on exacerbations in Vietnamese patients remains limited. This highlights the need for further exploration of clinical complexities in this population. **Objective:** The aim of this study was to characterize the clinical and paraclinical features of COPD and identify predictors of exacerbation. **Methods:** A cross-sectional, prospective study was conducted on 180 inpatients at Vietnam National Lung Hospital from January 2016 to June 2021. Clinical and paraclinical data were collected. **Results:** The mean patient age was 69.38 ± 9.40 years, with 92.8% male. Common symptoms included dyspnea (97.8%), cough (85.6%), and expectoration (80.0%). GOLD stage distribution was: GOLD III (53.7%), GOLD IV (29.3%), and GOLD II (17.0%). Significant predictors of exacerbation included smoking (OR=2.79), comorbidities (OR=3.95), increased dyspnea (OR=14.83), increased sputum (OR=3.13), decreased alveolar murmur (OR=4.11), wheezing (OR=2.70), white blood cell count ≥10 G/L (OR=4.79), GOLD group D (OR=9.75), and FEV1 <30% (GOLD IV) (OR=7.51) ($p < 0.05$). **Conclusion:** Clinical and paraclinical predictors can aid in forecasting and mitigating COPD exacerbations.

Keywords: COPD, exacerbation, factors, Vietnam.

1. BACKGROUND

Chronic obstructive pulmonary disease (COPD) is a prevalent and increasingly common condition worldwide. According to the World Health Organization, 65 million people globally suffer from moderate to severe COPD, making it the third leading cause of death globally, with projections of affecting over 210 million people by 2030 (1, 2). This disease is severe, debilitating, and imposes a burden on patients and healthcare systems alike. In the Asia-Pacific region, including Vietnam, COPD prevalence is notably high. Research by Ngo Quy Chau and colleagues in Hanoi found a 2% prevalence rate among adults aged 40 and above (3). Another national survey in 2006 by Dinh Ngoc Sy and collaborators reported a 4.2% prevalence rate in the same age group (4).

Exacerbations represent pivotal events in patients with chronic obstructive pulmonary disease (COPD), contributing to a deterioration in pulmonary function, a decline in health-related quality of life, an elevated risk of subsequent exacerbations, and increased mortality (5, 6). The prevention of exacerbations has been identified as a central objective in the management of COPD due to their profound impact on patient outcomes, which often include hospital admissions, disease progression, accelerated lung function decline, and heightened mortality rates (7). Despite these implications, there remains a notable scarcity of real-world data on COPD exacerbations among the Vietnamese population, highlighting the need for comprehensive investigation into the clinical complexities specific to this cohort.

2. OBJECTIVE

This study aims to analyze the clinical and laboratory characteristics of patients experiencing exacerbations of chronic obstructive pulmonary disease and identify predictive factors.

3. MATERIAL AND METHODS

Research Participants

Patients diagnosed with acute COPD and admitted for inpatient treatment at the Vietnam National Lung Hospital between January 2016 and June 2021, regardless of gender, were included in the study. Eligible participants were those with a previously diagnosed history of COPD at the Central Lung Hospital who met the criteria for an acute exacerbation upon admission. Only patients who provided consent participated in the study.

The COPD diagnostic criteria, based on GOLD 2015, required patients to be over 40 years old with a history of smoking or tobacco use (18). Clinical symptoms included a persistent cough, excessive sputum production over many years, progressively worsening shortness of breath, and recurrent respiratory infections. Physical examination findings included reduced breath sounds, wheezing, crackles, and bronchial breath sounds, as well as chest expansion and hyperresonance on percussion. Laboratory findings included chest X-rays showing bronchial and vascular patterns, along with emphysematous changes. Pulmonary function tests confirmed irreversible or partially reversible airflow obstruction, with an FEV1/FVC ratio of less than 70% after bronchodilator use.

The diagnosis of acute COPD exacerbation followed Anthonisen's 1987 criteria, which included increased sputum volume, the presence of purulent or mucopurulent sputum, and worsening dyspnea.

Research Period and Location of the Study

The study was conducted at the Vietnam National Lung Hospital from January 2016 to June 2021.

Research Design

A cross-sectional, comparative, and prospective study design was employed to analyze the data.

Data collection method

Sample size

Applied the sample size formula to a proportion

$$n = Z^2_{1-\alpha/2}\frac{p(1-p)}{\varepsilon^2.p^2}$$

in which:

- n: the study sample size.
- Statistical significance level α = 0.05 (corresponding to 95% confidence level).
- With 95% confidence level: Z1-α/2 = 1.96 (look up from the table with the selected α value).
- ε is the relative deviation between the sample parameter and the population parameter (choose ε = 0.15).
- p = 0.5 (Estimating the rate of common bacterial agents in patients with acute COPD exacerbations).

The actual sample size collected was 180 subjects.

Sample Collection Method

A convenient sampling method was used in this study, where patients were directly interviewed using a pre-built structured questionnaire.

Data Collection Method

Clinical Research

The researcher conducted direct interviews with patients to assess their condition, performed clinical examinations on all participants, and monitored the implementation of research-related tests. The collected research information was recorded in the research medical records.

Paraclinical Research

Various laboratory tests were conducted upon the patient's admission to the hospital, including blood count, blood biochemistry, CRP, PCT, and arterial blood gas analysis. Sputum culture was performed to isolate bacteria, and real-time PCR was used to identify atypical bacteria within the first 24 hours of admission. Pulmonary ventilation function was measured once the patient's clinical condition and/or blood gas levels had stabilized after the acute episode. Additionally, chest X-rays and electrocardiograms were conducted within the first 24 hours of admission.

4. RESULTS

The table 1 presented the smoking history of 180 patients in the study. Among them, only 6.7% were non-smokers, while 93.3% had a history of smoking. The highest proportion of smokers (38.3%) reported smoking between 20 and 40 packs per year, followed by 25.6% who smoked between 41 and 60 packs per year. Additionally, 18.8% smoked less than 20 packs per year, and 10.6% smoked more than 60 packs per year. The average number of pack-years among smokers was 27.7 ± 14.5. These findings highlighted the high prevalence of smoking in the study population, which could have contributed to respiratory conditions (Table 1).

The table 2 summarized the comorbidities among 180 patients in the study. Hypertension was the most common comorbidity, affecting 43.3% of the patients, followed by diabetes mellitus at 26.1%. Renal failure was present in 8.3% of cases, while heart failure af-

Bacteria		Quantity (n)	(%)
Pseudomonas aeruginosa,		14	20,9
Haemophilus influenzae,		12	17,9
Streptococcus pneumoniae,		8	11,9
Acinetobacter baumannii,		7	10,4
Moraxella catarrhalis,		6	9,0
Klebsiella pneumoniae,		4	6,0
Stenotrophomanas maltophilia,		2	3,0
Staphylococcus aureus,		2	3,0
Atypical bacteria	Legionella pneumophila,	8	11,9
	Mycoplasma pneumoniae,	3	4,5
	Chlamydia pneumoniae	1	1,5
Total		67	100

Table 1. Bacterial species isolated in sputum (n=67)

Antibiotic	Sensitive	Interme-diate	Resistant
Meropenem	5/7	0	2/7
Imipenem	5/7	0	2/7
Amikacin	2/7	0	5/7
Gentamycin	2/7	0	5/7
Tobramycin	2/7	0	5/7
Doxycycline	5/7	0	2/7
Ceftazidim	1/7	1/7	5/7
Ciprofloxacin	2/7	0	5/7
Minocycline	1/7	1/7	5/7
Ampicillin /Sulbactam	2/7	0	5/7
Trimethoprim/ Sultamethoxazole	0	2/7	5/7
Piperacillin /Tazobactam	1/7	1/7	5/7

Table 2. Antibiogram results of Acinetobacter baumannii (n=7)

Antibiotic	Sensitive	Intermediate	Resistant
Amoxixilin/clavulanic acid	4/6	1/6	1/6
Cefotaxim	3/6	1/6	2/6
Ceftriaxon	4/6	0	2/6
Ceftazidim	5/6	0	1/6
Penicillin G	2/6	1/6	3/6
Erythromycin	1/6	0	5/6
Clarythromycin	2/6	0	4/6
Amikacin	3/6	0	3/6
Gentamycin	2/6	1/6	3/6
Levofloxacin	5/6	0	1/6

Table 3. Antibiogram results of Moraxella catarrhalis (n=6)

fected 2.8% of the patients. Both osteoporosis and old pulmonary tuberculosis were observed in 2.2% of the study population. A total of 15.0% of the patients had no reported comorbidities. These findings highlighted the prevalence of chronic conditions, particularly hypertension and diabetes, among the study participants (Table 2).

The figure illustrated the duration of COPD and the number of exacerbations among the study participants. The average duration of illness was 5.78 ± 3.96 years. The majority of patients (50.0%) had COPD for 5–10 years, while 45.0% had the disease for less than 5 years. Only 5.0% had been living with COPD for more than 10 years. Regarding exacerbations in the past year, 27.2% of patients experienced two episodes, 26.1% had three episodes, and 22.8% had one episode. The average number of exacerbations per year was 2.76 ± 1.63. These findings highlighted the chronic nature of COPD and the frequency of acute exacerbations among patients (Figure 1).

The table summarized the symptoms observed among 180 patients in the study. The most common functional symptoms were dyspnea (97.8%), cough (85.6%), and increased sputum production (80.0%). Sputum color varied, with purulent sputum occurring in 47.8% of cases, green sputum in 23.9%, and yellow sputum in 8.3%. Among physical symptoms, reduced alveolar murmur was noted in 84.4% of patients, while 73.9% experienced wheezing and snoring. Moist rales and crackles were observed in 44.4% of cases, and 66.7% had a barrel-shaped chest. Respiratory muscle retractions were present in 41.7% of patients, while lower extremity edema and the Harzer sign were found in 12.8% and 4.4% of cases, respectively. These findings highlighted the prevalence of respiratory symptoms in the study population (Table 3)

The Table 4 summarized the paraclinical results of 180 patients in the study. The mean pH value was 7.34 ± 0.05, while the average PaO_2 level was 82.27 ± 20.18 mmHg. A total of 61.1% of patients had decreased PaO_2 levels (<80 mmHg). The mean $PaCO_2$ was 46.04 ± 11.84 mmHg, with 53.9% of patients showing increased $PaCO_2$ (≥45 mmHg). The mean HCO_3 level was 27.34 ± 5.11 mmol/L, with 35.0% of patients exhibiting increased HCO_3 levels (>26 mmol/L). Regarding inflammatory markers, 81.1% of patients had CRP levels ≥10 mg/L, and 23.5% had PCT levels ≥0.25 ng/mL. The majority of patients (65.5%) had a white blood cell count >10 G/l. Eosinophil counts varied, with 32.8% of patients having counts ≥300. In terms of disease severity, 86.7% of patients fell into Acute Exacerbation Group D. Based on FEV1 classification, GOLD III (30% ≤ FEV_1 ≤ 50%) was the most prevalent stage, affecting 53.7% of patients, followed by GOLD IV (FEV_1 ≤ 30%) at 29.3%, and GOLD II (50% ≤ FEV_1 ≤ 80%) at 17.0%. These findings highlighted the severity of disease progression and respiratory impairment in the study population (Table 4).

The Table 5 presented the results of a multivariate logistic regression analysis examining factors associ-

Characteristics	Bacterial results	Positive bacteria		Negative bacteria		OR 95%CI	p
		n	%	n	%		
White blood cell count (n=180)	≤ 10 G/l	17	27.4	45	72.6	1	0.04
	> 10 G/l	50	46.3	68	53.7	1.95 (0.96 - 4.06)	
	Total	67	37.2	113	62.8		
CRP level (n=180)	< 20 mg/l	19	24.1	60	75.9	1	0.001
	20 - 40 mg/l	17	45.9	20	54.1	2.68 (1.37 - 6.45)	
	> 40 mg/l	31	48.4	33	51.6	2.97 (1.07 - 6.65)	
	Total	67	37.2	113	62.8		
PCT (n=51)	< 0.25 ng/mL	31	79.5	8	20.5	1	0.01
	≥ 0.25 ng/mL	4	33.3	8	66.7	0.13 (0.02 - 0.66)	
	Total	35	70.6	16	29.4		

Table 4. Correlation between the results of bacteria isolated in sputum and some paraclinical characteristics

Characteristics		Gram negative (-) bacteria	Gram positive (+) bacteria	Atypical bacteria	P
Duration of illness (years)		5.59 ± 2.84	5.81 ± 2.71	5.95 ± 2.82	>0.05
Number of acute times per year (times)		2.57 ± 1.63	3.31 ± 2.91	2.60 ± 1.81	>0.05
Severity level	Type 1	29 (65.9%)	7 (63.6%)	8 (66.7%)	>0.05
	Type 2	15 (34.1%)	4 (36.4%)	4 (33.3%)	

Table 5. Relationship between gram positive (+), gram negative (-), and atypical bacteria groups with some clinical characteristics

ated with the severity of acute exacerbations in COPD patients. The analysis identified several statistically significant predictors of exacerbation ($p < 0.05$). Smoking increased the risk of exacerbation with an odds ratio (OR) of 2.79 (95% CI: 1.02 - 7.62). The presence of comorbidities was also a significant factor, with an OR of 3.95 (95% CI: 1.71 - 10.11). Among symptoms, increased dyspnea showed the strongest association with exacerbation severity (OR = 14.83; 95% CI: 1.37 - 160.84), followed by increased sputum production (OR = 3.13; 95% CI: 1.19 - 7.19) and decreased breath sounds (OR = 4.11; 95% CI: 1.71 - 7.54). Wheezing was also a significant predictor (OR = 2.70; 95% CI: 1.12 - 6.53). A white blood cell count ≥ 10 G/L was associated with a higher risk (OR = 4.79; 95% CI: 2.11 - 9.15). In terms of disease classification, being in GOLD Group D (OR = 9.75; 95% CI: 2.11 - 61.74) and having an FEV_1 obstruction level < 30% (GOLD IV) (OR = 7.51; 95% CI: 1.02 - 69.75) were significant indicators of exacerbation severity. These findings highlighted key clinical and physiological factors that contributed to the worsening of COPD symptoms (Table 5).

5. DISCUSSION

Exacerbation is an important deterioration event in patients with COPD that could aggravate the progression of the disease. Therefore, it is important to elucidate the clinical characteristics of these patients to identify better COPD prevention strategies (8).

After performing a multivariate logistic regression analysis of risk factors, we identified the following statistically significant predictors of COPD exacerbation severity ($p < 0.05$): smoking (OR=2.79; 95% CI: 1.02 - 7.62); comorbidities (OR=3.95; 95% CI: 1.71 - 10.11); increased dyspnea (OR=14.83; 95% CI: 1.37 - 160.84); increased sputum production (OR=3.13; 95% CI: 1.19 - 7.19); decreased alveolar murmur (OR=4.11; 95% CI: 1.71 - 7.54); wheezing (OR=2.70; 95% CI: 1.12 - 6.53); BC ≥ 10 G/L (OR=4.79; 95% CI: 2.11 - 9.15); being in GOLD group D (OR=9.75; 95% CI: 2.11 - 61.74); and having an FEV1 obstruction level < 30% (GOLD IV) (OR=7.51; 95% CI: 1.02 - 69.75).

Numerous studies have provided estimates regarding the risk of moderate to severe exacerbations based on eosinophil count. A positive correlation was found between elevated eosinophil levels and an increased risk of moderate or severe exacerbations, particularly in patients who were not receiving inhaled corticosteroid treatment. The exacerbation risk was consistently associated with various thresholds for higher eosinophil counts, including absolute counts of ≥ 200, ≥ 300, ≥ 340, ≥ 400, and ≥ 500 cells/mm^3, as well as percentages of blood eosinophils at ≥ 2%, ≥ 3%, ≥ 4%, and ≥ 5% (8–11).

The relationship between smoking status and the occurrence of moderate-to-severe or severe exacerbations has been consistently demonstrated in multiple studies, which reported a significant positive correlation (9, 11–13). Our findings align with these results. In contrast, no comparable association between age and exacerbations was observed in our study. Nonetheless, prior research has established a link between age and the frequency of moderate-to-severe exacerbations, indicating a notable increase in the risk of such exacerbations with each decade of age (14–17).

Larsson et al. (2021) demonstrated that patients experiencing two or more annual exacerbations exhibited a significantly higher mortality rate compared to those with no exacerbations or only one exacerbation (18). Furthermore, a greater frequency of exacerbations was linked to a more rapid decline in pulmonary function. Whittaker's study (year) further supported these findings, showing a correlation between the frequency and severity of exacerbations and an elevated risk of both future exacerbations and mortality (19).

The relationship between moderate-to-severe or severe exacerbations and COPD Assessment Test (CAT) scores was found to be both significant and positive (20). Furthermore, the likelihood of moderate-to-severe exacerbations was notably higher in patients with CAT scores of 10 or greater (21–23).

The study by Yong et al. demonstrated that a CAT score of 15 enhanced the predictive accuracy for exacerbations in comparison to scores of 10 or higher (24). Additionally, a significant positive correlation was identified between the risk of future exacerbations and the severity of the disease, which was determined by more pronounced lung function impairment, as indicated by lower FEV1 values (25, 26).

6. CONCLUSION

A study on 180 inpatients at the Vietnam National Lung Hospital from January 2016 to June 2021 showed that smoking, having comorbidities, increased dyspnea, increased sputum production, decreased alveolar murmur, wheezing, a white blood cell count ≥ 10 G/L, being in GOLD group D, and having an FEV1 obstruction level < 30% (GOLD IV) were statistically significant predictors of COPD exacerbation. Understanding clinical and paraclinical predictors helps

in predicting and reducing the risk of exacerbation in COPD.

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