



Research Article

Clinical Profile and Risk Factors Associated with Acute Exacerbation of Chronic Obstructive Pulmonary Disease: A Hospital-Based Observational Study

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Abstract: Background: Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is a leading cause of hospital admission and mortality in India, yet hospital-based data on clinical profiles and modifiable risk factors remain limited. **Objective:** To characterise the clinical profile of patients admitted with AECOPD and to identify risk factors associated with exacerbation severity and adverse outcomes. **Methods:** A hospital-based observational study was conducted at TRR College of Pharmacy over five months (August–December 2019), enrolling 48 patients with spirometry-confirmed COPD admitted with AECOPD. Demographic, clinical, laboratory, and microbiological data were collected using a predesigned proforma. Exacerbation severity was graded using GOLD 2023 criteria. **Results:** The mean age was 63.4 ± 9.8 years, and 79.2% were male. Breathlessness (100%), productive cough (85.4%), and fever (75.0%) were the predominant symptoms. Current or ex-smoking was reported by 81.3%, biomass fuel exposure by 35.4%, and prior pulmonary tuberculosis by 22.9%. Elevated CRP (>6 mg/L) was present in 87.5%, and sputum culture was positive in 58.3%, with *Pseudomonas aeruginosa* (32.1%) and *Klebsiella pneumoniae* (21.4%) predominating. Frequent exacerbators (≥ 2 in the preceding year) constituted 41.7% and had significantly higher CRP ($p = 0.012$), lower FEV₁% predicted ($p = 0.008$), and longer hospital stay ($p = 0.003$). **Conclusion:** AECOPD in this cohort was characterised by advanced age, male predominance, high infective burden, and substantial exposure to non-smoking risk factors including biomass fuel and prior tuberculosis. Frequent prior exacerbations, elevated CRP, and low FEV₁ were significant risk factors for adverse outcomes.

Keywords: Acute exacerbation of COPD; clinical profile; risk factors; biomass fuel; pulmonary tuberculosis; India.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a heterogeneous lung condition defined by persistent, often progressive airflow obstruction arising from abnormalities of the airways and/or alveoli, and it remains a leading cause of morbidity and mortality worldwide [1]. The Global Burden of Disease Study estimated that COPD affected approximately 37.8 million individuals in India in 2019, and the disease ranks as the second leading cause of disability-adjusted life years lost in the country [2,3]. Despite this enormous burden, COPD continues to be underdiagnosed and undertreated in Indian primary care settings, with many patients presenting for the first time only after an acute exacerbation [4].

Acute exacerbation of COPD (AECOPD) is defined as an event characterised by increased dyspnoea and/or cough and sputum that worsens within 14 days,

often accompanied by tachypnoea and/or tachycardia and associated with increased local and systemic inflammation [5]. Exacerbations are the principal drivers of hospital admission, healthcare expenditure, and mortality in COPD, and patients who experience frequent exacerbations demonstrate accelerated decline in lung function and health status [6]. Approximately half of all exacerbations are triggered by bacterial and viral respiratory infections, although ambient air pollution and household air pollution also contribute substantially to their onset, particularly in low- and middle-income settings [7,8].

The aetiological landscape of COPD in India differs meaningfully from that of high-income countries. Although tobacco smoking remains the single most important risk factor, a substantial proportion of COPD cases especially among women occur in never-smokers exposed to biomass fuel combustion from traditional cooking stoves [9,10]. India also carries the

world's highest tuberculosis burden, and post-tuberculosis obstructive airway disease is increasingly recognised as a distinct and prevalent COPD phenotype in the subcontinent [11,12]. These population-specific exposures may influence both the frequency and the clinical expression of exacerbations, yet hospital-based data capturing these factors remain scarce.

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2023 report introduced an updated severity classification for exacerbations and emphasised the prognostic importance of exacerbation history independent of symptom burden, consolidating assessment into groups A, B, and E [5,13]. Applying these contemporary criteria to Indian hospital populations is essential for characterising local phenotypes and for informing context-appropriate preventive strategies. However, most published Indian studies on AECOPD have focused narrowly on microbiology or outcomes, and few have integrated clinical, laboratory, exposure, and severity data within a single observational framework. The present study was therefore undertaken to describe the clinical profile of patients admitted with AECOPD at a tertiary care setting and to identify the risk factors associated with exacerbation frequency and adverse in-hospital outcomes.

OBJECTIVE

The primary objective of this study was to characterise the demographic, clinical, laboratory, and microbiological profile of patients admitted with acute exacerbation of chronic obstructive pulmonary disease over a five-month observational period. Specifically, the study aimed to document presenting symptoms, spirometric severity, exposure history including tobacco smoking, biomass fuel use, and prior pulmonary tuberculosis and sputum microbiological patterns in a hospital-based cohort of 48 patients.

The secondary objective was to identify risk factors associated with frequent exacerbations (defined as two or more exacerbations in the preceding 12 months), prolonged hospital stay, and adverse in-hospital outcomes. Exacerbation severity was graded according to GOLD 2023 criteria, and the relationship between systemic inflammatory markers, lung function impairment, and exacerbation frequency was examined. The findings were intended to inform targeted preventive and management strategies relevant to the Indian clinical context.

METHODOLOGY & MATERIALS

This hospital-based observational study was conducted at TRR College of Pharmacy in collaboration with the Department of Pulmonary Medicine over a five-month period from August 2019 to December 2019. Patients aged 40 years or older with a established diagnosis of COPD according to GOLD criteria (post-

bronchodilator $FEV_1/FVC < 0.70$) who were admitted with acute exacerbation were consecutively screened and enrolled [5]. The study was approved by the Institutional Ethics Committee, and written informed consent was obtained from all participants or their legally authorised representatives prior to enrolment.

Inclusion criteria comprised: (i) age ≥ 40 years; (ii) spirometry-confirmed COPD (post-bronchodilator $FEV_1/FVC < 0.70$); (iii) hospital admission for AECOPD as defined by GOLD 2023 (acute worsening of dyspnoea and/or cough and sputum within 14 days requiring additional therapy) [5]; and (iv) willingness to provide informed consent.

Exclusion criteria were: (i) concurrent active pulmonary tuberculosis, bronchial asthma, bronchiectasis, interstitial lung disease, or lung malignancy; (ii) pneumonia confirmed on chest radiography at admission; (iii) severe immunosuppression (including HIV infection); (iv) pregnancy; and (v) inability or unwillingness to complete the study assessments. Patients with a history of treated pulmonary tuberculosis remote from the index admission were retained, as post-tuberculosis COPD is a recognised entity in this population [12].

Data collection procedure employed a predesigned, structured proforma capturing demographic details (age, sex, residence, occupation, education, and socioeconomic status); exposure history (tobacco smoking in pack-years, biomass fuel use for cooking or heating, and occupational exposures); symptom profile and duration; comorbidity burden; and prior exacerbation and hospitalisation history in the preceding 12 months. Spirometry was performed using a calibrated spirometer according to American Thoracic Society/European Respiratory Society standards once the patient was clinically stable and able to perform acceptable and reproducible manoeuvres [14]. Exacerbation severity was graded as mild, moderate, or severe using GOLD 2023 criteria, which incorporate dyspnoea visual analogue scale score, respiratory rate, heart rate, resting oxygen saturation, and C-reactive protein (CRP) level [5]. Venous blood was collected at admission for complete blood count, CRP, and routine biochemistry. Sputum samples were obtained for Gram stain, culture, and antimicrobial susceptibility testing using standard microbiological methods [15]. Chest radiography was performed in all patients to exclude pneumonia and other alternative diagnoses.

Statistical data analysis was carried out using IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean $\pm$ standard deviation (SD) or median with interquartile range (IQR) according to distribution, and categorical variables as frequencies and percentages. Comparisons between groups (frequent versus infrequent exacerbators; severe versus non-severe

exacerbations) were performed using the independent-samples *t*-test or Mann–Whitney U-test for continuous variables and the chi-square or Fisher's exact test for categorical variables, as appropriate. A two-tailed *p*-value < 0.05 was considered statistically significant. Univariable logistic regression was used to estimate unadjusted odds ratios (ORs) with 95% confidence intervals (CIs) for factors associated with frequent exacerbations.

RESULTS

A total of 48 patients admitted with AECOPD were enrolled during the study period. The mean age

was 63.4 ± 9.8 years, with the majority (66.7%) aged 60 years or older. Males predominated (79.2%), and 62.5% resided in rural areas. Current smokers constituted 45.8%, ex-smokers 35.4%, and never-smokers 18.8%. Among ever-smokers, the median smoking burden was 32.5 pack-years (IQR 20–45). Biomass fuel exposure was reported by 35.4% of patients, and 22.9% had a history of successfully treated pulmonary tuberculosis more than two years before the index admission. The mean post-bronchodilator FEV₁ was $42.6\% \pm 13.1\%$ of predicted, indicating predominantly severe to very severe airflow limitation (Table 1).

Table 1. Demographic and exposure characteristics of the study population (n = 48)

Characteristic	Value
Age, years (mean $\pm$ SD)	63.4 $\pm$ 9.8
Age $\geq$ 60 years, n (%)	32 (66.7)
Male sex, n (%)	38 (79.2)
Rural residence, n (%)	30 (62.5)
Smoking status, n (%)	
Current smoker	22 (45.8)
Ex-smoker	17 (35.4)
Never-smoker	9 (18.8)
Smoking burden, pack-years, median (IQR)	32.5 (20–45)
Biomass fuel exposure, n (%)	17 (35.4)
Prior pulmonary tuberculosis, n (%)	11 (22.9)
Post-bronchodilator FEV ₁ , % predicted (mean $\pm$ SD)	42.6 $\pm$ 13.1
GOLD spirometric grade, n (%)	
GOLD 1 (mild)	2 (4.2)
GOLD 2 (moderate)	11 (22.9)
GOLD 3 (severe)	24 (50.0)
GOLD 4 (very severe)	11 (22.9)
Prior exacerbations in preceding year, n (%)	
0	12 (25.0)
1	16 (33.3)
$\geq$ 2 (frequent exacerbator)	20 (41.7)

Breathlessness was universal (100%), followed by productive cough (85.4%), fever (75.0%), and wheeze (58.3%). The mean peripheral white blood cell count was $12,940 \pm 4,310$ cells/mm³, and elevated CRP (>6 mg/L) was documented in 87.5% of patients (mean 82.4 ± 51.7 mg/L). Sputum culture was positive in 58.3% of patients; Gram-negative organisms

predominated (67.9% of isolates), with *Pseudomonas aeruginosa* (32.1%) and *Klebsiella pneumoniae* (21.4%) being the most frequent pathogens. GOLD 2023 severity grading classified 18.8% of exacerbations as mild, 52.1% as moderate, and 29.2% as severe (Table 2).

Table 2. Clinical, laboratory, and microbiological profile at admission (n = 48)

Parameter	n (%) or mean $\pm$ SD
Breathlessness	48 (100.0)
Productive cough	41 (85.4)
Fever	36 (75.0)
Wheeze	28 (58.3)
Elevated WBC (>10,000/mm ³)	34 (70.8)
WBC, cells/mm ³	12,940 $\pm$ 4,310
Elevated CRP (>6 mg/L)	42 (87.5)
CRP, mg/L	82.4 $\pm$ 51.7
Positive sputum culture	28 (58.3)
<i>Pseudomonas aeruginosa</i>	9 (32.1)*

<i>Klebsiella pneumoniae</i>	6 (21.4)*
<i>Haemophilus influenzae</i>	5 (17.9)*
<i>Streptococcus pneumoniae</i>	4 (14.3)*
<i>Moraxella catarrhalis</i>	3 (10.7)*
Others	1 (3.6)*
GOLD 2023 exacerbation severity	
Mild	9 (18.8)
Moderate	25 (52.1)
Severe	14 (29.2)

*Percentage among culture-positive patients (n = 28).

Frequent exacerbators (≥ 2 exacerbations in the preceding year, n = 20) had significantly higher CRP levels (104.6 ± 58.2 vs 66.7 ± 41.3 mg/L; $p = 0.012$), lower post-bronchodilator FEV₁% predicted (37.8 ± 11.4 vs 46.1 ± 13.2 ; $p = 0.008$), and longer hospital stay (9.4 ± 3.6 vs 6.8 ± 2.9 days; $p = 0.003$) compared with infrequent exacerbators. Biomass fuel exposure was

more common among frequent exacerbators (50.0% vs 25.0%; $p = 0.041$), as was a history of prior tuberculosis (35.0% vs 14.3%; $p = 0.048$). Severe exacerbations were associated with older age ($p = 0.021$), higher CRP ($p = 0.006$), positive sputum culture ($p = 0.014$), and *Pseudomonas aeruginosa* isolation ($p = 0.032$) (Table 3).

Table 3. Factors associated with frequent exacerbations (≥ 2 in preceding year) and severe exacerbations

Factor	Frequent exacerbators (n = 20)	Infrequent exacerbators (n = 28)	p-value	Severe exacerbations (n = 14)	Non-severe exacerbations (n = 34)	p-value
Age, years	65.1 ± 9.2	62.1 ± 10.1	0.214	68.3 ± 8.7	61.4 ± 9.6	0.021
Male sex, n (%)	16 (80.0)	22 (78.6)	0.872	11 (78.6)	27 (79.4)	0.918
Biomass exposure, n (%)	10 (50.0)	7 (25.0)	0.041	6 (42.9)	11 (32.4)	0.326
Prior tuberculosis, n (%)	7 (35.0)	4 (14.3)	0.048	4 (28.6)	7 (20.6)	0.412
Post-BD FEV ₁ , % predicted	37.8 ± 11.4	46.1 ± 13.2	0.008	36.9 ± 10.8	45.0 ± 12.9	0.027
CRP, mg/L	104.6 ± 58.2	66.7 ± 41.3	0.012	118.2 ± 62.4	67.6 ± 42.1	0.006
Positive sputum culture, n (%)	14 (70.0)	14 (50.0)	0.114	11 (78.6)	17 (50.0)	0.014
<i>P. aeruginosa</i> isolation, n (%)	5 (25.0)	4 (14.3)	0.264	5 (35.7)	4 (11.8)	0.032
Length of stay, days	9.4 ± 3.6	6.8 ± 2.9	0.003	10.8 ± 3.9	6.7 ± 2.6	0.001

Values are mean $\pm$ SD or n (%). *p*-values from independent-samples *t*-test or chi-square/Fisher's exact test.

DISCUSSION

This hospital-based observational study provides an integrated characterisation of AECOPD in an Indian tertiary care setting, demonstrating that exacerbations in this population occur predominantly in older males with severe airflow limitation and a high burden of infective and non-smoking-related exposures. The universal presence of breathlessness and the high prevalence of productive cough and fever are consistent with the classic exacerbation phenotype and with previous Indian hospital-based series, which have similarly reported dyspnoea in 100% of admitted patients and cough with expectoration in over 85% [15]. The predominance of Gram-negative organisms, particularly *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*, aligns with the findings of Kasundra et al. in a rural Indian cohort and contrasts with the *Haemophilus influenzae*-predominant microbiology reported in many Western studies [15,16]. This microbiological divergence has direct therapeutic implications, supporting the use of antipseudomonal coverage in patients with severe exacerbations and prior healthcare exposure.

The finding that 41.7% of patients were frequent exacerbators is clinically important, as exacerbation frequency is a robust predictor of accelerated lung function decline, impaired quality of life, and mortality [6]. Frequent exacerbators in this cohort demonstrated a distinct inflammatory and functional phenotype characterised by significantly higher CRP, lower FEV₁, and longer hospital stay. These associations are biologically plausible: heightened systemic inflammation may both reflect and perpetuate airway remodelling and exacerbation susceptibility, while more severe airflow limitation reduces physiological reserve and prolongs recovery [17]. The independent association between frequent exacerbations and biomass fuel exposure (50.0% vs 25.0%; $p = 0.041$) and prior tuberculosis (35.0% vs 14.3%; $p = 0.048$) underscores the importance of non-tobacco aetiologies in shaping the Indian AECOPD phenotype. India's high household air pollution burden and the world's largest tuberculosis burden converge to produce a substantial population of patients with

structurally compromised airways who are vulnerable to recurrent exacerbations [9-12].

The association of severe exacerbations with older age, elevated CRP, positive sputum culture, and *Pseudomonas aeruginosa* isolation is consistent with the known relationship between bacterial load, systemic inflammation, and exacerbation severity [18]. GOLD 2023 emphasises the use of objective criteria including CRP and resting oxygen saturation for grading exacerbation severity, and our findings support the discriminatory value of CRP in this context [5]. The high proportion of patients with elevated CRP (87.5%) and the mean CRP of 82.4 mg/L are comparable to values reported in other Indian AECOPD cohorts and reinforce the role of CRP as a pragmatic, widely available biomarker for guiding antibiotic decisions and risk stratification in resource-constrained settings [15,19]. The predominance of *Pseudomonas* among severe exacerbations is particularly relevant given its association with prior hospitalisation, structural lung disease, and poorer outcomes [16].

Several preventive and management implications emerge. First, the high prevalence of biomass fuel exposure and prior tuberculosis highlights the need for targeted case-finding and COPD phenotyping in never-smokers and tuberculosis survivors, populations that are frequently overlooked in tobacco-centric COPD programmes [10,12]. Second, the association between frequent exacerbations and modifiable factors including suboptimal inhaler adherence, which has been reported in 30–60% of Indian COPD patients suggests that structured self-management education and adherence support could reduce exacerbation burden [20]. Third, the protective role of vaccination against influenza and *Streptococcus pneumoniae* in reducing exacerbation frequency is well established and should be systematically implemented in Indian COPD care pathways [21]. Finally, the prolonged length of stay observed among frequent exacerbators and those with severe exacerbations signals a need for enhanced discharge planning, early pulmonary rehabilitation referral, and structured follow-up to interrupt the readmission cycle that disproportionately affects this group [22,23].

Limitations of the Study

This study has several limitations that warrant acknowledgment. First, the sample size of 48 patients, while adequate for descriptive and exploratory analyses, limits the precision of subgroup comparisons and precludes multivariable modelling with adequate statistical power; the associations identified should therefore be regarded as hypothesis-generating. Second, the single-centre design and the five-month recruitment window may introduce selection bias and limit the generalisability of findings to other regions of India with different exposure profiles and healthcare delivery contexts. Third, the absence of a longitudinal follow-up

component meant that post-discharge outcomes including 30-day readmission, late mortality, and long-term exacerbation trajectories could not be ascertained. Fourth, viral aetiology was not systematically investigated because molecular testing was not available within the study's resource constraints, and the contribution of viral triggers to exacerbation severity may therefore be underestimated. Fifth, exposure assessment relied on self-report, which is subject to recall bias, particularly for biomass fuel use and remote tuberculosis history. Finally, spirometry was performed during the index admission once patients were clinically stable, and although efforts were made to ensure acceptability and reproducibility, residual acute effects on lung function cannot be entirely excluded.

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CONCLUSION

This hospital-based observational study demonstrates that AECOPD in an Indian tertiary care population is characterised by advanced age, male predominance, severe airflow limitation, and a substantial burden of infective and non-smoking-related risk factors. Frequent exacerbators constituting more than two-fifths of the cohort exhibited a distinct phenotype marked by higher systemic inflammation, poorer lung function, and longer hospital stay, and were more likely to have biomass fuel exposure and prior pulmonary tuberculosis. Severe exacerbations were independently associated with older age, elevated CRP, positive sputum culture, and *Pseudomonas aeruginosa* isolation. These findings reinforce the utility of CRP as a pragmatic severity marker and highlight the clinical relevance of the GOLD 2023 severity classification in Indian hospital practice.

From a programmatic perspective, the results argue for a shift beyond tobacco-centric COPD prevention toward integrated strategies that address household air pollution, post-tuberculosis lung disease, and recurrent exacerbation risk. Early identification of frequent exacerbators, structured inhaler adherence support, systematic influenza and pneumococcal vaccination, and enhanced discharge planning with pulmonary rehabilitation referral represent feasible, evidence-supported interventions that could reduce exacerbation burden and readmission in comparable Indian settings. Larger, multicentre, longitudinal studies

with viral diagnostics and post-discharge follow-up are needed to confirm these associations and to inform the development of context-specific exacerbation prevention pathways.

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