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ORIGINAL ARTICLE

Clinical Spectrum and Determinants of Acute Exacerbations in Chronic Obstructive Pulmonary Disease (COPD) in Urban Pakistan

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ABSTRACT

Background: Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) are a major cause of morbidity, hospitalization, and mortality worldwide. In urban Pakistan, rapid urbanization, high smoking prevalence, air pollution, biomass fuel exposure, and suboptimal preventive care may significantly influence the clinical presentation and determinants of AECOPD.

Objective: To evaluate the clinical spectrum of AECOPD and identify key determinants associated with frequent and severe exacerbations among COPD patients in an urban Pakistani setting.

Methods: This hospital-based observational study was conducted at Arif Memorial Teaching Hospital and Shaikh Zayed Hospital, Lahore, from May 2023 to April 2024. A total of 120 adults with physician-diagnosed COPD presenting with acute exacerbations were enrolled. Demographic data, clinical features, smoking and environmental exposures, comorbidities, inhaler adherence and technique, vaccination status, and exacerbation history were recorded. Severity outcomes included hospitalization, need for non-invasive ventilation (NIV), intensive care unit admission, and in-hospital mortality. Multivariable logistic regression analysis was performed to identify independent determinants of frequent (≥2/year) and severe exacerbations.

Results: The mean age was 61.4 ± 9.8 years; 68.3% were males and 31.7% females. Frequent exacerbations were observed in 45% of patients. Hospitalization was required in 65%, NIV in 28.3%, and ICU care in 14.2% of cases. Independent predictors of frequent and severe AECOPD included current smoking, poor inhaler adherence, incorrect inhaler technique, lack of influenza vaccination, biomass fuel exposure, prior hospitalization for AECOPD, radiological pneumonia, and ischemic heart disease.

Conclusion: AECOPD in urban Pakistan is commonly severe and largely driven by preventable and modifiable factors. Strengthening preventive care, patient education, and integrated management strategies is essential to reduce exacerbation burden and improve outcomes.

Keywords: Chronic obstructive pulmonary disease; Acute exacerbation; Urban Pakistan; Smoking; Biomass fuel exposure; Inhaler adherence; Vaccination.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major global public health problem and currently ranks among the leading causes of morbidity and mortality worldwide. It is characterized by persistent airflow limitation, chronic airway inflammation, and progressive respiratory symptoms such as dyspnea, cough, and sputum production[1,2]. Acute exacerbations of COPD (AECOPD), defined as sudden worsening of respiratory symptoms beyond normal day-to-day variation requiring additional treatment, represent the most critical events in the clinical course of the disease. These exacerbations accelerate lung function decline, impair quality of life, increase healthcare utilization, and are a major contributor to COPD-related mortality[3].

Low- and middle-income countries bear a disproportionate burden of COPD, largely due to high rates of tobacco smoking, biomass fuel exposure, air pollution, and delayed diagnosis[4]. Pakistan, particularly its rapidly expanding urban centers, faces a unique and complex risk environment. Urban populations are exposed to intense traffic-related air pollution, industrial emissions, construction dust, overcrowded living conditions, and occupational hazards. Although biomass fuel exposure is traditionally associated with rural settings, it remains prevalent in peri-urban and low-income urban households, further increasing respiratory risk. In addition, smoking prevalence among adult males remains high, while exposure to second-hand smoke is common among women and children[5].

Acute exacerbations in urban Pakistani COPD patients are frequently severe, often leading to emergency department visits, hospital admissions, need for non-invasive ventilation, and prolonged hospital stays[7]. Infectious triggers, poor baseline lung function, comorbid cardiovascular and metabolic diseases, inadequate vaccination coverage, poor inhaler adherence, and incorrect inhaler technique further amplify the risk and severity of exacerbations. Despite these challenges, COPD care in Pakistan is often fragmented, with limited access to spirometry, pulmonary rehabilitation, structured patient education, and long-term follow-up, resulting in delayed presentation and suboptimal disease control[8].

Although international literature has extensively described the epidemiology and determinants of AECOPD, local data from urban Pakistan remain scarce[9]. Most available studies focus on prevalence or general clinical outcomes, with limited emphasis on the combined evaluation of clinical presentation, environmental exposures, healthcare-related factors, and comorbidities influencing exacerbation frequency and severity. Understanding these determinants within the local context is essential for developing targeted preventive strategies, optimizing acute management, and reducing the overall burden of COPD in urban Pakistani populations[10].

Therefore, this study aims to describe the clinical spectrum of acute exacerbations of COPD in urban Pakistan and to identify key determinants associated with frequent and severe exacerbations. The findings are expected to inform context-specific interventions, improve risk stratification, and support evidence-based policies for COPD management in urban healthcare settings[11].

MATERIALS AND METHODS

Study Design and Setting: This hospital-based observational study was conducted at Arif Memorial Teaching Hospital, Pakistan, and Shaikh Zayed Hospital, Lahore, Pakistan. Both institutions are tertiary-care centers that cater to a large urban population and receive a high volume of patients with chronic respiratory diseases. The study was carried out over a 12-month period from May 2023 to April 2024 to capture seasonal variations in acute exacerbations of chronic obstructive pulmonary disease (COPD).

Study Population: The study population consisted of adult patients aged 40 years and above with an established diagnosis of COPD who presented to the emergency department or were admitted to

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medical wards with acute exacerbation of COPD (AECOPD). COPD diagnosis was based on documented clinical assessment and prior spirometry demonstrating persistent airflow limitation (FEV1/FVC <70%) whenever available. An acute exacerbation was defined as a sudden worsening of respiratory symptoms, including increased dyspnea, cough, and/or sputum production, necessitating additional pharmacological treatment or hospitalization.

Patients were excluded if they had acute respiratory symptoms primarily due to alternative diagnoses such as acute heart failure, pneumonia without underlying COPD, pulmonary tuberculosis, interstitial lung disease, or bronchiectasis as the dominant pathology. Individuals with asthma as the primary diagnosis were also excluded unless a clearly documented COPD–asthma overlap syndrome was being managed as COPD. Patients unable to provide informed consent and without an attendant to consent were not enrolled.

Sample Size and Sampling Technique: A total sample size of 120 patients with AECOPD was included in the study. Participants were recruited using a non-probability consecutive sampling technique, whereby all eligible patients presenting during the study period were enrolled. The sample size was considered adequate to evaluate the clinical spectrum of exacerbations and to perform multivariable analysis for identifying determinants of frequent and severe exacerbations.

Data Collection Procedure: Data were collected using a structured, pre-designed proforma through patient interviews, physical examination, and review of medical records. Demographic information included age, sex, and indicators of socioeconomic status. Clinical data comprised duration of COPD, history of prior exacerbations in the preceding 12 months, previous hospitalizations, and use of non-invasive ventilation or intensive care. Presenting symptoms such as dyspnea, cough, sputum volume and purulence, wheezing, and fever were documented, along with vital signs including respiratory rate, heart rate, blood pressure, temperature, and oxygen saturation at presentation.

Environmental and behavioral exposures were assessed in detail, including smoking status (current, former, or never smoker), cumulative smoking exposure in pack-years, passive smoke exposure, use of biomass fuels for cooking or heating, residential proximity to high-traffic roads or industrial areas, and occupational exposure to dust, fumes, or chemicals. Information regarding comorbidities such as hypertension, ischemic heart disease, heart failure, diabetes mellitus, and chronic kidney disease was also recorded.

Medication-related variables included current inhaler therapy, self-reported adherence, and evaluation of inhaler technique through direct observation to identify critical errors. Preventive measures such as influenza and pneumococcal vaccination status and prior participation in pulmonary rehabilitation or structured patient education programs were documented.

Clinical Severity Assessment: Severity of exacerbation at presentation was assessed using clinical parameters and investigations. Oxygen saturation on room air and need for supplemental oxygen were recorded for all patients. Arterial blood gas analysis was performed when clinically indicated to assess hypoxemia and hypercapnia. Laboratory investigations included complete blood count, serum electrolytes, and C-reactive protein where available. Chest radiographs were reviewed for evidence of hyperinflation, consolidation, or cardiomegaly.

Outcome Measures: The primary outcomes included the clinical spectrum of AECOPD and identification of determinants associated with exacerbation frequency and severity. Patients were categorized as frequent exacerbators if they experienced two or more exacerbations in the preceding 12 months. Severe exacerbation was defined by the need for hospitalization, non-invasive ventilation, intensive care unit admission, or in-hospital mortality. Secondary outcomes included length of hospital stay and discharge status.

Statistical Analysis: Data were entered and analyzed using SPSS version 25. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, depending on data distribution, while categorical variables were presented as frequencies and percentages. Comparative analyses were performed using independent t-tests or Mann–Whitney U tests for continuous variables and chi-square or Fisher's exact tests for categorical variables. Multivariable logistic regression analysis was conducted to identify independent determinants of frequent and severe AECOPD, adjusting for potential confounders such as age, smoking history, baseline disease severity, environmental exposures, and comorbidities. A p-value <0.05 was considered statistically significant.

Ethical Considerations: Ethical approval for the study was obtained from the institutional review boards of Arif Memorial Teaching Hospital and Shaikh Zayed Hospital, Lahore. Written informed consent was obtained from all participants or their legal attendants prior to enrollment. Patient confidentiality was strictly maintained, and all data were anonymized and used solely for research purposes.

RESULTS

A total of 120 patients presenting with acute exacerbation of chronic obstructive pulmonary disease (AECOPD) were included in the final analysis during the study period from May 2023 to April 2024. Patients were enrolled from Arif Memorial Teaching Hospital and Shaikh Zayed Hospital, Lahore. The study population included both male and female patients, reflecting the urban Pakistani COPD burden, although males constituted a higher proportion due to greater smoking prevalence and occupational exposure.

Demographic and Baseline Clinical Characteristics: The mean age of the study population was 61.4 ± 9.8 years, with the majority of patients aged between 55 and 70 years, indicating that AECOPD predominantly affected older adults with long-standing disease. Of the total participants, 82 (68.3%) were males and 38 (31.7%) were females. While males predominated, a substantial proportion of females were included, largely representing non-smoking COPD phenotypes associated with biomass fuel exposure and indoor air pollution.

Smoking history revealed that 58 (48.3%) patients were current smokers, 44 (36.7%) were former smokers, and 18 (15.0%) were never smokers, the latter group being predominantly female. The mean cumulative smoking exposure among ever-smokers was 32.6 ± 14.2 pack-years. Biomass fuel exposure was documented in 41 (34.2%) patients, with a significantly higher frequency among females. Occupational exposure to dust, fumes, or chemicals was reported by 46 (38.3%) patients, primarily among males employed in industrial, transport, and construction-related occupations.

The majority of patients (69, 57.5%) had a COPD duration exceeding five years, suggesting advanced disease at presentation. Comorbid conditions were highly prevalent, with hypertension (51.7%), diabetes mellitus (37.5%), and ischemic heart disease (32.5%) being the most common. Baseline hypoxemia was frequent, as 72 (60.0%) patients presented with oxygen saturation below 90% on room air. Detailed baseline characteristics are presented in Table 1.

Table 1. Baseline demographic and clinical characteristics of patients with AECOPD (n = 120)

Variable	Value
Age (years), mean ± SD	61.4 ± 9.8
Male	82 (68.3%)
Female	38 (31.7%)
Current smokers	58 (48.3%)
Former smokers	44 (36.7%)
Never smokers	18 (15.0%)
Smoking exposure (pack-years), mean ± SD	32.6 ± 14.2
Biomass fuel exposure	41 (34.2%)
Occupational exposure	46 (38.3%)
COPD duration >5 years	69 (57.5%)
Hypertension	62 (51.7%)
Diabetes mellitus	45 (37.5%)
Ischemic heart disease	39 (32.5%)
SpO_2 <90% at presentation	72 (60.0%)

Clinical Presentation and Spectrum of Acute Exacerbations: The clinical presentation of AECOPD was predominantly severe. Progressive dyspnea was the most common presenting symptom, reported by nearly all patients, followed by increased cough and sputum production. Purulent sputum was observed in a large proportion of cases, indicating an infective etiology as the dominant trigger of exacerbation. Wheezing and chest tightness were frequently noted, while systemic symptoms such as fever and malaise were present in patients with suspected lower respiratory tract infection.

At presentation, a significant number of patients exhibited tachypnea and hypoxemia, and arterial blood gas analysis, performed when clinically indicated, revealed acute hypercapnic respiratory failure in a notable subset. Radiological evaluation showed hyperinflated lung fields in most patients, while 29 (24.2%) patients had radiographic evidence of pneumonia, which was associated with greater disease severity and prolonged hospitalization. The overall clinical spectrum and severity indicators are summarized in Table 2.

Table 2. Clinical severity and outcomes of acute exacerbations of COPD

Variable	Frequency (%)
Hospital admission required	78 (65.0%)
Non-invasive ventilation required	34 (28.3%)
ICU admission	17 (14.2%)
Radiological pneumonia	29 (24.2%)
Mean hospital stay (days)	6.8 ± 3.1
In-hospital mortality	7 (5.8%)

Exacerbation Frequency and Preventive Care Practices: Based on exacerbation history, 54 patients (45.0%) were classified as frequent exacerbators, having experienced two or more exacerbations in the preceding 12 months. Frequent exacerbators demonstrated a higher symptom burden, more advanced disease, and greater healthcare utilization compared to non-frequent exacerbators.

Preventive care measures were notably inadequate across the cohort. Poor inhaler adherence was documented in 67 (55.8%) patients, while incorrect inhaler technique was observed in 72 (60.0%) patients during direct assessment. Vaccination coverage was low, with 72.5% of patients not receiving influenza vaccination and 81.7% lacking pneumococcal vaccination. These deficiencies were more pronounced among frequent exacerbators, highlighting significant gaps in long-term COPD management. Comparative findings are shown in Table 3.

Table 3. Exacerbation frequency and preventive care characteristics

Variable	Frequent Exacerbators (n = 54)	Non-Frequent (n = 66)
Poor inhaler adherence	39 (72.2%)	28 (42.4%)
Incorrect inhaler technique	41 (75.9%)	31 (47.0%)
No influenza vaccination	44 (81.5%)	43 (65.2%)
No pneumococcal vaccination	48 (88.9%)	50 (75.8%)
Current smoking	34 (63.0%)	24 (36.4%)

Determinants of Frequent and Severe Acute Exacerbations: Multivariable logistic regression analysis identified several independent predictors of frequent and severe AECOPD. Current smoking significantly increased the likelihood of recurrent exacerbations. Poor inhaler adherence and incorrect inhaler technique emerged as strong, modifiable determinants, independently associated with both frequent and severe exacerbations. Lack of influenza vaccination, biomass fuel exposure, and prior hospitalization for AECOPD were also significant predictors after adjustment for age and sex.

Severe exacerbations requiring non-invasive ventilation or ICU admission were independently associated with radiological pneumonia, baseline hypoxemia, and the presence of ischemic heart disease. These findings emphasize the interaction between respiratory pathology, infection, and systemic comorbidities in determining exacerbation severity. The regression model results are presented in Table 4.

Table 4. Multivariable logistic regression analysis of determinants of frequent and severe AECOPD

Determinant	Adjusted Odds Ratio (AOR)	95% CI	p-value
Current smoking	2.84	1.41–5.72	0.003
Poor inhaler adherence	3.12	1.56–6.23	0.001
Incorrect inhaler technique	2.67	1.33–5.38	0.005
No influenza vaccination	2.21	1.09–4.49	0.028
Biomass fuel exposure	1.98	1.01–3.89	0.046
Prior AECOPD hospitalization	3.45	1.72–6.92	<0.001
Radiological pneumonia	3.76	1.61–8.74	0.002

Overall, the results demonstrate that AECOPD in urban Pakistan affects both males and females, with male predominance reflecting higher smoking and occupational exposure, while a substantial proportion of females were affected due to biomass fuel exposure and indoor pollution. The disease is characterized by frequent severe presentations, high hospitalization rates, and substantial preventable risk factors. The identification of modifiable determinants underscores the potential impact of targeted preventive strategies on reducing exacerbation burden and improving patient outcomes.

DISCUSSION

This study provides a comprehensive evaluation of the clinical spectrum and determinants of acute exacerbations of chronic obstructive pulmonary disease (AECOPD) in an urban Pakistani population, highlighting the substantial burden of severe exacerbations, frequent hospitalizations, and modifiable risk factors[9]. The findings demonstrate that AECOPD in this setting is not only common but often clinically severe, with a considerable proportion of patients presenting with hypoxemia, infective features, and respiratory failure requiring advanced ventilatory support. These observations underscore the critical impact of exacerbations on both patient outcomes and healthcare systems in low- and middle-income urban environments[10,11].

The demographic profile revealed a predominance of older adults, consistent with the progressive nature of COPD, and a higher proportion of male patients, reflecting the greater prevalence of smoking and occupational exposures among men in Pakistan[12]. Importantly, nearly one-third of the cohort comprised female patients, many of whom were never-smokers but had significant exposure to biomass fuel and indoor air pollution. This supports growing evidence that COPD in women, particularly in South Asia, is frequently driven by non-tobacco environmental exposures and remains under-recognized in clinical practice. The inclusion of a substantial female population strengthens the relevance of the findings and highlights the need for gender-sensitive approaches to COPD diagnosis and management[13].

Infective exacerbations emerged as the dominant clinical phenotype, as evidenced by high rates of purulent sputum, fever, leukocytosis, and radiological pneumonia. Patients with radiographic evidence of pneumonia experienced more severe exacerbations, longer hospital stays, and greater need for non-invasive ventilation or intensive care[14]. These findings align with international literature showing that bacterial and viral infections are the most common precipitants of AECOPD and are associated with worse short-term outcomes. In Pakistan, overcrowded living conditions, poor vaccination coverage, and delayed healthcare seeking behavior likely contribute to the high burden of infection-related exacerbations observed in this study[15].

A key strength of the study is the identification of several modifiable determinants of frequent and severe exacerbations. Current smoking was one of the strongest predictors, reaffirming its central role in exacerbation risk and disease progression[16]. Equally important was the strong association of poor inhaler adherence and incorrect inhaler technique with recurrent and severe exacerbations.

These findings highlight a critical gap in COPD care, as improper inhaler use can lead to inadequate drug delivery, poor symptom control, and increased exacerbation risk despite prescription of appropriate medications. Routine inhaler technique assessment and patient education are therefore essential components of effective COPD management in urban Pakistani healthcare settings[17].

Preventive care deficiencies were striking, particularly the low uptake of influenza and pneumococcal vaccinations. Under-vaccination independently increased the risk of frequent exacerbations, emphasizing the preventable nature of many AECOPD episodes[18]. Vaccination remains a cost-effective intervention, yet its implementation is limited by lack of awareness, poor access, and inadequate integration into routine care. Addressing these barriers could substantially reduce infection-driven exacerbations and associated hospitalizations[19].

Environmental exposures, including biomass fuel use and traffic-related air pollution, were also independently associated with exacerbation frequency[7-10]. While outdoor air pollution exposure is difficult to quantify precisely in hospital-based studies, the observed associations are biologically plausible and consistent with evidence linking particulate matter exposure to airway inflammation and exacerbation risk. These findings reinforce the need for public health strategies aimed at improving air quality and reducing indoor smoke exposure, particularly among vulnerable urban populations[20].

Comorbid cardiovascular and metabolic diseases significantly influenced exacerbation severity, with ischemic heart disease emerging as a key determinant of severe AECOPD[8]. This highlights the bidirectional relationship between COPD and cardiovascular disease, where systemic inflammation and hypoxemia exacerbate cardiac dysfunction, complicating acute management and worsening outcomes. Integrated care models addressing both respiratory and non-respiratory comorbidities are therefore essential to improve prognosis in COPD patients[13].

Despite its strengths, this study has limitations. Its hospital-based design may over-represent more severe cases and may not fully capture milder exacerbations managed in the community. Environmental exposure assessments relied partly on self-reported data, which may introduce recall bias. Additionally, spirometric data were not uniformly available for all patients at baseline. Nevertheless, the study provides valuable real-world insights into AECOPD in urban Pakistan and identifies actionable targets for intervention[15-20].

CONCLUSION

Acute exacerbations of COPD in urban Pakistan are characterized by a high burden of severe clinical presentations, frequent hospitalizations, and significant healthcare utilization. Both males and females are affected, with gender-specific risk profiles driven by smoking and occupational exposure in men and biomass fuel and indoor air pollution exposure in women. Frequent and severe exacerbations are strongly associated with modifiable factors, including active smoking, poor inhaler adherence and technique, inadequate vaccination, environmental pollutant exposure, prior exacerbation history, and cardiovascular comorbidities. These findings emphasize the urgent need for comprehensive, context-specific COPD management strategies in urban Pakistan. Interventions focusing on smoking cessation, inhaler education, vaccination programs, early recognition of exacerbations, and integrated management of comorbidities have the potential to substantially reduce exacerbation frequency and severity. Strengthening preventive care and patient education, alongside protocol-driven acute management, is essential to improve outcomes and reduce the growing burden of COPD in urban healthcare systems.

Authors' Contributions: Talha Sadiq[1]* conceptualized the study, designed the methodology, supervised data collection, and critically revised the manuscript. Muaaz Bin Saif[2] contributed to data acquisition, patient enrollment, and initial data analysis. Aleena Nazar[3] assisted in literature review, data interpretation, and manuscript drafting. Maira Iqbal[4] participated in clinical data collection, patient follow-up, and compilation of results. Urvah Tariq[5] contributed to statistical analysis, interpretation of findings, and preparation of tables. Labiqa Afzaal[6] assisted in manuscript editing, reference formatting, and final proofreading. All authors reviewed and approved the final manuscript and take responsibility for the integrity and accuracy of the work.

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Ethical Approval: Ethical approval for this study was obtained from the Institutional Review Boards of Arif Memorial Teaching Hospital, Pakistan, and Shaikh Zayed Hospital, Lahore, Pakistan. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Informed Consent: Written informed consent was obtained from all participants or their legal attendants prior to enrollment in the study.

Data Availability: The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

Conflict of Interest: The authors declare that there are no conflicts of interest regarding the publication of this article.

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