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Original Research Article

PREDICTORS OF 60 DAY COPD EXACERBATION WITH HOSPITAL READMISSION

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ABSTRACT

Background: Exacerbations of Chronic Obstructive Pulmonary Disease (COPD) are a primary cause of hospital admissions and readmissions, considerably impacting the healthcare burden. Identifying predictors of 60-day readmission can aid in optimizing management strategies and improving patient outcomes. **Aim:** To evaluate clinical, laboratory, and radiological factors associated with 60-day readmission in COPD patients hospitalized due to acute exacerbation of COPD.

Materials and Methods: A prospective cohort with nested case control study was conducted on 92 COPD patients admitted to a tertiary care center. Baseline characteristics, admission and discharge parameters, and follow-up data were analysed. Univariate and multivariate logistic regression models were used to identify independent predictors of readmission.

Results: The 60-day readmission rate was 35.9%. Significant predictors of readmission included severe COPD (Group E), frequent hospitalizations and ER visits, current smoking, comorbidities (diabetes, CAD, CKD), lower SpO_2 at admission, ICU admission and duration, need for NIV, longer hospital stays, higher inflammatory markers (TLC, CRP), higher CXR scores, and lower SpO_2 at discharge.

Conclusion: Several clinical, inflammatory, and radiological factors contribute to early readmission in COPD patients. Addressing these risk factors through comprehensive discharge planning, targeted interventions, and follow-up strategies may help reduce readmissions and improve COPD management.

Keywords: COPD, exacerbation, hospital readmission, predictors, chronic respiratory disease, inflammatory markers, comorbidities, oxygen saturation, chest X-ray.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a diverse pulmonary disorder marked by enduring respiratory symptoms (dyspnoea, cough, sputum production, and/or exacerbations) resulting from airway (bronchitis, bronchiolitis) and/or alveolar (emphysema) abnormalities that lead to persistent, frequently progressive, airflow obstruction.[1] COPD encompasses a spectrum of diseases, most notably chronic bronchitis and emphysema. The disease is characterized by persistent respiratory symptoms such as cough, sputum production, and dyspnoea, which often worsen over time. The pathophysiology involves the destruction of lung parenchyma, narrowing of airways, and inflammation, which results in the chronic airflow limitation seen in COPD patients.[2] COPD is one of the leading causes of morbidity and mortality worldwide, significantly impacting both individuals' quality of life and healthcare systems.[3]

Risk factors for COPD are numerous, with smoking being the most significant. Over 80% of COPD cases are attributed to tobacco smoke exposure, either active or passive. Other important risk factors include exposure to environmental pollutants, occupational dust and chemicals, genetic factors like alpha-1 antitrypsin deficiency, and a history of

frequent respiratory infections in childhood. The risk of COPD increases with the intensity and duration of smoking, as well as with advancing age, with the majority of patients diagnosed after the age of 40.[4,5,6]

The history of COPD dates back to the early 20th century, though its clinical recognition grew substantially in the mid-1900s as smoking became more widespread. The term "chronic obstructive pulmonary disease" was first introduced in the 1960s to encompass both emphysema and chronic bronchitis. It was not until the 1970s that the link between smoking and COPD was firmly established, leading to widespread public health campaigns to reduce smoking rates.[8] Over the years, significant progress has been made in diagnosing and managing COPD, but challenges remain, particularly in reducing smoking rates in low- and middle-income countries where the disease burden is rising.[9]

Hospital admissions for COPD exacerbations are a critical aspect of disease management. Exacerbations, which are acute worsening of symptoms, are often triggered by respiratory infections, environmental pollutants, or non-adherence to treatment regimens. Hospitalization is typically required when patients experience severe respiratory distress, hypoxemia, or complications such as pneumonia. The admission parameters often include clinical symptoms like increased dyspnoea, tachypnoea, and reduced oxygen saturation levels, alongside changes in lung function tests, such as a decrease in Forced Expiratory Volume (FEV1).[10]

The global burden of COPD is immense. According to the World Health Organization (WHO), COPD was the third leading cause of death globally in 2019, accounting for over 3 million deaths annually. The disease disproportionately affects low- and middle-income countries due to high smoking rates and limited healthcare resources. COPD's economic burden is also substantial, encompassing direct healthcare costs, lost productivity, and long-term care expenses. Despite advancements in treatment, the mortality rate for COPD remains high, and projections indicate that the global burden will continue to grow as smoking rates persist in certain regions and populations age.

MATERIALS AND METHODS

This prospective cohort study with a nested case-control design was conducted in the Department of Respiratory Medicine at Sree Narayana Institute of Medical Sciences, Chalakka, Ernakulam, Kerala, India, over a one-year period from May 2023 to April 2024. The study population comprised patients admitted to the respiratory wards and intensive care unit (ICU) with acute exacerbation of chronic obstructive pulmonary disease (COPD).

Patients admitted with acute exacerbation of COPD who provided written informed consent were included in the study. Patients with obstructive or restrictive ventilatory failure secondary to other respiratory diseases such as asthma, post-tubercular sequelae, or restrictive lung disorders were excluded. Patients admitted for reasons other than acute COPD exacerbation, those with newly diagnosed COPD whose diagnosis could not be confirmed by post-discharge spirometry within two months, patients undergoing planned admissions or admitted for unrelated illnesses during the follow-up period, and individuals unwilling to participate were also excluded.

Sample Size

The sample size was calculated using the standard formula for estimating a single population proportion, assuming an expected 60-day readmission rate of 38%, a 95% confidence level (Z = 1.96), and an allowable error of 10%. The minimum required sample size was calculated as 91 participants. After accounting for a 1% non-response rate, the final sample size was determined to be 92 patients.

A consecutive sampling technique was employed, wherein all eligible patients admitted during the study period who fulfilled the inclusion criteria were recruited until the desired sample size was achieved, thereby minimizing selection bias.

Study Procedure

The study commenced after obtaining approval from the Institutional Ethics Committee. Eligible patients were enrolled after obtaining written informed consent in English or the local language. Baseline demographic and clinical information, including previous hospitalizations, smoking history, comorbidities, and medication history, was collected. All participants underwent detailed general and systemic examinations. Disease severity and symptom burden were assessed using the COPD Assessment Test (CAT), Modified Medical Research Council (mMRC) dyspnea grading, and GOLD classification (Groups A, B, and E).

Patients received standard treatment for acute exacerbation of COPD according to institutional protocols. At the time of discharge, laboratory and clinical parameters including total leukocyte count, differential leukocyte count, C-reactive protein (CRP), chest radiograph score, oxygen saturation without supplemental oxygen, and sputum purulence were recorded.

All participants were prospectively followed for 60 days after discharge to identify hospital readmissions due to COPD exacerbation. Patients readmitted within the follow-up period fulfilling the predefined readmission criteria constituted the case group, whereas patients without readmission served as controls. Readmission status among patients not returning to the hospital was confirmed through telephone follow-up. Information regarding potential factors contributing to readmission, including medication adherence, continuity of care, regular follow-up, and complications, was also collected. The clinical and laboratory characteristics of the readmitted and non-readmitted groups were

subsequently compared to identify predictors of 60-day readmission.

Ethical Considerations

Ethical approval for the study was obtained from the Institutional Ethics Committee prior to commencement. Written informed consent was obtained from all participants before enrolment. Patient confidentiality was maintained throughout the study by anonymizing collected data, and all participants received a detailed patient information sheet explaining the study objectives and procedures.

Statistical Analysis

Data were entered into a master database and analyzed using IBM SPSS Statistics version 26. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were summarized as frequencies and percentages. Comparisons between groups were performed using the independent t-test or Mann–Whitney U test for continuous variables depending on data distribution, and the Chi-square test or Fisher's exact test for categorical variables. Variables associated with readmission on univariate analysis were entered into a multivariable logistic regression model to identify independent predictors of 60-day readmission. A two-tailed p value of <0.05 was considered statistically significant.

RESULTS

Table 1: Baseline demographic and clinical characteristics of study participants (N = 92)

Variable	Value
Age (years), mean ± SD	69.5 ± 8.5
Male sex	48 (52.2%)
COPD Group B	45 (48.9%)
COPD Group E	47 (51.1%)
MMRC grade, mean ± SD	3.11 ± 0.83
CAT score, mean ± SD	28.39 ± 3.96
Previous hospitalizations (last year), mean ± SD	1.03 ± 1.20
Previous ER visits (last year), mean ± SD	1.61 ± 1.48
Sputum production	85 (92.4%)
Current smokers	17 (18.5%)
Ex-smokers	36 (39.1%)
Non-smokers	39 (42.4%)
Previous COVID-19	57 (62.0%)
Pulmonary tuberculosis	24 (26.1%)
Diabetes mellitus	59 (64.1%)
Hypertension	79 (85.9%)
Coronary artery disease	42 (45.7%)
Chronic kidney disease	38 (41.3%)

The study population predominantly consisted of elderly patients with advanced COPD. More than half belonged to GOLD Group E, with high symptom burden reflected by elevated MMRC and CAT scores. Hypertension, diabetes mellitus, coronary artery disease, and chronic kidney disease were common comorbidities.

Table 2: Clinical and laboratory findings during hospitalization

Variable	Mean ± SD / n (%)
BMI (kg/m²)	22.64 ± 2.61
Admission SpO_2 (%)	77.46 ± 7.08
Admission TLC (/µL)	18,053 ± 5,401
Admission CRP (mg/L)	149.0 ± 40.7
Admission CXR score	3.16 ± 0.75
ICU admission	52 (56.5%)
NIV requirement (among ICU patients)	33 (63.5%)
ICU stay (days)	4.83 ± 1.15
Hospital stay (days)	10.08 ± 2.91

Patients demonstrated severe exacerbations with marked hypoxemia and systemic inflammation at admission. More than half required ICU care, and nearly two-thirds of ICU patients required non-invasive ventilation.

Table 3: Clinical improvement from admission to discharge

Parameter	Admission	Discharge	p-value
SpO_2 (%)	77.46 ± 7.08	87.50 ± 1.46	<0.001
TLC (/µL)	18,053 ± 5,401	11,349 ± 3,613	<0.001
CRP (mg/L)	149.04 ± 40.70	41.13 ± 14.45	<0.001
Chest X-ray score	3.16 ± 0.75	2.14 ± 0.97	<0.001

Significant improvements were observed in oxygen saturation, inflammatory markers, and radiographic findings at discharge (all p<0.001), indicating satisfactory response to treatment.

Table 4: Comparison between readmitted and non-readmitted patients

Variable	Significant finding	p-value
COPD Group E	Higher	<0.001
MMRC grade	Higher	<0.001
CAT score	Higher	<0.001
Previous hospitalizations	Higher	<0.001
Previous ER visits	Higher	<0.001
Current smoking	Higher	0.022
COVID-19 history	Higher	0.013
Diabetes mellitus	Higher	0.002
Coronary artery disease	Higher	<0.001
Chronic kidney disease	Higher	0.005
BMI	Lower	0.006
Admission SpO_2	Lower	0.007
Admission CXR score	Higher	0.002
ICU admission	Higher	<0.001
ICU duration	Longer	<0.001
NIV requirement	Higher	<0.001
Hospital stay	Longer	<0.001
Discharge TLC	Higher	0.019
Discharge CRP	Higher	0.001
Discharge CXR score	Higher	<0.001
Discharge SpO_2	Lower	<0.001

Patients readmitted within 60 days had significantly greater disease severity, poorer oxygenation, longer hospitalizations, more frequent ICU admissions, higher inflammatory markers, and a greater burden of comorbidities than patients without readmission.

Table 5: Independent predictors of 60-day readmission (Multivariable logistic regression)

Predictor	Odds Ratio	p-value
COPD Group E	24.88	<0.001
MMRC grade	3.01	0.003
CAT score	1.47	0.002
Previous ER visits	2.50	<0.001
Diabetes mellitus	3.61	0.001
BMI	0.69	0.005
Admission CXR score	2.19	0.027
ICU duration	4.45	<0.001
Hospital stay	3.08	<0.001
Discharge CRP	1.17	0.028
Discharge CXR score	7.44	<0.001
Discharge SpO_2	0.37	0.001
Sputum purulence at discharge	48.43	<0.001

Multivariable logistic regression identified COPD Group E, higher symptom burden (MMRC and CAT scores), diabetes mellitus, prolonged ICU and hospital stay, persistent inflammation, impaired oxygenation, abnormal chest radiographic findings, and sputum purulence at discharge as independent predictors of 60-day readmission. Sputum purulence at discharge emerged as the strongest predictor (OR 48.43).

Table 6: Summary of 60-day readmission outcomes

Outcome	Value
Readmitted within 60 days	33 (35.9%)
Not readmitted	59 (64.1%)
Mean time to readmission (days)	27.8 ± 11.4
Cause of readmission	COPD exacerbation (100%)
Irregular medication use	97.0%
Irregular follow-up	78.8%
Continued smoking after discharge	18.2%

Approximately one-third of patients experienced readmission within 60 days, with COPD exacerbation being the sole cause. Most readmitted patients reported poor medication adherence and inadequate follow-up, highlighting the importance of structured post-discharge care.

DISCUSSION

The current study and the study by Crisafulli et al,[11] highlight the significance of comorbidities, with diabetes mellitus emerging as a strong predictor of readmission in both. Our study reported high rates of diabetes (64.1%), hypertension (85.9%), and coronary artery disease (45.7%), while Crisafulli et al. also emphasized diabetes and previous hospitalizations as critical risk factors. Both studies noted that elevated CRP levels correlated with a heightened risk of readmission; however, our investigation identified CRP to be a strong univariate predictor but not significant in a multivariate model, whereas Crisafulli et al. identified CRP ≥7.6 mg/L at discharge as a significant predictor. Additionally, our study demonstrated that longer hospital stays, higher chest X-ray scores, and lower SpO2 levels at discharge were significant predictors of readmission, while Crisafulli et al. focused more on the integration of comorbidities and prior hospitalizations in their predictive model. Both studies suggest the need for closer monitoring and targeted interventions in high-risk patients, with our study providing a detailed analysis of smoking history, sputum production, and COVID-19 history as additional factors contributing to readmission risk.

The present study noted longer hospital stays, higher chest X-ray scores, and lower SpO2 levels at discharge as significant predictors of readmission, while Ruan et al,[12] highlighted male sex, length of stay, heart failure, diabetes, cancer, and malnutrition as major risk factors for 30-day readmission. Both studies found comorbidities to be crucial, with our study reporting high rates of diabetes (64.1%), hypertension (85.9%), and coronary artery disease (45.7%), aligning with Ruan et al.'s emphasis on the impact of heart failure and diabetes. While our study observed a 35.9% readmission rate within 60 days, Ruan et al. reported a range of readmission rates from 11% at 30 days to 37% at 365 days. Unlike our study, which found no significant association between sputum purulence and CRP in multivariate models, Ruan et al. identified comorbid conditions as consistent predictors. Additionally, our study's observation that Group E patients had more severe symptoms and poorer outcomes is consistent with Ruan et al.'s finding that longer hospital stays and comorbidities increased readmission risk.

Alqahtani et al,[13] found that peak inspiratory flow rate (PIFR) at discharge, frailty, and higher COPD Assessment Test (CAT) scores were the most significant predictors of both 30-day and 90-day readmissions. Both the studies observed that patients with previous exacerbations and longer hospital stays had a higher risk of readmission, aligning with our findings of increased readmission rates among Group E patients with severe disease. While our study indicated that poor medication adherence and smoking were contributing factors to readmission, Alqahtani et al. emphasized the role of depression and reduced PIFR in predicting readmission.

The systematic review by Lin P et al,[14] points out that male sex, multiple hospital admissions, a history of smoking, low BMI, and ≥3 comorbidities as significant risk factors for COPD readmission. While our study highlighted purulent sputum and low SpO2 levels at discharge as predictors of readmission, the meta-analysis also reported factors like a high Neutrophil-to-Lymphocyte ratio (NLR >7), eosinophil percentage ≥2%, and FEV1 <50 as relevant. Additionally, the review found 30-, 90-, and 365-day readmission rates of 19%, 31%, and 42%, respectively, compared to the current study's focus on a 60-day readmission rate with a notable association of Group E patients with severe symptoms and frequent hospital visits.

Quintana et al,[15] identified previous eCOPD-related hospital admissions, low FEV1%, use of diuretics, and patient-reported fatigue and psychological distress as key predictors for COPD readmissions within 60 days. Both studies emphasize the importance of disease severity and comorbidities, with our study reporting high rates of diabetes, hypertension, and coronary artery disease, while Quintana et al. pointed to the use of diuretics as a marker for cardiac disease. The present study observed a strong link between smoking and severe disease, particularly in Group E patients, while Quintana et al. also noted hospital-specific variations in readmission rates.

Chow et al,[16] mentions that heart failure, mental health conditions, and cancer as significant predictors of readmission. Both studies found that longer hospital stays and severe COPD exacerbations increased the likelihood of readmission. Chow et al. also pointed to anemia, low FEV1, and higher eosinophil counts as important factors. Furthermore, both studies noted the impact of previous hospitalizations and the use of non-invasive ventilation during hospitalization.

Fernández-García et al,[17] identified dependence on basic activities of daily living (BADLs) and a history of two or more admissions in the previous year as key predictors across 30, 90, and 365 days. The Fernández-García et al study also focused on the influence of social factors, noting that patients with caregiver dependence, poor family support, and social isolation were at a higher risk. Additionally, obesity and high-grade dyspnoea were identified as long-term predictors in their study.

CONCLUSION

This prospective cohort study demonstrated that more than one-third of patients hospitalized with acute exacerbation of COPD experienced readmission within 60 days despite significant clinical improvement during the index hospitalization. Severe disease (GOLD Group E), greater symptom burden (higher MMRC and CAT

scores), frequent previous hospitalizations and emergency visits, comorbidities such as diabetes mellitus, coronary artery disease, and chronic kidney disease, prolonged ICU and hospital stay, persistent systemic inflammation, abnormal chest radiographic findings, sputum purulence, and lower oxygen saturation at discharge were identified as significant predictors of readmission. Additionally, poor medication adherence, inadequate follow-up, and continued smoking emerged as important modifiable factors contributing to recurrent hospitalizations. These findings highlight the need for comprehensive discharge planning, optimization of comorbidity management, smoking cessation, close post-discharge surveillance, and individualized follow-up strategies for high-risk patients to reduce readmissions and improve long-term outcomes in COPD

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