



Monaldi Archives for Chest Disease

eISSN 2532-5264

<https://www.monaldi-archives.org/>

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Monaldi Arch Chest Dis 2026 [Online ahead of print]

To cite this Article:

Usman A, Irfan M, Aslam M, et al. **Frequency and factors leading to prolonged hospital stay and in-hospital mortality in patients admitted with acute exacerbation of chronic obstructive pulmonary disease.** *Monaldi Arch Chest Dis* doi: 10.4081/monaldi.2026.3756

Submitted: 2-10-2025

Accepted: 26-01-2026

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Frequency and factors leading to prolonged hospital stay and in-hospital mortality in patients admitted with acute exacerbation of chronic obstructive pulmonary disease

Ali Usman,¹ Muhammad Irfan,¹ Mehwish Aslam,¹ Akbar Shoukat Ali,¹ Nousheen Iqbal,¹
Muhammad Usman Ghani,¹ Talha Shahzad,¹ Ayesha Ather,¹ Bilal Ahmad Khan²

¹Section of Pulmonary and Critical Care, Department of Medicine, The Aga Khan University, Karachi; ²Institute of Public Health & Social Sciences, Khyber Medical University, Peshawar, Pakistan

Correspondence: Muhammad Irfan, Section of Pulmonary and Critical Care, Department of Medicine, The Aga Khan University, Karachi, Pakistan.

Tel.: + 92 21 34864664. E-mail: muhammad.irfan@aku.edu

Contributions: Ali Usman, Muhammad Irfan, Nousheen Iqbal, Talha Shahzad: conception, design of the work, data acquisition, drafting of the manuscript, and approval of the submitted version. Ali Usman, Mehwish Aslam, Muhammad Usman Ghani, Ayesha Ather, Bilal Ahmad Khan: conception data acquisition, drafting of the manuscript, and approval of the submitted version. Ali Usman, Mehwish Aslam, Akbar Shoukat Ali, Muhammad Usman Ghani, Ayesha Ather, Bilal Ahmad Khan: data management, data analysis, drafting of the manuscript, and approval of the submitted version. Muhammad Irfan, Nousheen Iqbal, Talha Shahzad: overall supervision, conception, design of the work, drafting of the manuscript, and approval of the submitted version.

Conflict of interest: the authors declare that there is no conflict of interest.

Ethics approval and consent to participate: given the retrospective nature of the study, a waiver of ethics approval and informed consent was obtained from the Ethics Review Committee (ERC) of the Aga Khan University (ERC # 2024-10107-29403). The study was performed in accordance with the ethical standards outlined in the 1964 Declaration of Helsinki and its future amendments.

Informed consent: not applicable.

Patient consent for publication: not applicable.

Availability of data and materials: the datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Acknowledgments: the authors thank the staff and patients of the Section of Pulmonary and Critical Care, Department of Medicine, The Aga Khan University Hospital (Karachi, Pakistan) for their support.

Abstract

Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) are a major cause of morbidity and mortality. This study aimed to determine the frequency and predictors of prolonged hospital stays and in-hospital mortality in patients admitted with AECOPD. A cross-sectional study was conducted at a tertiary care hospital in Karachi, Pakistan, from June to December 2024. A total of 150 patients admitted with AECOPD were enrolled. A prolonged stay was defined as >7 days. Data on demographics, clinical parameters, and outcomes were collected. Multivariable logistic regression was used to identify independent predictors. The mean age of participants was 72.5 ± 10.4 years, with 63.3% being male. Prolonged hospital stay occurred in 25.3% of patients, and in-hospital mortality was 10.0%. *Pseudomonas aeruginosa* infection [adjusted odds ratio (aOR) 11.46, 95% confidence interval (CI): 2.49-52.70; $p=0.002$] was an independent predictor of prolonged stay. Vasopressor use was the independent predictor of in-hospital mortality (aOR 40.35, 95% CI: 4.49-362.79; $p=0.001$). In conclusion, *Pseudomonas aeruginosa* infection is significantly associated with prolonged hospitalization in AECOPD, while the need for vasopressors is strongly associated with mortality. Early identification of these factors can help in risk stratification and improve patient outcomes.

Key words: chronic obstructive pulmonary disease, acute exacerbation, length of stay, mortality, pulmonary hypertension, *Pseudomonas aeruginosa*.

Introduction

Chronic obstructive pulmonary disease (COPD) is an inflammatory condition characterized by progressive airflow limitation [1]. It is a leading cause of death globally, resulting in an estimated 3.5 million deaths in 2021 [2]. A critical aspect of COPD management is acute exacerbations (AECOPD), which worsen respiratory symptoms, drive healthcare costs, and lead to hospitalizations, prolonged length of stay (LOS), and mortality [3].

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) defines AECOPD as an acute worsening of respiratory symptoms that requires additional therapy [4]. In-hospital mortality for AECOPD ranges from 2.5% to 14.8%, while prolonged LOS (>7 days) occurs in over 50% of cases in some studies [5,6]. Predictors include comorbidities, previous exacerbations, and specific infections [7].

While data from high-income countries exist, there is a scarcity of studies from low- and middle-income countries (LMICs) like Pakistan. This study aims to determine the frequency and identify factors associated with prolonged hospital stay and in-hospital mortality in patients admitted with AECOPD at a tertiary care centre in Karachi, Pakistan.

Materials and Methods

Study design and population

This retrospective cross-sectional study was conducted at the Aga Khan University Hospital, Karachi, Pakistan. After approval from the Ethics Review Committee (ERC # 2024-10107-29403), 150 patients admitted with AECOPD were enrolled using consecutive sampling.

Inclusion and exclusion criteria

Patients aged 30–70 years with a prior COPD diagnosis presenting with an acute exacerbation were included. Exacerbation was defined per GOLD criteria. Exclusion criteria included asthma, pneumonia, pulmonary embolism, other chronic respiratory diseases, or significant comorbid conditions like chronic renal failure or malignancy.

Data collection and operational definitions

Data were collected on demographics, smoking history, comorbidities, clinical presentation, and hospital course using a structured proforma. Prolonged hospital stay was defined as >7 days. In-hospital mortality was death from any cause during the admission.

Statistical analysis

Data were analysed using Stata 17. Continuous variables were reported as mean \pm standard deviation or median (interquartile range), and categorical variables as frequencies (%). Group comparisons used t-tests, Mann-Whitney U, Chi-square, or Fisher's exact tests. Variables that achieved a significance level of $p < 0.1$ in univariable analysis were entered into the multivariable logistic regression models. The final models are presented showing both statistically significant independent predictors and other variables retained in the analysis to provide complete transparency. Adjusted odds ratios (aORs) with 95% confidence intervals (CIs) are reported. A p -value < 0.05 was considered statistically significant.

Results

Among 150 patients admitted with AECOPD, the mean age was 72.51 ± 10.36 years, and most were male (63.33%). Half of the patients were classified as obese (50.67%), while 22.67% were normal weight. The majority had a history of smoking, with 50.67% being ex-smokers and 18.00% current smokers. Common comorbidities included type 2 diabetes mellitus (59.15%), heart failure (46.67%), and pulmonary hypertension (42.00%). Biomass exposure was reported in 43.33% of patients, and 74.67% had experienced a previous exacerbation. The median hospital stay was 3 days, with 25.33% experiencing prolonged hospitalization (>7 days), and in-hospital mortality was 10.00%. Hypercapnic respiratory failure occurred in 44.00% of patients, with non-invasive ventilation used in 62.67% and mechanical ventilation in 4.67%. At discharge, most patients were prescribed inhalers (85.33%), while 39.33% received long-term oxygen therapy and 31.33% continued home non-invasive ventilation. Positive cultures were observed in 28.00% of patients. The baseline characteristics are presented in Table 1.

When stratified by length of hospital stay, patients with prolonged hospitalization (≥ 7 days) were more likely to be male (84.21% vs. 56.25%, $p=0.002$) and have comorbidities such as type 2 diabetes mellitus (77.78% vs. 52.83%, $p=0.009$), pulmonary hypertension (76.32% vs. 30.36%, $p<0.001$), and heart failure (60.53% vs. 41.96%, $p=0.047$) compared to those hospitalized for less than 7 days. They also had higher rates of previous exacerbations (97.37% vs. 66.96%, $p<0.001$), smoking history (86.84% vs. 62.50%, $p=0.005$), and positive cultures, particularly *Pseudomonas aeruginosa* (47.37% vs. 4.46%, $p<0.001$). Patients with longer stays more frequently required advanced respiratory support, including non-invasive ventilation (97.37% vs. 50.89%, $p<0.001$), mechanical ventilation (18.42% vs. 0.0%, $p<0.001$), and vasopressors (42.11% vs. 3.57%, $p<0.001$). Hypercapnic respiratory failure (84.21% vs. 30.36%, $p<0.001$) and in-hospital

mortality (26.32% vs. 4.46%, $p < 0.001$) were also significantly higher in this group, while biomass exposure was less common (23.68% vs. 50.00%, $p = 0.005$) (Table 2).

Table 3 compares characteristics of survivors and non-survivors with AECOPD. Non-survivors were more likely to be male (93.33% vs. 60.00%, $p = 0.011$) and had higher prevalence of pulmonary hypertension (80.00% vs. 37.78%, $p = 0.002$), smoking history (93.33% vs. 65.93%, $p = 0.030$), previous exacerbations (100.00% vs. 71.85%, $p = 0.013$), and *Pseudomonas aeruginosa* infection (33.33% vs. 13.33%, $p = 0.041$). Non-survivors had more frequent hospitalizations in the previous year (median 3 vs. 1, $p < 0.001$), were more likely to require vasopressors (73.33% vs. 6.67%, $p < 0.001$) and non-invasive ventilation (86.67% vs. 60.00%, $p = 0.043$), and experienced hypercapnic respiratory failure more often (86.67% vs. 39.26%, $p < 0.001$). The median duration of hospital stay was significantly longer in non-survivors (8 vs. 3 days, $p < 0.001$).

In multivariable logistic regression analysis, *Pseudomonas aeruginosa* infection was the only factor significantly associated with prolonged hospital stay in patients with AECOPD (adjusted OR [aOR] 11.46, 95% CI: 2.49-52.70; $p = 0.002$). Although several variables, including sex, type 2 diabetes mellitus, pulmonary hypertension, heart failure, smoking status, prior hospitalizations, vasopressor use, non-invasive ventilation, and hypercapnic respiratory failure, showed associations in univariable analysis, none remained statistically significant after adjustment (Table 4).

Table 5 shows that, in the multivariable logistic regression analysis, vasopressor use emerged as the only independent predictor of in-hospital mortality among patients with AECOPD (adjusted OR 40.35, 95% CI: 4.49-362.79; $p = 0.001$). While several variables, including sex, pulmonary hypertension, prior hospitalizations, *Pseudomonas aeruginosa* and *Acinetobacter* infections, use of non-invasive ventilation, and hypercapnic respiratory failure, were associated with mortality in univariable analysis, these associations did not remain statistically significant after multivariable adjustment.

Discussion

This study found that one-quarter of patients with AECOPD experienced a prolonged hospital stay, and one in ten died during admission. The rate of prolonged stay (25.3%) is consistent with a large European study of 661 patients, which reported a 24% rate of prolonged hospitalization, defined as >14 days [8]. The identified predictors align with and are further elucidated by the global literature.

Our finding that *Pseudomonas aeruginosa* infection drastically increases the risk of prolonged stay is strongly supported by large-scale contemporary research. A multiregional epidemiological study of 22,053 COPD patients demonstrated that *Pseudomonas aeruginosa* was an independent predictor of hospitalization for exacerbation or all-cause death, with a hazard ratio (HR) of 2.8 [9]. Furthermore, a systematic review and meta-analysis concluded with moderate certainty that the isolation of *Pseudomonas aeruginosa* in COPD patients is associated with an almost doubled adjusted risk of all-cause mortality (HR 1.95) [10]. This pathogen is often associated with more severe baseline disease, frequent prior exacerbations, and structural lung damage, which complicate therapy and delay recovery, contributing to protracted hospital stays [8].

Although pulmonary hypertension did not retain independent significance in our final multivariable model for prolonged stay, its high prevalence (76.3%) in the prolonged stay group and significant univariable association underscore its clinical importance as a marker of advanced disease. Pulmonary hypertension is a well-documented and serious complication of COPD, with reported prevalence rates ranging from 20% to 70% in different populations [11]. Its presence is associated with worse exercise capacity, increased hospitalization risk, and higher mortality, often reflecting greater overall cardiopulmonary compromise [11]. The strong association observed here reinforces the need to consider it in the overall assessment of disease severity in hospitalized AECOPD patients.

The strongest predictor of mortality in our cohort was the need for vasopressors. It is critical to interpret this finding as a profound marker of critical illness severity, specifically shock and hemodynamic instability, rather than a direct cause of death. This aligns with broader critical care literature where vasopressor use signifies a grave prognostic state. Our observed mortality rate of 10.0% is corroborated by another recent study from Pakistan involving 355 AECOPD patients, which reported an almost identical in-hospital mortality rate of 9.5% [12]. That study also identified ischemic heart disease and the need for mechanical ventilation as significant predictors of poor outcomes, highlighting common themes of critical illness and cardiovascular comorbidity in the region [12]. Our finding powerfully quantifies the extreme risk associated with this clinical milestone. Consequently, the initiation of vasopressor therapy in a patient with AECOPD should be recognized as a critical inflection point demanding immediate escalation to a higher level of care, ideally an intensive care unit (ICU). Admission to the ICU itself has been independently associated with prolonged hospital stay in other studies [8].

While not achieving statistical significance in our final models, several factors showed notable effect sizes that warrant consideration and are supported by other research. The strong association

between *Acinetobacter* infection and mortality (aOR 7.88, p=0.116) may reflect a clinically important relationship that our study was underpowered to detect, highlighting the grave challenge of managing multidrug-resistant organisms in severe AECOPD. Similarly, the trend between frequent previous hospitalizations and both prolonged stay and mortality reinforces the well-established concept that healthcare utilization history is a key marker of underlying disease severity and instability [13]. Other studies have identified advanced age, the need for oxygen supplementation, and the use of systemic corticosteroids during hospitalization as factors associated with longer stays, reflecting the multifactorial nature of this outcome [14].

The present study has limitations. The single-centre design and modest sample size may limit generalizability. The cross-sectional nature can establish associations but not causality. The sample size may have limited our power to detect statistically significant associations for variables with high point estimates, such as *Acinetobacter* infection.

Conclusions

In conclusion, *Pseudomonas aeruginosa* infection is significantly associated with prolonged hospitalization in AECOPD, while the need for vasopressors is strongly associated with in-hospital mortality. The frequent co-occurrence of pulmonary hypertension further delineates a high-risk phenotype. Early identification of these factors can facilitate better risk stratification, guide targeted investigation and therapy, inform the critical decision for intensive care escalation, and improve management strategies and outcomes in resource-limited settings.

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Table 1. Demographic and clinical characteristics of patients with acute exacerbation of chronic obstructive pulmonary disease (n=150).

Characteristic	Value
Age (years)	72.51 ± 10.36
Sex (Male)	95 (63.33%)
BMI (kg/m ²)	25.98 ± 5.00
BMI category†	
Normal	34 (22.67%)
Underweight	6 (4.00%)
Overweight	34 (22.67%)
Obese	76 (50.67%)
Smoking status	
Never smoker	47 (31.33%)
Ex-smoker	76 (50.67%)
Current smoker	27 (18.00%)
Comorbidities	
Type 2 diabetes mellitus	84/142 (59.15%)
Pulmonary hypertension	63 (42.00%)
Heart failure	70 (46.67%)
- Preserved ejection fraction	50 (33.33%)
- Reduced ejection fraction	20 (13.33%)
Biomass exposure	65 (43.33%)
Previous exacerbation episode	112 (74.67%)
Hospitalizations (last 1 year)	1 (0 – 2)*
Positive culture	42 (28.00%)
Duration of hospital stay (days)	3 (2 – 7)*
Prolonged hospital stay (>7 days)	38 (25.33%)
In-hospital mortality	15 (10.00%)
Respiratory support	
Vasopressors	20 (13.33%)
Non-invasive ventilation (NIV)	94 (62.67%)
Mechanical ventilation	7 (4.67%)
Hypercapnic respiratory failure	66 (44.00%)
Discharge on home NIV	65 (43.33%)
Long-term management	
Inhalers on discharge	128 (85.33%)
Long-term oxygen therapy	59 (39.33%)
Long-term home NIV	47 (31.33%)

*Data presented as mean ± standard deviation, n (%), or median (interquartile range). †Based on Asian-Pacific Obesity Classification guideline (Normal 18.5-22.9 kg/m², Underweight <18.5 kg/m², Overweight 23.0-24.9 kg/m², Obese 25.0 kg/m²).

Table 2. Comparison of characteristics between patients with acute exacerbation of chronic obstructive pulmonary disease stratified by length of hospital stay.

Characteristic	<7 days (n=112)	7 days (n=38)	p-value
Age (years)	72.06 ± 10.81	73.84 ± 8.92	0.362
Sex (Male)	63 (56.25%)	32 (84.21%)	0.002
BMI (kg/m ²)	26.21 ± 4.77	25.28 ± 5.64	0.322
Type 2 diabetes mellitus	56/106 (52.83%)	28/36 (77.78%)	0.009
Pulmonary hypertension	34 (30.36%)	29 (76.32%)	<0.001
Heart failure	47 (41.96%)	23 (60.53%)	0.047
Biomass exposure	56 (50.00%)	9 (23.68%)	0.005
Smoking status	70 (62.50%)	33 (86.84%)	0.005
Previous exacerbation episode	75 (66.96%)	37 (97.37%)	<0.001†
Hospitalizations (last 1 year)*	1 (0 – 2)	2 (2 – 3)	<0.001
Positive culture	15 (13.39%)	27 (71.05%)	<0.001
<i>Pseudomonas aeruginosa</i>	5 (4.46%)	18 (47.37%)	<0.001†
Vasopressors	4 (3.57%)	16 (42.11%)	<0.001†
Non-invasive ventilation	57 (50.89%)	37 (97.37%)	<0.001†
Mechanical ventilation	0 (0.0%)	7 (18.42%)	<0.001†
Hypercapnic respiratory failure	34 (30.36%)	32 (84.21%)	<0.001
In-hospital mortality	5 (4.46%)	10 (26.32%)	<0.001†

*Data presented as mean ± standard deviation, n (%), or median (interquartile range). Categorical variables compared using Chi-square or †Fisher's exact test; continuous variables compared using independent t-test or ‡Mann-Whitney U test.

Table 3. Comparison of characteristics between survivors and non-survivors in patients with acute exacerbation of chronic obstructive pulmonary disease.

Characteristic	Survivors (n=135)	Non-Survivors (n=15)	p-value
Age (years)	72.30 ± 10.40	74.40 ± 10.15	0.459
Sex (Male)	81 (60.00%)	14 (93.33%)	0.011
BMI (kg/m ²)	26.08 ± 5.06	25.07 ± 4.52	0.462
Type 2 diabetes mellitus	74 (57.36%)	10 (76.92%)	0.171
Pulmonary hypertension	51 (37.78%)	12 (80.00%)	0.002
Heart failure	62 (45.93%)	8 (53.33%)	0.585
Biomass exposure	62 (45.93%)	3 (20.00%)	0.055
Smoking status	89 (65.93%)	14 (93.33%)	0.030
Previous exacerbation episode	97 (71.85%)	15 (100.00%)	0.013†
Hospitalizations (last 1 year)*	1 (0 – 2)	3 (2 – 3)	<0.001
Positive culture	33 (24.44%)	9 (60.00%)	0.006†
<i>Pseudomonas aeruginosa</i>	18 (13.33%)	5 (33.33%)	0.041
Vasopressors	9 (6.67%)	11 (73.33%)	<0.001†
Non-invasive ventilation	81 (60.00%)	13 (86.67%)	0.043
Mechanical ventilation	5 (3.70%)	2 (13.33%)	0.146†
Hypercapnic respiratory failure	53 (39.26%)	13 (86.67%)	<0.001
Duration of hospital stay (days)*	3 (2 – 4)	8 (4 – 10)	<0.001

*Data presented as mean ± standard deviation, n (%), or median (interquartile range). Categorical variables compared using Chi-square or †Fisher's exact test; continuous variables compared using independent t-test or ‡Mann-Whitney U test.

Table 4. Multivariable logistic regression analysis of factors associated with prolonged hospital stay in patients with acute exacerbation of chronic obstructive pulmonary disease.

Variable	Crude OR (95% CI)	Adjusted OR (95% CI)	p-value
Age (Years)	1.017 (0.981 - 1.054)	-	-
Sex (Male)	4.148 (1.607 - 10.710)	1.394 (0.137 - 14.197)	0.779
BMI (kg/m ²)	0.961 (0.889 - 1.039)	-	-
Type 2 diabetes mellitus	3.125 (1.305 - 7.484)	2.111 (0.557 - 7.996)	0.272
Pulmonary hypertension	7.392 (3.161 - 17.285)	3.028 (0.838 - 10.939)	0.091
Heart failure	2.121 (1.001 - 4.494)	2.651 (0.716 - 9.810)	0.144
Biomass exposure	0.310 (0.135 - 0.715)	0.779 (0.132 - 4.589)	0.783
Smoking status	3.960 (1.435 - 10.931)	3.208 (0.248 - 41.528)	0.372
Hospitalizations (previous year)	1.947 (1.408 - 2.692)	1.544 (0.879 - 2.710)	0.131
<i>Pseudomonas aeruginosa</i> infection	19.260 (6.412 - 57.852)	11.462 (2.493 - 52.700)	0.002
Vasopressor use	19.636 (5.988 - 64.398)	2.578 (0.453 - 14.662)	0.286
Non-invasive ventilation	35.702 (4.734 - 269.273)	7.965 (0.583 - 108.821)	0.120
Hypercapnic respiratory failure	12.235 (4.683 - 31.970)	2.085 (0.405 - 10.737)	0.380

OR, odds ratio; CI: confidence interval. The multivariable model included all variables with $p < 0.1$ in univariable analysis.

Table 5. Multivariable logistic regression analysis of factors associated with in-hospital mortality in patients with acute exacerbation of chronic obstructive pulmonary disease.

Variable	Crude OR (95% CI)	Adjusted OR (95% CI)	p-value
Age (Years)	1.020 (0.968 - 1.074)	-	-
Sex (Male)	9.333 (1.192 - 73.066)	6.001 (0.191 - 188.727)	0.308
BMI (kg/m ²)	0.957 (0.852 - 1.075)	-	-
Type 2 diabetes mellitus	2.477 (0.651 - 9.429)	-	-
Pulmonary hypertension	6.588 (1.774 - 24.469)	1.373 (0.193 - 9.775)	0.752
Heart Failure	1.346 (0.462 - 3.921)	-	-
Biomass exposure	0.294 (0.079 - 1.091)	1.595 (0.087 - 29.331)	0.753
Smoking status	7.236 (0.922 - 56.758)	2.597 (0.078 - 86.852)	0.594
Hospitalizations (previous year)	2.092 (1.420 - 3.082)	1.651 (0.914 - 2.985)	0.097
<i>Pseudomonas aeruginosa</i> infection	3.250 (0.996 - 10.605)	0.166 (0.018 - 1.485)	0.108
<i>Acinetobacter</i> infection	10.231 (1.329 - 78.763)	9.799 (0.644 - 149.032)	0.100
Vasopressor use	38.500 (10.190 - 145.461)	40.350 (4.488 - 362.793)	0.001
Non-invasive ventilation	4.333 (0.940 - 19.972)	0.242 (0.007 - 8.599)	0.436
Hypercapnic respiratory failure	10.057 (2.181 - 46.362)	5.965 (0.196 - 181.414)	0.305

OR, odds ratio; CI, confidence interval. The multivariable model included all variables with $p < 0.1$ in univariable analysis.