


Original Article

Prevalence of Eosinophilia in Chronic Obstructive Pulmonary Disease Exacerbation

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ABSTRACT

Chronic Obstructive Pulmonary Disease (COPD) is a major cause of morbidity and mortality worldwide. **Objectives:** To determine the prevalence of eosinophilia in COPD exacerbation, and to evaluate its association with exacerbation severity. **Methods:** This cross-sectional study was conducted at the Department of Pulmonology, Indus Hospital and Health Network, Karachi, Pakistan, during April 2024 to September 2024. A total of 141 diagnosed cases of COPD patients were analyzed. Eosinophilia was labeled as a blood eosinophil count $\geq 2\%$. Stratification analysis was performed to observe the effects of effect modifiers on the prevalence of eosinophilia, applying Chi-square or Fisher's exact test, taking $p < 0.050$ as statistically significant. **Results:** In a total of 141 patients, 101 (71.6%) were males, and the median age was 62.0 (52.0-71.0) years. Monthly family income was classified as low in 80 (56.7%) patients. Smoking status was 'never smoked' in 65 (46.1%), 'ex-smoker' in 61 (43.3%), and 'current smoker' in 15 (10.6%) patients. Hypertension and diabetes mellitus were reported in 92 (65.2%) and 73 (51.8%) patients. Eosinophilia was identified in 58 (41.1%) patients. Smoking status differed significantly with respect to the prevalence of eosinophilia ($p = 0.024$). Severity of COPD exacerbation differed by eosinophilia status, as increasing severity was significantly associated with eosinophilia ($p < 0.001$). **Conclusions:** Blood eosinophilia was frequently observed among patients admitted with COPD exacerbation and showed a significant association with smoking status and exacerbation severity.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a major cause of morbidity and mortality worldwide. Around 250 million people are estimated to suffer from COPD annually, whereas 5% of total annual deaths are attributed to COPD [1]. COPD is the 4th leading cause of mortality and is projected to rise as the 3rd leading cause of death in 2050 [2, 3]. Population-based evidence from South Asia indicates a substantial prevalence of spirometry-defined COPD, with a pooled estimate of 8.0-11.1% [4]. In Pakistan, community-level estimates remain heterogeneous, yet regional epidemiological data reported a COPD prevalence of 2.1% among adults aged over 40 years [5]. Eosinophilic inflammation is anticipated in COPD, and contemporary

literature exhibits that eosinophils may reflect therapeutic effects and phenotypes of COPD [6]. With recent developments, the role of controlling blood eosinophilia in COPD management has increased, and COPD with increased eosinophilia is also used as a biomarker of exacerbations [7, 8]. Significant variability in blood eosinophil levels has been shown throughout the course of COPD. In 25%-40% of COPD exacerbations, the eosinophilic phenotype is present [9]. Smoking is one of the primary determinants of COPD progression and exacerbation risk, and prior cohort data suggest that the relationship between blood eosinophils and exacerbations may vary by smoking status, indicating potential effect

modification [10]. Diabetes and hypertension are highly prevalent comorbidities in COPD and have been linked with higher exacerbation-related healthcare use and worse inpatient outcomes, which is clinically relevant because systemic corticosteroids used during exacerbations can worsen glycaemic control and cardiometabolic instability [11]. Evaluating smoking status and cardiometabolic comorbidity alongside eosinophil measurements can refine the interpretation of eosinophilic phenotypes during acute exacerbations and inform risk stratification and treatment decisions.

The prevalence of eosinophilic COPD exacerbation in Asian populations has only been briefly studied. Not much recent data from Pakistan is available about the evaluation of eosinophilia in newly diagnosed COPD patients. This study aims to determine the prevalence of blood eosinophilia among patients with acute exacerbation of COPD, and to evaluate its association with exacerbation severity.

METHODS

This cross-sectional study was performed at the Department of Pulmonology, Indus Hospital and Health Network, Karachi, Pakistan, during April 2024 to September 2024. A sample size of 141 was calculated through the online Open Epi sample size calculator, taking the anticipated proportion of eosinophilia in COPD as 15.6% [12], with 95% confidence level and 6% margin of error. Non-probability, consecutive sampling technique was adopted. Inclusion criteria were patients of any gender, aged 40-80 years, and diagnosed with COPD according to GOLD, as clinical history and spirometry showed persistent airflow limitation with a ratio of FEV1 / FVC < 0.70 pre- and post-bronchodilator [13]. Patients with a history of asthma and bronchiectasis, on long-term oral steroid use, or diagnosed with tuberculosis were excluded. This study was commenced after approval from the Institutional Review Board (IHHN_IRB_2024_03_002; dated 29th March 2024). Written informed consent was obtained from each participant or caregiver. Information like age, gender, monthly family income, and smoking status was collected from the patients. Weight and height were recorded at enrolment, and body mass index (BMI) was calculated as weight (kg) divided by height (m²). Venous blood was drawn under aseptic technique, and 2-3 mL was collected in an EDTA tube, gently inverted, transported promptly to the laboratory, and analyzed for CBC with differential on an automated hematology analyzer, and eosinophilia was defined as $\geq 2\%$ eosinophils [12]. Diabetes mellitus was defined as a prior documented diagnosis or use of glucose-lowering medication, or random plasma glucose ≥ 200 mg/dL at presentation. Hypertension was defined as a prior documented diagnosis or use of antihypertensive medication, or systolic blood pressure ≥ 140 mmHg and or

diastolic blood pressure ≥ 90 mmHg on presentation (measured after 5 minutes rest, repeated if elevated). Monthly family income was recorded in Pakistani Rupees per month and categorized into low ($\leq 55,000$), middle (55,001-80,000), and high ($> 80,000$) [14]. COPD exacerbation severity was categorized according to guideline-based event definitions as mild when managed with short-acting bronchodilators alone, moderate when requiring systemic corticosteroids and or antibiotics, and severe when requiring emergency department visit or hospital admission [13]. All information was recorded into a pre-designed proforma by the researchers themselves.

Statistical analyses were performed using IBM-SPSS Statistics, version 26.0. All continuous variables like age, height, weight, body mass index (BMI), and eosinophil count were assessed by the Shapiro-Wilk test to check for normality assumption and represented as mean and standard deviation (SD), or median and inter-quartile range (IQR). Frequency and percentage were computed for all categorical variables, such as gender, smoking status, hypertension, diabetic mellitus, monthly family income status, education status, COPD severity, and eosinophilia (yes/ no). Stratification analysis was performed to observe the effects of effect modifiers like age, BMI, gender, smoking status, hypertension, diabetic mellitus, monthly family income, education status, and COPD severity on the prevalence of eosinophilia. After stratification, the chi-square or Fisher exact test was used to observe the effect of effect modifiers on the outcome (eosinophilia), and odds ratios (OR) with 95% confidence interval (CI) were calculated, taking $p < 0.050$ as statistically significant.

RESULTS

In a total of 141 patients, 101 (71.6%) were males, and 40 (28.4%) were females. The median age was 62.0 (52.0-71.0) years. There were 94 (66.7) patients who had a BMI between 18.5 and 24.9 kg/m². Monthly family income status was classified as low in 80 (56.7%) patients. Smoking status was 'never smoked' in 65 (46.1%), 'ex-smoker' in 61 (43.3%), and 'current smoker' in 15 (10.6%) patients. Hypertension and diabetes mellitus were reported in 92 (65.2%) and 73 (51.8%) patients, respectively. The study shows details about the characteristics of patients studied (Table 1).

Table 1: Characteristics of Patients (n=141)

Characteristics		Frequency (%)
Gender	Male	101 (71.6%)
	Female	40 (28.43%)
Age Groups (years)	40 to 50	17 (12.1%)
	51 to 60	45 (31.9%)
	61 to 70	46 (32.6%)
	71 to 80	33 (23.4%)

BMI (kg/m ²)	<18.5	8 (5.7%)
	18.5 to 24.9	94 (66.7%)
	25.0 to 29.9	22 (15.6%)
	≥30.0	17 (12.1%)
Monthly Family Income	Low	80 (56.7%)
	Middle	49 (34.8%)
	High	12 (8.5%)
Education	Illiterate	58 (41.1%)
	Primary-Secondary	30 (21.3%)
	Matriculation	36 (25.5%)
	Intermediate	11 (7.8%)
	Graduation or above	6 (4.3%)
Smoking	Never Smoked	65 (46.1%)
	Ex-smoker	61 (43.3%)
	Current Smoker	15 (10.6%)
Hypertension	—	92 (65.2%)
Diabetes Mellitus	—	73 (51.8%)

Eosinophilia was identified in 58 (41.1%) patients with COPD exacerbation, while 83 (58.9%) had no eosinophilia. Eosinophilia prevalence did not differ with respect to gender ($p=0.437$), age groups ($p=0.518$), BMI ($p=0.181$), monthly family income ($p=0.167$), education status ($p=0.615$), hypertension ($p=0.209$), and diabetes mellitus ($p=0.499$). Smoking status differed significantly with respect to the prevalence of eosinophilia prevalence ($p=0.024$), as the current smoking status was recorded in 10 (17.2%) patients with eosinophilia, and 5 (6.0%) without eosinophilia, with OR of 4.5 (95% CI 1.4 to 14.9) compared with never-smokers, and ex-smokers were 28 (48.3%) among eosinophilia patients, and 33 (39.8%) in the non-eosinophilia group, with OR 1.9 (95% CI 0.9 to 4.0). The details about the association of eosinophilia with various demographic and clinical characteristics of patients are shown (Table 2).

Table 2: Association of Eosinophilia with Various Demographic and Clinical Characteristics (n=141)

Characteristics		Eosinophilia		95% CI	p-value
		Yes (n=58)	No (n=83)		
Gender	Male	39 (67.2%)	62 (74.7%)	Reference	0.512
	Female	19 (32.8%)	21 (25.3%)	1.4 (0.7-3.0)	
Age Groups (years)	40 to 50	7 (12.1%)	10 (12.0%)	Reference	0.518
	51 to 60	21 (36.2%)	24 (28.9%)	1.3 (0.4-3.9)	
	61 to 70	20 (34.5%)	26 (31.3%)	1.1 (0.4-3.4)	
	71 to 80	10 (17.2%)	23 (27.7%)	0.6 (0.2-2.1)	
BMI (kg/m ²)	<18.5	2 (3.4%)	6 (7.2%)	0.5 (0.1-2.4)	0.181
	18.5 to 24.9	40 (69.0%)	54 (65.1%)	Reference	
	25.0 to 29.9	6 (10.3%)	16 (19.3%)	0.5 (0.2-1.4)	
	≥30.0	10 (17.2%)	7 (8.4%)	1.9 (0.7-5.5)	
Monthly Family Income	Low	38 (65.5%)	42 (50.6%)	Reference	0.167
	Middle	15 (25.9%)	34 (41.0%)	0.5 (0.2-1.0)	
	High	5 (8.6%)	7 (8.4%)	0.8 (0.2-2.7)	
Education	Illiterate	26 (44.8%)	32 (38.6%)	Reference	0.615
	Primary-Secondary	14 (24.1%)	16 (19.3%)	1.1 (0.5-2.6)	
	Matriculation	11 (19.0%)	25 (30.1%)	0.5 (0.2-1.3)	
	Intermediate	4 (6.9%)	7 (8.4%)	0.7 (0.2-2.7)	
	Graduation or above	3 (5.2%)	3 (3.6%)	1.2 (0.2-6.6)	
Smoking	Never Smoked	20 (34.5%)	45 (54.2%)	Reference	0.024
	Ex-smoker	28 (48.3%)	33 (39.8%)	1.9 (0.9-4.0)	
	Current Smoker	10 (17.2%)	5 (6.0%)	4.5 (1.4-14.9)	
Hypertension	—	44 (75.9%)	48 (57.8%)	2.3 (1.1-4.8)	0.209
Diabetes Mellitus	—	32 (55.2%)	41 (49.4%)	1.3 (0.6-2.5)	0.499

Severity of COPD exacerbation differed by eosinophilia status, as increasing severity was significantly associated with eosinophilia ($p<0.001$) (Figure 1).

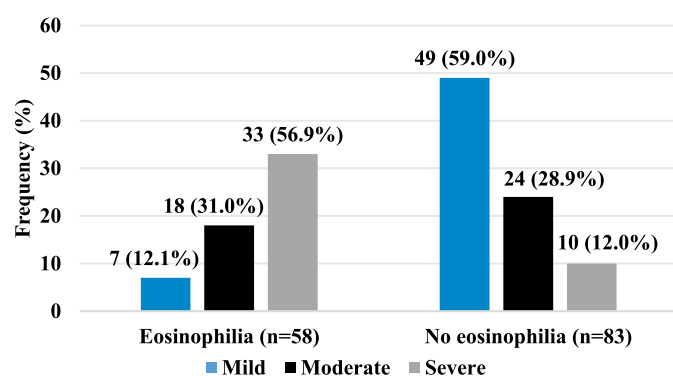


Figure 1: Association of Prevalence of Eosinophilia with Respect to Severity of COPD Exacerbation (n=141)

DISCUSSION

Blood eosinophilia was identified in 41.1% patients presenting with COPD exacerbation. This prevalence sits close to estimates reported by Hasegawa and Camargo Jr., where eosinophilia based on the same $\geq 2\%$ threshold was observed in 40% of hospitalized COPD patients with exacerbation, supporting the view that a relative eosinophil cut-off identifies a substantial eosinophilic phenotype in COPD patients [15]. Javed *et al.* in a local study from Faisalabad, found eosinophilia in 39.3% patients with acute exacerbation of COPD [16]. These estimates from different centers suggest that eosinophilia is frequently encountered during COPD exacerbations [17]. Ahmad *et al.* reported eosinophilia in 23.7% COPD patients [17]. The absence of a statistically significant difference in eosinophilia prevalence across age strata, or gender distribution in the present study, is consistent with reports that eosinophilic status is not primarily driven by age alone. A study from Saudi Arabia examined eosinophilic COPD and found no meaningful differences between eosinophilic and non-eosinophilic groups in age or gender distribution [18]. Kiani *et al.* described higher pack-year exposure and pulmonary hypertension prevalence with higher eosinophils at diagnosis, yet ICU admission, invasive ventilation requirement, and mortality during exacerbations were not clearly separated by eosinophil status, indicating that eosinophilia may not map neatly onto various indices or all markers of physiological compromise [19]. Monthly family income and educational attainment were also not associated with eosinophilia in the present study. Smoking status showed a significant association with eosinophilia, as current smoking was recorded in 17.2% patients with eosinophilia, and 6.0% without eosinophilia, corresponding to an OR of 4.5 (95% CI 1.4 to 14.9). Ex-smokers comprised 48.3% in the eosinophilia patients, and 39.8% in the non-eosinophilia patients, with an OR of 1.9 (95% CI 0.9 to 4.0). This relationship may reflect several mechanisms, as active smoking can promote airway epithelial injury and

dysregulated immune signaling, and may interact with corticosteroid exposure and infection patterns that shape blood eosinophil proportions during acute illness [20]. The present results indicate that smoking cessation counselling remains central not only for exacerbation prevention but also because smoking may be linked to inflammatory profiles that influence acute management decisions. Exacerbation severity differed by eosinophilia status in the present study, with increasing severity significantly associated with eosinophilia ($p < 0.001$). This observation is clinically important because it suggests that eosinophilic inflammation may cluster among greater acute care requirements, reinforcing the role of eosinophils as a marker of exacerbation phenotype rather than baseline demographics [21]. The link is consistent with longitudinal evidence that eosinophil elevation predicts future exacerbation burden. Vedel-Krogh *et al.* reported that higher baseline blood eosinophils were associated with increased incidence rate ratios for both severe and moderate exacerbations, indicating that eosinophil-driven inflammation is connected to subsequent exacerbation trajectories [22]. Chan *et al.* observed that eosinophil proportions $\geq 2\%$ were associated with higher exacerbation frequency over the subsequent 12 months and conferred an adjusted odds ratio of 2.98 for exacerbation risk [23]. Juthong and Kaenmuang found higher annual exacerbation rates and higher admission frequency in eosinophilic COPD defined by ≥ 300 cells/ μL , with admission burden differences aligning with the concept that eosinophilia tracks higher healthcare utilization [24]. These findings provide a possible mechanistic and prognostic context in which the present severity association is plausible, especially in an inpatient cohort enriched for clinically significant events.

The study was conducted at a single center with non-probability consecutive sampling, which may limit generalizability across different healthcare settings and referral patterns. Eosinophilia was defined using a proportional cut-off of $\geq 2\%$ rather than absolute eosinophil count thresholds, which complicates direct comparison with cohorts using absolute definitions. Pack-years and recency of smoking were not captured, which restricts quantified response assessment. The present analysis did not quantify treatment outcomes.

CONCLUSIONS

It was concluded that the blood eosinophilia was frequently observed among patients admitted with COPD exacerbation and showed a significant association with smoking status and exacerbation severity.

Authors' Contribution

Conceptualization: K

Methodology: AM, RK, MH, SA

Formal analysis: AM

Writing and Drafting: KA, K

Review and Editing: KA, K, AM, RK, MH, SA

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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