

## Frequency of Eosinophilia among Patients of Chronic Obstructive Pulmonary Disease with Acute Exacerbation

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### ABSTRACT

**Objective:** To determine the frequency of eosinophilia among patients of chronic obstructive pulmonary disease with acute exacerbation

**Methodology:** This cross-sectional study was carried out at Aziz Fatimah Hospital (AFH), Faisalabad from February 2020-May 2020. Ethical approval was taken from Institutional Ethical Committee of Aziz Fatimah Medical and Dental College. After obtaining informed consent, 135 patients of chronic obstructive pulmonary disease were enrolled by non-probability consecutive sampling technique according to inclusion and exclusion criteria. All the information was collected on predesigned proforma. Blood samples were drawn and sent to the AFH pathology laboratory for determination of eosinophilia. Statistical analysis was performed by SPSS 21. Mean and percentages were determined for continuous and categorical variables respectively. Chi square test was applied for differences in proportions.

**Results:** This study comprised of 135 patients of chronic obstructive pulmonary disease. Out of total participants 48.89% (n=66) were male and 51.11% (n=69) were females. Mean±SD of the age of the study subjects was 56.30±7.01 years. Eosinophilia was found in 39.26% (n=53) patients of chronic obstructive pulmonary disease with acute exacerbation.

**Conclusion:** Eosinophilia is frequently found in patients of chronic obstructive pulmonary disease with acute exacerbation.

**KEYWORDS:** Acute Exacerbation Chronic Obstructive Pulmonary Disease, Eosinophilia.

### INTRODUCTION

Chronic obstructive pulmonary disease (COPD) especially with frequent exacerbations increases the

economic burden up to 50-75% on health care system of any society because of more visits to OPD clinics and also increased number of hospitalizations.<sup>1</sup> In COPD there is progressive air flow limitation which interferes with normal life activities and is not fully reversible. Factors responsible for it may be abnormal inflammatory response to noxious gases or particles like tobacco smoke, biomass solid fuel, coal, crop residues etc. Moreover, in addition to this airway hypersensitivity which may cause exacerbation of the disease sometimes may even requires the change of treatment.<sup>2</sup> Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) means aggravation of symptoms and deterioration of the Pulmonary Function Tests (PFTs) by infection or change in quality of air, resulting in respiratory failure or even death.<sup>3,4</sup> COPD is considered to be a progressive, debilitating disease resulting in approximately 23% of all the respiratory diseases related mortalities, a fact which is especially observed in case of AECOPD.<sup>3,5</sup> It aggravates the situation by rapid progression of the disease, poor quality of life and higher mortality rate.<sup>6</sup> Apart from a predominant neutrophilic pattern of inflammation, various research studies show that

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eosinophils also play role in the underlying pattern of inflammation in about 1/3 patients of COPD. Although it is a fact that eosinophilia is commonly associated with bronchial asthma which is indicated by blood and sputum eosinophilia. This phenomenon is also seen in COPD patients and more consistently in cases of AECOPD.<sup>7</sup> It has also been observed that this fact depends upon specific population under study and on eosinophil threshold. Presence of eosinophilic inflammation in the COPD patients is very significant as it predicts response to inhaled corticosteroids (ICS) for prevention and systemic corticosteroids (SCS) for the treatment of AECOPD.

Detection of eosinophilia from the sputum is more time consuming and samples of sputum may also be inadequate. Comparatively determination of blood eosinophil count is easy and practically a surrogate biomarker for sputum eosinophilia, in COPD and AECOPD.<sup>8,9</sup> In this regard Pavord et al detected eosinophilia in 74% of patients in TRISTAN study whereas Couillard et al observed blood eosinophilia in 32.90% of COPD patients.<sup>3,10</sup> Both aforementioned studies signify the important role of eosinophilic inflammation in the pathophysiology of AECOPD, although a lot of variation in eosinophil count is seen in these studies. Recent research has elaborated role of eosinophils in prediction and treatment of COPD and acute exacerbation of COPD. High level of eosinophils in blood is now taken as a possible biomarker in the diagnosis and management of exacerbation of COPD.<sup>11</sup> Due to conflicting results reported by the previous researches, impact of eosinophilia on the prognosis of COPD exacerbations is still under debate. Some previous studies have documented the high rate of exacerbation with eosinophilia, while others suggested fewer aggravating attacks. Numerous studies have reported high blood eosinophils count in COPD patients results in longer hospital stay with high risk of mortality.<sup>12</sup>

Regarding pathogenesis, it is suggested that eosinophilia is because of expression of more complex chemokines including RANTES (regulated upon activation normal T-cell expressed and secreted) responsible for recruiting inflammatory cells including eosinophils at the sites of inflammation.<sup>13</sup> The aim of current study was to explore frequency of blood eosinophilia in COPD patients with acute exacerbations.

## METHODOLOGY

This cross-sectional study was conducted at Aziz Fatimah Hospital (AFH) Faisalabad from February

2020 to May 2020. Ethical approval was taken from Institutional Ethical Committee of Aziz Fatimah Medical and Dental College (IEC-42-20). Sample size of 135 was calculated by using WHO sample size calculator with prevalence (P) 2.9%<sup>7</sup>, Confidence level = 95 % and absolute precision required = 8% . This study recruited 135 subjects enrolled with non-probability consecutive sampling technique. COPD subjects of either gender with age between 40-80 years having acute exacerbation presenting to medical Out Patient Department (OPD) were enrolled. Subjects with asthma, pneumothorax, congestive cardiac failure or malignancy, with the history of major surgery in previous four weeks, patients who were on mechanical ventilation, patients receiving anticoagulation therapy and subjects presenting with azotemia (serum creatinine >1.5 mg/dl) were excluded from this study. Informed consent was taken from each participant. All relevant information like, age, gender, duration of disease, and medical history were recorded on pre-designed proforma. After aseptic techniques blood samples were drawn and sent to the AFH pathology laboratory for determination of blood eosinophil count. Eosinophilia cutoff value is taken as  $\geq 2\%$  (equivalent to about  $\geq 150$  cells  $\mu\text{L}^{-1}$ ).<sup>11</sup>

**Statistical analysis** was performed by SPSS 21. Mean and standard deviation was calculated for all quantitative variables like age and duration of COPD. Frequencies and percentages were calculated for all qualitative variables like gender, COPD and eosinophilia. Chi-square was applied for differences in proportions. P value  $\leq 0.05$  were taken as significant.

## RESULTS

A total of 135 cases of COPD with acute exacerbation fulfilling the selection criteria were enrolled in this study to determine the frequency of blood eosinophilia. Mean $\pm$ SD of the age of study participants was 56.30  $\pm$  7.01 years. Mean duration of COPD was calculated as 2.58 $\pm$ 0.78 weeks.

**Table 1: Frequency of Eosinophilia among Patients of Chronic Obstructive Pulmonary Disease with Acute Exacerbation (n=135)**

Eosinophilia	No. of patients (n)	Percentages (%)
Yes	53	39.26
No	82	60.74
Total	135	100

Eosinophilia cut off value was taken as  $\geq 2\%$  (equivalent to about  $\geq 150$  cells  $\mu\text{L}^{-1}$ ), p value  $\leq 0.05$  is taken significant.

On analyzing overall population current results shows that eosinophilia was found in 39.26% (n=53) of the total patients of chronic obstructive pulmonary disease with acute exacerbation, whereas 60.74% (n=82) did not have this finding (Table 1). Age distribution of the study participants is shown in the Table.2 Significant difference was not found concerning frequency of Eosinophilia among the various age groups of studied population with p-value 1.69 (Table2). Of total participants, 48.89 % (n=66) were male and 51.11% (n=69) were female. Eosinophilia was found almost equally in both genders, significant difference in percentages of eosinophilia among the gender was not found. (p value 1.09). (Table No. 3).

**Table 2: Comparison Eosinophilia among Different Age Groups (N=135)**

Age (years)	Frequency n (%)	Eosinophilia	
		Yes n (%)	No n (%)
40-60	84(62.22)	33(39.3)	51(60.7)
61-80	51(37.78)	20(39.2)	31(60.7)
Total	135(100)	53	82
P value		1.69	

Eosinophilia cut off value was taken as  $\geq 2\%$  (equivalent to about  $\geq 150$  cells  $\mu\text{L}^{-1}$ ), p value  $\leq 0.05$  is taken significant.

**Table3: Comparison Eosinophilia Frequency on Bases of Gender (n=135)**

Gender	Frequency n (%)	Eosinophilia	
		Yes n (%)	No n (%)
Male	66(48.89)	26(39.39)	40(60.6)
Female	69(51.11)	27(39.13)	42(60.8)
Total	135(100)	53(39.2)	82(60.7)
p value		1.09	

Eosinophilia cut off value was taken as  $\geq 2\%$  (equivalent to about  $\geq 150$  cells  $\mu\text{L}^{-1}$ ), COPD = Chronic Obstructive Pulmonary Disease. p value  $\leq 0.05$  was significant, p value  $\leq 0.05$  is taken significant.

## DISCUSSION

Chronic progressive diseases including COPD with frequent exacerbations will always remain the largest economic burden on the health care system globally.<sup>3</sup> Eosinophilic inflammation is most often associated with bronchial asthma, but researches done in this field have proved that about one third of patients with COPD also have blood and/or sputum eosinophilia, although its detection depends upon eosinophil threshold used and the patient population under study.<sup>7,8</sup> Several previous studies have proposed levels of eosinophil count as a predictor of response to treatment with inhaled corticosteroid (ICS) in patients of COPD with acute exacerbations.<sup>14,15</sup> On the other hand, this emerging role for blood eosinophil count as

biomarker in COPD patients as a guide for inhaled corticosteroid (ICS) therapy has been challenged recently. Previous ISOLDE study documented better effects of ICS in acute exacerbation with lower blood eosinophilic count when compared in subjects with eosinophilia.<sup>16</sup> Contrary to this FLAME study has reported superior effects of long-acting  $\beta_2$ -agonist (LABA), and long-acting muscarinic antagonist (LAMA) in preventing COPD exacerbations irrespective of eosinophil count.<sup>17</sup> On the basis of all these researches conducted in various large scale trials, it is now generally considered that a blood eosinophil count  $\geq 2\%$  (equivalent to about  $\geq 150$  cells  $\mu\text{L}^{-1}$ ) is a useful biomarker for the prediction of frequent exacerbations and their prevention with the use of inhaled steroids.<sup>11</sup> Due to this fact that there is lot of variation in the literature regarding the presence of eosinophilia in patients with AECOPD. Furthermore, limited data from Pakistan is available at national level in this respect. The goal of this study was early detection of blood eosinophilia in COPD patients which helps us to take appropriate measures early for its effective prevention and treatment so that the outcome of patients can be optimized and financial impact of the disease can be minimized.

Current results reveal that only 39.26% (n=53) of total patients of COPD with acute exacerbation showed eosinophilia. The eosinophilia was found equally in both age groups of the study. Another previous study conducted at Haripur Pakistan also reported similar results.<sup>12</sup> Current results were also in accordance to Couillard et al where eosinophilia was present in 32.9% patients of COPD.<sup>10</sup> Present results are also justified by ECLIPSE study that found 37.4% of patients with persistent high eosinophilia whereas 49% of patients showed intermittent elevation of eosinophils.<sup>18</sup> Researches are available showing higher percentages and found eosinophilia in 74.77% of COPD patients.<sup>3</sup> There is a marked variations concerning levels of eosinophils in current study with international studies. High prevalence of eosinophilia was reported by Poverd et al as compared with our study and another Pakistani study from Haripur. Disparity between Pakistani studies and previous international study by Poverd et al is probably due to the variability of demographics and diverse ethnicities as samples being taken from twenty-five different countries over the period of one year. Contrary to current results another follow up study of the long duration of eight years by Oshagbemi et al showed that 80% of patients of COPD had high eosinophil counts ( $\geq 340$  cells/ $\mu\text{L}$ ) at 6 months of their follow-up. This study suggests that variations in eosinophilic-count seen in patients with COPD

may be related to variations in disease stability (i.e. exacerbations) or pharmacologic therapy i.e, oral Corticosteroid courses.<sup>19</sup> Inconsistent result to our study have been reported from Copenhagen, Denmark by Jabarkhil et al, reporting eosinophilia only 13.2% of COPD patients.<sup>20</sup> However this aforementioned study concluded that COPD exacerbations in patients with eosinophilia have a better prognosis without the higher risk of subsequent exacerbation and lowers three-year mortality rate as compared to subjects with lower count of eosinophil.<sup>20</sup>

On comparing the eosinophilia among gender, current results shows eosinophilia was equally found COPD patients of both genders. Our results were not in line with ECLIPSE cohort study that reported persistent elevated blood eosinophils predominantly in old males.<sup>18</sup> Nevertheless high levels of eosinophils and eosinophil-associated pro-inflammatory factors in the air-ways and blood of patients with COPD are highly suggestive of the fact that eosinophils actively contribute to the inflammatory processes in these patients.<sup>21</sup> Future researches on a broader scales are required for elucidating the underline mechanism of eosinophilia for better management strategies for preventing COPD exacerbations and mortality to reduce the burden of this disease worldwide.

**Limitations:** It was a cross sectional study, so the casual inferences were not established. Sample size was small so results were not generalized to whole population.

## CONCLUSION

Eosinophilia is frequently found in patients of chronic obstructive pulmonary disease with acute exacerbation. Though, these results are preliminary and further studies, at national level, are required in this respect to substantiate this fact.

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**Conflicts of Interest:** None.

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### ***Authors' contribution:***

<b>Dr. Masood Javed</b>	Contributed to study design, acquisition of data and manuscript write up. Reviewed and approved the manuscript.
<b>Dr. Ghulam Abbas Sheikh</b>	Data acquisition, manuscript writing, Reviewed and approved the manuscript.
<b>Dr. Muhammad Rizwan</b>	Data analysis and interpretation of results, Revising manuscript critically for important intellectual content.
<b>Dr. Rizwan Rasul Khan</b>	Data collection, Data analysis and interpretation and write up of results. Reviewed and approved the manuscript.
<b>Dr. Nasir Mehmood</b>	Data collection, revised manuscript critically for important intellectual content and approved it.
<b>Dr. Mubarak Ali Anjum</b>	Data collection, drafting and formatting of final manuscript. Revised and approve the final manuscript.
	All authors are responsible for the integrity of the data and the accuracy of the data analysis.

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