

Frequency of Blood Eosinophilia in COPD Patients admitted with Acute Exacerbation

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Date Received: Jan 04, 2019
Date Revised: Feb 12, 2020
Date Accepted: Feb 27, 2020

Author Contributions

WA SA conceived idea, SA HA RF drafted the study, AW RF collected data, SA HA did statistics analysis and interpretation, SA RF critical review manuscript, All approved final version to be published

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

Abstract

Background: Chronic Obstructive Pulmonary Disease (COPD) is a heterogeneous disorder displaying variable clinical and pathophysiological features. Different phenotypes have been recognized that differ in respect to their biomarker profiles and response to treatment. Eosinophilic airway inflammation has been identified in significant number of COPD patients.

Objective: The objective of our study was to determine the frequency of blood eosinophilia in COPD patients admitted with acute exacerbation.

Methodology: This was a cross-sectional study conducted at pulmonology unit Khyber Teaching Hospital, Peshawar Pakistan from December 2016 to June 2017. All the COPD patients admitted with acute exacerbation (diagnosed by spirometry i.e. post bronchodilator FEV1/FVC less than 70) were enrolled in the study. Exclusion criteria were strictly followed to control confounding factors in our study. The age and gender of the patient was documented and blood eosinophil count was measured for each patient using a standardized method to eliminate bias. All the data was collected on a structured proforma and analyzed via SPSS v.19. Results were presented as tables/graphs and descriptive statistics were performed for qualitative variables.

Results: Out of 139 patients, 73 (52.5 %) were male and 66 (47.5%) were female. The mean age of the study population was 58.65 + 8.1. Most of the patients were concentrated in the age group 51-60(44.88%). Furthermore, 33 (23.74%) of COPD patients were found to have blood eosinophilia. Among the 33 patients found to have eosinophilia, 20 (68.42%) were male and 13 (31.57%) were female.

Conclusion: Approximately one quarter of COPD patients were found to have blood eosinophilia in this study. More than half of the COPD patients admitted with acute exacerbation, having eosinophilia were male.

Key Words: Blood Eosinophilia; Chronic Obstructive Pulmonary Disease; GOLD

This article may be cited as: Ahmad W, Ashraf S, Wahab A, Farooqi R, Ahmad H. Frequency of Blood Eosinophilia in COPD Patients admitted with Acute Exacerbation. Pak J Chest Med 2020; 26 (1):28-32

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a common obstructive airway disease characterized by airflow limitation that is progressively worsening, not fully reversible (with post-bronchodilator FEV1/FVC less than 0.7 and the FEV1 <80% predicted).^{1,2}

COPD is one of the important causes of mortality and morbidity across the globe.¹ All over the world about

210 million people have COPD.³ According to WHO facts sheet, globally more than 3 million people died of COPD in 2012 (6% of all deaths). According to BREATHE STUDY that was conducted in 10 countries including Pakistan, the overall prevalence of COPD in these countries is 3.6% and about 6.9 million people suffer from COPD symptoms in Pakistan.⁴ The clinical syndrome of COPD comprises of various phenotypes, including a subset of patients with eosinophilic airway inflammation.⁵ Prevalence of blood eosinophilia—a

marker for eosinophilic airway inflammation and its clinical characteristics have been reported in significant number of COPD patient in different studies.^{5,6} Previously eosinophilic inflammation was established as a characteristic feature of asthma rather than COPD,⁶ but now it has been recognized that eosinophilic airway inflammation exists in a good proportion of COPD patients, even after carefully excluding the patients with any features of asthma, such as b-agonist reversibility, bronchial hyper responsiveness, atopy or a childhood history of asthma.⁶ According to study conducted by K. Hasegawa, Carlos A et al blood eosinophilia (≥ 300 cells/ μ L) was reported in 17% of the COPD patient; while using an alternative cut-off level ($\geq 2\%$), elevated eosinophil count was observed in 40% of the patients.⁴ In a study by Price D et al, blood eosinophilia was found in 10% of the COPD patients.⁷ COPD patient with blood eosinophil counts persistently $> 2\%$, are less symptomatic, have good functional class and quality of life as determined by higher FEV1, and lower SGRQ and mMRC scores^{6,8} but higher frequency of readmission for AECOPD was observed during 1-year follow-up^{5,7}.

COPD patient with eosinophilia have shown greater response to corticosteroid treatment so eosinophilic airway inflammation in COPD can be used as a predictive biomarker of corticosteroid responsiveness during clinical stability and exacerbations.⁶ Clinical recovery can be enhanced and rates of exacerbation can be decreased significantly by titrating corticosteroid therapy according to eosinophil level. During exacerbation of COPD, sputum and blood eosinophil numbers are increased in a similar way so blood eosinophils can be used as a surrogate marker for airway eosinophilia to direct oral corticosteroid therapy in the treatment of COPD, to enhance clinical recovery and decrease the exacerbation rates.⁶ This study was conducted to determine the frequency of blood eosinophilia in patients with COPD in our setup that can help in guiding the targeted treatment.

Objective

Objective of the present study was to determine the

frequency of blood eosinophilia in COPD patients admitted with acute exacerbation.

Methods

This was a descriptive study conducted at pulmonology unit Khyber teaching hospital Peshawar from 10th Dec 2016 till 10th June 2017. Sample size was 139 with 95% confidence interval, 5% margin of error and prevalence of 10%.⁷ Consecutive, Non-Probability sampling technique was applied. All adult patients including both genders with spirometry proven COPD admitted due to acute exacerbation were included. Patient with asthma and other diseases or drugs causing pulmonary eosinophilia were excluded. After taking consent and appropriate management of these patients; age, gender and spirometric findings were noted. Blood eosinophils count of every patient was determined in KTH lab by a trained haematologist and by the same analyzer "medonic hematology analyzer". Eosinophilia was defined as Peripheral blood eosinophil count $\geq 2\%$ or Peripheral blood eosinophil count ≥ 300 cells/microliters.

All the data was collected on a designed proforma and was analyzed by using SPSS10. Categorical variables like gender; eosinophilia were computed via frequency and percentages. Numerical variables like age were computed via mean+ standard deviation. Blood eosinophilia was stratified among age groups and gender to see the effect modification. All the results were presented in the form of tables and graphs.

Results

In this study, a total of 139 patients with chronic obstructive pulmonary disease admitted with acute exacerbations and fulfilling the inclusion criteria were assessed for the presence of eosinophilia in blood. Out of 139 patients, 73 (52.5 %) were male and 66 (47.5%) were female. The mean age of the study population was 58.65 years + 8.096. Most of the patients were concentrated in the age group 51-60 (43.9%) as shown in table 1.

Out of 139 patients, 33 (23.74%) of COPD patients were found to have blood eosinophilia while 106

Table 1. Distribution of study cases on the basis of age groups

Age group (Years)	Frequency	Percent (% age)
< 50	32	23.0
51-60	61	43.9
61-70	46	33.1
Total	139	100.0

(76.26%) tested negative for blood eosinophilia (Figure 1). Among the 33 patients found to have eosinophilia, 20 (68.42%) were male and 13 (31.57%) were female (Table 2).

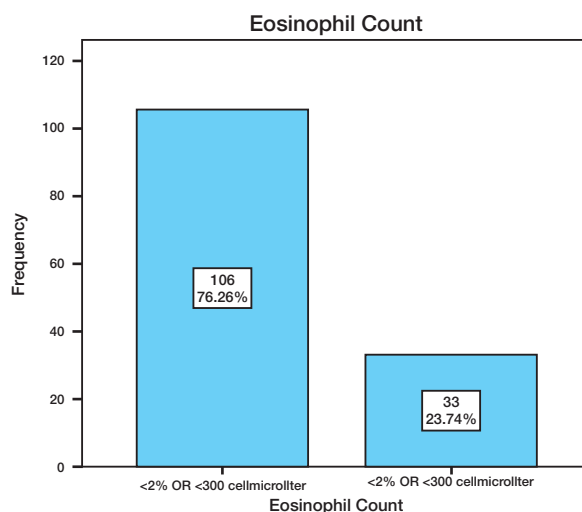


Fig 1. Frequency of blood eosinophilia in COPD patients(n=139)

Table 2. Eosinophil Count * Age group Crosstabulation

Eosinophil Count	Age group (Years)			Total
	<50	51-60	61-70	
≤2% OR ≤300cell/microliter	29	43	34	106
>2% OR >300cells/microlitre	3	18	12	33
Total	32	61	46	139

Discussion

Chronic obstructive pulmonary disease (COPD) is a heterogeneous condition, with patients displaying variable clinical and pathophysiological features.⁶ The clinical syndrome of COPD comprises of various phenotypes, including a subset of patients with eosinophilic airway inflammation.⁵ Airway eosinophilia has been shown to be associated with corticosteroid responsiveness in COPD. Peripheral blood eosinophil count has been recognized as a surrogate marker for airway eosinophilia during COPD exacerbations and it reflects the severity of the exacerbation.⁶ Blood eosinophil counts can be used to guide systemic corticosteroid treatment during an exacerbation of COPD resulting in reduced total exposure to systemic corticosteroids without adversely affecting the outcome of treatment.¹⁰

The frequency of blood eosinophilia has been reported by various study groups from as low as 9% to as high as 37.4%.^{6,12} In this study, we have come across a significant number of patients who

presented to us with exacerbations of COPD and with a blood eosinophil count of >2%, amounting to 23.74% of the total study population. Our study results were closer to those of K. Hasegawa et al (17%)¹¹ and Bafadhel et al (28%).¹⁰ This wide range of prevalence of blood eosinophilia may be multifactorial i.e. due to different cut-off values of eosinophil count, different exclusion criteria's, and concurrent or preceding use of drugs effecting eosinophil count i.e. corticosteroids, aminophylline, differences in population, different stages of COPD. From this study we can postulate that approximately 25% of our study population that presented with COPD exacerbation had airway eosinophilia. As studies have shown that during exacerbation of COPD, sputum and blood eosinophil numbers are increased in a similar way, so blood eosinophils can be used as a surrogate marker for airway eosinophilia to direct corticosteroid therapy in the treatment of COPD, so as to enhance clinical recovery, decrease the exacerbation rates and limiting the side effects of therapy by minimizing its unnecessary use.^{6,14}

A study performed by Bafadhel et al in 2011 showed that out of their study sample, approximately 28% of COPD exacerbation patients had airway eosinophilia.¹⁰ The findings of Bafadhel et al are marginally higher when compared to our study. A similar study done by Singh D et al showed that 37.4% of COPD patients had airway eosinophilia and that it carried a better initial outlook in terms of baseline investigations.⁶ Conversely, Hasegawa K et al and Price D et al showed a significantly lower proportion of patients with airway eosinophilia approximating 17% and 10% respectively.^{7,11} Price D et al further postulates an increase in COPD exacerbations in patients with airway eosinophilia and that reducing airway eosinophilia with corticosteroids may decrease hospital admissions and the number of exacerbations.⁷

In another study conducted by Saltürk et al 2015, the prevalence of eosinophilic exacerbations and clinical characteristics of these exacerbations were studied. It was found that, “9.6% of the enrolled subjects had eosinophilic COPD”.¹² A relatively better clinical outcome was observed in this group. The non-eosinophilic COPD exacerbation group had a higher APACHE II score and worse arterial blood gas on admission. Moreover, in non-eosinophilic group the use of NIMV were more, they had a higher NIMV failure rate, a longer ICU stay, a significantly higher rate of septic shock and resistant pathogen infection, and an increased ICU mortality despite similar steroid and antibiotic usage.

Patients with COPD respond to corticosteroid therapy in different ways and this response is related to the presence of eosinophilic airway inflammation.¹³ By targeting the treatment to normalize the sputum or blood eosinophils, the clinical recovery will be enhanced, the number of hospital admissions will be reduced and disease progression will be modified.^{14,15}

In light of recent studies, eosinophils have been establishing itself as an important bio-marker of corticosteroid responsiveness. Keeping in view the heterogeneity of COPD, the management of COPD patients should be standardized depending upon the individual biomarker profile. Managing obstructive airway diseases without considering its biological complexity and its various phenotypic presentations ultimately leads to under/over-prescription of medications. By considering eosinophils in COPD, treatments with a higher likelihood of response with minimal adverse effects can be ensured and a more 'tailor-made' approach can be used in the future.

Conclusion

About quarter of the patients in our study were found

to have blood eosinophilia. More than half of COPD patients admitted with acute exacerbation, with eosinophilia were males.

Limitations

It was a descriptive study conducted at one center so the results may not be generalized. Moreover peripheral blood eosinophil count was taken into account that may not be the true reflection of airway eosinophilia. The study was conducted in COPD patient hospitalized with acute exacerbation, so the results may not be true reflection of ambulatory patients with exacerbation or COPD patients having stable disease.

Recommendations

Further studies need to be performed at a local level to know the clinical presentations of various phenotypes of COPD acute exacerbations. More robust study designs should be employed to confirm/refute the usefulness of eosinophilia in guiding COPD exacerbation therapy. Furthermore, it would be advisable to include other variables including treatment outcomes, exacerbation frequencies with a comparison between the various phenotypes of COPD especially when treated with and without corticosteroids and the differences in treatment outcomes in patients who are smokers vs. non-smokers.

References

1. Vestbo j,Hurd,SS, Agusti AG, Jones PW, Vogelmeier C,Anzueto A,et al ,Global strategy for diagnosis and management and prevention of chronic obstructive disease :GOLD executive summary .American journal of respiratory and critical care medicine.2013 Feb 15 ;187(4):347-65
2. Pakistan Chest Society; Guidelines for management of COPD, 2005 April.
3. Guzman E D, Mannino D M, Epidemiology and Prevalence of Chronic Obstructive Pulmonary Disease CLINIC IN CHEST MEDICINE March 2014; 35(1): 7–16
4. Alzaabi A,Javaid A,khan JA,Chronic obstructive pulmonary disease in the adult population within the Middle East and North Africa region, Respiratory Medicine 2012 Dec 31;106:S3–15
5. Hasegawa K,Carlos A. Camargo Jr. Prevalence of blood eosinophilia in hospitalized patients with acute exacerbation of COPD Respirology 2015;21(4): 761–764
6. Singh D, Kolsum U, Brightling CE, Locantore N, Agusti A, Tal-Singer R. Eosinophilic inflammation in COPD: prevalence and clinical characteristics.

- European Respiratory Journal. 2014 Dec 1;44(6):1697-700.
7. Price D, Rigazio A, Postma D, Papi A, Guy B, Agusti A et al. Blood eosinophilia and the number of exacerbations in COPD patients. *European Respiratory Journal*. 2014 Sep 1;44(Suppl 58):4416.
 8. Loureiro CC. Blurred lines. Eosinophilic COPD: ACOS or COPD phenotype?. *Revista Portuguesa de Pneumologia (English Edition)*. 2016 Mar 21.
 9. Fernandes FL. Eosinophils in COPD: why should I care?. *Jornal Brasileiro de Pneumologia*. 2016 Aug;42(4):237-8.
 10. Bafadhel M, McKenna S, Terry S, Mistry V, Pancholi M, Venge P, Lomas DA, Barer MR, Johnston SL, Pavord ID, Brightling CE. Blood eosinophils to direct corticosteroid treatment of exacerbations of chronic obstructive pulmonary disease: a randomized placebo-controlled trial. *American journal of respiratory and critical care medicine*. 2012 Jul 1;186(1):48-55
 11. Hasegawa K, Camargo CA. Prevalence of blood eosinophilia in hospitalized patients with acute exacerbation of COPD. *Respirology*. 2016 Jan 1.
 12. Saltürk C, Karakurt Z, Adiguzel N, Kargin F, Sari R, Celik ME, Takir HB, Tuncay E, Sogukpinar O, Ciftaslan N, Mocin O. Does eosinophilic COPD exacerbation have a better patient outcome than non-eosinophilic in the intensive care unit?. *International journal of chronic obstructive pulmonary disease*. 2015;10:1837
 13. Brightling CE, Monteiro W, Ward R, Parker D, Morgan MD, Wardlaw AJ, Pavord ID. Sputum eosinophilia and short-term response to prednisolone in chronic obstructive pulmonary disease: a randomised controlled trial. *The Lancet*. 2000 Oct 28;356(9240):1480-5.
 14. Bafadhel M, Davies L, Calverley PM, Aaron SD, Brightling CE, Pavord ID. Blood eosinophil guided prednisolone therapy for exacerbations of COPD: a further analysis. *European Respiratory Journal*. 2014 Sep 1;44(3):789-91.
 15. Saha S, Brightling CE. Eosinophilic airway inflammation in COPD. *Int J Chron Obstruct Pulmon Dis* 2006;1:39–47.