

BLOOD EOSINOPHILIA IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE EXACERBATIONS

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Abstract;

Background; The short-term benefits of inhaled corticosteroids for patients with chronic obstructive pulmonary disease (COPD) are greater in patients with evidence of eosinophilic airway inflammation. This study was conducted to determine the frequency of blood eosinophilia in patients with acute exacerbations of COPD. **Objective:** To determine the frequency of blood eosinophilia in chronic obstructive pulmonary disease exacerbations. **Material and methods;** A total of 159 patients with acute exacerbations of COPD were registered and their eosinophil count was done. All data was entered on SPSS-20 and analyzed. **Setting:** Study was conducted in the pulmonology department of Nishtar Hospital Multan. **Study design:** Descriptive cross sectional study. **Sampling technique:** Non probability consecutive. **Results;** Of these 159 study cases, 87 (54.7%) were male patients while 72 (45.3%) were female patients. Mean age of our study cases was 57.87 \pm 8.99 years (with minimum age of our study cases was 44 years while maximum age was 70 years). Mean body mass index (BMI) of our study cases was 23.89 \pm 2.74 kg/m², 32 (20.1%) were overweight and 16 (10.1%) were obese. Smoking was seen in 48 (30.2%) patients and 5% were light smokers, 10.1% were moderate smokers and 15.1% were heavy smokers. Mean duration of COPD was 8.18 \pm 2.34 years (with minimum duration of illness was 6 years while maximum duration was 14 years). Mean duration of acute exacerbation of COPD was noted to be 6.21 \pm 1.71 days (ranging from 4 to 10 days). Blood eosinophilia was noted in 87 (54.7%) of our study cases.

Conclusion; Blood eosinophil count is a promising biomarker of response to inhaled corticosteroids in patients with COPD and very high frequency of blood eosinophilia was noted in our study. Blood eosinophilia was significantly associated with increasing age, heavy smoking and duration of COPD.

Keywords; Blood eosinophilia, COPD, acute exacerbations.

Introduction:

Chronic obstructive pulmonary disease is a highly prevalent and progressive respiratory disease. Although mortality for COPD is decreasing in developed countries, it remains a major cause of morbidity and mortality worldwide. According to WHO estimates, 65 million people have moderate to severe chronic obstructive pulmonary disease. More than 3 million people died of COPD in 2005, which corresponds to 5% of



all deaths globally. The health, social and economic impact of COPD (the third leading cause of death in the United States) is high. In 2010, the global cost associated with COPD in the USA was 50 billion dollars, of which 20 billion of indirect costs and 30 billion of direct costs.³ These costs tend to increase in a way directly proportional to the severity of the illness and to moderate and severe exacerbations, especially those requiring hospitalization.

Chronic obstructive pulmonary disease is characterized by the presence of an airflow limitation that is not fully reversible, and is usually progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases. Until recently, COPD was thought to cause only pulmonary abnormalities, but recent studies have demonstrated the presence of systemic and extra-pulmonary effects. Acute exacerbations of chronic obstructive pulmonary disease are associated with substantial morbidity and mortality and are heterogeneous with respect to inflammation⁶ and etiology. An acute exacerbation of COPD is associated with increased frequency and severity of coughing. It is often accompanied by worsened chest congestion and discomfort. Shortness of breath and wheezing are present in many cases. Exacerbations may be accompanied by increased amount of cough and sputum productions and a change in appearance of sputum. Although primarily associated with asthma, eosinophilic airway inflammation is also present in 20-40% COPD patients.⁸ Previous studies have shown that a sputum eosinophilia is associated with a positive response to corticosteroid treatment in stable COPD,9 and the sputum eosinophil count can be used to titrate corticosteroid therapy to reduce exacerbations of COPD. 10 Studies have also shown that peripheral blood eosinophil count is a valid biomarker of this pattern of inflammation. 11,12 In a study conducted by Bafadhel M, McKenna S, Terry S, Mistry V, Reid C, Haldar P et al it was found that 28% of the COPD exacerbations were eosinophil-associated exacerbations and peripheral blood eosinophil was the biomarker.¹¹

In another study conducted by Bafadhel M, McKenna S, Terry S, Mistry V, Pancholi M, Venge P et al, it was found that in 85 (51.2%) COPD exacerbations out of 166 exacerbations blood eosinophil level was more than 2 $\frac{9}{6}$ 12

Method and material:

All the patients of either sex aged; 30 – 70 years, were taken from pulmonology department with diagnosis of acute exacerbation of COPD with history of COPD for at least 5 years. Patients with co-existent congestive cardiac failure (confirmed by echocardiography showing EF less than 55%), co-existent asthma, co-existent pulmonary tuberculosis, co-existent pneumothorax, co-existent pleural effusion and patients with co-existent interstitial lung disease were excluded from our study. A total of 159 patients with acute exacerbation of COPD fulfilling inclusion and exclusion criteria were enrolled by non-probability consecutive technique. Demographic data like age (in years) and gender (male/female) was noted. Informed consent was taken from patients. All investigations were done from Nishtar Hospital Multan laboratory which includes complete blood count, sputum culture, chest radiograph, echocardiography and spirometery.

Results;

Our study included a total of 159 study cases meeting inclusion criteria of our study. Of these 159 study cases, 87 (54.7%) were male patients while 72 (45.3%) were female patients. Mean age of our study cases was 57.87 \pm 8.99 years (with minimum age of our study cases was 44 years while maximum age was 70 years). Mean age of the male patients was 57.77 \pm 8.35 years while that of female patients was 58.00 \pm 9.76 years (p = 0.873). Our study results have indicated that majority of our study cases i.e. 119 (74.8%) were aged 51 - 70 years of age. Mean height of our study cases was 163.52 \pm 10.21 centimeters while mean weight of our study cases was 61.34 \pm 11.71 kilograms. Mean body mass index (BMI) of our study cases was 23.89 \pm 2.74 kg/m², 32 (20.1%) were overweight and 16 (10.1%) were obese. Smoking was seen in 48 (30.2%) patients and 5% were light smokers, 10.1% were moderate smokers and 15.1% were heavy smokers. Mean duration of COPD was 8.18 \pm 2.34 years (with minimum duration of illness was 6 years while maximum duration was 14 years). our study results have documented that majority of these patients had disease duration ranging from 5 - 10 years. Mean duration of acute exacerbation of COPD was noted to be 6.21 \pm 1.71 days (ranging from 4 to 10 days). Our study results have documented that majority of our patients i.e. 119 (74.8%) presented within one week. Blood eosinophilia was noted in 87 (54.7%) of our study cases



$\label{eq:condition} Table~No.~1$ Stratification of Blood eosinophilia with regards to duration of COPD.

(n = 159)

	Blood Eosinophilia		
Duration of COPD	Yes	No	P – value
	(n = 87)	(n = 72)	
5 – 10 Years	64	64	
(n = 128)	04	04	
More than 10 years	23	08	0.017
(n=31)	23	00	0.017
Total	159		

Table No. 2 Stratification of Blood eosinophilia with regards to acute exacerbation of COPD.

(n = 159)

	Blood Eosinophilia		
Duration of acute exacerbation	Yes	No	P – value
	(n = 87)	(n = 72)	
Up to 1 week	63	56	
(n = 119)	03	30	
More than 1 week	24	16	0.468
(n=40)	27	10	0.400
Total	159		



Discussion;

Eosinophilic inflammation is thought to be a characteristic feature of asthma rather than COPD. However, studies have shown that a subset of COPD patients with eosinophilic airway inflammation exists, even after the careful exclusion of patients with any features of asthma, such as β -agonist reversibility, bronchial hyperresponsiveness, atopy or a childhood history of asthma. Interestingly, these patients exhibit the greatest response to corticosteroid treatment ¹³⁻¹⁵.

Our study included a total of 159 study cases meeting inclusion criteria of our study. Of these 159 study cases, 87 (54.7%) were male patients while 72 (45.3%) were female patients. Our results are consistent with that of findings of Zaman et al ¹⁶ from Peshawar who also reported overall male gender predominance in COPD patients. A study conducted by Waqas et al ¹⁷ has reported 70 % male patients predominating over female gender with 30 % frequency, these findings are similar to that of our study results. Hassan et al ¹⁸ reported 53 % male patients with COPD which is same as that of our study results. Motiani et al ¹⁹ reported 80 % male patients compared with 20 % female patients with COPD which is showing same trend as that of our study results.

Mean age of our study cases was 57.87 ± 8.99 years (with minimum age of our study cases was 44 years while maximum age was 70 years). Mean age of the male patients was 57.77 ± 8.35 years while that of female patients was 58.00 ± 9.76 years (p = 0.873). Our study results have indicated that majority of our study cases i.e. 119 (74.8%) were aged 51 - 70 years of age. Khan et al 2 also reported similar results. Phulpoto et al 21 reported 56.8 ± 7.8 years mean age of COPD patients, these findings are close to our study results. Motiani et al 19 reported 60.87 ± 10.93 years mean age of the patients, which is similar to that of our study results. Thakrar et al 22 reported 63.54 ± 10.656 years mean age, which is close to our study results. Mean height of our study cases was 163.52 ± 10.21 centimeters while mean weight of our study cases was 61.34 ± 11.71 kilograms. Mean body mass index (BMI) of our study cases was 23.89 ± 2.74 kg/m 2 , 32 (20.1%) were overweight and 16 (10.1%) were obese. Smoking was seen in 48 (30.2%) patients and 5% were light smokers, 10.1% were moderate smokers and 15.1% were heavy smokers. Zaman et al 16 from Peshawar also reported 34% smoking in these patients which is close to our study results and they also observed that all these smokers were male patients which is in compliance with that of our study results.

Blood eosinophilia was noted in 87 (54.7%) of our study cases. A very recent study published in 2016 from America has reported 40 % blood eosinophilia which is close to our study results ²³. A study conducted by Pascoe et al ²⁴ also reported blood eosinophilia in 66% patients with acute exacerbations of COPD which is close to our results. In a study conducted by Bafadhel M et al it was found that 28% of the COPD exacerbations were eosinophil-associated exacerbations and peripheral blood eosinophil was the biomarker. ¹¹ In another study conducted, it was found that in 85 (51.2%) COPD exacerbations out of 166 exacerbations blood eosinophil level was more than 2 %. ¹² these results are in compliance with our study results.

Conclusion;

Blood eosinophil count is a promising biomarker of response to inhaled corticosteroids in patients with COPD and very high frequency of blood eosinophilia was noted in our study. Blood eosinophilia was significantly associated with increasing age, heavy smoking and duration of COPD.

References:

- 1. Decramer M, Janssens W, Miravitlles M. Chronic obstructive pulmonary disease. Lancet.2012;379(9823):1341–51.
- 2. López-Campos JL, Ruiz-Ramos M, Soriano JB. Mortality trends in chronic obstructive pulmonary disease in Europe, 1994–2010: a joinpoint regression analysis. Lancet Respir Med. 2014;2(1):54–62.
- 3. Guarascio AJ, Ray SM, Finch CK, Self TH. The clinical and economic burden of chronic obstructive pulmonary disease in the USA. Clinicoecon Outcomes Res. 2013;5:235–45.



- 4. Rabe KF, Hurd S, Anzueto A, Barnes PJ, Buist SA, Calverley P,et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med 2007;176:532–55.
- 5. Agusti AG, Noguera A, Sauleda J,Sala E, Pons J, Busquets X. Systemic effects of chronic obstructive pulmonary disease. Eur Respir J 2003;21:347–60.
- 6. Bhowmik A, Seemungal TA, Sapsford RJ, Wedzicha JA. Relation of sputum inflammatory markers to symptoms and lung function changes in COPD exacerbations. Thorax 2000;55:114–20.
- Papi A, Bellettato CM, Braccioni F, Romagnoli M, Casolari P, Caramori G et al.Infections and airway inflammation in chronic obstructive pulmonary disease severe exacerbations. Am J Respir Crit Care Med 2006;173:1114–21
- 8. Saha S, Brightling CE. Eosinophilic airway inflammation in COPD. Int J Chron Obstruct Pulmon Dis2006;1:39–47.
- 9. Shim C, Stover DE, Williams MH. Jr Response to corticosteroids in chronic bronchitis. J Allergy Clin Immunol 1978;62:363–7
- 10. Brightling CE, Monteiro W, Ward R, Parker D, Morgan MD, Wardlaw AJ et al. Sputum eosinophilia and short-term response to prednisolone in chronic obstructive pulmonary disease: a randomised controlled trial. Lancet 2000;356:1480–5
- 11. Bafadhel M, McKenna S, Terry S, Mistry V, Reid C, Haldar P et al. Acute exacerbations of COPD: identification of biological clusters and their biomarkers. Am J Respir Crit Care Med 2011;184:662–71
- 12. Bafadhel M,McKenna S, Terry S, Mistry V, Pancholi M, Venge P, et al. Blood eosinophils to direct corticosteroid treatment of exacerbations of Chronic Obstructive Pulmonary Disease, a randomized placebocontrolled trial. Am J Respir Crit Care Med. 2012 Jul 1;186(1):48–55.
- 13. Lee JS, Park DA, Hong Y, Jo KW, Lee SW, Huh JW, Oh YM, Lee SD. Systematic review and metaanalysis of prophylactic antibiotics in COPD and/or chronic bronchitis. Int J Tuberc Lung Dis. 2013;17(2):153-62.
- Miravitlles M, Izquierdo I, Herrejón A, Torres JV, Baró E, Borja J, ESFERA investigators COPD severity score as a predictor of failure in exacerbations of COPD. The ESFERA study. Respir Med.2011;105(5):740–7.
- 15. Singh D¹, Kolsum U², Brightling CE³, Locantore N⁴, Agusti A⁵, Tal-Singer R⁶, et al. Eosinophilic inflammation in COPD: prevalence and clinical characteristics. Eur Respir J. 2014 Dec;44(6):1697-700.
- 16. Zaman M, Wahab F, Khan N, Ashraf S. Management of patients admitted with COPD exacerbation in Chest Unit and Medical Units of Khyber Teaching Hospital, Peshawar. Pak J Chest Med. 2007;13(4):11-6.
- 17. Waqas MS, Malik AN, Javed M. Effectiveness of conventional chest physiotherapy versus manual hyperinflation during postural drainage of ventilated COPD patients. Rawal Med J. 2014;39(1):32-4.
- 18. Hassan SH, Sheikh SA, Munfeat F. Spirometry and vital parameters in assessment of asthma and COPD in rural population of Karachi. Pak J Chest Med. 2007;13(1):15-20.
- Motiani B, Haidri FR, Rizvi N. Frequency of depression in chronic obstructive pulmonary disease (COPD) patients
 Pak J Med Sci. 2011;27(5):1112-5.
- Khan MH, Javaid A. Bronhodilator response to nebulized salbutamol in elderly patients with stable COPD J Postgrad Med Inst. 2007;21(3):222-6.
- 21. Riaz MA, Qayyum S, Rizvi N, Khuhawar SM. Proportion of gastroesophageal reflux symptoms in patients with chronic obstructive pulmonary disease. J Pak Med Assoc. 2005;55(7):276-9.
- 22. Thakrar R, Alaparthi GK, Kumar SK, Vaishali K, Zulfeequer CP, Aanad R. Awareness in patients with COPD about the disease and pulmonary rehabilitation: A survey.Lung India 2014;31:134-8.
- 23. Hasegawa K¹, Camargo CA Jr¹. Prevalence of blood eosinophilia in hospitalized patients with acute exacerbation of COPD. Respirology. 2016 May;21(4):761-4.
- 24. Pascoe S¹, Locantore N², Dransfield MT³, Barnes NC⁴, Pavord ID⁵. Blood eosinophil counts, exacerbations, and response to the addition of inhaled fluticasone furoate to vilanterol in patients with chronic obstructive pulmonary disease: a secondary analysis of data from two parallel randomised controlled trials. Lancet Respir Med. 2015 Jun;3(6):435-42.