



FREQUENCY OF BLOOD EOSINOPHILIA IN NEWLY DIAGNOSED CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) is a diverse illness and has various phenotypes both clinical and pathological. Globally ‘Chronic Obstructive Lung Disease’ (GOLD) described COPD as “A common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases”.

Objective: The purpose of this study was to record the incidence of blood eosinophilia in individuals with recently diagnosed COPD

Methods: The study was conducted in Hayatabad Medical Complex (HMC), Peshawar for 6 months between 1st July 2023 to 31st December 2023. The study design was observational cross-sectional study. The study involved 250 participants who had just received a COPD diagnosis. The sample technique was purposive sampling. Individuals with COPD who were ‘40 to 80 years’ old were included in the trial; however, individuals who were on ‘TB medication’ or who had ‘asthma’, ‘asthma COPD overlaps (ACO)’, or ‘bronchiectasis’ were not. The study was approved by the Ethical Review Board of Hayatabad Medical Complex (HMC), Approval No:1835 dated: 18th May 2023.

Results: 250 COPD patients were identified and assessed for Eosinophilia in blood in which 195 (78%) men, and 55 (22%) women with mean age of 65.63 ±11.35 years. Most of the COPD patients had no history of smoking 138 (55.2%) followed by Presently smoking 77 (30.8%), and past -

Smokers 35 (14%). Approximately 76 (50.8%) of the COPD patients had exposure to Biomass. Freshly confirmed individuals with COPD were divided into four categories based on the GOLD standard: mild (38, 15.2%), moderate (90, 36%), severe (79, 31.6%), and very severe (43, 17.2%). 110 patients (44%) had confirmed eosinophilic COPD, and 140 patients (56%) had diagnosed non-eosinophilic COPD.

Conclusion: It was determined that a high frequency of blood eosinophilia was present among individuals with recently diagnosed COPD, the majority of whom had moderate-to-severe COPD. Thus, when treating COPD patients, eosinophilia should be taken into account.

Keywords: Eosinophilia, Chronic Obstructive Pulmonary Disease, Spirometry

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a diverse illness and has various phenotypes both clinical and pathological.^{1,2} Globally Chronic Obstructive Lung Disease (GOLD) described COPD as “A common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases”.³ Globally, WHO reported 251 million population affected by COPD.⁴ COPD is considered the 4th leading cause of death and is expected to become 3rd leading cause by 2030.^{5,6} In 2015, WHO reported 3.17 million deaths due to COPD globally.⁴ It is considered as a disease which has no cure but if diagnosed to time, properly managed and exposure to risk factors is reduced it will lead to hindrance in its advancement. The commonest risk factor for COPD is tobacco smoke followed by old age, gender with male predilection and exposure to pollution (indoor + outdoor).⁷

Accurate treatment of COPD needs proper diagnosis through identification of biomarkers which are non-invasive and dependable biomarker.⁸ High levels of eosinophils have been noticed in the blood of COPD patients which signifies its important role in COPD pathogenesis.⁸⁻¹⁰ When the patients of COPD has $\geq 2\%$ eosinophils in blood, they are diagnosed with eosinophilia. With time and new advancements, the management of COPD patients with regard to controlling high levels of eosinophils in their blood has improved. Increased levels of COPD is used as a biomarker for exacerbations.¹¹⁻¹³ Few investigations have reported 20% of patients with COPD had high levels of eosinophils in their blood, however, a precise ‘prevalence of eosinophilia in patients’ of COPD is not known. A study conducted by Negewo NA, et al reported that 15.6% patients of COPD have high levels of eosinophils in blood⁹ whereas another study conducted by ‘Hasegawa K et al’ reported in 16.5% of COPD patients.¹⁴

The goal of the investigation is to identify blood a high level of eosinophils in newly diagnosed individuals with COPD so that patients can receive the proper medication, which is essential to slowing the advance of the illness and improving results. Only freshly diagnosed individuals with COPD have been included because no COPD medication will alter the amount of eosinophils level in blood or the course of the disease. Blood eosinophilia is one of the variables that are thought to determine how well sufferers of COPD respond to medication.

Being aware of these variables can aid in timely and appropriate management as well as in lowering the related mortality and morbidity. Inhaled corticosteroids are recommended for the management of individuals with COPD with blood eosinophilia. This will improve symptom alleviation and delay the course of the illness. Various data revealed a strong association between elevated blood eosinophil counts and a higher incidence of worsening symptoms in COPD patients. The worsening reduces when eosinophilic COPD is managed with inhaled corticosteroid. Currently, no comparable research on blood eosinophilia among individuals with recently diagnosed COPD has been carried out in Pakistan. Consequently, the purpose of this study was to record the incidence of blood eosinophilia in individuals with recently diagnosed COPD.

METHODS

The study was conducted in Hayatabad Medical Complex (HMC), Peshawar for 6 months between 1st July 2023 to 31st December 2023. The study design was observational cross-sectional study. The study involved 250 participants who had just received a COPD diagnosis. The sample technique was purposive sampling. Individuals with COPD who were '40 to 80 years' old were included in the trial; however, individuals who were on 'TB medication' or who had 'asthma', 'asthma COPD overlaps (ACO)', or 'bronchiectasis' were not. The study was approved by the Ethical Review Board of Hayatabad Medical Complex (HMC), Approval No:1835 dated: 18th May 2023.

Participants with COPD have been identified based on GOLD criteria, which included a medical record and pulmonary function tests demonstrating a chronic restriction in breathing ('ratio of FEV1/FVC' '< 0.70' both before and after inhaler). The presence of '≥ 2% eosinophils' in blood is referred to as a condition called eosinophilia. The blood counts of eosinophils ≥ 2% in a patient with COPD was classified as eosinophilic COPD. An individual was categorised as an active smoker if they reported using over twenty packs of cigarettes in their lifetime or more than a single cigarette per day for a year. Ex-smokers were those who had stopped smoking for a minimum of twelve months prior to the study's inclusion, and non-smokers were those who hadn't previously smoked or consumed fewer than one cigarette per day for a period of time not exceeding one year. An individual was classified as having experienced biomass exposure if they had been subjected to chemicals or indoor wood fires used for heating or cooking purposes for a minimum of six months.

Following the identification of individuals with expected COPD, a comprehensive medical history and data on demographics was gathered from the patients, including their ages, gender, work, habit of smoking, and biomass exposure. Every patient had a pulmonary function tests to confirm their COPD diagnosis. A qualified technician with at least three years of experience conducted the pulmonary function tests, and a consultant pulmonologist with three years of experience completed the interpretation process. Every individual had a sample of their blood taken in an aseptic setting, and the collected specimen was delivered to a laboratory for a full blood count, or CBC, in order to validate the eosinophilia diagnosis.

Each one individual's laboratory data, such as 'FEV1', 'FVC', 'FEV1/FVC', 'COPD severity' ('mild, moderate, severe, very severe'), 'eosinophil count', and 'eosinophilia (yes/no)', were gathered and further examined using SPSS version 23. 'Age', 'FEV1/FVC ratio', 'eosinophil count', 'frequency and percentages of gender', 'age', 'occupation', 'risk factor' ('smoking status and biomass exposure'), 'severity of COPD', and 'eosinophilia' were all determined via descriptive statistics. To ascertain the relationship between risk factors such as 'gender', 'age', 'smoking status', 'biomass exposure', and 'COPD severity' and the 'frequency of eosinophilia', the 'Chi-square Test' was utilized. 'Significant data is defined as $P < 0.05$ '.

RESULTS

In our investigation, the participant's records were gathered and assessed to confirm COPD following diagnosis of eosinophilia in participants with newly diagnosed COPD. Table-I specifies the characteristics of participants with confirmed COPD which were collected during assessment of COPD. There were 195 (78%) men, and 55 (22%) women. Most of the participants of COPD were in age group of 62-71 years, 89 (35.6%) followed by 72-81 years, 59 (23.6%), 52-61 years, 54 (21.6%), and 40-51 years 48 (19.2%). Most of the COPD patients had no history of smoking 138 (55.2%) followed by Presently smoking 77 (30.8%), and past -Smokers 35 (14%). Approximately 76 (50.8%) of the COPD patients had exposure to Biomass.

Descriptive statistical analyses of various continuous variables collected during the data gathering process include age, which has a mean of 65.63 ± 11.35 years, and clinical characteristics, such as spirometric variables (FEV1 $54.3 \pm 16.5\%$, FVC $77.4 \pm 17.6\%$, and FEV1/FVC $50.8 \pm 13.9\%$), and blood eosinophil count, which was measured during spirometry and CBC and has a mean of $4.1 \pm 3.8\%$.

Freshly confirmed individuals with COPD were divided into four categories based on the GOLD standard: mild (38, 15.2%), moderate (90, 36%), severe (79, 31.6%), and very severe (43, 17.2%).

110 patients (44%) had confirmed eosinophilic COPD, and 140 patients (56%) had diagnosed non-eosinophilic COPD. According to Table II, the spirometric level of severity for eosinophilic COPD was as follows: mild 18 (7.2%), moderate 37 (14.8%), severe 28 (11.2%), and very severe 32 (12.8%). Table II further demonstrates the ‘insignificant difference’ between ‘Eosinophilic’ and ‘Non-eosinophilic COPD’ with respect to ‘Gender’ (p=0.23), ‘Age’ (p=0.25), ‘Smoking’ (p=0.8), and ‘Biomass Exposure’ (p=0.4), whereas the ‘severity of COPD’ (p=0.02) shows a significant difference.

Characteristics	Frequency (n=250)	Percentage
Gender		
Men	195	78%
Women	55	22%
Age		
40-51	48	19.2%
52-61	54	21.6%
62-71	89	35.6%
72-81	59	23.6%
History of Smoking		
No history of smoking	138	55.2
Past history of smoking	35	14%
Presently smoking	77	30.8%
Exposure to biomass		
Yes	127	50.8%
No	123	49.2%

Characteristics	COPD with eosinophil levels ≥ 2	COPD with eosinophil levels <2	P-value
Gender			
Men	58 (23.2%)	79 (31.6%)	0.23
women	52 (20.8%)	61 (24.4%)	
‘Age’			
40-51	17 (6.8%)	37 (14.8%)	0.25
52-61	25 (10%)	30 (12%)	
62-71	28 (11.2%)	51 (20.4%)	
72-81	27 (10.8%)	35 (14%)	
History of Smoking			
No history of smoking	28 (11.2%)	50 (20%)	0.8
Past history of smoking	19 (7.6%)	26 (10.4%)	
Presently smoking	54 (21.6%)	73 (29.2%)	
Exposure to biomass			
Yes	56 (2.4%)	68 (27.2%)	0.4
No	47 (18.8%)	79 (31.6%)	
COPD Severity			
Mild	18 (7.2%)	13 (5.2%)	0.02
Moderate	37 (14.8%)	59 (23.6)	
Severe	28 (11.2%)	48 (19.2%)	
Very severe	32 (12.8%)	15 (6%)	

DISCUSSION

Persistent breathing problems and a persistent restriction in airflow are hallmarks of the complex combination of diseases known as COPD, which is directly linked to higher rates of illness and death. It is crucial to identify clinical phenotypes of COPD early on using proven biomarkers, such as blood eosinophilia, in order to establish targeted treatment plans to treat COPD appropriately.^{15, 16}

In patients who have COPD, blood eosinophils are employed as a predictive marker. Elevated blood eosinophil counts have been linked to higher hospital admissions, death, and COPD exacerbation. It is critical to identify elevated blood eosinophil counts in COPD patients as soon as possible. This will help to minimise the risk of severe exacerbations and ensure adequate care.⁹⁻¹² Thus, with the aim to

slow the development of COPD and enhance the results, 'new COPD patients were identified and their blood eosinophilia' incidence measured in this research. The two key conclusions of the current investigation are the spotlight. First, determining the individual's COPD using the GOLD criteria and any relevant risk factors that may exist. Next, determining if that individual has Eosinophilic COPD. The present research assessed 250 newly identified COPD sufferers with a mean age of 65.63 ± 11.35 years, comprising 195 (78%) males and 55 (22%) women. A number of research studies on COPD patients produced 'comparable results'. For example, 'Couillard S. et al' reported 52% of the patients were male and 50% were female, with a mean age of 70 ± 9 years. 'Oshagbemi OA', et al. reported 56% of the patients were male and 45% of the female had a mean age of 67 ± 11 years.¹⁷⁻¹⁸ Bélanger M. et al reported 53.0% of the patients were male and 47.0% were female with a mean age of 69 ± 10 years.¹⁹

Studies from the past and present indicate that getting older is a significant risk factor for COPD patients. According to recent study, the age category of 62–71 years, 89 (35.6%), 72–81 years, 59 (23.6%), 52–61 years, 54 (21.6%), and 40–51 years, 48 (19.2%) is where the majority of people with COPD reside. Other researchers have reported similar findings. For example, Hasegawa K. et al. found that 31% of patients aged 71-80 had COPD, compared to 25.5% of patients aged 61-70, 22% of patients aged 81 and over, 17% of patients aged 51-60, and 6% of patients aged 41-50.¹⁴ A study conducted by 'Oshagbemi OA, et al.¹⁸ reported the higher prevalence of COPD' in 61-69 years having 61.9% patients, followed by 41-60 years having 20% patients and ≥ 70 years with 17% patients.¹⁸

The onset of COPD is significantly influenced by two key factors: biomass exposure and smoking. According to the present study, 44.8% of the participants had a smoking history, with 73 (29.2%) reporting currently smoking and 26 (10.4%) reporting ex-smoking, while 127 (50.8%) have a history of biomass exposure. Multiple research studies report varying rates of both smoking and biomass exposure. For example, Bakr RM, et al.²¹ indicated 42.0% of patients had biomass exposure, while 'Couillard S, et al'¹⁷ 'Oshagbemi OA', et al¹⁸ 'Bélanger M, et al'¹⁹ and 'Casanova C, et al'²⁰ reported smoking in 52%, 43%, 53%, and 28% of patients, respectively. Every study showing how smoking and biomass exposure play a significant part in the formation of COPD.

Individuals with COPD were classified into four groups based on the GOLD standard: mild (38, 15.2%), moderate (90, 36%), severe (79, 31.6%), and extremely severe (43, 17.2%). According to 'Couillard S. et al'¹⁷ mild 8.4%, moderate 48.5%, severe 34.5%, and very severe 8.5% COPD disease were identified in patients; similarly, 'Bélanger M. et al'¹⁹ found that individuals had mild 5.5%, moderate 44.5%, severe 41.1%, and very severe 8.1% COPD. Every study demonstrates the comparable trend of COPD worsening.

The research's other key finding was that COPD patients with eosinophilic COPD were present. According to the present research, 110 patients (44%) had eosinophilic COPD, while 140 patients (56%) had non-eosinophilic COPD. Blood eosinophilia has been reported in 33.1% and 35.9% of COPD patients, respectively, according to 'Couillard S. et al'.¹⁷ and 'Bélanger M. et al'¹⁹; in contrast, blood eosinophilia was found in 16.1% and 18.1% of COPD patients, according to 'Negewo NA, et al'⁹ and 'Hasegawa K, et al'¹⁴. The severity of COPD determines the incidence of blood eosinophilia; as aggravation rises, so does the percentage of eosinophilia in the bloodstream. Consequently, an increased risk of blood eosinophilia is reported in every investigation with a greater incidence of COPD intensity.

Since COPD requires inhaled steroids, the research we conducted has shown that eosinophilia is more prevalent in COPD patients. This will have an impact on public knowledge regarding COPD care.

Limitations of the study: Our investigation has demonstrated that eosinophilia is more common in COPD patients, which is not surprising given that COPD necessitates inhaled steroids. This will affect the general public's understanding of COPD treatment.

CONCLUSION

It was determined that a high 'frequency of blood eosinophilia' was present among individuals with recently diagnosed COPD, the majority of whom had moderate-to-severe COPD. Thus, when treating COPD patients, eosinophilia should be taken into account.

REFERENCES

1. Mirza S, Benzo R. Chronic obstructive pulmonary disease phenotypes: implications for care. *Mayo Clin Proc.* 2017;92(7):1104-1112. doi: 10.1016/j.mayocp.2017.03.020
2. Vestbo J, Agusti A, Wouters EF, Bakke P, Calverley PM, Celli B, et al. Should we view chronic obstructive pulmonary disease differently after ECLIPSE? A clinical perspective from the study team. *Am J Respir Crit Care Med.* 2014;189(9):1022-1030. doi: 10.1164/rccm.201311-2006PP
3. Global initiative for chronic obstructive lung disease. GOLD 2019 Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease [Internet]. 2019. Available from: <https://goldcopd.org/wp-content/uploads/2018/11/GOLD-2019-v1.7-FINAL14Nov2018-WMS.pdf>. Accessed on Sept. 3, 2019.
4. World Health Organization. Chronic obstructive pulmonary disease (COPD) [Fact sheet]. Geneva: World Health Organization; 2017. Available from: [https://www.who.int/news-room/fact-sheets/detail/chronic-obstructivepulmonary-disease-\(copd\)](https://www.who.int/news-room/fact-sheets/detail/chronic-obstructivepulmonary-disease-(copd)).
5. Riley CM, Sciruba FC. Diagnosis and outpatient management of chronic obstructive pulmonary disease: a review. *JAMA.* 2019;321(8):786-797. doi: 10.1001/jama.2019.0131.
6. World Health Organization. Chronic obstructive pulmonary disease (COPD) Geneva, Switzerland: WHO; 2015. Available from: <http://www.who.int/respiratory/copd/en/> Accessed on Sept. 3, 2019.
7. Leem AY, Park B, Kim YS, Jung JY, Won S. Incidence and risk of chronic obstructive pulmonary disease in a Korean community-based cohort. *Int J Chron Obstruct Pulmon Dis.* 2018;13:509-517. doi: 10.2147/COPD.S148618.
8. Eltboli O, Brightling CE. Eosinophils as diagnostic tools in chronic lung disease. *Expert Rev Respir Med.* 2013;7(1):33-42. doi: 10.1586/ers.12.81
9. Negewo NA, McDonald VM, Baines KJ, Wark PAB, Simpson JL, Jones PW, et al. Peripheral blood eosinophils: a surrogate marker for airway eosinophilia in stable COPD. *Int J Chron Obstruct Pulmon Dis.* 2016;11:1495-1504. doi: 10.2147/COPD.S100338
10. Vedel-Krogh S, Nielsen SF, Lange P, Vestbo J, Nordestgaard BG. Blood eosinophils and exacerbations in chronic obstructive pulmonary disease. The Copenhagen general population study. *Am J Respir Crit Care Med.* 2016;193(9):965-974. doi: 10.1164/rccm.201509-1869OC
11. Kerkhof M, Sonnappa S, Postma DS, Brusselle G, Agusti A, Anzueto A, et al. Blood eosinophil count and exacerbation risk in patients with COPD. *Eur Respir J.* 2017;50(1):1700761. doi: 10.1183/13993003.00761-2017
12. Oh YM, Lee KS, Hong Y, Hwang SC, Kim JY, Kim DK, et al. Blood eosinophil count as a prognostic biomarker in COPD. *Int J Chron Obstruct Pulmon Dis.* 2018;13:3589-3596. doi: 10.2147/COPD.S179734
13. Eltboli O, Mistry V, Barker B, Brightling CE. Relationship between blood and bronchial submucosal eosinophilia and reticular basement membrane thickening in chronic obstructive pulmonary disease. *Respirol.* 2015;20(4):667-670. doi: 10.1111/resp.12475
14. Hasegawa K, Camargo CA Jr. Prevalence of blood eosinophilia in hospitalized patients with acute exacerbation of COPD. *Respirol.* 2016;21(4):761-764. doi: 10.1111/resp.12724
15. Vestbo J, Hurd SS, Agusti AG, Jones PW, Vogelmeier C, Anzueto A, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med.* 2013;187(4):347-365. doi: 10.1164/rccm.201204-0596PP
16. Han MK, Agusti A, Calverley PM, Celli BR, Criner G, Curtis JL, et al. Chronic obstructive pulmonary disease phenotypes: the future of COPD. *Am J Respir Crit Care Med.* 2010;182(5):598-604. doi: 10.1164/rccm.200912-1843CC

17. Couillard S, Larivee P, Courteau J, Vanasse A. Eosinophils in COPD exacerbations are associated with increased readmissions. *Chest*. 2017;151(2):366-373. doi: 10.1016/j.chest.2016.10.003
18. Oshagbemi OA, Burden AM, Braeken DCW, Henskens Y, Wouters EFM, Driessen JHM, et al. Stability of blood eosinophils in patients with chronic obstructive pulmonary disease and in control subjects, and the impact of sex, age, smoking, and baseline counts. *Am J Respir Crit Care Med*. 2017;195(10):1402-1404. doi: 10.1164/rccm.201701-0009LE
19. Belanger M, Couillard S, Courteau J, Larivee P, Poder TG, Carrier N, et al. Eosinophil counts in first COPD hospitalizations: a comparison of health service utilization. *Int J Chron Obstruct Pulmon Dis*. 2018;13:3045-3054. doi: 10.2147/COPD.S170743
20. Casanova C, Celli BR, de-Torres JP, Martinez-Gonzalez C, Cosio BG, Pinto-Plata V, et al. Prevalence of persistent blood eosinophilia: relation to outcomes in patients with COPD. *Eur Respir J*. 2017;50(5):pii:1701162. doi: 10.1183/13993003.01162-2017
21. Bakr RM, Elmahallawy II. Prevalence characteristics of COPD in never smokers. *Egypt J Chest Dis Tuberc*. 2012;61(3):59-65. doi: 10.1016/j.ejcdt.2012.10.035