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Original Article

Absolute Eosinophil Count as a Clinical Marker for Chronic Obstructive Pulmonary Disease Patients

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ABSTRACT

Objective: To determine the predictive value of absolute eosinophil count as a clinical biomarker for acute exacerbations in COPD patients and their clinical outcomes.

Study design: Prospective Observational Study

Place and duration of Study: Pakistan Emirates Military Hospital Rawalpindi Pakistan from May to Dec 2023.

Methodology: A total of 300 COPD patients fulfilling inclusion criteria were enrolled in the study. After detailed history and examination and assessment of severity of COPD, a 5ml blood venous blood was drawn and sent for CBC and absolute eosinophil count. The patients were divided into Group A and B based on absolute eosinophil count of less or more than 300/ul. They were admitted to indoor patient department depending upon severity of the disease into high dependency unit or pulmonology ward. The patients were followed up till discharge from the hospital or death in the hospital.

Results: Out of total 300 patients, 122(40.7%) were categorized into Group A and 178(59.3%) were categorized into Group B based on absolute eosinophil count of less or more than 300/ul respectively. Group B patients were found to have statistically significant ($p<0.05$) more exacerbation of COPD, disease severity, admission into HDU and mortality in comparison to Group A patients.

Conclusion: Absolute eosinophil count can be used as biomarker to predict acute exacerbations and outcome in COPD patients. Patients with absolute eosinophil count of >300/ul were found to be having more severe disease, acute exacerbation, admissions to HDU, mechanical ventilation requirement and mortality.

Keywords: Absolute eosinophil count, Chronic Obstructive Pulmonary Disease, Clinical Marker

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is among the leading diseases carrying significant morbidity and mortality across the globe.[1] COPD can result from exposure to several noxious substances such as smoking. Persistent exposure to noxious substances lead to permanent structural changes in lung airways leading to airflow obstruction along with inflammation.[2] In our country a significant proportion of people suffer from this disease and carries major impact on health burden. These patients need frequent hospital visits and admissions once the disease has advanced significantly.

The inflammatory process underlying COPD involve various cellular and immunological responses. Among these neutrophils, alveolar macrophages and cytotoxic T cells are most important.[3] The role of Eosinophils in acute inflammatory process in COPD has also been an established fact in some patients though they play major role in acute asthma inflammation.[4]

Approximately 33 percent of COPD have sputum eosinophilia and rise in eosinophil count during acute exacerbations of COPD.[5] A rise in sputum or blood eosinophils count can be used to predict response to inhaled corticosteroids (ICS) and systemic corticosteroids for prevention or exacerbations managements in COPD patients respectively.[6]

Several studies have utilized various threshold for defining low and high eosinophil count in COPD patients. The majority of studies used a cut off of 2%. There is serious harmful effect on ICS withdrawal on exacerbations risk with eosinophil count of >300 cells/µL.[7] There is a growing evidence suggesting that higher eosinophil count is associated with higher

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exacerbations episodes and risk of exacerbations in COPD patients.[8] COPD patients underwent several clinical courses that can affect their clinical outcome. This study is designed to study the raised eosinophil count as predictive biomarker for COPD exacerbations and by obtaining peripheral blood eosinophil count may help guide therapy. Higher levels of blood eosinophils in patient with exacerbations predict response to inhaled corticosteroid therapy.

METHODOLOGY

This prospective observational study was carried out at Pak Emirates Military Hospital (PEMH) Rawalpindi, Pakistan from May 2023 to December 2023. The study was conducted after due approval of ethical review committee A/28/ERC/614/23. The sampling technique employed was non probability consecutive sampling. Sample size was calculated using WHO sample size calculator using a mean reduction of 62 % in exacerbations of COPD patients having raised eosinophils counts using ICS.[9] A written informed consent was taken from all participants of the study.

Inclusion Criteria: All diagnosed patients of COPD clinically or on spirometry irrespective of gender having age more than 40 years were enrolled.

Exclusion Criteria: patients who had more than 10 smoked packs year smoking history, or had been exposed to wood burning smoke were also included in the study. We have excluded all patients of pneumonia, lung cancer, active pulmonary tuberculosis, bronchiectasis, asthma and interstitial pulmonary diseases from the study. In addition patients on systemic steroids of more than 20mg daily dose were also excluded from study.

A total of 300 COPD patients were enrolled in the study. After detailed history and examination and assessment of severity of COPD, a 5ml blood venous blood was drawn from ante cubital vein and sent for CBC and absolute eosinophil count. They were admitted to indoor patient department depending upon severity of the disease into high dependency unit or pulmonology ward. They were further divided into two Groups on basis of absolute eosinophil count of more or less than 300/ul. The patients were followed up till discharge from the hospital or death in the hospital.

Data was recorded, entered and analyzed in statistical package for social sciences (SPSS) version 26.0. For quantitative data, mean± standard deviation (SD) and for qualitative data frequency and percentage were calculated. Chi square test was applied to determine statistical significance among two variables and p value of ≤ 0.05 was considered statistically significant.

RESULTS

A total of 300 patients were recruited in this study. Among them 190(63.3%) and 110(36.7%) were male and female respectively. A high eosinophil count in blood of more than 300/ul was found in 178(59.3%) patients and they were assigned Group B of the study. Whereas, 122(40.7%) were found to be have an eosinophilic count of less than 300/ul were assigned Group A of the study. A comparison among both Groups for various studied variables is shown in Table.

Table: Comparison between Group A and B of Studied Variables (n=300)

Variables	Group A n= 122(40.7%)	Group B n=178(59.3%)	*p*- value
	Eosinophilic Count < 300/ul	Eosinophilic Count ≥ 300/ul	
Smokers	37(30.3%)	104(58.4%)	<0.0001
Severe Chronic Obstructive Pulmonary Disease diagnosed on Spirometry	37(30.3%)	102(57.3%)	<0.0001
No of patients having ≥ 1 exacerbation in last 1 year	14(11.4%)	62(34.8%)	<0.0001
Mechanical Ventilation Required	10(8.1%)	54(30.3%)	<0.0001
Admission required in high dependency units	21(17.2%)	101(56.7%)	<0.0001
Mortality	6(4.9%)	31(17.4%)	<0.001

DISCUSSION

The third most leading cause of death worldwide is COPD.[10] The acute exacerbations of COPD are defined by Global Initiative for chronic obstructive pulmonary disease (GOLD) as an acute episode resulting in aggravation of respiratory symptoms requiring additional management with subsequent decline in respiratory function and bad prognosis.[11,12] There are various phenotypes of COPD and inflammation of airways due to eosinophils is one of these phenotypes which account for approximately 30-40% of COPD patients.[13] An acute exacerbation of COPD has an association with high blood eosinophil count. Several randomized clinical trials support utility of ICS to prevent acute exacerbation of COPD in patients with high blood eosinophil count.[14]

Studies have also supported the role of systemic corticosteroids in preventing FEV1 decline in patients with high sputum eosinophil count.[15] At the same time estimation of sputum eosinophil is technically a difficult task in comparison to blood eosinophil count estimation. Blood and sputum eosinophil count in COPD patients are associated to each other. In a COPD patient having an eosinophil count of more than 2% has a positive predictive value of 90% for raised sputum eosinophils.[16] In addition a blood eosinophil count of more than 2% is also associated with increased exacerbations in COPD patients.[17] This fact marks the basis of our study to determine association of raised eosinophils count in COPD patients with acute exacerbations and outcomes.

In our study 62 (34.8%) having blood eosinophil count of more than ≥ 300/ul experience ≥1 in last one year. This result is quite comparable to the result reported by Kerkhof et al[18] where it was found that 42% patients with elevated eosinophil count experience ≥1 exacerbations in a calendar year. The acute exacerbation rate was also reported 13% higher than control Group in the study. In our study it was found 20.4% higher than control Group. Similarly a study was conducted on The Copenhagen population reported that there is a three folds increased risk of exacerbation in COPD patients having a blood eosinophil count of more than 350/ul.[8] An eosinophil associated airway inflammation is present both during an acute exacerbation phase as well as during stable COPD. However a raised eosinophil count of more than 2% or ≥ 150 cells/ul is a predictor of higher exacerbation frequency. Studies have also reported that in patients having a higher eosinophil count during stable COPD experience higher exacerbation frequency.[17]

In our study patients with higher eosinophil count also require more high dependency unit care, mechanical ventilation and a higher mortality rate in comparison to patient with lower eosinophil count. The likely explanation of these findings is more exacerbation in higher eosinophil count patient which leads to more respiratory compromise with falling FEV1, more prone to hospital acquired infections due to frequent indoor treatments and poor quality of life.

In addition to raised eosinophil count, several other markers and factors have also been reported in the literature as a risk factor for exacerbation of COPD. These risk factors include high white blood cell count, C reactive protein, fibrinogen, gastro-esophageal reflux disease and poor quality of life.19 In our study we have studied one these risk factors. There is a strong need to study other risk factors along with raised eosinophil count to establish most important risk factors in our population.

CONCLUSION

Absolute eosinophil count can be used as biomarker to predict acute exacerbations and outcome in COPD patients. Patients with absolute eosinophil count of >300/ul were found to have more severe disease, acute exacerbation, admissions to HDU, mechanical ventilation requirement and mortality.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

AUR & MI: Data acquisition, data analysis, critical review, approval of the final version to be published.

MAS & MWK: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

AK & BR: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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