**Original article**

**Elevated blood eosinophils and serum IGE levels as biomarkers in prediction of COPD exacerbations**

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**ABSTRACT**

**INTRODUCTION:** Airway eosinophilia, hallmark feature of Asthma, is now a recognized inflammatory pattern in COPD. In 10–40% of COPD, eosinophilic airway inflammation has been reported.Smoking (nicotine), a risk factor promotes allergic reactions which cause elevated IgE levels.

**METHODOLOGY:** 140 COPD patients were studied prospectively for a period of 1 year (Aug 2021 to Aug 2022) in a tertiary care hospital. Patients with clinical diagnosis of COPD and post-bronchodilator FEV1/FVC ratio of less than 0.7 as per GOLD criteria considered. Based on ANTHONISEN’S criteria classified as stable COPD & COPD exacerbation. Peripheral blood collected for Absolute Eosinophil Count (AEC) & Serum IgE.

**RESULTS:** Among 140 COPD patients, Males-119(85%), Females-21(15%) were between 45-75 years of age group. COPD population belonging to GOLD I,GOLD II,GOLD III,GOLD IV staging were 21(15%), 40(28.5%), 58(41.4%), 21(15%) respectively. Of which, stable COPD were 53 (37.8%) & COPD exacerbations 87(62%). The AEC in stable COPD (468.9) & COPD exacerbation (890.8) while, Serum IgE in stable COPD (1289.5) & COPD exacerbation (2309) was observed. Current smokers showed elevated AEC (747) & Serum IgE levels (2214) compared to nonsmokers with AEC (660) & Serum IgE (646) respectively.

**CONCLUSION:** AEC & Serum IgE levels can be considered as biomarkers of COPD exacerbations that allow identification of patients who most likely respond to ICS.

**INTRODUCTION:**

Chronic obstructive pulmonary disease (COPD) is currently the fourth leading cause of death worldwide. By the year 2020, COPD is predicted to become the third leading cause of death worldwide 1. In 10–40 %of COPD cases, eosinophilic airway inflammation has been reported during both stable disease and exacerbations. Recently, peripheral blood eosinophil counts can help in predicting the COPD exacerbations1. Chronic obstructive pulmonary disease (COPD) comprises of two diseases namely chronic bronchitis and emphysema1,2.During COPD exacerbations, inflammation in the airways increases. While this inflammation in patients with COPD is primarily neutrophilic, in some patients it is associated with an increased sputum eosinophil count of more than 3%3. Neutrophilic airway inflammation appears to be poorly responsive to corticosteroid treatment , and the absence of bacterial inflammation may therefore favour a greater corticosteroid response4.Airway eosinophilia, a hallmark feature of asthma, is now a recognized inflammatory pattern in chronic obstructive pulmonary disease (COPD) & COPD is a heterogeneous disease for which there are limited choices with respect to therapeutic mechanisms of action5. In 10–40% of COPD cases, eosinophilic airway inflammation has been reported during both stable disease and exacerbations. ECLIPSE (Evaluation of COPD.

 Longitudinally to Identify Predictive Surrogate Endpoints) study cohort, only 37% of the patients with COPD had persistently increased blood eosinophils at or above 2%6. Smoking is a major risk factor for COPD, and nicotine promotes the development of allergic reactions which causes increase in IgE levels and sensibillisation to different allergens. IgE level of COPD patients was higher than normal range, which could be due to the degree of tobacco smoking, or local production of IgE in the bronchial mucosa7.

**METHODS AND MATERIALS:**

AIM OF THE STUDY: To study the association between eosinophils and serum IgG levels in exacerbations of COPD.

STUDY DETAILS: we conducted a cross sectional observation study. Study was conducted after obtaining approval from the ethics committee, patients who were diagnosed COPD were included. During the study brief history of the patient, smoking history, were noted down and patients were subjected to a battery of investigations as a routine protocol. The tests include blood eosinophil levels, PFT, serum IgE levels.

STATISTICAL ANALYSIS: the data obtained was tabulated in to Microsoft exel sheets. The exel sheet was then analyzed using SPSS software version 19. The data was analyzed to obtain mean, standard deviation, range, and percentages where ever necessary for tabulation. The p value of 0.05 was considered significant. Comparison between two variables was done using chi square test.

 **RESULTS:**

 A total of 140 patients were included in the study. Study showed the male predominance 119(85%) & of female 21(15%) with the most common age group in the range of 50-70 years (83.5%). Here, the absolute eosinophil count & serum IgE levels increased with the staging respectively. The cut off of 2 % (300) for absolute eosinophil count and 150UI/ML for serum IgE levels was taken. Both the biomarkers were elevated in stable COPD & COPD exacerbation but comparatively higher in COPD exacerbation with the P value of 0.001 being statistically significant.

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| **Sl. No** | **Variable** |  **Percentage** | **P value** |
| 1 | Age (years) | 40 - 50 | 11(7.8%) | < 0.001 |
| 51 - 60 | 61 (43.5%) |
| 61 - 70 | 56 (40%) |
| 71 - 80 | 12 (8.5%) |
| 2 | Gender | Male | 119 (85%) | <0.001 |
| Female | 21 (15%) |
| Absent | 144 (48%) |
| 4 |  AEC (mean) | Stable copd (468.98)Unstable copd (890.8) | <0.001 |
| 5 | Serum IgE (mean) |  Stable copd (1289.5) Unstable copd (2309) | < 0.001 |

**DISCUSSION:**

In our study, we observed the significance of Blood Eosinophils & Serum IgE levels among the stable COPD & COPD exacerbation. We also observed the relation of these two biomarkers in the COPD exacerbation. Study showed the male predominance 119(85%) & of female 21(15%) with the most common age group in the range of 50-70 years (83.5%) {CHART 1} Prevalence of STAGE I 21(15%) in stable COPD 13(61.9%) & COPD exacerbation 8(38%), STAGE II 40 (28.5%) in stable COPD 16(40%) & COPD exacerbation 24(60%), STAGE III 58(41.4%) in stable COPD 19(32.7%) & COPD exacerbation 39(67%), STAGE IV 21(15%) in stable COPD 5(24%) & COPD exacerbation 16(76%). That is, predominantly seen in STAGE II & STAGE III.{TABLE 1}

 The no of exacerbations in the last one year & duration of illness increased with staging I,II,III,IV. Whereas, the FEV1 declines with the stage I, II, III, IV. There was no much significant change in the hospitalisation between the various stages. The absolute eosinophil count in STAGE I (305),STAGE II (612),STAGE III (846),STAGE IV (1065) & serum IgE levels in stage I (790),stage II (1728),stage III(1988),stage IV (3247). Here, the absolute eosinophil count & serum IgE levels increased with the staging respectively.

 The factors like, occupational exposure to dust & fumes, biomass exposure & the poor ventilation were comparatively higher in COPD exacerbation states. Whereas, bronchodilator usage was twofold higher in COPD exacerbation with mean of FEV1 in stable COPD (54.3) & COPD exacerbation (48.9) respectively. The cut off of 2 % (300) for absolute eosinophil count and 150UI/ML for serum IgE levels was taken. Both the biomarkers were elevated in stable COPD & COPD exacerbation but comparatively higher in COPD exacerbation with the P value of 0.01 being statistically significant. Like, previous studies showed the relationship between smoking & the elevation in the blood eosinophils & serum IgE levels. The cause for the elevation of the absolute eosinophil count & serum IgE levels was observed in our COPD study population. We could see that smoking was related with the elevation in the biomarkers. Especially, smokers (current, former, passive smokers) & patients with > 10 pack years were associated with increased duration of illness & increased exacerbation rates.

**CONCLUSION:**

Elevated blood eosinophils & serum IgE levels were observed in stable COPD & COPD exacerbation but comparatively was higher in COPD exacerbation. Hence, blood eosinophils can be used as a prognostic biomarker in COPD exacerbation. Smoking is related with longer duration of illness, increased exacerbations, elevated blood eosinophils & serum IgE levels. Further, studies to be done to analyze biomarkers in COPD & ACOS.

**LIMITATIONS:**

We did not analyse the difference in long-term drug therapy, particularly inhaled corticosteroids in these patients. We were not able to reproduce a correlation between sputum and blood eosinophils in a general population setting. Therefore, we cannot exclude that the correlation between sputum and blood eosinophils is different among relatively healthy, treatment-naive individuals with COPD from the general population.

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