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Original article:

Peripheral blood eosinophilia in COPD: prevalence and clinical characteristics

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Abstract

Background: Current evidence suggests that blood eosinophil levels are associated with COPD treatment response and natural history. This study assessed the prevalence of blood eosinophil count as a biomarker and investigated the clinical characteristics of COPD with peripheral blood eosinophilia.

Materials and methods : Cross-sectional observational data from 120 subjects with age greater than 40 years with spirometry defined COPD and with absolute eosinophil count were analysed. Prevalence of peripheral blood eosinophilia and differences in clinical characteristics by absolute eosinophil count above and below 440 cells/cmm were evaluated.

Results: Among COPD patients 38% had peripheral blood eosinophilia. Older age and male gender were associated with peripheral blood eosinophilia in COPD. Among COPD with eosinophilia other associated characteristics included higher BMI, lower FEV_1 and FVC.

Conclusion: The results suggests that the different level of blood eosinophils in the two groups may have influenced the pulmonary function tests independently and identify subgroups of subjects with specific disease characteristics.

Key words: Chronic obstructive lung disease. peripheral blood eosinophilia, prevalence

Introduction:

The prevalence of eosinophilic inflammation in COPD patients is unknown. We do not know whether patients with blood eosinophilia represent a stable COPD phenotype over time. Apart from corticosteroid responsiveness, little is known about the other clinical characteristics of this subset of patients. COPD exacerbations are responsible for a considerable amount of the morbidity and healthcare costs associated with the condition. Some patients with COPD are especially prone to develop exacerbations and have been termed frequent exacerbators[1,5,6]. There has been considerable interest in factors predicting exacerbation frequency, and thus applying strategies to reduce the risk for hospital admission. studies have shown that the strongest predictor of future exacerbation is the exacerbation frequency during the previous year. There has been considerable interest recently in the role of the blood eosinophil count in COPD, and especially in predicting responses in exacerbation rates with inhaled corticosteroid therapy [1-4]. A number of studies have shown that the higher the blood eosinophil count, the greater the exacerbation reduction response to inhaled corticosteroids. Studies of blood eosinophils in inhaled corticosteroid therapy trials have suggested that the higher the blood eosinophil count, the greater the exacerbation frequency[7], and thus the blood eosinophil count may be a biomarker

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for the presence of a frequent exacerbator[8]. In the Copenhagen study, patients with COPD with higher blood eosinophil counts were more likely to have reported more infections and wheezing during colds, suggesting they may have had increased susceptibility to viral infection. The increased blood eosinophil count may reflect a past history of more frequent exacerbations with respiratory viruses, and studies are now required to investigate. The data obtained in the study by Vedel-Krogh and colleagues shows that one should use absolute blood eosinophil counts rather than the percentage of eosinophils in blood[10]. Most of the data on relationships between blood eosinophils, exacerbations and corticosteroid sensitivity have come from retrospective analyses of studies[7]. Study from Vedel-Krogh and colleagues has shown that patients with COPD who develop severe exacerbations may have distinct pathophysiological processes and form a specific phenotype[10]. Eosinophils in COPD is a biomarker of the frequent exacerbator and steroid responsiveness[7]. Present study was undertaken to find out the prevalence of peripheral blood eosinophilia in COPD phenotypes and its clinical characteristics.

Materials and Methods

This cross sectional observational study was conducted in the department of pulmonary medicine, Medical college, Thrissur in 120 patients with COPD who visits the OPD of pulmonary medicine. Inclusion criteria were COPD subjects aged 40 – 90 years with a smoking history of more than 10 pack-years with post-bronchodilator FEV_1/FVC ratio <0.7. Patients with asthma, malignancy, exacerbation COPD, ischemic heart disease, uncontrolled hypertension, heart failure were excluded. After careful history and physical examination; COPD was confirmed by pulmonary function tests. Post bronchodilator FEV_1/FVC ratio was taken to confirm COPD. Baseline blood samples were obtained. Absolute eosinophil count were measured during automated full blood count analysis. Absolute eosinophil count above 440cells/cmm is considered as having peripheral blood eosinophilia. The percentage of COPD patients who peripheral blood eosinophilia is assessed and its clinical characteristics were analysed in subgroups as COPD with and without peripheral blood eosinophilia. Institutional ethical committee approval was obtained and informed consent was taken from all patients.

Results

Among 120 patients 45 patients (38%) showed peripheral blood eosinophilia with absolute eosinophil count above 440cells/cmm. The clinical characteristics are given in Table1.

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Table1: Differences in clinical features between the COPD population with and without peripheral blood eosinophilia

	COPD patients total (n=120)		
	With peripheral blood	Without peripheral blood	
	eosinophilia	eosinophilia	
	(AEC>440/cmm (n=45)	(AEC<440/cmm (n=75)	P value
Age	65 (range 56 - 70)	64.36 (range 48 - 80)	0.786
Sex (% male)	93.34%	80%	0.253
Smoking history	93.34%	80%	o.253
BMI (kg/m^2)	22.1	19.8	0.129
Pre FEV_1 %	38.1	46.4	0.116
Pre FVC %	54.7	66	0.028
Post FEV_1 %	43.5	52.3	0.091
Post FVC %	64.6	76	0.011
Absolute eosinophil	886	296	0.000
count (cells/cmm)			

Distribution of absolute eosinophil count among patients with peripheral blood eosinophilia is given in figure 1.

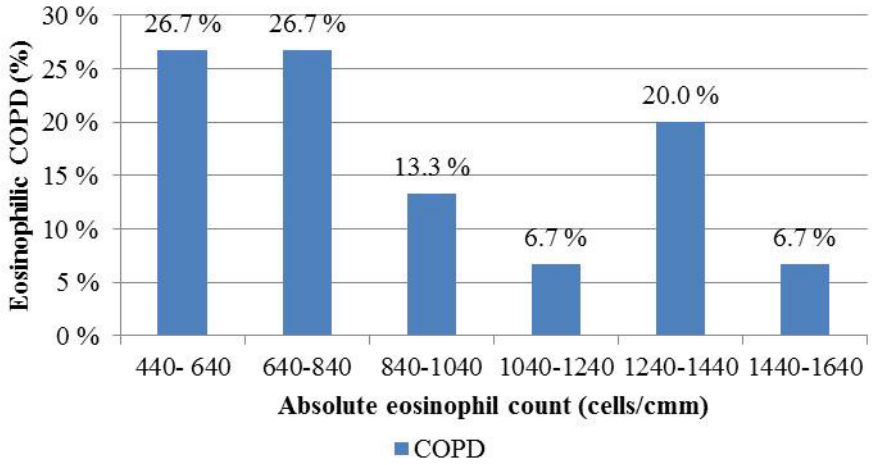

Figure 1: Graph showing associations of eosinophilic COPD and peripheral blood eosinophilia.

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Discussion

The results of the present study show 39% of COPD patients had peripheral blood eosinophilia greater than 440cells/cmm. The results are relevant to clinical practice. In this study absolute eosinophil count above 440 cells/cmm was associated with slightly older, greater proportion of males and history of smoking, high BMI, low FEV_1, FVC compared with COPD patients with absolute eosinophil count less than 440cells/cmm.

Generally, eosinophilic inflammation is regarded as a factor in asthma rather than in COPD [11,12]. Elevated sputum eosinophil levels, due to eosinophilic airway inflammation are found in 10% of corticosteroid-naïve and 40% of corticosteroid-treated patients with COPD[14]. It has been established that there is a strong correlation between sputum eosinophilia and peripheral eosinophilia in COPD[18]. Blood eosinophil levels have been suggested as a practical, quick, cost-effective surrogate marker for sputum eosinophil levels as sputum samples for eosinophil analysis are often unavailable outside of a research setting [8,9]. The studies have suggested the usefulness of the eosinophil count in predicting the therapeutic response to ICS.[13,14] Eosinophis greater than 2% cut-off used by many researchers investigating ICS response in patients with COPD therefore falls within the normal range. Peripheral eosinophilia is a biomarker of response to inhaled corticosteroids (ICS). Subgroup analyses performed in three large-scale studies showed that the benefit of ICS in preventing exacerbations was found only in the subgroup of patients with an eosinophil count greater than 2 percentage [8]. The response to ICS in terms of the rate of decline in pulmonary function also seems to be marked by eosinophilia. When treated with ICS, patients with an eosinophil count greater than 2% showed a marked reduction in the annual rate of decline in FEV_1 (from 74.5mL to 40.6mL). In the absence of this marker, there was no change in the rate of decline in pulmonary function.[8] Queiroz et al. investigated the inflammatory profile in the sputum from 37 patients with COPD, the proportion of eosinophils in the sputum correlated inversely with FEV_1,especially in patients with GOLD stage III COPD. Eltboli and colleagues [15] reported that there is a strong correlation between peripheral blood and bronchial eosinophils and reticular basement membrane thickening and suggested that the peripheral blood eosinophil count does identify COPD subjects with a greater tissue eosinophilia. A recent study documented that airway wall thickness is independently associated with a stronger decline in lung function [16]. An individual's blood eosinophil levels change over time and are influenced by COPD phenotype, medicines and co-morbidities, e.g. obesity [14]. It has been demonstrated that a systematic evaluation of sputum eosinophilia can help to prevent exacerbations [17]. In ECLIPSE cohort study 37.4% subjects had eosinophil counts persistently above 2% at all visits. There was an increased rate of emphysema progression in subjects with eosinophil counts persistently less than 2%. Blood eosinophils above versus below $0.343x10^9$ cells per liter had an excess risk of exacerbations with multivariable-adjusted incidence rate ratio of 1.76 (95%confidence interval, 1.56 – 1.99) for severe exacerbations and 1.15 (1.05 – 1.27) for moderate exacerbations.

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Conclusion

Present study shows that COPD patients are having prevalence of 39% for peripheral blood eosinophilia. COPD patients with and without peripheral blood eosinophilia are having different clinical characteristics and pulmonary function. Previous studies have shown the importance of peripheral blood eosinophilia as a marker of therapeutic response to inhaled corticosteroids, lung function changes and frequent exacerbation.

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