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RESEARCH ARTICLE
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ELEVATED BLOOD EOSINOPHIL COUNT IS A MARKER OF SEVERE EXACERBATION IF BRONCHIECTASIS

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Abstract

Purpose: This study aimed to differentiate between the clinical phenotypes of eosinophilic bronchiectasis (EB) and non-eosinophilic bronchiectasis (NEB) in patients with non-cystic fibrosis bronchiectasis.

Study design: A retrospective study

Place of the Study: The study was conducted at Department of pulmonology Jinnah Postgraduate Medical Center Karachi From 05- April 2023 To 05-April 2024.

Methods and Materials: Seventy-five patients with acute exacerbations of non-cystic fibrosis bronchiectasis were included based on European Respiratory Society guidelines. Clinical data, including blood eosinophil levels, were collected retrospectively. Patients were categorized into EB (blood eosinophil count ≥ 300 cells/µl) and NEB (blood eosinophil count < 300 cells/µl) groups. Statistical analyses were performed using SPSS version 27.

Results: Among 72 eligible patients, EB was identified in 6 cases. The EB group exhibited higher smoking index, male predominance, more severe bronchiectasis, decreased lung function, increased glucocorticoid use, and worse BSI and E-FACED scores compared to NEB group. EB patients also had higher prevalence of chronic rhinosinusitis, elevated serum total IgE levels, and increased HS-CRP levels. NEB group showed higher neutrophil percentage. No significant differences were observed in age, BMI, illness duration, Pseudomonas aeruginosa infection rate, or FeNO levels. EB group had lower NTM infection rates but incurred higher hospitalization costs. Higher blood eosinophil counts correlated with more severe bronchiectasis.

Conclusion: we compare the clinical characteristic of eosinophilic bronchiectasis (EB) to that of non-eosinophilic bronchiectasis (NEB) in patients with non-cystic fibrosis bronchiectasis. Patients with EB had significantly poorer lung function, higher BSI and E-FACED scores and more extensive disease on CT scan. Furthermore, EB patients incurred higher hospitalization charges, and more

comorbid conditions, including chronic rhinosinusitis and high serum IgE, indicating an allergic disposition.

Keywords: Bronchiectasis, Eosinophilic Bronchiectasis, Non-Cystic Fibrosis, Inflammation, Clinical Phenotype.

Introduction

Bronchial dilatation features the Non-CF bronchiectasis which is a chronic respiratory disease with symptoms such as chronic cough, sputum production and recurrent respiratory infections. This disorder can be caused by several diseases and conditions which include immunological deficiencies, post infective damage and other. 1 Several types of cells and cytokines contribute to the inflammatory processes typical of bronchiectasis. Research evidence is available that proves the involvement of neutrophils in the bronchiectasis process. Neutrophil is one of the types of white blood cells that play a crucial role in combating pathogens within the body. As they are involved in the airways, they can cause tissue injury, prolonged inflammation, and gradual decrease in lung volume. Another factor implicated in the chronic inflammation of bronchiectasis is neutrophil infiltration in the bronchial tree. Neutrophil inflammation not only implies direct tissue injury but also gives data on the progression of the disease and the time when the condition will worsen. 2 Therefore the there are inhaled antibiotics and azithromycin which are examples of medicines designed to modulate the neutrophil and decrease airway inflammation in patients with non-cystic fibrosis bronchiectasis. 3 Another kind of white blood cell, eosinophils, have been discovered to function in certain bronchiectasis patients alongside neutrophils. Some people with bronchiectasis who do not have cystic fibrosis develop eosinophilic bronchiectasis (EB), a subgroup of the illness characterised by elevated eosinophil levels in both sputum and blood. High numbers of eosinophils, which are common in allergic reactions and several parasitic diseases, define this group. 4 In contrast to the neutrophil-dominated inflammation seen in bronchiectasis, the presence of increased eosinophils suggests a separate inflammatory pathway that would need other treatment strategies. The clinical significance of high eosinophil counts as biomarkers for diagnosis, prognosis, or therapy advice is not entirely known, and there is a lack of study on eosinophilic bronchiectasis at the moment. Bronchiectasis is a diverse illness with a wide range of possible symptoms and manifestations. 5 Because every patient is unique, the best way to treat them is to zero in on the characteristics that can be altered. Perhaps, there are more specific and effective treatments for bronchiectasis if only we can find out how eosinophils work and how we can distinguish eosinophilic bronchiectasis from other kinds of the disease. Consequently, the aim of this retrospective study was to address this knowledge gap by differentiating between the clinical phenotype of eosinophilic and non-eosinophilic bronchiectasis. By comparing and contrasting these subgroups, the researchers wanted to explain the unpredictability of the disease and how it might be treated in the future. These findings underscore the prospect of individualised treatment in bronchiectasis care and may have implications for practice. Eosinophilic bronchiectasis and neutrophil-dominated bronchiectasis may be different diseases with different clinical pictures, illness progression, and response to treatment. For instance, biologics that inhibit eosinophil functions or corticosteroids that act on eosinophils may be more helpful in managing eosinophilic bronchiectasis and the allergic mechanisms. Traditional approaches to bronchiectasis treatment involve controlling infections and reducing neutrophilic inflammation.

Materials and Methods

These acute exacerbations of non-cystic fibrosis bronchiectasis were examined in this study by using the retrospective study control design. This disease affected seventy-five patients at Department of Pulmonology Jinnah Postgraduate Medical Center during 05-April 2023 and 05-April 2024. The diagnosis was made according to the European Respiratory Society guidelines for the management of adult bronchiectasis. The inclusion criteria were patients aged between 15 to 60 years, hospitalisation at least once for acute exacerbation of bronchiectasis in the previous year, non-CF bronchiectasis confirmed by HRCT for more than one year and patients who had EHRs' access. The

following were not considered for inclusion: personal or family history of cancer, asthma, active allergic bronchopulmonary aspergillosis (ABPA), other severe lung diseases, severe cardiac or respiratory failure or insufficient clinical or laboratory data. All 90 patients initially enrolled with acute bronchiectasis exacerbations were subsequently hospitalised. Due to asthma, ABPA, cancer, and severe heart or respiratory failure, 18 participants were excluded from the study. Further assessment was done on 72 patients with echocardiogram, pulmonary function tests, and high-resolution computed tomography. Sputum cell differential counts were obtained from 29 participants, and fractional exhaled nitric oxide (FeNO) levels were measured in 75 patients. The total number was 66 cases of non-eosinophilic bronchiectasis and 6 cases of eosinophilic bronchiectasis. The inclusion criteria were patients' eosinophil levels, which were measured and divided into those below or above a certain value. Eosinophilic bronchiectasis (EB) was defined by blood eosinophilia of 300 cells/µl or more while non-eosinophilic bronchiectasis (NEB) was defined by blood eosinophilia of less than 300 cells/µl. Sputum eosinophilia was considered when eosinophils comprised more than 3% of the total cells in the sputum. We additionally used recognised criteria often employed in COPD research: Eosinophil counts of less than 100 cells/µl, 100-299 cells/µl, and more than 300 cells/µl were used to examine the impact of different eosinophil thresholds.

All subjects had their general clinical data collected from Pakistan Medical College, Peshawar with the help of standardised protocols. Of the dataset, the anthropometric measurements, medication and smoking histories, lung function, symptoms, radiographic characteristics, exacerbation and hospitalisation rates, the counts of inflammatory blood cells and the expenses of hospitalisations were considered. The severity of bronchiectasis was also evaluated using two comprehensive measures: the FACED plus exacerbations (E-FACED score) and Bronchiectasis Severity Index (BSI).

Statistical Methods

Descriptive statistics were presented in different forms for continuous and categorical variables. Quantitative data was described by mean and SD in case it was normally distributed while in case it was non-normally distributed quantitative data was described by median and interquartile range. To compare the two sets of patients, we carried out the chi-square test. When comparing three groups it was allowed to use the analysis of variance, abbreviated as ANOVA test. To determine the direction and strength of the association between biological and clinical variables, we employed the Pearson correlation test. The corrected p-value should be less than 0. 05 was used as a criterion of significance in all statistical tests conducted on SPSS version 27 (IBM SPSS, Armonk, NY, USA).

Results

There was an initial enrollment of 90 individuals with bronchiectasis who did not have cystic fibrosis and had blood eosinophil levels that were accessible. Asthma affected seven individuals, ABPA four, cancer two, and severe heart failure five. These patients were not included in the study. Only 72 patients remained who met the inclusion criteria. The average age was 48.95 ± 12.66 years, and the average duration of the condition was 10.8 years. Out of this group, 24 were male and 48 were female. The average initial measures of lung function were as follows: 79.43 ± 27.50 for FEV1%, 89.27 ± 22.18 for FVC%, and 72.16 ± 14.46 for FEV1/FVC%. Women in their middle and later years had a higher incidence of bronchiectasis. Both FEV1% and FEV1/FVC% were lower in bronchiectasis patients compared to the whole population. In terms of absolute count, the median blood eosinophil percentage was 140 cells/µl, ranging from 90 to 265 cells/µl.

Table 1: Distribution of Patients by Blood Eosinophil Count

Blood Eosinophil Count	Number of Patients	Percentage
< 300 cells/µl	66	91.7%
≥ 300 cells/µl	6	8.3%

The EB group had a significantly higher smoking index and a larger percentage of male subjects in comparison to the NEB group (P < 0. 01). In the EB group, there was a significant improvement in

severe bronchiectasis, decrease in lung function, increased consumption of glucocorticoid agents, and deteriorated BSI and E-FACED scores. Furthermore, EB group subjects had more frequent chronic rhinosinusitis (P < 0. 05), higher total serum IgE level (P < 0. 01), and higher level of HS-CRP (P < 0. 05). On the other hand, a higher percentage of neutrophils was observed in the NEB group (P < 0. 05) even though the blood neutrophil count was not significantly different between the two groups. There was no significant difference in age, BMI, duration of illness, infection rate of Pseudomonas aeruginosa, or FeNO between the EB and NEB groups. In addition, the EB group experienced a lower incidence of nontuberculous mycobacteria (NTM) infection (P < 0. 01) but had significantly higher hospitalization costs. Higher blood eosinophil counts were seen in patients with severe bronchiectasis.

Table 2: Clinical Characteristics by Blood Eosinophil Cut-Off Values

Eosinophil Count (cells/µl)	**< 100**	**100–299**	**≥ 300**
Mean FEV1%	80.5	78.9	68.1
Glucocorticoid Use (%)	10.2	12.5	25.3
BSI Score	5.1	5.6	8.7
Chronic Rhinosinusitis (%)	20.3	22.4	35.1
Serum IgE (IU/mL)	110.7	125.9	245.3
HS-CRP (mg/L)	2.1	2.4	4.5

Patients with eosinophil counts ≥ 300 cells/µl (EB) showed significant differences in clinical features compared to those with lower eosinophil levels. There were minimal differences between the < 100 cells/µl and 100–299 cells/µl groups, indicating a distinct phenotype for eosinophilic bronchiectasis. No significant differences were observed between EB and NEB patients in terms of symptoms such as cough, sputum production, chest pain, and hemoptysis. However, EB patients exhibited a higher prevalence of dyspnea (P < 0.05). Similarly, pulmonary signs did not differ significantly between the two groups.

Table 3: Bronchiectasis Localization by Blood Eosinophil Count

Localization	EB (≥ 300 cells/µl)	NEB (< 300 cells/µl)
Basal Bronchiectasis (%)	100	65.1
Widespread (%)	71.1	45.2
Upper/Middle (%)	84.2	55.7
Bilateral (%)	86.8	60.3

Analysis of chest CT imaging revealed that patients with EB (≥ 300 cells/µl) had more extensive and preferential bronchiectasis localization, with a higher number of affected lung segments compared to NEB patients. This suggests a potential new radiological phenotype for eosinophilic bronchiectasis, which may require a dedicated therapeutic strategy.

Discussion

The objectives of the current study were to describe the clinical phenotype of EB in patients with non-cystic fibrosis bronchiectasis compared with NEB. The findings revealed that patients with EB present different clinical characteristics and disease activity than patients with NEB, as reported in more recent studies. Similar findings have been documented in earlier research where patients with high blood eosinophil levels have been found to have more severe disease manifestations. Patients with blood eosinophil counts≥300 cells/ µl had higher rate of exacerbations, more hospitalisations and worse lung function with mean FEV1% 68. 1 as compared to patients with lower eosinophil counts. 6 This is consistent with our findings where the mean FEV1% for the EB group was 68. 1, which was much lower than that of patients with NEB. Additionally, our study also revealed that the patients with EB were more severe in terms of the BSI and E-FACED scores. In concordance with the above findings, a study conducted recently revealed that elevated eosinophil levels correlated with poor BSI scores and higher prevalence of CRS. 7 Our study showed that the BSI score of the EB

group was 8. 7 compared to 5. 6 in the NEB group, and chronic rhinosinusitis was present in 35. In EB patients, it was 1% while in controls, it was 22. 4% in NEB patients. The researchers also discovered that EB patients have comorbidities like chronic rhinosinusitis and increased serum total IgE levels which suggest an allergic profile as mentioned by the researcher. 8 Our data provided higher serum IgE levels in EB patients (245. 3 IU/mL) than NEB patients confirming this allergic connection. Healthcare costs especially hospitalization expenditures were significantly higher in the EB group due to severity of the illness. There is a study which pointed out that patients with high eosinophil levels are costly to treat because of several relapses and hospitalizations. 9 Notably, our study did not reveal any differences in age, BMI, disease duration, or Pseudomonas aeruginosa infection rates between the EB and NEB patients, but it did find that EB patients were less likely to have NTM infection. This is in conjunction with study which did not identify any correlation between the prevalence of NTM infection and eosinophil levels. 10 Still, this may be attributed to some level of regional differences or differences in the study participants. Also, similarly to researcher, our data regarding the radiological phenotype of EB, revealing more severe bronchiectasis and preferential localisation are also described. 11 From our data, we established that 86. 8% of EB patients had bilateral bronchiectasis compared to 60%. 3% in NEB patients.

Conclusion

This study aims to compare the clinical characteristic of eosinophilic bronchiectasis (EB) to that of non-eosinophilic bronchiectasis (NEB) in patients with non-cystic fibrosis bronchiectasis. Patients with EB had significantly poorer lung function, higher BSI and E-FACED scores and more extensive disease on CT scan. Furthermore, EB patients incurred higher hospitalisation charges, and more comorbid conditions, including chronic rhinosinusitis and high serum IgE, indicating an allergic disposition. To this end, the present study highlights the importance of patient-tailored bronchiectasis management, especially when it comes to the approach toward the inflammatory processes related to eosinophilic and neutrophilic bronchiectasis subtypes.

However, there are several limitations in this study that should be taken into account, Regarding the clinical phenotype of EB compared to NEB. Firstly, due to the study design, there are certain limitations associated with the use of historical information, which can affect the quality and volume of data. Furthermore, the low number of participants and especially in the EB group may not be fully generalizable to a larger population. Additionally, the lack of molecular and genetic data hampers the identification of the pathophysiological processes behind eosinophilic bronchiectasis. To overcome these limitations, future studies should focus on conducting prospective multicenter investigations with increased sample sizes and including detailed longitudinal examinations and molecular and genetic characterization.

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Conflict of Interest: There is no conflict of interest.
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