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Prevalence of Peripheral Blood Neutrophilic and Eosinophilic Phenotype in Bronchiectasis Patients in Bangladesh

*Ali MMI[1], Hasan MT[2], Miah MAH[3], Dey PK[4], Ahammad M[5], Kadir SMU[6]

Abstract

Bronchiectasis is a heterogeneous condition characterized by chronic airway inflammation. Phenotypic classification into neutrophilic, eosinophilic, and non-neutrophilic types is crucial for understanding disease pathophysiology and guiding management. A cross-sectional study was conducted in the Department of Respiratory Medicine, Cumilla Medical College Hospital, Bangladesh, from January 2023 to June 2024, to assess prevalence of those phenotypes and clinical implications. A total of 150 adult bronchiectasis patients diagnosed via clinical features, high-resolution computed tomography (HRCT), and pulmonary function tests. Blood samples were analyzed to determine phenotypes: neutrophilic (ANC >7.5×10⁹/L), eosinophilic (AEC >0.3×10⁹/L), and non-neutrophilic (neither criteria met). Clinical, demographic, and radiological data were collected and analyzed. The neutrophilic phenotype was predominant (63.3%), followed by eosinophilic (23.3%) and non-neutrophilic (13.4%). Neutrophilic patients were older (mean 45.3±10.5years) and more likely to be smokers (57.9%; p=0.015). Frequent exacerbations (>2 per year) were highest in neutrophilic (68.4%; p=0.001), and severe HRCT findings were more prevalent in this group (57.9%; p=0.048). Eosinophilic patients had milder disease and fewer exacerbations (57.1%), aligning with a Th2-driven inflammatory mechanism. Logistic regression showed smoking as a significant risk factor for severe disease (OR=2.08, p=0.019). Neutrophilic bronchiectasis is the most common and severe phenotype, closely linked to smoking and frequent exacerbations. Eosinophilic and non-neutrophilic phenotypes showed milder clinical courses highlighting the need for management strategies tailored to specific phenotypes.

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Introduction

Bronchiectasis is a chronic respiratory disease marked by permanent dilation and thickening of the bronchial walls, mainly caused by recurrent or prolonged airway inflammation and infection.[1] This structural alteration impairs mucociliary clearance, predisposing individuals to persistent infections and chronic inflammation.[2] Clinically, the presenting signs of bronchiectasis include chronic cough, excessive sputum production, hemoptysis and recurrent respiratory infections, significantly impacting patients' quality of life and posing a substantial healthcare burden.[3] The disease's aetiology is multifactorial, including post-infectious sequelae, immune deficiencies, connective tissue diseases, and idiopathic causes.[4,5] High-resolution computed tomography (HRCT) scan has revolutionized the diagnosis of bronchiectasis, helping to identify the structural changes precisely.[6] Bronchiectasis has shown variability in the underlying inflammatory profiles, resulting in the classification of distinct phenotypes.[2] Among these, the neutrophilic and

1. *Dr. Mirza Mohammad Idris Ali, Assistant Professor, Department of Respiratory Medicine, Comilla Medical College, Cumilla, Bangladesh.
2. Dr. Mohammad Towfique Hasan, Associate Professor, Department of Respiratory Medicine, Sir Salimullah Medical College, Dhaka, Bangladesh.
3. Dr. Mohammad Amir Hossain Miah, Assistant Professor, Department of Respiratory Medicine, Comilla Medical College, Cumilla, Bangladesh.
4. Dr. Pulak Kumar Dey, Associate Professor, Department of Respiratory Medicine, National Institute of Diseases of the Chest and Hospital, Dhaka, Bangladesh.
5. Dr. Mostaque Ahammad, Assistant Professor, Department of Medicine, Comilla Medical College, Cumilla, Bangladesh.
6. Dr. Syeed Mehbub Ul Kadir, Assistant Professor, National Institute of Ophthalmology and Hospital, Dhaka, Bangladesh.

Address of Correspondence:
Email: mirzaidris@ymail.com

eosinophilic phenotypes have emerged as clinically significant subtypes, distinguished by their predominant inflammatory cell populations in the airways.[7] The neutrophilic phenotype is characterized by elevated neutrophil counts, often linked to bacterial infections and more severe disease manifestations, including frequent exacerbations and persistent airway destruction.[8] In contrast, the eosinophilic phenotype is defined by increased eosinophil counts, frequently associated with underlying allergic or immune-mediated mechanisms.[9] The roles of these phenotypes may influence disease progression, frequency of exacerbations, and therapeutic responses, underscoring the significance of individualized management strategies.[10]

Peripheral blood biomarkers, such as absolute neutrophil count (ANC) and absolute eosinophil count (AEC), offer a non-invasive and practical approach to phenotype classification in clinical settings.[11] Identifying the neutrophilic and eosinophilic phenotypes through peripheral blood analysis may provide insights into disease pathophysiology and serve as a guide for tailored interventions.[12] For instance, neutrophilic Bronchiectasis may benefit from strategies aimed at controlling bacterial infections and neutrophilic inflammation, while eosinophilic bronchiectasis may require approaches targeting eosinophilic inflammation, such as corticosteroid therapy.[13]

Despite their clinical significance, limited data are available regarding their prevalence and associated characteristics in the South Asian population, particularly in Bangladesh. Understanding the distribution of these phenotypes and their relationship with clinical outcomes is critical for optimizing disease management. It may also contribute to improved prognostication and resource allocation in resource-limited settings. Therefore, our study aims to determine the prevalence of neutrophilic and eosinophilic phenotypes of bronchiectasis in patients attending a tertiary care hospital in Bangladesh. Additionally, this study examines the connection between these phenotypes and clinical characteristics, such as disease severity, frequency of exacerbations, and quality of life. The study aspires to pave the way for personalized therapeutic approaches to enhance patient outcomes by identifying potential differences in treatment responses among these phenotypes. The findings of this research are expected to provide valuable insights into the phenotype distribution of Bronchiectasis in Bangladesh and inform clinical practice in similar settings globally.

Methods

This cross-sectional study was conducted in the Department of Respiratory Medicine, Cumilla Medical College Hospital, Bangladesh, from January 2023 to June 2024, with a sample size of 150 adult patients aged 18 years or older diagnosed with bronchiectasis. Diagnosis was based on clinical features, high-resolution computed tomography (HRCT), and pulmonary function tests. Patients with coexisting chronic respiratory diseases, such as acute or chronic obstructive pulmonary disease, were excluded. Data compilation involved a standardized form capturing demographic information, clinical history, HRCT findings, pulmonary function tests, and laboratory data, including peripheral blood counts of neutrophils and eosinophils. Absolute neutrophil count (ANC) and absolute eosinophil count (AEC) were used to classify patients into phenotypes: neutrophilic (ANC $>7.5\times10^9$/L), eosinophilic (AEC $>0.3\times10^9$/L), and non-neutrophilic (not meeting the

criteria for the other two groups). Clinical data included the frequency of exacerbations, disease duration, and chronic symptoms such as persistent cough, sputum production, or shortness of breath. Sputum culture and sensitivity or GeneXpert tests were documented to exclude pulmonary tuberculosis. Then, peripheral blood samples were collected under aseptic conditions, and laboratory analysis was conducted in the Department of Clinical Pathology of the same institution.

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 29.0 for Windows to calculate descriptive statistics for phenotype prevalence and demographic and clinical characteristics. Relationships between phenotypes and clinical outcomes, such as exacerbation frequency and chronic symptom duration, were analyzed using chi-square tests, independent t-tests, and logistic regression. Continuous variables were expressed as mean±standard deviation (SD) and categorical variables were presented as percentages. A p-value <0.05 was considered statistically significant.

Ethical approval was obtained from the Institutional Review Board of Cumilla Medical College, Cumilla, Bangladesh.

Results

Among 150 patients, the majority 95(63.3%) of them were classified as having a neutrophilic phenotype. The eosinophilic phenotype was observed in 35(23.3%) patients. The remaining 20(13.4%) patients were categorized as non-neutrophilic, indicating the presence of inflammatory profiles that met the thresholds for neither neutrophilic nor eosinophilic classification (Table-I). Regarding demographic characteristics of the patients, the neutrophilic phenotype had a mean age of 45.3 years, those with the eosinophilic phenotype were slightly younger at 42.8 years, and the non-neutrophilic group was older at 50.2 years, with a significant difference among the groups (p=0.042). Males predominated in the neutrophilic (60/35) and eosinophilic (25/10) groups, while the non-neutrophilic group had an equal male-to-female ratio (10/10); however, the difference was not statistically significant (p=0.193). Smoking history showed a significant association, with 57.9% of neutrophilic, 34.3% of eosinophilic, and 25.0% of non-neutrophilic patients being smokers (p=0.015) (Table-II). Of clinical characteristics, frequent exacerbation (>2 episodes per year) was the most common finding in the neutrophilic group (68.4%), followed by the eosinophilic group (57.1%) and the non-neutrophilic group (25.0%) with a statistically significant difference (p=0.001). Chronic symptoms lasting more than five years were observed in 84.2% of neutrophilic patients, 80.0% of eosinophilic patients, and 60.0% of non-neutrophilic patients, which shows a significant association (p=0.023). Severe disease based on HRCT findings was most prevalent in the neutrophilic group (57.9%), compared to 42.9% in the eosinophilic group and 35.0% in the non-neutrophilic group with a significant difference among groups (p=0.048) (Table-III). Logistic regression analysis identified factors associated with severe forms of disease in bronchiectasis patients. The eosinophilic phenotype had an odds ratio (OR) of 0.62 (95% CI: 0.30–1.28), suggesting a lower likelihood of severe disease, though the result was not statistically significant (p=0.194). The non-neutrophilic phenotype demonstrated a significantly reduced likelihood of severe disease, with an OR of 0.35 (95% CI: 0.14–0.85; p=0.021). Conversely, being a smoker was associated with a significantly increased likelihood of

severe disease, with an OR of 2.08 (95% CI: 1.12–3.85; p=0.019). These findings indicate that smoking is a risk factor for severe disease, whereas non-neutrophilic phenotype may confer a protective effect (Table-IV).

Table-I: Prevalence of different phenotype (N=150)

Phenotype	Frequency	Percentage
Neutrophilic	95	63.3
Eosinophilic	35	23.3
Non-Neutrophilic	20	13.4

Table-II: Demographic characteristics by phenotype (N=150)

Variables	Neutrophilic (n=95)	Eosinophilic (n=35)	Non-Neutrophilic (n=20)	p-value
Age (mean±SD)	45.3±10.5 years	42.8±11.2 years	50.2±9.8 years	0.042*
Sex(Male/ Female)	60/35	25/10	10/10	0.193
Smokers (%)	55 (57.9%)	12 (34.3%)	5 (25.0%)	0.015*

Table-III: Clinical characteristics by phenotype (N=150)

Variables	Neutrophilic Frequency (Percentage)	Eosinophilic Frequency (Percentage)	Non-Neutrophilic Frequency (Percentage)	p-value
Frequent exacerbation (>2/year)	65 (68.4)	20 (57.1)	5 (25.0)	0.001*
Chronic symptoms (>5 years)	80 (84.2)	28 (80.0)	12 (60.0)	0.023*
Severe Disease (HRCT Findings)	55 (57.9)	15 (42.9)	7 (35.0)	0.048*

Table-IV: Logistic regression for severe disease

Variables	Odds Ratio (OR)	95% CI	p-value
Eosinophilic Phenotype	0.62	0.30 – 1.28	0.194
Non-Neutrophilic	0.35	0.14 – 0.85	0.021*
Smokers	2.08	1.12 – 3.85	0.019*

Discussion

Our study identified the neutrophilic phenotype as the predominant subtype (63.3%), consistent with findings by Martínez-García *et al.,* who reported that neutrophilic inflammation is closely linked to bronchiectasis severity and exacerbations.[14] The eosinophilic phenotype (23.3%) was less common, yet clinically significant, as it may reflect a Th2-driven inflammatory pathway, aligning with the findings of Chen *et al.* and Oscullo *et al.*[15,16] The non-neutrophilic phenotype representing 13.4% of patients, underscores the heterogeneity of the disease and may be associated with milder clinical manifestations, as suggested by Schäfer *et al.*[17]

The distribution of phenotypes may also reflect geographical, genetic, and environmental differences in disease expression. A study done by Nomura et al. highlighted the varying prevalence of eosinophilic bronchiectasis across different populations, further underscoring the importance of localized data.[18] Our findings expand upon these observations by providing region-specific insights, contributing to the global understanding of bronchiectasis phenotypes.

The neutrophilic phenotype was significantly associated with older age, smoking history, and severe disease manifestations, consistent with Keir & Chalmers, who emphasized the role of chronic infections and environmental factors, such as

smoking, in neutrophilic inflammation.[19] Smoking, in particular, was a key risk factor for severe disease in our study, with an odds ratio of 2.08 (p=0.019). This aligns with the findings of Papaioannou *et al.* as they reported that smoking exacerbates neutrophilic airway inflammation leading to more severe outcomes.[20]

In contrast, the eosinophilic phenotype exhibited a milder disease course with fewer exacerbations and structural abnormalities. This supports the findings of Kwok *et al.,* as they demonstrated the potential for inhaled corticosteroids (ICS) to improve outcomes in eosinophilic bronchiectasis, particularly in patients with elevated blood eosinophils.[21] However, as Martínez-García *et al.* noted, excessive ICS use may have a U-shaped relationship with disease severity, emphasizing the need for careful therapeutic application.[14]

Although less prevalent, the non-neutrophilic phenotype warrants further investigation. Its association with milder symptoms may suggest a distinct endotype or adaptive immune response, as speculated by Simpson *et al*.[22] Understanding these mechanisms can offer new avenues for targeted therapies.

The neutrophilic phenotype was associated with a higher prevalence of severe disease on HRCT (57.9%), corroborating findings by Gramegna *et al.,* who highlighted the destructive role of neutrophil elastase in promoting airway remodelling and inflammation.[23] Conversely, the eosinophilic and non-neutrophilic phenotypes were associated with less severe HRCT findings, suggesting a different pathophysiological mechanism of airway damage, as discussed by Oscullo *et al*., and Nomura *et al*.[16,18] Meanwhile, severe disease manifestations in neutrophilic patients underline the need for aggressive management strategies. Schäfer *et al.* pointed out that early intervention in this phenotype may prevent irreversible airway damage.[17] The lower HRCT severity in eosinophilic and non-neutrophilic phenotypes highlights their potential responsiveness to conservative treatments.

Phenotypic classification has significant implications for the management of bronchiectasis. Neutrophilic patients may benefit from treatments targeting infection and neutrophilic inflammation, such as macrolides or neutrophil elastase inhibitors, as suggested by Gramegna *et al*.[23] Eosinophilic phenotype patients, on the other hand, may respond favourably to ICS or biological therapies targeting the Th2 pathway, such as mepolizumab, as demonstrated by Carpagnano *et al.* and Oriano *et al*.[24,25] For non-neutrophilic patients, symptom-focused management and monitoring may be more appropriate, given their milder disease course. These findings underscore the need for phenotype-guided therapeutic approaches to optimize patient outcomes. Keir & Chalmers stated that an individualized approach considering phenotype, biomarkers, and clinical features is crucial in addressing bronchiectasis's diverse presentations and improving prognosis.[19]

This study provides valuable insights into the prevalence of bronchiectasis phenotypes and clinical implications, particularly in a developing country. However, certain limitations should be acknowledged. The reliance on peripheral blood markers may not fully reflect airway-specific inflammation. Future studies incorporating sputum and bronchoalveolar lavage analysis could provide a more comprehensive understanding. Additionally, the cross-sectional design limits causal interpretations, and longitudinal studies are warranted to evaluate phenotype evolution and treatment response.

Conclusion

The neutrophilic phenotype was linked to more severe disease and frequent exacerbations, whereas the eosinophilic and non-neutrophilic phenotypes showed distinct but less severe profiles. These findings emphasize the significance of phenotypic classification in managing bronchiectasis and support the creation of therapeutic strategies tailored to specific phenotypes to improve patient outcomes. Future research should concentrate on longitudinal studies and integrating advanced biomarkers to enhance phenotype-based management strategies.

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