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Original Article

Evaluation of Inflammatory Response in Patients with Bronchiectasis: Eosinophilic and Non-eosinophilic Phenotypes

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ABSTRACT

OBJECTIVE: To examine the distribution of eosinophilic and non-eosinophilic phenotypes, defined by routine complete blood count, in a Turkish bronchiectasis cohort, and to evaluate their associations with demographic and radiological characteristics as geographic validation of European findings.

MATERIAL AND METHODS: We retrospectively analyzed 120 patients with bronchiectasis at Yozgat Bozok University Research and Application Hospital. Patients were classified as eosinophilic (≥300 cells/μL) or non-eosinophilic (<300 cells/μL) based on peripheral blood eosinophil count. Demographic, laboratory, and computed tomography radiological extent data (number of lobes involved) were compared between groups. Correlation analyses, exploratory logistic regression, and receiver operating characteristic analyses were performed, with multiple-comparison correction and sensitivity analyses (alternative cutoffs, exclusion of inhaled corticosteroid users).

RESULTS: Twenty-five patients (20.8%) were eosinophilic and 95 (79.2%) were non-eosinophilic. The eosinophilic group was younger (52.1±12.0 vs. 60.3±13.5 years; $P = 0.005$; Cohen's d = −0.62), but this lost significance after multiple-comparison correction; other demographic and laboratory variables did not differ. Radiological extent was similar between groups ($P = 0.606$) and did not correlate with eosinophil count (rho = 0.11, $P = 0.227$). In an exploratory multivariate model, only age was independently associated with the eosinophilic phenotype (adjusted odds ratio = 0.95, 95% confidence interval 0.92–0.99; $P = 0.009$). Eosinophil count, neutrophil count, and C-reactive protein showed limited discrimination for extensive radiological involvement, with area under the curves of 0.52, 0.50, and 0.58, respectively; lobar distribution did not differ ($P = 0.655$ and 1.000). Radiological findings were similar after excluding inhaled corticosteroid users (n = 23).

CONCLUSION: Hemogram-based phenotyping was feasible, but eosinophil count alone had limited value in predicting radiological extent or distribution. These preliminary single-center, retrospective data will be included in a planned multicenter study pending ethical approval.

KEYWORDS: Bronchiectasis, eosinophilic phenotype, non-eosinophilic phenotype, peripheral blood eosinophil count, bronchiectasis radiological extent

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INTRODUCTION

Bronchiectasis is a chronic lung disease characterized by permanent bronchial dilation resulting from progressive injury driven by sustained inflammation and recurrent infection. Its global prevalence has risen markedly over the past decade,[1] disproportionately affecting older adults and imposing a substantial morbidity burden[2]; European Bronchiectasis Registry (EMBARC) data further document wide geographic variation in disease distribution and clinical burden.[3] Taken together, these data confirm that bronchiectasis is a growing global health concern that requires a deeper biological understanding.[4]

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Bronchiectasis pathophysiology reflects a self-perpetuating cycle in which impaired mucociliary clearance and microbial colonization amplify inflammation[5]; it is now recognized as an active, biologically heterogeneous process rather than simple structural damage,[6] driven by distinct inflammatory endotypes with direct implications for targeted, patient-specific treatment.[7]

Neutrophilic mechanisms have traditionally dominated this model: airway neutrophils release elastase, matrix metalloproteinases, and reactive oxygen species that disrupt epithelial integrity,[8] and neutrophil extracellular traps and elastase activity have been linked to disease severity and exacerbation risk.[9] However, a subset of patients shows eosinophil-predominant airway inflammation, indicating that a single inflammatory model cannot capture the full disease spectrum.[10]

Eosinophilic inflammation in bronchiectasis has consequently become a major research focus.[10,11] A multicenter European cohort study by Shoemark et al.[12] showed that eosinophilic bronchiectasis differs from the non-eosinophilic phenotype in clinical, radiological, and microbiological features, and the EMBARC-BRIDGE study further supported the eosinophilic endotype as a distinct clinical entity;[13] T-helper/T-regulatory balance appears to shape this divergence beyond simple cell counts.[14]

Eosinophilic bronchiectasis has been linked to disease severity and treatment response;[15] eosinophil levels rise during exacerbations,[16] and Martínez-García et al.[17] described a U-shaped, nonlinear relationship between blood eosinophil count and severity that is modified by inhaled corticosteroids. Comorbid chronic rhinosinusitis further defines a distinct immunological subgroup.[18] Together, these findings support blood eosinophil count as a practical phenotyping biomarker, although its consistency across populations remains debated.

Radiological assessment complements laboratory phenotyping. High-resolution computed tomography (HRCT) remains the diagnostic cornerstone,[19] and radiological features such as distribution pattern, extent, and bronchial wall thickness may reflect the underlying inflammatory subtype, adding a structural dimension to phenotyping models. EMBARC data show that comorbid asthma marks a distinct eosinophil-predominant subgroup.[20] Accurate phenotyping, therefore, matters for matching patients with the right treatment.

Despite this evidence, most phenotyping studies rely on induced sputum, bronchoalveolar lavage, or advanced immunoassays that are not routinely feasible in clinical practice.[7] Existing eosinophilia data, including those of Shoemark et al.[12] and Martínez-García et al.,[17] derive largely from Western European and Mediterranean reference-center cohorts,[13,15] leaving the reproducibility of these phenotypes unknown in populations such as Türkiye's. In Türkiye, a recent large retrospective cohort of hospitalized patients with bronchiectasis reported peripheral eosinophilia (≥300 cells/μL) in 5.6% of patients and a statistically significant but very small independent association between baseline eosinophil count (analyzed as a continuous variable) and mortality (hazard ratio 1.003);[21] however, eosinophilic and non-eosinophilic phenotypes were not compared with respect to demographic and radiological characteristics. This gap motivates external geographic validation of routine, low-cost complete blood count (CBC)-based phenotyping in real-world settings.

This retrospective study therefore aimed to provide geographic external validation in a Turkish bronchiectasis cohort of the CBC-defined eosinophilic and non-eosinophilic classification described in European cohorts by characterizing the distribution of these phenotypes and examining their associations with thoracic CT findings and demographic and laboratory characteristics to determine whether blood eosinophil count can serve as a practical, independent biomarker for phenotype-specific disease characterization.

Main Points

- This study provides geographic external validation, in a Turkish bronchiectasis cohort, of a simple, routinely available complete blood count-based classification of eosinophilic and non-eosinophilic inflammatory phenotypes previously described in European cohorts.
- Among 120 patients, 20.8% were classified as the eosinophilic phenotype and 79.2% as the non-eosinophilic phenotype; the eosinophilic group was significantly younger, although this difference did not survive correction for multiple comparisons.
- Peripheral blood eosinophil count showed no clear association with radiological disease extent or distribution in correlation, multivariate regression, and sensitivity analyses across multiple thresholds, and only limited discrimination in receiver operating characteristic analyses.
- These findings suggest that, while hemogram-based phenotyping is feasible in real-world clinical practice, eosinophil count alone has limited utility in predicting the radiological extent of bronchiectasis.
- The study provides external validation data from an underrepresented geographic population and lays the groundwork for a planned larger multicenter study on inflammatory phenotypes in bronchiectasis.

MATERIAL AND METHODS

Study Design and Ethical Approval

This single-center, retrospective, cross-sectional study was conducted jointly by the Departments of Chest Diseases and Radiology at Yozgat Bozok University Research and Application Hospital. The patients analyzed here will also be included in a planned larger multicenter study (currently at the ethical approval stage), which will apply the same eligibility criteria for the same study period (January 1-December 31, 2025) at additional centers. The present single-center analysis was conducted under its own ethical approval and was not part of a predefined multicenter protocol; therefore, this analysis represents preliminary data, and the findings will be re-evaluated in the larger sample (see Discussion). The protocol was approved by the Yozgat Bozok University Ethics

Committee (protocol no. 2026-GOKAEK-268; decision no. 123; date: 15.04.2026) and was conducted in accordance with the Declaration of Helsinki. Given the retrospective, anonymized design, individual informed consent was waived and data confidentiality was maintained throughout.

Patient Selection

Patients aged 18–90 years who presented to the chest diseases outpatient clinic between January 1 and December 31, 2025 with bronchiectasis radiologically confirmed on thoracic imaging by an experienced radiologist were retrospectively identified from the hospital information system and radiology archive. As all eligible patients during this period were included, no a priori power analysis was performed. Inclusion required age 18–90 years, HRCT-confirmed bronchiectasis per accepted diagnostic criteria,[19] and available CBC results plus complete clinical and radiological data. Patients were excluded for the following reasons: cystic fibrosis, active hematological or solid-organ malignancy, primary immunodeficiency, active parasitic infection, systemic corticosteroid use at the time of CBC collection, or incomplete data. After applying these criteria, 120 patients were enrolled.

Radiological Assessment

Thoracic computed tomography (CT) images, acquired on a GE Revolution Maxima 128-detector scanner with a standard thoracic protocol, were reviewed by an experienced radiologist who was blinded to clinical and CBC data and were evaluated using published international consensus criteria for bronchiectasis.[19] Two parameters were recorded: anatomical distribution (right and left lungs; individual lobes) and an extent score (range 1–5; all patients had at least one affected lobe), calculated as the number of lobes showing bronchiectasis (right upper, middle, and lower lobes; left upper lobe, including the lingula; left lower lobe). This lobar approach was derived from the scoring system of Reiff et al.[22]; however, unlike the original system, which also grades the severity of bronchial dilatation, only the number of affected lobes was recorded, so the score reflects radiological extent rather than severity. Extensive involvement was defined as involvement of ≥3 lobes, i.e., above the cohort median score of 2.0. This threshold was data-driven rather than predefined and consistent with the lobar-involvement criterion of the Bronchiectasis Severity Index.[23] Because dichotomization at a sample-derived cut-off may limit generalizability, the score was analyzed as a continuous variable in the primary comparisons, and the ≥3 threshold was used only in secondary analyses [receiver operating characteristic (ROC) analysis and proportion of extensive involvement].

Laboratory Parameters and Inflammatory Phenotype Classification

Peripheral blood eosinophil and neutrophil counts were obtained from routine CBC results, drawn from standard clinical follow-up without study-specific testing, on the same day as thoracic CT in 75 patients (62.5%) and within three days after CT in 45 patients (37.5%). CBCs were performed using the hospital's routine automated hematology analyzer (Sysmex XN-1000; Sysmex Corporation, Kobe, Japan), and absolute eosinophil and neutrophil counts were expressed as cells/μL. Phenotype classification used the literature-validated threshold of ≥300 cells/μL (eosinophilic) versus <300 cells/μL (non-eosinophilic).[12,13] Because no independent measure of neutrophilic airway inflammation (e.g., sputum neutrophil percentage) was available, patients with eosinophil counts <300 cells/μL were designated as non-eosinophilic rather than neutrophilic; the blood neutrophil count was analyzed as a separate laboratory parameter and was not used for phenotype classification. Additionally, sensitivity analyses used alternative cutoffs of 150, 200, and 400 cells/μL. Asthma and chronic obstructive pulmonary disease (COPD) diagnoses were obtained from patient history. All patients with these diagnoses (n = 23) reported using inhaled corticosteroids (ICS)-containing combination inhalers, although the agent, dose, and duration were not available. No clinical findings suggestive of an asthma or a COPD exacerbation were noted in these patients at presentation. Information on bronchiectasis exacerbation at the time of blood sampling could not be obtained from the patient's history. Likewise, systematic data on the use of antibiotics or other anti-inflammatory treatments (e.g., long-term macrolides) at the time of blood sampling could not be obtained.

Statistical Analysis

Descriptive statistics and primary comparisons were performed in SPSS v20.0, while Spearman correlation, multivariate logistic regression, ROC/area under the curve (AUC) analyses, multiple-comparison corrections, and threshold sensitivity analyses were performed in Python 3.12 using SciPy (v1.16.3), statsmodels (v0.14.6), scikit-learn (v1.6.1), pandas (v2.2.2), and NumPy (v2.0.2). Continuous variables are reported as mean±standard deviation or median [interquartile range (IQR)] and compared with Welch t-tests, Mann-Whitney U, ANOVA, or Kruskal-Wallis as appropriate; categorical variables were compared with chi-square or Fisher's exact tests. For the 12 comparisons in Table 1, the Benjamini-Hochberg FDR correction was applied as the primary method, with the Bonferroni correction reported as a conservative sensitivity check. A multivariate logistic regression model [age, sex, radiological extent score, C-reactive protein (CRP)] was constructed for the eosinophilic phenotype, as an exploratory analysis given the limited number of events (n = 25). Results are reported as odds ratios [95% confidence interval (CI)] and model AUC. ROC analysis further assessed eosinophil count, neutrophil count, and CRP for predicting extensive radiological involvement. Given the modest sample size, Cohen's d (calculated using the pooled standard deviation) and events per variable were calculated to contextualize the statistical power. Because the events-per-variable ratio was low, two more parsimonious models (age and radiological extent score, age alone) were fitted post hoc, and the minimum detectable effect size (Cohen's d) for the eosinophilic versus non-eosinophilic comparison was calculated (80% power, two-sided $\alpha = 0.05$). Statistical significance was set at $P < 0.05$. To assess the potential confounding effect of ICS use, the association between phenotype and radiological extent was repeated as a sensitivity analysis after excluding patients with such use (those with asthma or COPD; n = 23). ROC analyses were additionally repeated using alternative thresholds for extensive involvement (≥2 and ≥4 lobes) as sensitivity analyses, and 95% CIs for AUC values were calculated using the DeLong method.

Table 1. Comparison of demographic, laboratory, and radiological characteristics between eosinophilic and non-eosinophilic phenotype groups

Variable	Whole cohort (n = 120)	Eosinophilic phenotype (n = 25)	Non-eosinophilic phenotype (n = 95)	*P* value	Effect size/OR (95% CI)
Age, years	58.6±13.6	52.1±12.0	60.3±13.5	0.005[a] *	d = −0.62
BMI, kg/m²	28.4 (24.9–31.8)	27.3 (24.6–31.8)	28.5 (24.9–31.2)	0.941[b]	r = 0.01
CRP, mg/L	5.8 (3.0–13.8)	5.0 (3.5–6.0)	6.7 (2.7–17.0)	0.475[b]	r = 0.07
ESR, mm/h	15.0 (9.0–27.0)	14.0 (9.0–20.0)	15.0 (9.0–28.0)	0.696[b]	r = 0.04
Neutrophil count, cells/µL	5395.0 (4157.5–7622.5)	4850.0 (4200.0–6550.0)	5430.0 (4135.0–7705.0)	0.598[b]	r = 0.05
Radiological extent score (1–5)	2.0 (1.8–4.0)	2.0 (2.0–4.0)	2.0 (1.0–4.0)	0.606[b]	r = 0.05
Sex, male, n (%)	55 (45.8)	14 (56.0)	41 (43.2)	0.252[c]	OR = 1.66 (0.69–3.96)
Any comorbidity, n (%)	91 (75.8)	18 (72.0)	73 (76.8)	0.615[c]	OR = 0.76 (0.29–1.99)
Asthma, n (%)	8 (6.7)	2 (8.0)	6 (6.3)	0.671[d]	OR = 1.46 (0.32–6.75)
COPD, n (%)	15 (12.5)	2 (8.0)	13 (13.7)	0.734[d]	OR = 0.65 (0.16–2.70)
Cardiovascular disease, n (%)	53 (44.2)	12 (48.0)	41 (43.2)	0.664[c]	OR = 1.22 (0.51–2.90)
Smoking status, n (%)				0.252[c]	V=0.15
Never	74 (61.7)	14 (56.0)	60 (63.2)		
Former	33 (27.5)	6 (24.0)	27 (28.4)		
Current	13 (10.8)	5 (20.0)	8 (8.4)		

[a]Welch t-test. [b]Mann-Whitney U test. [c]Chi-square test. [d]Fisher's exact test. *$P < 0.05$ (unadjusted). No variable retained significance after Benjamini-Hochberg FDR or Bonferroni correction for multiple comparisons. Continuous variables: mean±SD or median (interquartile range); categorical variables: n (%).

BMI: body mass index, CI: confidence interval, COPD: chronic obstructive pulmonary disease, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, FDR: false discovery rate, OR: odds ratio, SD: standard deviation, V: Cramér's V. quartiles were calculated by linear interpolation

RESULTS

A total of 120 patients met study criteria [mean age 58.6±13.6 years; 65 female (54.2%), 55 male (45.8%); median body mass index (BMI) 28.4 kg/m², IQR 24.9–31.8]. By smoking history, 61.7% had never smoked, 27.5% were former smokers, and 10.8% were current smokers (mean burden 29.3±19.9 pack-years). At least one comorbidity was present in 75.8% of participants; the most common comorbidities were cardiovascular (44.2%) and metabolic (31.7%); asthma and COPD were present in 6.7% and 12.5%, respectively. The median radiological extent score was 2.0 (IQR 1.8–4.0), and all-lobe involvement (score 5) was present in 16.7% of patients.

Based on classification by eosinophil count, 25 patients (20.8%) were assigned to the eosinophilic phenotype and 95 patients (79.2%) to the non-eosinophilic phenotype (Figure 1A). Among the 12 compared variables, only age reached unadjusted significance: the eosinophilic group (52.1±12.0 years) was significantly younger than the non-eosinophilic group (60.3±13.5 years; Welch t-test, $P = 0.005$; Cohen's d = −0.62) (Figure 1B), a difference that did not retain significance after correction for multiple comparisons. No significant differences were found for sex, BMI, CRP, erythrocyte sedimentation rate (ESR), neutrophil count, smoking status, comorbidity prevalence, asthma, or COPD (Table 1). All 23 patients with asthma (n = 8) or COPD (n = 15) were using ICS-containing combination inhalers; 4 (17.4%) were in the eosinophilic group and 19 (82.6%) were in the non-eosinophilic group.

Radiological extent scores did not differ between the eosinophilic and non-eosinophilic groups [median 2.0 vs. 2.0; Mann-Whitney U test, $P = 0.606$; r = 0.05 (negligible)]. Sensitivity analyses using alternative eosinophil thresholds (150, 200, 400 cells/µL) yielded consistently non-significant differences ($P = 0.431$, 0.212, 0.548; r = 0.070, 0.112, 0.054), confirming that this null finding is not threshold-dependent (Table 2).

After excluding patients with known ICS use (those with asthma or COPD; n = 23), the analysis included 97 patients (21 eosinophilic, 76 non-eosinophilic). Radiological extent scores remained similar between groups (median 2.0 vs. 2.0; Mann-Whitney U, $P = 0.689$; r = 0.041), eosinophil count did not correlate with extent score (rho = +0.106, $P = 0.301$), and the proportion of patients with extensive involvement (score ≥3) was comparable (42.9% vs. 46.1%; Fisher's exact test, $P = 1.000$). The eosinophilic group remained younger in this subset (51.2±12.7 vs. 59.2±13.9 years; Welch t-test, $P = 0.017$).

Spearman's correlation analysis showed no association between eosinophil count and radiological extent score (rho = +0.11, $P = 0.227$; Figure 2), age (rho = -0.12, $P = 0.186$), BMI (rho = +0.05, $P = 0.601$), CRP (rho = -0.11, $P = 0.240$), ESR (rho = +0.002, $P = 0.984$), or comorbidity count (rho = -0.03, $P = 0.734$); neutrophil count likewise did not correlate with extent score (rho = +0.07, $P = 0.458$).

In multivariate logistic regression (age, sex, radiological extent score, CRP; n = 120, 25 events; model AUC = 0.71, 95% CI 0.59–0.83), only age was independently associated with the eosinophilic phenotype [adjusted odds ratio (OR) = 0.95, 95% CI 0.92–0.99, $P = 0.009$], suggesting a higher likelihood of the eosinophilic phenotype in younger patients, although the estimate is imprecise given the small number of events [events per variable (EPV) ≈6.25] and should be regarded as exploratory; sex, extent score, and CRP were not independently associated with the phenotype (Table 3).

To address the low events-per-variable ratio of the full model, two more parsimonious models were fitted post hoc. Age remained the only variable independently associated with

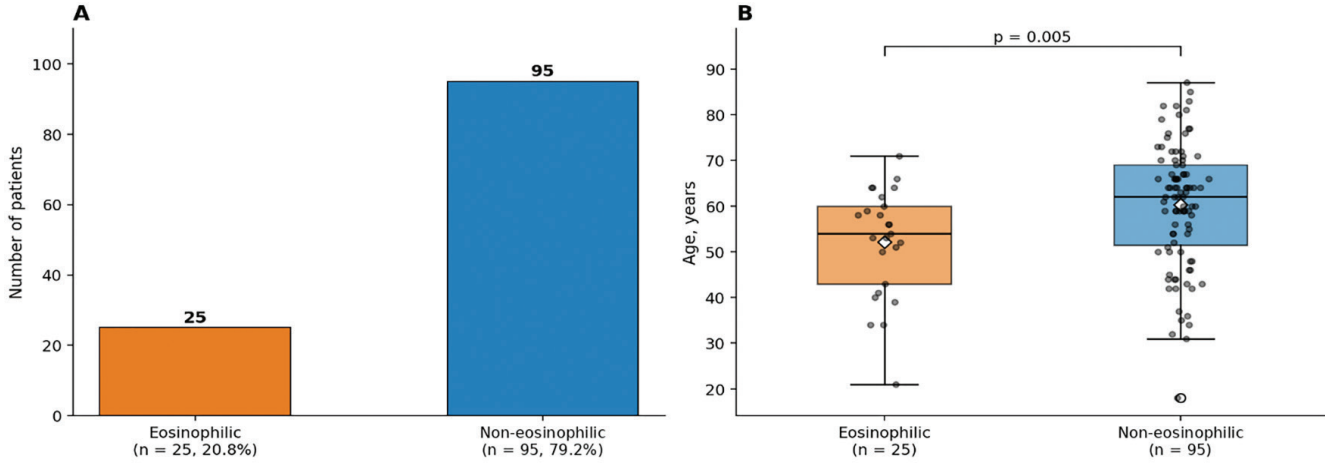


Figure 1. Distribution of inflammatory phenotypes and age comparison between groups (n = 120). A) Distribution of eosinophilic (n = 25, 20.8%) and non-eosinophilic (n = 95, 79.2%) phenotypes in the study cohort based on a peripheral blood eosinophil count threshold of ≥300 cells/μL. (B) Age distribution by inflammatory phenotype. The eosinophilic group was significantly younger than the non-eosinophilic group in the unadjusted analysis (52.1±12.0 vs. 60.3±13.5 years; Welch t-test, $P = 0.005$; Cohen's d = −0.62); this difference did not retain significance after correction for multiple comparisons. Diamonds indicate group means; dots represent individual patients; horizontal lines indicate medians; boxes represent interquartile ranges; whiskers extend to 1.5× interquartile range

Table 2. Sensitivity analysis of the eosinophil count threshold used for phenotype classification

Threshold (cells/μL)	Eosinophilic, n (%)	Non-eosinophilic, n (%)	Mann-Whitney U, *P* value	Effect size, r
150	56 (46.7)	64 (53.3)	0.431	0.070
200	40 (33.3)	80 (66.7)	0.212	0.112
300 (primary)	**25 (20.8)**	**95 (79.2)**	**0.606**	**0.046**
400	15 (12.5)	105 (87.5)	0.548	0.054

The outcome variable in all analyses is the radiological extent score (Mann-Whitney U test; eosinophilic vs. non-eosinophilic groups). The 300 cells/μL threshold (bold) represents the primary analysis. Effect sizes (r) were negligible across all thresholds

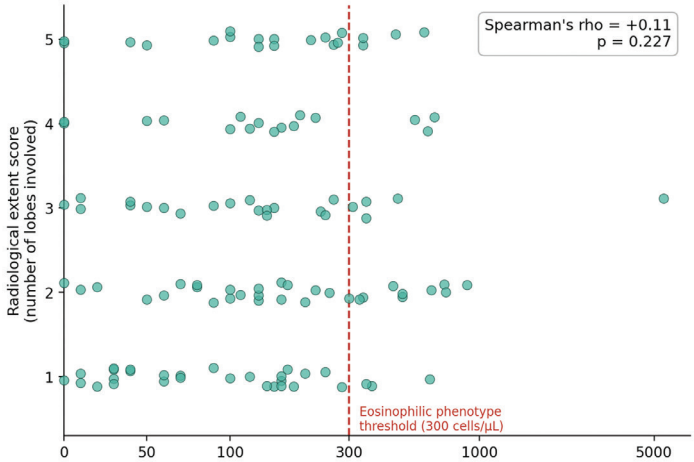


Figure 2. Relationship between peripheral blood eosinophil count and radiological extent score (n = 120). Scatter plot of peripheral blood eosinophil count (x-axis, symmetric logarithmic scale) against radiological extent score (y-axis, number of affected lobes, 1–5). The vertical dashed red line indicates the eosinophilic phenotype threshold (300 cells/μL). No significant association was identified between eosinophil count and radiological extent score (Spearman's rho = +0.11, $P = 0.227$)

the eosinophilic phenotype in both the age-and-extent-score model (age: adjusted OR = 0.96, 95% CI 0.92–0.99, $P = 0.010$; extent score: adjusted OR = 1.05, 95% CI 0.77–1.44, $P = 0.745$; EPV = 12.5; AUC = 0.68) and the age-only model (OR = 0.96, 95% CI 0.92–0.99, $P = 0.010$; EPV = 25; AUC = 0.69). The minimum detectable effect size for the comparison between the eosinophilic (n = 25) and non-eosinophilic (n = 95) groups, with 80% power and a two-sided $\alpha = 0.05$, was d = 0.64.

ROC analysis of eosinophil count, neutrophil count, and CRP for extensive radiological involvement (extent score ≥3, n = 59/120) showed no clinically meaningful discrimination for any marker (AUC 0.52, 0.50, and 0.58, respectively; all 95% CIs spanning 0.50) (Figure 3).

AUC values were: eosinophil count 0.52 (95% CI 0.42–0.62); neutrophil count 0.50 (95% CI 0.39–0.60); CRP 0.58 (95% CI 0.48–0.69). The diagonal dashed line represents the reference line of no discrimination (AUC = 0.50). None of the markers demonstrated clinically meaningful discriminatory ability.

To assess whether these findings depended on the definition of extensive involvement, the ROC analyses were repeated using alternative thresholds (≥2 lobes, n = 90/120; ≥4 lobes, n = 36/120) (Table 4). At ≥3 and ≥4 lobes, no marker showed meaningful discrimination (all 95% CIs included 0.50). At the ≥2-lobe threshold, discrimination was modest for eosinophil count (AUC 0.62, 95% CI 0.50–0.73) and CRP (AUC 0.65, 95% CI 0.53–0.77), whereas neutrophil count did not discriminate (AUC 0.58, 95% CI 0.47–0.69); these exploratory findings were not adjusted for multiple comparisons.

Lateralization and distribution patterns did not differ between phenotypes: bilateral involvement occurred in 60.0% of the eosinophilic group versus 53.7% of the non-eosinophilic group (Fisher's exact test, $P = 0.655$), and diffuse all-lobe involvement occurred in 16.0% of the eosinophilic group versus 16.8% of the non-eosinophilic group ($P = 1.000$).

Table 3. Multivariable logistic regression analysis of factors associated with the eosinophilic phenotype

Variable	Adjusted OR (95% CI)	*P* value
Age, years	0.95 (0.92–0.99)	0.009 *
Sex (male vs. female)	1.98 (0.77–5.10)	0.158
Radiological extent score	1.06 (0.77–1.46)	0.736
CRP, mg/L	0.98 (0.96–1.01)	0.148

*$P < 0.05$. The model included age, sex, radiological extent score, and CRP as covariates (n = 120, 25 events; EPV≈6.25; model AUC = 0.71). Given the low EPV, the estimates are exploratory and should be interpreted with caution.
AUC: area under the curve, CI: confidence interval, CRP: C-reactive protein, EPV: events per variable, OR: odds ratio

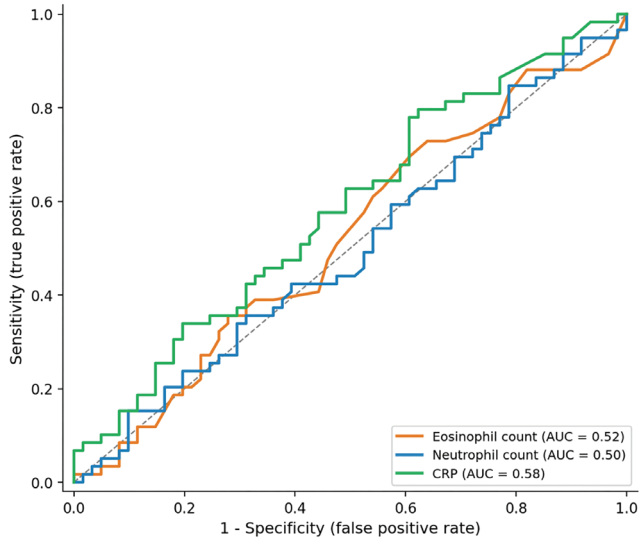


Figure 3. ROC curves for peripheral blood inflammatory markers in discriminating extensive radiological disease (radiological extent score ≥3, n = 120)

AUC: area under the curve, ROC: receiver operating characteristic

Overall, peripheral blood eosinophil count showed no clear association with radiological extent or distribution in univariable, correlation, multivariate, and localization analyses and demonstrated only limited discrimination in ROC analyses. The only between-group difference in age was nominal and did not survive correction for multiple comparisons.

DISCUSSION

Among 120 patients with bronchiectasis, 20.8% (n = 25) were classified as eosinophilic and 79.2% (n = 95) as non-eosinophilic phenotype based on peripheral blood eosinophil count (≥300 vs. <300 cells/μL). This proportion is broadly comparable to, though slightly lower than, the 22.6% reported by Shoemark et al.[12] in a five-country European cohort of 1,007 patients and the 27% reported by Campisi et al. [15] in 153 patients, a modest discrepancy that may reflect cohort size, selection criteria, or threshold application; nonetheless, simple hemogram-based classification yielded a comparable subgroup distribution even in a population with distinct geographic and epidemiological characteristics.[24] Thus, rather than identifying a new phenotype, the present study provides external geographic validation of the eosinophilic subgroup previously described in European cohorts.[12,13]

The eosinophilic group was significantly younger (52.1±12.0 vs. 60.3±13.5 years), though this did not survive multiple-comparison correction. Campisi et al.[15] similarly reported a

Table 4. Sensitivity analysis of the threshold used to define extensive radiological involvement in the ROC analyses

Threshold for extensive involvement, n (%)	Eosinophil count, AUC (95% CI)	Neutrophil count, AUC (95% CI)	CRP, AUC (95% CI)
≥2 lobes: 90 (75.0)	0.62 (0.50–0.73)	0.58 (0.47–0.69)	0.65 (0.53–0.77)
≥3 lobes (primary): 59 (49.2)	**0.52 (0.42–0.62)**	**0.50 (0.39–0.60)**	**0.58 (0.48–0.69)**
≥4 lobes: 36 (30.0)	0.54 (0.43–0.65)	0.51 (0.39–0.62)	0.57 (0.45–0.68)

Values are presented as AUC with 95% confidence intervals (DeLong method). The ≥3-lobe threshold (bold) represents the primary analysis; the ≥2- and ≥4-lobe analyses are exploratory and were not adjusted for multiple comparisons.
AUC: area under the curve, CI: confidence interval, CRP: C-reactive protein, ROC: receiver operating characteristic

possible age association, attributed to immunological changes over disease course; our consistent but only nominally significant finding suggests our sample size may have been insufficient to confirm this association robustly. Because the multivariable model was based on only 25 events (EPV≈6.25), its estimates are imprecise, and the age association should be regarded as hypothesis-generating rather than confirmatory.

Neither correlation nor between-group comparison revealed an association between eosinophil count and radiological extent (rho = +0.11, $P = 0.227$), contrasting with the U-shaped, nonlinear relationship reported by Martínez-García et al.[17] using eosinophil count as a continuous variable; we instead applied a predefined categorical threshold.[12,13] Sensitivity analyses across alternative cutoffs (150, 200, 400 cells/μL) confirmed that this null finding was independent of threshold choice, thereby supporting its robustness. The discrepancy with Shoemark et al.'s[12] multicenter findings of radiological differences by phenotype more plausibly reflects differences in sample size, severity distribution, and radiological methodology than a categorical-versus-continuous distinction; single time-point eosinophil measurement, given known biological variability,[24] may also limit its ability to reflect overall radiological extent.

ROC analysis likewise showed no clinically meaningful discrimination of extensive radiological involvement using eosinophil count, neutrophil count, or CRP (AUC 0.50–0.58), consistent with reviews noting limited standalone predictive value of peripheral blood parameters, which are better incorporated into broader biomarker panels than being interpreted in isolation.[25,26] This was also true at a stricter threshold (≥4 lobes), whereas eosinophil count and CRP showed modest discrimination when extensive involvement was defined more inclusively (≥2 lobes; AUC 0.62 and 0.65), which warrants confirmation in larger cohorts. Similarly, laterality and extent of radiological involvement did not differ by phenotype; while EMBARC-CT data suggest structural disease patterns may relate to clinical phenotype,[27] a direct link to the eosinophilic–non-eosinophilic distinction is not yet established. At the level of lobar distribution and laterality, our findings support treating inflammatory phenotype and radiological pattern as largely independent dimensions.

Several factors may account for this predominantly negative pattern of findings. Much of the existing literature derives from Western European and Mediterranean cohorts,[12,13,17] and geographic or ethnic variation, as suggested by a Chinese cohort study of type-2 biomarkers,[28] may affect generalizability to populations such as Türkiye's. Notably, in the Turkish hospitalized cohort mentioned above, peripheral eosinophilia (≥300 cells/μL) was present in only 5.6% of patients,[21] compared with 20.8% in our outpatient cohort; this difference may reflect differences in setting and patient selection, and the two studies are not directly comparable. Alternatively, the absence of an association may reflect genuine biology rather than methodological limitation: hemogram-based phenotyping may not capture radiological extent, a finding that itself has value in questioning its generalizability. Induced sputum cytology or advanced immunological methods would capture eosinophilic inflammation more sensitively than routine CBC parameters.[7] Even so, blood eosinophil count retains value as an accessible, low-cost first-line assessment tool;[29] given growing evidence for anti-interleukin (IL)-5/IL-5Rα therapies in the type-2-high endotype,[30] it may still contribute to broader phenotyping algorithms.

Strengths of this study include real-world, retrospective enrollment, radiological assessment blinded to clinical and laboratory data, and consistent application of multiple-comparison correction; the Turkish data provide geographic external validation of previously described CBC-based phenotype classifications and may help characterize the heterogeneous global presentation of bronchiectasis, given the predominance of Western European cohorts in the existing literature.[12,13,17,29]

Study Limitations

Limitations include the single-center, retrospective, cross-sectional design, which precludes causal inference and limits generalizability; we, therefore, report post-hoc power and effect size estimates. The small eosinophilic subgroup (n = 25; ratio ≈1:4) limited power to a minimum detectable effect of d = 0.64, meaning smaller or moderate differences may have gone undetected. The multivariate model's events-per-variable ratio (EPV≈6.25) fell below the recommended threshold of ≥10; the post-hoc, more parsimonious models reported in the Results (age and extent score; age alone; EPV 12.5 and 25) again identified age as the only independently associated variable (OR = 0.96, $P = 0.010$) with comparable discrimination (AUC = 0.68–0.69 vs. 0.71), suggesting this result is not sensitive to model complexity. Nevertheless, because of the small number of events, these estimates may be unstable or overfitted and may require confirmation in larger samples. After Bonferroni and Benjamini-Hochberg correction of the 12 Table 1 comparisons, no difference retained statistical significance; therefore, the age finding should be interpreted as nominal. Exacerbation frequency, pulmonary function, and microbiological data[23,31] were not assessed, limiting the clinical scope of phenotype characterization; phenotype classification also relied on a single eosinophil measurement at diagnosis, which may misclassify patients given known temporal fluctuation with exacerbations, seasonality, and atopic comorbidity, and precludes assessment of eosinophil stability or its relationship with sputum microbiome data.[24] The CT score reflected only the number of lobes involved (radiological extent); severity-related features, such as the degree of bronchial dilatation, bronchial wall thickening, and mucus plugging, were not assessed, and therefore our findings cannot be extrapolated to radiological severity. Although blood samples were obtained on the same day as CT or within three days thereafter, information on bronchiectasis exacerbation at the time of sampling could not be obtained from the patient history; the time of day of sampling was not standardized; and systematic data on antibiotic or other anti-inflammatory treatment (e.g., long-term macrolides) at that time were unavailable. Eosinophil counts may vary during exacerbations, across the day, and with such treatments. ICS use was ascertained from patient history only for patients with asthma or COPD, without information on agent, dose, or duration; ICS may have suppressed eosinophil counts, misclassifying some patients as non-eosinophilic. The non-eosinophilic group is biologically heterogeneous and may

include patients with neutrophilic, mixed, or paucigranulocytic airway inflammation, cannot be distinguished from one another without sputum cytology. These limitations motivate a planned multicenter study (currently at the ethical approval stage) that will include the patients from the present cohort and will screen additional centers using the same eligibility criteria and study period. The present single-center analysis, therefore, represents preliminary data, and the analyses will be repeated in the larger sample, incorporating exacerbation frequency, pulmonary function, and microbiological data.

CONCLUSION

This study demonstrates that hemogram-based inflammatory phenotyping is feasible in patients with bronchiectasis under real-world conditions and provides external geographic validation data from a Turkish cohort within a literature dominated by cohorts from Western Europe. Of 120 patients, 25 (20.8%) had the eosinophilic phenotype; this group was nominally younger than the non-eosinophilic group (a difference that did not survive correction for multiple comparisons). However, peripheral blood eosinophil count alone showed limited predictive power for radiological extent or distribution (AUC = 0.52), and even the multivariate model incorporating age, sex, extent score, and CRP achieved only moderate discrimination (AUC = 0.71). The eosinophil count alone, therefore, appears insufficient to capture the full heterogeneity of bronchiectasis. The planned multicenter study, which will include the present cohort, will examine CBC parameters alongside exacerbation frequency, pulmonary function, and microbiological findings, with the aim of advancing understanding of inflammatory heterogeneity and supporting phenotype-specific, personalized treatment in bronchiectasis.[25,29]

Ethics

Ethics Committee Approval: This study was approved by the Yozgat Bozok University Ethics Committee (protocol no: 2026-GOKAEK-268, decision no: 123, date: 15.04.2026) in accordance with the ethical principles of the Declaration of Helsinki of the World Medical Association.

Informed Consent: Given the retrospective, anonymized design, individual informed consent was waived and data confidentiality was maintained throughout.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Ü.T.T., Concept: Ü.T.T., Design: H.Ş.T., Data Collection or Processing: M.F.E., M.M.K., Literature Search: Ü.T.T., M.F.E., M.M.K., Writing: Ü.T.T., H.Ş.T.

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