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The association of neutrophil-to-lymphocyte ratio with bronchiectasis severity assessed by the FACED classification in adults with post-tuberculosis bronchiectasis

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Abstract
The neutrophil-to-lymphocyte ratio (NLR) has emerged as a simple, cost-effective biomarker of systemic inflammation in various respiratory diseases. However, its association with bronchiectasis severity in patients with post-tuberculosis bronchiectasis remains limited. This study aimed to investigate the association between NLR and bronchiectasis severity as assessed by the FACED classification and to identify factors contributing to disease severity in patients with post-tuberculosis bronchiectasis. This retrospective cross-sectional study involved 49 patients with post-tuberculosis bronchiectasis. Bronchiectasis severity was assessed using the FACED score. NLR was calculated from routine complete blood counts. The Mann-Whitney U test compared NLR between mild and moderate severity groups, and factors associated with moderate severity were also analyzed. The median NLR was significantly higher in patients with moderate bronchiectasis compared to those with mild disease (7.16 *vs*. 3.25, p=0.043), driven primarily by significantly lower lymphocyte percentage in the moderate group (11.20 *vs*. 22.05, p=0.043). Moderate severity was significantly associated with forced expiratory volume in 1 second <50% predicted (p<0.001), radiological extension involving more than two lobes (p=0.010), and a modified Medical Research Council dyspnea score ≥2 (p=0.049). No significant associations were observed for age, sex, comorbidities, smoking status, or Pseudomonas colonization. Taken together, NLR is significantly elevated in patients with moderate bronchiectasis compared to those with mild disease, primarily reflecting relative reduced lymphocyte percentage in more severe disease. As an easily obtainable, inexpensive biomarker, NLR may serve as a practical tool for initial risk stratification in post-tuberculosis bronchiectasis, particularly in resource-limited settings.

Introduction

Bronchiectasis is a chronic respiratory disease characterized by irreversible dilation of the bronchi and bronchioles, resulting from a "vicious cycle" of recurrent airway inflammation, infection, and structural damage.[1] This condition leads to progressive decline in lung function, persistent symptoms including chronic cough, sputum production, and recurrent exacerbations that significantly impair patients' quality of life and increase healthcare burden.[2] The European Respiratory Society (ERS) 2025 guidelines for the management of bronchiectasis in adults provide comprehensive recommendations for diagnosis, treatment, and monitoring of this condition.[3] In developing countries, post-tuberculosis bronchiectasis remains a major contributor to the overall disease burden, representing a distinct clinical entity with specific pathophysiological characteristics that warrant focused investigation.[4] Early identification of disease severity and risk stratification are crucial for optimizing therapeutic strategies and improving long-term outcomes in these patients.

The FACED score, which comprises forced expiratory volume in 1 second (FEV1%) predicted, age, chronic colonization by *Pseudomonas aeruginosa*, radiological extension, and dyspnea [modified Medical Research Council (mMRC) scale], is one of the most validated multidimensional scoring systems for assessing bronchiectasis severity and predicting mortality.[5] The score has been validated in multiple international cohorts, including the SEPAR Spanish Bronchiectasis Registry,[6] and the EMBARC registry,[7] demonstrating its prognostic value across diverse populations. However, the ERS guidelines recommend the Bronchiectasis Severity Index (BSI) as a more comprehensive tool that incorporates additional variables including hospitalization history, exacerbation frequency, and body mass index, providing improved prognostic accuracy for exacerbations and hospitalizations.[8] Nevertheless, the BSI's complexity limits its routine use in resource-limited settings. Therefore, there is an ongoing need to identify simple, inexpensive, and easily obtainable biomarkers that can complement or serve as surrogates for comprehensive severity assessment.

The neutrophil-to-lymphocyte ratio (NLR) has emerged as a promising biomarker of systemic inflammation across various respiratory diseases. Derived from routine complete blood count, NLR reflects the balance between neutrophilic (innate) and lymphocytic (adaptive) immune responses, with elevated ratios indicating heightened systemic inflammatory burden.[9] Beyond respiratory diseases, NLR has been associated with cardiovascular disease, metabolic syndrome, and various malignancies, highlighting its role as a general marker of systemic inflammation.[10] Previous studies have demonstrated the utility of NLR in predicting disease severity, exacerbation risk, and prognosis in conditions such as chronic obstructive pulmonary disease,[11] community-acquired pneumonia,[12] and lung cancer.[13] However, evidence regarding the association between NLR and bronchiectasis severity in post-tuberculosis populations remains limited. This study aimed to investigate the association between NLR and bronchiectasis severity as assessed by the FACED classification in patients with post-tuberculosis bronchiectasis, and to identify factors contributing to disease severity in this specific population.

Materials and Methods

This retrospective cross-sectional study was conducted at the Persahabatan Hospital, Jakarta, Indonesia. A total of 49 patients with bronchiectasis were consecutively identified from medical records of patients treated between May to October 2025. The inclusion criteria were: age 18 years or older, bronchiectasis confirmed by high-resolution computed tomography (HRCT) of the thorax, and a documented history of pulmonary tuberculosis. Patients were excluded if they had: acute exacerbation of bronchiectasis at the time of enrollment; active malignancy; acute infection not related to bronchiectasis (*e.g.*, urinary tract infection or skin infection); systemic corticosteroid use within the preceding 2 weeks; pregnant or lactating, or inability to perform spirometry. As this was a retrospective study using de-identified medical records, the Institutional Review Board (IRB) granted approval with a waiver of prospective informed consent. The study protocol was approved by the IRB of Persahabatan Hospital (Number 0098/KEPK-RSUPP/03/2026). This study was conducted in compliance with the ethical standards of the responsible institution on human subjects as well as with the Helsinki Declaration.

Demographic and clinical data including age, sex, education level, comorbidities, smoking history, and Brinkmann index were collected through structured interviews and medical record reviews. Dyspnea severity was assessed using the modified Medical Research Council (mMRC) scale. Pulmonary function testing was performed using a calibrated spirometer following the American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines, with pre-bronchodilator forced expiratory volume in one second (FEV1) expressed as a percentage of predicted value.[14] Radiological extent of bronchiectasis was determined by HRCT, categorized as involvement of 1-2 lobes or more than 2 lobes.[15] Sputum cultures were obtained to identify *Pseudomonas aeruginosa* colonization. Peripheral venous blood samples were collected from all participants under standardized conditions. Complete blood counts were analyzed using an automated hematology analyzer to obtain neutrophil and lymphocyte percentage, from which the NLR was calculated.

Statistical analysis was performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was assessed using the Shapiro-Wilk test. Continuous variables were presented as mean ± standard deviation (SD) or median with interquartile range (IQR), as appropriate, while categorical variables were expressed as frequencies and percentages. The Mann-Whitney U test was used to compare neutrophil percentage, lymphocyte percentage, and NLR between mild and moderate bronchiectasis groups, as the data were not normally distributed. For variables with expected cell counts <5, Fisher's exact test was applied, whereas chi-square tests were used for variables meeting the chi-square assumptions. A p-value of less than 0.05 was considered statistically significant for all analyses.

Results

A total of 49 subjects were enrolled in this study. As described in Table 1, the mean age of the participants was 48.3±10.9 years, with the majority (95.9%) aged below 70 years. The cohort was predominantly female (53.1%), and most subjects had a middle level of education (53.1%). Hypertension was the most common comorbidity (16.3%), while 67.3% of subjects had no comorbid conditions, including COPD. Regarding smoking history, 40.8% were former smokers, 55.1% were never smokers, and only 4.1% were current smokers. Among former smokers and current smokers, the Brinkmann index was predominantly moderate (59.1%). Most of patients had mMRC score 0 and 1, had more than 2 lobes of lesion extenstion by HRCT, had no colonization of Pseudomonas, and had FEV1% > 50%. Among the 49 patients, the FACED score distribution was as follows: score 0-2 (mild) in 36 patients (73.5%), score 3-4 (moderate) in 13 patients (26.5%), and score ≥5 (severe) in 0 patients (0%). The median neutrophil was 70.2, median lymphocyte was 20.5, and median neutrophil-to-lymphocyte ratio (NLR) was 3.4 (range 0.6-16.3) (Table 1).

Comparison between mild and moderate bronchiectasis groups revealed no significant difference in neutrophil percentage (p=0.095). However, lymphocyte percentage were significantly lower in the moderate severity group (median 11.20; IQR 7.65-22.80) compared to the mild group (median 22.05; IQR 14.87-30.35; p=0.043). Consequently, the NLR was significantly higher in patients with moderate bronchiectasis (median 7.16; IQR 2.29-11.85) than in those with mild disease (median 3.25; IQR 1.93-4.86; p = 0.043) (Table 2).

We identified several factors associated with moderate bronchiectasis severity based on the FACED classification. A higher modified Medical Research Council (mMRC) dyspnea score of 2 was significantly associated with moderate severity (OR 7.2; 95% CI 1.00-51.39; p=0.049). Greater radiological involvement (>2 lobes on HRCT) was also significantly associated with moderate severity (OR 7.7; 95% CI 1.48-39.9; p=0.010). As expected, a lower FEV1% predicted (<50%) was strongly associated with moderate severity (OR 19.2; 95% CI 3.5-105.29; p<0.001). No significant associations were observed for age, gender, educational level, comorbidities, history of smoking, Brinkmann index, or *Pseudomonas* colonization in this analysis as presented in Table 3.

Discussion

The present study demonstrated a significant association between the NLR and bronchiectasis severity as assessed by the FACED classification, with moderate bronchiectasis patients exhibiting

a significantly higher NLR compared to those with mild disease (median 7.16 *vs*. 3.25, p=0.043). This finding supports the growing body of evidence that NLR, a readily available and cost-effective biomarker derived from routine complete blood count, reflects the underlying systemic inflammatory burden in various respiratory diseases, including bronchiectasis.[16] Bronchiectasis is characterized by predominant neutrophilic inflammation, where neutrophil recruitment into the airways leads to the release of proteolytic enzymes such as neutrophil elastase and matrix metalloproteinases, contributing to progressive airway destruction.[17] The elevation of NLR in more severe disease likely represents not only increased neutrophilic activity but also reduced lymphocyte percentage, which may indicate immunosuppression or chronic stress response associated with advanced disease.[10]

The significantly lower lymphocyte percentage in the moderate severity group may reflect alterations in the relative composition of the leukocyte differential in more advanced disease. While the reduced lymphocyte percentage could suggest a relative decrease in lymphocyte proportion, we acknowledge that without absolute lymphocyte counts, we cannot conclude true lymphopenia. However, this finding is consistent with previous observations that chronic inflammatory conditions, for examples in patients with more extensive diseases,[18] and frequent exacerbation,[19] may be associated with shifts in leukocyte proportions, potentially reflecting changes in immune cell trafficking or distribution. Further studies incorporating absolute cell counts and functional immune assessments are needed to elucidate the underlying mechanisms.

Our findings are consistent with recent studies investigating NLR in bronchiectasis. Kwok *et al.* (2024), in a cohort of 473 Chinese patients with non-cystic fibrosis bronchiectasis, demonstrated that patients in the highest NLR quartile were at increased risk of hospitalization for bronchiectasis exacerbation with an adjusted odds ratio of 2.02 (95% CI 1.00-4.12, p=0.05).[20] Previous study also revealed that a higher NLR was associated not only with more severe bronchiectasis according to the commonly used scores (FACED, E-FACED and BSI), but also with poorer quality of life, more comorbidities, infection by pathogenic microorganisms, and greater application of treatment.[21] Similarly, a preliminary study by Ghosh et al. investigating systemic inflammation in stable bronchiectasis found that NLR was statistically significant increase in bronchiectasis patients with a sign of low-grade inflammation compared to controls (p=0.0156).[22]

The absence of patients with severe bronchiectasis (FACED score ≥5) in our cohort merits discussion. This likely reflects the patient population at our tertiary referral center, where most patients are diagnosed and managed at an earlier stage of disease. Additionally, post-tuberculosis bronchiectasis in our setting often presents with milder disease severity compared to other etiologies, as previously reported.[4] This distribution limits the generalizability of our findings to patients with severe disease and underscores the need for multicenter studies including a broader spectrum of disease severity.

The FACED score components that demonstrated significant associations with moderate severity in our study, namely FEV1<50% predicted (p<0.001), radiological extension >2 lobes (p=0.010), and mMRC dyspnea score ≥2 (p=0.049), are consistent with the original FACED validation study. Martínez-García *et al.* originally identified these five independent predictors of mortality in bronchiectasis, with FEV1<50% (OR 5.2) and age >70 years (OR 4.9) being the strongest contributors.[4] Notably, while the original FACED score incorporates age, chronic Pseudomonas colonization, and dyspnea, our analysis did not find significant associations for age, Pseudomonas colonization, or education level with moderate severity. This may be due to the relatively small sample size (n=49) and the predominance of patients with mild disease (73.5%) in our cohort.

The significant association between mMRC dyspnea score ≥2 and moderate severity (OR 7.2, 95% CI 1.00-51.39, p=0.049) aligns with the prognostic value of dyspnea in bronchiectasis. The FACED score assigns one point for MRC dyspnea grade ≥II, reflecting the impact of respiratory symptoms on functional status and quality of life.[23] Similarly, the radiological extension of bronchiectasis affecting more than two lobes was associated with increased severity (OR 7.7, 95% CI 1.48-39.9, p=0.010), underscoring the importance of anatomical disease burden in determining clinical outcomes. These findings reinforce the construct validity of the FACED classification in our predominantly post-tuberculosis bronchiectasis cohort.

We acknowledge that our secondary endpoint, in identifying factors associated with moderate

severity, is limited by both the small sample size and the characteristics of our study population. The finding that mMRC score ≥2 was significantly associated with moderate severity, despite mMRC contributing only one point to the FACED score, likely reflects the distribution of disease severity in our cohort rather than a true dissociation. Similarly, while the FACED score includes age ≥70 years as a component, we were unable to demonstrate this association, likely due to the underrepresentation of elderly patients (only 2 patients ≥70 years) rather than a true lack of association. These findings highlight the need for larger, more balanced cohorts to adequately evaluate all components of the FACED score.

Several comorbidities included in our analysis, particularly hypertension and diabetes mellitus, are known to independently affect NLR values through chronic low-grade inflammation and altered immune cell profiles. While our sample size precluded stratified analysis by comorbidity status, we acknowledge that these conditions may have influenced our findings. Interestingly, we did not observe significant associations between individual comorbidities and moderate severity, though this may reflect the limited statistical power in each subgroup. Future studies with larger cohorts should adjust for these potential confounders in multivariable models.

Several limitations should be acknowledged. First, the cross-sectional design precludes determination of causality or longitudinal changes in NLR with disease progression. Second, the relatively small sample size (n=49) was because that our study conducted at a single tertiary referral center over a limited time period and the retrospective nature of the study limited our ability to identify additional eligible patients beyond those captured in the medical records. The predominance of patients with mild disease (73.5%) and the complete absence of severe cases (FACED score ≥5) in our cohort limits the generalizability of our findings to broader patient populations. This distribution likely reflects both the patient population at our institution and the natural history of post-tuberculosis bronchiectasis, which may present with milder disease compared to other etiologies. Third, our study population consisted exclusively of patients with a history of pulmonary tuberculosis, which may represent a distinct etiological subgroup with specific inflammatory characteristics. Fourth, we did not measure other inflammatory biomarkers such as C-reactive protein or procalcitonin, which could provide additional context for the systemic inflammatory response. Fifth, the presence of chronic comorbidities such as hypertension and diabetes mellitus, which are known to affect inflammatory markers, may have influenced our findings. Larger studies with detailed medication histories and biomarker panels are needed to disentangle these effects.

The underrepresentation of elderly patients (≥70 years) in our cohort, with only two patients in this age group, is also a limitation. The FACED score assigns one point for age ≥70 years, and the original validation study identified older age as a strong predictor of mortality. Our inability to demonstrate an association between age and moderate severity likely reflects insufficient statistical power rather than a true lack of association.

Conclusions

This study demonstrates that the NLR is significantly elevated in patients with moderate bronchiectasis compared to those with mild disease, as assessed by the FACED classification. The significant association was observed alongside a marked reduction in lymphocyte percentage among patients with more severe disease, though we acknowledge that absolute lymphocyte counts were not measured to confirm true lymphopenia. Furthermore, the FACED components, including FEV1<50% predicted, radiological extension involving more than two lobes, and mMRC dyspnea score ≥2, were significantly associated with moderate severity in univariable analysis, reinforcing the validity of this multidimensional scoring system in our post-tuberculosis bronchiectasis cohort.

Given its accessibility, low cost, and ease of calculation from routine complete blood count, NLR represents a practical and promising biomarker for initial risk stratification in bronchiectasis, particularly in resource-limited settings. However, larger prospective studies incorporating absolute cell counts and comprehensive immune assessments are warranted to establish its prognostic utility and to better understand the underlying immunological changes associated with disease progression.

Abbreviations

CAD: coronary artery disease; DM: diabetes mellitus; FACED: FEV1% predicted, age, chronic colonization by *Pseudomonas aeruginosa*, radiological extension, and dyspnea; FEV1: forced expiratory volume in one second; HRCT: high-resolution computed tomography; IQR: Interquartile Range; mMRC: modified Medical Research Council; NLR: neutrophil-to-lymphocyte ratio.

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Table 1. Subject characteristics.

Variables	Total, n=49
Age (year old), (mean± SD)	48.3±10.9
Age, n (%)	
<70-year-old	47(95.9)
≥70-year-old	2 (4.1)
Gender, n (%)	
Female	26 (53.1)
Male	23 (46.9)
Education level, n (%)	
Elementary	18 (36.7)
Middle	26 (53.1)
High	5 (10.2)
Comorbidity, n (%)	
None	33 (67.3)
Diabetes mellitus (DM)	4 (8.2)
Hypertension	8 (16.3)
Coronary artery disease (CAD)	1 (2.0)
Hyperthyroid	1 (2.0)
Combination	
DM and CAD	0 (0)
Hypertension and CAD	0 (0)
DM and hypertension	2 (4.1)
History of smoking, n (%)	
Non smoker	27 (55.1)
Former smoker	20 (40.8)
Smoker	2 (4.1)
Brinkmann index, n= 22 (%)	
Mild	6 (27.3)
Moderate	13 (59.1)
Severe	3 (13.6)
mMRC score, n (%)	
0	20 (40.8)
1	18 (36.7)
2	9 (18.4)
3	1 (2.0)
4	1 (2.0)
Lesion extension by HRCT, n (%)	
1-2 lobes	23 (46.9)
>2 lobes	26 (53.1)
Colonization of *Pseudomonas*	
No	45 (91.8)
Yes	4 (8.2)
FEV1% prediction	
FEV1% ≥ 50%	30 (61.2)
FEV1% < 50%	19 (38.8)
FACED Bronchiectasis Severity, n (%)	
Mild	36 (73.5)
Moderate	13 (26.5)
Neutrophil, Lymphocyte and Neutrophil-to-Lymphocyte Ratio	
Neutrophil % [median (min-max)]	70.2 (34.1-91.7)
Lymphocyte % [median (min-max)]	20.5 (5.5-58.8)
Neutrophil-to-Lymphocyte Ratio [median (min-max)]	3.4 (0.6-16.3)

CAD, coronary artery disease; DM, diabetes mellitus; FACED, FEV1% predicted, age, chronic colonization by *Pseudomonas aeruginosa*, radiological extension, and dyspnea; FEV1, forced expiratory volume in one second; HRCT, high-resolution computed tomography; mMRC, modified Medical Research Council; NLR, neutrophil-to-lymphocyte ratio.

Table 2. Association of neutrophil, lymphocyte and NLR with the bronchiectasis severity.

Variables	Bronchiectasis Severity		Total	p
	Mild	Moderate		
Neutrophil % [median (IQR)]	68.95 (57.67-73.87)	80.20 (69.75-89.40)	49	0.095
Lymphocyte % [median (IQR)]	22.05 (14.87-30.35)	11.20 (7.65-22.80)	49	**0.043***
Neutrophil-to-Lymphocyte Ratio [median (IQR)]	3.25 (1.93-4.86)	7.16 (2.29-11.85)	49	**0.043***

*Statistically significant; Mann Whitney test.

Table 3. Factors contributing to bronchiectasis severity.

Variables	Bronchiectasis Severity		Total	p	OR (95% CI)
	Mild	Moderate			
Age (year old), (mean± SD)	48.89±10.93	46.92±11.09		0.58[t]	
Age, n (%)					
<70-year-old	35	12	47		Ref
≥70-year-old	1	1	2	0.464[f]	2.9 (0.16-50.3)
Gender, n (%)					
Female	20	6	26		Ref
Male	16	7	23	0.560[p]	1.4 (0.40-5.21)
Education level, n (%					
Elementary	12	6	18		Ref
Middle	22	4	26	0.178	2.7 (0.64-11.6)
High	2	3	5	0.291	0.3 (0.04-2.56)
Comorbidity, n (%)					
None	7	26	33		Ref
Diabetes mellitus (DM)	1	3	4	0.862	1.2 (0.11-13.8)
Hypertension	4	4	8	0.111	3.7 (0.73-18.7)
Coronary artery disease (CAD)	0	1	1	0.922	1.1 (0.04-31.9)
Hyperthyroid	1	0	1	0.161	10.6 (0.39-287.8)
Combination					
DM and CAD	0	0	0	N/A	N/A
Hypertension and CAD	0	0	0	N/A	N/A
DM and hypertension	0	2	2	0.828	0.7 (0.03-16.3)
History of smoking, n (%)					
Non smoker	22	5	27		Ref
Former smoker	12	8	20	0.110	0.3 (0.09-1.27)
Smoker	2	0	2	0.901	1.2 (0.05-29.28)
Brinkmann index, n= 22 (%)					
Mild	5	1	6		Ref
Moderate	5	8	13	0.092	0.1 (0.01-1.40)
Severe	2	1	3	0.577	0.40 (0.01-10.0)
mMRC score, n (%)					
0	18	2	20		Ref
1	12	6	18	0.093	4.5 (0.77-26.13)
2	5	4	9	**0.049***	7.2 (1.00-51.39)
3	0	1	1	0.079	22.2 (0.69-708.06)
4	1	0	1	0.609	2.4 (0.07-78.67)
Lesion extension by HRCT, n (%)					
1-2 lobes	21	2	23		Ref
>2 lobes	15	11	26	**0.010[f*]**	7.7 (1.48-39.9)
Colonization of *Pseudomonas*					
No	34	11	45		Ref
Yes	2	2	4	0.648[p]	1.3 (0.37-4.84)
FEV1% prediction					
FEV1% ≥50%	28	2	30		Ref
FEV1% <50%	8	11	19	**<0.001[f*]**	19.2 (3.5-105.29)

[*]Statistically significant, [t]T test, [f]Fisher test, [p]Pearson test.