RESEARCH PAPER

Association of Blood Eosinophil and Neutrophil Counts with Severe Asthma Exacerbations in Adults: A Multicenter Cross-Sectional Study

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ABSTRACT

Background: Asthma exacerbations are associated with increased airway inflammation and may lead to significant morbidity in adults. Blood eosinophil and neutrophil counts have been proposed as inflammatory biomarkers related to exacerbation severity. This study aimed to evaluate the association between blood eosinophil and neutrophil counts and severe asthma exacerbations in adult patients.

Methods: A multicenter analytical cross-sectional study was conducted in 2025 at Hasanuddin University Hospital, Ibnu Sina Hospital, and Jaury Academic Hospital, Indonesia. A total of 108 adult patients with asthma exacerbations were enrolled. Clinical characteristics and laboratory parameters were collected from all participants. Exacerbation severity was determined based on clinical presentation, physical examination, and supporting investigations. Statistical analyses were performed using the Chi-square test, independent t-test, and Mann–Whitney U test. A P value < 0.05 was considered statistically significant.

Results: Of the 108 participants, 78 (72.2%) experienced non-severe asthma exacerbations, while 30 (27.8%) presented with severe exacerbations. Elevated eosinophil counts were identified in 26.9% of patients, whereas increased neutrophil counts were observed in 54.6%. Elevated eosinophil counts were significantly associated with severe asthma exacerbations (P = 0.031; OR = 7.2; 95% CI: 2.79–18.57). Similarly, increased neutrophil counts showed a significant association with severe exacerbations (P = 0.014; OR = 6.5; 95% CI: 2.24–18.67).

Conclusion: Higher blood eosinophil and neutrophil counts were significantly associated with severe asthma exacerbations in adults. These inflammatory biomarkers may contribute to the assessment of exacerbation severity in clinical practice.

Keywords: *Asthma exacerbation severity; eosinophils; neutrophils; adult asthma; inflammatory biomarkers.*

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INTRODUCTION

Asthma is a heterogeneous chronic inflammatory airway disease characterized by airway hyperresponsiveness, excessive mucus production, and structural airway changes. The prevalence of asthma varies widely across countries, affecting approximately 1–29% of the population worldwide. Recent global estimates indicate that approximately 358 million individuals are living with asthma. In the United States alone, nearly 28 million people are affected by the disease. Asthma prevalence differs according to socioeconomic status, ethnicity, age, and sex. In addition, asthma remains a major public health burden, accounting for approximately one million emergency department visits annually and substantial asthma-related mortality (1-3).

Asthma exacerbation is defined as an acute or subacute worsening of asthma symptoms, including dyspnea, cough, and wheezing, accompanied by a reduction in expiratory airflow, such as peak expiratory flow (PEF) or forced expiratory volume in one second (FEV1). Exacerbations may be triggered by allergens, respiratory infections, medications, environmental exposures, or emotional stress. Airway inflammation involving eosinophils and neutrophils plays an important role in the pathogenesis of asthma exacerbations. Lipopolysaccharide-induced neutrophilic activation may disrupt epithelial tight junction proteins, thereby

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aggravating airway inflammation. Furthermore, impaired clearance of neutrophil extracellular traps (NETs) by alveolar macrophages may lead to persistent airway inflammation, particularly in neutrophilic asthma. Excessive NET formation in severe asthma has also been associated with inflammasome activation and increased interleukin-1β secretion by monocyte-macrophages (2,4).

Recent evidence has demonstrated increased extracellular trap formation in patients with asthma. Extracellular traps are web-like structures composed of DNA and activated proteins released by inflammatory cells, including neutrophils, eosinophils, basophils, macrophages, mast cells, dendritic cells, and monocytes. Activated neutrophils contribute to airway inflammation through degranulation, phagocytosis, and the release of NETs, which function in host defense against pathogens. However, excessive NET formation may induce tissue injury and amplify inflammatory responses within the airways (2,4).

Eosinophils also contribute substantially to asthma pathogenesis, particularly in allergic and eosinophilic phenotypes. Eosinophil extracellular traps (EETs) play a role in immune defense against extracellular pathogens by providing a structural scaffold for cytotoxic proteins. Compared with NETs, EETs possess a more stable chromatin structure and are more resistant to proteolytic degradation, allowing prolonged persistence within tissues. In chronic uncontrolled asthma, excessive EET production may interact with other inflammatory cells and further exacerbate airway inflammation. Previous studies have demonstrated that elevated EET levels are associated with increased asthma severity (4).

Considering the important role of eosinophils and neutrophils in airway inflammation, this study aimed to evaluate the association between blood eosinophil and neutrophil counts and severe asthma exacerbations in adult patients.

METHODS

Study Design And Setting

This study was an analytical observational study with a cross-sectional design. Data were obtained from secondary sources through medical record review of patients presenting with asthma exacerbations. The study was conducted in 2025 at Hasanuddin University Hospital, Ibnu Sina Hospital, and Jaury Academic Hospital, Indonesia. The study population consisted of adult patients presenting to the Emergency Department with asthma exacerbations of varying severity.

Ethical Approval

Ethical approval was obtained from the Human Biomedical Research Ethics Committee, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia. The study was approved under Recommendation Number 1067/UN4.6.4.5.31/PP36/2025 and Protocol Number UH25070517.

Study Population

Inclusion Criteria

Patients aged ≥18 years with a clinical diagnosis of asthma exacerbation of any severity were included in the study.

Exclusion Criteria

Patients were excluded if they had a diagnosis of chronic obstructive pulmonary disease (COPD) or other significant comorbid conditions that could influence inflammatory parameters, including acute pulmonary edema, congestive heart failure, chronic kidney disease, chronic liver disease, or malignancy.

Data Collection and Variables

Clinical and laboratory data were extracted from medical records. Variables included demographic characteristics, clinical presentation, asthma exacerbation severity, absolute blood eosinophil count, and absolute blood neutrophil count.

Asthma exacerbation severity was classified based on clinical assessment, physical examination findings, and supporting investigations documented in the medical records.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics version 25.0. Continuous variables were presented as mean ± standard deviation or median (interquartile range), depending on data distribution, while categorical variables were presented as frequencies and percentages.

Comparisons between groups were performed using the independent t-test or Mann–Whitney U test for continuous variables, and the Chi-square test for categorical variables. A p-value <0.05 was considered statistically significant. Odds ratios (OR) with corresponding significance values were used to assess the association between hematological parameters and asthma exacerbation severity.

RESULTS

Characteristics of Study Subjects

A total of 108 patients with asthma exacerbations met the inclusion criteria. The majority were female (n=79; 73.1%), while 29 patients (26.9%) were male. The age of participants ranged from 18 to 76 years, with a mean age of 44 years. Most patients were aged <60 years (n=89; 82.4%). Regarding asthma exacerbation severity, 78 patients (72.2%) presented with non-severe exacerbations, while 30 patients (27.8%) had severe exacerbations. In hematological parameters, 79 patients (73.1%) had low absolute eosinophil counts, while 29 patients (26.9%) had elevated eosinophil counts. For neutrophil counts, 59 patients (54.6%) had elevated levels, whereas 49 patients (45.4%) had non-elevated levels.

Tabel 1: Characteristics of study subjects (n=108)

Variable	Category	n	(%)
Gender	Man	29	26,9
	Woman	79	73,1
Age	< 60 years old	89	82,4
	≥ 60 years old	19	17,6
Asthma Exacerbation Severity	Non-severe	78	72,2
	Severe	30	27,8
Absolute Eosinophil Category	Non-elevated	79	73,1
	Elevated	29	26,9
Absolute Neutrophil Category	Non-elevated	49	45,4
	Elevated	59	54,6

Association between Eosinophil Count and Asthma Severity

The mean eosinophil count was higher in patients with severe exacerbations compared with those with non-severe exacerbations. Patients with severe exacerbations (n=30) had a mean eosinophil count of 3.56 ± 2.46, while those with non-severe exacerbations (n=78) had a mean of 2.54 ± 3.14. The difference was statistically significant (p=0.031, Mann–Whitney U test).

Table 2. Comparison of eosinophil counts by asthma severity

Severity of Asthma Exacerbation	n	Mean	SD	Mann-Whitney test *(p value)*
Severe	30	3,56	2,46	**0,031**
Non-severe	78	2,54	3,14	

Elevated eosinophil counts were significantly associated with severe asthma exacerbations (p<0.001). Among patients with elevated eosinophils, 17 (58.6%) had severe exacerbations, while 12 (41.4%) had non-severe exacerbations. In contrast, among those with non-elevated eosinophils, only 13 (16.5%) had severe exacerbations. Patients with elevated eosinophil counts had a 7.2-fold higher risk of severe exacerbations compared with those with non-elevated levels (OR: 7.2; 95% CI: 2.79–18.57).

Table 3. Association between eosinophil count and asthma severity

Absolute Eosinophil Category		Severity of Asthma Exacerbation		Total	Chi-Square (*p value*)	Odds Ratio (95% CI)
		Severe	Non-severe			
Elevated	n	17	12	29	**<0,001**	**7,2 (2,79-18,57)**
	%	58,6%	41,4%	100,0%		
Non-elevated	n	13	66	79		
	%	16,5%	83,5%	100,0%		
Total	n	30	78	108		
	%	27,8%	72,2%	100,0%		

Association between Neutrophil Count and Asthma Severity

Mean neutrophil counts were higher in patients with severe exacerbations (76.64 ± 14.39) compared to those with non-severe exacerbations (69.31 ± 13.35). This difference was statistically significant (p=0.014, independent t-test).

Table 4. Comparison of neutrophil counts by asthma severity

Severity of Asthma Exacerbation	n	Mean	SD	Independent-t test *(p value)*
Severe	30	76,64	14,39	**0,014**
Non-severe	78	69,31	13,35	

Elevated neutrophil counts were also significantly associated with severe asthma exacerbations (p<0.001). Among patients with elevated neutrophils, 25 (42.4%) had severe exacerbations, while 34 (57.6%) had non-severe exacerbations. Patients with elevated neutrophil counts had a 6.5-fold increased risk of severe exacerbations

compared to those with non-elevated levels (OR: 6.5; 95% CI: 2.24–18.67).

Table 5. Association between neutrophil count and asthma severity

Absolute Neutrophil Category		Severity of Asthma Exacerbation		Total	Chi-Square (*p value*)	Odds Ratio (95% CI)
		Severe	Non-severe			
Elevated	n	25	34	59	**<0,001**	**6,5 (2,24-18,67)**
	%	42,4%	57,6%	100,0%		
Non-elevated	n	5	44	49		
	%	10,2%	89,8%	100,0%		
Total	n	30	78	108		
	%	27,8%	72,2%	100,0%		

DISCUSSION

Asthma exacerbation is a potentially life-threatening clinical condition characterized by progressive worsening of respiratory symptoms, including dyspnea, cough, wheezing, and chest discomfort, accompanied by a decline in pulmonary function. Airway inflammation involving eosinophils and neutrophils plays a central role in the pathophysiology of exacerbations (5-8). In this study, the majority of patients were female (73.1%), consistent with previous findings reporting a higher prevalence of asthma exacerbations in women.

Marinelli et al. (2025) reported that asthma exacerbations are more frequent in adult women than men. This difference is thought to result from a complex interaction of hormonal, anatomical, environmental, and behavioral factors (9). Anatomically, women generally have smaller airway calibers relative to lung size, which may increase airway resistance and susceptibility to hyperresponsiveness. In addition, sex hormones contribute significantly to asthma pathophysiology: estrogen and progesterone may exacerbate airway inflammation, whereas testosterone appears to exert a protective effect. At the molecular level, sex-related differences in inflammatory regulation have also been reported, including higher expression of anti-inflammatory microRNAs (Let-7 family) in males, which suppress IL-13 signaling, while females exhibit higher levels of IL-13, TSLP, and sST2 (10-12).

In this study, the mean age of patients was 44 years, with most subjects aged under 60 years (82.4%). This finding is consistent with previous studies reporting that asthma exacerbations commonly occur in middle-aged adults (13,14). However, differences in age distribution across studies may reflect variations in population characteristics, particularly the proportion of late-onset asthma.

Regarding severity, most patients experienced non-severe exacerbations (72.2%), while 27.8% had severe exacerbations. These findings are consistent with Goodall et al. (2025), who reported that the majority of asthma patients experienced moderate exacerbations despite standard inhaled corticosteroid/long-acting β-agonist (ICS/LABA) therapy (15,16). Poor asthma control in these populations has been associated with multiple factors, including medication adherence and inadequate symptom monitoring.

Association between Eosinophils and Asthma Severity

This study demonstrated a significant association between elevated eosinophil counts and severe asthma exacerbations. Patients with higher eosinophil levels were more likely to experience severe exacerbations (p=0.031), and the risk was significantly increased (OR: 7.2; 95% CI: 2.79–18.57; p<0.001).

These findings are supported by Schleich et al. (2020), who reported that blood eosinophil count is an independent predictor of asthma exacerbations, particularly in patients with persistent airway eosinophilia despite corticosteroid therapy (17,18). Similarly, Bleecker et al. (2023) demonstrated that patients with higher blood eosinophil levels (≥300 cells/μL) had higher annual exacerbation rates and poorer asthma control compared to those with lower eosinophil levels (19,20).

Biologically, eosinophils contribute to airway inflammation through cytotoxic granule proteins such as eosinophil cationic protein (ECP), major basic protein (MBP), eosinophil peroxidase (EPO), and eosinophil-derived neurotoxin (EDN). They also release lipid mediators, including cysteinyl leukotrienes (LTC4, LTD4, LTE4), which promote bronchoconstriction, mucus hypersecretion, and vascular permeability. In addition, eosinophils secrete pro-inflammatory cytokines such as IL-1β, IL-6, TNF-α, and TGF-β, which contribute to airway remodeling and fibrosis (21-23). These mechanisms explain the association between eosinophilia and more severe asthma phenotypes observed in this study.

Association between Neutrophils and Asthma Severity

A significant association was also observed between neutrophil counts and asthma severity. Patients with severe exacerbations had higher mean neutrophil counts compared to those with non-severe exacerbations (76.64 ± 14.39 vs 69.31 ± 13.35; p=0.014). Elevated neutrophil counts were significantly associated with severe exacerbations (OR: 6.5; 95% CI: 2.24–18.67; p<0.001).

Neutrophils contribute to airway inflammation through multiple mechanisms, including epithelial injury, release of neutrophil elastase, and induction of epithelial–mesenchymal transition. Increased TGF-β1 expression in asthmatic airways further promotes airway remodeling and fibrosis, contributing to disease severity (24,25). Additionally, neutrophils may amplify type 2 inflammation by enhancing eosinophil recruitment during acute exacerbations.

Mao et al. (2023) similarly reported higher neutrophil counts in patients with severe asthma, supporting their role as a biomarker of disease severity (26). The neutrophilic asthma phenotype is increasingly recognized and is often associated with Th17/IL-17-mediated inflammation, which contributes to steroid resistance and more severe disease manifestations.

Furthermore, Jin et al. (2025) reported that the neutrophil-to-lymphocyte ratio (NLR) was significantly elevated in asthma patients compared with controls, reinforcing the role of systemic inflammation in asthma severity (27). Bullone et al. also demonstrated that neutrophilic asthma is associated with a higher frequency of exacerbations and increased healthcare utilization, including emergency department visits and hospitalizations (28).

Clinical Implications

The findings of this study suggest that both eosinophils and neutrophils are important inflammatory biomarkers associated with asthma exacerbation severity. Their measurement may provide additional clinical value in risk stratification and management of adult asthma patients.

CONCLUSIONS

The findings of this study indicate that both blood eosinophil and neutrophil counts are important inflammatory markers associated with asthma exacerbation severity in adults. Elevated levels of eosinophils and neutrophils are significantly associated with severe asthma exacerbations, reflecting their role in airway inflammation and disease progression. These findings suggest that routine assessment of these hematological parameters may be useful in identifying patients at higher risk of severe exacerbations and may support improved clinical decision-making in the prevention and management of asthma, with the aim of reducing morbidity and mortality.

Ethics committee approval: This research was approved by the Ethics Committee for Biomedical Research on Humans, Faculty of Medicine, Hasanuddin University, Makassar, South Sulawesi, Indonesia. Based on Recommendation Number 1067/UN4.6.4.5.31/PP36/2025 with Protocol Number UH25070517.

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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