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# Frequency distribution of neutrophil and eosinophil count in children with asthmatic attack referring to Taleghani hospital in Gorgan in 2016-2020

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## Abstract

**Introduction:** The total eosinophil count is a marker of asthmatic activity and can be helpful in the early diagnosis of asthma attacks and in determining appropriate steroid doses. However, in some asthmatic patients, the blood eosinophil count may be within the normal range, and the eosinophil level may not necessarily be elevated in patients with bronchial asthma.

**Objectives:** This study aimed to assess the frequency distribution of eosinophil and neutrophil percentages in peripheral blood smears of children experiencing asthma attacks.

**Patients and Methods:** A cross-sectional study was conducted using medical records of children with severe asthmatic attacks treated at Ayatollah Taleghani hospital in Gorgan between 2016 and 2020. Peripheral blood samples were collected from the participants to evaluate the neutrophil and eosinophil counts.

**Results:** Out of the 180 medical records analyzed, only 1.7% of patients had eosinophil counts above the normal range, while 86.7% had neutrophil counts above the normal range. The results showed an inverse relationship between the age of patients and their peripheral blood eosinophil levels, although this relationship was not statistically significant ( $r=-0.06$ ,  $P=0.41$ ). There was a significant relationship between the neutrophil percentage and the age of the patients; however, this relationship was also not statistically significant ( $r=0.03$ ,  $P=0.96$ ).

**Conclusion:** The percentage of eosinophils in peripheral blood can be a reliable predictor for assessing the severity of asthma.

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## Introduction

Asthma is a prevalent respiratory disease characterized by inflammation of the lower airway tract, leading to increased bronchial sensitivity and variable, reversible airflow obstruction (1). Children with asthma commonly present with a symptom triad of wheezing, shortness of breath, and cough. Pediatric asthma can be classified into two key endotypes: "type 2-high" and "type 2-low" asthma. Allergic or eosinophilic asthma, which often begins in childhood, falls under the type 2-high category and is characterized by eosinophilic airway inflammation, elevated IgE levels, fractional exhaled nitric oxide (FeNO), and a positive response to inhaled corticosteroids (2).

The prevalence of asthma varies significantly across different studies, ranging from 2.7% in Kerman to 35.4% in Tehran Province. Most asthma symptoms nationwide have been reported at 13.14% (3). Genetic predisposition and environmental factors, such as allergens and viral infections,

## Key point

The total eosinophil count can be a helpful indicator of asthmatic activity and aid in diagnosing asthma attacks and adjusting steroid doses. It also acknowledges that normal eosinophil levels do not exclude the presence of bronchial asthma. The study aimed to examine the distribution of eosinophil and neutrophil percentages in the peripheral blood smear of children experiencing asthma attacks. The results indicated that only a few patients had elevated eosinophil counts, while most had high neutrophil counts. The conclusion emphasizes that the eosinophil percentage in peripheral blood can be a reliable predictor for assessing asthma severity.

contribute to the development of asthma (4).

Pathophysiologically, asthma involves thickening of the airway tract wall, submucosal edema, vasodilation, and cellular infiltration, particularly by lymphocytes and eosinophils. Even in individuals with mild or asymptomatic asthma, biopsy samples have shown significant eosinophil activity in the submucosa of the airway tract. These findings support the hypothesis that eosinophil and

neutrophil infiltration and activation in the airway tract contribute to respiratory tract inflammation during asthma attacks (5). When using a biomarker to diagnose a disease, the biomarker must remain relatively stable during the stationary phase of the disease. Studies have suggested an increase in CD4+CRT2+ T cell numbers in patients with severe asthma compared to those with mild/moderate disease, particularly in patients experiencing frequent asthma exacerbations (6).

There is no gold standard for accurately diagnosing asthma. The use of either peripheral blood film or spirometry in the diagnosis of asthma is limited in children over five years old, making the diagnosis challenging (2).

In recent years, eosinophil count has gained attention as a valuable tool for assessing the severity of pulmonary asthma. This hypothesis has been supported by pulmonary function tests and clinical examinations (7). Studies have indicated that the ratio of eosinophils in mucus compared to blood eosinophils is a more sensitive marker for predicting respiratory tract inflammation in asthma (7).

Peripheral blood film is fundamental and informative hematological tool clinicians use for screening, diagnosing, monitoring disease progression, and assessing therapeutic response. Leukocytosis is suspected when the white blood cell (WBC) count exceeds five leucocytes/hpf, while leucopenia is defined as less than two leucocytes/hpf. Eosinophils are slightly more prominent than polymorphs and typically have a bilobed nucleus. They are characterized by the presence of orange-red granules in the cytoplasm. Significant eosinophilia may be observed in allergies and parasite infections (8).

Considering the relationship between atopy, asthma, eosinophilia in the blood and lungs, as well as the role of blood eosinophils as an indirect marker of respiratory tract inflammation, the total eosinophil count appears to be a suitable marker for assessing the activity of asthma attacks and can aid in both diagnosis and determining appropriate steroid dosages (7).

## Objectives

This study aimed to investigate the frequency distribution of eosinophil and neutrophil percentages in peripheral blood smears of children experiencing asthma attacks treated at Taleghani Hospital in Gorgan between 2016 and 2020.

## Patients and Methods

### Study design

The present cross-sectional study was performed within four years on the medical files of 180 children with severe asthmatic attacks referring to Ayatollah Taleghani hospital in Gorgan in 2016-2020. Asthma diagnosis in these patients has been based on the results of spirometry tests and confirmation by an asthma or allergy subspecialist or lung specialist. Based on the inclusion criteria, 4-14-year-old children were referred to the hospital with asthma

attacks. Those hospitalized between 2016- and 2020 were included, among whom the patients whose asthma was associated with allergic rhinitis, stomach reflux, and congenital lung disease were excluded.

We used these criteria as diagnostic criteria for asthma (9):

- Presence of the symptoms of wheezing, coughing, and breathing difficulty
- Using an improvement in symptoms after a trial of preventer medication alone to diagnose asthma
- Perform spirometry as part of the diagnostic work-up of children aged 5–16 years with suspected asthma: A forced expiratory volume in 1 s (FEV1)/forced vital capacity (FVC) below the lower limit of normal (LLN) or <80%, or an FEV1 <LLN or <80% predicted should be considered supportive of an asthma diagnosis.
- An increase in FEV1  $\geq 12\%$  and/or  $\geq 200$  mL following inhalation of 400  $\mu\text{g}$  of a short-acting  $\beta_2$ -agonist as diagnostic of asthma. BDR <12% does not exclude asthma.
- If a child with asthma symptoms has a FeNO value of  $\geq 25$  ppb, it may indicate a diagnosis of asthma. However, a FeNO value of <25 ppb does not necessarily rule out asthma.
- A cut-off of  $\geq 12\%$  in PEF variability should be considered a positive test. A PEF variability of <12% does not exclude asthma.

A peripheral blood sample was taken from all study patients. According to similar studies, a normal eosinophil percentage in peripheral blood is considered to be between 0-5%, while a normal neutrophil percentage in peripheral blood is regarded as between 54-62% (8).

### Statistical analysis

For the statistical analysis, we entered the study data into SPSS 20 software and analyzed it. We used the mean and standard deviation to describe the quantitative data, and for the qualitative data, we used frequency and percentage. We used independent samples t-test and Pearson's correlation coefficient to compare the frequency distribution of quantitative data. For the frequency distribution of qualitative variables, we employed the chi-square test. We considered all statistical test results significant with  $P < 0.05$ .

## Results

During the study, we investigated 180 medical files of patients aged between 4-14 years who had been admitted to the hospital with an asthma attack. Of these patients, 114 were boys, accounting for 63.37%. We measured the eosinophil and neutrophil levels in their peripheral blood sample. The mean age of the patients was  $7.07 \pm 2.56$  years. The average duration of hospitalization was  $2.2 \pm 1.08$  days, ranging from 1-6 days. The mean eosinophil count of the patients examined in the study was  $1.96 \pm 1.17$ , ranging from 1-6. The mean neutrophil percentage of the

patients was  $74.16 \pm 11.01\%$ , ranging from 45-89%. Among the patients, 47.3% received anticholinergic drugs, 37.2% received corticosteroids, 7.2% received both, and 7.2% were under treatment with other medications.

Considering the normal percentage of peripheral blood eosinophil as 0-5% (8), the eosinophil count lay within the normal range in 177 patients (98.3%), and the eosinophil count was reported above normal in only three patients (1.7%). Considering the normal percentage of peripheral blood neutrophil as 54-62%, in 22 patients (12.2%), the peripheral blood neutrophil percentage lied within the normal range, and in 2 (1.1%), it was below the normal range, and 154 (86.7%) showed above normal neutrophil percentage.

We used Spearman correlation test to compare the relationship between patients' age and eosinophil and neutrophil values. Based on its results, there was an inverse relationship between the age of patients and their peripheral blood eosinophil level, though this relationship was not significant ( $r=-0.06$ ;  $P=0.41$ ). The neutrophil percentage had a significant relationship with the age of the studied patients, but again this relationship was insignificant ( $r=0.03$ ;  $P=0.96$ ). In this study, the mean frequency distribution of neutrophils and eosinophils in the peripheral blood of the studied patients had no significant relationship with their gender (Table 1).

In this study, again, according to the correlation test, the eosinophil percentage of peripheral blood among hospitalized patients had a direct and significant relationship with the number of days of hospitalization ( $r=0.429$ ;  $P<0.001$ ). Regarding the peripheral blood neutrophil

percentage and number of days of hospitalization, this relationship was direct but insignificant ( $r=0.13$ ;  $P=0.81$ ). In this study, no significant association was observed between the type of treatment received and the duration of hospitalization (Table 2).

## Discussion

This study investigated the relationship between the frequency distribution of peripheral blood neutrophils and the eosinophil percentage of patients and the severity of asthma attacks in 180 treatments 4-14 years of age suffering from asthma. The eosinophil frequency was within the normal range in 177 patients (98.3%), and in only three patients (1.7%), eosinophilia was above the normal range. The results indicated that the peripheral blood eosinophil percentage did not have considerably increased compared to the normal range. On the other hand, 48% of patients in our study showed eosinophil levels above the median range, which reflects a relative increase of the peripheral blood eosinophil in asthma attacks. Tran et al, in a cross-sectional study, found that the peripheral blood eosinophil count of patients with asthma was significantly higher than the normal range ( $P=0.0001$ ) (10). In this study, again, the peripheral blood neutrophil was within the normal range in 22 patients (12.2%), below the normal range in 2 patients (1.1%), and 154 patients (86.7%) showed above-normal range levels. The peripheral blood neutrophil percentage has been higher than normal among patients with asthma attacks. The results of the present research were in line with the prospective study of Kansal et al done in August 2017 to investigate the role of peripheral blood neutrophils on the severity of asthma. They took bronchial biopsies of 73 asthmatic patients (37 severe patients and 36 mild patients). They found that blood neutrophil was significantly higher in severe asthma compared to mild asthma patients ( $P=0.003$ ) (11).

In this study, the frequency of eosinophils of patients had no relationship with their age. Dogru et al conducted a prospective study in 2016 to investigate the relationship between eosinophils and the neutrophil frequency of peripheral blood and age plus the duration of hospitalization of 469 asthmatic patients. Similar to the present study, they found no significant relationship between the peripheral blood eosinophil percentage and the age or gender of patients. Accordingly, it can be concluded that the patient's age cannot be a good indicator to predict the incidence or relapse of asthma attacks or the number of days of hospitalization (12). Our study showed no significant relationship between the peripheral blood neutrophil percentage and patients' age. Dogru et al in 2016, in their prospective research, observed that, similar to the present study, there was no significant relationship between the peripheral blood neutrophil level of patients and their age, gender, history of atopic dermatitis, contact with allergens, or cigarette smoke (12).

In this study, the frequency distribution of neutrophils

**Table 1.** Correlation analysis of neutrophil and eosinophil count with the age of study participants

		Age (y)
Eosinophil	Correlation coefficient	-0.061
	P value*	0.412
	N	180
Neutrophil	Correlation coefficient	0.003
	P value*	0.964
	N	180

\*P value was calculated with Spearman correlation analysis.

**Table 2.** Correlation analysis of neutrophil and eosinophil count with hospitalization days of study participants

		Age (y)
Eosinophil	Correlation coefficient	0.429
	P value*	0.00
	N	180
Neutrophil	Correlation coefficient	0.130
	P value*	0.081
	N	180

\*P value was calculated with Spearman correlation analysis.

and eosinophils of patients had no significant relationship with their gender. The study by Dogru et al also had similar findings and reported no special significant relationship between the patient's gender and their peripheral blood eosinophil percentage (12). Elsewhere, Tran et al in their cross-sectional study in August 2014 to explore the peripheral blood eosinophil of asthmatic patients, reported that there was no significant relationship between the peripheral blood eosinophil percentage of patients and their gender (10).

In this study and similar to the findings of Tran plus Dogru and other studies, the peripheral blood eosinophil level of patients had a significant relationship with their number of days of hospitalization (10, 12). Malinovsky et al conducted a cross-sectional study on 1248 asthmatic patients based on the data of the asthma-associated emergency office of the US. They reported that there was a direct and significant relationship between the peripheral blood eosinophil percentage of these patients and their number of days of hospitalization (5). Other studies, such as Kansal et al and Chapman et al, also reported similar findings (11, 13).

This study found no significant relationship between the peripheral blood neutrophil percentage of patients and their number of hospitalization days. This finding aligns with the results of Java et al in 2006, who reported no significant relationship between the peripheral blood neutrophil percentage and the severity of asthma attacks. According to this study, during severe asthma attacks, CD35 and CD11b markers are elevated (14). However, no specific elevation was found in CD62L or CD18, a kind of memory T cells released following an inflammatory response from the surface of neutrophils (15). However, these findings did not concur with the results of the cross-sectional research by Ricciardolo et al in 2018. They reported that the peripheral blood neutrophil was higher among patients with severe asthma than in mild cases (16). Also, there was a negative relationship between peripheral blood neutrophil percentage and the number of asthma attacks in the future and the duration of hospitalization. Based on these findings, it can be concluded that the peripheral blood neutrophil percentage of patients cannot be regarded as a reliable indicator to predict the number of hospitalization days and severity of asthma.

In our study, there was no significant relationship between receiving corticosteroids and patients' hospitalization duration. Abaya et al in 2019 conducted a case-control study on asthmatic patients in a Philadelphia hospital. They reported that the administration of corticosteroids failed to create a significant difference in the rate of second referral within the next 72 h following the prescription in patients with an asthma attack (15). Further, the duration of hospitalization of patients undergoing inhalation of corticosteroids did not have any significant difference from other patients. Briefly, consuming corticosteroids in patients with mild to moderate asthma has no considerable

impact on their course of hospitalization (15).

## Conclusion

It has been found that there is a strong correlation between the length of a patient's hospital stay and their percentage of peripheral blood eosinophils. This means that the peripheral blood eosinophil percentage is a trustworthy indicator of the severity of asthma in patients. Eosinophil is a significant factor in causing asthma as it damages the respiratory system's epithelium.

## Authors' contribution

**Conceptualization:** Seyed Ali Aghapour.

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**Formal analysis:** Mousa Ghelichi-Ghojogh.

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## Conflicts of interest

The authors decline any kind of conflict of interest.

## Ethical issues

The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of Golestan University of Medical Sciences approved this study (Ethical code#IR.GOUMS.REC.1399.269). Accordingly, written informed consent was taken from all participants before any intervention. This study was extracted from MD., thesis Shima Shirzaeinezhad (Thesis #111654) at this university. Additionally, ethical issues (including plagiarism, data fabrication, and double publication) were completely observed by the authors.

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