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Research Article

Blood Eosinophils as a Predictor of Acute Attacks of Asthma in Children

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Abstract

Background: Childhood asthma represents a heterogeneous challenging disease, particularly in its severe forms. The identification of different asthma phenotypes has stimulated research in underlying molecular mechanisms, such as the endotypes, and paved the way to the search for related specific biomarkers, which may guide diagnosis, management and prediction of treatment response. **Methods:** The present study was a cross-sectional hospital-based study carried out at the Pediatric Departments of Minia University. It was conducted on 60 children known as asthmatic, who attended Minia University Hospital, their age range was (3 -12) years. They were divided into 2 groups: **Group I**: It was included 30 asthmatic children presented to the pediatric department with asthma exacerbation according to GINA 2021**, and Group II**: It was included 30 stable asthmatic children. **Results**: There were statistically significant higher values of (TLC and eosinophil count) detected in the asthma exacerbation group than asthma stable group with p values (0.008, <0.001) respectively. Blood eosinophils have a significant moderate positive correlation with the number of asthma exacerbations (R=0.58, p value= <0.001), blood eosinophils have a significant moderate negative correlation with the asthma control status (R=-0.58, p value= <0.001), the highest values of blood eosinophils were in uncontrolled group (p-value <0.001), **Conclusion:** blood eosinophil counts were associated with the risk of future exacerbation in severe asthma despite receiving multiple therapy. Eosinophils are involved in the pathogenesis of asthma exacerbation. Blood eosinophils are reportedly associated with the frequency of asthma exacerbation.

Keywords; Childhood asthma, Blood Eosinophils, hematological biomarker.

Introduction

Asthma is a chronic heterogeneous disease of the lower airways characterized by chronic inflammation and airway hyper-reactivity leading to cough, wheeze, difficulty in breathing, and chest tightness.[1]

Severe asthma is a relatively uncommon condition in children but one which causes morbidity, occasionally mortality, and is a challenging condition to manage. There are several definitions of severe asthma, which have a common theme of poor control despite high dose inhaled corticosteroid treatment.

Severe asthma is defined by the European Respiratory Society/American Thoracic Society (ERS/ATS) criteria as either asthma requiring escalation to step 5 medical therapy (=high-dose ICS in combination with a second controller and/or additional systemic corticosteroid therapy) to maintain asthma control or

asthma that remains uncontrolled despite step 5 therapy.[2, 3].

Eosinophils are involved in the development of asthma exacerbation, Eosinophils, which tend to accumulate at sites of allergic inflammation, contribute to the development of bronchial asthma. They release a number of mediators, including s radical oxygen species, cytokines, such as granulocyte-macrophage colony-stimulating factor (GM-CSF) and interleukin (IL)-8, and lipid mediators, such as cysteinyl leukotrienes (cysLTs) [4]. the role of eosinophils in the development of airway remodeling has been established at a relatively early phase. Eosinophil-deficient mice are reportedly protected from peribronchiolar collagen deposition. Eosinophils produce trans-forming growth factor (TGF)-β, which may contribute to airway fibrosis. Additionally, eosinophils can produce cysLTs and be a major cellular source of cysLTs in the airways of individuals with seasonal allergic asthma or aspirin-exacerbated respiratory disease, which also contribute to airway remodeling. Anti-IL-5 mAb suppresses airway remodeling (reduction of tenascin, lumican, and procollagen III) as well as airway eosinophils expressing mRNA for TGF-β1 and concentrations of TGF-β1 in the bronchoalveolar lavage (BAL) fluid of asthmatics[4].

Patients and methods

The present study was a cross-sectional hospital-based study carried out at Pediatric Departments of Minia University. It was conducted on 60 children known as asthmatic, they were attended to Minia University Hospital, their age range was (3 -12) years.

They were divided into 2 groups: **Group I**: It was included 30 asthmatic children presented to the pediatric department with asthma exacerbation according to GINA 2021, **Group II:** It was included 30 stable asthmatic children.

All subjects included in the study were subjected to the following:

1) **Careful history taking:**

Considering age, sex, age of first attack of wheezes, age of diagnosis, last exacerbation, severity, controller therapy, family history of asthma, history of atopic dermatitis or allergic rhinitis.

2) **Examination:**

Through general and chest examination.

*** General examination**: including vital data, general systemic examination to exclude other chronic diseases.

*** Complete chest examination:** inspection, palpation, percussion and auscultation.

3) **Laboratory investigation:** CBC, blood eosinophils count.

Results

In this study the exacerbation group includes 30 children, their age range (3-12) years, 23 of them were males and 7of them were females, and they diagnosed to have asthma (3±0.6) years ago and their age of 1st wheezes was (1-3) years, while the controlled asthma group includes 30 children, their age range (3-12) years, 8 0f them were males and 22 of them were females, and they diagnosed to have asthma (3.1±0.6) years ago and their age of 1st wheezes was (1.4-3) years. (table 1)

In this study there was a statistically significant higher values of (TLC, eosinophil count) detected in the asthma exacerbation group than stable asthmatic group with p value (0.008, <0.001) respectively. Table (2)

Blood eosinophils have significant moderate positive correlation with number of exacerbation (R=0.58, p value= <0.001), blood eosinophils have significant moderate negative correlation with control status (R=-0.58, p value= <0.001). Table (3), while the highest values of blood eosinophils were recorded in uncontrolled asthmatic group (p value <0.001). Table (4). The most potent predictor marker for asthma exacerbation is blood eosinophils (OR=9.699) Table (5)

Table (1): Demographic and clinical data of diseased groups:

		Group 1 (asthma exacerbation patients) During attack	Group 2 (controlled asthma patients) Between attacks	P value
		N=30	N=30	
Age	**Median IQR**	4 (3.5-7)	9 (7-11)	**<0.001***
Sex	**Male Female**	23(76.7%) 7(23.3%)	8(26.7%) 22(73.3%)	**<0.001***
BMI	**Range Mean ± SD**	(11.8-20.4) 16±2.1	(12.2-18.2) 16.3±1.4	0.439
Age of 1st wheezes	**Median IQR**	1.8 (1-3)	2 (1.4-3)	0.392
Age at diagnosis	**Range Mean ± SD**	(1-4) 3±0.6	(2-4) 3.1±0.6	0.649

Table (2): Blood biomarkers in the studied groups:

		Asthmatic patients in exacerbation	Stable asthmatic patients	P value
		N=30	N=30	
TLC	**Median IQR**	14 (10.9-16)	11 (9-13.1)	**0.008***
Eosinophils	**Median IQR**	2 (1.8-3)	0 (0-1)	**<0.001***

- Mann Whitney test for non- parametric quantitative data between the two groups
- *: Significant level at P value < 0.05

Table (3): Correlation between blood biomarkers and clinical variables in children with asthma

All cases (n=60)	Eosinophils	
	R	P value
Asthma Control status	-0.586	<0.001*
Asthma Severity	0.314	0.014
No of exacerbation since last year	0.583	<0.001*

- (P) Pearson's correlation
- (S) Spearman's correlation

*: Significant level at P value < 0.05

Table (4): Blood biomarkers in relation to control status in asthmatic children:

All cases (n=60)	Control status			P value
	Uncontrolled	Partially controlled	Well controlled	
	N=24	N=16	N=20	
Eosinophils	2/(1-3)	1/(0.25-2)	0/(0-1)	**<0.001***

- Kruskal Wallis test for non-parametric quantitative data between the three groups followed by Mann Whitney test between each two groups
- *: Significant level at P value < 0.0

Table (5): Simple logistic regression analysis of blood biomarkers for prediction of asthma exacerbation

	OR	95% CI	P value
Eosinophils	9.699	3.308-28.438	<0.001*

- CI: Confidence Interval
- *: Significant level at P value < 0.05

Discussion

Childhood asthma represents a heterogeneous challenging disease, particularly in its severe forms. The identification of different asthma phenotypes has stimulated research in underlying molecular mechanisms, such as the endotypes, and paved the way to the search for related specific biomarkers, which may guide diagnosis, management, and predict response to treatment [5].

Some patients with severe asthma experience acute attacks despite receiving multiple therapy. The risk of acute attacks and heterogeneous response to treatment may be associated with specific inflammatory molecules that are responsive or resistant to corticosteroids[6].

Biomarker analysis may help in tailoring treatment and predicting the future risk of exacerbation in patients with severe asthma [7-9].

As regard the value of blood biomarkers in both groups, we found that TLC had higher values in group I (exacerbation group) than group II (stable group) p value 0.008. In agreement with result done by Rabah et al., who found that highTLC associated with asthma exacerbation and reflect disease severity.

We found significant higher values of eosinophils in group I (exacerbation group) than group II (stable group), p value <0.001 and by simple logistic regression analysis of blood biomarkers for prediction of asthma exacerbation, eosinophils were the most potent predictor for exacerbation (OR=9.6, CI=3.3-28.4, P value <0.001). These findings were the same as a study done by Nakagome and Nagata who found that blood eosinophil counts are important factors for predicting asthma exacerbation, moreover we found that highest values of eosinophils in uncontrolled patients. in agreement with this results study was Choi et al., who found that blood eosinophilia is associated with more severe symptoms and lower response to anti-inflammatory medications.

Conclusion

We determined that previous history of severe-to-serious exacerbation, blood eosinophil counts was associated with the risk of future exacerbation in severe asthma despite receiving multiple therapy. Eosinophils are involved in the pathogenesis of asthma exacerbation and it is associated with the frequency of asthma exacerbation.

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