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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 spurred further investigation into the underlying molecular mechanisms, including endotypes, and has opened the door to discovering specific biomarkers that could assist in diagnosing, managing, and predicting the treatment outcomes. **Methods:** The present study was a cross-sectional hospital-based study carried out at the Pediatric Departments of Minia University. It was conducted upon 60 children known to be asthmatic; their age range was (3 -12) years. They were divided into 2 groups: Group I: It included 30 asthmatic children admitted to the Pediatric Department with asthma exacerbation diagnose according to GINA 2021; Group II: It 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:** Although the patients were treated with different therapies, elevated blood eosinophil levels were associated with a higher risk of future exacerbations in severe asthma. The underlying mechanisms of asthma flare-ups remain a key area of study.

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 less common condition in children, yet it leads to significant morbidity, and sometimes mortality, making it difficult to manage. Various definitions of severe asthma exist, but they all share the common characteristic of

inadequate 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 play a key role in asthma exacerbations by its accumulating at sites of allergic inflammation, which contributes to the development of bronchial asthma. They release a range of inflammatory mediators, including reactive oxygen species, cytokines such as granulocyte-macrophage colony-stimulating factor (GM-CSF) and interleukin-8 (IL-8), as well as lipid mediators like cysteinyl leukotrienes (cysLTs)[4]**.** The involvement of eosinophils in airway remodeling has been demonstrated in early stages. Studies have shown that eosinophil-deficient mice are protected from collagen deposition around the bronchi. Additionally, transforming growth factor (TGF)-β, produced by eosinophils, may contribute to airway fibrosis. Additionally, eosinophils are a major source of cysteinyl leukotrienes (cysLTs) in the airways of individuals with seasonal allergic asthma or aspirin-exacerbated respiratory disease, both of which contribute to airway remodeling. Treatment with anti-IL-5 monoclonal antibodies (mAb) has been shown to reduce airway remodeling (including decreased levels of tenascin, lumican, and procollagen III), as well as lower the expression of mRNA for TGF-β1 in airway eosinophils and reduce the concentrations of TGF-β1 in the bronchoalveolar lavage (BAL) fluid of asthmatic patients. [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 to be asthmatic; their age range was (3 -12) years.

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

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

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.

1) **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:** Blood sample was collected through venous blood sampling by sterile venipuncture under complete aseptic conditions in an EDTA-containing tube for CBC analysis. The complete blood count was determined by an automated cell counter (Celltac ES, Nihon Kohden, Germany).

Results

In this study the exacerbation group included 30 children, their age range was (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 included 30 children, their age range (3-12) years, 8 of 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

- *: Significant level at P value < 0.05

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***

*: 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*

*: 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***

*: 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

Asthma exacerbations are associated with significant childhood morbidity and mortality. Recurrent asthmatic attacks lead to progressive lung functions loss and can sometimes be fatal or near-fatal, even in mild asthma. The identification of different asthma phenotypes attract the attention for researches in underlying molecular mechanisms, such as the endotypes, and paved the way to the search for the related specific biomarkers, which may guide diagnosis, management, and predict response to treatment [5].

Severe asthma children experience acute attacks even with receiving polytherapy. The acute attacks risk and different response to managements may be related to specific inflammatory molecules that are responsive or resistant to corticosteroids[6].

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

In the current study regards the value of blood biomarkers of both groups, the TLC had higher values in group I (exacerbation group) than group II (stable group) p value 0. 008. Many studies were in agreement with these results [10-11].

This study found significant higher values of blood eosinophils in group I (exacerbation group) than group II (stable group), p value <0.001 and 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.[4] Moreover, this study found that highest values of eosinophils was 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.[12]

Ameta analysis done by Mallah et.al, reported that blood eosinophil counts ≥ 200 cells/µL are associated with asthma exacerbation. Blood eosinophil count is a modifiable factor that could be contributed in asthma management strategies [13].

However, Zeiger, R. S et al, found that Blood eosinophil counts of 300/mm3 or more in children with persistent asthma may identify children at increased risk for future asthma exacerbations, indicating a possible higher disease burden among these patients.

On the other hand, Gibson, P. et.al, found that children with more frequent asthma exacerbation exhibit increasing airway inflammation that is characterized by sputum eosinophilia and bronchial epithelial desquamation rather than blood eosinophilia.[15]

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 patho-genesis of asthma exacerbation and it is associated with the frequency of asthma exacerbation.

References

1. Hammad, H. and B.N.J.C. Lambrecht, The basic immunology of asthma. 2021. 184(6): p. 1469-1485.
2. Seys, S.F., et al., Severe asthma: Entering an era of new concepts and emerging therapies: Highlights of the 4th international severe asthma forum, Madrid, 2018. 2019. 74(11): p. 2244-2248.
3. Eyerich, S., et al., New biological treatments for asthma and skin allergies. 2020. 75(3): p. 546-560.
4. Nakagome, K. and M. Nagata, Involvement and Possible Role of Eosinophils in Asthma Exacerbation. Front Immunol, 2018. 9: p. 2220.
5. Chung, K.F.J.A.J.O.R. and C.C. medicine, Predicting Response to Triamcinolone in Severe Asthma by Machine Learning. Solving the Enigma. American Thoracic Society. 2019, p. 1299-1300.
6. Ko, H.-K., et al., Blood tryptase and thymic stromal lymphopoietin levels predict the risk of exacerbation in severe asthma. 2021. 11(1): p. 1-10.
7. Tay, T.R., J.W. Lee, and M.J.M.J.A. Hew, Diagnosis of severe asthma. 2018. 209(2 Suppl): p. S3-S10.
8. Chung, K.F.J.T.L., Targeting the interleukin pathway in the treatment of asthma. 2015. 386(9998): p. 1086-1096.
9. Chung, K.F.J.T.L.R.M., Neutrophilic asthma: a distinct target for treatment? 2016. 4(10): p. 765-767.
10. Nguyen-Thi-Dieu, T., Le-Thi-Thu, H., & Duong-Quy, S. (2017). The profile of leucocytes, CD3+, CD4+, and CD8+ T cells, and cytokine concentrations in peripheral blood of children with acute asthma exacerbation. *Journal of International Medical Research*, *45*(6), 1658-1669.
11. Vedel-Krogh, S., Fallgaard Nielsen, S., Lange, P., Vestbo, J., & Nordestgaard, B. G. (2017). Association of blood eosinophil and blood neutrophil counts with asthma exacerbations in the Copenhagen General Population Study. *Clinical Chemistry*, *63*(4), 823-832.
12. Choi, Y., S. Sim, and H. S. Park. 'Distinct functions of eosinophils in severe asthma with type 2 phenotype: clinical implications', Korean J Intern Med, 35: 823-332020.
13. Mallah, N., Rodriguez-Segade, S., Gonzalez-Barcala, F. J., & Takkouche, B. (2021). Blood eosinophil count as predictor of asthma exacerbation. A meta-analysis. *Pediatric Allergy and Immunology*, *32*(3), 465-478.
14. Zeiger, R. S., Schatz, M., Li, Q., Chen, W., Khatry, D. B., Gossage, D., & Tran, T. N. (2015). The association of blood eosinophil counts to future asthma exacerbations in children with persistent asthma. *The Journal of Allergy and Clinical Immunology: In Practice*, *3*(2), 283-287.
15. Gibson, P. G., Simpson, J. L., Hankin, R., Powell, H., & Henry, R. L. (2003). Relationship between induced sputum eosinophils and the clinical pattern of childhood asthma. *Thorax*, *58*(2), 116-121.