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The Significance of Blood Eosinophilia in Atopic Dermatitis

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ABSTRACT

Background: Atopic dermatitis (AD) is chronic relapsing, pruritic, inflammatory skin disease. It usually accompanies other atopic problems like asthma and allergic rhinitis. Eosinophil plays a role in patients with AD.
Objectives: To assess blood eosinophils in patients with AD and to evaluate the factors that are affecting the blood eosinophilia.
Materials and methods: This prospective study was conducted at Hit General Hospital in the period from October 2018-October 2019. The age, gender, and personal or family history of asthma or allergic rhinitis of the patients with AD were recorded. The severity of the disease was assessed by the SCORAD score. The total number of eosinophil was measured for each subject. The data were analyzed using SPSS version 22.
Results: Out of 70 patients with AD, 38 (54.3%) were females, and 32 (45.7%) males. The age of the patients ranged from 8 months to 30 years (mean 7.59±7.40). The highest age group affected was 2-12 years 40 (57.1%). The SCORAD score ranged from 6-80 (mean 24.19±17.59). The majority of our patients with mild course 50 (71.1%). The majority of the cases were without a history of asthma (n=53,75.7%), and around 50% without allergic rhinitis. The range of eosinophil count was 42-3360 (mean 636.44±491.37). The majority of the subjects (n=53,75.7%) with mild eosinophilia (500-1500/ mm^3). The age, gender, and patients with a history of allergic rhinitis or asthma had no significant effect on the number of eosinophils (P-Value >0.05). While, there was a high statistically significant difference between the eosinophils count, and the severity of AD (P-Value=0.000).
Conclusion: From these findings we concluded that blood eosinophilia is a relatively common laboratory finding of AD. Blood eosinophilia was influenced by the severity of AD.

Keywords: Atopic Dermatitis; allergic rhinitis; asthma; Eosinophilia.

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INTRODUCTION

Atopic dermatitis (AD) is a chronic relapsing eczematous condition of the skin often associated with a personal or family history of bronchial asthma and allergic rhinitis. Pruritus, scratching and rubbing lead to lichenification most typically in the antecubital and popliteal flexural areas [1, 2]. The word atopy comes from Greek (a- topos= without a place). It was introduced by Cooke in 1923 and refers to the strange grouping of asthma, hay fever, and eczema in the medical classifications [1]. AD was extensively studied by Sulzberger in 1932 [3]. The Incidence of atopic diseases in the population is between 2- 20% and slightly more in girls than boys [3]. The highest incidence of AD is among children and about 3% of all infants suffer from AD. The prevalence of AD is 10.7% [3–5].

The cause of AD is unknown, but it may be the result of interaction between hereditary, immunological, pharmacological, environmental, and psychological factors [1]. AD is a multifactorial etiology that inherited from a mother rather than a father. The clinical features of AD are a chronic recurrent eczematous disease that may be presented in 3 phases infantile, childhood, and adult phase [6, 7].

There are major and minor criteria for the diagnosis of AD that are established by Hanifin and Rajka [8]. The major criteria (must have 3 or more) include pruritus, typical mor-

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phology and distribution (flexural lichenification in adults, and facial and extensor involvement in infancy), Dermatitis (chronically or chronically relapsing), and Personal or family history of atopy-asthma, allergic rhinitis, and AD. The minor criteria (must have 3 or more) include xerosis/ichthyosis, pityriasis alba, keratoconus, recurrent conjunctivitis, cataract (anterior subcapsular), keratosis pilaris.-facial pallor, white dermographism, elevated IgE, a tendency to hand eczema, a tendency to repeated cutaneous infection, food intolerance, and wool intolerance.

The eosinophils are potent inflammatory cells involved in allergic reactions [9]. The unique feature of eosinophil is the specific granules that stain with eosin [10]. The eosinophil is a polymorphonuclear leukocyte, 12-17 μ in diameter which has the capacity for phagocyting and destroying allergen and invading organisms through its numerous enzymes. The nucleus of the eosinophil is bilobed [11].

The functions of eosinophil are phagocytosis, modulation of inflammation, and host defense against invading helminth parasites. The life span of eosinophil in the circulation ranges from 1/2 to 12 hours with only 1% of the eosinophils circulating under normal conditions, and the normal total eosinophil count is 40 to 500/mm^3 representing the lower and upper limits of the normal adult range. Normal percentage of eosinophil is 1-5 % of total WBC count [10, 11]. The grading of blood eosinophil count divided into 3 levels: mild; 500-1500/mm^3, moderate; 1500-5000/mm^3, and severe; more than 5000/mm^3 [7, 12].

We aimed to examine the blood eosinophils in patients with AD and to assess the factors that might affect the blood eosinophilia.

MATERIALS AND METHODS

The study was conducted at the Hit General Hospital during the period from October 2018 to October 2019. The present study ethically approved by the scientific committee of the Hospital and the informed consent was taken from all patients or their caregivers. Seventy patients with AD were enrolled in the study. The diagnosis of AD was made according to the HanifinRajka criteria [8]. The age, gender, and history of personal or family history of allergic rhinitis or asthma were taken from the patients or their caregivers.

Any patients with lymphadenopathy, hepatosplenomegaly, helminthic diseases, cardiac problems, chest X-ray or ECG changes, and elevated liver enzymes were excluded from the study.

After taking a history, a thorough clinical examination to assess the severity of eczema depending on the SCORAD index was performed [13]. This index composed of three component extent, intensity, and subjective. The extent depends on the involved area of the body. Calculation of the area depends on the Wallace's Rule of Nine: head and neck 9%, upper limb left 9%, upper limb right 9%, lower limb left 18%, lower limb right 18%, anterior trunk 18%, back 18%, and genitalia 1%. The intensity is measured according to 6 signs redness, edema, oozing or crust, scratching, lichenification, and dryness. Three points for each sign and the total points will be 18 for intensity. The last component of the score is subjective symptoms including itching, and sleeplessness, 10 points for each and the total are 20 points. Finally, the SCORAD Index is a summation of all these 3 scales with an equation: A/5+7B/2+C, where A (0-100) is the area or extension of eczema, B defined as intensity depending on 6 lesions (0-18), and lastly, C is defined as a subjective feeling of itching (0-10), and sleeplessness (0-10), the total of both (0-20). The patients were divided according to the SCORAD index into mild (<25), moderate (26-50), and severe (>50).

The patients were classified into 3 groups, group 1 (<2 years), group 2 (2-12 years), and group 3 (>12 years). Evaluation of the blood eosinophil count using these steps: 1- Take 2 ml of blood from the patient put one drop on the slides and one drop of Leishman stain, wait 2 minutes for all cells to be stained, then the sample is diluted with distilled water and wait 10 minutes then wash and read with high power field microscopy to calculate the number of eosinophil cells per 100 white blood cells (WBC) to calculate the percentage of eosinophil. 2- Take 0.02 ml of blood with a pipette and add 0.4 ml of glacial acetic acid, then put one drop of this mixture on the Neubauer chamber and read on lower power to calculate the WBC counts. 3- Multiply the eosinophil percentage by total WBC counts to deduce the total eosinophil count. Eosinophilia classified into mild 500-1500/ mm^3, moderate 1500-5000/mm^3, and severe >5000/mm^3.

The data were analyzed using SPSS (Statistical Package for the Social Sciences) version 22. A comparison of eosinophilia was done according to the age, gender, and severity of AD. Pearson Chi-Square was used to compare the variables. A P-Value of less than 0.05 considered a statistically significant difference. .

RESULTS

The age of the patients ranged from 8 months-30 years with a mean of 7.59±7.40. The highest age group affected was 2-12 years 40 (57.1%) Table 1. Out of 70 patients, 38 (54.3%) were females and 32 (45.7%) males, with male/female ratio 0.84/1 Table 2. The SCORAD score ranged from 6-80 with a mean of 24.19±17.59. The majority of our patients with mild course 50 (71.1%) Table 3. The majority of the patient was without a history of asthma 53 (75.7%) or about 50% without allergic rhinitis Tables 4 and 5.

The range of eosinophil count was 42-3360 with a mean of 636.44±491.37. The majority of the cases (n=53, 75.7%) with mild eosinophilia (500-1500/ mm^3). There was no statistically significant difference between the eosinophil count, and the age, gender, and patients with a history of allergic rhinitis or asthma (P-Value >0.05). While, there was a high statistically significant difference between the eosinophil count, and the severity of AD (P-Value=0.000) Tables 1-5.

DISCUSSION

In the last few decades, the incidence of AD is increasing particularly in developed nations [14–17]. AD becomes a

Table 1. The relationship between the eosinophil count and the age groups in 70 patients with AD.*

Age group	Eosinophil count/mm^3 [Number (%)]			Total
	Normal <500	Mild 500-1500	Moderate 1500-5000	
< 2 years	3 (16.7)	13 (72.2)	2 (11.1)	18(25.7)
2-12 years	10 (25)	29 (72.5)	1 (2.5)	40(57.1)
> 12 years	1 (7.1)	11 (20.8)	0 (0.0)	12(17.1)
Total	14 (20)	53 (75.7)	3 (4.3)	70(100)

* P-Value = 0.323.

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Table 2. The relationship between the eosinophil count and the gender in 70 patients with AD.*

Gender	Eosinophil count/mm^3 [Number (%)]			Total
	Normal <500	Mild 500-1500	Moderate 1500-5000	
Males	4 (12.5)	25 (78.1)	3 (9.4)	32(45.7)
Females	10 (26.3)	28 (73.7)	0 (0)	38(54.3)
Total	14 (20)	53 (75.7)	3 (4.3)	70(100)

* P-Value = 0.072.

Table 3. The relationship between the eosinophil count and the severity of AD in 70 patients.*

Age group	Eosinophil count/mm^3 [Number (%)]			Total
	Normal <500	Mild 500-1500	Moderate 1500-5000	
Mild (0-25)	11 (78.6)	39 (73.6)	0 (0)	50(71.4)
Moderate (26-50)	3 (25)	9 (72.5)	0 (0)	12(17.1)
Severe (>50)	0 (0)	5 (62.5)	3 (37.5)	8(11.5)
Total	14 (20)	53 (75.7)	3 (4.3)	70(100)

* P-Value = 0.000.

Table 4. The relationship between the eosinophil count and the history of asthma in 70 patients with AD.*

Asthma	Eosinophil count/mm^3 [Number (%)]			Total
	Normal <500	Mild 500-1500	Moderate 1500-5000	
Yes	2 (11.8)	13 (76.5)	2 (11.8)	17(24.3)
No	12 (22.6)	40 (75.5)	1 (1.9)	53(75.7)
Total	14 (20)	53 (75.7)	3 (4.3)	70(100)

* P-Value = 0.158.

Table 5. The relationship between the eosinophil count and the history of allergic rhinitis in 70 patients with AD.*

Allergic rhinitis	Eosinophil count/mm^3 [Number (%)]			Total
	Normal <500	Mild 500-1500	Moderate 1500-5000	
Yes	2 (11.8)	13 (76.5)	2 (11.8)	17(24.3)
No	12 (22.6)	40 (75.5)	1 (1.9)	53(75.7)
Total	14 (20)	53 (75.7)	3 (4.3)	70(100)

* P-Value = 0.452.

health concern worldwide because it carries huge health providing costs, significant comorbidity, an effect on the quality of life, and its burden are similar to other chronic diseases e.g. diabetes mellitus, epilepsy, and cystic fibrosis [14, 15, 18].

AD affects both children and adults in up to 20% and 3% respectively [19]. About 70% of AD patients begin in the pediatric population (less than 5 years) [20], while, 1-10% of patients seen in a hospital-based population in adults [14]. A prior retrospective study by Tay et al. from Singapore reported that 61.2% of AD starts at the age of 10 years, and only 13.6% begins at the age of 21 years [21]. Dhar et al. study from India [10] showed that the mean age of onset of the AD was 4.55 years ± 3.63. The mean age of our cases was 7.59±7.40 with the majority of cases below 12 years (n=58, 82.8%). The current study and the previous studies support that AD is more prevalent in children than adults. However, the age in our study doesnt affect the blood eosinophil count (P-Value > 0.05).

The present study showed that females were affected more than males. This finding is consistent with other investigations results [5, 22]. Our investigation reported that the gender of AD patients does not affect the level of blood eosinophil (P-Value > 0.05).

AD is often the first step in the development of other atopic conditions, like asthma, food allergy, and, allergic rhinitis the known as "atopic march", characterized by a typical sequence of atopic conditions preceding the development of other allergic problems later in life [14, 17, 19]. Only 30% of children with AD develop asthma, and allergic rhinitis in 35% [23]. Celakovska et al. [22] reported that 46% of AD cases had a history of asthma and 75% with allergic rhinitis. These high percentages of allergic conditions are due to their studied sample age of 14 years and more. The eosinophil number and the IgE level showed a statistically significant difference with a history of asthma in subjects with AD but not with allergic rhinitis [10]. Our results showed that 48.6%, and 24.3% of the AD cases had allergic rhinitis and asthma respectively. The high frequency of allergic rhinitis of the current study in comparison with Luoma et al. study [23] is due to the difference of the age of the studied samples (below 5 years in Luoma et al. study vs children and adults in our study). Asthma and allergic rhinitis were not affecting the eosinophil count (P-Value > 0.05). A similar finding also reported by Celakovska et al. study [22].

Eosinophil plays a role in AD owing to the presence of eosinophilia in AD subjects and the infiltration of the eosinophil in AD lesions. Moreover, eosinophil production, recruitment, and activation are associated with cytokines and chemokines release in patients with AD [24]. Around 3/4 of our cases showed mild eosinophilia (500-15000 mm^3). However, 20% of our active cases were with normal numbers of the blood eosinophil, therefore, the measurement of eosinophil counts is not considered a diagnostic tool of AD. A previous study from Japan showed that the peripheral eosinophil counts roughly correlated with the severity of AD [25]. Very high blood eosinophil numbers in severe forms of AD who had a personal or family history of respiratory atopy, while normal or moderately elevated counts were obtained in severe cases of 'pure' AD who had neither a personal nor a family history of respiratory atopy. It was suggested that disease severity and personal or family history of respiratory atopy are important factors in determining high blood eosinophil levels in AD [25]. An Indian study reported that the absolute eosinophil number and the IgE level had a statistically significant difference with the severity of AD [10]. The non-homogeneous distribution of the absolute eosinophil number and the IgE level was reflected in the large range and higher standard deviation. One way analysis of variance found a significant association of the absolute eosinophil number and the IgE level with a family history of AD only when both parents were affected [10]. Jerenowicz et al. study reported that subjects with severe AD had higher eosinophilia than subjects with mild-to-moderate AD, but the difference was not significant. In AD patients with positive SPT tests and detectable specific IgE in sera, and also in patients with symptoms of other atopic diseases,

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the peripheral blood eosinophilia was more prominent compared to patients with negative SPTs and without symptoms of other atopic diseases, but the difference was not statistically significant [26]. Our results also showed that there was a high statistically significant difference between the peripheral blood eosinophil numbers and the severity of AD as diagnosed by the SCORAD index [13].

The shortcomings of this study include no control group, small sample size, and the study did not take the age of onset of AD and the sites of the lesions into consideration.

In conclusion, blood eosinophilia is a relatively common laboratory finding in cases with AD. It was not influenced by the age or gender of the patients. Also, it was not affected by the presence of a history of asthma or allergic rhinitis. The level of blood eosinophil can be used as a prognostic factor for AD patients because it has a significant effect on the severity of the disease. However, the level of blood eosinophil is not used as one of the diagnostic criteria of AD.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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