

## Evaluation of the Role of Serum Interleukin-1 Beta in Patients with Atopic Dermatitis

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### ABSTRACT

**Background:** Atopic dermatitis (AD) is a common eczematous skin disease that is chronically relapsing. Interleukin -1-beta (IL-1 $\beta$ ) is a pivotal agonist member of the IL-1 family that plays a master role in the induction of an adequate immune response to regulate the sweeping of the diseased cells physiologically. **Objective:** The aim was to clarify the possible participation of a certain IL (IL-1 beta) in the pathogenesis of atopic dermatitis. **Patients and Methods:** This case-control study has been conducted in the Dermatology, Venereology and Andrology Department at Zagazig University Hospitals. Our present study included 30 atopic patients and 30 apparently healthy control subjects of matched age and sex. Serum IL-1 $\beta$  level was measured. **Results:** Gender had no significant effect on serum IL-1 $\beta$  in all groups. Duration of the disease showed a non-significant positive one in atopic patients. The severity of the disease showed a significant positive correlation in atopic patients and similarly, the disease score did. There was a significant difference in serum IL-1 $\beta$  among the three degrees of severity in a topic patients. **Conclusion:** IL-1 $\beta$  serum level was found in patients with moderate to severe cases of atopic dermatitis, marking the systemic inflammatory nature of these diseases. On the other hand, IL-1 $\beta$  serum level was around normal values in the control group. These mentioned findings were supported by the statistical evaluations on the relationship between serum IL-1 $\beta$  level, severity scores of AD (SCORAD score) and clinical observations.

**Keywords:** Assessment, Atopic Dermatitis, Serum Interleukin-1 beta

### INTRODUCTION

Atopic dermatitis is an inflammatory, chronically relapsing, non-contagious and pruritic skin disorder that is very common in children but may occur at any age; it may start as early as age 2-6 months, and may persist into adulthood. It is the most common form of dermatitis. Atopic dermatitis usually occurs in people with 'atopic tendency'. This means they may develop any or all of three closely linked conditions; atopic dermatitis, asthma and allergic rhinitis. Often these conditions run within families so, the family history is useful in diagnosing atopic dermatitis in infants <sup>(1)</sup>.

Atopic dermatitis arises because of a complex interaction of genetic and environmental factors. These include defects in skin barrier function making the skin more susceptible to irritation by contact irritants. This malfunctioning skin barrier also provides a golden key to pathogens especially staphylococcus aureus to colonize the skin and then aggravating the inflammatory process. Atopic dermatitis manifests itself, not only as an acute but also as a chronic disease <sup>(2)</sup>.

The disease is distinguished in acute, relapsing form (episodes of acute eczema with intervals between them) and chronic form (episodes of acute eczema without intervals). The main first symptom of AD is persistent severe pruritus. AD is defined in most people by acute flares with inflamed, red, sometimes blistered and weepy patches. In-between flares, the skin may appear normal or suffer from chronic eczema with dry, thickened and itchy areas <sup>(3)</sup>.

Many factors can alter the way eczema looks and feels. There are some general patterns where the eczema is found on the body according to the age of the affected

person as following: on cheeks, arms, legs and groin in infants, on feet and antecubital and popliteal fossae in children/adolescents, and on hands, feet, ankles and groin in adults. There is a great interest to the disease not only due to its special clinical manifestation but also due to its pathogenetic mechanism <sup>(4)</sup>.

IL-1 $\beta$  is mainly produced in blood monocytes; macrophages and dendritic cells. IL-1 $\beta$  transmits its signal through binding to its cell surface receptor IL-1R-1. IL-1 $\beta$  promotes T-cell activation, up regulates the IL-2 receptor on lymphocyte surface, stimulates B-lymphocytes for proliferation and antibody production and enhances Th17, Th1 and Th2 lymphocyte differentiation <sup>(5)</sup>.

IL-1 $\beta$  requires the intracellular cysteine protease caspase-1 for biological activity. Activation of caspase-1 is mediated by a cytosolic multiprotein oligomer called the inflammasome. The activity of the inflammasome is triggered not only by microbial infection, but also by a noninfectious both exogenous and endogenous stimuli. The dysregulation of inflammasome activity is associated with numerous proinflammatory and nonmicrobial diseases in human including atopic dermatitis <sup>(6)</sup>.

The aim of the study is to clarify the possible participation of a certain IL (IL-1 beta) in the pathogenesis of atopic dermatitis.

### PATIENTS AND METHODS

This case-control study has been conducted in the Dermatology, Venereology and Andrology Department at Zagazig University Hospitals. The present study had been carried out on 60 individuals. Participants were divided into 2 groups, a diseased group, and a control

group as follows: Group A: 30 patients with Atopic dermatitis, 16 males and 14 females, and Group B: 30 apparently healthy individuals, 18 males, and 12 females.

**Inclusion criteria:**

1. The age of subjects of both sexes is from 10 to 35 years old.
2. 30 patients with persistent atopic dermatitis.
3. 30 healthy control of matched age and sex. They had no history of atopic dermatitis, or other inflammatory skin disorders.

**Exclusion criteria**

1. Patients who are receiving systemic or topical therapy for 6 weeks before their visit into our clinic.
2. Patients with chronic systemic diseases such as diabetes mellitus, hypertension, liver, renal or cardiac disease.
3. Patients with collagen vascular disorders.
4. Pregnant and lactating females.

**Ethical approval:**

An approval of the study was obtained from Zagazig University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of participation in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

All subjects in this study were subjected to the following before collecting the blood samples:

**1. Detailed history taking:**

- **Personal history:** Including; age, sex, occupation, and demographic data.
- **Present history:** Including; onset, course, and duration of the disease.

- **Drug history:** Including; a history of the previous and current treatment of atopic dermatitis.
- **Medical illnesses history:** Such as diabetes, hypertension, liver, renal disease, or others.
- **Family history** of atopic dermatitis.

**2. Dermatological examination:**

➤ **For patients with Atopic dermatitis:** The severity of atopic dermatitis was assessed according to **SCORing Atopic Dermatitis (SCORAD)** index. SCORAD index is a valid, interpretable composite score that combines the intensity of clinical signs of atopic dermatitis, the extent of them and the severity of its symptoms. They are calculated through a certain mathematical equation to give the final score of maximally 103<sup>(7)</sup>.

**3. Measurement of serum interleukin-1 beta.**

*Statistical analysis*

Data analysis was performed using the Statistical Package for the Social Sciences software (IBM Corporation, v. 20.0, Armonk, NY). Data were expressed as numbers and percentage for qualitative data and arithmetic mean ± Standard deviation (SD) for quantitative data. The differences in serum IL-B between control and diseased groups and between males and females were evaluated by one-way analysis of variance (ANOVA). ROC curve (Receiver operator characteristic curve) it is a graphic presentation of sensitivity against 1- specificity. It is done by comparing values of cases to detect a cutoff of certain outcome. When differences among them were found to be statistically significant (P<0.05), each group was compared with every other group using Turkey’s post hoc test. Correlation between serum IL-1β and variables was analyzed using Pearson’s correlation coefficients.

**RESULTS**

Age and serum IL-1β significantly varied between the 2 groups. Atopic patients tend to be significantly younger (**Table1**).

**Table (1): Demographic Data and Clinical Data of participants**

		Atopic N=30	Control N=30	P*
Age (years)		17.73±6.94	23.50±7.40	<0.001
Gender	Male	16 (53.33%)	18 (60%)	
	Female	14 (46.67%)	12 (40%)	
Duration (years)		9.83±5.69		
Severity		Mild=12 (38.71%) Moderate=12 (38.71%) Severe=6 (19.35%)		
Score		50.68±20.65		

Mean value of serum IL-β was significantly higher among atopic dermatitis than control (**Table 2**).

**Table (2): Comparison between serum IL-β in diseased versus control groups**

Serum IL-β	Atopic dermatitis	Control	P
	2455.67±286.34	717.78±28.43	<0.001

Age showed a non-significant positive correlation in atopic patients, and a non-significant negative one in control subjects. Also duration of the disease showed a non-significant positive one in atopic patients. However, the severity of the disease showed a significant positive correlation in atopic patients. Similarly, the disease score showed a significant strong positive correlation in atopic patients (Table 3).

**Table (3): Correlation of serum IL-β with other variables in atopic and control groups**

	Atopic		Control	
	r	p	r	p
Age	0.17	0.366	-0.08	0.690
Duration	0.15	0.432		
Severity	0.81	<0.001		
Score	0.86	<0.001		

Gender had no significant effect on serum IL-1β in the 2 groups as there was no significant difference in serum IL-1β between males and females in atopic or control group (Table 4).

**Table (4): Comparison of serum IL-1β according to gender**

	Male	Female	p
Atopic dermatitis	2376.06±126.73	2546.65±186.49	0.724
Control	691.83±95.18	747.45±65.83	0.515

There was a significant difference in serum IL-1β among the three degrees of severity in atopic patients. Serum IL-1β level had statistically significant higher levels in severe group (Table 5).

**Table (5): Comparison of serum IL-1β according to disease severity in atopic groups**

	Mild	Moderate	Severe	P*
Atopic dermatitis	1575.38±261.97	2300.70± 356.58	4526.19±1450.46	<0.001

While receiver operating characteristic curve analyses indicated that the area under the ROC curve was 1 (Table 6).

**Table (6): ROC curve analysis of serum IL-1β for detecting the presence of atopic dermatitis**

Cut off ( pg/ml)	P	AUC	Sensitivity %	Specificity %
1160.72	<0.001	1.00	100	100

## DISCUSSION

Our results revealed a significant elevation in serum IL-1β levels of AD patients compared to the control group. Similarly, Liu *et al.* <sup>(8)</sup> estimated the significant-high serum level of IL-1β in psoriatic patients before receiving the treatment with etanercept and its lowering in serum after 6 months of treatment. Also Tarentini *et al.* <sup>(9)</sup> stated that the IL-1β level in psoriatic skin lesions is significantly elevated more than it is in the normal skin biopsy.

Considering the demographic data in our results, gender had no significant effect on serum IL-1β in the 2 groups. At the same time, age showed a non-significant positive correlation in atopic patients and a non-significant negative one in control subjects.

In our study, the severity of the disease showed a significant positive correlation with IL-1β in atopic

patients. Similarly, the disease score showed a significant strong positive correlation with IL-1β in atopic patients.

Interestingly, we recorded from our results that serum IL-1β was significantly different according to the three degrees of severity of AD. On the contrary, we found that serum IL-1β was not significantly correlated with the disease duration in the atopic ones.

AbdelHay *et al.* <sup>(10)</sup> stated that IL-1β was significantly highly expressed in atopic patients, which could explain its role in the pathogenesis of AD. It was also found that IL-1β had a master role as an initiator of inflammation in AD. This study agreed with our results that gender had no significant effect on serum IL-1β in all patients of the tested group. At the same time, we disagreed when we have detected a significant

difference in serum IL-1 $\beta$  among the three degrees of severity in atopic patients.

Other studies like **Szymanski *et al.*** <sup>(11)</sup> reflected that keratinocytes isolated from AD patients had exhibited increased secretion of IL-1 $\beta$ , and further studies histochemically illustrated its main role in the pathogenesis of AD through inducing overexpression of TSLP in keratinocytes <sup>(12)</sup>.

**Schwartz *et al.*** <sup>(13)</sup> concluded that IL-1 $\beta$  plays a critical role in the initiation and maintenance of skin inflammation in a mutant mouse model of defective skin barrier. It stated also that IL-1 $\beta$  was significantly elevated in skin blisters of patients with AD that have FLG mutations and treatment with anti-IL-1 $\beta$ -antibody alleviated dermatitis exacerbation.

Another important study that used the ELISA technique to measure serum IL-1 $\beta$  in AD patients revealed consistent results to our study and cleared out that the IL-1 $\beta$  level in peripheral blood serum was higher in AD patients compared with healthy donors <sup>(14)</sup>.

Up to our knowledge, our current study is the first one to measure the serum level of IL-1 $\beta$  in patients with AD together in comparison to a healthy control group. Our results cleared with no doubt that serum IL-1 $\beta$  level rises significantly in this condition, unlike the healthy state, and this high level is closely related to the etiopathogenesis of AD and the initiation of the consequent inflammatory cascade at the level of different skin cell types.

Moreover, we interestingly found the positive correlation between serum level of IL-1 $\beta$  and the severity of these two diseases that is calculated by a specific scoring system, IL-1 $\beta$  is expected to be a target molecule in treating both diseases besides the concurrent available biological therapies.

## CONCLUSION

According to the data recorded in the literature and the current survey results, the augmented IL-1 $\beta$  serum level was found in patients with moderate to severe cases of atopic dermatitis, marking the systemic inflammatory nature of these diseases. The study suggested that IL-1 $\beta$  serum level significantly increases with atopic dermatitis diseases activity. On the other hand, IL-1 $\beta$  serum level was around normal values in the control group.

These mentioned findings were supported by the statistical evaluations on the relationship between serum IL-1 $\beta$  level, severity scores of AD (SCORAD score) and clinical observations. Moreover, serum IL-1 $\beta$  level was affected somehow by the duration of disease in the disease group but not affected by age nor gender. On this topic, measurement of serum IL-1 $\beta$  level could be used as both, diagnostic and prognostic marker for atopic dermatitis.

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