

The Sera levels of Interleukin-13 in Patients with Atopic Dermatitis in Thi-Qar province

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Abstract—The Interleukin-13 (IL-13) is a component of the innate immune system that is primarily produced by Th2 cells and is found in high concentrations in skin lesions of atopic dermatitis. The study comprised 90 people of both genders, 45 of whom were patients who attending to Al-Nassirya teaching Hospital, Dermatology, during a period between November 2021 to March 2022, and the same number served as controls. Blood samples were obtained from both groups, and the serum levels of IL-13 were estimated using an ELISA-ready kit. The findings of the current study referred that young adult, and the females gender were as more effective in Atopic Dermatitis, and the female to male ratio was 1.14: 1. On the other hand, the results indicated there were elevated sera levels of IL-13 in AD patients in contrast to the controls group. Also, there is no significant difference in IL-13 sera levels among patients groups regarding to severity of AD ($P > 0.05$). we concluded from a significant difference between the healthy control group and patients that IL-13 involved in the pathogenesis of AD.

Keywords— Atopic Dermatitis , Inflammation , IL-13

I. Introduction

Atopic dermatitis AD (atopic eczema) is a chronic inflammatory skin condition marked by severe itching and recurring eczematous lesions. Despite the fact that it is most frequent in childhood, affecting two out of every ten children, it is also highly common in adults. It is the most prevalent non-fatal skin infection, according to the WHO Global Burden of Diseases study, and it is a major cause of morbidity (Weidinger *et al.*, 2016).

Although the pathogenesis of AD is unknown, it is thought to be caused by a complex interplay of epidermal barrier malfunction, immunological dysregulation, and environmental and microbial factors (Otsuka *et al.*, 2017). The prevalence of AD has risen, with estimates ranging from 10–20 percent of children to 1–3 % of adults in developed nations (Ring *et al.*, 2019). AD often starts in childhood; roughly 45 percent of all cases begin during the first six months of life, 60 percent within the first year, and

85 percent before the age of five. Indeed, there will be a large number of newborns who will Children with AD have much increased transepidermal water loss on their second day of life, which is an excellent predictor of future food allergies (Li *et al.*, 2019).

IL-13 is a key regulator of multiple typical features of AD including epidermal hyperplasia, skin barrier failure, and the production of eosinophil and T cell chemokines, and it's produced at higher levels in lesional skin (Renert-Yuval and Guttman-Yassky, 2020).

IL-13 is a biologically active molecule that plays a central role in the inflammation underpinning the clinical manifestation of AD, such as itching and skin lesions (Wynn, 2003).

AD was formerly assumed to be a Th2 disease characterized by interleukin (IL-4) signaling. This belief stems from the fact that this cytokine was formerly assumed to play a role in regulating IgE production, which is normally high in most patients. However, more recent data has emerged that IL-13 is the primary cytokine implicated in AD inflammation. IL-13 is a physiologically active molecule that is involved in the inflammation that underpins the clinical signs of AD, such as itching and skin sores (Wynn, 2003).

II. MATERIALS AND METHODS

A. Design of Study

A total 90 participants of whom 45 were Atopic dermatitis (AD) patients from both genders [21 (46.67%) males, and 24 (53.33%) females] who attending to Al-Nassirya teaching Hospital, Dermatology, in the period between November 2021 to March 2022. In addition to 45 healthy individuals [29 (64.44%) males, and 16 (35.56%) females] non AD as a control group. The age range was (1-65 years).

B. Methods

Three ml of venous blood were collected in gel tubes and were allowed to clot at room temperature the sera were separated by centrifugation at 3000 rpm for 15 min to obtain sera and were stored at -20°C in the deep freeze. The serum levels of IL-13 were estimated using IL-13 ELISA-ready kit (Elabsience- USA).

C. Ethical permission

To conduct the study, The hospital, as well as all patients and healthy persons, gave their consent form to be signed. Dermatologists at the hospital assisted in the selection of patients.

D. Estimation of Atopic dermatitis severity

Atopic dermatitis patients was diagnosed by dermatology physician before take place in the current study. Patients were divided into three groups based on their severity. The degree of atopic dermatitis is characterized as mild, moderate, or severe, depending on the affected skin area, the severity of the skin lesion, and subjective symptoms (itch and insomnia), which is referred to as "SCORAD: SCORing Atopic Dermatitis".

E. Statistical Analysis

The Statistical analysis was done by using the SPSS program. It was determined at $P < 0.05$ and the results were shown as mean \pm SD. Student's t-test and one way ANOVA.

III. RESULT AND DISCUSSION

A. Distribution of AD Patients and Healthy People According to Gender

Figure(1) showed the investigation groups' descriptions. There were 90 Iraqi subjects in this study, 45 of them were atopic dermatitis patients 21 (46.67%) males, and 24 (53.33%) females, and there were 45 healthy individuals 29 (64.44%) males, and 16 (35.56%) females.

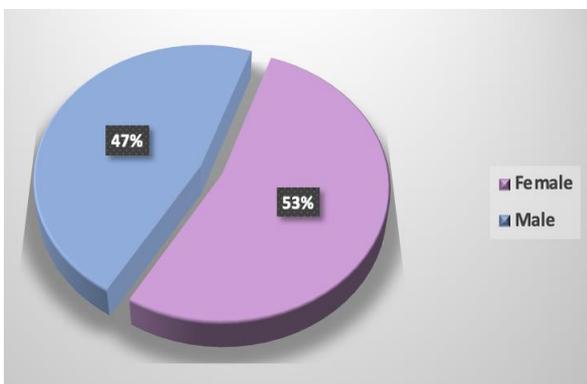


Figure (1): Distribution of AD Patients According to Gender

In this study distribution according to gender was found that the female to male ratio was 1.14:1, this finding agree with local paper by Al-Taei (2005) and Bahnan *et al.* (2019). Also, these results were consistent with those of a study conducted in Iran which also revealed a higher proportion of females (53.4%) compared to males (46.6%) (Kalmarzi, *et al.*, 2016). In addition, the current data agree relatively with other authors (Yu, *et al.*, 2012; Mina, *et al.*, 2015). While the result, disagree with Kim *et al.* (2012) who found that percentage of males is larger than females, and they were inconsistent with the Korean study which showed a higher proportion of males (51.8%) compared to females (48.2%) (Chu *et al.*, 2017).

Despite the prevalence of atopic dermatitis among male and female, the study result referred that female patient was more than male and this may be explained that the ratio of male to female varies depending on the criteria used in different studies and women in general are more frequent visitors to skin care clinics than men in search of medical advice. Also, Wang *et al.* (2004) study has concluded that female increasing percentage can be gained ongoing age due to intrinsic factors like hormonal changes during puberty and menstrual cycle and extrinsic factors such as contact with a lot of substances in their life that are prone to irritation, Inflammation and exposure to chemicals from cleaning material, cosmetic substance and dust mites from housekeeping works.

Work related skin disease is common and usually presents as hand eczema. According to studies, it is evident that females report skin disease more often than males (Obermeyer *et al.*, 2021). Epidemiological studies of hand eczema also showed that women are more often affected than men, in particular young women. The most common type of hand eczema is irritant contact dermatitis, which is often caused by wet work. Many female-dominated occupations involve extensive wet work, e.g., hairdressing, catering, cleaning and healthcare work.

These occupations are also high-risk occupations for hand eczema (Johansson *et al.*, 2022). Experimental studies of skin irritation have not confirmed differences between genders; thus, the higher prevalence of irritant contact dermatitis among females is most likely due to exposure, occupational and non-occupational. Nickel allergy is the most common contact allergy, which is most frequent in young females, Hand eczema has an impact on quality of life and females seem to report a higher degree of discomfort than males (Rautiainen and Reynolds, 2002).

B. Distribution of AD Patients According to Severity

Patients were divided into three categories according to severity by using the SCORAD index as shown in Figure -2, 23 patients (51.11%) were mild AD patients, 17 (37.78%) were moderate AD patients, and 5 (11.11%) were patients with severe AD.

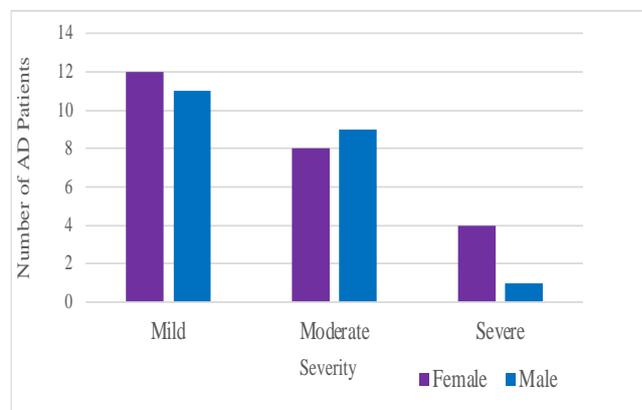


Figure (2): Distribution of Atopic Dermatitis Patients



Figure (3): Signs of Atopic dermatitis in the study patients; A: Redness, B: Oozing and Crusting, C: Skin Thickening/ Lichenification, and D: Scratch Marks.

Figure (3) showed signs of Atopic dermatitis in this study patients. The patients were divided into three groups according to SCORAD index results:

I- **Mild AD:** which included 23 patients (12 females and 11 males).

II- **Moderate AD:** which included 17 patients (8 females and 9 males).

III- **Severe AD:** which included 5 patients (4 females and 1 male).

The differences in which AD patients are sub-grouped, results from different reasons such as specific immunologic stimuli including food, aeroallergens and elicitation of AD by infection of the skin with different microorganisms as well as continuous exposure to irritants and a combined influence of a specific group of cytokine genes that are thought to be important immunological mechanisms in the pathogenesis of AD (Leung *et al.*, 2004).

C. Distribution of AD Patients According to Body Mass Index

The results of this study as seen in Figure (4), showed a high percentage of AD according to BMI in the healthy group, it may be due to the random collection of patients' samples in different age groups. patients' samples in different age groups.

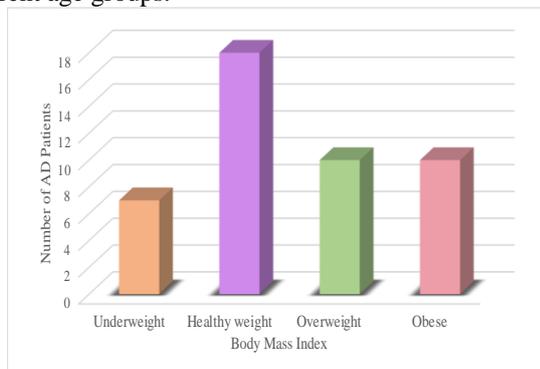


Figure (4): IL-13 levels in AD patients according to BMI

A previous study suggested that BMI may have a causal role in the development of AD which founded evidence of a small overall association between atopic eczema and being overweight or obese. However, there was no association with obesity among those with the most severe eczema (Ascott *et al.*, 2021).

2. Serum Levels of Interleukin 13 (IL-13)

In order to clarify the clinical significance of serum IL-13, the serum IL-13 concentration was measured in AD patients and compared to healthy controls. Patients with AD showed an elevated mean sera levels of IL-13 (33.25 pg/ml), as compared with the healthy control (21.64 pg/ml), there was a significant difference between the healthy control group and patients ($p \leq 0.05$) as seen in Table (1).

Table (1): Sera levels of IL-13 in patients and healthy.

Groups	No.	IL-13 Mean \pm SD
Patient	45	33.25 \pm 3.01
Control	45	21.64 \pm 1.93
P value		0.000*
T-test value		21.811

A higher mean concentration was observed for total AD patients compared to control. These findings were in agreement with previous studies (Terao *et al.*, 2003; Morsiet *et al.*, 2005) in which serum IL-13 concentration was increased in AD patients. These results indicated that this cytokine might exert a direct systemic effect on AD disease.

The results of this study in conjunction with the previous studies described above showed that IL-13 plays a role in decreased skin barrier function and chronic inflammation through several cellular or molecular mechanisms thus considered to play an important role in the pathogenesis of AD and as a potential therapeutic target for AD in the future (Hijnenet *et al.*, 2013).

Previous studies have shown that skin barrier defects, a decrease in antimicrobial peptides, increased skin pH, or Th2 cytokines such as IL-4 and IL-13 are potential contributing factors to the increased risk of skin infections in AD (Ong and Leung, 2016b).

The relationship between sera means levels of IL-13 and groups of patients with atopic dermatitis according to severity showed an increased mean levels of IL-13 (33.76 pg/ml) in patients with mild AD with no significant difference as compared with patients with both moderate and severe AD (32.93 pg/ml, $p = 0.41$) and (31.97 pg/ml, $p = 0.26$) respectively. Also, there was no significant difference in mean levels of IL-13 between moderate and severe AD patients ($p = 0.49$) as shown in Table (2). The results revealed

an increase in the levels of IL-13 in mild AD patients compared with others groups with no significant differences and followed by patients suffering from moderate AD.

Table (2): Serum levels of IL-13 in patients' groups

Groups	NO.	Mean ± S.D	Comparisons	p value	T-test value
Mild	23	33.76 ± 3.32	Mild-Moderate	0.41	0.833
Moderate	17	32.93 ± 2.83	Moderate-Severe	0.49	0.703
Severe	5	31.99 ± 1.66	Mild-Severe	0.26	1.152

Recently, IL-4 and IL-13 have also been shown to promote the neurogenic itch by acting directly on pruritogenic sensory neurons and via IL-31 interaction. IL-4 and IL-13 cytokines contribute substantially to the barrier impairment seen in AD. They have been shown to downregulate filaggrin and loricrin, crucial proteins expressed in the skin barrier, compromising the structure of the skin, the ability of the barrier to protect against pathogens and allergens, and the ability to maintain an adequate amount of moisture in the skin surface. IL-4 and IL-13 act on keratinocytes in the epidermis, causing hyperplasia as well as attenuated differentiation, preventing their complete maturation. IL-13 also reduces the expression of skin barrier proteins and lipids via its impact on keratinocytes, mediated by the expression of MMP-9. Thus, IL-4 and IL-13 play an integral role in the Th2 immune response in AD, contributing to both immune activation as well as skin barrier dysfunction (Dubin *et al.*, 2021). In conclusion according to the findings of this study, IL-13 levels were higher in patients with AD. These findings indicated that this marker involved in AD pathogenesis .

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