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REVIEW ARTICLE

Serum Level of IL-4 and IL-13 and Their Association with Disease Pathogenesis in Patients with Eczema

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Abstract:

Background: As the most common chronic skin illness with a genetic foundation, eczema is an inflammatory skin condition driven by cytokines. People with AD suffer from a significant burden that affects their physical, mental, social, and financial well-being. The cytokines are important in eczema disease. Interleukins regulate immunity. Lack impairs immunity or causes autoimmune disorders.

Objectives: This study is aiming to investigate whether inflammatory cytokine (IL-4, IL-13) levels in the blood correlate with eczema disorder.

Methods: This case-control study is based on 60 patients who have been diagnosed with eczema disorder with a 60-person apparently healthy control group. 4 ml of blood samples have been collected from each individual by using a sterile syringe under aseptic conditions and collected in a gel tube for serum separation. The serum levels of IL4 and IL13 IL4,IL13,were measured using the sandwich ELISA method according to the instruction manual.

Results: According to the research findings, individuals with eczema disorder had considerably higher levels of IL-4 and IL-13 (P = 0.001). A positive correlation between IL-4 and IL-13 levels has also been demonstrated, which may indicate that these changes play a role in the development of eczema disease.

Conclusions: This study established that the levels of IL-4 and IL-13 are strongly related with the risk of eczema in individuals in Diwaniyah Province, Iraq.

Keywords: atopic dermatitis (AD), interleukins (IL)

Introduction

Eczema, sometimes referred to as atopic dermatitis (AD), is an inflammatory skin disorder that affects the skin's ability to retain moisture and form a barrier. AD is the most common chronic skin disease that is inherited, and its effects on a person's physical, mental, social, and financial well-being are significant [1]. Eczema prevalence varies across the world; in industrialized countries, it is estimated that up to 20% of children and 3% of adults have the condition. Although the exact number of causes of eczema is unknown, new research has revealed that immunological factors are one of the disease's causes. [2]. There are three primary clinical patterns for atopic dermatitis: acute, subacute, and chronic [3, 4]. The pH of the skin may be adversely affected by the use of abrasive alkaline cleansers in skin care products, changing the skin's composition and encouraging inflammation. Environmental contaminants can activate both innate and adaptive immunity mechanisms. stress, humidity, and temperature [5]. Interleukins IL are proteins that have the ability to promote cell growth, differentiation, and functional activation. There is a common pathogenic mechanism that underlies many atopic illnesses, and the cytokines IL-4 and IL-13 play a key role in controlling this pathogenesis [6]. Interleukin-4 is a key cytokine for helper T cell subset 2 [7]. IL-4 is involved in numerous immunological and, to a greater and greater extent, non-immune processes [8]. Moreover, using an in vitro AD method, IL-4 modifies the cell's extracellular lipids in a way that is similar to the aberrant stratum corneum lipid structure seen in actual AD skin [9]. Recent studies have shown that the significant expression of IL-4 in skin lesions, especially in long-term AD lesions, supports the notion that IL-4 plays a critical role in the pathogenesis of AD at an early stage. [10, 11]. One type 2 T helper cytokine is IL-13 [12]. Although Th2 cells are primarily responsible for producing IL-13, mast cells and basophils can also produce it [13, 14]. Interleukin (IL)-13 could have an important function in the etiology of AD, according to recent research [15]. This study aims. Determining IL-4 and IL-

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13 in serum of both patients and the control group.

Materials and Methods

The case-control study was conducted by recruiting 60 patients with eczema and 60 apparently healthy individuals to evaluate the association between IL-4 and IL-13 levels and eczema. All participants visited the dermatology clinic at Al-Diwaniyah Teaching Hospital between October 2024 and the end of February 2025, where they were clinically examined by a dermatologist. A questionnaire was completed for both groups, including information such as name, age, sex, and family history. Ethical approval for this study was obtained from the College of Medicine, University of Al-Qadisiyah.

Blood sample collection

Using a disposable syringe, 4 mL of venous blood was drawn into a gel tube under aseptic conditions. After allowing the blood to clot, the serum was extracted using centrifugation for five minutes at 3000 rpm. The mixture was separated into tiny Eppendorf tubes to conduct immunological tests to measure the concentrations of IL-4 and IL-13 levels in both eczema patients and apparently healthy group samples.

In the current study

The Elabscience ELISA kits IL-4 (Cat. No. E-EL-H0101) and IL-13 (Cat. No. E-EL-H0104) were used based on the Sandwich ELISA principle. The micro ELISA plate provided in the kits was pre-coated with an antibody specific to human IL-4 and IL-13. The samples or standards were added to the wells and bound to the specific pre-coated antibodies. Then, a biotinylated detection antibody specific for human IL-4 and IL-13, followed by an avidin-conjugated horseradish peroxidase (HRP), was added to the wells and incubated. Unbound components were washed away. A substrate solution was then added to the wells. Only wells that contained IL-4 or IL-13, the biotinylated detection antibody, and the avidin-HRP conjugate developed a blue color. The enzyme-substrate reaction was terminated by the addition of a stop solution, turning the color to yellow. The optical density (OD) was measured at 450 nm using a spectrophotometer. The OD value was directly proportional to the concentration of human IL-4 and IL-13 in the sample. The concentration was calculated by comparing the sample OD values to the standard curve.

The statistical analysis

Excel 2010 and SPSS 26 were used in the study to collect, process, and display quantitative data. The normal distribution of the variables was evaluated using the Kolmogorov-Smirnov normality test. Group means were compared using independent sample t-tests. Group means were compared using ANOVA testing. To examine relationships between categorical data, the chi-square test was employed. A 95% confidence interval and odds ratio were used to assess the risk. The numerical variables were evaluated using the Pearson correlation coefficient. The significant level was evaluated using the receiver operator characteristic (ROC) curve [16].

Ethical approval

The Ethics Committee of the College of Medicine, University of Al-Qadisiyah, Diwaniyah, Iraq, granted clearance for this study on September 30, 2024, under approval number 4047. The Declaration of Helsinki's ethical guidelines were followed when conducting the study. Before being included, each participant provided written informed permission. All personal information was kept completely private and used only for research.

Results

In this study, 60 people with eczema and 60 healthy ones as controls were included. Table (1) shows their age and other info. The average age of patients was 34.70±7.61 years, and controls had 36.56±7.25 years. There was no big age difference between the two groups (P=0.701). Age group distribution also didn't show any real difference (P=0.841), which agrees with other research.

About sex, 15 (25%) of the eczema group were male and 45 (75%) female. In the control group, 20 (33.3%) were male and 40 (66.7%) female. No big sex difference (P=0.315). For residency, most patients (55 or 91.7%) were from cities and 5 (8.3%) from villages. In the control group, 48 (80%) were urban and 12 (20%) rural. Still, no clear difference (P=0.067). So overall, both groups were matched in age, sex, and where they lived—which is important for this type of study.

Table (1): Demographic Profile of Eczema Patients and Healthy Control Group.

Characteristic	Eczema Patients n = 60	Healthy control n = 60	P
Age (years)			
Mean ±SD	34.70 ± 7.61	36.56 ± 7.25	0.701 †NS
< 30 years, n	28 (46.7%)	25 (41.7%)	0.841 ¥ NS
30-39 years, n	8 (13.3%)	8 (13.3%)	
≥ 40 years	24 (40.0%)	27 (45.0%)	
Sex			
Male, n (%)	15 (25.0%)	20 (33.3%)	0.315 ¥ NS
Female, n (%)	45 (75.0%)	40 (66.7%)	
Residency			
Urban, n (%)	55 (91.7%)	48 (80.0%)	0.067 ¥ NS
Rural, n (%)	5 (8.3%)	12 (20.0%)	

n: number of cases; SD: standard deviation; †: independent samples t-test; ¥: Chi-square test; NS: not significant at P > 0.05.

Distribution according to severity

The frequency distribution of eczema patients according to severity was shown in figure (1), as follows: 30 (50.0%) of eczema patients were mild cases, 22 (36.7%) of eczema patients were severe cases, and only 8 (13.3%) of eczema patients were moderate cases, and the difference was significant (p=0.002).

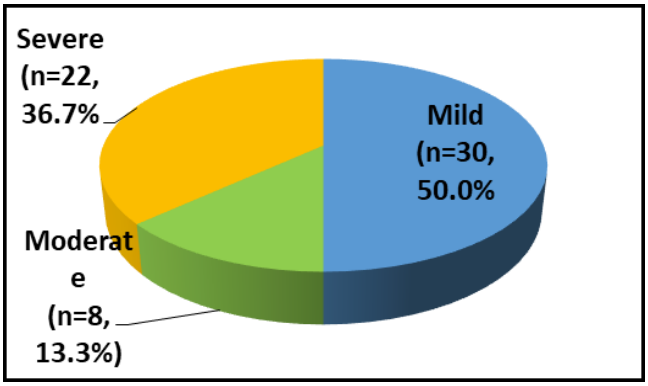

Figure (1): Distribution of patients according to severity

Pro-inflammatory Cytokine (IL-4 and IL-13) Analysis Results

Table 2 displays a comparison of the blood levels of IL-4 and IL-13 between the patient group and the control group. The patients' group had considerably greater mean serum IL4 than the control group (P = 0.001). The patients' group had a considerably greater mean serum IL-13 than the control group (p = 0.001).

Table (2): Comparison of the patients' group and the control group's serum concentrations of IL-4 and IL-13.

Characteristic	Patients Group N = 60	Control Group N = 60	P
Serum IL-4 (pg/ml) level			
Mean ±SD	86.37 ± 11.1 (pg/ml)	32.15 ± 7.4 (pg/ml)	0.001** † HS
Range	65.21-121.00	15.68-49.00	
SerumIL-13 (pg/ml) level			
Mean ±SD	38.51 ± 3.93 (pg/ml)	16.46 ± 5.7 (pg/ml)	0.001** † HS
Range	30.26-47.26	9.82-31.20	

SD: standard deviation; †: Independent T test; **: significant at P >0.05

Logistic regression correlations between IL4 and IL13. The logistic regression model shows that the correlation serum parameter, such as IL-4, directly correlates with IL-13 among eczema patients, as in figure (4). This result might refer to the fact that the eczema condition enhances the production of IL-4 in relation to the expression of IL-13.

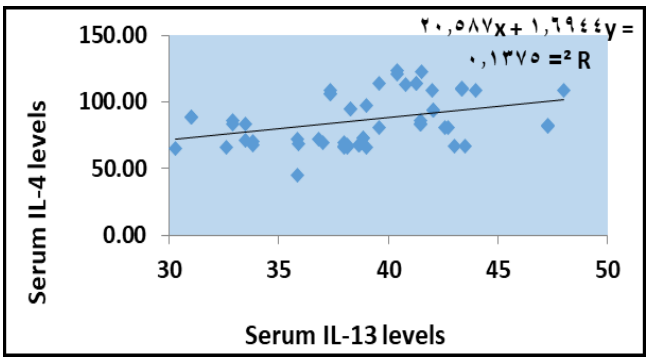

Figure (2): The Logestic scatter IL-4 and IL-13 levels among patients.

Correlation between immunological in eczema patients. The correlation between immunological in eczema patients was shown in tables (3). In patients with eczema, there is a positive association between IL-4 and IL-13 levels (r=0.377 and p=0.003).

Table (3): Correlation between immunological factors in eczema patients.

Parameters	IL-4		IL-13	
	R	P	R	P
IL-4	1			
IL-13	0.377	0.003*	1	

r: correlation coefficient.

Discussion

Concerning sex and its relation to AD, several authors gave controversial results. They either found that females are more prone than males to AD, or some reported the reverse result, while others described similar sex distribution and suggested no difference. Our finding is comparable to that reported by [17]. But our finding disagrees sharply with. [18], who discovered that the proportion of men is higher than that of women. The severity of AD in infants is connected with factors such as the duration of nursing, exposure to cigarette smoke, dietary allergens, atopy in the family, aeroallergen sensitivity, high serum total IgE level, eosinophilia, and poor socioeconomic status [19]. showed that, independent of any other possible risk factors, eczema that started in the first year of life, was accompanied by asthma, hay fever, or both, and was connected to living in an urban setting was linked to a more severe disease [20]. Severe atopic dermatitis is linked to factors such as advanced maternal age, a previous cesarean delivery, the use of an incubator, and winter births [21].

According to the current study, the mean levels of IL-4 in the eczema patients and healthy control groups were 86.37 ± 11.1 (pg/ml) and 32.15 ± 7.4 (pg/ml), respectively; the difference between the two groups was significant (P=0.001). According to the current findings, eczema sufferers' mean levels of IL-4 are much higher than those of seemingly healthy individuals. Similarly, a separate study conducted in Anbar and Babylon Provinces, Iraq, found that eczema patients had significantly higher serum IL-4 levels than the healthy group. This substantial difference highlights the role of IL-4 in the pathogenesis of eczema [22, 23, and 2]. Our findings are consistent with those of Kyoko Kaminishi et al., who found a significant increase in IL-4 levels in the blood; these data taken together suggested that the pathogenetic process of AD may be significantly influenced by the predominance of Th2 cells and the resulting overexpression of IL-4 in peripheral blood [24].

Eczema patients had higher mean levels of IL-13 than healthy controls, with a significant difference (P=0.001) between the two groups. The mean levels of IL-13 were 38.51 ± 3.93 and 16.46 ± 5.7, respectively. According to the current findings, eczema sufferers' mean levels of IL-13 are much higher than those of seemingly healthy individuals. According to a similar study, eczema sufferers' blood IL-13 levels were substantially greater than those of the healthy group in the Thi-Qar region of Iraq. This significant variation emphasizes how IL-13 contributes to the pathophysiology of eczema. [17]. IL-13 is a pleiotropic cytokine that was first cloned from activated human T-lymphocytes. Human mast cells, basophils, alveolar macrophages, B lymphocytes, and activated Th2 cells can all release IL-13 [25].

The current results of this study demonstrated a positive relationship between IL-4 and IL-13 in ECZEMA disease, and this is consistent with the results of the previous studies [22, 26].

In most people with atopic dermatitis, the IgE level in blood is really high. That's why IL-4 was thought for a long time to be the main cytokine causing AD, since it helps control IgE making. But now, more studies show IL-13 might actually be more important than IL-4 in AD inflammation [27, 28]. New treatments with biologics also point to IL-13 playing a bigger role. Both IL-4 and IL-13 act on skin cells (keratinocytes), making them grow too much and not fully mature. IL-13 also lowers the amount of skin barrier proteins and fats by affecting keratinocytes through something called MMP-9. So, IL-4 and IL-13 are key parts of the Th2 immune response in AD; they trigger immune reactions and also damage the skin barrier [26].

Conclusion: This study suggests that both cytokines (IL4 and IL13) contribute to the pathogenesis of the eczema disorder, and there was a statistically significant correlation between them and eczema patients. These cytokines may be used as prognostic markers, depending on the ROC curve.

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Conflicts of interest

A lack of disputes among interests exists.

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