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Study the impact of the Interleukins and Vit.E in patients with Atopic Eczema in Anbar Governorate

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ABSTRACT

Background: Atopic dermatitis (AD), also referred to as atopic eczema, is a type of inflammatory skin disease that affects the skin's moisture-retention ability and skin barrier. It has been demonstrated in animal models that IL-4 is both required for the genesis of AD and capable of eliciting every histological sign of the disease. IgE levels rise, inflammation within the skin intensifies, pathogenic bacteria skin infections are encouraged, and pruritus is mediated when IL-4 is overexpressed. Prior studies have indicated that IL-13 plays a crucial role in the pathophysiology of AD, especially when it comes to a number of disease-causing factors such as the degeneration of the skin barrier, thickening of the epidermis, itching, inflammation, and infection. In cell membranes, vitamin E functions as an antioxidant. Nonetheless, research has demonstrated its connection to the skin, and deficiencies are visible in the majority of skin conditions, such as atopic dermatitis.

Methods: We included 75 AD patients, 25 of whom were infants, 25 of whom were children, and 25 of whom were adults. ((51)) healthy controls were divided into 17 infants, 17 children, and 17 adults who were unaffected by the illness and had no prior history of AD. Serum levels of vitamin E, interleukin-13, and interleukin-4 are measured.

Results: Compared to controls, serum levels of interleukin-4 and interleukin-13 were considerably higher in AD patients, while serum levels of vitamin E were significantly lower in AD patients.

Introduction

Eczema, also known as atopic dermatitis (AD): a typical chronic disorder of the skin that compromises skin's barrier function and moisture absorption capacity [1]. The disease has a serious negative influence on the physical, mental, social, and economic well-being of patients as well as their families. Innovations and access to new medications are still vital despite recent improvements in our understanding of and ability to treat the disease. A lot of people find it difficult to control their medical issues [2]. Up to 85% of AD patients report that their symptoms began before the age of five, and 50% of patients report having more allergy symptoms during the first year of life [3].

Atopic dermatitis (AD) and allergic illnesses have been linked to filaggrin, a significant epidermal protein [4]. The epidermal barrier is compromised in AD due to firagrin deficiency [5]. Comprehending environmental diversity is crucial for identifying disease phenotypes [6]. Scoring systems indicate that just 10% of people have a severe form of AD, 20% have a moderate form, and 70% have a mild form [7]. Except for their thighs and buttocks, most of their body is covered in blisters that itch or dry, scaly skin that is blistering [8]. Atopic dermatitis can be categorized into three main clinical patterns: acute, sub-acute, and chronic [9,10]. 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

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and adaptive immunity mechanisms. stress, humidity, and temperature [11].

Atopic dermatitis and interleukins, such as IL-13 and IL-4, are strongly associated. Proteins called interleukins (IL) can stimulate cell division, proliferation, and functional activation [12]. Interleukin-4 is a key cytokine for helper T cell subset 2 [13]. IL-4 is involved in numerous immunological and, to a greater and greater extent, non-immune processes [14]. 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 [15]. According to recent research, the idea that IL-4 plays a crucial role in the pathogenesis of AD at an early stage is supported by the substantial expression of IL-4 in skin lesions particularly rises in long-term AD lesions [16, 17]. One type 2 T-helper cytokine is IL-13 [18]. Although Th2 cells are primarily responsible for producing IL-13, mast cells and basophils can also produce it [19, 20]. Interleukin (IL)-13 could have an important function in etiology of AD, according to recent research [21].

A recent publication has connected levels of circulating eosinophils, total serum IgE, and IL-13, a biomarker of AD detected in skin samples, to the severity of the disease. Furthermore, elevated cutaneous IL13 levels have been associated with a number of atopic stigmata, such as thinning of the lateral brow (the Hertoghe sign) and maternal atopic rhinitis [22]. Similar to the decreased expression of filaggrin seen in acute AD lesions, keratinocytes grown *in vitro* in the presence of IL-4 and IL-13 show considerably less filaggrin expression than healthy skin [23, 24]. Controlling host immunological processes is one of the many functions of vitamin E, an efficient antioxidant [25]. The body's primary lipid-soluble antioxidant is vitamin E, which also has antioxidant properties in cell membranes that prevent the propagation of free radical reactions [26].

A class of tocopherols and tocotrienols, with the highest biological activity being α-tocopherol, is referred to as vitamin E [27]. Transport proteins involved in signal transduction or the enzymes that make lipid mediators can both directly bind vitamin E. Vitamin E may modify the performance of signal transduction enzymes by influencing the interaction of protein chains in the membrane and the transportation of enzymes to the membrane of the plasma [28]. Vegetable oils are one of the main nutritional sources of vitamin E. Vitamin E can also be found in nuts [29]. Soybeans. sunflower, corn, walnuts, cottonseeds, palms, and the bran of rice, peanut, and wheat germ oils contain comparatively higher vitamin E contents than other oils. [29,30]

In order to identify certain interleukins and vitamin E as pathological markers of AD in the Anbar Governorate, the current study set out to measure these amounts in serum.

2.(Materials and methods)

The Fallujah Maternity and Children Hospital's laboratory served as the study's location (Since infants may suffer from eczema) from December 2022 to June 2023. 52 controls and 75 cases were included in the study. In this study, there were 17 healthy Infants ranging in age from 1 to 12 months, Seventeen children with good health, their ages between two to twelve years, and 17 healthy people with age between 12 to 68 years. Additionally, 25 patients' Infants, whose ages varied from 1 to 12 months, and 25 patients' children, whose ages ranged from 2 to 12 years, were incorporated into the research.

Samples were collected from the governorate of AL-Anbar. Every patient completed a thorough questionnaire with their name, age, gender, the spot of the injury on their body, and any past medical conditions on it. Every patient verbally consented to take part in research. The person's blood (Five milliliters) was meticulously drawn from their veins and placed in straightforward disposable tubes. Venous blood samples were taken using gel tubes. Serum samples were produced by centrifuging samples in gel tubes for ten to fifteen minutes at 3000 rpm after they had been allowed to coagulate for ten to fifteen minutes at 37°C. The separated serum samples were then stored at -20°C, then biochemistry analysis was down. Sun Long Biotech Co.LT (China) assessed the serum levels of various parameters (interleukin-4, interleukin-13, and vitamin E) using the method known as ELISA.

Statistics analysis

Results were presented as mean ± SD after the data were analyzed using linear regression analysis. A statistical analysis was performed by SPSS (23.0 version). Significance statistical definition was a ($p < 0.05$).

.3. Results and discussion

Interleukin-4 (ng/ml): Infants patients had a significantly higher level of the protein (24.955 ± 11.963) than the control group (11.538 ± 5.211) ($p < 0.001$). Furthermore, compared to control group (16.426 ± 4.356), there was a substantial increase ($p < 0.001$) in children's patient group (24.045 ± 8.221). In the adult group as well, the patients' scores (27.243 ± 4.965) were considerably greater ($p < 0.001$) than control group (17.699 ± 5.401).

Interleukin-13 (ng/ml): Compared to the control group (27.327± 10.140), the Infants group ($p < 0.001$) patients had a significantly higher level of interleukin-13 (41.206 ± 13.914). Furthermore, compared to the control group (37.599 ± 8.088), there was a substantial increase ($p < 0.001$) in the number of patients in the children's group (48.472 ± 19.162). The results also revealed a significant increase ($p < 0.001$) between the patients (42.802 ± 12.895) and the control group (32.466 ± 9.821) in the adults group.

Vitamin E (pg/ml): Infants patients (0.64 ± 0.218) had a notably lower vitamin E concentration than the group under control. (28.499 ± 12.214) ($p < 0.001$). Furthermore, a substantial ($p < 0.001$) reduction in the number of patients (0.623 ± 0.241) compared to the control group (23.186 ± 11.787) was observed in the children's group. Additionally, in the adult group, the results revealed that the patients' (0.573 ± 0.242) weight was significantly lower than that of the control group (21.662 ± 7.365) ($p < 0.001$). The outcome as displayed in Figures 1, 2, and 3 and Tables 1, 2, and 3.

Table (1) Mean ± Standard Deviation of Interleukin-4 concentration

interleukin-4 (ng/mL)	Control	Patient	*P*-value
	Mean ± SD	Mean ± SD	
Infants	11.538 ± 5.211	24.955 ± 11.963	0.001
Children	16.426 ± 4.356	24.045 ± 8.221	0.001
Adults	17.699 ± 5.401	27.243 ± 4.965	0.001

Table (2) Mean ± Standard Deviation of Interleukin-13 concentration

interleukin-13 (ng/mL)	Control	Patient	*P*-value
	Mean ± SD	Mean ± SD	
Infants	27.327 ± 10.140)	41.206 ± 13.914	0.001
Children	37.599 ± 8.088)	48.472 ± 19.162	0.001
Adults	32.466 ± 9.821)	42.802 ± 12.895	0.001

Table (3) Mean ± Standard Deviation of Vitamin E concentration

Vitamin E (ng/mL)	Control	Patient	*P*-value
	Mean ± SD	Mean ± SD	
Infants	28.499 ± 12.214	0.64 ± 0.218	0.001
Child	23.186 ± 11.787	0.623 ± 0.241	0.001
Adults	21.662 ± 7.365	0.573 ± 0.242	0.001

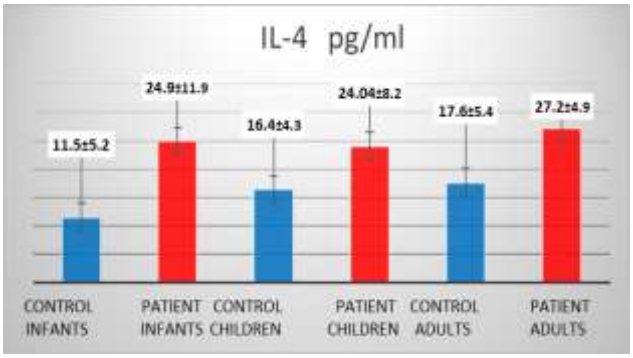

Figure (1): Mean ± S. D for IL-4 concentration

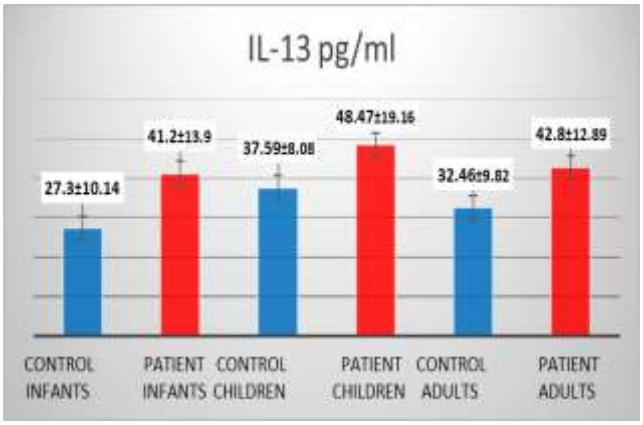

Figure (2): Mean ± S. D for IL-13 concentration

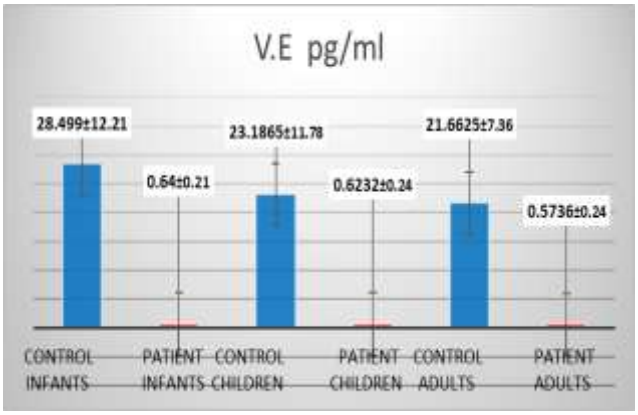

Figure (3): Mean ± S. D Vit. E concentration

Person's analysis of infant's stages, results of the linear regression analysis show that, in the group of infants with atopic eczema, there is a strong positive connection (r = 0.868) between the serum concentration of IL-13 and IL-4, as well as a substantial negative association (r = -0.505) between the serum concentration of Vitamin E and IL-4. These relationships are displayed in Figure (4,5) and Table (4).

Table (4): Correlation between IL-4 with IL-13 and Vit.E

Parameters	Correlation coefficient R	*P*-value
IL-13 (ng/mL)	0.868	0.001
Vit. E (ng/mL)	-0.505	0.001

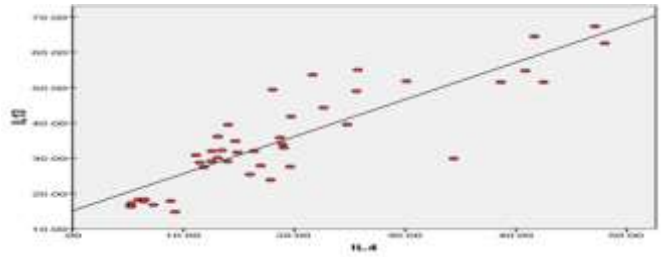

Figure (4) Correlation between IL-4 with IL-13

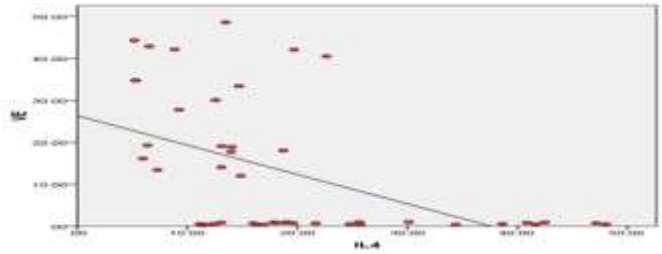

Figure (5) Correlation between IL-4 with Vit. E

Additionally, the results of the linear regression analysis show that, in the infant group with atopic eczema, there is a weak negative correlation ($p < 0.05$), with r = (-0.444), between the serum (vit. E) level and IL-13. These relationships are displayed in Figure (6) and Table (5).

Table (5): Correlation between IL-13 with Vit. E

Parameters	Correlation coefficient R	*P*-value
Vit. E (ng/mL)	-0.444	0.002

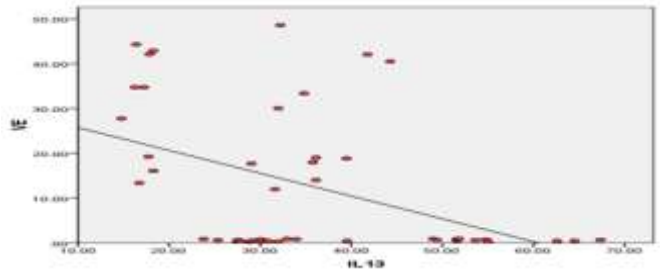

Figure (6) Correlation between IL-13 with Vit. E in infants' patient group

Furthermore, the outcomes of the linear regression analysis show that, in the children with atopic eczema patient group, there is a not strong negative association ($p < 0.05$), r = (-0.359), between the serum (Vit. E) level and IL-4, and a significant positive correlation ($p < 0.05$), r = (0.842), between the two. Table displays these relationships (6).as well as Figure (7).

Table (6) Correlation between IL-4 with (IL-13 and Vit. E) in children patient group

Parameters	Correlation coefficient R	*P*-value
IL-13 (ng/mL)	0.842	0.001
Vit. E (ng/mL)	-0.359	0.016

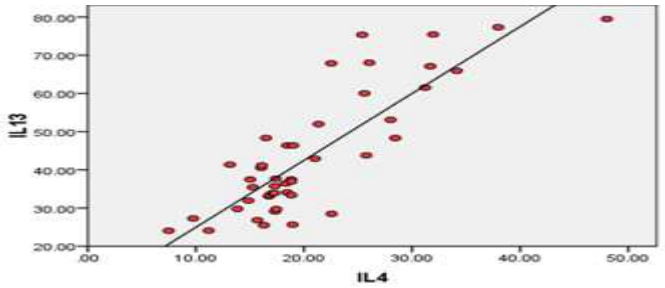

Figure (7) Correlation between IL-4 with IL-13 in patient children group

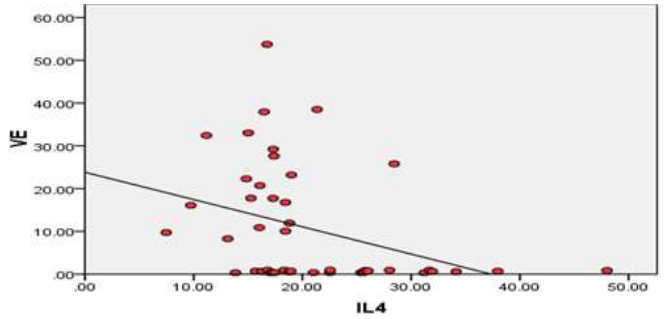

Figure (8) Correlation between IL-4 with Vit.E in patient children group

Further, IL-13 and (Vit. E) did not significantly correlate in the group of children with atopic eczema, according to this study. These connections can be shown in Figure 9 and Table (7).

Table (7) Correlation between IL-13 with Vit. E in patient children group

Parameters	Correlation coefficient R	*P*-value
Vit. E (ng/mL)	-0.262	0.082 NS

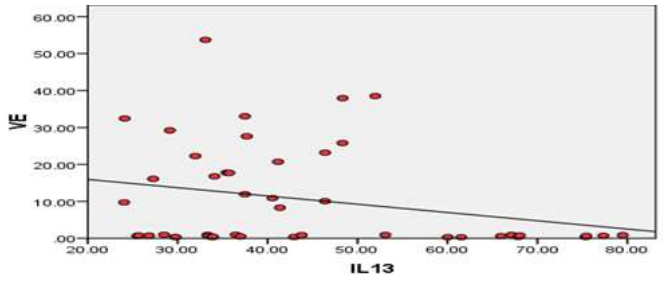

Figure (9) Correlation between IL-13 with Vit E in patient children group

Similarly, a linear regression analysis of the study's data revealed that, in the group consisting of adults with atopic eczema, there is a strong positive association ($p < 0.05$), $r = (0.673)$, between the serum (IL-13) concentration and IL-4, as well as a significant adverse relationship ($p < 0.05$), $r = (-0.549)$, between the serum (Vit E) concentration and IL-4. Table (8) and Figures (10 and 11) demonstrate these connections.

Table (8) Correlation between IL-4 with (IL-13 and Vit.E) in patient adults group

Parameters	Correlation coefficient R	*P*-value
IL-13 (ng/mL)	0.673	0.001
Vit. E (ng/mL)	-0.549	0.001

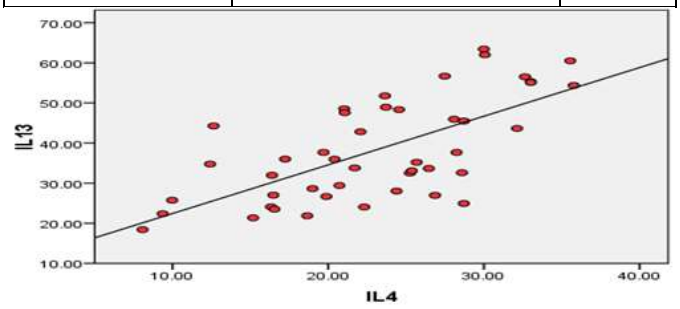

Figure (10) Correlation between IL-4 with IL-13 in patient adults group

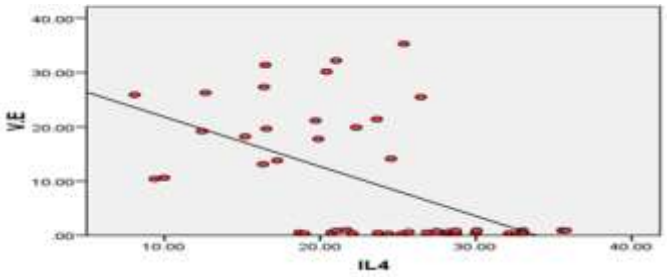

Figure (11) Correlation between IL-4 with Vit E patient adults group

Moreover, the results of the linear regression analysis show that the content of vitamin E in the serum and IL-13 have a weakly negative correlation ($p < 0.05$), with $r = (-0.318)$. These associations are displayed in Figure (12) and Table (9).

Table (9) Correlation between IL-13 with Vit. E in the atopic eczema patient adults' group

Parameters	Correlation coefficient R	*P*-value
Vit. E (ng/mL)	-0.318	0.033

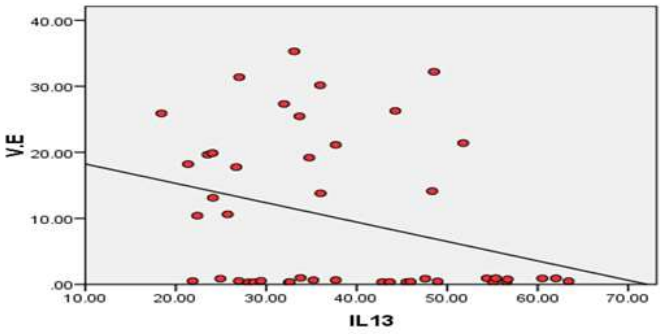

Figure (12) Correlation between IL-13 with Vit. E in patient adults group

The cytokine interleukin-4 (IL-4) is produced by mast cells, basophils, and T helper type 2 cells. That cytokine is connected to pathological conditions including allergies and asthma in addition to its physiological roles. The body uses inflammatory mediators called cytokines, or inflammatory mediators, to fight off infections and other external dangers [31]. Although the multifunctional cytokine (IL-4) is necessary to regulate immune responses, it is more successful in limiting the expansion of TH2, which may lead to an increase in cytokine levels. replying to multiple cases, numerous of which have links to allergies, asthma, and autoimmune suppression [32, 33].

Our results align with those of Kyoko Kaminishi et al., who observed a notable rise in IL-4 levels in the blood. Collectively, these findings imply that Th2 cell predominance and the consequent overexpression of IL-4 in peripheral blood may have a significant impact on the pathogenetic process of AD [34]. Khaldon Bodoor et al. state that they investigated into the role of IL-4 in AD. Compared to controls, patients with atopic dermatitis showed greater serum levels of IL-4, -13, -31, and -33. The severity of the disease or itching was not linked to elevated serum levels of these interleukins [35]. Similar outcomes were noted by Ami Totsuka et al. when researchers showed that since Th2 cytokines are enhanced in AD, blood levels of IL-4 were evaluated in AD patients. and the serum levels of IL-4 were noticeably higher in AD patients too [36].

Activated human T cells were used to clone the pleiotropic cytokine interleukin-13 (IL-13). IL-13 can be released by human mast cells, basophils, activated Th2 cells, alveolar macrophages, and B lymphocytes [37]. The cytokine IL-13, which is generated by pleiotropic Th2 (T helper2) cells, is essential for the development of fibrosis, asthma, allergies, and other eosinophilic illnesses. IL-13 is caused by a multitude of immune cell's innate and non-innate, and it has been demonstrated to express aberrantly in a range of autoimmune illnesses. Furthermore, some allergic disease outcomes have been improved by IL-13-targeting therapy [38, 39]. Our conclusions line up with those of Francisca Gonçalves et al., who observed a marked rise in blood concentrations of IL-13. AD patients also have increased numbers of T cells that generate IL-13 and circulating IL-13. In light of this, it would seem that IL-13 is more important when considering the pathophysiology of AD [40]. Due to the unique effectiveness of the IL-dual-lamellar antibody receptor in AD, as shown by Masutaka Furue et al., it is most likely that the skewed milieu of IL-4 and IL-13 is important in etiology of AD [41]. Additionally, Benjamin Ungar et al. obtained similar results when they demonstrated that, in comparison to healthy controls, skin biopsies from AD patients reveal higher numbers of T cells that produce IL-13 and higher serum levels of IL-13 [42].

Tocopherols and tocotrienols are both referred to by the same name (vitamin E), with the main distinction being in their aliphatic tails. It has been shown to have a greater antioxidant impact than because of its unsaturated side chain [43]. Apart from its antioxidant characteristics, vitamin E can also decrease inflammation and enhance the expression of genes related to keratinocyte differentiation, indicating potential therapeutic benefits against AD [44, 45]. Our findings align with those of Cheryl Wei Ling Teo et al., who found that patients with AD had lower serum levels of vitamin E. They also confirmed in their research that the treatment contains vitamin E. It is thought to be an adjuvant treatment for infections and other skin disorders as well as AD [43]. When comparing skin biopsies from AD patients to healthy controls, Kelly A. Reynolds et al. discovered similar results: skin biopsies

from AD patients reveal greater amounts of vitamin E, although serum levels of vitamin E are lower [46]. Our results are in line with those of Alexandra R. Vaughn et al., who observed low serum vitamin E levels in AD patients and concluded that consuming more vitamin E-rich foods may protect against AD. Researchers who studied infants and their moms found a link between (vitamin E) intake and atopy mothers during pregnancy and a decreased risk of eczema in their family [47].

5. Conclusion

The results of this investigation indicate a positive relationship between AD and interleukin-4,13. There is a negative association between AD and vitamin E. Those with high levels of these interleukins and low vitamin E may be at higher risk for developing atopic dermatitis. As a result, serum interleukins and vitamin E may be benefit markers for predicting the beginning and development of AD.

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دراسة تأثير الانترلوكينات و فيتامين E في مرضى الاكزيما في محافظة الانبار

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الخلاصة:

التهاب الجلد التأتبي**(AD)** ، والذي يشار إليه أيضًا باسم الأكزيما التأتبية، هو نوع من أمراض الجلد الالتهابية التي تؤثر على قدرة الجلد على الاحتفاظ بالرطوبة وحاجز الجلد. لقد ثبت في النماذج الحيوانية أن **IL-4** ضروري لنشوء مرض الأكزيما وقادر على استنباط كل الاعراض النسيجية للمرض. ينتج عن التعبير عن **IL-4** بشكل مفرط ازدياد إنتاج **IgE** ، وتفاقم التهاب الجلد، وتنامي الالتهابات الجلدية البكتيرية والحكة. أشارت الدراسات السابقة إلى أن **IL-13** يلعب دورًا حاسمًا في الفيزيولوجيا المرضية للأكزيما، خاصة عندما يتعلق الأمر بعدد من العوامل المسببة للأمراض مثل تدهور حاجز الجلد، وسماكة البشرة، والحكة، والالتهاب، والعدوى. يعمل فيتامين **E** كمضاد للأكسدة في أغشية الخلايا. ومع ذلك، فقد أثبتت الأبحاث ارتباطه بالجلد ومعظم الأمراض الجلدية، مثل التهاب الجلد التأتبي.

طرق العمل: تضمنت الدراسة 75 مريضاً، 25 منهم من الرضع، و 25 من الأطفال، و 25 من البالغين **((51))** .تم تقسيم المجموعة الضابطة من الأصحاء إلى 17 رضيعًا و17 طفلًا و17 بالغًا لم يتأثروا بالمرض وليس لديهم تاريخ سابق لمرض الزهايمر. يتم قياس مستويات فيتامين**E** ، والإنترلوكين 13، والإنترلوكين 4 في الدم.

النتائج: بالمقارنة مع المجموعة الضابطة، كانت مستويات الإنترلوكين 4 والإنترلوكين 13 أعلى بكثير في مرضى الزهايمر، في حين كانت مستويات فيتامين **E** في المصل أقل بشكل ملحوظ في مرضى الزهايمر.

الكلمات المفتاحية: *التهاب الجلد التأتبي/الأكزيما (AD/E)، إنترلوكين-4 (IL-4)، إنترلوكين-13(IL-13)، فيتامين هـ (فيتامين هـ)، الإجهاد التأكسدي (OS).*