

Measuring the level of IL-4 and IL-25 in the serum of eczema patients

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ABSTRACT

Eczema is an inflammatory skin disease and may be the result of environmental factors, genetic factors, and immune factors. Itching, persistent scratching, skin redness, and dryness are the primary signs of the illness. Many cytokines are essential to the pathophysiology of the disease, including the role of interleukin-4 and interleukin-25 as major players in the immune pathogenesis of eczema. This study was conducted with the aim of evaluating some seromic criteria that clarify the effect of some immune and inflammatory factors on the pathological condition in eczema patients and comparing them with the healthy group. This can help determine whether there is a relationship between the level of interleukin-4 and the high level of interleukin-25 and the clinical symptoms of the disease. The current study was conducted in Marjan Medical City in Babylon Governorate. Samples of 50 patients with eczema were collected after being diagnosed by dermatologists, and samples of 50 ostensibly healthy people were collected as a control group. The enzyme-associated immuno-absorption method (Elisa) was used to measure the level of interleukin-4 and interleukin-25 in the serum of all patients and the control group. Serum levels of interleukin-4 and interleukin-25 are significantly higher in eczema patients at the probability level ($P < 0.05$), while they decrease in the control group for the same criteria rates. According to the results of the current investigation, patients with eczema reported higher levels of interleukin-4 and interleukin-25 in the serum than the control group.

Keywords: cytokines, interleukin-4, interleukin-25, inflammatory factors

INTRODUCTION

The prevalence of eczema varies globally, as according to estimates, up to 20% of children and 3% of adults in developed nations suffer from eczema. The causes of eczema are multiple and not limited accurately, but recent studies on eczema have shown that among the causes of the disease are neurological and immune causes. The occurrence of eczema is attributed to the increase of immune cell leaches and their accumulation in the affected area. The concentration of some cellular motors of both interleukin-4 and interleukin-25 increases [1]. This increase in concentrations may be one of the reasons that may contribute to the pathogens' pivotal roles. In the beginning, perpetuating the distinctive inflammatory sequence of eczema, histological studies show hyperkeratosis of the skin cells, which leads to an increase in their thickness and increased

peeling and confirmed degeneration in the form of plaques, causing episodes of itching throughout the day. The affected skin also appears to have infiltration from the T cells surrounding the consciousness and an increase in the number of attracted eosinophils [2,3]. Lymphatic infiltration appears mostly from T cells for activated memory. The skin barrier has been identified for eczema patients. They found that there is a breakdown of the skin's protective layer on a large scale associated with the occurrence of mutations and the Filaggrin lack of functionality gene. This deficiency or disorder is caused by the gene to weaken the capacity of the skin to hold onto moisture and the occurrence of the skin, which causes effects in the entry of irritants and allergens [4]. The disorder caused by the mediation of immunity is the basis of eczema, with the prominent role of the Th2 cells, which release a different set of cyto-

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kines, including interleukin-4, which promotes the B cell's activation and the generation of immunoglobulin IgE, which induces mast cells and eosinophils, creating a complex inflammatory response that can form the structure of a micro-immune environment within the skin [5,6]. The biological role of interleukin-4, which is secreted from the Th2 cells play a crucial part in the pathological physiology of eczema, and the cells secrete the Th2 cells and the mast cells, and the eosinophil cytokines exert their biological effects. It triggers the release of a series of intracellular signals by binding to the interleukin-4 receptors [7,8]. These signals then activate the transcription factors that cause the induction of genes linked to Th2 cells, resulting in the production of various classes of inflammatory cytokines that are correlated with the severity of the illness. The infected keratin cells do the act of scratching with the secretion of cytokines that help in the migration of the Th cells to the skin, and interleukin-25 works as a major regulator of the response of Th2 cells, eczema is characterized by the excessive immune response caused by these cells due to the effect of interleukin-25 on them [9]. This causes the release of many cytokines, including interleukin-4 other inflammatory cytokines such as interleukin-13 and interleukin-5, which works to cause an imbalance in the epidermal barrier and an increase in the number of other immune cells and their attraction such as acid and mast cells to the affected skin, thus releasing these attractive cells inflammatory cytokines that cause the creation of a complex inflammatory environment that increases eczematous lesions [10]. Interleukin-25 is produced mainly from the epithelial cells of the skin and shows its role in the immune system in coordinating immune responses, especially the Th2 cells [11]. Interleukin-25 is associated with its receptors to activate the final signaling pathways for infections, abnormally regulating the disease. The group of different immune cells leaching to the affected areas of the skin can, through their specific receptors, activate a series of reactions that include the release of different types of IL-4, IL-6 and IL-8 and other cytokines [12]. It has recently become clear that all T cells do not produce the same cytokine, but the secretory model depends on the subtypes of induced or activated cells. In general, cytokines do not have specific target cells, but they are of multiple strengths and exert their effect on different cell models and participate in the inflammatory reaction in the place of contact with the cells. This process, in the end, leads to eczema. It is very likely that the B cells also stimulate T cells during the agitation phase and leads to the formation of mixed antibodies, and we are not aware of the importance of these mixed antibodies in dermatitis. It seems that immune complexes can sometimes form during the acute impulse phase [13]. Clinical experi-

ences indicate that both dermatitis and eczema are able to cause generalized reactions. This phenomenon is also called the phenomenon of proliferation, where vesicle papules appear that begin in terms of dermatitis or eczema. These follicular papules are first related to hair follicles and then appear in the form of eczema changes that diffuse in areas far from the first impulse. This reaction is explained in two ways: either the catalyst or the cause of the disease is transmitted through the blood to other areas of the skin, where it encounters sensitized T lymphocytes. Or that the lymphocytes, which are made by T-lymphocytes in the place of contact, enter blood circulation and become responsible for lesions far from the initial impulse, and symmetric reactions appear to spread over large areas of the skin [14].

MATERIALS AND METHODS

There were 50 eczema patients in the study, aged between 12-58 years, who attended the Dermatology Clinic in Marjan Medical City, Department of Dermatology and Venereology in Babylon, and who were clinically diagnosed with eczema. All patients who received treatment for eczema during the previous 3 months were excluded from participating in the study, and the participants' personal data, namely age, was collected. The patient samples were divided according to age, and on the basis of gender, the number of male patients was 37 and females were 13. (5 ml) of venous blood was drawn [15], and the levels of interleukin-4 and interleukin-25 were measured in the two groups. They were investigated and evaluated. Using enzyme-linked immunosorbent assay (ELISA) utilizing statistical analysis (using SAS version 9.2) and reviewing data results in accordance with the company's manual processes (Abcam). (T tests are used in data analysis by SAS Institute Inc., Cary, North Carolina, USA).

RESULTS

The results of this investigation showed that IL-4 levels have increased significantly ($P < 0.05$) between a set of patients and a group of healthy individuals (58.06 ± 262.83), (22.13 ± 127.08) (pg/ml), respectively, and significant. There was also an increase in morale between the two groups of patients and controls for both the following characteristics: age and sex with interleukin-4, as shown in Table 1, and a significant increase in IL-25 levels between a set of patients and a group of healthy individuals. (145.69 ± 586.78), (49.45 ± 210.77) (pg/ml), respectively, and significant. There was also an increase in morale between the two groups of patients and controls for both the following characteristics: age and sex with interleukin-25, as shown in Table 2. Addi-

tionally, a strong positive association was found between interleukin-4 and interleukin-25 at a value of 0.880, as shown in the table 3.

TABLE 1. Investigations of IL-4 for patients and controls

Variable	Patients N=50	Control N=50	Sig
IL-4 (pg/ml) Mean ± SD	58.06 ± 262.83	22.13 ± 127.08	0.00
Age (years) Mean ± SD	62.15 ± 810.99	22.75 ± 337.32	0.00
Sex			
Male	22.25 ± 744.54	11.90 ± 212.70	0.00
Female	25.76 ± 641.99	7.15 ± 191.81	

TABLE 2. Investigations of IL-25 for patients and controls

Variable	Patients N=50	Control N=50	Sig
IL-25 (pg/ml) Mean ± SD	145.69 ± 586.78	49.45 ± 210.77	0.00
Age (years) Mean ± SD	158.19 ± 314.06	34.48 ± 744.82	0.00
Sex			
Male	93.67 ± 702.65	65.17 ± 231.98	0.01
Female	90.23 ± 706.51	60.66 ± 231.62	0.00

TABLE 3. Correlation between IL-4 and IL-25

Sample	links	IL-25
IL-4	correlation	.880
	sig.	.000

DISCUSSION

The causes of eczema are many and not specific, and the causes of eczema have not been accurately understood. Many studies have shown that among the causes of the disease are genetic and other neurological or environmental factors or immune factors, represented by increasing the synthesis of some cytokines, including interleukin-4 and interleukin-25 and by producing inflammatory compounds at high levels and increasing their secretion [16]. Through what the study's findings revealed, it was observed that the amounts of immune standards are morally high for eczema patients in contrast to the control cohort. The findings indicated that the increase in interleukin-4 has increased in the serum of eczema patients, which shows that this increase in levels affects skin cells, which reflects the significant impact on the disease. Interleukin-4 works by binding to its receptors on the surfaces of some immune cells, strengthening its capacity to play a part in the structuring and production of antibodies from activated B cells and the production of immunoglobulin IgE, which is one of the antibodies that induces allergic receptors on mast cells and stimulates eosinophils to produce eotaxin, a chemi-

cal attractant that works to increase the infiltration and localization of eosinophils in the skin. Interleukin-4 also works by way of its impact on skin-resident activated mast cells and eosinophils to create a complex inflammatory environment within tissues and skin cells and works to increase the disease [17,18].

These results agreed with the study of Wichmann K which confirmed that the increase in the rise of interleukin 4 is through its production of Th2 cells attracted to the injury sites in the skin in eczema, and interleukin-4 works to stimulate the process of naive T cell development and its transformation into Th2 cells. The study's findings demonstrated that the interleukin-4 criterion has a moral difference in terms of age [19]. Studies by Koga C, Kabashima K, Toda M, and Leung DY show that age has an impact on the emergence and development of eczema, especially in early ages, where it appears to increase the progression and development of the spread of the disease in young ages. In middle age, the disease may develop into other allergies like psoriasis and asthma. Regarding age, in the advanced age stages, the disease may rapidly spread and then take stability [20,21], while other studies by Jensen JM and Pfeiffer S show that age has no role or effect on the Interleukin-4, and he mention and indicated that eczema is a palliative allergic disease that occurs through several factors that lead to the development and exacerbation of the body's reaction to it, leading to the appearance of eczema at any age stage. Age is not considered a catalyst for the emergence of the disease [22].

As for the high level of interleukins with sex, a moral increase in interleukin-4 was recorded. These results agreed with what Gutowska-Owsiak D indicated, that sexual hormones have no effect on modifying the inflammatory pathways caused by interleukin-4 in the skin barrier, while other studies have indicated that sex has an effect on the appearance of symptoms of the disease, especially in women, in a more positive way [23]. This is due to the fact that the rate of skin moisture is higher in women than in men, and men lose more transdermal basal water than women do, which lessens the permeability of the skin and the skin barrier by progesterone and androgens. Another study was suggested because De Greef A said that the rate of infection in women is higher than that of men due to the imbalance in the proportions between Th1 cells and Th2 cells. The height of Th2 cells is higher than the Th1 cells, which is reflected inside the body in the change in the proportion of cytokines released inside the body and the affected skin, including the release of inflammatory cytokines with high concentrations [24].

With regard to interleukin-25, the results of the current study, which was conducted on eczema, indicated higher concentrations in patient serum as

compared to the control group serum due to the activation of inflammation pathways within the affected area having a special effect on skin cells, which increases the production and secretion of interleukin-25 from skin epithelial cells in the affected area and from dendritic cells, which is connected to the increase in IgE antibodies and the increase in the release of Th2 cells' cytokine secretions, which infiltrated the affected area in the skin. Interleukin-25 works to prevent keratin cells from producing filaggrin and stimulate the Th2 cells to release inflammatory cytokines, which are related. A common link between inflammation and breaking down the function of the skin barrier [25,26].

In terms of age, there was a moral difference with interleukin-25, where the results show and agree with what the research indicated by Nakajima S. who noted that eczema may appear at different age stages and does not affect or depend on a certain age group. But during different phases of life, the disease's incidence and severity can change [27]. The results did not agree with what the research of Chovatiya R and Paller AS indicated, which notes that age can affect the development of eczema and its course through the fact that the disease has heterogeneous and internal patterns represented by high inflammatory cytokines. As it ages, there are more abnormalities in the skin's immune system, represented by an increase and a decrease in the number of antibody IgE and eosinophils, which reflect negatively on the skin and stimulate the appearance of eczema [28].

There was a moral association with the high concentration rate of interleukin 25 with sex, and there is no effect of sex on changing the levels of interleukin-25. This is where our study agreed with Chen YL, who mentions eczema is a complex skin disease that affects various factors, including genetics, environmental stimuli, and immune responses. The society works to create a mixture of genetic and hormonal factors and does not depend on sex alone [29]. The mechanism in which the cytokines appear or work still needs more understanding and studies to find out the mechanism of the complex interaction that works on the development of eczema, while Shin HW refers to sex as having a great impact on the high levels of inflammatory cytokines, as the female sex prevails in the high rates of infection with eczema compared to men and the consolation of those physiological reasons related to sexual hormones in women, which are disturbed during pregnancy or childbirth. In general, other studies show that sexual hormones may increase their secretion from the adrenal gland, testicles, or ovary glands, and therefore, the immune responses to the skin barrier is prone to being affected by these sexual hormones of the skin and be more sensitive to stimulate the appearance of the disease [30].

There was a moral association with the high concentration rate of interleukin-25 with sex, and there is no effect of sex on changing the levels of interleukin-25. This is where our study agreed with Haddad EB and Zara L, which indicated that eczema is a complex skin disease that affects various factors, including genetics, environmental stimuli, and immune responses. Society works to create a mixture of genetic and hormonal factors and does not depend on sex alone [31,32]. The mechanism in which the cytokines appear or work still needs more understanding and studies to find out the mechanism of the complex interaction that works on the development of eczema, while Cayrol C and Girard JP refers to sex has as having a great impact on the high levels of inflammatory cytokines [33], as the female sex prevails in the high rates of infection with eczema compared to men and the consolation of those physiological reasons related to sexual hormones in women, which are disturbed during pregnancy or childbirth. In general, other studies show that sexual hormones may increase their secretion from the adrenal gland, testicles, or ovary glands, and therefore, the immune responses to the skin barrier is prone to being affected by these sexual hormones of the skin and be more sensitive to stimulate the appearance of the disease [34].

As for the relationship between interleukin-4 and interleukin-25, it has found that there is a positive relationship with a moral difference, due to the fact that the cytokines are not isolated, or isolated from the rest of the cytokines in their work, but there is a network of complex interactions with the cytokines among them, and this is shown by the present study's findings, especially the relationship that showed between interleukin-4 and the interaction with interleukin-25, which affects the exacerbation of eczema disease and increases the amplification of immune responses, including the cells that responded are Th2 cells, leading to an exacerbation of the disease and an increase in the movement and penetration of more immune cells reacting to the skin damage areas [35].

CONCLUSION

Both serotype levels of interleukin-4 and interleukin-25 were significantly elevated in eczema patients. The investigation's findings demonstrated that the immune levels were higher, that there were notable variations in comparison to the control group. Additionally, a strong positive association between the interleukins was discovered by the study.

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