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Determination of Epidermal Growth Factor and Interleukin 6 in Patients with Atopic Dermatitis in Karbala Province

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Abstract

The most prevalent chronic skin inflammatory illness, Atopic Dermatitis (AD), significantly lowers the quality of life for those who suffer from it. The clinical course, age at onset, and degree of allergy and non-allergic comorbidities associated with AD vary widely. Epidermal growth factor receptor controls a number from keratinocyte processes, including as migration, adhesion, survival, and differentiation. The contrast between differentiation and cell cycle progression is one of these pleiotropic effects that stand out. Also, Interleukin 6 promotes the healing of corneal epithelial wounds. These cytokines may cause corneal neovascularization because they affect different kinds of cells. measurement the concentrations of EGF and interleukin 6 in the serum of men with Atopic Dermatitis and its correlated with severity of the disease. Serum Samples for the current study were collected from 60 serum samples from men with Atopic dermatitis and 60 samples from the control group. All samples were collected from outpatient dermatology clinics in karbala province. The ages of all men ranged between 28 years and 40 years. By ELISA kits, the epidermal growth factor concentrations and interleukin 6 were measured in serum). Results showed significantly increased in levels of EGF and interleukin 6 ($p< 0.05$) in patient with Atopic Dermatitis compared with control group. These findings imply that EGF might, in an inflammatory setting, collaborate with other cytokines to strengthen the immunological barrier, The pathophysiology of dermatitis is significantly influenced by IL6, and the clinical severity of AD disease development is correlated with elevated levels of this protein.

1. Introduction

Atopic Dermatitis, often called Eczema, is among the most common conditions that results in inflammation of the skin (1). These conditions are typified by a rash, red skin, and itching. Minor blisters may occur in short-term cases, but the skin may thicken in situations that last a long time. The affected skin area may be little or the entire body (2). It is believed that both environmental and genetic factors contribute to the etiology. Although it can occur in adults, eczema is more frequently found in youngsters (3). The illness is often characterized by dry, itchy, and infection-prone skin. Eczema is sometimes referred to as the "itch that rashes" because it causes dry skin that becomes rashly when scratched or rubbed. Skin hydration is the most important treatment for eczema, and topical steroids are used for flare-ups (4). Atopic

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dermatitis prevalence varies greatly throughout the world because of regional, national, age-group, and data-gathering methodology variations (5, 6).

Atopic dermatitis affects between 15–30% of children and 2–10% of adults during the course of their lives. The first year of birth is when about 60% of instances will manifest. In contrast to metropolitan regions, atopic dermatitis is more prevalent in rural areas. This occurrence highlights the connection between environmental and lifestyle factors and the mechanisms of atopic dermatitis. One of the three conditions referred to as the "Atopic march" is atopic dermatitis. This has to do with the correlation among those who suffer from atopic dermatitis, asthma, and allergic rhinitis. Approximately 75% of individuals with severe atopic dermatitis will develop allergic rhinitis, and 50% will develop asthma (7). The assessment of atopic dermatitis prevalence is complicated by the disease's fundamental characteristics, such as the absence of reliable diagnostic tests, the scarcity of commonly recognized biomarkers, and the recurrent nature of the condition, which cause estimates to vary throughout research (8). Atopic dermatitis has a hereditary component, according to research. A frequent modification has been found in the gene Filaggrin, which is crucial for the skin cells development. This gene produces the hard, flat corneocytes that make up the skin's outermost layer of defense. The corneo- cytes in a patient with normal skin cells are arranged in a compact pack. Because of the random arrangement of skin cells, a patient with a mutation in filaggrin will have a defective skin barrier (9). A 'leaky' skin barrier brought on by this malfunction permits water loss and reduces defense against dangerous chemicals. Beta-defens in levels are also lower in the skin of eczema sufferers. Host defense peptides called beta-defensins are essential for warding off specific bacteria, viruses, and fungi. Particularly with *Staph aureus*, a reduction in these peptides increases colonization and infection (10). There is growing acknowledgment of the varied character of atopic dermatitis and its complicated and multifaceted pathophysiology (11). The idea that atopic dermatitis is an inflammatory skin disease with a systemic component has been supported by significant advancements in atopic dermatitis research over the past ten years, even though the precise mechanisms of the pathogenesis are still unknown. Environmental variables, a compromised skin barrier, the skin microbiota, and immunological dys regulation in those with atopic dermatitis susceptibility genes interact to cause atopic dermatitis (12). Platelets, keratinocytes, and macrophages all secrete EGF, which is crucial for wound healing. EGF receptor (EGFR) ligands are abundant in epidermal keratinocytes, and EGFR signaling significantly influences keratinocyte proliferation and differentiation. Consequently, EGF is essential for skin growth and homeostasis (13). In previous study using an acute Atopic Dermatitis mouse model, skin trans-epidermal water loss factor was significantly reduced in mice treated with EGF, while EGFR signaling blocking increased this factor. EGF has a protective function in the epidermal barrier in addition to its role in wound healing and epithelial homeostasis, and atopic dermatitis is characterized by defects in the epidermal barrier (14).

EGFR signaling reduces allergen-induced IL-6 production and Th17 responses in the skin, according to one study, which also suggested that EGF has an immune-modulatory function in inflammatory skin tissue (15). Numerous cytokines and growth factors, including

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EGF, are involved in the intricate process of wound healing, which also includes inflammation, cellular proliferation, differentiation, and remodeling (16). Numerous researchers have sought to examine the role of rhEGF in treating acute or chronic wounds because it is difficult to modulate this process. By encouraging re-epithelialization and angiogenesis, rhEGF is known to aid in wound healing. It can also activate and proliferate myo-fibroblasts through the PI3K/AKT and ERK/MAPK signaling pathways (17). EGF was also demonstrated to shield fibroblasts from oxidative stress in a rat model by scavenging harmful oxidation products that had previously generated during the acute wound healing phase (18). The skin's primary source of interleukin (IL)-6 is epidermal keratinocytes, and elevated levels of this pleiotropic cytokine have been linked to a variety of skin conditions, including psoriasis. Numerous cell types, including those of dermal and epidermal origin, are influenced by IL-6 in their proliferation and differentiation (19).

Relatively little is known about IL-6's function in the skin, despite the fact that its connection to inflammation and specific disease states is well documented. It has been demonstrated that an inflammatory response after cutaneous injury is necessary for healing, and inflammatory proteins like IL-6 may play a vital role in this process (20).

Interleukin-6 (IL-6) is the primary member of the superfamily of cytokines. Speedily created in response to infections and damage of tissue, IL-6 supports host defense by stimulating immunological responses, hematopoiesis, and acute phase responses. IL-6 supports the innate immune response, powerfully by generating C-reactive protein, many complement system proteins, and the coagulation cascade, and also controls body thermogenesis by serving as an endogenous pyrogenes (21).

Multiple positive and negative feedback processes involving several cell types underpin a physiological immune response, and their effectiveness and homeostasis depend on a coordinated choreography. Cytokines play crucial roles in event coordination. During acute inflammation, macrophages immediately produce TNF-α, IL-1, and chemokine's in response to inflammatory stimuli. Early neutrophil recruitment into the inflammatory region is triggered by TNF-a, which also triggers IL-8 (22). When IL-8 activates neutrophils, IL-6R is cleaved and removed from the neutrophil surface, so encouraging IL-6 to "trans-signal" to cells lacking the IL-6 receptor. Furthermore, TNF-α causes monocytes and macrophages to express the IL-6 gene (23).

Methods

Samples for the current study were collected from 60 serum samples from men with Atopic Dermatitis and 60 samples from the control group (men without Atopic Dermatitis). All samples were collected from outpatient dermatology clinics in karbala province. The ages of all men ranged between 28 years and 40 years. All men were free of chronic diseases. The current study began in the period ranging from September 2023 to February 2024. Using a disposable syringe (5 ml), venous blood samples were obtained from each participant while they were seated. Blood samples were placed in tubes (without coagulants materials), serum

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samples separating from blood, Then, these tubes were centrifuged for 10 min at 3000 rpm, and used another plan tube and gave a special number to keep the serum (24). The levels of EGF and IL-6 were measured by using an ELISA device, according to the manufacturer's method (EPIDERMAL GROWTH FACTOR and HUMAN IL-6 kit).

Statistical Analysis

The program known as SPSS stands for statistical package for social sciences. Significance was expressed using the mean ± standard deviation of the mean independent-sample T-test, and ANOVA test with a *p* less than 0.05 (25).

Results

A results in table (1) showed higher significantly ($p< 0.05$) in levels of EGF in patient with Atopic Dermatitis and interleukin 6 (IL-6) (95.1 ± 13.77, 26.34 ± 3.28 and 15.20 ± 5.82, 4.6 ± 0.79 respectively) when compared with control group. In the table 2, the results showed an increase in the concentration of interleukin 6 directly proportional to the severity of the disease.

Table (1) the means of Epidermal Growth Factor and interleukin 6 in patients with Atopic Dermatitis and control group.

Groups	**EGF (pg / ml) Mean ± SD**	**IL-6 (pg / ml) Mean ± SD**
Patients (60)	95.1 ± 13.77	15.20 ± 5.82
Control(60)	26.34 ± 3.28	4.6 ± 0.79
P	0.000*	0.001*

Table (2) the means of interleukin 6 in patients with Atopic Dermatitis.

Groups	**IL-6 (pg / ml) Mean ± SD**	**Comparison**	***P*-value**

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(Mild) Patients	9.51 ± 0.95	Mild and Moderate	**0.001***
(Moderate) Patients	13.17 ± 1.07	Moderate and Severe	**0.004***
(Severe) Patients	23.42 ± 1.64	Mild and Severe	**0.000***

Discussion

In the current study presented a significantly ($p < 0.05$) increased in EGF and interleukin 6 concentrations in the patient with Atopic Dermatitis groups compared with control. Also, the concentration of interleukin increases with the severity of the disease. EGF is essential for fostering cell survival (26). After binding to its receptor Epidermal growth factor Receptor, It initiates a series of signals that lead to a modification in the transcription of genes (27). In addition to being crucial for cellular proliferation, EGFR signaling also plays a role in angiogenesis, metastasis, and apoptosis inhibition, among other cellular processes that advance cancer (28).

Although clinical evidence suggests that EGFR blockade may potentially contribute to epithelial cancer therapy by enhancing the innate and adaptive antitumor immune response, experimental evidence now shows that its influence extends to the inflammatory and immune functions of the epidermis. The complex signaling system known as EGFR is essential for both maintaining the tumorigenic state and normal physiology (29).

The present study agreed with the study (30) the concentration of EGF in peoples with eczema when comparison with control peoples. The results shown a rise significant in the IL-6 levels in AD severe patients compared with others groups. These results relatively agree with data recorded by Ilves and Harvima (31). Th2-polarized CD-41 T cells, which are linked to atopic dermatitis, are a complex disease that cans production IL-13, IL-5 and IL-6. Activated T cells and macrophages release IL-6. It controls bone metabolism, hematopoietic responses, inflammation and pathogen responses, and the immune system (32). Dendritic cells from atopic patients may overproduce IL-6, which is unrestricted in AD individuals' cutaneous reaction to allergen exposures, but its exact function in causing atopic dermatitis is yet unknown(33). We can conclude that the concentration of epidermal growth factor and interleukin 6 increases directly with the severity of the disease.

Ethical approval

The ethical guidelines derived from the Declaration of Helsinki were followed when conducting the study. Before a sample was taken, the patients' verbal and analytical consent was obtained.

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