

## Role of Immunoglobulin E in the Pathogenesis of Psoriasis: Review Article

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### ABSTRACT

**Background:** In the general population, psoriasis affects two to three percent of people and is characterized by aberrant epidermal proliferation and inflammation. Several clinical subtypes exist for it. The most prevalent form of this disorder is chronic plaque psoriasis (CPP) that is characterized by well-defined, erythematous plaques with silvery scales on knees, scalp, and elbows. There is a chance that any part of the skin could be affected. High IgE levels are frequently linked to parasite infections and atopic dermatitis, allergic contact dermatitis and bullous pemphigoid. Research suggests that psoriasis pathogenesis could be correlated with an increase in IgE expression, which could be a prospective therapy target. **Objective:** Study the relation to immunoglobulin E in the pathogenesis of psoriasis.

**Methods:** The databases were searched for articles published in English in 4 data bases [PubMed – Google scholar-science direct] and Boolean operators (and, or, not) had been used such as [Immunoglobulin E and pathogenesis of Psoriasis OR IgE] and in peer-reviewed articles between January 2001 and October 2020.

**Conclusion:** Overexpression of Immunoglobulin E may have a role in the pathogenesis of psoriasis through several mechanisms. Hence, it could be a viable target to assess severity of psoriasis and follow up of treatment goals.

**Keywords:** Psoriasis, Pathogenesis, Immunoglobulin E.

### INTRODUCTION

Psoriasis is a common chronic skin disorder characterized by inflammation and abnormal epidermal proliferation. The worldwide prevalence is about 2%, but varies according the regions <sup>(1)</sup>. Chronic plaque psoriasis (CPP), the most common form of the condition is usually manifested as well-demarcated erythematous, scaly plaques on elbows, knees, scalp, but any skin surface may be affected as well. Psoriatic erythroderma (PE) represents the generalized form of the disease that affects all body sites. The specific pathogenesis of psoriasis is not completely understood, but the underlying mechanisms involve a complex interplay between epidermal keratinocytes, T lymphocytes as well as other leukocytes, and vascular endothelium <sup>(2)</sup>. The T-helper (Th) 1 and Th17 cells are responsible for the inflammation of psoriasis. Inflammation is not limited to the psoriatic skin, and has been shown to affect different organ systems. Thus, it has been postulated that psoriasis is a systemic entity rather than a solely dermatological disease <sup>(3)</sup>.

The discovery of immunoglobulin E (IgE) was major stimuli to the investigation of allergic diseases <sup>(4)</sup>. Within a decade of its discovery, reports began to incriminate IgE as a possible contributor to the pathogenesis of several chronic inflammatory disorders <sup>(5)</sup>. Although serum IgE concentrations are low in normal health condition, they are high in atopy, parasitic infestation, human immunodeficiency virus (HIV) infection, and certain types of cancer<sup>(6)</sup>.

### Methods:

A search strategy has been performed to determine the related literature. Initially, the objective of review was identified: Immunoglobulin E in the pathogenesis of Psoriasis. Relevant keywords included: Immunoglobulin

E, and pathogenesis of psoriasis, more synonymous key words had been used.

These databases were searched for articles published in English in 4 data bases [PubMed – Google scholar- science direct] and Boolean operators (AND, OR, NOT) had been used such as [Immunoglobulin E and pathogenesis of Psoriasis OR IgE] and in peer-reviewed articles between January 2001 and October 2020; a 19-year date range was selected, and no language limitations, and filtered in selected data basis for the last 19 years, however, the range of time interval for researches is wide as there's scarcity of data on the particular reviewed, accurate and depth in the retrieved literature. Documents in a language apart from English have been excluded as sources for interpretation was not found. Papers apart from main scientific studies had been excluded: documents unavailable as total written text, conversation, conference abstract papers and dissertations.

### Psoriasis:

#### Epidemiology:

Psoriasis is a widespread, chronic inflammatory skin disease that is characterized by well delineated, scaly, erythematous plaques. As a result, the patient's quality of life may be significantly affected. It is difficult to pinpoint a single cause for the development of psoriasis. Hence, psoriasis could result from the interaction between several factors including; genetic, environmental, and immunologic factors <sup>(7)</sup>.

The onset of psoriasis can occur at any time, regardless of the patient's age. It seems that the onset of disease has a bimodal distribution, peaking in young adults, in the 20-30-year-old range and then again in the 50–60-year-old range (early-onset psoriasis and late-onset psoriasis,



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respectively). Those who develop psoriasis at a young age are more likely to have a hereditary predisposition to the disease. As a result of this, early-onset psoriasis is typically associated with more severe illness. As a general rule, the disease worsens and improves throughout a patient's life, and it is doubtful that the disease will go away without therapy <sup>(8)</sup>.

### **Clinical Picture:**

The most prevalent type of psoriasis is psoriasis vulgaris, with clearly defined plaques on the skin's surface. Red or salmon pink plaques are present with white or silvery scales covering their surface. Lesions that are rapidly developing may become annular. The extensor aspects of the elbows and knees; the scalp, lumbosacral area, and the umbilicus are the most prevalent locations for lesions to appear. New lesions appear at the site of trauma or pressure in active inflammatory psoriasis, a phenomenon known as Koebner phenomenon <sup>(9)</sup>.

### **Pathogenesis:**

Accelerated epidermal proliferation and abnormal keratinocyte differentiation are the hallmarks of psoriasis pathogenesis. Immunologic, environmental, and genetic factors all have a role in the etiology of the disease <sup>(10)</sup>.

#### **1-Genetics factors:**

Mendelian inheritance is not involved in the pathogenesis of psoriasis, although there is a family history of psoriasis in most patients. The relative risk for first- and second-degree relatives of patients is significantly elevated as compared to the general population when a positive family history is present. Psoriasis is strongly linked to the human leucocyte antigen-Cw6 gene (HLACw6). PSORS loci have been linked to psoriasis in over a dozen separate studies thus far. Psoriasis-related gene variations can be divided into two broad categories: genes relevant to either the skin or the immune system <sup>(11)</sup>.

Some SNPs in the genes encoding the interleukin-23 (IL-23) cytokine (p40 as well as p19 subunit) and its receptor (IL-23R) are associated with a higher risk of developing psoriasis. T helper 17 (Th17) cells that generate IL-17A/F play a critical role in the development of psoriasis <sup>(12)</sup>.

#### **2-Factors related to the Environment:**

Psoriasis exacerbations can be triggered by alcohol, trauma, infections (e.g., human immunodeficiency virus, streptococci, staphylococci), cold weather, and drugs (e.g., beta-blockers, aspirin, lithium, antimalarials, iodides, steroid withdrawal) <sup>(13)</sup>.

#### **Psoriasis and immunoglobulin E:**

Allergic disorders are characterized by raised Immunoglobulin E (IgE) levels, such as in patients with eczema, asthma, and rhinitis <sup>(14)</sup>.

Patients with psoriasis have been found to produce excessive amounts of IgE. Higher levels of total IgE were detected in blood of psoriasis patients compared to healthy controls. Patients with a longer history of skin abnormalities had a greater total IgE concentration <sup>(15)</sup>.

Patients with psoriatic erythroderma had a considerably higher mean serum IgE level than those with psoriasis vulgaris <sup>(16)</sup>. All these findings indicate a possible role of IgE in the pathogenesis of psoriasis. B lymphocytes produce IgE, which is dominated by Th2 cytokines; IL-13 and IL-4, in the majority of cases. However, keratinocytes are unable to produce IL-13 and IL-4, which are downregulated in psoriasis patients. Therefore, the overproduction of IgE in psoriasis patients may be caused by various other mechanisms <sup>(17)</sup>.

#### **Relation between IgE and immune cells in psoriasis:**

The high-affinity Fc receptor (receptor I for the Fc portion of IgE, called FcRI) and the low-affinity Fc receptor (FcRII) have been found on basophils and mast cells <sup>(18)</sup>. FcεRI is a tetrameric membrane protein complex that consists of four chains ( $\alpha\beta\gamma\delta$ ) <sup>(19)</sup>. Activation of this pathway results in the production of numerous mediators (e.g; leukotrienes, tryptase, histamine) that play an important role in allergic disorders **(11)**. IL-6, IL-8, IL-12, IL-17, IL-22, IFN- $\gamma$  and TNF- $\alpha$  as well as vascular endothelial growth factor (VEGF) and nitric oxide (NO) are all released by mast cells and have been linked to psoriatic inflammation <sup>(20)</sup>.

IFN- $\gamma$  and IL-22 can also be produced by mast cells directly interacting with T cells, resulting in the production of memory CD4+ T cells. IL-22 is a key cytokine in the onset of epidermal hyperplasia in psoriasis and increases keratinocyte proliferation. T-cell proliferation and polarization toward Th1 and Th17 responses are stimulated by cellular interactions between mast cells and DCs <sup>(21)</sup>. Interestingly, mast cells have been found to be elevated in lesional skin of patients with psoriasis <sup>(22)</sup>.

Additional to this, FcεRI is also found on DCs and macrophages in the form of a trimeric complex  $\alpha\gamma\delta$ . It has been shown that activation of FcεRI on these cells enhances antigen presentation and increases the inflammatory response in the skin <sup>(23)</sup>.

Moreover, IgE binding to FcεRI has previously been shown to improve neutrophil survival and result in the production of IL-8. A known chemotactic agent for neutrophils, such as IL-8, may further contribute to the self-amplifying loop of psoriatic inflammation by promoting neutrophil recruitment <sup>(15)</sup>.

## **DISCUSSION**

A variety of humoral changes have been demonstrated in psoriatic skin. Psoriasis patients, especially those with severe disease, have elevated serum levels of IgA and often IgG and even antinuclear antibodies <sup>(24)</sup>.

IgE is generally acknowledged as a typical mediator of allergic response, which is low in healthy subjects and elevated in atopic conditions. Factors regulating IgE levels include age, gene-by-environmental interactions, genetic factors, sex and season <sup>(25)</sup>. IgE recognizes exogenous antigens and signals through Fcε receptors (FcεRs), including FcεR I and FcεR II, triggering an immunologic response. The possible association of

serum IgE levels and psoriasis has been previously reported<sup>(26, 27)</sup>.

**Kasumagic-Halilovic**<sup>(28)</sup> study demonstrated that total serum IgE was significantly increased in psoriatic patients (46.7%) in comparison to healthy subjects (10%). Also, **Chen et al.**<sup>(29)</sup> who analyzed serum IgE levels in 98 patients with psoriasis, and found serum levels of IgE to be elevated in 53.06% of total patients with psoriasis compared to 12% of the control group. **Li et al.**<sup>(30)</sup>, who also recorded a significant increase in serum IgE (81.3%) in patients with PE.

In addition, **Yan et al.**<sup>(31)</sup> demonstrated that 39% of patients with psoriasis had elevated serum IgE concentrations and they observed that lesional skin of patients with psoriasis contains more IgE+ and FcεRI+ cells.

IgE and FcεRI were coexpressed on mast cells, epidermal Langerhans cells, dermal dendritic cells, macrophages and a small number of neutrophils. They concluded that IgE might participate in the development of psoriasis by activating FcεRI-bearing cells<sup>(28)</sup>. Nevertheless, of serum IgE concentrations in psoriatic patients were in contrast to some previous studies<sup>(32, 33, 34)</sup>, which did not find an increase in IgE levels.

## CONCLUSION

Overexpression of Immunoglobulin E may have a role in the pathogenesis of psoriasis through several mechanisms. Hence, it could be a viable target to assess severity of psoriasis and follow up of treatment goals.

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