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CURRENT UNDERSTANDING OF PSORIASIS IMMUNOPATHOGENESIS: A NARRATIVE REVIEW

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ABSTRACT Psoriasis is a common chronic inflammatory skin disease affecting approximately 2-3% of the global population. Its prevalence varies, being higher in populations of European descent and lower in Asian and African populations, with rates in adults ranging from 0.5% to 11.4%. The incidence of psoriasis is increasing, likely due to heightened awareness, better diagnostic criteria, and environmental factors. Psoriasis can occur at any age, with peak incidences in early-onset psoriasis (before age 40) and late-onset psoriasis (after age 40). Early-onset psoriasis is often linked to a stronger genetic predisposition and a more severe disease course. Risk factors include genetic predisposition, with about 40% of patients having a family history. Specific genetic markers like HLA-Cw6 increase susceptibility.

KEYWORDS : Psoriasis, Epidemiology, Genetic predisposition, Environmental triggers, Chronic inflammation.

INTRODUCTION

Psoriasis is a chronic inflammatory skin disease that significantly impacts patients' quality of life due to its persistent and often severe symptoms. Characterized by well-demarcated erythematous plaques with silvery scales, psoriasis can affect various parts of the body, including the scalp, elbows, knees, and lower back. (1).

The immunopathogenesis of psoriasis involves a complex interplay of genetic, environmental, and immunological factors. Key elements in this process include the activation of T-cells and dendritic cells, along with the overproduction of cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-17 (IL-17), and interleukin-23 (IL-23). These cytokines play a pivotal role in the inflammatory cascade that leads to the hyperproliferation and abnormal differentiation of keratinocytes observed in psoriatic lesions (1,2).

Methods

This narrative review was conducted through a systematic search of several databases, including PubMed, Scopus, and Web of Science. The search strategy focused on identifying studies related to the immunopathogenesis of psoriasis. Key terms used in the search included "psoriasis," "immuno-pathogenesis," "cytokines," "T-cells," and "genetic factors." Inclusion criteria were studies published in English within the last ten years, focusing on human subjects and addressing the mechanisms underlying psoriasis. Studies were excluded if they were not relevant to immuno-pathogenesis, focused solely on clinical treatments without discussing underlying mechanisms, or involved animal models without human data. A total of 15 studies were included in this review, providing a comprehensive overview of current understanding in the field.

Epidemiology

Psoriasis is a relatively common chronic inflammatory skin disease that affects approximately 2-3% of the global population. The prevalence of psoriasis varies widely across different geographic regions and ethnic groups, with higher rates observed in populations of European descent and lower rates in Asian and African populations. A systematic review reported prevalence rates ranging from 0.5% to 11.4% in adults and 0% to 1.4% in children. The incidence of psoriasis appears to be increasing, which may be attributed to heightened awareness, improved diagnostic criteria, and environmental factors (2,3).

Risk Factors for Psoriasis

Psoriasis is influenced by a combination of genetic and environmental factors. A strong genetic predisposition is evident, with approximately 40% of patients having a family history of the disease. Specific genetic loci, such as those involving HLA-Cw6, are associated with increased susceptibility. Environmental triggers include infections (particularly streptococcal throat infections), skin trauma, and lifestyle factors such as smoking, alcohol consumption, and obesity. Certain medications, including beta-blockers and lithium, can exacerbate or trigger psoriasis. Additionally, psychological stress is known to worsen the condition, highlighting the multifactorial nature of psoriasis risk factors (4).

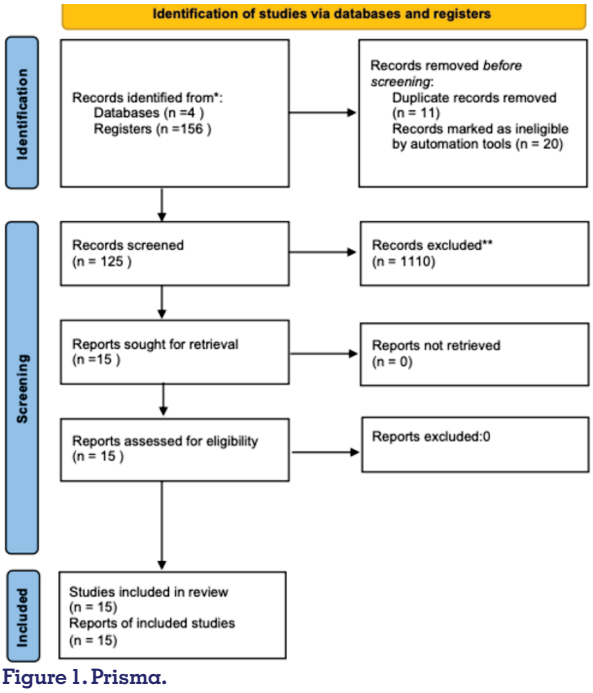

Figure 1. Prisma.

Pathophysiology

Psoriasis is a complex, immune-mediated disease characterized by hyperproliferation and abnormal differentiation of keratinocytes, leading to the formation of the hallmark erythematous plaques with silvery scales. The pathogenesis involves a multifaceted interplay between genetic predisposition, environmental triggers, and immune system dysregulation (4,5).

Central to the pathophysiology of psoriasis is the activation of the immune system, particularly T-cells and dendritic cells. Genetic factors, such as the HLA-Cw6 allele, contribute to the susceptibility and severity of the disease. Environmental triggers, including infections, stress, and trauma, can activate these immune cells. Activated dendritic cells produce cytokines like interleukin-23 (IL-23), which in turn stimulates the proliferation and activation of Th17 cells. Th17 cells release pro-inflammatory cytokines, including IL-17 and IL-

22, which promote keratinocyte proliferation and the inflammatory response. Tumor necrosis factor-alpha (TNF-α) also plays a pivotal role in amplifying the inflammatory cascade (5).

Clinical Manifestations of Psoriasis

Psoriasis presents with a wide spectrum of clinical manifestations, reflecting its chronic and inflammatory nature. The most common form, plaque psoriasis (psoriasis vulgaris), accounts for about 80-90% of cases. It is characterized by well-demarcated, erythematous plaques with silvery scales, commonly affecting the scalp, elbows, knees, and lower back (6,7).

Guttate psoriasis is another clinical variant, typically seen in younger individuals and characterized by the sudden onset of small, droplet-shaped lesions over the trunk and proximal extremities. This form is often triggered by streptococcal infections. Inverse psoriasis involves smooth, red lesions that occur in skin folds such as the axillae, groin, and under the breasts. The lack of scales and the moist environment of these areas make it easily mistaken for fungal infections. Pustular psoriasis, which can be localized or generalized, presents with sterile pustules on an erythematous base. Localized pustular psoriasis, such as palmoplantar pustulosis, affects the palms and soles, while generalized pustular psoriasis (von Zumbusch variant) can be life-threatening, with widespread pustules, fever, and systemic symptoms (7,8).

Diagnosis of Psoriasis

The diagnosis of psoriasis is primarily clinical, based on the characteristic appearance of the skin lesions. Dermatologists typically identify psoriasis by examining the erythematous, well-demarcated plaques with silvery scales, commonly located on the scalp, elbows, knees, and lower back. A detailed patient history is essential to identify potential triggers, family history, and the presence of comorbid conditions such as psoriatic arthritis (9,10).

In atypical cases or when the diagnosis is uncertain, a skin biopsy may be performed. Histopathological examination of the biopsy typically reveals features such as hyperkeratosis, parakeratosis, acanthosis, and elongated rete ridges. The presence of Munro's microabscesses (collections of neutrophils in the stratum corneum) and spongiform pustules of Kogoj (neutrophil collections in the epidermis) are additional supportive findings. Laboratory tests are generally not required for the diagnosis of psoriasis but may be used to rule out other conditions or to assess comorbidities. In cases of suspected psoriatic arthritis, imaging studies such as X-rays, MRI, or ultrasound can be useful to detect joint involvement and the extent of joint damage (10).

Treatment of Psoriasis: Topical and Systemic Therapies

Psoriasis management involves a combination of topical and systemic therapies, tailored to the severity of the disease and individual patient needs. The primary goal is to reduce inflammation, control symptoms, and improve the patient's quality of life (10,11).

Topical Therapies

Topical treatments are the first-line therapy for mild to moderate psoriasis and can be used in conjunction with systemic treatments for more severe cases (11).

Corticosteroids: Topical corticosteroids are the most commonly prescribed treatments for psoriasis. They reduce inflammation and slow down the turnover of skin cells. Corticosteroids come in various strengths, from mild to very potent, and are chosen based on the location and severity of the lesions. Side effects, such as skin thinning and tachyphylaxis, limit their long-term use (11).

Vitamin D Analogues: Calcipotriene (calcipotriol) and calcitriol are synthetic forms of vitamin D used topically. They help normalize skin cell growth and have a favorable safety profile. They are often used in combination with topical corticosteroids to enhance efficacy and reduce side effects(11).

Coal Tar: This traditional therapy helps reduce scaling, itching, and inflammation. It is available in shampoos, creams, and ointments. Although effective, coal tar can be messy and has a strong odor, which can limit patient compliance(11).

Topical Retinoids: Tazarotene, a vitamin A derivative, is effective in reducing plaque thickness and scaling. It is often used in combination with corticosteroids to mitigate its irritant effects (11,12).

Systemic Therapies

Systemic treatments are reserved for moderate to severe psoriasis or cases unresponsive to topical treatments. They include traditional systemic agents, biologics, and newer oral therapies.

Methotrexate: This immunosuppressant reduces inflammation and slows down skin cell proliferation. It is effective for both skin and joint symptoms of psoriasis. Regular monitoring of liver function and blood counts is necessary due to potential side effects, including hepatotoxicity and bone marrow suppression (13).

Cyclosporine: A potent immunosuppressant, cyclosporine is highly effective for severe psoriasis. Its use is limited to short-term treatment due to risks of nephrotoxicity and hypertension. Regular monitoring of kidney function and blood pressure is essential (13).

Acitretin: An oral retinoid, acitretin normalizes skin cell growth. It is often used in combination with phototherapy. Its use is limited in women of childbearing potential due to teratogenicity, and it can cause mucocutaneous side effects and elevated lipid levels (13,14).

Phototherapy

Phototherapy involves exposing the skin to ultraviolet (UV) light under medical supervision. It includes narrowband UVB, broadband UVB, and psoralen plus UVA (PUVA). Phototherapy is effective for widespread psoriasis and can be combined with other treatments. Side effects include an increased risk of skin cancer with long-term use (15).

REFERENCES

1. Nast A, Gisondi P, Ormerod AD, et al. European S3-Guidelines on the systemic treatment of psoriasis vulgaris--Update 2015--Short version--EDF in cooperation with EADV and IPC. J Eur Acad Dermatol Venereol 2015; 29:2277.
2. Armstrong AW, Puig L, Joshi A, et al. Comparison of Biologics and Oral Treatments for Plaque Psoriasis: A Meta-analysis. JAMA Dermatol 2020; 156:258.
3. Gottlieb AB, Strober B, Krueger JG, et al. An open-label, single-arm pilot study in patients with severe plaque-type psoriasis treated with an oral anti-inflammatory agent, apremilast. Curr Med Res Opin 2008; 24:1529.
4. Papp KA, Kaufmann R, Thaçi D, et al. Efficacy and safety of apremilast in subjects with moderate to severe plaque psoriasis: results from a phase II, randomized, double-blind, placebo-controlled study. Lancet 2012; 380:738.
5. Papp K, Bachelez H, Costanzo A, et al. Clinical similarity of biosimilar ABP 501 to adalimumab in the treatment of patients with moderate to severe plaque psoriasis: A randomized, double-blind, multicenter, phase III study. J Am Acad Dermatol 2017; 76:1093.
6. Blauvelt A, Papp KA, Griffiths CE, et al. Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the continuous treatment of patients with moderate to severe psoriasis: Results from the phase III, double-blinded, placebo- and active comparator-controlled VOYAGE 1 trial. J Am Acad Dermatol 2017; 76:405.
7. Reich K, Armstrong AW, Langley RG, et al. Guselkumab versus secukinumab for the treatment of moderate-to-severe psoriasis (ECLIPSE): results from a phase 3, randomised controlled trial. Lancet 2019; 394:831.
8. Lebwohl MG, Papp KA, Marangell LB, et al. Psychiatric adverse events during treatment with brodalumab: Analysis of psoriasis clinical trials. J Am Acad Dermatol 2018; 78:81.
9. Reich K, Papp KA, Blauvelt A, et al. Bimekizumab versus ustekinumab for the

treatment of moderate to severe plaque psoriasis (BE VIVID): efficacy and safety from a 52-week, multicentre, double-blind, active comparator and placebo controlled phase 3 trial. Lancet 2021; 397:487.
10. Griffiths CE, Reich K, Lebwohl M, et al. Comparison of ixekizumab with etanercept or placebo in moderate-to-severe psoriasis (UNCOVER-2 and UNCOVER-3): results from two phase 3 randomised trials. Lancet 2015; 386:541.
11. Gordon KB, Blauvelt A, Papp KA, et al. Phase 3 Trials of Ixekizumab in Moderate-to-Severe Plaque Psoriasis. N Engl J Med 2016; 375:345.
12. Thaçi D, Puig L, Reich K, et al. Secukinumab demonstrates sustained efficacy in clearing skin and improving patient-reported outcomes in patients with moderate-to-severe psoriasis through 2 years of treatment: Results from the CLEAR study. J Am Acad Dermatol 2019; 81:1405.
13. Sandhu K, Kaur I, Kumar B, Saraswat A. Efficacy and safety of cyclosporine versus methotrexate in severe psoriasis: a study from north India. J Dermatol 2003; 30:458.
14. Lebwohl M, Yeilding N, Szapary P, et al. Impact of weight on the efficacy and safety of ustekinumab in patients with moderate to severe psoriasis: Results from the PHOENIX 1 and PHOENIX 2 studies. J Am Acad Dermatol 2010; 63:448.
15. Strober BE, Poulin Y, Kerdel FA, et al. Switching to adalimumab for psoriasis patients with a suboptimal response to etanercept, methotrexate, or phototherapy: efficacy and safety results from an open-label study. J Am Acad Dermatol 2011; 64:671.