

The Epidemiology, Etiology, and Therapeutic Approaches of Psoriasis: A Review Article

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ABSTRACT: Psoriasis is a common condition, affecting approximately 3-7% of the population in Western countries. It does not only affect the skin, as the buildup of skin cells can also result in the development of psoriatic arthritis that progresses to joint destruction. It is a chronic condition affecting over 60 million people worldwide. The incidence of psoriasis varies globally, with some countries reporting rates as low as 0.1% and others as high as 11.8%. This review discusses in detail the different aspects related to the epidemiology, etiology, and therapeutic approaches of psoriasis.

KEYWORDS: Epidemiology, Etiology, Therapeutic Approaches, Psoriasis

1. INTRODUCTION TO PSORIASIS

Psoriasis is a common condition, affecting approximately 3-7% of the population in Western countries. It does not only affect the skin, as the buildup of skin cells can also result in the development of psoriatic arthritis that progresses to joint destruction (M. Martins et al., 2020).

1.1. DEFINITION AND CLASSIFICATION

Psoriasis is a chronic inflammatory skin disease that usually presents with reddish plaques covered with silvery scales (Sarac et al., 2016). It is thought to result from a complex interplay of environmental and genetic factors leading to increased epidermal proliferation and abnormal inflammatory response. Epidemiological studies have revealed a global distribution of psoriasis, affecting approximately 2–3% of the population in most countries. In addition to its broad spectrum of severity (mild, moderate, or severe), psoriasis can have a spectrum of clinical features resulting in its classification into different types (plaque, guttate, inverse, pustular, and erythrodermic) (Yan et al., 2021).

1.2. HISTORICAL OVERVIEW

Psoriasis is probably as old as mankind. Today, it is a well defined skin disease, in which genetic, environmental and immunologic factors participate in etiopathogenesis. However, despite its frequency, chronicity and visibility, it is quite hard to find a description of psoriasis in the works of the ancient physicians (Brajac & Gruber, 2012).

Psoriasis is present worldwide, but with varying prevalence. Traditional co-morbidities associated with psoriasis include psoriasis arthritis (PsA) and inflammatory bowel disease. Recent studies have established solid evidence for psoriasis being associated with a range of lifestyle co-morbidities, the metabolic syndrome and the derived consequences diabetes and cardiovascular disease (Rønholt & Iversen, 2017).

2. EPIDEMIOLOGY OF PSORIASIS

There have been several systematic reviews and meta-analyses of psoriasis epidemiology taking into account European, Asian, African, and North American countries, but there are limited studies observing Western Pacific, Eastern Mediterranean, and South Asian countries. Furthermore, several country-specific estimates of the prevalence of psoriasis at the national level are also not available. In children, psoriasis epidemiology is poorly defined compared to adult-onset psoriasis. Within Europe, there are notable differences with the lowest prevalence in the southern European countries like Spain and Greece (Burden-Teh et al., 2016).

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2.1. GLOBAL PREVALENCE

Psoriasis is a common chronic inflammatory skin condition affecting around 2-3% of the world's population (Peng et al., 2021). The incidence of psoriasis varies globally, with some countries reporting rates as low as 0.1% and others as high as 11.8%. The goal of this systematic review and meta-analysis was to examine the global epidemiology of psoriasis, updating findings from previous reviews in 2005 and 2013. Due to the cultural and social stigmas surrounding psoriasis, there remains great uncertainty in estimating the worldwide prevalence of the disease, especially in underdeveloped countries (Parisi et al., 2020)..

2.2. DEMOGRAPHIC PATTERNS

Psoriasis is a common skin disease that affects people of all ages. Prevalence varies considerably in different regions, with rates higher than 10% in women aged over 75 years in Norway and Iceland, and lower rates of 0-0.4% in the Arabian Peninsula. Gender differences in the risk of developing psoriasis have been debated. Some studies indicate a higher incidence in women, while other data show higher rates in men, particularly for more severe disease. Striking ethnic differences in the occurrence of psoriasis have been observed. There is a higher incidence in Caucasians than in African blacks, Mongoloids, and Arabian peoples. Psoriasis patients are reported to experience psychiatric comorbidities with heightened risk of depression or distress. The demographic and psychiatric pattern in psoriasis patients should be taken into consideration when assessing and mitigating disease burden (Parisi et al., 2020 ;Li & Jiang, 2022).

3. ETIOLOGY OF PSORIASIS

Psoriasis is a chronic inflammatory disorder of the skin characterized by a rapid increase in the proliferation of keratinocytes, leading to marked alterations in the epidermal structure and appearance of well-circumscribed, erythematous plaques covered with silvery scales. Although the underlying mechanism is still obscure, it is accepted that genetic predisposition and environmental trigger(s) play an important role in the development of the disease (Elena Branisteanu et al., 2022). Genetic analysis in familial psoriasis has identified a major susceptibility locus on chromosome 6p21 containing the HLA-Cw6 gene. Several other susceptibility loci have also been identified, including PSORS1 on chromosome 17q, PSORS2 on chromosome 4q, PSORS3 on chromosome 1p, PSORS4 on chromosome 1q, PSORS5 on chromosome 3q, and PSORS7 on chromosome 19p. Familial and non-familial psoriatic patients share common HLA susceptibility genes, most notably HLA-Cw6, but several associations have been found with the HLA-B, HLA-DQ, and HLA-DR genes as well (Mateu-Arrom & Puig, 2023).

3.1. GENETIC FACTORS

Among known psoriasis patients, 30-50% of the cases can be said to have a family member with psoriasis. This mode of development suggests a strong genetic component in psoriasis pathogenesis. A number of familial aggregation studies have been done, demonstrating heritability rates of psoriasis ranging from 62 to as high as 90%. Moreover, concordance rates for monozygotic twins of around 74% were determined, while the concordance rates for dizygotic twins were below 25%. This shows that genetic factors are predicted to play a primary role in the pathogenesis of psoriasis. Moreover, in genes where genes are located at around 6p21 in the MHC class I, MHC class II and other immune response genes region, a strong association with psoriasis was reported. However, no single genetic defect has been shown to cause psoriasis in such pedigree analyses, implying an involvement of multiple genes, each with a modest effect on disease pathogenesis (Chandran, 2010).

Candidate gene studies have provided insights into the role of several genes in psoriasis pathogenesis, including genes implicated in T lymphocyte development, cellular adhesion, the immune response, apoptosis, and the cytokine network (Nedoszytko et al., 2020).

3.2. IMMUNOLOGICAL MECHANISMS

Psoriasis is an immune cell-mediated inflammatory skin disease. While recent studies have demonstrated that certain antimicrobial peptides (AMPs) are linked to the development of psoriasis, these mechanisms of action have not been fully understood. However, it is clear that the IL23/IL17 axis plays an important role in the development of psoriasis; the effectiveness of new biologic treatments such as TNF α inhibitors, IL23 inhibitors, and IL17 inhibitors has verified these findings. It has been shown that immune-related cells, such as dendritic cells (DCs) and macrophages, are related to the development of psoriasis, in addition to other molecules such as Toll-like receptors (TLRs) and various cytokines, including IFN α , TNF α , IL12, IL22, IL23, and IL17 (Tokuyama & Mabuchi, 2020).

The purpose of this review is to summarize a comprehensive overview of the epidemiology, pathogenesis, and treatment of psoriasis. Among these treatment options, a description of a new treatment option, including a Janus kinase inhibitor, tyrosine kinase 2 inhibitor, modulator of sphingosine 1-phosphate receptor 1, and Rho-associated kinase 2 inhibitor, is also described. Furthermore, a comprehensive overview of the epidemiology and treatment of psoriasis will be provided. Psoriasis was essentially considered a disease of epidermal keratinocyte proliferation until the early 1980s. Since the mid-1980s, there has been compelling evidence that the cell-mediated adaptive immune response is critical in the treatment of psoriasis (Elena Branisteanu et al., 2022).

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4. CLINICAL FEATURES OF PSORIASIS

Psoriasis is a non-infectious chronic skin condition that generally displays red plaques well-defined by silver-white scales on the extensors, scalp, and sacrum. Apoptotic keratinocytes lead to parakeratosis by pseudostratification of keratinocytes and psoriatic changes in the vascular system among hyperproliferating keratinocytes and dysfunctional dendritic cells. The redness of papules is due to vascular changes and neovascularity. The silver-white scales are due to the acceleration of the management of the keratinization process and subsequent incomplete maturation (Sarac et al., 2016).

Psoriasis varies widely in clinical appearance showing different forms or types. These types are important for its diagnosis and determine treatment protocols. Although plaque type is the most common type, it can show its effects as guttate, inverse, pustular, erythrodermic, or specifically on nails, palms, and soles. Psoriasis can also have different types according to histopathological findings (Dhabale & Nagpure, 2022).

4.1. TYPES OF PSORIASIS

Plaque psoriasis, or Psoriasis Vulgaris, is the most common type of psoriasis, affecting 80% to 90% of patients suffering from the disease (Dhabale & Nagpure, 2022). It is characterized by well-demarcated, raised, red lesions with adherent silvery scales, most commonly located on the knees and elbows but also occurring on the scalp and lower back. Plaque psoriasis can be localized (involving only a few regions of the body) or generalized (disseminated to multiple body regions). It is associated with multiple comorbidities, including psoriatic arthritis, obesity, hypertension, hyperlipidemia, diabetes mellitus, cardiovascular disease, chronic kidney disease, nonalcoholic fatty liver disease, and psychiatric disorders (Hu et al., 2021).

4.2. COMMON SYMPTOMS

Psoriasis is a chronic, erythematous, scaly skin disease affecting 2-4% of the world's population. Psoriasis is characterized by the excessive proliferation and inadequate differentiation of epidermal keratinocytes. In the newly formed epidermis, keratinocytes proliferate at a normal rate and lose their viability. The major physical symptoms associated with psoriasis are red scaly patches resembling a bib of the common name "psoriasis bib." Of these, the most irritating is pruritus, one of the 5 classical symptoms in ancient Greece dermatology and a high prevalence in psoriasis patients, while the other 4 are reddening, swelling, keratosis, and pain. The raised, rough skin makes it difficult to wear clothes. The cutaneous affliction appearance is stressful, and psoriasis patients have a high risk of comorbidities such as hypertension, coronary artery disease, diabetes, and increased mortality (Marek-Jozefowicz et al., 2022).

Psoriasis affects the entire life of patients; the initial symptoms are usually in the teenage or 20-30s, and psoriasis runs a chronic lifelong course. This long-term chronicity in the daily life of the patients leads to significant psychological damage. Psoriasis is one of the most serious dermatologic diseases, with an overall substantial impairment in the quality of life; an adverse effect on professional, social, and sexual activities; and a knock-on effect on the care of relatives. Furthermore, psoriasis patients are recognized as a high-risk group for suicidal ideation, which is 5.6 times that of the general population. Individuals who experienced more substantial pruritus had a higher risk of suicidal ideation than individuals who experienced less (J. Connor et al., 2015).

5. DIAGNOSIS AND ASSESSMENT

Psoriasis diagnosis is based upon the patient's history, clinical signs, and physical examination, confirming the presence of typical lesions on a clinical basis. In the complicated cases with a greater differential diagnosis, skin biopsy specimens for histopathological examination are collected. Other ancillary methods can also be employed, such as imaging methods for skin, joint, and bone, biochemical and blood examinations, etc.; drugs that can induce or exacerbate psoriasis should also undergo investigation based upon clinical indications (Tampa et al., 2024).

The response to treatment can be objectively assessed by measuring a well-targeted number of outcome parameters. There is agreement worldwide that each patient under treatment for psoriasis should undergo regular monitoring of treatment efficacy and safety (Codrut Nicolescu et al., 2022).

5.1. CLINICAL EXAMINATION

The clinical examination is the next important step once the history-taking of a patient with psoriasis is initiated. Physical examination needs to include visual inspection of the skin, nails, and scalp. Psoriasis presents as classic scaly plaques. Silvery white scale on a bright red plaque is a classic but needs to be supported with evidence of other signs. The most common sites for psoriasis vulgaris are elbows, knees, scalp, umbilicus, and gluteal cleft. Inverse psoriasis presents as bright red, glistening plaques in intertriginous areas like the groin and axilla. Scalp psoriasis may involve only the hairline or the entire scalp. Nail changes like pitting, onycholysis, oil spot nail, and hyperkeratosis support the diagnosis of psoriasis (Sarac et al., 2016).

5.2. LABORATORY TESTS

The diagnosis of psoriasis is based on clinical examination. However, laboratory tests might be helpful when there is uncertainty regarding the diagnosis or to determine the underlying disorders. Determining the current activity of psoriasis is not a common

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practice in everyday clinical practice; however, in some cases, laboratory tests may be useful in monitoring the course of psoriasis (Kowalska-Kępczyńska et al., 2021).

Blood tests are conducted mainly to assess the background disorders associated with psoriasis. However, blood tests might be useful in monitoring the course of psoriasis in some cases. A skin biopsy is not indicated when the diagnosis is obvious, or the lesions are typical for psoriasis (Arican et al., 2005).

6. TREATMENT MODALITIES

Psoriasis is a chronic inflammatory disorder of the immune system affecting the skin and joints. Psoriasis frequently appears as red plaques with silvery scale on the elbows, knees, and scalp. Severe psoriasis affects a considerable portion of a person's body and may lead to an impaired quality of life due to persistent itch, pain, and disfigurement. Psoriasis is a systemic inflammatory disease. Patients with psoriasis frequently develop comorbid conditions, such as the metabolic syndrome, increased cardiovascular risk, and psoriatic arthritis (Lee & Kim, 2023). Ghafel (2021) observed that vitamin C perform as effective immunomodulator and antioxidant action to decrease psoriasis severity.

For patients with limited skin involvement (less than 10% body surface area), topical treatment is the first line of therapy. Topical treatment options include glucocorticoids (GCs), vitamin D3 analogs, tazarotene, calcineurin inhibitors, and coal tar preparations. Topical GCs are the most commonly prescribed treatment for psoriasis (Cather & Crowley, 2014).

6.1. TOPICAL THERAPIES

Psoriasis is a chronic immune-mediated inflammatory disease. The alopecic and co-morbid complex manifestation has a significant impact on patients' quality of life. Beyond the systemic treatments of the disease, the requirement for topical therapies is high, especially in the mild to moderate community, for the sake of accessibility, adverse effect profiles, and cost effectiveness (Imafuku et al., 2018). Topical therapies are fundamental in managing the symptoms of psoriasis. The skin is the main organ affected by this immune-mediated disease and is readily accessible for topical application. Types of topical therapy commonly used for patients with psoriasis include corticosteroids, vitamin D analogs, retinoids, calcineurin inhibitors, coal tar, phosphodiesterase 4 inhibitors, and salicylic acid. Treatments are differentiated based on their potency, efficacy, side effects, method of application, and costs. These medications have accompanying information regarding the mechanisms, dosing regimens, and side effects for each of the products. All topical treatments carry potential adverse effects that are different among every individual (Patel et al., 2017).

6.2. SYSTEMIC THERAPIES

Systemic therapies treat psoriasis from within the body and therefore target the underlying causes of disease. They can be oral (orally administered) or injected (self-administered or given in a doctor's office). Systemic therapies can take several weeks, if not months, for patients to see a difference in their plaques as they work on a larger scale by suppressing the immune system (Belge et al., 2014).

Traditional systemic medications include a variety of oral medications that have been prescribed for psoriasis for decades. Most of these medications suppress the immune system and can lead to significant side effects and require regular laboratory monitoring. Methotrexate (MTX) is one of the most commonly prescribed systemic medications for patients with psoriasis. It is often considered a standard of care and is usually started first in patients needing systemic medications because it has a well-established safety and side effect profile. Acitretin (acitretin) is a systemic retinoid medication that is also prescribed for psoriasis. Patients benefiting from acitretin therapy should be counseled about possible side effects and required pregnancy testing. Patients receiving cyclosporin therapy should be counseled about side effects and the need for routine laboratory monitoring (Kivelevitch et al., 2014).

7. NOVEL THERAPEUTIC APPROACHES

Researchers are continually on the lookout for new and novel therapeutic options that can improve outcomes for individuals with psoriasis. This has resulted in new biologics, topical treatments that enhance drug delivery, and evaluation of the benefits of combining existing therapies. Psoriatic disease is a chronic relapsing inflammatory condition affecting 2–3% of the population. The pathophysiology of psoriatic disease is complex and begins with an abnormal immune response primarily in predisposed individuals causing infiltration of effector memory T cells, dendritic cells, and neutrophils in the skin and synovium. In the skin, under the defense interaction between the innate and adaptive immune systems, keratinocytes become activated, undergo disordered differentiation, and secrete a host of pro-inflammatory cytokines (Thakur & Mahajan, 2022). This further induces a plethora of activation of inflammatory cells, such as dendritic cells, mast cells, and natural killer cells; persistence of the inflammatory cascade; and amplification of the immune response resulting in angiogenesis, hyperplasia of blood vessels, and changes in extracellular matrix. Moreover, psoriatic lesions can progress from the early inflammatory to chronic stage, as chronic plaques mature, in part to the generation of highly activated CD8+ T cell clones (Lee & Kim, 2023)..

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7.1. BIOLOGICAL AGENTS

Biologics are a type of treatment for psoriasis that target specific parts of the immune system. In psoriasis, the immune system functions abnormally, leading to inflammation, increased skin cell production, and other immune system activities. There are several different types of biologics, and depending on how they work, they are classified as TNF-alpha inhibitors, IL-12/23 inhibitors, IL-17 inhibitors, or IL-23 inhibitors. These biological agents are given by injection or infusion, and they are usually given once a month after starting on weekly doses (Gaspari & Tyring, 2015).

Biological agents are usually included as a treatment option in moderate to severe cases of psoriasis. They can work very well, often clearing psoriasis almost completely. They can also, in many cases, reduce or stop inflammation in other parts of the body, such as joints, where it can cause psoriatic arthritis. Most biological agents have been seen to be quite safe overall, with a few possible side effects that may occur in some people. Only a few people stop having treatment with a biologic due to side effects (Kivelevitch et al., 2014).

7.2. SMALL MOLECULE INHIBITORS

Psoriasis is a chronic, systemic inflammatory disease that primarily affects the skin and joints. The estimated global prevalence of psoriasis is 2.6% (with a range of 0.09%–6.5%) (Lee & Kim, 2023). However, psoriasis prevalence rates differ by country and ethnicity. Generally, higher estimates are reported for Europe and North America compared to Asia and Africa. It occurs equally in both sexes, but higher male prevalence rates ($\geq 3\%$) are reported in some Western countries. The median age of psoriasis onset is 27 years but remarkably varies across geographic areas. In Asian countries, psoriasis typically develops at younger ages (19 years), while it presents later (39 years) in northern European countries. Psoriasis develops at two peaks in both sexes: the young-onset form (below 35 years) is more common in females, while the late-onset form (beyond 35 years) is predominant in males (Drakos et al., 2024).

8. COMPLEMENTARY AND ALTERNATIVE MEDICINE

Complementary and alternative medicine (CAM) encompasses a wide range of diagnostic and therapeutic techniques that fall outside the realm of conventional biomedicine. Its use by patients with psoriasis has been highlighted by many studies. Psoriasis is a chronic skin disease with an autoimmune background that affects different body areas. Although the exact cause of psoriasis is still unknown, it is believed to include a combination of genetic dysregulation, inflammatory mechanisms, environmental factors, and an abnormal immune response involving T cells and dendritic cells (Wnuk-Kłosińska et al., 2021).

Traditional Chinese medicine (TCM), applied to psoriasis patients, was assessed in an upper-level, nonrandomized, uncontrolled trial. TCM is an ancient holistic system based on the principles of yin-yang balance, Qi circulation, and the five elements theory. The TCM treatment included acupuncture, herbal decoctions, and dietary suggestions. Pastrnak et al. selected studies that compared TCM to placebo or no treatment controls, pharmacological therapies, or Western medicine, with psoriasis diagnosis supported by established criteria. Twelve studies were included in the analysis, mostly conducted in the People's Republic of China. The results indicate that TCM improves psoriasis symptoms more than placebo and other Western treatments. The efficacy of herbal remedies (HT) in its treatment was evaluated in 34 trials. HT was found to have a beneficial effect on PASI, BSA, and quality of life (QoL) improvement (Lee et al., 2019).

9. PSYCHOSOCIAL IMPACT OF PSORIASIS

A considerable burden falls on individuals living with psoriasis, whether assessment is made from the perspective of emotional, psychological, social, occupational, or educational responsibilities (Jankowiak et al., 2020). Psoriasis is not life-threatening; however, feelings can be provoked that make it worse than many diseases. Emotional reactions include embarrassment and anger at the unfairness, inconvenience, and discomfort of the condition; anxious preoccupations concerning control, spread, lack of understanding from others, and fear of ridicule; and feelings, often unshared, of isolation, depression, and low self-image (A. Gupta et al., 1987).

10. MANAGEMENT OF PSORIASIS IN SPECIAL POPULATIONS

Psoriasis can present unique challenges to manage. Pregnant women with psoriasis may experience concern for fetal safety versus the risks of flare of their psoriasis. Because most psoriasis medications and treatment options have limited data regarding pregnancy and lactation, dermatologists may limit or avoid treatment entirely despite knowledge that untreated psoriasis can worsen maternal and fetal outcomes. Psoriasis in children and adolescents raises concern for treatment options that may interfere with growth and/or immune development. Psoriasis in the elderly poses the challenge of polypharmacy and comorbidities predisposing to increased risk of adverse events. The majority of systemic treatments for psoriasis are approved for use in patients aged >18 years; therefore the use of psoriasis treatments in pediatric populations requires consideration of the developmental stage and a more cautious approach. This article focuses on best practices for the management of psoriasis in these special populations (Di Cesare et al., 2022 ; Mahé, 2020).

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