Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/wsfm2880

REVIEW ON SEASONAL INCIDENCE OF PSORIASIS EXACERBATIONS DURING WINTER IN INDIA: CLINICAL INSIGHTS AND OBSERVATIONS

Dhwiti Patel[1*], Ms. Sonika Rathi[2], Dr. Pragnesh Patani[3]

[1*]Khyati College of Pharmacy, Palodia, Ahmedabad
[2]Assistant Professor, Department of Pharmacology, Khyati College of Pharmacy, Palodia, Ahmedabad
[3]Principal, Khyati College of Pharmacy, Palodia, Ahmedabad

***Corresponding Author:** Dhwiti Patel
*Khyati College of Pharmacy, Palodia, Ahmedabad, Email: pateldhwiti17@gmail.com

Abstract:
The cause of a disease over approximately 125 million people worldwide with active cases of psoriasis. The patients with the disease psoriasis experience substantial morbidity and increased rates of inflammatory arthritis, cardiometabolic diseases, and mental health disorders. As per the data published on the site of WHO Global report on psoriasis that a new comprehensive worldwide systematic review of the epidemiology of psoriasis was undertaken. Psoriasis is a common disease, occurring more frequently with advancing age and as per the data of the researches it was estimated that the prevalence of psoriasis in adults ranged from 0.53% to 11.48%, and in children from 0.5 % to 1.40%. The available data comes from approximately 20 countries, there is a vast difference of knowledge in low and middle income settings. As it was conducted by several sources about the increase in the number of active cases so in this article we rigorously and systematically analyze the research work. This article contain all the nursery information related to the disease psoriasis and also with the advance treatments and recent advancements.

Keywords: Psoriasis, TNF, plaque, seasonal, pustular, climatotherapy.

Introduction:

Psoriasis is a chronic autoimmune disease which causes redness, flaky skin, and scaly areas on the skin due to fast proliferation of skin cells. [1] It is a lifelong disease associated with morbidities like hepatic, psoriatic arthropathy, cardiovascular disease. The term "psora," which means "itch," in Greek is whence the condition gets its name, Because of this disease's rapid and excessive proliferation of epidermis cells, which give the skin a fishy appearance and eventually peel off as exfoliation, the skin continuously scales as flakes known as psoriatic plaques. [3] World Health Organisation has confirmed psoriasis as serious non-communicable disease in 2014. [2] mets, also known as syndrome X, is a group of symptoms that raises the risk of obesity, cardiovascular disease (CVD), diabetes mellitus type 2, and other morbidities.[3] Numerous research have demonstrated the connection between Metabolic Syndrome and various dermatological conditions, including rosacea, systemic lupus erythematosus, hidradenitis suppurativa, psoriasis, lichen planus, and androgenetic alopecia.[4] Although the precise pathophysiology of Mets is still unknown, there may be a connection between skin disorders and non-alcoholic fatty liver disease, elevated homocysteine, leptin, and resistin, many

pro-inflammatory cytokines, prothrombotic factors, decreased serum adiponectin, and these conditions.[5] Given that psoriasis is primarily caused by chronic inflammation, long-term metabolic change appears to be most likely, which raises the risk of mets, [4] Sunlight exposure is thought to help psoriasis, especially in cases where skin types III and IV (rarely and never tanned) are affected.5. When it comes to treating psoriasis, ultraviolet B (UVB) phototherapy and climatotherapy—which include utilizing sunlight aggressively—are excellent options. The concept of seasonal variation and psoriasis with an automatic improvement in the summer—defined as the sunny period—has most likely been shaped by the beneficial effects of light therapy. On the other hand, it's commonly believed that psoriasis is negatively impacted by colder weather and less sunlight. [5]

Active cases during winter in India: [6-9]

Psoriasis onset takes place on average at the age of 27.8 years. The lower extremities were reported to be suffering most often at the time of the study, followed by the trunk, elbow, and scalp; the knee and face were mentioned less frequently. Half of the patients had involvement of their fingernails at some point during the course of their illness. Sunlight and hot temperatures were favorable to most patients. Moreover, a third of the ladies reported feeling better during their pregnancies. [7] The male to female ratio among psoriasis patients was 1.1:1. The age groups of 21–30 and 41–50 years, which made approximately 25% of the total, had the highest prevalence. Clinically, the most common pattern (fifty percent) was chronic plaque psoriasis. In decreasing order of incidence, the palms and soles (33%) and scalp (20.8%) were the most often involved areas. About 4.1% of patients had erythroderma. 12.5% of people had psoriasis in their family. [8]

Table 1: Age distribution among psoriasis and Vitiligo patients

Age group	Psoriasis %	Vitiligo %
0-10	-	6.5
11-20	12.5	26.08
21-30	25	21.7
31-40	20.8	21.7
41-50	25	15.2
51-60	16.6	6.5
>60	-	2.175

Just 30% of psoriatic patients clearly worsened during the winter. The most prevalent places were the skin and scalp; 54% of patients had altered nails when they were initially diagnosed, and in 8 cases, nail involvement was the only sign of psoriasis. Only seven individuals had frank arthritis, but joint symptoms were present in ten percent of cases. Nail anomalies were always linked to the existence of joint affection. In contrast to people in western nations, psoriatic arthritis is not only uncommon but also manifests in a milder form in Indian patients. Just 30% of psoriatic patients clearly worsened during the winter. The most prevalent places were the skin and scalp; 54% of patients had altered nails when they were initially diagnosed, and in 8 cases, nail involvement was the only sign of psoriasis.[9]

Table 2: Types and its characteristics of psoriasis [10]

Types of Psoriasis	Its Characteristics
Plaque psoriasis	Itchy, dry, covered with scales
Nail psoriasis	Abnormal grown nails and discoloration
Guttate psoriasis	Scaling spots all over trunk, arm
Inverse psoriasis	Inflamed skin in smooth patchwork
Erythrodermic psoriasis	Peeling form of rash
Pustular psoriasis	Blisters with pus

Pathophysiology

According to histological investigations, psoriasis causes the superficial vascular plexus's surface area to expand fourfold while also causing an increase in endothelial cell proliferation. [11, 12] Cytokines such as tumour growth factor-α (TGF-α), IFN-γ, and tumour necrosis factor-α (TNF-α) stimulate the manufacture of this substance by keratinocytes, activated T lymphocytes, and endothelial cells. The psoriatic epidermis has an overexpression of VEGF (vascular endothelial growth factor), and the papillary microvessels have an overexpression of KDR and Flt-1, the receptors for VEGF. Transgenic mice with an excess of VEGF in their epidermis experience psoriasis-like symptoms. [13] There is a link between plaque VEGF, PASI (psoriasis area and severity index), and serum VEGF levels, and erythrodermic psoriasis is associated with higher serum VEGF concentrations. [11, 14, 12] In patients with severe psoriasis, the source of pulmonary oedema and microalbuminuria has been suggested to be the hyperpermeability brought on by VEGF. [12] The discovery that ciclosporin is a very effective treatment for psoriasis was initially made in the 1980s, and it suggested that T cells play a major part in the process. In rare cases, recipients of bone marrow transplants from afflicted patients have acquired psoriasis. [15] xenotransplant animal models also provide evidence for the significance of T cells. In non-lesional skin transplanted from psoriasis patients, psoriasis develops spontaneously in AGR129 mice. These mice are deficient in their innate immune response and lack T and B cells. [16] These plaques' growth is correlated with the graft's resident T cells' proliferation. Psoriasis is classified as a Th1 illness and is characterized by IL12-induced production of TNF-α and IFN-γ. The success of a monoclonal antibody that targets the p40 component of IL12 in early clinical studies lends credence to this immunological paradigm. [17] Nonetheless, there is mounting data supporting the significance of Th17 cells, a new subset of T cells, in autoimmune illness. Th17 cells are driven by IL23 (which shares the p40 subunit with IL12) to produce both IL17 and IL22. IL22 is a novel target for treatment because it has been demonstrated lately to be a primary driver of acanthosis in psoriasis. [18]

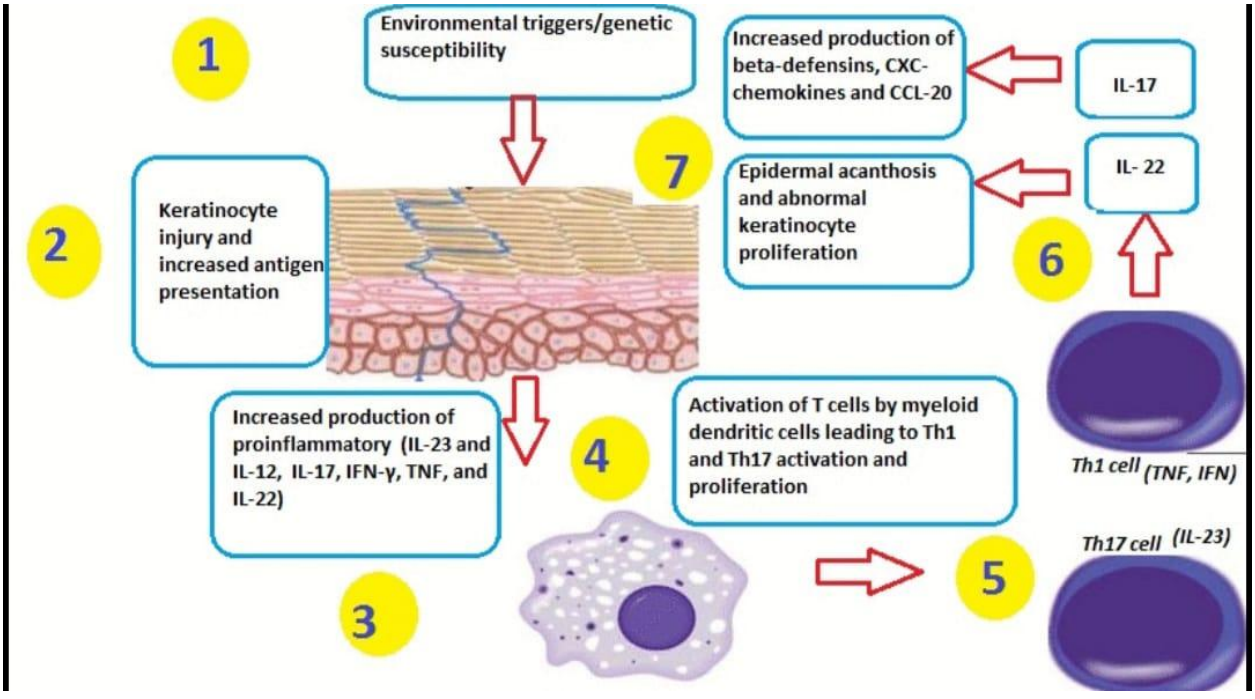

Fig.1 An overview of psoriasis's pathophysiology

Dendritic cells are abundant in psoriatic plaques and through their cytokine production patterns, they affect T cell activation and differentiation. TNF-α is also largely produced by dendritic cells, and the effectiveness of anti-TNF-α therapy for psoriasis has brought attention to the significant function that this pro-inflammatory cytokine plays in the disease. Psoriatic plaques have higher levels of TNF-α, a crucial component of both innate and adaptive immune responses, and the disease's severity is correlated with blood levels of this protein. [19] Natural killer T cells (NK T cells), neutrophilic

granulocytes, keratinocytes, antimicrobial peptides, and toll-like receptors (TLR) are further components of the innate immune response linked to the pathogenesis of psoriasis. While circulating concentrations of NK T cells tend to decrease in proportion to disease activity, NK T cell presence in psoriatic plaques is much higher than in non-lesional skin. [20] Psoriatic keratinocytes express more TLR1 and TLR2 than other cell types. In fact, the treatment for psoriasis, monomethylfumarate, disrupts TLR signaling. [21]

Lifestyle of patients

- **Alcohol -** Plaque psoriasis is more common in persons with alcohol addiction. Moreover, alcohol consumption is the catalyst that starts the disease, keeps it going, and makes the psoriasis worse. [22, 23] Chronic alcohol intake increase T-cell activation, CD80 and CD86 expression, and inflammatory markers (including tumor necrosis factor alpha [TNF-α], soluble TNF receptor, and pro-inflammatory cytokines) at the cytokine level. Additionally, it up regulates genes that promote the proliferation of lymphocytes and keratinocytes, the latter of which is probably connected to the interference of the skin barrier caused by exocrine glands excreting ethanol. [24] Periodic alcohol use may also have an immunosuppressive effect, making skin infections more likely to occur, such as staphylococcal and cutaneous streptococcal infections, which can be triggers for psoriasis. However, prolonged alcohol intake reduces the effectiveness and heightens the toxicity of systemic antipsoriatic therapies, and drinking make worse therapeutic compliance. [25]
- **Smoking -** Compared to non-psoriatic smokers, smokers with psoriasis had a lower chance of quitting. [26] The pathogenetic connection is the generation of free radicals, which cause damage by activating the pathways of mitogen-activated protein kinase (MAPK), nuclear factor kappa (NF-k), and Janus kinases-signal transducer and activator of transcription (JAK-STAT). [26] These pathways also result in the generation of reactive oxygen species (ROS), a reduction in the expression of protective antioxidant genes, and skin damage. [27] Moreover, nicotine stimulates the innate immune system and increases dendritic cell production of interleukin-12 (IL-12). Finally, smokers with psoriatic patients show a decreased adherence to therapy and a poor response to treatment. [27, 26]
- **Stress and sleep disturbances -** A malfunction of the hypothalamic-pituitary-adrenal axis is probably responsible for the pathogenetic association observed between stress and the onset and worsening of psoriasis. Patients with psoriasis who respond well to stress have been reported to have greater psoriasis area severity indexes (pasis) than their less responsive counterparts. [25] Psoriatic patients have high rates of anxiety and depression and are at risk of acting suicidally, regardless of the severity of their disease. They also frequently have sleep disruptions caused by skin complaints including uncomfortable and itching. [22]
- **Diet -** Low-calorie diets, such as the ketogenic diet, have been shown in breaking rcts to be effective in advance the improvement of psoriasis. This diet plan has also been shown to enhance the response to complete therapy using biologics, phototherapy, or low-dose cyclosporine. [28] Mediterranean diet is high in a variety of anti-inflammatory nutrients, including polyphenols, antioxidants, and monounsaturated fats found in extra virgin olive oil, which is an important source of monounsaturated fatty acids, which is associate to a lower risk of coronary heart disease and altered immune and inflammatory responses. [25] Due to a lower minimal erythemal dose brought on by consuming more foods high in furocumarin, a strict vegan diet may crucially improve treatment response to phototherapy and reduce the number of narrow-band UVB sessions required to achieve psoriatic relieving. There is increased risk of adverse effects which includes severe erythema, important to consider in this context. [29] Psoriatic patients show deficiencies in vitamin D and vitamin B12. High sugar, fatty acids, and dairy food can all aggravate psoriasis by causing inflammation. While high sugar and bad fats promote systemic inflammation and may exacerbate symptoms, dairy may cause immunological responses in certain people. You can better control flare-ups and maintain the health of your skin by cutting these out of your diet. [30]

Foods that may trigger psoriasis symptoms

Eggs, milk and cheese, and red meat frequently come up as psoriasis trigger foods. Arachidonic acid, a polyunsaturated fatty acid, is most likely responsible for this. All foods and food products that contain gluten must be avoided when sticking to such a diet. This covers malt, wheat, barley, and the derivatives of these grains. Vegetables classified as nightshades, such as potatoes, tomatoes, eggplants, and peppers, belong to the Solanaceae plant family. Solanine, an alkaloid found in several vegetables, can be harmful in excessive doses. For some people, this induces inflammation and difficulties with digestion, which can lead to breakouts of psoriasis. Citrus fruits are acidic and may occasionally irritation the skin or worsen inflammation, people with psoriasis often avoid eating them.[52] Spices that cause inflammation and intestinal irritation, such black pepper, cayenne, and chili powder, may exacerbate the symptoms of psoriasis. Some people may also experience allergic reactions or inflammatory reactions when they use curry powder, which usually consists of a mixture of several spices. Furthermore, certain people may be more prone to inflammation while eating mustard seeds. Because individual reacts differently to spices, it's best to keep an eye on how particular spices impact your symptoms and modify your diet accordingly, maybe gravitating toward anti-inflammatory spices like turmeric and ginger instead.[53]

Diagnosis

Based on the overall score of skin symptoms, which includes a rating of erythema, pustules, and edema together with a systemic inflammation score of fever, white blood cell count, serum C-reactive protein, and albumin levels, the severity of psoriasis is classified as mild, moderate, or severe. [31] Psoriasis flare-related cutaneous symptoms can include itching, burning, and discomfort. Extra cutaneous symptoms of the condition can include arthralgia, jaundice, abnormalities of the nails, and edema of the lower extremities due to its systemic nature. [32] Drugs like amoxicillin and terbinafine, ointments like calcipotriol and betamethasone, or abrupt or rapid tapering off of systemic corticosteroids or cyclosporine can all cause psoriasis flares. [33, 34, 35]

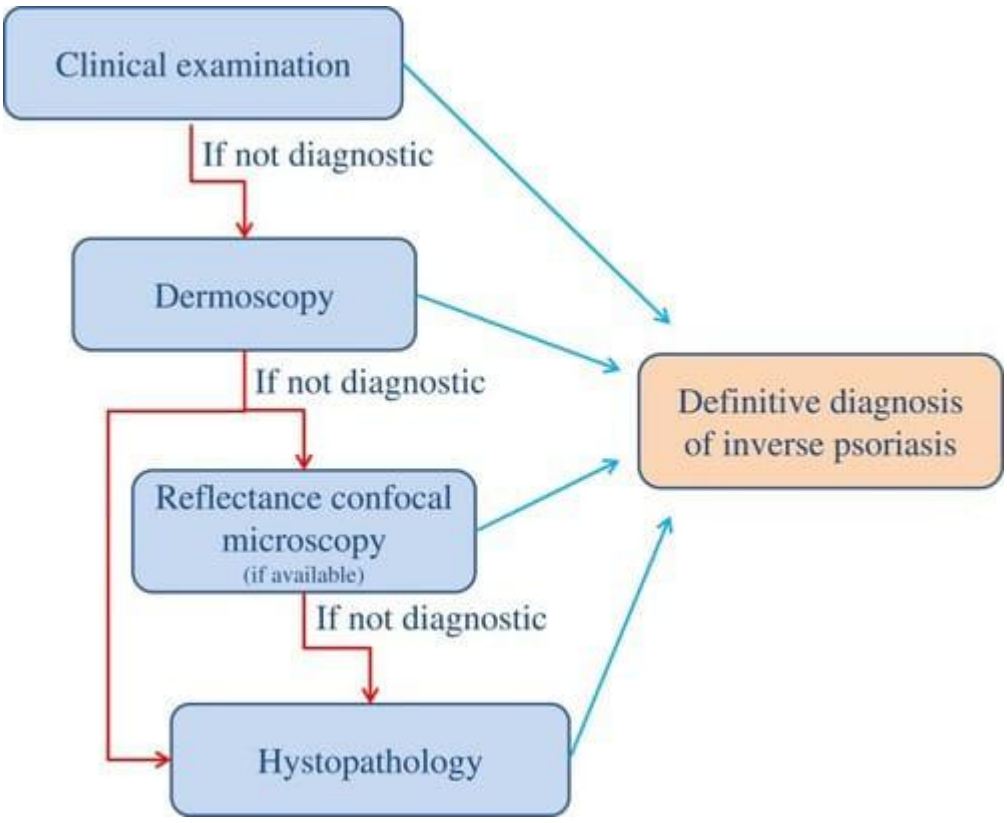

Fig.2 Diagnosing inverse psoriasis

Dermatoscopy has improved the clinical diagnosis of psoriasis in recent years. Specifically, on an erythematous backdrop, low magnification (X10) dermoscopy reveals the distinctive presence of whitish scales and "red dots" evenly dispersed across the entire plaque. [36] A non-invasive technique for morphofunctional assessment of the subcutaneous fat, dermis, epidermis, and skin appendages is high-frequency ultrasound (HFUS). It enables direct determination of the thickness of different skin structures and high-resolution imaging. [37, 38] Dermatoscopy can help with the non-invasive diagnosis of dermatological disorders, such as plaque psoriasis, according to numerous studies in the literature. This method offers information at the sub-macroscopic level that is helpful for differential diagnosis. [39]

Treatment and management

- Retinoid, which regulate gene transcription, include IL6, are derived from vitamin A and bind to nuclear receptors, retinoic acid receptors, and retinoid X receptors. Retinoids slow down proliferation of cells by stimulating keratinocyte differentiation and decreasing epidermal hyperplasia. Japan uses etretinate, a second-generation retinoid; many different countries uses acitretin, a metabolically active form of etretinate that has a shorter half-life and is eliminated more rapidly than etretinate. [40,41]
- Dihydrofolate reductase (DHFR), an enzyme involved in the production of tetrahydrofolate, is inhibited by methotrexate (MTX). In addition to inhibiting DNA synthesis, MTX causes suppression of the synthesis of purines, methionine, and thymidylates. Methotrexate improves psoriasis by aiming against the overactive immune system that results in the disease. It prevents the action of dihydrofolate reductase, an enzyme essential for DNA synthesis. By lowering this enzyme, methotrexate works control psoriasis symptoms by inhibiting the skin cells' explosive the proliferation and reducing the inflammatory response of the immune system. [42]
- Cyclosporine a (cya) is an inhibitor of calcineurin. Cya combines with cyclophilin to generate a compound that inhibits calcineurin's phosphatase activity and reduces the release of inflammatory cytokines, including those in T cells. Cyclosporine is an immunosuppressant that works by inhibiting T-cells—a group of white blood cells involved in the immune response—from working, which helps control psoriasis. Psoriasis results from the immune system attacking healthy skin cells by mistake, which causes inflammation and a high turnover rate of skin cells. Cyclosporine lessens the hyperactive immune response by inhibiting T-cell activation, which reduces the inflammation, scaling, and redness linked to psoriasis. [41,43]
- Tumor necrosis factor-alpha (TNF-alpha), a cytokine that is important in inflammation and the hyperproliferation of skin cells in psoriasis, is the target that infliximab binds to in order to treat psoriasis. By blocking TNF-alpha, infliximab lessens inflammation and slows down the skin's rapid cell turnover, which helps to improve the look and feel of psoriasis. as tnfα inhibitors, infliximab, adalimumab, and certolizumab pegol are presently prescribed for the treatment of psoriasis. [44]
- As a member of the IL1 superfamily, IL36 is crucial for attracting and stimulating Th17 cells and neutrophils in psoriasis. [45]
- First-generation JAK inhibitor tofacitinib mainly targets JAK3, JAK2, and JAK1. [46] During weeks 16–24 in the phase 3 trials, the PASI75 response to tofacitinib was 39.5–54.3% (5 mg twice daily) and 59.2–81.1% (10 mg twice daily), whereas the placebo response was 5.6–12.5%. [47]
- Hydrogels provide several benefits, such as their biocompatibility, PH and temperature sensitivities, injectability, water absorption capacity of about 10–20 times molecular weight, and ease of modification. Liposomal MTX hydrogels were developed. For the purpose to manage psoriasis, hydrogels moisten the skin, decrease inflammation, protect lesions from irritating substances, and occasionally give medicine directly to the affected areas. They improve the effectiveness of treatments, relieve discomfort, and keep the skin hydrated [48]
- Recent research has focused on using nanoparticles as the drug's carrier, with the aim of reducing side effects, increasing efficacy and dosage frequency, improving site specificity, and treating the disease from its core. Conventional nanoparticles such as liposomes, ethosomes, neosomes, and polymeric nanoparticles were used in the early research. Nanoparticles may trigger responses from the immune system, toxicity, and changes in cell function when they penetrate cells and tissues. The

way they interact with biological systems and affect health is influenced by their small size and surface features. [49]

- Pain and itching sensations are temporarily reduced when capsaicin activates the TRPV1 receptors on nerve cells. It improves the amount of a neurotransmitter that is involved in pain and inflammation, resulting in decreased redness, itching, and inflammation.The ability of liposomes, niosomes, and emulsomes carrying capsaicin (CAP) to provide targeted and regulated distribution, hence enhancing the drug's topical delivery. [50]
- Although topical CAP treatment is very helpful for psoriatic diseases, its blistering and stinging effects on the skin limit its use. Adding the medication to an appropriate carrier system would be preferred to lessen these side effects. [51]

Conclusion

Seasonal shifts in psoriasis incidence and flare-ups could indicate a pattern impacted by a range of behavioral and environmental factors. According to research, the winter months can make psoriasis worse because of the decreased sunshine exposure and increased dryness. On the other hand, temperatures during the summer that are warmer and brighter might help certain people since more UV radiation has a healing benefit. Individuals may have different effects from seasonal changes; for example, some people may find summertime exacerbations because of elements like heat and sweating. All things considered, treating psoriasis frequently requires modifying treatment plans to take into account individual reactions and seasonal fluctuation. Its care can be challenging since the condition is caused by a combination of environmental variables, immune system dysregulation, and hereditary predisposition. Combining systemic drugs, lifestyle modifications, and topical therapy with ongoing monitoring to customize interventions to the patient's changing needs is often the basis of an effective treatment plan. It is especially important to integrate supportive care and mental health issues because psoriasis has a substantial impact on patients' quality of life, affecting not just physical symptoms but also psychological well-being. With the goal of improving patient outcomes and management techniques down the road, ongoing research is crucial to the development of targeted therapeutics and the knowledge of disease causes.

References

1. Smith CH, Barker JN. Psoriasis and its management. Bmj. 2006 Aug 17; 333(7564):380-4.
2. Raharja A, Mahil SK, Barker JN. Psoriasis: a brief overview. Clinical Medicine. 2021 May 1; 21(3):170-3.
3. Kuchekar AB, Pujari RR, Kuchekar SB, Dhole SN, Mule PM, Vidyapeeth B, Wadi B. Psoriasis: A comprehensive review. Int J Pharm Life Sci. 2011 Jun; 2(6):857-77.
4. Agarwal K, Das S, Kumar R, De A. Psoriasis and its association with metabolic syndrome. Indian Journal of Dermatology. 2023 May 1; 68(3):274-7.
5. Jensen KK, Serup J, Alsing KK. Psoriasis and seasonal variation: a systematic review on reports from Northern and Central Europe—little overall variation but distinctive subsets with improvement in summer or wintertime. Skin Research and Technology. 2022 Jan; 28(1):180-6.
6. Henseler T, Christophers E. Psoriasis of early and late onset: characterization of two types of psoriasis vulgaris. Journal of the American Academy of Dermatology. 1985 Sep 1; 13(3):450-6.
7. Vol. 1-78 (1893-1938) were published under the journal's former title Dermatologische Zeitschrift and Vol. 79-183 (1939-1991) under Dermatologica.
8. Kumar S, Nayak CS, Padhi T, Rao G, Rao A, Sharma VK, Srinivas CR. Epidemiological pattern of psoriasis, vitiligo and atopic dermatitis in India: Hospital-based point prevalence. Indian dermatology online journal. 2014 Nov 1; 5(Suppl 1): S6-8.
9. Bedi T R. Clinical profile of psoriasis in North India. Indian J Dermatol Venereol Leprol 1995; 61:202-205
10. Dhabale A, Nagpure S. Types of psoriasis and their effects on the immune system. Cureus. 2022 Sep; 14(9).

11. MacDonald A, Burden AD. Psoriasis: advances in pathophysiology and management. Postgraduate medical journal. 2007 Nov; 83(985):690-7.
12. Creamer D, Allen MH, Sousa A, Poston R, Barker JN. Localization of endothelial proliferation and microvascular expansion in active plaque psoriasis. British Journal of Dermatology. 1997 Jun; 136(6):859-65.
13. Xia YP, Li B, Hylton D, Detmar M, Yancopoulos GD, Rudge JS. Transgenic delivery of VEGF to mouse skin leads to an inflammatory condition resembling human psoriasis. Blood. 2003 Jul 1; 102(1):161-8.
14. Bhushan M, McLaughlin B, Weiss JB, Griffiths CE. Levels of endothelial cell stimulating angiogenesis factor and vascular endothelial growth factor are elevated in psoriasis. British Journal of Dermatology. 1999 Dec 1; 141(6):1054-60.
15. Snowden JA, Heaton DC. Development of psoriasis after syngeneic bone marrow transplant from psoriatic donor: further evidence for adoptive autoimmunity. British Journal of Dermatology. 1997 Jul 1; 137(1):130-2
16. Boyman O, Hefti HP, Conrad C, Nickoloff BJ, Suter M, Nestle FO. Spontaneous development of psoriasis in a new animal model shows an essential role for resident T cells and tumor necrosis factor-α. The Journal of experimental medicine. 2004 Mar 1; 199(5):731-6.
17. Kauffman CL, Aria N, Toichi E, mccormick TS, Cooper KD, Gottlieb AB, Everitt DE, Frederick B, Zhu Y, Graham MA, Pendley CE. A phase I study evaluating the safety, pharmacokinetics, and clinical response of a human IL-12 p40 antibody in subjects with plaque psoriasis. Journal of Investigative Dermatology. 2004 Dec 1; 123(6):1037-44.
18. Zheng Y, Danilenko DM, Valdez P, Kasman I, Eastham-Anderson J, Wu J, Ouyang W. Interleukin-22, a TH17 cytokine, mediates IL-23-induced dermal inflammation and acanthosis. Nature. 2007 Feb 8; 445(7128):648-51.
19. Mussi A, Bonifati C, Carducci M, D'Agosto G, Pimpinelli F, D'Urso D, D'Auria L, Fazio M, Ameglio F. Serum TNF-alpha levels correlate with disease severity and are reduced by effective therapy in plaque-type psoriasis. Journal of biological regulators and homeostatic agents. 1997 Jul 1; 11(3):115-8.
20. Cameron AL, Kirby B, Griffiths CE. Circulating natural killer cells in psoriasis. British Journal of Dermatology. 2003 Jul 1; 149(1):160-4.
21. Baker BS, Ovigne JM, Powles AV, Corcoran S, Fry L. Normal keratinocytes express Toll-like receptors (tlrs) 1, 2 and 5: modulation of TLR expression in chronic plaque psoriasis. British Journal of Dermatology. 2003 Apr 1; 148(4):670-9.
22. Musumeci ML, Nasca MR, Boscaglia S, Micali G. The role of lifestyle and nutrition in psoriasis: Current status of knowledge and interventions. Dermatologic Therapy. 2022 Sep; 35(9): e15685.
23. Zhu Kj, Zhu cy, Fan Ym. Alcohol consumption and psoriatic risk: a meta-analysis of case–control studies. The Journal of dermatology. 2012 Sep; 39(9):770-3.
24. Zuccotti E, Oliveri M, Ratto D, Di Iorio C, Occhinegro A, Rossi P, girometta C. Nutritional strategies for psoriasis: current scientific evidence in clinical trials. European Review for Medical & Pharmacological Sciences. 2018 Dec 1; 22(23).
25. Madden SK, Flanagan KL, Jones G. How lifestyle factors and their associated pathogenetic mechanisms impact psoriasis. Clinical Nutrition. 2020 Apr 1; 39(4):1026-40.
26. Armstrong AW, Harskamp CT, Dhillon JS, Armstrong EJ. Psoriasis and smoking: a systematic review and meta-analysis. British journal of dermatology. 2014 Feb 1; 170(2):304-14.
27. Katsimbri P, Korakas E, Kountouri A, Ikonomidis I, Tsougos E, Vlachos D, Papadavid E, Raptis A, Lambadiari V. The effect of antioxidant and anti-inflammatory capacity of diet on psoriasis and psoriatic arthritis phenotype: nutrition as therapeutic tool. Antioxidants. 2021 Jan 22; 10(2):157.
28. Pacifico A, Conic RR, Cristaudo A, Garbarino S, Ardigò M, Morrone A, Iacovelli P, di Gregorio S, Pigatto PD, Grada A, Feldman SR. Diet-related phototoxic reactions in psoriatic patients undergoing phototherapy: results from a multicenter prospective study. Nutrients. 2021 Aug 25; 13(9):2934.

29. Rastmanesh R. Psoriasis and vegetarian diets: a role for cortisol and potassium. Medical hypotheses. 2009; 3(72):368.
30. Tsai TY, Yen H, Huang YC. Serum homocysteine, folate and vitamin B12 levels in patients with psoriasis: a systematic review and meta-analysis. British Journal of Dermatology. 2019 Feb 1; 180(2):382-9.
31. Fujita H, Gooderham M, Romiti R. Diagnosis of generalized pustular psoriasis. American Journal of Clinical Dermatology. 2022 Jan; 23(Suppl 1):31-8.
32. Ly K, Beck KM, Smith MP, Thibodeaux Q, Bhutani T. Diagnosis and screening of patients with generalized pustular psoriasis. Psoriasis: Targets and Therapy. 2019 Jun 20:37-42.
33. Tobin AM, Langan SM, Collins P, Kirby B. Generalized pustular psoriasis (von Zumbusch) following the use of calcipotriol and betamethasone dipropionate ointment: a report of two cases. Clinical and experimental dermatology. 2009 Jul 1; 34(5):629-30.
34. Katz M, Seidenbaum M, Weinrauch L. Penicillin-induced generalized pustular psoriasis. Journal of the American Academy of Dermatology. 1987 Nov 1; 17(5):918-20.
35. Samotij D, Szczęch J, Reich A. Generalized pustular psoriasis: divergence of innate and adaptive immunity. International Journal of Molecular Sciences. 2021 Aug 22; 22(16):9048.
36. Micali G, Verzì AE, Giuffrida G, Panebianco E, Musumeci ML, Lacarrubba F. Inverse psoriasis: from diagnosis to current treatment options. Clinical, cosmetic and investigational dermatology. 2019 Dec 31:953-9.
37. Negrutiu M, Danescu S, Popa T, Focsan M, Vesa SC, Szasz F, Baican A. Imaging Approach in the Diagnostics and Evaluation of the Psoriasis Plaque: A Preliminary Study and Literature Review. Diagnostics. 2024 May 7; 14(10):969.
38. Grajdeanu IA, Statescu L, Vata D, Popescu IA, Porumb-Andrese E, Patrascu AI, Taranu T, Crisan M, Solovastru LG. Imaging techniques in the diagnosis and monitoring of psoriasis. Experimental and therapeutic medicine. 2019 Dec; 18(6):4974-80.
39. Errichetti E, Stinco G. Dermoscopy in general dermatology: a practical overview. Dermatology and therapy. 2016 Dec; 6:471-507.
40. Tokuyama M, Mabuchi T. New treatment addressing the pathogenesis of psoriasis. International journal of molecular sciences. 2020 Oct 11; 21(20):7488.
41. Ogawa E, Sato Y, Minagawa A, Okuyama R. Pathogenesis of psoriasis and development of treatment. The Journal of dermatology. 2018 Mar; 45(3):264-72.
42. Raaby L, Zachariae C, Østensen M, Heickendorff L, Thielsen P, Grønbæk H, Skov L, Kyvsgaard N, Madsen JT, Heidenheim M, Funding AT. Methotrexate use and monitoring in patients with psoriasis: a consensus report based on a Danish expert meeting. Acta dermato-venereologica. 2017; 97(4):426-32.
43. Maza A, Montaudié H, Sbidian E, Gallini A, Aractingi S, Aubin F, Bachelez H, Cribier B, Joly P, Jullien D, Le Maître M. Oral cyclosporin in psoriasis: a systematic review on treatment modalities, risk of kidney toxicity and evidence for use in non-plaque psoriasis. Journal of the European Academy of Dermatology and Venereology. 2011 May; 25:19-27.
44. Gall JS, Kalb RE. Infliximab for the treatment of plaque psoriasis. Biologics: Targets and Therapy. 2008 Mar 1; 2(1):115-24.
45. Bachelez H, Choon SE, Marrakchi S, Burden AD, Tsai TF, Morita A, Turki H, Hall DB, Shear M, Baum P, Padula SJ. Inhibition of the interleukin-36 pathway for the treatment of generalized pustular psoriasis. New England Journal of Medicine. 2019 Mar 7; 380(10):981-3.
46. Papp KA, Menter MA, Abe M, Elewski B, Feldman SR, Gottlieb AB, Langley R, Luger T, Thaci D, Buonanno M, and Gupta P. Tofacitinib, an oral Janus kinase inhibitor, for the treatment of chronic plaque psoriasis: results from two randomized, placebo-controlled, phase III trials. British Journal of Dermatology. 2015 Oct 1; 173(4):949-61.
47. Bissonnette R, Iversen L, Sofen H, Griffiths CE, Foley P, Romiti R, Bachinsky M, Rottinghaus ST, Tan H, Proulx J, Valdez H. Tofacitinib withdrawal and retreatment in moderate-to-severe chronic plaque psoriasis: a randomized controlled trial. British Journal of Dermatology. 2015 May 1; 172(5):1395-406.

48. Garg T, Rath G, Goyal AK. Nanotechnological approaches for the effective management of psoriasis. Artificial Cells, Nanomedicine, and Biotechnology. 2016 Aug 17; 44(6):1374-82.
49. Hazari SA, Kaur H, Karwasra R, Abourehab MA, Khan AA, Kesharwani P. An overview of topical lipid-based and polymer-based nanocarriers for treatment of psoriasis. International Journal of Pharmaceutics. 2023 May 10; 638:122938.
50. Gupta R, Gupta M, Mangal S, Agrawal U, Vyas SP. Capsaicin-loaded vesicular systems designed for enhancing localized delivery for psoriasis therapy. Artificial cells, nanomedicine, and biotechnology. 2016 Apr 2; 44(3):825-34.
51. Carter RB. Topical capsaicin in the treatment of cutaneous disorders. Drug development research. 1991; 22(2):109-23.
52. Park MK, Li W, Paek SY, Li X, Wu S, Li T, Qureshi AA, Cho E. Consumption of polyunsaturated fatty acids and risk of incident psoriasis and psoriatic arthritis from the Nurses' Health Study II. British Journal of Dermatology. 2017 Jul 1; 177(1):302-6.
53. Wolters M. Diet and psoriasis: experimental data and clinical evidence. British Journal of Dermatology. 2005 Oct 1; 153(4):706-14.