International Journal of Research and Review
Vol. 10; Issue: 10; October 2023
Website: www.ijrrjournal.com
Review Paper *E-ISSN: 2349-9788; P-ISSN: 2454-2237*

The Association of Psoriasis and Multiple Sclerosis: A Narrative Review

Nadyah Abdullah Owaidhah[1], Mohammed Abdullah Alahmadi[2], Shuruq Talea Asiri[3], Shahad Fayez Albalawi[4], Hadeel Abdulrahman Aljoufi[4]

[1]Department of Family and Community Medicine, Assistant Professor Family Medicine, Taibah University, Al-Madinah al-Munawwarah, Saudi Arabia.
[2]Department of Medicine and Surgery, Taibah University, Al-Madinah al-Munawwarah, Saudi Arabia.
[3]Department of Medicine and Surgery, Najran University, Najran City, Saudi Arabia.
[4]Department of Medicine and Surgery, Jouf University, Al-Jouf City, Saudi Arabia.

Corresponding Author: Mohammed Abdullah Alahmadi

DOI: https://doi.org/10.52403/ijrr.20231036

ABSTRACT

Multiple sclerosis (MS) and psoriasis (PsO) are inflammatory diseases that share genetic risk variations and inflammatory mechanisms. The precise connection between PsO and MS has been the subject of earlier investigations, but it is still unclear because there is little conflicting data to support such a connection. There are several risk factors in common between PsO and MS, and disease-modifying treatments are powerful treatments for both PsO and MS, indicating a shared pathophysiology. In this narrative review, we have revised the causes, pathophysiology, diagnosis, and treatment of each condition. Also, we summaries the current research on any potential connections between PsO and MS. We come to the conclusion that more research is required to determine whether PsO and MS may have a meaningful association. In order to enable fast referral to a neurologist, if necessary, physicians may decide that it is prudent to assess individuals with PsO for MS.

Keywords: Psoriasis, Multiple sclerosis, Autoimmune disease, Co-morbid patients.

INTRODUCTION

Psoriasis (PsO) is a chronic skin condition marked by inflammation, with a significant genetic predisposition and autoimmunity. Evidence shows that inflammation goes beyond the skin and affects various organ systems. This leads to a hypothesis that PsO should be viewed as a systemic disorder rather than solely a dermatological issue (1). The fundamental processes at play entail intricate interactions between the adaptive and innate immune systems. T cells can engage with dendritic cells, macrophages, and keratinocytes through the secretion of cytokines (2). Comorbidities associated with PsO encompass inflammatory bowel disease, psoriatic arthritis (PsA), cardiovascular disease (CVD), diabetes mellitus (DM), metabolic syndrome, and specific types of cancer. It has been observed that individuals with PsO may also experience multiple sclerosis (MS) as a comorbidity, and the reverse relationship has been noted as well (3).

The leading non-traumatic source of neurological disability among young people is MS, which is an autoimmune condition branded by neurodegeneration and demyelination in the nervous system (4). MS has distinctive features such as inflammation, neurodegeneration, and gliosis. The pathological process involves the degradation of myelin sheaths that normally protect neurons, caused by the infiltration of lymphocytes and macrophage (5).

The connection between these two conditions is perhaps unsurprising,

considering that PsO and MS are inflammatory disorders with similar inheritance risk factors and inflammatory pathways. However, it's important to note that there is currently limited and unclear evidence supporting a direct link between these two disorders (3).

Our objective is to present a thorough examination of PsO and Ms, with a particular emphasis on the connection between the two conditions. To offer a more precise assessment of this association and adopt a more prudent approach in our patient care, our intention is to integrate the latest scientific evidence related to this linkage. In terms of our research approach, we conducted a thorough review of articles accessible through PubMed and Google Scholar.

Prevalence of PsO and MS

MS:

A descriptive study conducted in Saudi Arabia has shown a notable increase in the prevalence of MS, although it remains considerably lower than that in Western countries and neighboring nations such as Kuwait, Qatar, and the UAE. However, when comparing the findings to historical rates, the projected MS prevalence in Saudi Arabia stands at 40.40 cases per 100,000 people, which places the Kingdom in the low-risk zone according to the Kurtzke classification. Notably, Saudi nationals are estimated to have a significantly higher prevalence rate, specifically at 61.95 cases per 100,000 Saudi nationals. Furthermore, the study indicates that females, younger individuals, and those with higher levels of education exhibit higher prevalence rates of this condition (6).

Table 1. The prevalence of MS per 100,000 individuals across different global regions in the years 2013 and 2020.

	Number of countries included	2013 prevalence per 100,000 population [95% CI]	2020 prevalence per 100,000 population [95% CI]	Increase; absolute (%)
Global	81	29.26 [29.21, 29.30]	43.95 [43.90, 44.01]	14.69 (50%)
African	6	5.52 [5.41, 5.62]	8.76 [8.64, 8.89]	3.24 (59%)
Americas	15	62.89 [62.72, 63.05]	117.49 [117.27, 117.71]	54.6 (87%)
E. Mediterranean	14	23.91 [23.77, 24.04]	33.00 [32.85, 33.15]	9.09 (38%)
European	35	108.25 [108.01, 108.49]	142.81 [142.53, 143.08]	34.56 (32%)
Southeast Asia	4	5.44 [5.41, 5.48]	8.62 [8.58, 8.66]	3.18 (58%)
Western Pacific	7	3.64 [3.61, 3.67]	4.79 [4.75, 4.82]	1.15 (32%)

Resulting as the global prevalence of MS has risen since 2013 (7).

PsO:

Conversely, a worldwide investigation revealed that affluent regions such as Australasia, Western Europe, Central Europe, and North America exhibited the highest instances of psoriasis prevalence. Furthermore, the United States, India, and China had the most elevated prevalence rates of psoriasis among adults, proceeded by Germany, Brazil, France, and the United Kingdom. It's noteworthy that the prevalence of psoriasis was closely linked to age, with a higher occurrence among adults and a lower occurrence among children (8).

Figure 1. Prevalence of psoriasis among adults by country, it varied across countries due to differences in regional and country specific age structures (8).

Etiology and pathogenesis of PsO and MS
PsO
PsO is a persistent immunological condition characterized by chronic inflammation that impacts both the skin and joints. It is recognized by abnormal skin cell growth, particularly in the epidermal layer (9,5). Psoriasis is classified as an autoimmune disorder with potential multifactorial causes, including factors like injury, such as chemical or radiation exposure. Certain medications, like NSAIDs, beta-blockers, lithium, chloroquine, and steroids, can exacerbate psoriasis symptoms (1). A significant genetic factor plays a central role in the disease, accounting for 60-90% of its occurrence and potentially being passed down through heredity (10,11).
PsO involves unregulated growth and impaired differentiation of keratinocytes, primarily driven by ongoing inflammation and activated T cells (1). The persistent inflammation in psoriasis arises from various cytokines and is initiated by the activation of T cells. Specifically, antigen-presenting cells in the skin produce cytokines like IL-12 and IL-23 as part of this process (9). Thick plaques develop as a result of the dysregulation in the turnover rate of keratinocytes, leading to epidermal hyperplasia (acanthosis). These plaques cover inflammatory infiltrates composed of macrophages, dermal dendritic cells, neutrophils, and T cells (1).

MS:
While the exact pathophysiology of MS remains unclear, it is generally understood to be an immune-mediated inflammatory disorder influenced by both genetic and environmental factors, much like PsO (9,12). MS, often considered as a central nervous system autoimmunity primarily driven by CD4 T cells, is recognized for its distinctive lesions primarily found in white matter. Recent studies have shed light on the intricate nature of MS's origins. Factors such as innate immunity, CD8 T cells, B cells, pathology within grey matter, widespread irregularities in brain tissue that appears normal, and primary degenerative processes, including oligodendroglial pathology, may all play roles in this complex condition (13).
The formation of autoreactive T-helper cells is initiated by antigen-presenting cells presenting an unidentified self-antigen, which might include myelin-associated antigens. Subsequently, these cells breach the blood-brain barrier and release inflammatory mediators such as interferon (IFN)-gamma, IL-1 TNF-alpha, and lymphotoxin, culminating in the earlier inflammation phase seen in MS. This immune cell-driven inflammatory milieu is responsible for processes like demyelination, gliosis, macrophage activation, and neuroaxonal degeneration, ultimately leading to the formation of pathological plaques in MS. These plaques are characterized by extensive areas of demyelinated white and grey matter, affecting both the spinal cord and brain (9).

The common between the PsO and MS:
Both conditions exhibit distinct characteristics that define them. It's possible that a link exists between PsO and MS, stemming from genetic and environmental factors leading to an overactive immune system. Additionally, there may be a connection between PsO and MS due to broader immune system dysregulation (9).

Diagnosis of Psoriasis and Multiple Sclerosis
PsO
PsO is typically diagnosed based on clinical observations. Diagnosis and categorization of PsO rely on a thorough examination of the lesion's morphology. Clinical phenotypes like plaque, guttate, and pustular PsO illustrate the diversity of the condition. The most common form is plaque PsO, which can manifest anywhere on the body but is most frequently found on the knees and elbows. These lesions typically begin as dry, well-defined reddish macules or papules covered with silvery scales. Guttate PsO, commonly affecting children and

teenagers, is characterized by small, uniform droplet-like lesions measuring less than 1 cm in diameter on the trunk and limbs. Pustular psoriasis, whether localized or widespread, is identified by multiple tenders, sterile pustules with a reddish, mottled base. Skin biopsy isn't always required for diagnosis, and its usefulness can vary based on the age of the lesions (14-16).

MS

The diagnosis of MS depends on clinical evaluation and is supplemented by research findings. The 2017 McDonald criteria, which consider both DIS (dissemination in space) and DIT (dissemination in time), are employed for diagnosis. A common MRI finding in MS is the presence of multiple sclerotic plaques, with the periventricular region being a frequent location. MRI is the preferred imaging method for confirming MS. While not usually necessary for patients with typical clinical and MRI results, a cerebrospinal fluid (CSF) examination can provide additional supportive evidence of MS (17-19).

Treatment of Psoriasis and Multiple Sclerosis

PsO

PsO is a persistent condition marked by relapses, often necessitating prolonged treatment. Treatment aims to eliminate scales and inhibit the excessive growth of skin cells. Various treatment options include topical remedies like creams and ointments, phototherapies such as psoralen with ultraviolet A radiation (PUVA) and narrowband ultraviolet B radiation (NB-UVB), as well as oral or intravenous medications (9).

Treatment options for PsO are influenced by factors such as the condition's severity, the presence of coexisting health issues, and the accessibility of medical care. Patients with PsO are typically categorized into two groups, based on the clinical severity of their lesions, the extent of skin involvement, and the impact on their quality of life: mild or moderate to severe psoriasis (1). Individuals with mild-to-moderate PsO may find relief through topical treatments, including corticosteroids, vitamin D analogues, and coal tar. However, due to potential skin staining and irritation, these options are less commonly favoured compared to alternatives like calcineurin inhibitors, retinoids, anthralin, and phototherapy. In cases of moderate-to-severe PsO, healthcare providers often recommend systemic and biologic therapies, such as TNF-alpha inhibitors like adalimumab, etanercept, and infliximab. For oral systemic treatments in PsO management, options encompass methotrexate (MTX), acitretin, cyclosporine (CYA), and apremilast (5).

PsO in challenging-to-treat areas such as the scalp, face, nails, genitalia, palms, and soles can pose substantial functional challenges and typically exhibit less-than-optimal treatment responses. Specialized attention is necessary in managing these cases. It's important to note that steroids should be used only temporarily on the face or genitalia due to the potential risk of skin atrophy and telangiectasia (9).

MS

Several therapies are available for the management of individuals with relapsing-remitting MS (RRMS). These options include medications like natalizumab, mitoxantrone, and dimethyl fumarate. It is advisable for patients to initiate these treatments promptly following their MS diagnosis (20).

The ultimate treatment goal is to prevent the development of secondary MS. After the initial medication dose, it is essential to monitor patient adherence. One example of a humanized monoclonal antibody used for this purpose is natalizumab. Intravenous natalizumab is employed in the treatment of various conditions, and it works by restricting the migration of leukocytes into the central nervous system through the prevention of their adherence to vascular endothelial cells. Additionally, preparations

of interferon-beta can alter the functioning of T and B cells by potentially modifying cytokine expression and possibly reducing the expression of matrix metalloproteinases (21).

Patients with progressive-relapsing MS, primary progressive MS, or secondary progressive MS typically manifest underlying neurodegenerative processes. Consequently, disease-modifying medications often exhibit a lower degree of efficacy, with effects on disease progression varying and potentially ranging from positive outcomes to no significant impact. Interestingly, it appears that younger patients tend to derive greater benefits from these treatments (20,21).

The common between Psoriasis and Multiple sclerosis

Treatments for both MS and PsO overlap, involving the use of common therapies such as fumarates, a combination of IFN-beta with MTX, and IL-17 inhibitors. MTX and CYA are recommended for PsO treatment to reduce relapses and improve MS symptoms. Dimethyl fumarate operates by diminishing Th1 and Th17 cells, which are elevated in both PsO and MS, thereby reducing pro-inflammatory cytokine production. The shared success of fumarates in both conditions, as well as the effectiveness of IL-17A inhibitors, may be attributed to common polymorphisms in the IL-23 receptor gene associated with both MS and PsO. Furthermore, patients with MS can also benefit from phototherapy, a treatment effective in managing PsO and increasing vitamin D levels, which are often insufficient in those at a higher risk of developing MS (5).

Correlation of Psoriasis and Multiple Sclerosis

Although the precise nature of their connection remains unclear, previous research has identified a **correlation between PsO and MS.**

In earlier investigations, a case-control study was conducted to validate the link between MS and PsO. This study involved a cohort of 214 MS patients and a control group consisting of 192 individuals with headaches. The findings revealed a higher-than-expected prevalence of psoriasis among the MS patients. Specifically, plaque psoriasis was observed in 9 out of 214 (4.21%) MS patients, while only 1 out of 192 individuals in the control group had psoriasis, and this prevalence was not influenced by gender. Remarkably, six out of the nine psoriasis-affected MS patients began interferon-β treatment after their MS diagnosis, and four of them experienced worsening of their psoriasis symptoms. However, the patient with both conditions did not experience any exacerbations during treatment with additional disease-modifying medications (22).

A Danish research study investigated the potential for new-onset MS in individuals with mild (n=58,628) or severe (n=9952) PsO using a national registry. The study found that MS incidence rates were notably higher among those with both mild and severe PsO when compared to a reference group, suggesting a potential correlation between the severity of PsO and an increased risk of developing MS. Specifically, for every 10,000 person-years with MS, the incidence rates were 3.22 (95% CI, 2.57-4.04) for moderate PsO and 4.55 (95% CI, 2.52-8.22) for severe PsO, whereas the reference population had an incidence rate of 1.78 (1.74-1.82). After adjusting for factors such as age, gender, socioeconomic status, smoking, medication, comorbidities, and UV phototherapy, a higher risk of MS was observed (incidence rate ratio [IRR]=1.84 for mild PsO; incidence rate ratio [IRR]=1.84 for moderate PsO). In patients with severe PsO, the risk was even greater (incidence rate ratio [IRR]=2.61, 95% CI 1.44-4.74). Similar findings were obtained when analyzing data while considering PsA diagnosis, prior TNF-inhibitor medication use, or a family history of MS (23).

A retrospective study explored the impact of PsO on the progression and activity of multiple sclerosis (MS). The study involved

a cohort of 3,456 patients who had both MS and PsO and had been under observation for over 5 years. These cases were compared to a control group comprising individuals diagnosed solely with MS. According to the findings, 1.3% of MS patients also had a concurrent diagnosis of PsO, and among these, 78% (35 out of 45) had PsO before receiving an MS diagnosis. Notably, individuals with PsO experienced delayed onset of MS compared to those with relapsing-remitting MS (24).

A population-based study examined psoriasis prevalence between 1998 and 2008 in individuals with MS in comparison to a matched cohort from the general population. The findings revealed that the MS population had a higher incidence and prevalence of psoriasis. Specifically, the crude prevalence of psoriasis per 100,000 individuals was 4,666.1 (95% CI: 3,985.2-5,429.9) among those with MS, whereas it stood at 3,313.5 (95% CI: 3,057.4-3,585.3) in the matched population. Over this period, both psoriasis incidence and prevalence exhibited a gradual increase. When accounting for factors such as sex, age at the index date, socioeconomic status, and doctor visits, the incidence of incident psoriasis was found to be 54% higher in the MS group (HR 1.54; 95% CI: 1.07-2.24). This association may be attributed to genetic similarities between MS and psoriasis, along with shared environmental factors like smoking that could potentially be addressed through intervention. Further research exploring this relationship could provide insights into the etiology of MS, particularly in light of the observed benefits of fumarates in both conditions. In any case, it is essential to consider psoriasis as part of comprehensive MS management, as it affects approximately 5% of the MS population and is linked to increased comorbidity and a diminished quality of life (25).

Following the recommended PRISMA guidelines, a systematic review and meta-analysis were conducted, incorporating data from studies that compared the occurrence or magnitude of psoriasis cases among the families or relatives of individuals with MS versus those of control cases without MS. The meta-analysis revealed that family members of MS patients were at an elevated risk of developing psoriasis, as indicated by a combined unadjusted analysis of five eligible studies (OR 1.45, 95% CI 1.07, 1.97). This suggests a potential predisposition for psoriasis among the relatives of MS patients (26).

A systematic review and meta-analysis of observational data conducted in 2018 revealed higher odds ratios (OR) and hazard ratios (HR) for PsO in individuals with MS (OR 1.29, 95% CI, 1.14-1.45; HR 1.92, 1.32-2.80) (27).

The narrative review's findings regarding the potential association between PsO and MS reveal a notable lack of consensus and clarity. The available data exhibit variability and contradictions, with smaller studies suggesting a possible link while larger ones fail to consistently confirm it. Consequently, further research is imperative to either substantiate or refute this connection, which could have substantial implications for the diagnosis and management of both conditions, potentially unveiling common underlying mechanisms, genetic factors, or environmental triggers. Meanwhile, healthcare providers, including dermatologists, may consider the cautious screening of Psoriasis patients for signs of MS to enable timely referral and appropriate care in cases where it may be warranted (5).

CONCLUSION

While the exact cause of this association remains uncertain, it could potentially be attributed to shared genetic factors and common environmental elements, such as smoking, which could be potential targets for therapeutic interventions. It's noteworthy that patients with MS exhibit a higher prevalence and incidence of PsO. However, the existing data on the relationship between PsO and MS are predominantly conflicting and inconclusive. Some smaller-scale studies suggest a possible connection, but

larger studies conducted so far have not identified a substantial link between PsO and MS. To gain a deeper understanding of the mechanisms underlying this association, further research is necessary.

Declaration by Authors

Ethical Approval: Not Required
Acknowledgement: None
Source of Funding: None
Conflict of Interest: The authors declare no conflict of interest.

REFERENCES

1. Rendon A, Schäkel K. Psoriasis pathogenesis and treatment. Int J Mol Sci. 2019;20(6):1–28.
2. Benshlomo O. No Titleการบริหารจัดการการบริการที่มีคุณภาพในโรงพยาบาลสังกัดกระทรวงสาธารณสุข. วารสารวิชาการมหาวิทยาลัยอีสเทิร์นเอเชีย. 2023;4(1):88–100.
3. Hauser SL, Cree BAC. Treatment of Multiple Sclerosis: A Review. Am J Med [Internet]. 2020;133(12):1380-1390.e2. Available from: https://doi.org/10.1016/j.amjmed.2020.05.049
4. Dighriri IM, Aldalbahi AA, Albeladi F, Tahiri AA, Kinani EM, Almohsen RA, et al. An Overview of the History, Pathophysiology, and Pharmacological Interventions of Multiple Sclerosis. Cureus. 2023;15(1):1–12.
5. Silfvast-Kaiser AS, Homan KB, Mansouri B. A narrative review of psoriasis and multiple sclerosis: links and risks . Psoriasis Targets Ther. 2019; Volume 9:81–90.
6. Aljumah M, Bunyan R, Al Otaibi H, Al Towaijri G, Karim A, Al Malik Y, et al. Rising prevalence of multiple sclerosis in Saudi Arabia, a descriptive study. BMC Neurol. 2020;20(1):1–7.
7. Walton C, King R, Rechtman L, Kaye W, Leray E, Marrie RA, et al. Rising prevalence of multiple sclerosis worldwide: Insights from the Atlas of MS, third edition. Mult Scler J. 2020;26(14):1816–21.
8. Parisi R, Iskandar IYK, Kontopantelis E, Augustin M, Griffiths CEM, Ashcroft DM. National, regional, and worldwide epidemiology of psoriasis: Systematic analysis and modelling study. BMJ. 2020;369.
9. Raharja A, Mahil SK, Barker JN. Psoriasis: A brief overview. Clin Med J R Coll Physicians London. 2021;21(3):170–3.
10. Dand N, Mahil SK, Capon F, Smith CH, Simpson MA, Barker JN. Psoriasis and genetics. Acta Derm Venereol. 2020;100(100-year theme: Psoriasis):54–64.
11. Nguyen CT, Bloch Y, Savvas N, Adamopoulos IE. arthritis : A molecular insight. 2020;15–22.
12. Galetta KM, Bhattacharyya S. Multiple sclerosis and autoimmune neurology of the central nervous system. Med Clin. 2019;103(2):325–36.
13. Rahmanzadeh R, Brück W, Minagar A, Sahraian MA. Multiple sclerosis pathogenesis: missing pieces of an old puzzle. Rev Neurosci. 2018;30(1):67–83.
14. Raychaudhuri SK, Maverakis E, Raychaudhuri SP. Diagnosis and classification of psoriasis. Autoimmun Rev. 2014;13(4–5):490–5.
15. Johnson MAN, Armstrong AW. Clinical and histologic diagnostic guidelines for psoriasis: A critical review. Clin Rev Allergy Immunol. 2013;44(2):166–72.
16. Kimmel GW, Lebwohl M. Psoriasis: Overview and Diagnosis. 2018;1–16.
17. Thompson AJ, Banwell BL, Barkhof F, Carroll WM, Coetzee T, Comi G, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. Lancet Neurol. 2018;17(2):162–73.
18. Brownlee WJ, Hardy TA, Fazekas F, Miller DH. Diagnosis of multiple sclerosis: progress and challenges. Lancet [Internet]. 2017;389(10076):1336–46. Available from: http://dx.doi.org/10.1016/S0140-6736(16)30959-X
19. Ford H. Clinical presentation and diagnosis of multiple sclerosis. Clin Med J R Coll Physicians London. 2020;20(4):380–3.
20. Thomas L. Multiple sclerosis. Vol. 2, Nursing standard (Royal College of Nursing (Great Britain) : 1987). 1988. 27 p.
21. Wehner NG, Gasper C, Shopp G, Nelson J, Draper K, Parker S, et al. Immunotoxicity profile of natalizumab. J Immunotoxicol. 2009;6(2):115–29.
22. Fellner A, Dano M, Regev K, Mosek A, Karni A. Multiple sclerosis is associated with psoriasis. A case-control study. J Neurol Sci. 2014;338(1–2):226–8.

23. Egeberg A, Mallbris L, Gislason GH, Skov L, Hansen PR. Risk of multiple sclerosis in patients with psoriasis: A Danish nationwide cohort study. J Invest Dermatol. 2016;136(1):93–8.
24. Miron G, Gurevich M, Baum S, Achiron A, Barzilai A. Psoriasis comorbidity affects multiple sclerosis neurological progression: a retrospective case – control analysis. J Eur Acad Dermatology Venereol. 2017;31(12):2055–61.
25. Marrie RA, Patten SB, Tremlett H, Wolfson C, Leung S, Fisk JD. Increased incidence and prevalence of psoriasis in multiple sclerosis. Mult Scler Relat Disord. 2017;13(February):81–6.
26. Charlton O, Phan K, Smith SD, Parratt J. Psoriasis in family members of patients with multiple sclerosis. Mult Scler Relat Disord. 2019;36(September).
27. Shen MH, Ng CY, Chang KH, Chi CC. Association of multiple sclerosis with vitiligo: a systematic review and meta-analysis. Sci Rep. 2020;10(1).

How to cite this article: Nadyah Abdullah Owaidhah, Mohammed Abdullah Alahmadi, Shuruq Talea Asiri, Shahad Fayez Albalawi, Hadeel Abdulrahman Aljoufi. The association of psoriasis and multiple sclerosis: a narrative review. *International Journal of Research and Review*. 2023; 10(10): 291-298. DOI: *https://doi.org/10.52403/ijrr.20231036*

******