IOSR Journal of Multidisciplinary Research (IOSR -JMR)
ISSN: 3048-7439 Volume 3, Issue 3, Series 2, May. - June. (2026), PP 46-50
www.iosrjournals.org

Comorbidities of Psoriasis: An Updated Review

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Abstract:
psoriasis is a multifactorial autoimmune disease, which affects 4.5 million people globally. It has been linked to various comorbidities and environmental factors. The associated comorbidities include contrary heart disease, metabolic syndrome, and psychiatric abnormalities. Studies on psoriasis patients assessing dermatological life quality index (DLQI) showed reduced patient's life quality. Psychiatric comorbidities including anxiety and depression affect psoriasis patients at high rates. Suicidal ideation and behaviors showed increase by 2.05-fold and 1.26-fold respectively. Coronary artery disease risk increased by 1.14-fold in psoriasis various severity categories. While, the prevalence of coronary heart diseases in severe psoriasis cases was 70%. Stroke risk also increased by 38% in severe psoriasis patients. Moreover, the risk of metabolic comorbidities in psoriasis patients raised by 2.63-folds. However, diabetes prognosis worsens, and obesity prevalence doubled in severe psoriasis cases compared to mild psoriasis cases. A study also showed improvement in psoriasis symptoms while treating diabetes. Certain hypoglycemic agents such as liraglutide and metformin showed best results. Autoimmune comorbidities like psoriatic arthritis and inflammatory bowel diseases are more prevalent in psoriasis too. The strong association between psoriasis and other comorbidities have been established in many studies. Therefore, it is necessary to address this complicated relationship between psoriasis and other associated diseases. A multidisciplinary approach, comorbidities management, and lifestyle modifications are crucial for psoriasis patient improvment. Meanwhile, further studies is required for better understanding of this relationship.

Date of Submission: 06-06-2026 Date of Acceptance: 17-06-2026

I. Introduction:

Psoriasis, a chronic inflammatory skin condition, is characterized by red plaques covered with scales, primarily found on the extensor surfaces, scalp, and lumbosacral region[1]. According to the 2019 Global Burden of Disease Study, approximately 4.5 million people worldwide are affected by psoriasis[2]. The incidence of this condition varies across different regions, with higher age-standardized rates seen in high-income countries and territories[2].

Psoriasis has a considerable impact on the quality of life of patients, as indicated by higher scores on the dermatological life quality index (DLQI) when compared to individuals without the condition[3–6] Factors that predict a lower quality of life for psoriasis patients include a larger affected body surface area and nail changes associated with the condition[6].

In addition to the cutaneous manifestations, autoimmune and metabolic comorbidities associated with psoriasis contribute to a decline in patients' quality of life[7,8]. Psoriasis is linked to psychiatric disorders, including a higher susceptibility to major depressive disorder[9–12]. Studies have reported a 13.9% prevalence of moderate-to-severe depression in individuals with psoriasis vulgaris[13]. Psoriasis patients also face a 48% increased risk of unspecified anxiety disorder and a 2.51-fold higher risk of developing anxiety symptoms[14]. All in all, the significant impact of psoriasis on patients' quality of life, and its association with debilitating comorbidities necessitate a comprehensive and holistic approach to health in psoriasis patients. In accord, our current review article aims to summarize evidence on the prevalence of various comorbidities in patients with psoriasis and predictors of their risk.

II. Comorbidities Associated with Psoriasis

1- Cardiovascular Comorbidities

Psoriasis is known to be associated with systemic inflammation, evident by the rising levels of pro-inflammatory cytokines and inflammatory biomarkers in patients with psoriasis[15]. These changes could precipitate endothelial injury and dysfunction, the hallmark in the pathogenesis of atherosclerosis[16]. Moreover, inflammation changes the structure of lipoproteins into oxidized forms that reduce endothelial nitric oxide synthetase (eNOS) activity by enhancing the metabolism of nitric oxide by asymmetric dimethylarginine (ADMA), an endogenous competitive eNOS inhibitor[17–20]. These along with the strong association between psoriasis and altered lipid

metabolism and dyslipidemia, could predispose psoriasis patients to early and progressive fatty streak and atheroma development. In patients with psoriasis, mean ADMA and homocysteine levels were higher when compared to controls[20].

Epidemiologically, Kaiser et al. performed a meta-analysis and revealed a 1.14-fold increase in the risk of coronary artery disease (CAD) in patients with psoriasis, with a higher risk (odds ratio (OR) = 1.71) for severe CAD[21]. Dhana and colleagues also performed a meta-analysis and showcased a correlation with psoriasis severity, as patients with severe disease had higher pooled relative risk (RR) when compared to patients with mild disease[22]. This was also confirmed by a systematic review and meta-analysis on the association between psoriasis and major cardiovascular events (MACEs) including myocardial infarction (MI) and stroke. The risk of stroke was 10% and 38% higher in patients with mild and severe psoriasis, respectively, whereas the risk of MI was 20% and 70% higher in patients with mild and severe psoriasis. Furthermore, risk of cardiovascular death was increased by 37% in patients with severe psoriasis[23]. The association might be bidirectional, specifically in regard to hypertension, a major risk factor for MI and stroke. Kim and colleagues found a higher risk for psoriasis in patients with hypertension when compared to normotensive patients during a 10-year follow-up period[24]. All in all, patients with psoriasis are at higher risk of developing hypertension and cardiovascular morbidity with a positive correlation with patients' psoriatic disease severity, which warrants careful consideration and screening for heart disease in patients with psoriasis.

2- Metabolic Comorbidities

The association between psoriasis and metabolic abnormalities have been illustrated in both molecular and epidemiological studies in both preclinical and clinical models. Metabolic syndrome defined in the National Cholesterol Education Program's Adult Treatment Panel III report (ATP III). The selected criteria included abdominal obesity, atherogenic dyslipidemia, raised blood pressure, insulin resistance ± glucose intolerance, proinflammatory and prothrombotic states[25]. A meta-analysis of five studies with 241 patients reported a 2.63-folds increase in the risk of metabolic syndrome in patients with psoriasis. In studies that included chronic and severe disease, a higher risk for metabolic syndrome was observed[26]. In regard to components of metabolic syndrome, patients with psoriasis were shown to have a higher risk for obesity, with doubling of the risk between mild and severe disease populations[27]. This might be mediated by psoriasis-induced dysfunction in adipose tissue macrophages which exacerbate insulin resistance and inhibit lipolysis[28,29]. In line, a strong correlation was illustrated between homeostatic model assessment of insulin resistance (HOMA-IR) and psoriasis area and severity index (PASI)[29].

Similar to obesity and biologically aligned with insulin resistance, patients with psoriasis do not only have a higher frequency of diabetes mellitus, but also experience a more severe disease prognosis with poor prognosis[30,31]. Interestingly, increasing evidence suggests that several hypoglycemic agents used in the management of type 2 diabetes mellitus could exert beneficial effects in patients with psoriasis[32]. For example, the use of glucagon-like peptide-1 receptor agonist liraglutide resulted in a significant decrease in the values of PASI and dermatological quality of life index (DLQI) from baseline[33]. Also, metformin reduced erythema, scaling, and induration (ESI) when compared to controls during a 12-weeks period. This was coupled with improvements in body mass index (BMI), fasting plasma glucose, serum triglycerides, high-density lipoprotein (HDL), LDL, systolic and diastolic blood pressures, and total cholesterol[34].

Overall, psoriasis is strongly associated with metabolic diseases such as obesity and diabetes mellitus, leading to a higher risk of metabolic syndrome and a more severe disease prognosis. In addition, numerous oral hypoglycemic medications show promise in improving psoriasis symptoms and metabolic health.

Psychiatric Comorbidities

Psoriasis is linked to psychiatric disorders, including a higher susceptibility to major depressive disorder[9]. For instance, individuals with psoriasis have a higher susceptibility to major depressive disorder compared to healthy individuals [10–12,35,36] A recent cross-sectional study revealed a prevalence of 13.9% for moderate-to-severe depression in individuals with psoriasis vulgaris [13]. Moreover, a recent meta-analysis demonstrated a 48% increased risk of unspecified anxiety disorder among psoriasis patients[14]. Additionally, patients with psoriasis were found to be at a 2.51-fold higher risk of developing anxiety symptoms [14]. A cross-sectional investigation in Egypt highlighted high prevalence of depression, anxiety, stress, and insomnia symptoms in patients with psoriasis[37]. Moreover, Singh et al. summarized evidence from 18 studies with a total of 1,767,583 participants, of whom 330,207 had psoriasis, and showed 2.05-folds and 1.26-folds higher odds of suicidal ideation and suicidal behaviors in patients with psoriasis, respectively[38]. In summary, psoriasis is strongly associated with psychiatric disorders, including a significantly higher risk of major depressive disorder, anxiety disorders, and suicidal tendencies compared to individuals without psoriasis.

Autoimmune Comorbidities

As previously discussed in the introduction, psoriasis represents an immune-mediated, inflammatory skin condition. The immune dysregulation in psoriasis is driven by accelerated inflammation via the tumor necrosis factor-α/interleukin-23/interleukin-17 axis[39]. Interleukin-17 up-regulates the proliferation of keratinocytes and down-regulates their differentiation, thus resulting in the hyperkeratotic scaling that is a central feature in psoriasis[40]. Moreover, The accelerated TNF-α/IL-23/IL-17 axis coincides with other characteristic histopathological features of psoriasis including aberrant differentiation and neutrophilic microabscess[41]. The critical function of CD8+ T cells within the epidermis has been established in psoriasis, where these cells are responsible for the production of pathogenic IL-17A[42–45]. In xenotransplanted mice models, inhibiting CD8+ T cells effectively prevented the development of psoriasis[43]. All in all, molecular evidence supports the autoimmune components of psoriasis etiopathogenesis which could be the link between psoriasis and other autoimmune conditions.

Most notable, psoriatic arthritis is prevalent in as much as 20% of patients with psoriasis, with the majority of affected patients being seronegative and a minority possessing positive rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibodies (anti-CCP)[46]. Predictors for psoriatic arthritis included age at onset of psoriasis, duration, nail involvement, erythematous lunula, onychorrhexis, oil drop, and subungual hyperkeratosis[47].

Another strongly associated autoimmune condition is inflammatory bowel diseases (IBD). According to a meta-analysis, the risk of Crohn's disease and Ulcerative Colitis (UC) was 153% and 71% higher than that in healthy controls, respectively[48]. According to a Mendellian randomization study, the association between psoriasis and IBD was higher in patients with genetically predisposed IBD[49]. In another investigation, Cox-regression survival analysis smoking as independent risk factor for psoriasis in patients with IBD, with immuno-suppressive therapy inversely correlating with the risk of psoriasis[50]. Other autoimmune conditions were also associated with psoriasis including autoimmune thyroid disease and rheumatoid arthritis among others[51,52]. Intriguingly, psoriasis comorbidity could impact the prognosis of these conditions, as evident by the three times higher risk for hospitalization in systemic lupus erythematosus (SLE) patients with psoriasis compared to patients with SLE alone[53]. In summary, psoriatic arthritis is common in psoriasis patients, and psoriasis is associated with other autoimmune conditions that can affect their prognosis.

III. Discussion

An initial aim of this study was to review the evidence on the association of psoriasis with other morbidities. This included cardiovascular, metabolic, psychiatric, and autoimmune conditions. The significance of these results could not be underestimated given the significant impact of multimorbidity on patients' quality of life. Belachew and colleagues reported a decreased health-related quality of life (HRQoL) in patients with psoriasis, with an enhanced decrement in patients with comorbidities[54]. An atherogenic lipid profile was shown in pediatric patients with psoriasis as 15.3% had elevated cholesterol, 18% had low HDL, and 12.6% had increased LDL[55]. These finding warrant screening for cardiovascular risk factors in patients with psoriasis for early detection and management[55]. In line, in a population of patients with psoriasis and psoriatic arthritis, comorbidities had a deleterious impact on patients' HRQoL, warranting optimal screening and management of patients' conditions to maximize improvements in quality of life[56].

The presence of comorbidities could also influence patients' treatment plan. As illustrated above, oral hypoglycemic agents were shown to improve PASI and DLQI scores in psoriasis patients with concomitant diabetes[57]. In addition, psoriasis might be trigger by the use of certain anti-hypertensive medications, specifically angiotensin-converting enzyme (ACE) inhibitors[58]. This association might have an implication on the management of patients with psoriasis and hypertension, ischemic heart disease, or diabetic nephropathy. Other antihypertensive medications that were linked to psoriasis included thiazide diuretics and beta blockers[59].

The association of psoriasis with cardiovascular and metabolic conditions honors the role of lifestyle modification in the management of these comorbidities. A diet high in fibers was consistently linked to lower PASI scores, lower MACE frequency, MI and stroke risk, and glycemic control[60–64]. In line, physical exercise was shown to positively improve DLQI and PASI scores in psoriasis patients[65]. However, patients could be limited by psoriasis's cutaneous manifestations and symptoms (e.g., pruritis) which could halt patients' intentions of physical exercise in patients with chronic plaque psoriasis[65,66].

Future directions include studies establishing the potential of screening programs, lab tests, and surveys for the early and sensitive detection of psychiatric and physical comorbidities in patients with psoriasis. This is crucial as patients with psoriasis are predisposed and might benefit less from regular screening schedules and protocols. Moreover, our review emphasizes the necessity of multidisciplinary team care and personalized medicine in the management of psoriasis patients, especially in the presence of comorbidities.

IV. Conclusion

Psoriasis significantly impacts patients' quality of life and is associated with a range of comorbidities, including cardiovascular, metabolic, psychiatric, and autoimmune conditions. These comorbidities underscore the importance of early detection and management, potentially affecting treatment choices. Lifestyle modifications, such as diet and exercise, can play a pivotal role in managing these conditions. Future research should focus on developing effective screening methods and personalized care for psoriasis patients with comorbidities, emphasizing a multidisciplinary approach to their management.

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