

Psoriasis Comorbidities: Obesity, Diet, and Metabolic Syndrome

Psoriasis is a systemic inflammatory disease that most commonly manifests on the skin and joints but is associated with several comorbidities affecting various organs/domains of health. In the early 2000s, multiple studies revealed that psoriasis patients had significantly higher rates of conditions like cardiac/cerebral vascular disease, obesity, type II diabetes mellitus, hyperlipidemia, and hypertension, the last four collectively being referred to as metabolic syndrome.^[1] Later on, higher prevalence of some other conditions like metabolic dysfunction-associated steatotic liver disease (MASLD), chronic kidney disease, depression, inflammatory bowel disease, and sexual dysfunction were also described.^[2] To reflect this multidimensional and multisystem nature of psoriasis, the term 'psoriatic disease' has been introduced. It is critical for dermatologists to understand, identify, and if possible prevent these comorbidities because of the following facts:

- Many of the comorbidities, especially cardiovascular and cerebrovascular disease, are associated with increased risk of mortality. This risk is higher than non-psoriatic patients suffering from these conditions, probably because of delayed diagnosis in this group of patients.
- Their severity is correlated with the severity of psoriasis, and this relationship is bidirectional, reflecting common pathophysiologic pathways underpinning them.
- They contribute significantly to the impaired quality of life associated with psoriatic disease.
- They complicate the treatment of psoriasis by limiting the choice of systemic treatments.
- They (especially obesity and overweight) are associated with poorer response to treatment and faster relapses.

Overweight and obesity are well known as independent risk factors for psoriasis as shown in several large studies.^[3] A recent study showed that the risk of psoriasis was doubled in patients with high abdominal adiposity and clinically obese patients with BMI > 35 had an even higher increase in psoriasis risk.^[4] The association of these two apparently unrelated conditions, one characterized by inflamed scaly plaques on the skin and the other by abnormal deposition of fat in various parts of the body, is deeply linked by shared pathological pathways. Excess adipose tissue aggravates psoriasis by producing various adipokines that have proinflammatory effects and also by promoting insulin resistance that affects keratinocyte proliferation and inflammation. On the other hand, psoriatic skin inflammation could precipitate obesity by direct and indirect mechanisms including promotion of insulin resistance and the adipogenic effect of IL17, one of the key cytokines in

psoriasis.^[5] Therefore, it becomes extremely important to address obesity in psoriasis patients. Conventionally, tools such as BMI, waist circumference, and waist-to-hip ratio have been used to diagnose obesity and grade cardiometabolic risk. But in recent years, it has become clear that these measurements, especially BMI, may not accurately reflect the amount and distribution of fat in the body, which are both important considerations in assessing its impact on the person's health. In this issue of the journal, a study by Fatima *et al.*^[6] uses dual-energy X-ray absorptiometry (DEXA) scan to accurately assess the body composition and adiposity of psoriasis patients and report a correlation with psoriasis severity. This and other methods like magnetic resonance imaging and computed tomography scans can assess body fat in different locations much more accurately. However, it remains to be seen how much added benefit accrues to our patients by using these expensive methods compared to simple measurements like waist-to-hip ratio.

The importance of obesity in psoriasis patients is further established by the fact that weight loss leads to improvement in the severity of psoriasis, in both untreated and treated patient populations.^[7] This leads us to the various methods employed to reverse obesity, ranging from dietary manipulations and exercise to bariatric surgery. The role of diet in psoriasis is not just mediated via obesity, but there is also a direct effect of various types of diets on psoriasis, even in nonobese patients. Randomized trials have shown that psoriasis patients show significantly higher reductions in psoriasis area and severity index (PASI) scores when they follow a low-calorie diet along with standard treatment, with both conventional and biologic agents.^[7] We have also long known about the low prevalence of psoriasis in countries and regions who follow the so-called mediterranean diet, and several studies have studied this phenomenon as well. Recently, other types of diets like ketogenic diet and gluten-free diet have been studied vis-à-vis their impact on psoriasis. In this issue, Neema *et al.*^[8] report the impact of the intermittent fasting on the disease severity and durability of response in methotrexate-treated patients with psoriasis. In spite of significant weight and waist circumference reduction in the fasting group, they did not find better clearance of psoriasis, although their patients maintained their improvement better than nonintermittent fasting patients after stopping methotrexate treatment. These are intriguing findings since prolonging treatment-free remission is a very important aim in a chronic, incurable disease like psoriasis. However, contradictory findings have been reported elsewhere^[9] and this aspect of psoriasis research merits much more serious work.

It is quite clear that diets aimed at reducing weight improve the severity of psoriasis in obese patients. Dietary advice however always goes hand-in-hand with advice about physical exercise, alcohol and smoking avoidance and so can be difficult to study in isolation. Nonetheless, a well-balanced, low-calorie diet should always be recommended to all psoriasis patients along with a healthy lifestyle since these complements medical treatment and improves almost all associated comorbidities. Further studies on dietary interventions in psoriasis can focus on the anti-inflammatory effect of various food items so that the psoriatic inflammation may be mitigated along with the benefits of reducing body weight and adiposity. These benefits would lead to the improvement in metabolic syndrome, thereby reducing cardiovascular and cerebrovascular morbidity and mortality as well as treatment response to various antipsoriatic medications.

Metabolic syndrome refers to the accumulation of certain lifestyle diseases like obesity, hyperlipidemia, glucose intolerance, and hypertension in a patient, which are linked to high risk of cardiovascular morbidity and mortality, type II diabetes, and chronic kidney disease. Multiple studies have shown that psoriasis patients are at high risk to develop metabolic syndrome and this risk rises with older age and the severity of psoriasis. This risk is at least twofold higher than comparable nonpsoriatic controls and increases with time.^[10] It is also well known that effective treatment of psoriasis particularly with biologic agents seems to reduce this risk. That is why it is important that patients with psoriasis be screened regularly and appropriate advice and referral given in time to mitigate the effects of metabolic syndrome.

Currently, the diagnosis of metabolic syndrome requires multiple anthropometric measurements and blood tests, which is time-consuming and labor-intensive. Therefore, many biomarkers have been studied in an attempt to accurately diagnose metabolic syndrome in a minimally invasive manner. These include proinflammatory cytokines, adipokines, neuropeptides, markers of pro-oxidant status, and prothrombotic factors.^[11]

However, there is no single perfect biomarker and combinations of the above are currently being studied. In this issue, Akl *et al.*^[12] report the association of the TGF beta superfamily cytokine, Growth Differentiating Factor-15 (GDF-15) with psoriasis. Not only was this cytokine positively associated with PASI score and disease duration but also it was more commonly elevated in the blood of psoriasis patients with metabolic syndrome. GDF-15 has been linked to different domains of metabolic syndrome, especially obesity and cardiovascular disease, and animal studies have reported weight loss via reduced appetite on administration of GDF-15 analogs.^[13] It remains to be seen if this marker

can usefully add to the growing list of biomarkers of metabolic syndrome with or without psoriasis and serve as a potential drug target in patients with obesity and psoriasis.

To conclude, identifying and effectively managing comorbidities in psoriasis patients is a priority and dermatologists should equip themselves with the skills and practices needed to achieve this aim. This is predicated on increased awareness from both physicians and patients, which in turn needs reliable and easily assessed clinical parameters and biomarkers. Further studies on the identification and management of comorbidities can improve the overall quality of life of a psoriasis patients in a much more profound way than mere drug treatment can. Hopefully, we will soon have much better tools in our hands to achieve this lofty aim to provide truly comprehensive treatment of psoriatic disease.

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Access this article online	
Website: https://journals.lww.com/idoj	Quick Response Code 
DOI: 10.4103/idoj.idoj_420_25	

How to cite this article: Saraswat A. Psoriasis comorbidities: Obesity, diet, and metabolic syndrome. *Indian Dermatol Online J* 2025;16:367-9.

Received: 15-Apr-2025. **Accepted:** 17-Apr-2025.

Published: 28-Apr-2025.

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