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# Challenges in Managing Metabolic Syndrome in Psoriasis: A Narrative Review of Pharmacological and Surgical Treatments

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**Abstract**

**Introduction:** Psoriasis is a chronic inflammatory disorder associated with multiple systemic comorbidities, most notably metabolic syndrome, which affects approximately one-third of individuals with the disease. Metabolic syndrome-characterized by obesity, insulin resistance, dyslipidemia, and hypertension-exacerbates systemic inflammation, further complicating disease management and treatment outcomes.

**Aim of Study:** This review explores the multidisciplinary approach to managing metabolic syndrome in psoriasis, with a particular focus on pharmacological and surgical interventions. It examines the challenges associated with these treatments and their implications for therapeutic efficacy.

**Brief Description of the State of Knowledge:** Psoriasis and metabolic syndrome share a complex, reciprocal relationship driven by chronic inflammation and metabolic dysregulation. While lifestyle modifications remain the cornerstone of management, many patients require additional pharmacological or surgical interventions. However, the presence of metabolic syndrome can alter the safety and effectiveness of systemic and biologic psoriasis therapies, underscoring the need for a personalized treatment approach.

**Conclusions:** Effective management requires interdisciplinary collaboration. Pharmacological treatments should minimize metabolic risks, while bariatric surgery may benefit selected patient groups. Further studies are needed to optimize treatment strategies and improve outcomes.

**Keywords:** metabolic syndrome, obesity, psoriasis, hypoglycemic agents, bariatric surgery.

## 1. Introduction

Psoriasis is a chronic immune-mediated disease that affects the skin, nails, and joints, with a global prevalence ranging from 0,09% to 11,4%, although data gaps exist in lower-income countries due to inadequate reporting [1-3]. Its incidence is increasing, particularly among adults and affluent populations [4, 5]. Psoriasis significantly impacts quality of life, causing physical discomfort, severe emotional distress, social stigma, and economic burden [2]. Genetic, immunologic, and environmental factors seem to all contribute to a pro-inflammatory state with the involvement of various immune cells (including, but not limited to, T-lymphocytes and dendritic cells), keratinocytes, and cytokine imbalances which lead to cutaneous and systemic manifestations of psoriasis [6, 7]. Several reports have demonstrated increased susceptibility to metabolic disturbances among psoriasis patients. A meta-analysis by Choudhary et al., which reviewed 63 observational studies, reported that metabolic syndrome was present in up to 30.29% of psoriasis patients, compared to 21.70 % in the control group [8].

Metabolic syndrome (originally named syndrome X) is a constellation of risk factors predisposing patients to type 2 diabetes and cardiovascular complications [9]. Estimates show it affects up to 25% of the adult population worldwide [10]. For decades, abdominal obesity and insulin resistance have been recognized as key factors in metabolic syndrome, and expert groups have proposed several diagnostic criteria [11]. The ones formulated by the International Diabetes Fenedarion in 2006 define metabolic syndrome as the presence of central obesity and at least 2 of the following: elevated blood pressure (≥130 mmHg systolic or ≥85 mmHg diastolic, or currently on drug treatment for hypertension), increased fasting glucose (≥100 mg/dL or currently on drug treatment for elevated blood glucose), increased triglycerides (≥150 mg/dL or current treatment for elevated triglycerides), reduced HDL-C (<40 mg/dL in men and <50 mg/dL in women or individuals receiving drug treatment for reduced HDL-C) [10].

Views on the pathophysiology of metabolic syndrome have changed since it was first mentioned in scientific literature. Initially attributed to insulin resistance, metabolic syndrome is now recognized as a chronic inflammatory condition, with pro-inflammatory cytokines (IL-6, TNF-α, CRP) and adipokines playing a key role [12].

Seeing how inflammation seems to be a crucial factor in both conditions, attempts have been made to pinpoint the exact pathophysiological processes underlying the link between psoriasis and metabolic syndrome. Release of pro-inflammatory cytokines, oxidative stress, endoplasmic reticulum stress, altered adipokine profile, and, more recently, dysregulation within the gut microbiome have all been postulated as plausible mechanisms behind this association. These alterations are interconnected and tend to exacerbate one another, resulting in a vicious cycle that needs to be addressed to ensure successful treatment (see Figure 1.) [13].

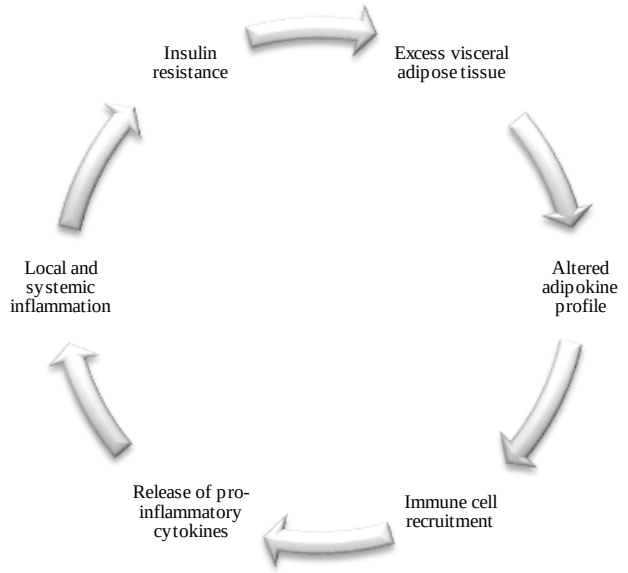


**Figure 1.** A simplified diagram illustrating the self-perpetuating cycle of chronic low-grade inflammation in metabolic syndrome. Psoriasis can further contribute to this cascade by amplifying systemic inflammation.

This narrative review explores available treatment strategies for patients with metabolic syndrome and psoriasis, focusing solely on pharmacological and surgical interventions. It emphasizes critical considerations in pharmacological management and highlights the importance of an interdisciplinary approach to optimize patient outcomes.

## 2. Materials and Methods

PubMed and Google Scholar databases were searched using relevant keywords for studies published until February 2, 2025. Only English-language articles were considered, with titles and abstracts screened first, followed by a full-text evaluation of selected papers.

## 3. Discussion

### 3.1. Pharmacological treatment

The primary approach to managing patients with metabolic syndrome involves targeting modifiable risk factors such as obesity, physical inactivity, inadequate nutrition, alcohol consumption, and smoking [11]. This can be effectively accomplished through lifestyle modification counseling, which should be offered to all patients. Pharmacological treatment should be considered in patients who do not respond to lifestyle modification and in those at significant cardiovascular risk, in whom combined lifestyle modification and drug therapy may be given upon diagnosis [11]. When implemented, pharmacological therapies should primarily aim to improve the lipid profile and control high blood pressure and blood glucose [11]. The specific therapeutic goals remain the same as for patients without metabolic syndrome and should be achieved by following current treatment guidelines [14, 15].

However, certain exceptions should be considered when managing metabolic syndrome components in patients with psoriasis. These exceptions may stem from factors such as potential drug interactions or the effects of the underlying disease itself. This section focuses on key evidence and specific challenges in managing metabolic syndrome among patients with psoriasis.

#### 3.1.1. Antihypertensive drugs

A meta-analysis of evidence from 24 observational studies shows that patients with psoriasis are 1.58 times more likely to suffer from hypertension compared to controls, with prevalence rates correlated positively with disease severity. The odds are even higher (2.07) for patients with psoriatic arthritis [16].

However, among medications with known potential to exacerbate psoriasis, antihypertensive drugs have long been associated with causing psoriasis flares [17]. A retrospective analysis by Gold et al. evaluated patient records of 588 patients with psoriasis, 26 of whom were administered beta-blockers. The authors observed that 72.4% of these patients experienced psoriasis aggravation [18]. More recently, these associations were studied in a systematic review with meta-analysis by Song et al. who found that all of the antihypertensive drugs included in the studies were significantly implicated in psoriasis incidence. The reported odds ratios for angiotensin-converting enzyme inhibitors (ACEi), beta-blockers, calcium-channel blockers (CCBs) and thiazide diuretics were 1.67 (95% CI: 1.31-2.13), 1.40 (95% CI: 1.20-1.63), 1.53 (95% CI: 1.23-1.89) and 1.70 (95% CI: 1.40-2.06), respectively. This was the first large-scale study to report the link between antihypertensive therapy and psoriasis incidence, although significant data heterogeneity was noted [19]. Conversely, a UK-based case-control analysis of 36 702 psoriasis patients and an equal number of controls did not identify a substantial risk of developing psoriasis associated with using beta-blockers or other antihypertensives [20]. Another analysis, a prospective cohort study involving 77 728 US female nurses, determined a 1.39 hazard ratio (95% CI: 1.11–1.73) for newly diagnosed psoriasis in women who used beta-blockers regularly for 6 years or longer. The authors found no significant association between shorter use of beta-blockers or other anti-hypertensive drugs [21].

In joint guidelines issued in 2019 by the American Academy of Dermatology and the National Psoriasis Foundation, the experts recommended that antihypertensive medication use in psoriasis patients can be the same as in the general population [22]. A similar stance was presented by the European Academy of Dermatology and Venereology (EADV) in their 2013 guidelines on managing comorbidities in psoriasis patients [23]. However, the authors of the aforementioned 2022 meta-analysis, which included over 6 million participants, recommend monitoring patients on antihypertensive therapy (conducted by either general practitioners or dermatologists) in light of their findings demonstrating an association between antihypertensive drugs and the onset of psoriasis [19].

### 3.1.2. Glucose-lowering drugs

While less effective than lifestyle changes, metformin has been shown to significantly reduce the risk of developing diabetes in prediabetic patients [24]. Nevertheless, only a single randomized controlled study has been conducted on the effects of metformin in psoriasis patients with metabolic syndrome. The authors compared the metformin group with placebo and pioglitazone. They found a statistically significant improvement in cardiometabolic parameters as well as a reduction in PASI scores in the metformin and pioglitazone groups. No significant adverse reactions were observed in either group [25].

Thiazolidinediones (TZDs), including the previously mentioned pioglitazone, represent another class of antidiabetic drugs. These medications act as agonists of peroxisome proliferator-activated receptor γ (PPARγ), a key receptor implicated in several pathological mechanisms underlying psoriasis, such as inflammation, impaired keratinocyte differentiation, and oxidative stress [26]. Given these associations, the potential role of TZDs in psoriasis has attracted increasing research interest. A systematic review and meta-analysis by Chang et al. demonstrated a significant improvement in PASI scores in patients treated with pioglitazone, either as monotherapy or in combination with other treatments. The authors also noted that the incidence of its controversial side effects, such as nausea, elevated liver enzymes, and weight gain, did not differ significantly between the intervention and control groups [27]. Similarly, a meta-analysis of randomized controlled trials conducted by Chen et al. confirmed the efficacy and safety of pioglitazone use in psoriasis [28].

GLP-1 receptor agonists (GLP-1RAs), a relatively new class of glucose-lowering drugs, have gained popularity for their exceptional efficacy in managing type 2 diabetes mellitus and obesity. Their anti-inflammatory properties are thought to contribute significantly to their therapeutic effects and may improve various inflammatory diseases by acting directly on innate immune cells [29]. These promising preliminary findings have spurred further clinical investigations into the impact of GLP-1RAs on psoriasis. However, while their cardiovascular benefits are well-established, evidence regarding their effects on psoriatic lesion severity remains limited and less conclusive [30, 31].

### 3.1.3. Lipid-lowering drugs

In clinical practice, statins are considered the cornerstone of the pharmacological treatment of dyslipidemia [32]. The benefits of statins for individuals with psoriasis are not limited to cholesterol control, as statins have been shown to reduce all-cause mortality rates in the general population when used for primary prevention, without increasing the risk of adverse events [33].

Due to their pleiotropic activity, which includes antioxidant, anti-inflammatory, and anti-proliferative properties, they have also been hypothesized to improve the course of psoriasis. Indeed, apart from improving lipid profiles, reducing vascular endothelial inflammation, and thus cardiovascular risk, several studies have reported a positive impact of statins on the severity of skin lesions in patients with psoriasis [34-37]. A meta-analysis by Socha et al. found that patients receiving atorvastatin or simvastatin showed significantly greater PASI score improvement than controls and the effect was more prominent in patients with severe disease [38]. However, a different meta-analysis of the effects of statins on disease severity in psoriasis patients produced inconclusive results, with a statistically significant reduction in PASI scores after 8 weeks of statin administration, but no difference was observed at week 12 [39]. Furthermore, although uncommon, cases of psoriasis flare-ups following statin administration have been reported in the literature [40-42].

Recently, the Psoriasis Task Force of the European Academy of Dermatology and Venereology (EADV) formulated consensus recommendations on the use of statins in psoriasis with the aim of providing dermatologists with a practical guide on lipid profile management [43].

Evidence regarding the use of fibrates in triglyceridemia in patients with psoriasis is scarce. We found only two such studies involving a total of 24 patients suffering from psoriasis. Imamura et al. reported a reduction in serum triglyceride levels and improvement of skin lesions in 2 patients who were administered 750 mg of clofibrate daily [44]. Vahlquist et al. observed a statistically significant reduction of serum triglycerides following 8 weeks of treatment with gemfibrozil in patients with acitretin-induced hyperlipidemia [45]. To date, a single case report has documented a psoriasis flare-up occurring two weeks after gemfibrozil administration, characterized by the onset of generalized, pruritic, papulosquamous skin lesions [46].

Finally, pre-clinical analyses have demonstrated the anti-inflammatory potential of fenofibrate, which acts by inhibiting IL-17A, a key inflammatory cytokine involved in psoriasis pathogenesis, as well as suppressing Th17 lymphocyte populations [47]. These findings shed light on the potential applications of fenofibrate in regulating the mechanisms underlying autoimmune diseases.

### 3.1.4. Challenges in psoriasis pharmacological treatment in patients with coexisting metabolic abnormalities

One of the inevitable challenges in the management of metabolic syndrome in patients with psoriasis is the potential side effects of psoriasis treatments, especially when used long-term. Some of the metabolic complications of selected systemic therapies for psoriasis are summarised in Table 1. Compared to conventional systemic therapies, biologic agents approved for psoriasis treatment appear to exhibit a more favorable safety profile [48].

| Drug | Potential metabolic and cardiovascular adverse effects |
|---|---|
| **Conventional systemic drugs** | |
| Acitretin | • Hyperlipidemia (hypercholesterolemia, high LDL/HDL ratio, hypertriglyceridiemia) [49] |
| Cyclosporine A | • Hypertension (common, affects approximately 10% of patients, usually mild to moderate) [50-52]<br>• Hyperlipidemia [52]<br>• Hyperglycemia [52]<br>• Hyperuricemia [52, 53] |
| **Biologics** | |
| Secukinumab (IL-17 inhibitor) | • Cardiac adverse events: coronary artery disease, pericarditis, atrial fibrillation [54] |
| Adalimumab, etanercept, inxliximab (TNF-α inhibitors) | • Weight gain (could be indicative or new-onset or exacerbation of pre-existing heart failure) [55]<br>• Hypoglycemia (adalimumab) [56] |
| Bimekizumab (IL-17 inhibitor) | • Hypertension [57] |

**Table 1.** Metabolic safety profiles of selected oral systemic treatments in patients with psoriasis.

Of note, co-existing metabolic syndrome or its components may increase the risk of developing adverse ev ents during conventional systemic psoriasis treatment. One such example is cyclosporin, whose characteristic side effect is nephrotoxicity. Since it is a hydrophobic molecule with a hypothesized affinity for adipose tissue, its pharmacokinetics have long been predicted to be affected by body fat concentration. It has been reported in the literature that the average serum cyclosporine levels are positively correlated with obesity, making these patients more susceptible to cyclosporine-induced nephrotoxicity [58].

Furthermore, in obese patients with moderate-to-severe plaque psoriasis, cyclosporine combined with a low-calorie diet leading to weight reduction yielded an improved response compared to the control group, highlighting the importance of counseling lifestyle modifications alongside pharmacological treatment [59]. Similar findings were reported in a study conducted on 262 obese patients with moderate-to-severe plaque psoriasis treated with anti-TNF-α biologic agents. The authors found significant improvements in PASI scores among those in the intervention group who followed a caloric restriction plan, leading to weight loss over a 24-week follow-up period [60]. More researchers have questioned the clinical efficacy of biologic therapies in obese psoriatic patients, with several studies linking obesity or other components of metabolic syndrome to poorer treatment response [61-63].

Additionally, existing research shows that this particular patient population may be more prone to non-compliance with anti-psoriatic treatment. A retrospective study by Jacobi et al. found that patients with psoriasis and concomitant metabolic syndrome had poorer adherence to biologic agents, suggesting this comorbidity as a potential predictor of treatment discontinuation. Furthermore, the authors observed that patients with comorbidities generally had significantly shorter biologic drug survival times than controls [64].

Similar findings were published by Feldman and colleagues, who reported higher discontinuation and switching rates during biologic treatment in patients with metabolic disease and an associated significant rise in costs [65]. Drop-out rates during methotrexate treatment were also observed to be higher among patients with metabolic syndrome [66].

### 3.2. Bariatric Surgery

Bariatric surgery may be considered for psoriasis patients who meet the approved indication criteria [67]. However, existing evidence supporting its benefits in psoriasis remains limited and primarily observational. In one study involving 34 obese psoriasis patients, most of whom (88%) underwent Roux-en-Y gastric bypass surgery, 62% reported improvements in skin lesions and significant therapy de-escalation post-surgery [68]. Even more promising results were obtained in another observational study, which reported that at 6 months post-surgery, 70% of patients were free of psoriasis and observed treatment de-escalation in some patients [69]. A prospective study of 32 patients who underwent various bariatric procedures reported significantly lower postoperative PASI scores and reduced nail involvement at a mean follow-up of 70.6 months, although no differences in joint involvement were observed [70]. Cases of complete postoperative remission of psoriasis have also been documented [71-73]. Conversely, a retrospective Swedish study of 50 obese psoriasis patients found no significant differences in PASI or life quality index scores between the operated and control groups [74].

On the other hand, Pérez-Pérez et al. reported a case of a woman whose psoriasis flare-ups became more frequent and severe after bariatric surgery, necessitating treatment escalation [75]. Additionally, a single case report has described the onset of psoriasis shortly after weight loss surgery, where a large plaque developed at the surgical wound site a few days following Roux-en-Y gastric bypass surgery, with more lesions developing on the elbows, knees, and shins later on [76].

One commonly raised concern around weight loss surgery in psoriasis is the theoretical potential to induce local flares at surgical sites due to the Koebner phenomenon [77]. Given that over 95% of bariatric procedures are now performed laparoscopically, in the vast majority of cases, only minimal tissue damage and scarring ensues [78]. For lack of specific surgical guidelines, avoiding trocar placement within psoriatic lesions seems prudent, and close monitoring of surgical sites for psoriatic flares is advisable.

In light of these mixed results, further research is essential to elucidate and establish the optimal surgical methods for managing obesity in patients with coexisting psoriasis.

## 4. Conclusions

Psoriasis is a common chronic inflammatory dermatosis closely linked to metabolic syndrome and other cardiometabolic comorbidities. Both conditions share underlying pathophysiological mechanisms, including chronic low-grade inflammation, which can exacerbate psoriasis symptoms. Metabolic syndrome is deemed one of the most prevalent comorbidities in psoriasis with potentially grave consequences, highlighting the need for early recognition and comprehensive management.

While lifestyle modification remains the mainstay of therapy, pharmacological interventions play a crucial role in managing both psoriasis and its associated metabolic dysfunctions. Certain antidiabetic, lipid-lowering, and antihypertensive medications may be integrated into the treatment plan to optimize overall health outcomes. However, careful consideration is required in this patient group, as certain drug classes have been implicated in triggering psoriasis flares, while some antipsoriatic treatments may potentially exacerbate metabolic disturbances.

Bariatric surgery presents a promising therapeutic option for patients with severe metabolic syndrome and obesity. Evidence suggests that weight loss following bariatric procedures can significantly improve psoriasis severity, insulin sensitivity, and systemic inflammation.

Given the complex interplay between psoriasis and metabolic syndrome, a multidisciplinary approach involving dermatologists, clinical nutritionists, cardiologists, diabetologists, endocrinologists, and metabolic surgeons is essential to ensure a holistic and personalized treatment strategy.

## Disclosure

### Author's Contribution

Conceptualization: AB, WK;
Methodology: AB, WK;
Software: n/a;
Check: WD, KSz, DW, RT, MMa;
Formal analysis: AB, WK;
Investigation: AB, WK, SD, MM;
Resources: AB;
Data curation: AB, WK, SD, MM, AK, WD, KSz;
Writing - rough preparation: AB, SD, WK;
Writing - review and editing: AB, SD, WK, MM, AK;
Visualization, RT, MMa;
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