

## ASSOCIATION OF OBESITY AND PSORIASIS: A TEN YEARS SYSTEMATIC REVIEW

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### ABSTRACT

**Background:** Psoriasis as a chronic inflammatory condition is often linked with metabolic disorders such as obesity, diabetes, dyslipidemia, and fatty liver disease. Research indicates a strong association between obesity and psoriasis, with obese individuals having a higher risk and severity of the condition. This study aims to systematically the association between psoriasis and obesity in literatures of the last 10 years.

**Methods:** This systematic review complied with the PRISMA 2020 standards and focused on full-text English literature published between 2014 and 2024. Articles such as editorials and review papers from the same journal, as well as submissions lacking a DOI, were excluded from consideration. Literature was sourced from online platforms like PubMed and SagePub.

**Result:** We found 698 articles on PubMed and 1157 articles on SagePub. Restricting our search to the past decade (2014-2024), PubMed presented 606 articles, whereas SagePub presented 633 articles. From these, we selected 5 papers meeting our criteria, with 2 from PubMed and 3 from SagePub.

**Conclusion:** Psoriasis is a chronic inflammatory skin disease caused by a complex interplay between immune and host cells. Obesity and nutrition play pivotal roles in its onset and severity through adipocytokin levels. Inflammation in psoriasis increases free radical production, necessitating antioxidants to maintain redox balance, suggesting that diets rich in antioxidants may help alleviate symptoms.

**Keyword:** Psoriasis, obesity

## INTRODUCTION

Psoriasis is a common chronic skin disease affecting 2-4% of the population, characterized by red, scaly patches mainly on the scalp, lower back, elbows, and knees. It significantly impacts quality of life, often accompanying conditions such as psoriatic arthritis. Patients with psoriasis face increased risks of various health issues, including skin cancer, diabetes, obesity, and cardiovascular events. Its development is attributed to genetic factors, immune dysfunction, and environmental influences, leading to pro-inflammatory responses involving specific immune cells and cytokines.<sup>1</sup>

Psoriasis is significantly influenced by genetics, with evidence suggesting a higher risk of the disease among the offspring and siblings of affected individuals, as well as its familial occurrence. Genetic associations primarily involve the major histocompatibility complex (MHC) locus on chromosome 6, which contains human leukocyte antigen (HLA) genes, along with other immune-modulating genes like complement factors and TNF- $\alpha$ . Notably, the HLA-C allele Cw6 shows a strong association, being present in 46% of psoriasis patients compared to only 7% of controls. Genome-wide linkage studies have identified additional genomic regions linked to psoriasis, including PSORS1 and non-MHC loci such as PSORS2-5. Recent genome-wide association studies (GWAS) have further expanded our understanding, revealing additional risk factors for psoriasis. These include genes associated with chronic inflammation (e.g., IL12B, IL23A, IL23R, TNFAIP3, TNIP1), epidermal/antimicrobial genes such as SLC12A8 and HBD (human  $\beta$ -defensin gene), and the LCE (late cornified envelope) gene cluster.<sup>2</sup>

Psoriasis as a chronic inflammatory condition is often linked with metabolic disorders such as obesity, diabetes, dyslipidemia, and fatty liver disease. Research indicates a strong association between obesity and psoriasis, with obese individuals having a higher risk and severity of the condition. Obesity, defined as a BMI over 30 kg/m<sup>2</sup>, may double the likelihood of developing psoriasis and impact treatment effectiveness. Additionally, obesity could increase the risk of adverse reactions to systemic medications used for psoriasis management. Weight loss may lead to improvements in psoriasis symptoms and treatment response in overweight and obese patients.<sup>3</sup>

The potential connection between autoimmunity and obesity has gained significance with the recognition that white adipose tissue acts as an active endocrine organ, secreting various molecules involved in immunity, inflammation, and metabolic regulation. These soluble mediators contribute to a pro-inflammatory state in obese individuals, which is implicated in the link between obesity and inflammatory/autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus, and diabetes mellitus. Recent research has also highlighted the role of innate lymphoid cells in perpetuating obesity-induced insulin resistance. In psoriasis, emerging epidemiological evidence suggests a higher adiposity among patients, possibly exacerbated by adipocyte secretion of pro-inflammatory mediators.<sup>1</sup>

This overlap in immunological mechanisms between psoriasis and obesity underscores the importance of understanding their association and its clinical implications. This study aims to systematically review the association between psoriasis and obesity in literatures of the last 10 years.

## METHODS

### Protocol

The author meticulously followed the guidelines set forth in the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 to ensure that the study fully complied with its requirements. This methodological approach was specifically chosen with the aim of guaranteeing the precision and reliability of the conclusions derived from the investigation.

### Criteria for Eligibility

This systematic review examined evidence concerning obesity and psoriasis over the past decade, carefully compiling and analyzing data to offer insights and improve patient treatment strategies. The main aim of this paper is to underscore the significance of the identified key points collectively.

The inclusion criteria for this study are: 1) Papers must be in English, and 2) Papers must be published between 2014 and 2024. The exclusion criteria are: 1) Editorials; 2) Submissions lacking a DOI; 3) Previously published review articles; and 4) Duplicate entries in journals.

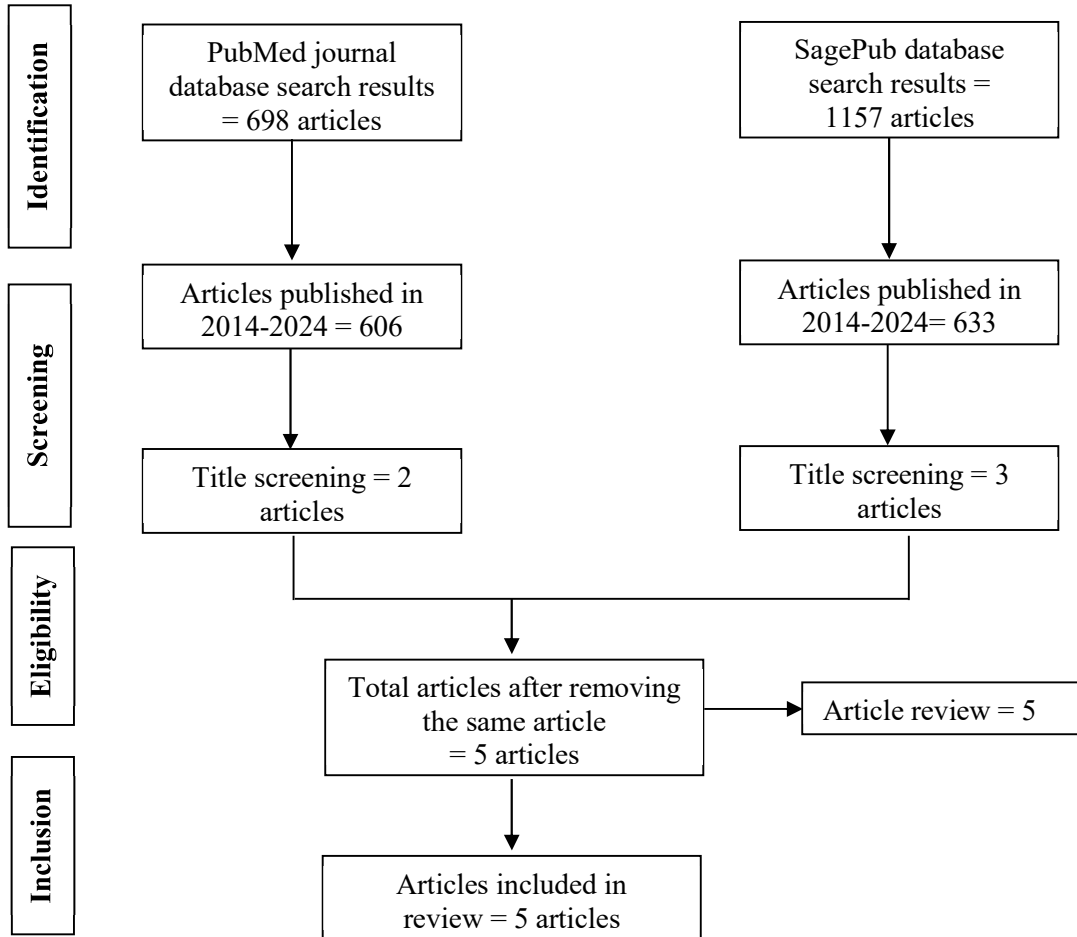
### Search Strategy

We used "psoriasis" and "obesity" as keywords. The search for studies to be included in the systematic review was carried out using the PubMed and SagePub databases by inputting the words: (*"epistaxis"[MeSH Terms] OR "epistaxis"[All Fields] OR ("recurrence"[All Fields] OR "recurrence"[MeSH Terms] OR "recurrence"[All Fields] OR "recurrences"[All Fields] OR "recurrencies"[All Fields] OR "recurrency"[All Fields] OR "recurrent"[All Fields] OR "recurrently"[All Fields] OR "recurrents"[All Fields]) AND ("epistaxis"[MeSH Terms] OR "epistaxis"[All Fields])*) OR (*"posterior"[All Fields] OR "posteriors"[All Fields]) AND ("epistaxis"[MeSH Terms] OR "epistaxis"[All Fields])*) OR

((("anterior"[All Fields] OR "anteriores"[All Fields] OR "anteriorization"[All Fields] OR "anteriorized"[All Fields] OR "anteriors"[All Fields]) AND ("epistaxis"[MeSH Terms] OR "epistaxis"[All Fields]))) AND ((fft[Filter]) AND (randomizedcontrolledtrial[Filter]) AND (fft[Filter]) AND (2014:2024[pdat])).

**Data retrieval**

The authors evaluated studies by examining their abstracts and titles to determine their eligibility. Relevant studies were chosen based on their adherence to the inclusion criteria, aligning with the objectives of the article. A consistent trend observed across multiple studies led to a definitive conclusion. The selected submissions had to meet the eligibility criteria of being in English and previously unpublished.



**Figure 1. Article search flowchart**

This systematic review exclusively incorporated literature that conformed to all predefined inclusion criteria and directly pertained to the topic under investigation. Studies failing to meet these criteria were systematically excluded, and their respective findings were omitted from consideration. The subsequent analysis explored various details revealed during the research process, encompassing elements such as titles, authors, publication dates, locations, study methodologies, and parameters.

**Quality Assessment and Data Synthesis**

Each author independently assessed the research outlined in the publication's title and abstract to determine which publications warranted further exploration. The subsequent stage entails assessing all articles that fulfill the predefined criteria for inclusion in the review. Decisions regarding the inclusion of articles in the review will be based on the findings uncovered during this evaluation process. This criteria serves to streamline the paper selection process for further assessment, providing a comprehensive discussion of previous investigations and the factors that render them suitable for inclusion in the review.

**RESULT**

We identified 698 articles from the PubMed database and 1157 from SagePub. After applying a ten-year filter (2014-2024), PubMed yielded 606 articles, and SagePub produced 633 articles. Ultimately, five papers meeting the criteria were chosen for the study, with two from PubMed and three from SagePub. Table 1 presents the selected literature included in this analysis.

**Table 1. The literature included in this study**

Author	Origin	Method	Sample	Result
<b>Norden, et al.<sup>4</sup> (2022)</b>	Multicenter, USA	Retrospective cohort analysis	1,5 million patients	The incidence of psoriasis increases with higher body mass index (BMI) categories, with overweight and obese individuals showing significantly greater risks compared to those with a BMI below 25.0. Specifically, the hazard ratio for developing psoriasis is notably higher in overweight, obese class 1, and obese class 2/3 individuals.
<b>Ozkaya, et al.<sup>5</sup> (2016)</b>	Multicenter, Turkey	Retrospective study	938 patients	Patient data from psoriasis outpatient clinics spanning from February 2007 to July 2013 were retrospectively reviewed using the Psoriasis-Turkey (PSR-TR) registration system. This included information such as patients' age, onset age, body mass index (BMI), waist circumference, psoriasis area and severity index (PASI), and arthritis details. Patients with joint pain were referred to rheumatology clinics. The diagnosis of arthritis was based on the CASPAR criteria. The study enrolled 443 males and 495 females, with mean ages of 43.9 years for females and 44.6 years for males. Psoriatic arthritis was

				identified in 25% of patients. Analysis revealed a statistically significant relationship between PASI, BMI, waist circumference (WC), and arthritis.
<b>Coban, et al.<sup>6</sup> (2016)</b>	Denizli, Turkey	Prospective cohort study	35 patients and 50 controls	The study involved 35 psoriasis patients and 50 controls, with blood samples collected at the beginning and end of a 12-week follow-up period. Various parameters were assessed in both groups, including serum glucose, insulin, insulin resistance index, lipids, and several adipokines. Additionally, blood pressure, body mass index, and psoriasis severity were evaluated. Results showed an improvement in psoriasis severity and a decrease in serum levels of hs-CRP, omentin, and chemerin in patients. At the start of the follow-up, psoriasis patients had lower levels of adiponectin and visfatin, and higher levels of vaspin and resistin compared to controls. Visfatin levels were negatively correlated with LDL and cholesterol, while vaspin and omentin levels were positively correlated with diastolic blood pressure. Reduced adiponectin levels were negatively correlated with diastolic blood pressure and LDL.
<b>Acar, et al.<sup>7</sup> (2019)</b>	Kirsehir, Turkey	Cohort study	46 patients	This study recruited 46 psoriasis patients matched for age, sex, and body mass index (BMI) with controls. Various measurements including Psoriasis Area and Severity Index (PASI), waist and hip circumferences, waist/hip ratio (WHR),

				<p>and total body fat mass (TBFM) were recorded. Fasting serum levels of leptin, resistin, and high molecular weight (HMW) adiponectin were measured, and insulin resistance was assessed using homeostasis model assessment (HOMA-IR). The patient group exhibited significantly higher resistin levels and lower HMW adiponectin levels compared to controls, after adjusting for anthropometric variables. However, serum leptin, resistin, and HMW adiponectin levels did not significantly correlate with PASI scores. HOMA-IR was positively correlated with leptin and negatively correlated with HMW adiponectin. Leptin and resistin correlated directly with BMI, while HMW adiponectin correlated inversely with BMI. Although there were no significant differences in TBFM and waist and hip circumferences between the groups, WHR was notably higher in the patient group.</p>
<b>Rocha, et al.<sup>8</sup> (2022)</b>	Sao Paulo, Brazil	Cross sectional study	81 patients	<p>Between August 2012 and March 2014, a cross-sectional study was conducted, gathering sociodemographic, lifestyle, biochemical, and dietary intake data, along with serum levels of lycopene and <math>\alpha</math>-tocopherol, and assessing psoriasis severity using the Psoriasis Area and Severity Index. The study involved 81 participants, predominantly female</p>

				(56%) and non-white (62%), with various degrees of psoriasis severity. Most participants did not meet daily fruit and vegetable intake recommendations, and while adequate levels of $\alpha$ -tocopherol were common (88%), lycopene levels were insufficient for the majority (86%). Notably, psoriasis severity exhibited a linear association with serum lycopene levels.
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Norden, et al.<sup>4</sup> (2022) identified the incidence of psoriasis and its correlation with body mass index (BMI) categories. This study showed that overweight and obese individuals have significantly greater risks of psoriasis compared to those with BMI below 25.0. The hazard ratio for developing psoriasis is higher in overweight, obese class 1, and obese class 2/3.

Ozkaya, et al.<sup>5</sup> (2016) identified a correlation between psoriatic arthritis (PsA) and elevated body mass index (BMI), increased waist circumference (WC), and higher psoriasis area and severity index (PASI) scores. Psoriatic arthritis is characterized by chronic inflammation, and the persistent inflammatory condition triggered by obesity may contribute to the development of PsA.

Coban, et al.<sup>6</sup> (2016) showed that adipokine levels in plasma can potentially serve as indicators for assessing the disease activity of psoriasis and its comorbidities. This study demonstrated an improvement in psoriasis severity and a decrease in serum levels of hs-CRP, omentin, and chemerin in patients. At the start of the follow-up, psoriasis patients had lower levels of adiponectin and visfatin, and higher levels of vaspin and resistin compared to controls.

Acar, et al.<sup>7</sup> (2019) demonstrated that psoriasis patients showed altered levels of adipocytokines, suggesting a potential link between psoriasis and metabolic comorbidities. Additionally, despite similar total body fat mass, psoriasis patients exhibit a different fat distribution, with a higher prevalence of abdominal obesity.

Rocha, et al.<sup>8</sup> (2022) showed that inflammation leads to increased production of free radicals, necessitating antioxidants to maintain redox balance. Patients with psoriasis commonly reported a diet lacking in vegetables and fruits but abundant in ultra-processed foods and fatty acids. While adequate levels of  $\alpha$ -tocopherol were found in circulation, patients exhibited low serum lycopene levels. Interestingly, psoriasis severity showed a linear relationship with serum lycopene levels.

**DISCUSSION**

Psoriasis is a persistent skin condition that involves an excess production of inflammatory cytokines such as tumor necrosis factor-alpha (TNF-a), interferon-gamma, interleukin (IL)-1 beta, IL-17, IL-22, and IL-23. Similarly, Obesity is characterized by a proinflammatory state, where white adipose tissue releases cytokines like TNF-a, IL-6, PAI-1, and C-reactive protein (CRP). This leads to an increase in visceral fat tissue due to elevated levels of TNF-a, IL-6, and PAI-1. The overproduction of inflammatory cytokines in adipose tissue, including TNF-a, IL-1, IL-6, and IL-8, is a significant feature of obesity and may contribute to the development of psoriasis.<sup>4,5</sup>

The chronic inflammation associated with psoriasis can lead to various metabolic and vascular disorders. Psoriatic arthritis (PsA), Crohn’s disease, pustular diseases, metabolic syndrome, malignancies, respiratory system diseases, smoking, infectious diseases, and comorbidities such as depression and alcohol use are commonly linked with psoriasis. Recent research indicates that obesity is an inflammatory condition, with visceral fat acting as an immune endocrine tissue. Adipokines produced by fat tissue have autocrine, paracrine, and endocrine effects.<sup>5</sup>

Compared to individuals of normal weight or underweight, there was a notable escalation in the risk of developing psoriasis among those categorized as overweight, obese class I, and obese class 2/3, with increases of 19%, 43%, and 83% respectively. Research conducted outside the United States has corroborated the association between obesity and psoriasis.



A study in Italy revealed higher odds of psoriasis among overweight individuals with a BMI between 26 to 29 as well as among obese individuals with a BMI of 30 or higher, compared to those with a BMI below 26.<sup>4</sup>

Psoriasis patients demonstrate altered levels of adipocytokines, suggesting a potential link between psoriasis and metabolic comorbidities. Additionally, despite similar total body fat mass, psoriasis patients exhibit a different fat distribution, with a higher prevalence of abdominal obesity.<sup>7</sup> Adipocytokines, including adiponectin, resistin, and visfatin, contribute to insulin resistance and low-grade inflammation. While adiponectin and resistin have opposing effects on glucose metabolism, these cytokines also play roles in chronic inflammation development and tissue damage. Leptin, the first adipokine identified, possesses immunoregulatory functions, influencing T cell proliferation and inducing T helper type 1 immune reactions, as well as activating inflammatory cells such as monocytes and neutrophils. Previous studies suggested that leptin might exacerbate psoriasis. A decrease in serum levels of hs-CRP, omentin, and chemerin helped demonstrate an improvement in psoriasis.<sup>5,6</sup>

Adiponectin exists in plasma as various oligomeric complexes, including trimeric, hexameric, and high molecular weight (HMW) structures. Its biological functions are believed to be influenced by its molecular weight, with HMW adiponectin being the most active form and a more sensitive marker for inflammation and metabolism. Adiponectin exhibits anti-inflammatory properties, inhibiting T-cell activation and proliferation, reducing levels of pro-inflammatory cytokines like TNF- $\alpha$ , IL-6, and IFN- $\gamma$ , and diminishing the phagocytic activity of macrophages. Consequently, adiponectin is proposed to act as a protective anti-inflammatory factor in psoriasis. Previous studies showed that the levels of leptin, resistin, and HMW adiponectin provide insight into obesity-related inflammation. This study suggests that adipocytokines could contribute to the link between psoriasis and its metabolic complications.<sup>7</sup>

Inflammation leads to increased production of free radicals, necessitating antioxidants to maintain redox balance. The diet provides exogenous antioxidants crucial for managing inflammatory diseases. These include polyunsaturated fatty acids (EPA), docosahexaenoic acid, selenium, zinc, vitamin C, flavonoids, carotenoids, and vitamin E. Notably, lycopene, a carotenoid, exhibits high potency owing to its resistance to retinol conversion, susceptibility to oxidation, and efficient scavenging of reactive oxidants. Furthermore,  $\alpha$ -tocopherol, a variant of vitamin E, holds universal recognition as an antioxidant. Patients with psoriasis commonly reported a diet lacking in vegetables and fruits but abundant in ultra-processed foods and fatty acids. While adequate levels of  $\alpha$ -tocopherol were found in circulation, patients exhibited low serum lycopene levels. Interestingly, psoriasis severity showed a linear relationship with serum lycopene levels.<sup>8</sup>

## CONCLUSION

Psoriasis is a chronic inflammatory skin disease caused by a complex interplay between immune and host cells. Obesity and nutrition play pivotal roles in its onset and severity through adipocytokine levels. Inflammation in psoriasis increases free radical production, necessitating antioxidants to maintain redox balance, suggesting that diets rich in antioxidants may help alleviate symptoms.

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