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REVIEW

The association between psoriasis and obesity: a systematic review and meta-analysis of observational studies

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OBJECTIVE: Psoriasis is an inflammatory skin disease affecting 2–4% of the world population. The objective of this study was to perform a systematic review and meta-analysis synthesizing the epidemiological associations between psoriasis and obesity.

DATA SOURCES: We searched for observational studies from MEDLINE, EMBASE and Cochrane Central Register from 1 January 1980 to 1 January 2012. We applied the Meta-Analysis of Observational Studies in Epidemiology guidelines in the conduct of this study.

STUDY SELECTION: We identified 16 observational studies with a total of 2.1 million study participants (201831 psoriasis patients) fulfilling the inclusion criteria.

RESULTS: Using random-effects meta-analysis, the pooled odds ratio (OR) for obesity among patients with psoriasis was 1.66 (95% confidence interval (CI) 1.46–1.89) compared with those without psoriasis. From the studies that reported psoriasis severity, the pooled OR for obesity among patients with mild psoriasis was 1.46 (95% CI 1.17–1.82) and the pooled OR for patients with severe psoriasis was 2.23 (95% CI 1.63–3.05). One incidence study found that psoriasis patients have a hazard ratio of 1.18 (95% CI 1.14–1.23) for new-onset obesity.

CONCLUSIONS: Overall, compared with the general population, psoriasis patients have higher prevalence and incidence of obesity. Patients with severe psoriasis have greater odds of obesity than those with mild psoriasis.

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Keywords: psoriasis; obesity; epidemiology; prevalence; incidence; meta-analysis

INTRODUCTION

Psoriasis is a common inflammatory skin disease that affects 2–4% of the world population.¹ Patients with psoriasis present with erythematous, scaly patches and plaques that can affect any part of their body.² The impact of psoriasis on patients' quality of life is similar to that for patients living with insulin-dependent diabetes, depression and angina.³

Increasing epidemiological evidence suggests that patients with psoriasis may be more obese compared with the general population. Although the exact mechanism underlying the epidemiological association between psoriasis and obesity is uncertain, researchers have theorized that adipocyte elaboration of pro-inflammatory cytokines may exacerbate psoriasis.^{4–7} Understanding the epidemiological relationship between psoriasis and obesity is also important for delineating risk factors for other comorbid diseases that may result from obesity. For example, obesity is a risk factor for cardiovascular diseases, type II diabetes mellitus, obstructive sleep apnea and osteoarthritis.⁸ Better understanding the strength of the relationship between psoriasis and obesity will therefore help ensure that future observational studies include adequate adjustment for the presence of comorbid obesity among patients with psoriasis.

In this systematic review and meta-analysis of observational studies, we synthesized the current literature on the association between psoriasis and obesity based on epidemiological studies from around the world. $^{9\text{-}24}$

MATERIALS AND METHODS

We searched MEDLINE, EMBASE and Cochrane Central Register using the following search criteria: 'Psoriasis' [Mesh] AND (('Obesity'[Mesh]) OR ('Body Mass Index'[Mesh])). Our search was limited to English language, human subject studies published from 1 January 1980 to 1 January 2012. Furthermore, we manually searched the reference sections of retrieved articles for any additional studies that were not included in the initial search. To be eligible for inclusion in the systematic review, the original studies needed to fulfill the following criteria: case–control, cross-sectional, cohort or nested case–control design; evaluation of obesity in conjunction with psoriasis; and analyses that compared psoriasis patients with control groups. Specifically, the studies must have evaluated the prevalence or incidence of obesity as defined by physical examination, patient self-report, medical chart review or medical billing codes. Whenever body mass index (BMI) was available, we included studies that defined obesity as a BMI ≥ 30 kg m⁻².

A total of 130 articles were retrieved from the initial search, and 8 additional studies were found from review of the reference sections (Figure 1). After manually reviewing all abstracts, 77 full-text articles were further examined. In all, 15 of these studies were excluded because they were reviews; 1 was a duplicate study; 5 assessed only psoriatic arthritis patients; 7 did not include a non-psoriasis control group; 8 were letters, commentaries or editorials without original data; and 25 did not report measures of association between psoriasis and obesity. After these exclusions, 16 publications were included in the meta-analysis. For the purposes of meta-analysis, one publication¹⁸ was treated as two studies, because two separate control populations were used in that publication.

Two reviewers (CTH and AWA) independently extracted the data and performed the systematic review, and any disagreements were

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Figure 1. Selection process for study inclusion in the meta-analysis.

Table 1. Study population characteristics: psoriasis and obesity						
Study	Study setting	Study design	Total number of patients		Mean age	
			Control	Psoriasis	Control	Psoriasis
^a Naldi <i>et al.</i> ¹⁷	Italy; outpatient (dermatology	Retrospective case-control	690	560	Median age of	Median age of 38
^a Herron <i>et al.</i> ¹⁴	USA; outpatient (dermatology clinics)	Prospective cross-sectional	4080	557	45.7	49.8
^a Neimann <i>et al</i> . ¹⁸	UK; outpatient (GPRD)	Prospective case-control	Mild Ps: 465 252 Severe Ps: 14 065 Combined: 479 317	Mild Ps: 127 706 Severe Ps: 3 854 Combined: 131 560	Mild Ps:45.7 Severe Ps: 46.3	Mild Ps: 46.4 Severe Ps: 49.8
Cohen <i>et al.</i> ¹¹ ^a Kaye <i>et al.</i> ¹⁵	Israel; outpatient (CHS database) UK; outpatient (GPRD)	Retrospective case-control Prospective nested case- control: incidence of obesity	6643 219 784	340 44 164	47 Not reported	47.7 Not reported
Cohen et al. ¹²	Israel; outpatient (CHS database)	Retrospective case-control	48 677	16850	51	42.7
Xiao et al. ²³	China; outpatient (medical records)	Retrospective cross- sectional	1521	3092	43.6	Mild Ps: 43.6 Severe Ps: 46.3
^a Driessen <i>et al.</i> ¹³	Netherlands; outpatient (clinic database)	Retrospective cross-	396	107	51.2	48.5
Takahashi <i>et al.</i> 21	Japan; outpatient (dermatology	Retrospective case-control	154	151	57.2	53.1
^a Schmitt <i>et al.</i> ¹⁹	Germany; outpatient (GKV-	Retrospective case-control	3147	3147	57.1	57.1
^a Augustin <i>et al</i> . ¹⁰	Germany; outpatient (health	Retrospective cross-	1 310 090	33 981	Not reported	Not reported
^a Al-Mutairi <i>et al</i> . ⁹	Kuwait; outpatient (medical	Retrospective case–control	1835	1835	52.7	52.3
^a Warnecke et al. ²²	Germany; inpatients and outpatients (dermatology department)	Retrospective case-control	100	100	51.9	51.8
^a Zhang <i>et al.</i> ²⁴	China; outpatient (dermatology	Retrospective cross-	1166	4452	36.7	36.5
^a Shapiro <i>et al</i> . ²⁰	Israel; inpatient (dermatology	Retrospective case–control	1079	1079	68.7	68.6
Langan <i>et al</i> . ¹⁶	UK; outpatient (THIN database)	Retrospective case-control	40 650	4065	Not reported	Not reported

Abbreviation: CHS, Clalit Health Services; GPRD, General Practice Research Database; THIN, The Health Improvement Network. ^aDenotes that obesity was the primary study outcome.

adjudicated by consensus. The Meta-Analysis of Observational Studies in Epidemiology guidelines were used to guide analysis.²⁵ For each study included, we recorded the study year, country in which the study population lived, setting in which the study took place, study design, numbers of case and control subjects, age, gender, whether the results were adjusted for comorbidities, data collection processes (prospective or retrospective), whether the results were a primary or secondary analysis of the publication and whether psoriasis disease severity was assessed. To measure study quality, we used a previously validated six-point scale, with values of 0 or 1 assigned to study design, assessment of exposure, assessment of psoriasis severity.²⁶ Studies with a score of 0–3 were categorized as lower quality, whereas studies with scores of 4–6 were categorized as higher quality.²⁶

The majority of studies were case–control in design and reported adjusted odds ratios (ORs). Studies that reported prevalence (n = 15) were analyzed using meta-analysis, whereas the one study that reported incidence¹⁵ was summarized. To estimate the pooled OR, we initially used both fixed-effects and random-effects models of DerSimonian and Laird.²⁷ For each study of prevalence, the crude ORs were identified based on the publication. In cases where multivariate adjustment was reported, the effect size and reported upper and lower bounds of the 95% confidence interval (CI) were log-transformed. The inverse variance method was then used to calculate the pooled OR. Study heterogeneity, reported pooled ORs are based on random-effects modeling.

Publication bias was assessed using visual inspection of a funnel plot of the study size vs s.e., with formal statistical testing using the Begg adjusted rank correlation test.^{28,29} To explore sources of study heterogeneity, we performed meta-regression using prespecified variables and random effects meta-analysis. Prespecified sources of heterogeneity included study country, subject location (ambulatory or inpatient), multivariate adjustment for confounders, prospective vs retrospective study design, ascertainment of prevalence vs incidence, primary vs secondary analysis,



ascertainment of psoriasis disease severity, measure of outcome and study quality (0–3 vs 4–6). All analyses were performed using STATA Version 11.2 (STATA Corp., College Station, TX, USA). No funding sources supported this work. All authors have read and agree to the manuscript as written.

RESULTS

We identified 16 observational studies with a total of 2.1 million study participants fulfilling our inclusion criteria. Among them, 201831 patients had psoriasis (Table 1). Fifteen of these studies reported prevalence among patients with psoriasis, whereas only one study¹⁵ assessed the incidence of obesity among patients with preexisting psoriasis. Obesity was defined in most studies as a BMI \geq 30, but a few studies used only medical diagnostic codes for obesity. Many of these studies assessed obesity as a secondary outcome in conjunction with prevalence of metabolic syndrome, but most studies adjusted for obesity independently.

All studies reported measures of association between psoriasis and obesity; the studies that found a statistically significant association after controlling for other covariates reported adjusted ORs ranging from 1.03 to 1.9 (Table 2). Meta-analysis revealed significant between-study heterogeneity ($l^2 = 98\%$). Using random-effects meta-analysis to account for between-study heterogeneity, the pooled OR for obesity among patients with psoriasis was 1.66 (95% Cl 1.46–1.89, Figure 2).

Visual inspection of a funnel plot revealed possible publication bias, but formal testing with the Egger test did not reveal any definite publication bias (P=0.1). Meta-regression was also performed using prespecified variables to assess possible sources of study heterogeneity (Table 3). Studies that performed multivariate

Study	Study period	Outcome ascertainment	Obesity in control patients (BMI in kg m ⁻²)	Obesity in psoriasis patients (BMI in kg m ⁻²)	Measure of association (95% Cl)
^a Naldi <i>et al.</i> ¹⁷	1988–1997	Interview/clinical examination	BMI≥30: <i>n</i> =57 (8.3%)	BMI≥30: <i>n</i> = 71 (12.9%)	BMI≥30: AOR 1.9 (1.2–2.8)
^a Herron <i>et al</i> . ¹⁴	Not reported	Questionnaire	Mean BMI of 26.2 (s.d. 5.1) Median BMI of 25.7	Mean BMI of 29.1 (s.d. 7.3) Median BMI of 27.8	OR 2.39 (1.98–2.90)
^a Neimann <i>et al.</i> ¹⁸	1987–2002	OXMIS/Read	BMI > 30: Mild Ps: <i>n</i> = 36 117 (13.1%) Severe Ps: <i>n</i> = 1 093 (13.0%)	BMI > 30: Mild Ps: <i>n</i> = 13 404 (15.8%) Severe Ps: <i>n</i> = 545 (20.7%)	BMI > 30: Mild Ps: OR 1.29 (1.26-1.32) Mild Ps: AOR 1.27 (1.24-1.31) Severe Ps: OR 1.84 (1.60-2.11) Severe Ps: AOR 1.79 (1.55-2.05)
Cohen et al. ¹¹	Not reported	Diagnosis in database	Obesity: <i>n</i> = 1 561 (23.5%)	Obesity: <i>n</i> = 100 (29.4%)	OR 1.4 (1.1–1.7) AOR 1.3 (1.0–1.7)
^a Kaye <i>et al.</i> ¹⁵	1991-2005	OXMIS/Read	BMI≥30: <i>n</i> = 11 996 (5.5%)	BMI≥30: <i>n</i> = 2 760 (6.3%)	BMI≥30: HR 1.18 (1.14–1.23)
Cohen <i>et al.</i> ¹²	Not reported	Diagnosis of obesity in database	Obesity: <i>n</i> = 1 768 (3.6%)	Obesity: n = 1 419 (8.4%)	OR 2.4 (2.3–2.6) AOR 1.7 (1.5–1.9)
Xiao et al. ²³	1999–2007	Medical code consistent with obesity	Obesity: n = 183 (12.03)	Obesity: Mild Ps: <i>n</i> = 227 (14.02%) Severe Ps: <i>n</i> = 296 (20.10%)	Mild Ps: OR 1.41 (1.08–1.85) Mild Ps: AOR 1.42 (1.06–1.91) Severe Ps: OR 1.51 (1.15–1.98) Severe Ps: AOR 1.52 (1.13–2.04)
^a Driessen <i>et al.</i> ¹³	Not reported	Manual chart review;	Mean BMI of 24.9 (s.d.	Mean BMI of 28.5 (s.d.	BMI \ge 30: OR 5.49 (3.09-9.74)
Takahashi <i>et al.</i> ²¹ ^a Schmitt <i>et al.</i> ¹⁹	2006–2008 2003–2004	Manual chart review ICD-10	Obesity: $n = 36$ (22.7%) Obesity: $n = 329$ (10.5%)	Obesity: $n = 60$ (39.7%) Obesity: $n = 490$ (15.6%)	OR 2.24 (1.36–3.69) OR 1.58 (1.36–1.83) AOR 1.63 (1.39–1.90)
^a Augustin <i>et al.</i> ¹⁰ ^a Al-Mutairi <i>et al.</i> 9	2005 2003–2007	ICD-10 Manual chart review	Obesity: <i>n</i> = 136 118 (10.4%) BMI > 30: <i>n</i> = 195 (17%)	Obesity: $n = 6$ 055 (17.8%) BMI > 30: Mild Ps: $n = 372$ (32.5%) Severe Ps: $n = 49$ (41%)	PR 1.72 (1.68–1.76) BMI > 30: Mild Ps: OR 2.36 (1.93–2.87) Severe Ps: OR 3.42 (2.30–5.10)
^a Warnecke <i>et al.</i> ²²	2009–2010	Questionnaire/ clinical assessment	BMI>30: n=33 (33%) Mean BMI of 27.7 (s.d. 5.6)	BMI > 30: $n = 44$ (44%) Mean BMI of 30.1 (s.d. 7.7)	AOR 1.03 (0.97–1.09)
^a Zhang <i>et al.</i> ²⁴	1997–2009	Clinical assessment	$BMI \ge 30$: $n = 30$ (2.6%); Mean BMI of 22.86 (s.d. 3.37)	BMI \ge 30: $n = 179$ (4.0%); Mean BMI of 23.29 (s.d. 3.25)	BMI≥30: OR 1.68 (1.13-2.49)
^a Shapiro <i>et al</i> . ²⁰	1993-2006	ICD-9	Obesity: $n = 94$ (8.7%)	Obesity: $n = 143$ (13.3%)	OR 1.60 (1.22–2.11)
Langan <i>et al.</i> ¹⁶	Not reported	Read codes (THIN database)	BMI 30–35: <i>n</i> = 7 678 (20.5%) BM/>35: <i>n</i> = 4 907 (13.1%)	BMI 30–35: <i>n</i> = 887 (23.5%) BMI > 35: <i>n</i> = 662 (17.5%)	BMI > 30: OR 1.38 (1.29–1.48) AOR 1.25 (1.16–1.34)

Abbreviations: AOR, adjusted odds ratio; BMI, body mass index; CI, confidence interval; HR, hazard ratio; ICD, International Classification of Disease; OXMIS, Read, Oxford Medical Information System and Read diagnostic codes; PR: prevalence ratio; THIN, The Health Improvement Network database. ^aDenotes that obesity was the primary study outcome.

	Year of		%
Study	Publication	OR (95% CI)	Weigh
Naldi	2005	1.90 (1.24, 2.90)	4.21
Herron	2005	- • 2.39 (1.97, 2.89)	6.71
Neimann	2006	• 1.27 (1.24, 1.31)	7.88
Neimann	2006	1.79 (1.56, 2.06)	7.22
Cohen	2007	1.30 (1.00, 1.69)	5.88
Cohen	2008	+ 1.70 (1.51, 1.91)	7.40
Xiao	2009	1.48 (1.23, 1.78)	6.80
Driessen	2009	5.49 (3.09, 9.75)	3.02
Takahashi	2010	2.24 (1.36, 3.69)	3.56
Schmitt	2010	1.63 (1.39, 1.91)	7.06
Augustin	2010	• 1.72 (1.68, 1.76)	7.89
Al-Mutairi	2010	2.59 (2.15, 3.12)	6.78
Warnecke	2011	► 1.03 (0.97, 1.09)	7.78
Zhang	2011	1.68 (1.13, 2.49)	4.48
Shapiro	2012	1.32 (0.99, 1.76)	5.63
Langan	2012	◆ 1.25 (1.16, 1.34)	7.71
Overall		1.66 (1.46, 1.89)	100.00
NOTE: Weig	hts are from random effects analys		

Figure 2. Meta-analysis of the prevalence of obesity in the psoriasis patients.

Table 3. Potential prespecified sources of heterogeneity exploredamong the studies reporting an association between psoriasis andobesity

Prespecified source of heterogeneity	Number of estimates	Stratified fixed-effects meta-analysis OR (95% CI)	Meta-regression P-value for heterogeneity
Study location USA Europe Other	1 8 7	2.39 (1.98–2.90) 1.56 (1.31–1.86) 1.69 (1.39–2.06)	0.78
Source population Inpatient Outpatient	2 14	1.12 (0.89–1.41) 1.75 (1.54–1.99)	0.09
Statistical adjustment Not adjusted	6	2.32 (1.79–3.01)	0.004
Adjusted	10	1.41 (1.26–1.58)	0.13
Lower (0–3) Higher (4–6)	6 11	2.19 (1.70–2.81) 1.48 (1.30–1.68)	0.15
Outcome ascertainment			0.86
Billing data Chart	1 11	1.72 (1.68–1.76) 1.66 (1.44–1.91)	
Examination	4	1.66 (0.97–2.83)	
Analysis of outcome			0.42
Secondary	5	1.75 (1.49–2.06) 1.48 (1.24–1.77)	
Severity of psoriasis			0.55
No distinction	10	1.62 (1.32–1.97)	
severe	Ö	1.74 (1.43–2.12)	

adjustment reported a significantly lower strength of association between psoriasis and prevalence of obesity (OR 1.41, 95% Cl 1.26–1.58 for studies with adjusted OR vs OR 2.32, 95% Cl 1.79–3.01 for studies with unadjusted OR, P = 0.004 for comparison).

Four studies reported the relative association of mild psoriasis with obesity (Figure 3).^{9,16,18,23} The pooled OR for obesity among patients with mild psoriasis was 1.46 (95% CI 1.17–1.82). Five studies reported the relative association of moderate-to-severe psoriasis with obesity (Figure 4), with a pooled OR of 2.23 (95% CI 1.63–3.05).^{9,13,16,18,23}

Although obesity likely predates the diagnosis of psoriasis in most cases, one study examined obesity incidence over time among patients with psoriasis. This study was conducted using the General Practice Research Database, a UK-based cohort of patients treated in general medical practices. Among a cohort of 44 164 patients with psoriasis, 2760 patients (6.3%) had a new diagnosis of obesity during follow-up. When compared with a matched cohort without psoriasis, those with psoriasis had a hazard ratio of 1.18 (95% CI 1.14–1.23)¹⁵ for new-onset obesity.

DISCUSSION

This systematic review and meta-analysis showed that the current literature supports an association between psoriasis and obesity. Specifically, compared with the general population, psoriasis patients are at significantly increased odds of obesity. Our meta-analysis of the cross-sectional and case–control studies showed that psoriasis patients have >50% increased odds of being obese compared with the general population. Where psoriasis severity data were available, the pooled OR for those with moderate-to-severe psoriasis was also significantly higher than that for patients with mild psoriasis.

Although the precise mechanism underlying the association between psoriasis and obesity is unknown, several lines of basic and translational research suggest that adipocytes and inflammatory-type macrophages may contribute to both disease processes. Adipose tissue is an active endocrine organ that has a key role in lipid and glucose metabolism, inflammation and coagulation, and insulin-mediated processes.^{30,31} Macrophages are the key immune



Figure 3. Meta-analysis of the prevalence of obesity in patients with mild psoriasis.



Figure 4. Meta-analysis of the prevalence of obesity in patients with severe psoriasis.

cell type that perpetuates inflammation within adipose tissue. Activated macrophages in adipose tissue stimulate adipocytes to secrete inflammatory mediators that establish and maintain an inflammatory state in obesity. Adipose tissue, especially visceral adipose tissue, then secretes bioactive products collectively known as adipocytokines or adipokines. The co-existence of psoriasis and obesity is at least in part attributed to the function of adipokines and their downstream effects.

The role of the various adipokines in psoriasis is an area of active investigation. For example, leptin is an adipokine that serves as an afferent signal of the nutritional and fat mass status to the hypothalamus and thereby regulates appetite and body weight.³² Hyperleptinemia has been associated with increased intima-media thickness of the common carotid artery and with arterial thrombosis.^{33,34} Studies in psoriasis have shown that leptin levels are elevated in psoriasis patients^{6,35–37} compared with healthy controls, and psoriasis is an independent risk factor for hyperleptinemia.³⁵ Although an increase in pro-inflammatory adipokines is seen in psoriasis, a decrease in regulatory adipokines is also observed in psoriasis. For example, an inverse relationship exists between obesity and adiponectin, a cytokine that has an anti-inflammatory and regulatory role in atherosclerosis.³⁸ In psoriasis, the adiponectin level was decreased in psoriasis patients compared with healthy controls.⁴ Furthermore, adiponectin level in psoriasis patients was inversely correlated with psoriasis severity and tumor necrosis factor- α levels.³⁶

Although obesity likely predates or co-exists with psoriasis, one study examined new-onset obesity in patients with existing psoriasis.¹⁵ The authors found a slightly increased risk for developing obesity in psoriasis patients compared with controls. It is possible that some psoriasis patients are reluctant to engage in physical activities where their skin disease may be visible to others. Thus, in addition to genetic and immune-mediated mechanisms, behavioral factors may have an additional role in explaining the association between psoriasis and obesity. Although a few studies suggest that the use of tumor necrosis factor antagonists may be associated with weight gain in psoriasis patients, 39-43 larger studies are necessary to elucidate the effect of systemic medications on obesity. This is one potential rationale for the stronger association between obesity and severe psoriasis. Alternative explanations might include a more active systemic inflammatory disease leading to greater alterations in adipocyte function, dysregulated metabolism and concomitant development of obesity and severe psoriasis.

This systematic review and meta-analysis must be interpreted in the context of the available primary studies. The methods for identifying psoriasis and obesity differed among the studies; while some studies used diagnostic codes to identify obesity, others used BMI measurements. Psoriasis severity was assessed in a minority of studies. The variations in the study findings were likely attributable to the differences in study design, patient population, and ascertainment of predictors and outcomes. Despite the potential heterogeneity among the studies, the directionality of the association between psoriasis and obesity is nearly uniform among the studies, and the overall finding from the meta-analysis is strongly supportive of the association between psoriasis and obesity.

In summary, this systematic review and meta-analysis revealed that psoriasis patients have >50% odds for obesity compared with those without psoriasis. Patients with more severe psoriasis are at higher odds of obesity compared with those with mild psoriasis. In patients with preexisting psoriasis, their likelihood of developing new-onset obesity is higher than those without psoriasis. Clinical recommendations to reduce weight in obese patients with psoriasis may have beneficial effects in both obesityassociated comorbidities and possibly their psoriasis severity. Future studies are necessary to elucidate the mechanisms underlying the association between obesity and psoriasis and to determine the impact of systemic medications used for psoriasis indications on modifying obesity.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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