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Original Article

Association between psoriasis and metabolic syndrome: a meta-analysis from 12 case control studies

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Abstract: Objective: Numerous studies have evaluated the increased prevalence of comorbid diseases and risk factors in psoriatic patients, a meta-analysis was conducted to evaluate the correlation between psoriasis and metabolic syndrome. Methods: Studies on the correlation between psoriasis and metabolic syndrome were identified by searches of PubMed, EMBASE, Cochrane Library, Web of Science databases from 1980 to March, 2016. The pooled odds ratio (OR) and corresponding 95% confidence interval (CI) were calculated to assess the strength of association. Results: 12 case control studies with a total of 3831 psoriasis patients were included in this meta-analysis. The results showed that metabolic syndrome was more prevalent in psoriasis patients than in controls. The odds ratio (OR) was 2.07 (95% CI: 1.61-2.67, random effect model). In addition, among these studies, 7 and 11 studies evaluated the correlation between psoriasis and obesity and hypertension, and the result demonstrated that higher prevalence was found in the psoriasis patients, the OR were 1.64 (95% CI: 1.08-2.47, random effect model) and 2.24 (95% CI: 1.62-3.10, random effect model), respectively. No significant publication bias was found in the studies. Conclusions: Patients with psoriasis have a higher prevalence of metabolic syndrome and hypertension compared with the controls. However, more prospective, controlled and randomized studies still need to be performed in the future.

Keywords: Psoriasis, metabolic syndrome, obesity, hypertension, meta-analysis

Introduction

Psoriasis is a chronic and relapsing, inflammatory, immune-mediated disease affecting approximately 1% to 3% of the general population [1, 2]. During recent few decades, several studies have found that psoriasis patients may have increased prevalence of cardiovascular risk and adverse cardiovascular outcomes [3-5]. Yet, some population-based studies have also suggested a relationship between psoriasis and metabolic syndrome. Metabolic syndrome affects approximately 15% to 25% of the general population [6]. Various organizations have proposed criteria for the diagnosis of metabolic syndrome, including the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATPIII) [7, 8], the International Diabetes Foundation [9], the World Health Organization, and the European Group for the Study of Insulin Resistance. According to the updated NCEP ATP III from 2005, metabolic syndrome is diagnosed when a person has at least 3 of these 5 conditions: (1) fasting glucose 100 mg/dL or greater (or receiving drug therapy for hyperglycemia), (2) blood pressure 130/85 mm Hg or higher (or receiving drug therapy for hypertension), (3) triglycerides 150 mg/dL or higher (or receiving drug therapy for hypertriglyceridemia), (4) high-density lipoprotein cholesterol complex (HDL-C) less than 40 mg/dL in men or less than 50 mg/dL in women (or receiving drug therapy for reduced HDL-C), and (5) waist circumference 102 cm (40 inches) or greater in men or 88 cm (35 inches) or greater in women; if Asian American, 90 cm (35 inches) or greater in men or 80 cm (32 inches) or greater in women. Recent literature suggests that psoriasis patients may have increased prevalence of metabolic syndrome [10-12]. In view of the abundance of literature, we have conducted an extensive meta-analysis of case control studies to get an overview of the literature to

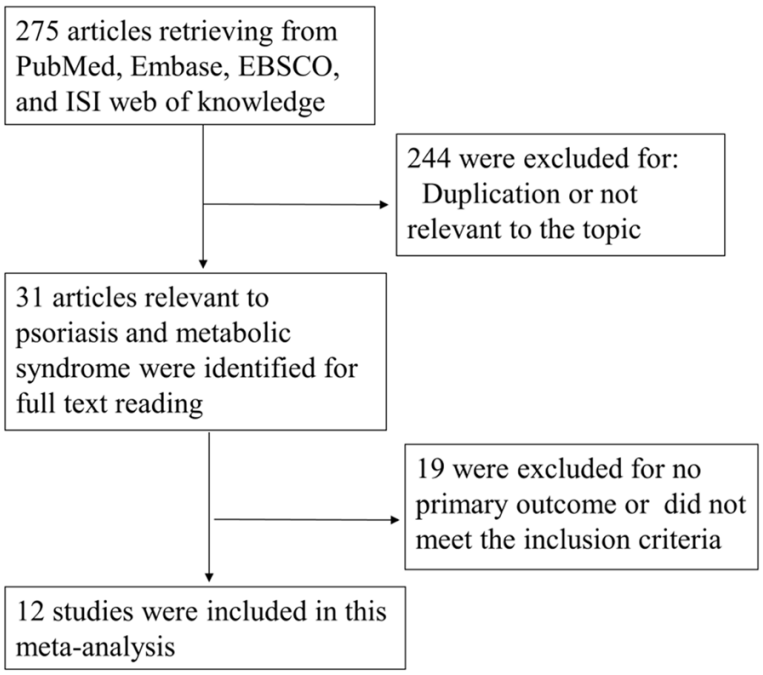

Figure 1. Flow chart of study selection.

investigate the association of psoriasis and metabolic syndrome.

Methods

The study was conducted in accordance to Meta-analysis of Observational Studies in Epidemiology (MOOSE) recommendations [13].

Search strategy

Several databases were electronically searched to retrieve studies on psoriasis and metabolic syndrome until March 2016, including PubMed, Embase, EBSCO, and ISI web of knowledge. We used the following search criteria: ("Psoriasis") AND "Metabolic Syndrome", limiting our search to English-language and human-subjects case control studies published between 1980 and March, 2016. Moreover, we check the reference lists of retrieved articles to identify more relevant studies.

Inclusion and exclusion criteria

The included studies were all case-control types, we excluded the cross sectional studies in order to increase the constancy and high quality of this meta-analysis. All studies reported prevalence of metabolic syndrome, and therefore the results are presented as pooled ORs.

Data extraction

Two reviewers independently searched and selected literatures, and then extracted relevant data according to a data extraction form, and disagreements were solved by discussion. The extracted data including: the first author, year of publication, country of origin, sample size, patients, outcome assessment et al.

Outcomes

The primary outcome measured was the prevalence of metabolic syndrome in the psoriasis group and control group. The secondary outcomes were the record of obesity and hypertension incidence.

Statistical analysis

OR and their corresponding 95% CI were used to evaluate the association between two groups. Heterogeneity among included studies was checked by chi-square-based Q test and I^2 test. If the data showed no heterogeneity ($P > 0.10$, $I^2 < 50\%$), Mantel-Haenszel fix effect model was used, otherwise DerSimonian-Laird random effect model was used. Sensitivity analyses were conducted by omitting individual studies sequentially. Data were analyzed using STATA 11.0 SE (Stata Statistical Software, College Station, TX, USA, www.stata.com) software.

Results

Literature search

275 relevant studies were obtained by searching electronic databases. Of these, 244 were excluded on the basis of their title and abstract. The full texts of the remaining 31 articles were retrieved and read by two independent investigators. From these 23 articles, 19 articles were excluded because they did not match the inclusion criteria. The remaining 12 articles [10-12,

Table 1. Characeristics of included studies in the analysis

Study	Country	Patients	Age (P, years)	Age (C, years)	Outcome assessment for MS	Sample size (P/C)
Sommer 2007	Germany	Department of Dermatology 1996-2002	54.4 (18-95)	58.5 (20-100)	Manual chart review	581/1044
Gisondi 2007	Italy	Outpatient clinics	62.1 (15.1)	63.8 (20.4)	Clinical assessment; NCEP ATP III criteria	338/334
Chen 2008	Taiwan, China	Dermatology outpatient from 2006 to 2007	57.39 (19.15)	55.63 (5.41)	Clinical assessment	77/81
Chen 2009	Taiwan, China	Dermatology outpatient from 2006 to 2007	58.85 (2.72)	56.00 (1.37)	Clinical assessment	40/37
Takahashi 2010	Japan	Outpatient clinic from 2006 to 2008	53.1 (21.4)	57.2 (23.4)	Manual chart review	151/154
AL-MUTAIRI 2010	Kuwait	Outpatients from 2003 to 2007	52.3 (11.9)	52.7 (13.5)	Manual chart review	1835/1835
Nisa 2010	India	Outpatient (dermatology department)	37.34 (18-62)	36.33 (20-69)	Clinical assessment; NCEP ATP III criteria	150/150
Mebazaa 2011	Tunisia	Outpatient (dermatology clinic)	46.28 (19.42)	48.64 (9.43)	Clinical assessment; NCEP ATP III criteria	164/216
Zindancı 2012	Turkey	Psoriasis vulgaris patients	45.4 (19-79)	43.4 (19-70)	International Diabetes Federation Criteria	115/140
Damevska 2013	Macedonia	Clinic of Dermatology from 2011 to 2012	51.52 (15.56)	51.98 (15.72)	Clinical assessment; NCEP ATP III criteria	122/122
Pehlevan 2014	Turkey	Outpatient clinic in 2010	46.8 (11.5)	36.9 (11.5)	Clinical assessment; NCEP ATP III criteria	59/22
KOKPOL 2014	Thailand	Outpatient Clinic from 2008 to 2009	50.04 (13.81)	49.96 (14.39)	International Diabetes Federation Criteria	199/199

Notes: P: psoriasis patients, C: control group, NCEP ATP III: National Cholesterol Education Program Adult Treatment Panel III.

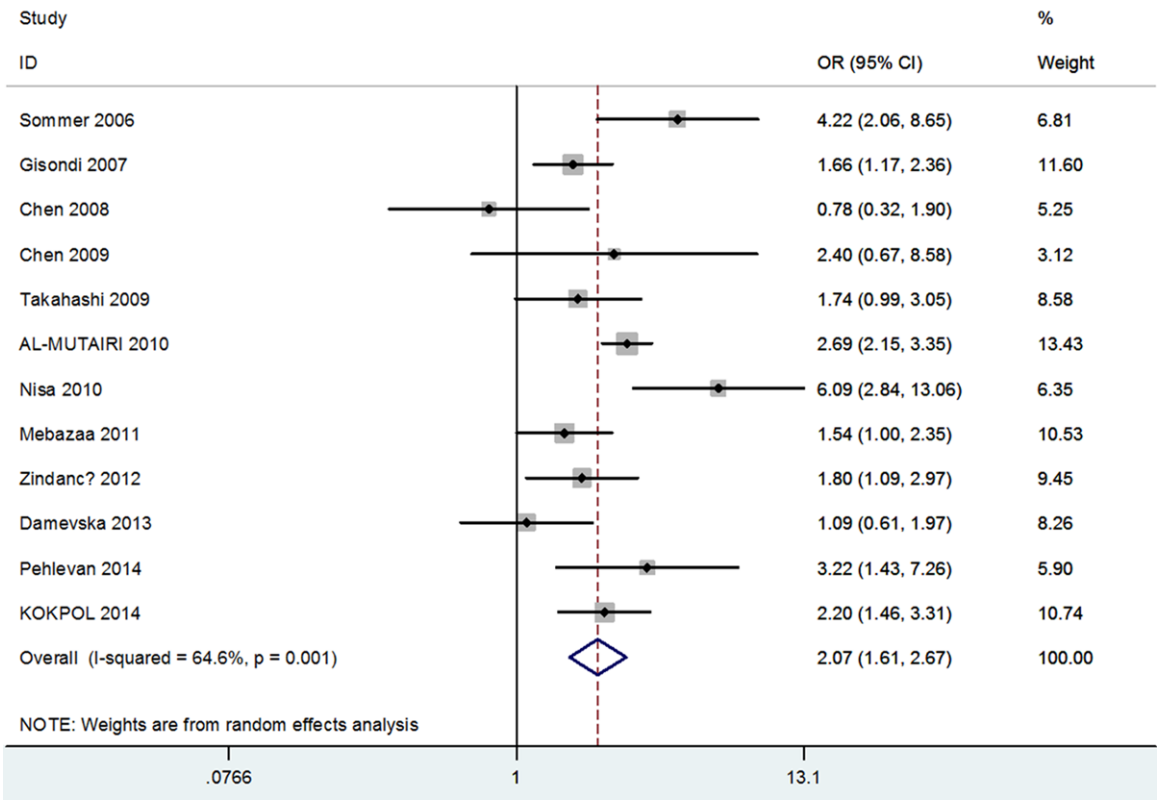

Figure 2. Forest plot with the random effects model in psoriasis and metabolic syndrome.

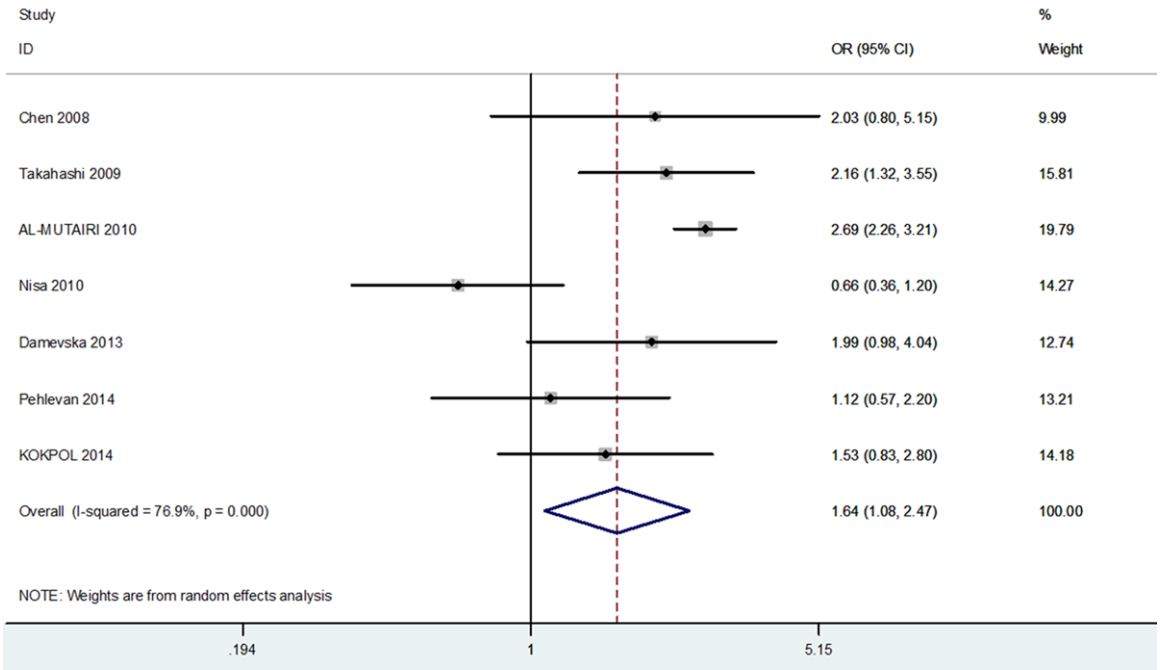

Figure 3. Forest plot with the random effects model in psoriasis and obesity.

14-22] which contained 3831 psoriasis patients met all entry criteria and were included in the meta-analysis. The screening process is illustrated in **Figure 1**.

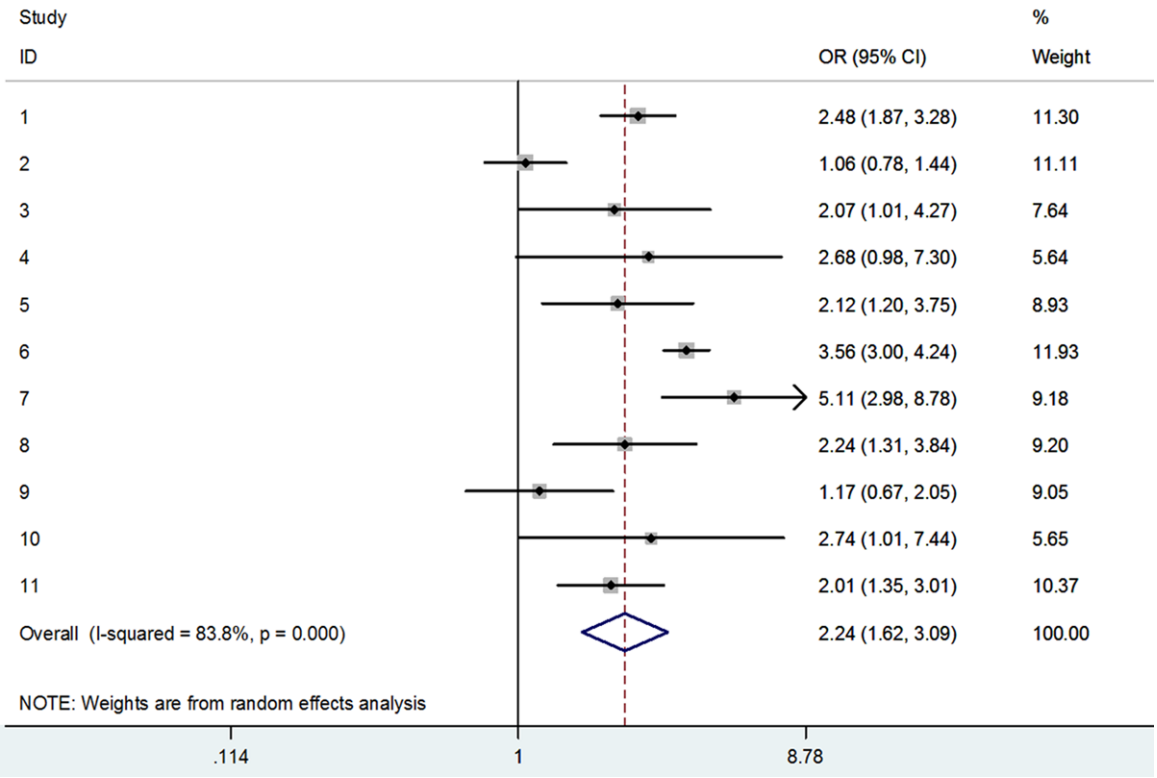

Figure 4. Forest plot with the random effects model in psoriasis and hypertension.

Study characteristics

The characteristics of the included studies in this meta-analysis were given in **Table 1**. All studies were published in high quality English journals. Among all these studies, 2 of China, 1 of Germany, 1 of Japan, 1 of Italy, 1 of Kuwait, 1 of India, 1 of Tunisia, 1 Of Macedonia, 1 of Thailand and 2 of Turkey.

Association between psoriasis and metabolic syndrome

12 case control studies with a total of 3831 psoriasis patients and 4394 controls were included in this meta-analysis. As the **Figure 2** demonstrated, the result showed that metabolic syndrome was more prevalent in psoriasis patients than in controls. The odds ratio (OR) was 2.07 (95% CI: 1.61-2.67, random effect model, I^2>50%).

Association between psoriasis and obesity and hypertension

Moreover, among these studies, 7 and 11 studies evaluated the correlation between psoriasis and obesity and hypertension, separately, and the results demonstrated that higher prevalence were found in the psoriasis patients, the OR were 1.64 (95% CI: 1.08-2.47, random effect model) and 2.24 (95% CI: 1.62-3.10, random effect model), respectively, as indicated in **Figures 3**, **4**.

Sensitivity analysis

Sensitivity analyses were conducted by omitting individual studies sequentially. The results did not change under some conditions, the indicators for heterogeneity were reduced. Sensitivity study suggested that the results were stable and statistically robust.

Publication bias

No significant publication bias was observed.

Discussion

The present meta-analysis was conducted to investigate the association of psoriasis and metabolic syndrome. 12 clinical case control studies were identified, and the data was

pooled and analyzed. Overall, the metabolic syndrome was more prevalent in psoriasis patients than in controls. To our knowledge, this is the first meta-analysis examining the relationship between psoriasis and metabolic syndrome including all case control studies.

The mechanism between psoriasis and metabolic syndrome may be associated with these processes: chronically elevated levels of free fatty acid (FFA) leads to adipocyte dysfunction which could inhibit insulin secretion and lead to the development of type 2 diabetes. Along with increased TNF-a and IL-6 lead to increased glucose production in the liver, as well as reduced glucose uptake in the muscle. The combined dysfunction results in an overall state of impaired glucose tolerance. Furthermore, elevated FFA levels induce apoptosis of pancreatic b-islet cells through an endoplasmic stress response [23]. However, some argue that the effect of systemic drugs on the cardiovascular risk is a sum of anti-inflammatory effect and atherogenic side effect [24]. Methotrexate increases homocysteine levels, cyclosporine and acitretin induce hyperlipidemia [25]. Thus, the high prevalence of the metabolic syndrome in patients with psoriasis may be, in part, due to the systemic anti psoriatic drugs.

Numerous studies have showed that psoriasis is associated with metabolic disorders such as hypertension, type II DM, dyslipidemia, abdominal obesity, insulin resistance, and cardiac disorders in patients with psoriasis [26-29] when compared to controls.

The higher prevalence of metabolic syndrome in psoriasis than in the general population had been reported in a systematic review [30]. The pooled OR of 41 853 multinational psoriatic patients compared with the general population was 2.26 (95% CI, 1.70-3.01). However, this systematic review consisted of 12 selected observational studies which contained cross sectional and case control studies which might increase the inconsistency, we excluded the cross sectional studies and added new studies of latest years in this analysis, in order to provide more persuasive evidence for clinical practice. In addition, we also investigate the association between obesity, hypertension and psoriasis which the systematic review above did not include and investigate.

In conclusion, based on our results of pooled analysis, psoriasis predisposes to the development of MS, obesity and hypertension. Therefore, were commend evaluating psoriasis patients for the presence of metabolic diseases which may influence the patients' health for their life quality.

Disclosure of conflict of interest

None.

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