Psoriasis: Targets and Therapy

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REVIEW

Epidemiology of Hypertension in Psoriasis: An Analysis of Trends from 2006 to 2023

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Background: Psoriasis and hypertension (HTN) are known to be closely related. However, at present, no study has systematically examined the epidemiology of this disease pattern on a global scale.

Methods: We examined six databases from their inception until November 1, 2023 and used the Agency for Healthcare Research and Quality and the Newcastle-Ottawa Scale to assess the quality of observational studies. Data analysis was conducted in R. Meta-regression, sensitivity, and subgroup analyses were used to evaluate interstudy heterogeneity. Egger's test and funnel plots were used to evaluate publication bias.

Results: We reviewed 200 studies involving 15,010,888 patients. The overall prevalence of HTN among the patients with psoriasis was 32.22%. Overall, South America had the highest prevalence of hypertension among adult patients with psoriasis (52.36%), the three countries with the highest prevalence were Serbia, Singapore and Brazil. The prevalence of mild and severe psoriasis comorbid with HTN was 31.71% [95% CI: 24.40–40.05%] and 33.19% [95% CI: 27.17–39.81%], respectively. The prevalence of HTN in psoriasis vulgaris was 29.71% [95% CI: 25.10–35.15%], while that in psoriatic arthritis was 34.54% [95% CI: 31.27–38.14%].

Conclusion: Patients with psoriatic arthritis are more predisposed to requiring hypertension risk screening than patients with psoriasis vulgaris. More population-based prospective observational studies are required to elucidate the mechanisms underlying the coexistence of hypertension in patients with psoriasis.

Keywords: psoriasis, hypertension, epidemiology, comorbidity, prevalence

Introduction

Psoriasis is a widespread, chronic inflammatory skin disease with a global reach and a prevalence that increases with age, ranging from 0.51% to 11.43% in adults and 0% to 1.37% in children.[1,2] As a systemic inflammatory disease, it is widely regarded to be associated with metabolic syndrome, hyperlipidemia, obesity, and mental health.[3–6]

Multiple studies have confirmed that hypertension (HTN), a well-known cardiovascular risk factor, is more prevalent in patients with psoriasis than in the general population.[7–10] Systematic reviews and meta-analyses have shown that the prevalence of HTN in patients with psoriasis is significantly higher than that in the general population, with an adjusted odds ratio of 1.43 (95% confidence interval (CI): 1.25–1.64).[9] Although the precise mechanism underlying this relationship remains unclear, it is likely to involve dysregulation of the renin–angiotensin system, elevated endothelin-1 levels, and increased oxidative stress often observed in patients with psoriasis.[11–13] In addition, a prospective study showed that certain medications used to treat psoriasis, such as cyclosporine, may increase in blood pressure.[14]

At present, a notable gap exists in the literature on the epidemiology of psoriasis, namely the lack of data on the comorbidity rate of HTN in patients with psoriasis at a global level. This study addresses this gap by providing

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a comprehensive meta-analysis comprising a broader range of participants than previous studies, as well as subgroup analyses of study populations across seven dimensions to develop an effective psoriasis management program: generation, country, region, sex, psoriasis severity, type of psoriasis, and study design.

Methods

This study was conducted in accordance with the Cochrane Handbook on Systematic Review of Interventions in accordance with the PRISMA (The Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 (eTable 1 in the Supplement) and Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines (eTable 2 in the Supplement), and was registered on PROSPERO (CRD42023482880).

Search Strategy

To identify relevant psoriasis studies that included HTN as outcome measures, three review authors (F.S-W., S.X-Y., and W.C-X.) systematically searched the PubMed, Embase, Cochrane Central Register, Chinese National Knowledge Infrastructure, Wanfang, and Sinomed databases from the beginning of inception until November 1, 2023. Medical subject headings and free text words were combined to retrieve all relevant studies. The search strategy is shown in eTable 3 in the Supplement.

Inclusion and Exclusion Criteria

The inclusion criteria were as follows: (1) studies reporting the prevalence and/or incidence of HTN in psoriasis; (2) observational studies, including cohort studies, case-control studies, cross-sectional studies, computer-based conjoint analysis experiments, real-life studies, and retrospective studies; (3) patients presenting specific diagnostic criteria of psoriasis or psoriatic arthritis (PSA), regardless of age, gender, country or ethnicity; (4) patients were clearly diagnosed HTN; (5) studies with approval from ethics committees and signed informed consent from participants; and (6) studies reported in Chinese and/or English containing conference abstracts.

Studies were excluded if they met the following criteria: (1) different reports of the same study; (2) non-observational studies; (3) studies with unavailable data; (4) studies without a full text to determine whether they met the inclusion criteria.

Data Extraction

Two researchers (W.J. and S.X-Y.) carefully screened qualified articles according to the predetermined inclusion and exclusion criteria. The same researchers independently completed the self-designed data extraction form, which included: first author, publication year, study year, study type, region (country), generation, diagnostic criteria for psoriasis and HTN, severity and type of psoriasis, number of cases of HTN in psoriasis, and prevalence and/or incidence of comorbidities.

Statistical Analysis

We synthesized the results of the meta-analysis using R (version 4.2.2). The 95% CI was used to evaluate the prevalence. Across studies, a fixed-effects model was used if homogeneity was present ($P > 0.1$, $I^2 < 50\%$); otherwise, a random-effects model was used. Heterogeneity was assessed using subgroup, meta-regression, and sensitivity analyses. Publication bias was determined using Egger's linear test. If a publication bias was identified, the trim-and-fill method was used to estimate the number of missing studies and correct for publication bias. Significance was set at $P < 0.05$.

Quality Assessment

The pooled studies were independently assessed by two authors (W.J. and S.X-Y.). The Agency for Healthcare Research and Quality (AHRQ) tool was used to assess the risk of bias in cross-sectional studies, and the Newcastle-Ottawa Scale (NOS) was used for case-control and cohort studies. Each article was assigned a single specific score according to the following scale: 0–3, low quality; 4–7, medium quality; and 8–11, high quality.

Results

Characteristics of the Included Studies

A total of 3181 studies were initially included in our meta-analysis. After removing duplicates, 2558 articles remained. We further refined these to 592 eligible studies, including 200 studies from 31 countries and regions across five continents from 2006 to 2023, in our final analysis (Figure 1). Two studies were conducted on children and the other on adults. Among these, 52 studies focused on PSA, while 148 focused on psoriasis. Regarding the type of HTN, 13 studies specifically mentioned arterial HTN and 2 essential HTN. Further details are provided in eTable 4 of the Supplement.

Study Quality

We did not find any qualified evaluation tools for the HUNT, dual-center study, register, chart review, or computer-based conjoint analysis experiment; therefore, we crossed these types of studies from the quality evaluations. Seven articles were found to be of low quality, 17 were of high quality, and the remaining studies were rated as medium quality. Details of the quality assessment are provided in eTables 5 and 6 of the Supplement.

Outcomes

The overall prevalence of HTN in patients with psoriasis was 32.22% [95% CI: 29.85–34.65%], which is similar to the prevalence in adults. In pediatric patients with psoriasis, the prevalence was 1.66% [95% CI: 1.53–1.81%], whereas it was 32.34% [95% CI: 29.93–34.79%] in adults (eFigures 1 and 2 in the Supplement). Since only two studies on the

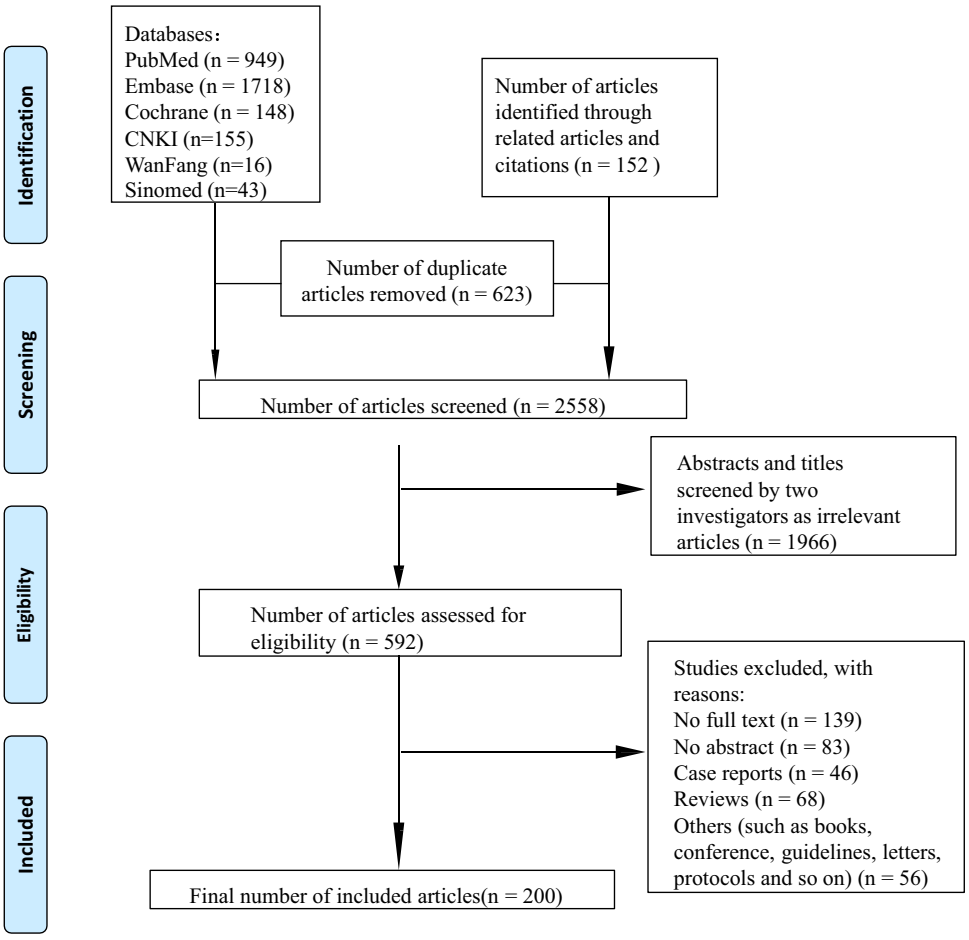

Figure 1 Flow diagram according to the preferred reporting items for systematic reviews and meta-analyses checklist.

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prevalence of HTN in pediatric patients with psoriasis were included, we restricted our analysis to the prevalence of HTN in adults with psoriasis.

The prevalence of HTN varied between male and female adult patients with psoriasis, with a prevalence of 34.47% [95% CI: 27.58–41.36%] in male patients and 28.71% [95% CI: 23.11–34.31%] in female patients (eFigure 3 in the Supplement). Then, the prevalence of HTN in patients with psoriasis was analyzed in each continent. The meta-analysis results showed that the prevalence in Asia was 26.98% [95% CI: 23.22–30.92%], 31.56% in Europe [95% CI: 28.01–35.21%], 25.18% in Africa [95% CI: 9.64–45.05%], 35.49% in North America [30.67–40.47%], and 52.36% in South America [95% CI: 38.85–65.69%]. In Asia, data on the prevalence of HTN in patients with psoriasis was available for nine countries, among which the highest prevalence was observed in Singapore at 63.11% [95% CI: 56.71–69.29%] and the lowest in India at 19.79% [95% CI: 69.00–50.64%]. In North America, a prevalence of 36.08% [95% CI: 30.53–41.82%] was observed in the United States, 31.43% [95% CI: 24.56–38.73%] in Canada, and 35.11% [95% CI: 25.83–44.99%] in Mexico. In terms of the prevalence in South America, a prevalence of 54.22% [95% CI: 39.72–68.36%] and 35.0% [95% CI: 21.17–50.26%] was reported in Brazil and Colombia, respectively. In Europe, prevalence was reported in 16 countries, among which the highest prevalence was observed in Serbia at 67.21% [95% CI: 61.20–72.95%], while the lowest was 23.63% [95% CI: 16.63–31.45%] in Turkey. Further details are provided in Figures 2 and 3, as well as eFigures 4 and 5 in the Supplement.

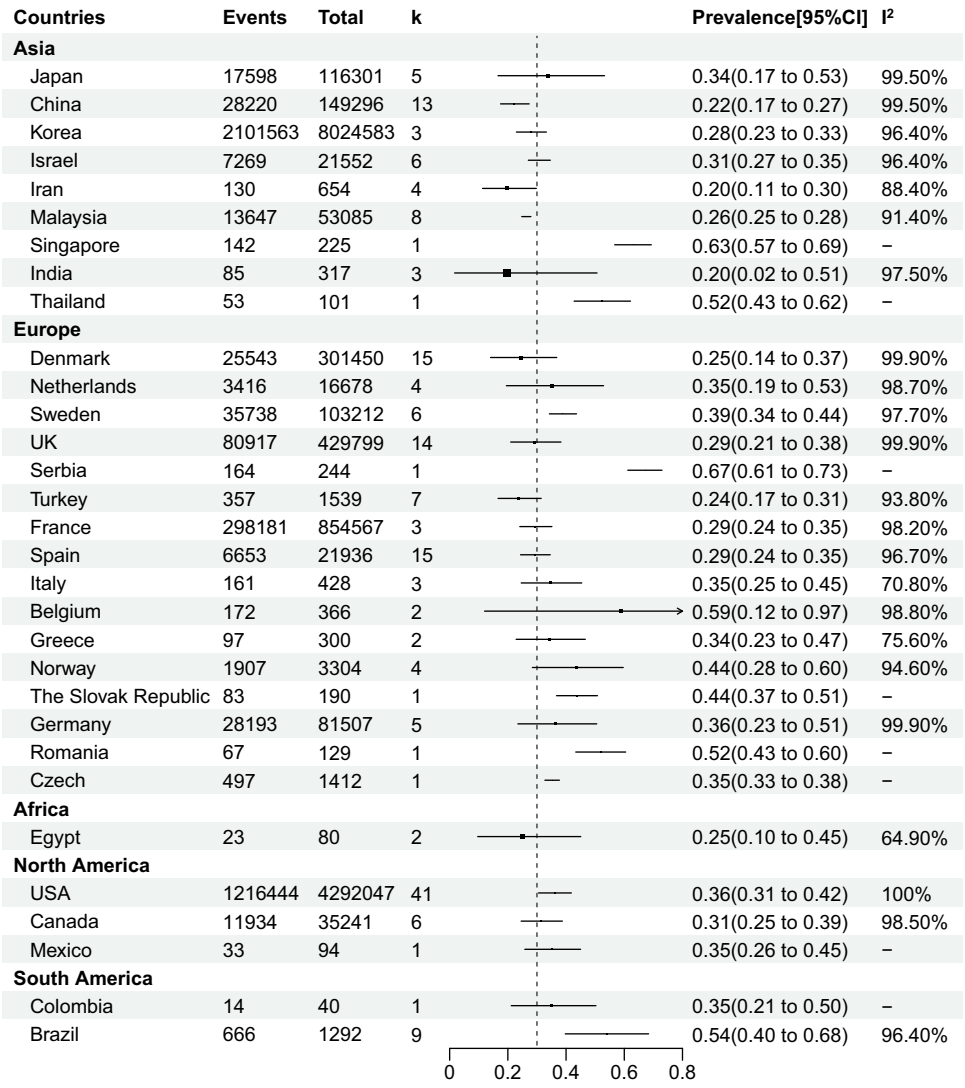

Figure 2 Forest plot of global prevalence according to different countries. k, No. of literature.

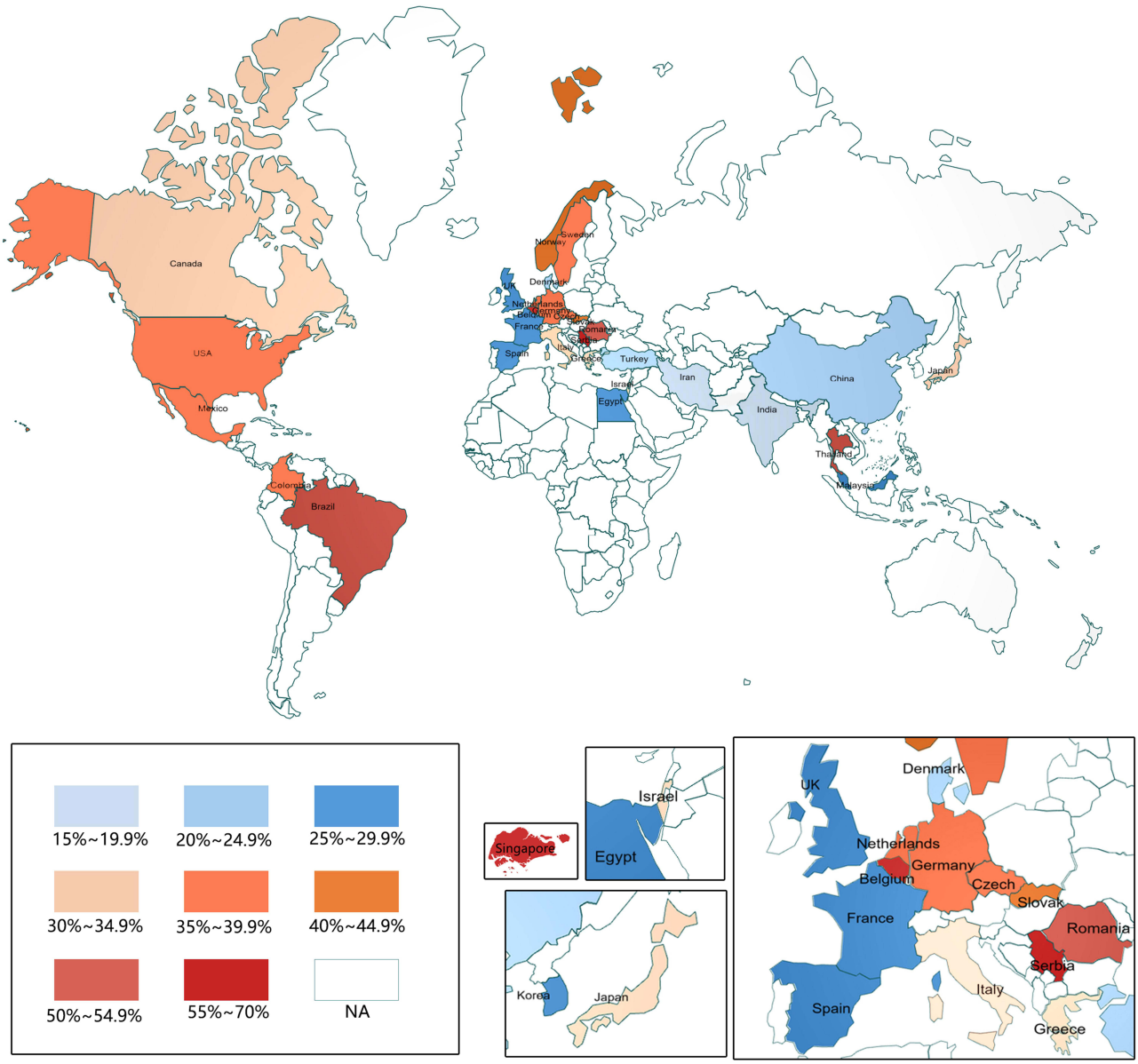

Figure 3 Mapping of global prevalence of hypertension in patients with psoriasis.

The severity and type of psoriasis was found to affect the prevalence of HTN. Mild psoriasis was defined as the psoriasis area and severity index (PASI) score < 10 or not received systemic medications, while severe psoriasis was characterized by systemic or biologic interventions in patients or a PASI score ≥10. The meta-analysis results showed that the prevalence of mild psoriasis comorbid with HTN was 31.71% [95% CI: 24.40–40.05%], while that of severe psoriasis was 33.19% [95% CI: 27.17–39.81%]. The prevalence of HTN in patients with psoriasis vulgaris was 29.71% [95% CI: 25.10–35.15%], while that of PSA was 34.54% [95% CI: 31.27–38.14%] (eFigures 6 and 7 in the Supplement).

A variety of prevalence rates have been reported in different types of studies. For example, in cross-sectional studies, prevalences of 33.56% [95% CI: 30.13–37.07%], 28.37% [95% CI: 23.40–33.62%], and 33.65% [95% CI: 29.22–38.24%] have been reported (eFigure 8 in the Supplement). Further details are provided in Table 1.

Meta-Regression

Because of the significant heterogeneity of the meta-analysis, we performed meta-regression analyses. The results revealed that the prevalence reported by age groups, different continents, sex, quality, different types of psoriasis, and studies were all responsible for the heterogeneity (Table 2).

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Table 1 Prevalence of Hypertension in Patients with Psoriasis

Study or Subgroup	Prevalence [95% CI]	I^2
1 Overall prevalence	32.22% [29.85–34.65%]	100%
1.1 Prevalence in adults	32.34% [29.93–34.79%]	100%
(1) Gender		
Male	34.47% [27.58–41.36%]	53.3%
Female	28.71% [23.11–34.31%]	46.7%
(2) Study design		
Cross-sectional study	33.56% [30.13–37.07%]	99.9%
Cohort study	28.37% [23.40–33.62%]	100%
Other	33.65% [29.22–38.24%]	100%
(3) Region		
Asia	26.98% [23.22–30.92%]	99.8%
Europe	31.56% [28.01–35.21%]	100%
Africa	25.18% [9.64–45.05%]	64.9%
North America	35.49% [30.67–40.47%]	100%
South America	52.36% [38.85–65.69%]	96.1%
(4) Severity of psoriasis		
Mild	31.71% [24.40–40.05%]	99.9%
Severe	33.19% [27.17–39.81%]	99.3%
(5) Type of psoriasis		
Psoriasis vulgaris	29.71% [25.10–35.15%]	99.2%
Psoriatic arthritis	34.54% [31.27–38.14%]	99.6%
1.2 Prevalence in pediatrics	1.66% [1.53–1.81%]	0%

Table 2 Meta-Regression Analysis of Prevalence of Hypertension in Psoriasis

Possible Source of Heterogeneity	Number of Studies	ES (95% CI)	P-value
(1) Generation	190		<0.0001
Adults	187	–0.089 [–0.216, 0.039]	0.172
Pediatrics	2	–0.564 [–0.839, –0.290]	<0.0001
(2) Region	189		0.0002
Asia	44	0.028 [–0.246, 0.302]	0.842
North America	48	0.120 [–0.154, 0.394]	0.391
Europe	85	0.078 [–0.194, 0.349]	0.574
South America	10	0.290 [–0.002.0.582]	0.0514
Africa	2	–	–
(3) Gender	17		<0.0001
Male	17	0.055 [–0.035, 0.146]	0.233
Female	17	–	–
(4) Type of psoriasis	85		<0.0001
Psoriasis vulgaris	33	–	–
Psoriatic arthritis	51	0.145 [–0.039, 0.328]	0.122
(5) Severity of psoriasis	33		<0.0001
Mild	24	–	–
Moderate	1	0.072 [–1.701, 1.845]	0.937
Severe	33	0.072 [–0.391, 0.534]	0.761
(6) Study design	186		<0.0001
Cohort study	43	–	–
Cross-section study	81	0.056 [–0.011, 0.124]	0.100
Other	64	0.057 [–0.013, 0.128]	0.111

(*Continued*)

Table 2 (Continued).

Possible Source of Heterogeneity	Number of Studies	ES (95% CI)	P-value
(7) Quality of study	121		<0.0001
Low	44	0.005 [–0.078, 0.086]	0.911
Medium	46	0.024 [–0.057, 0.106]	0.557
High	31	–	–

Sensitivity Analysis

Sensitivity analysis indicated that regardless of which study was excluded, the effect sizes of the other studies combined were within the CI range, suggesting that the results of the merger were robust (eFigure 9 in the Supplement).

Publication Bias

Funnel plots and Egger's tests were performed for publication bias analysis. The result indicated there was no publication bias ($P > 0.05$) (eFigure 10 in the Supplement).

Discussion

Psoriasis is highly correlated with cardiovascular disease, with HTN-induced atherosclerosis considered to be the predominant condition.[15] In clinical practice, it is crucial to conduct cardiovascular risk assessments to manage patients with psoriasis.[16] Current research indicates deficiencies in the diagnosis and treatment of HTN in patients with psoriasis, possibly due to poor treatment adherence and inadequate therapy.[17] Although numerous studies have investigated the correlation between psoriasis and HTN, precise data on the global prevalence of both conditions are currently lacking. By incorporating 200 observational studies spanning from 2006 to 2023, this study found that the total global prevalence of HTN in patients with psoriasis was 32%, which is consistent with the prevalence in adults, but higher than that in children and pediatrics (1.66%). These findings suggest that patients with psoriasis should undergo detailed screening and management of HTN.

Multiple studies have indicated that the risk of developing HTN is higher among male patients with psoriasis,[7,18–20] which is consistent with our study conclusions. Our research found that the prevalence of HTN among male patients with psoriasis was 34.47%, compared to 28.71% in females. This may be attributed to the fact that smoking and alcohol consumption are often higher among male patients with psoriasis than among female patients, both are significant risk factors for HTN.[21] In addition, being female may have a protective effect on the cardiovascular system by reducing the risk of developing HTN.[22,23]

Meta-analysis also revealed regional differences in the prevalence of HTN, with the highest prevalence observed in South America (52.36%) and the lowest in Africa (25.18%), the latter of which was similar to that in Asia (26.98%). However, caution is warranted as only two South American countries (Colombia and Brazil) and one African country (Egypt) were surveyed. The prevalence in North America was slightly higher than that in Europe, at 35.49% and 31.56%, respectively. To date, no research has been conducted on the impact of regional differences in the incidence of HTN on psoriasis. Next, we explored the underlying reasons for differences in the prevalence of psoriasis comorbid with HTN across continents and countries.

Disparities in medical resources and accessibility across different regions may lead to imbalances in the diagnosis and treatment of psoriasis and HTN. In areas where medical resources are scarce, patients may not be able to receive accurate diagnoses and effective treatment in a timely manner.[24] Moreover, the severity of psoriasis may vary across regions, which can affect the prevalence of HTN.[10] Genetic factors, lifestyle factors (eg diet, exercise, smoking, and alcohol consumption), and differences in HTN diagnostic criteria may also contribute to differences in the prevalence of psoriasis comorbid with HTN across regions.[25] For example, certain populations may be more prone to both psoriasis and HTN due to genetic factors. Additionally, lifestyle factors, such as a high-salt diet and lack of exercise, may increase the risk of

HTN.[26] In Brazil, characterized by the consumption of processed foods and high fatty acid content, the typical "Western diet" exacerbates the production of inflammatory cells and factors involved in glucose metabolism and is emerging as a significant risk factor for both psoriasis and HTN.[27,28]

Recent evidence indicates that patients with psoriasis often exhibit systemic endothelial dysfunction, increased oxidative stress, and alterations in the renin-angiotensin system, all of which may serve as common pathways linking the pathogenesis of psoriasis to the development of HTN.[11,13,29] A meta-analysis conducted by Armstrong et al[30] revealed that psoriasis is associated with a higher prevalence of HTN, with both mild and severe psoriasis showing this association. However, while Al-Metairie et al[31] demonstrated that the correlation between severe psoriasis and HTN was significantly stronger than that between severe and mild psoriasis, suggesting that the severity of psoriasis may be directly proportional to the risk of HTN, Langan et al[32] did not observe a clear trend. Our findings indicate that the prevalence of HTN was similar among patients with mild and severe psoriasis (33.71% and 31.19%, respectively), which is consistent with Langan's results.

Psoriasis vulgaris, the most common subtype of psoriasis, is predominantly characterized by skin lesions, such as erythema and scales.[33] However, PSA involves not only skin lesions but also joint inflammation, which manifests as joint pain, swelling, and restricted movement.[34] Studies have found that the prevalence of HTN is higher in patients with PSA than in those with psoriasis vulgaris alone.[35,36] Our study also confirmed that the prevalence of PSA was 34.54%, significantly higher than that of plaque psoriasis (29.71%). This suggests that patients with PSA have two inflammatory entities (skin and joints), and that this greater inflammatory burden may increase the risk of HTN and other factors of metabolic syndrome.[35,37] In addition, patients with PSA often require medication, such as nonsteroidal anti-inflammatory drugs and corticosteroids, which can predispose them to an increase in blood pressure.[38]

Multiple systematic reviews have demonstrated an association between psoriasis and HTN, offering updated prevalence estimates stratified by continent, severity, and psoriasis type.[9,30] However, these reviews only included a limited number of studies conducted before 2015 and did not present the prevalence of psoriasis comorbid with HTN in the form of a map. By contrast, our meta-analysis includes a variety of observational studies and comprehensively analyzes the prevalence of psoriasis and HTN comorbidities across seven subgroups. Moreover, our study highlights the risk of comorbid HTN in patients with PSA owing to the substantial inflammatory burden and the impact of therapeutic medications in these individuals.

This study has several limitations. First, caution must be exercised when interpreting summary estimates due to the heterogeneity of the studies included in our analysis. A random-effects model was used to address the fact that meta-analyses should be pursued whenever possible to acknowledge heterogeneity.[39] In addition, most of the studies we aggregated were of moderate quality, with only a handful achieving high quality. This distribution likely introduced a risk of bias. The prevalence estimates listed by continent were not adjusted according to the sample size of each study, which may have led to inaccurate results. Additionally, our inclusion criteria restricted our analysis to studies published in Chinese or English, which may have led to selection bias. Most pooled studies relied solely on the international classification of diseases (ICD-9) diagnostic codes to identify patients with psoriasis; however, previous studies have shown that ICD-9 diagnostic codes can exhibit misclassification when identifying certain diseases, which affects the completeness and accuracy of medical records.[40,41] Lastly, the included studies did not explicitly state the patients' medication history, suggesting that cyclosporine treatment may have influenced the observed association between psoriasis and uncontrolled HTN.[42]

Conclusions

Psoriasis has been found to be associated with a heightened risk of developing HTN. The present study bridges a gap in the epidemiological data on comorbidities, namely the lack of data on the comorbidity rate of HTN in patients with psoriasis at a global level. Herein, the prevalence of HTN was found to be significantly higher in adult males compared with children and adult females. Moreover, a robust correlation was observed between psoriasis severity and HTN incidence. These findings highlight the need to identify and manage patients with HTN and psoriasis, emphasizing the need to encourage patients with psoriasis to adopt a healthy lifestyle and diet to mitigate the risk of cardiovascular comorbidities associated with this skin condition.

Abbreviations

AHRQ, Agency for Healthcare Research and Quality; CI, Confidence Interval; MOOSE, Meta-analysis of Observational Studies in Epidemiology; NOS, Newcastle-Ottawa Scale; HTN, Hypertension; PASI, Psoriasis Area and Severity Index; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PSA, Psoriatic Arthritis; ICD, International Classification of Diseases.

Data Sharing Statement

The corresponding author of this article (Xin Li) had full access to all study data and took responsibility for the integrity of the data and accuracy of the data analysis. Data supporting the findings of this study are available from the corresponding author (Xin Li) upon request.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; agreed on the journal to which the article has been submitted; and agreed to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest in this work.

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