Prevalence of autoimmune thyroid disease in patients with psoriasis: a meta-analysis

Xiaochao Zhang, Suhan Zhang, Ruifang Wu, Siying Li, Yuwen Su, Peng Zhang

ABSTRACT

Objective Psoriasis is a chronic inflammatory disease with autoimmune etiology. A possible link between psoriasis and autoimmune thyroid disease (AITD) has been suggested in some studies with inconsistent findings. This meta-analysis aims to determine the association between psoriasis and AITD.

Design A meta-analysis of observational studies.

Data sources PubMed, EMBASE, Scopus and the Cochrane Library were searched up to 1 November 2021.

Eligibility criteria for selecting studies We included non-randomised studies, each with over 50 cases in every group, focusing on the rate of comorbidity between psoriasis and AITD.

Data extraction and synthesis Two independent reviewers screened the articles and extracted data. The restricted maximum-likelihood was applied to perform the meta-analysis. OR and 95% CIs were pooled to compare the prevalence of AITD in psoriasis and control groups. Heterogeneity was assessed with I² statistic.

The Newcastle-Ottawa Scale and Agency for Healthcare Research and Quality were applied for quality assessment. The risk of bias was assessed with Risk Of Bias In Non-randomised Studies-of Interventions (ROBINS-I).

Results Eleven available studies with data on 253,131 patients with psoriasis and 1,376,533 controls were included. Meta-analysis showed that patients with psoriasis had a higher prevalence of AITD (OR 1.76, 95% CI 1.35 to 2.28, Z=4.25, p<0.01), especially loss-of-function disorder of the thyroid gland. Both thyroglobulin antibodies positive rate (OR 1.98, 95% CI 1.27 to 3.01, Z=3.00, p<0.01) and thyroid peroxidase antibodies positive rate (OR 2.15, 95% CI 1.31 to 3.52, Z=3.05, p<0.01) were also increased in the psoriasis group compared with the control group.

Conclusions Our study indicates that the rate of co-occurring AITD was significantly increased in patients with psoriasis. It suggests that the increased risk of AITD should be concerned in patients with psoriasis.

PROSPERO registration number CRD42020206005.

INTRODUCTION

Psoriasis is a chronic inflammatory disease with autoimmune etiology, affecting approximately 125 million people around the world. The skin lesions of psoriasis occur mainly on the scalp, trunk and exterior surfaces of the limbs, and manifest as erythema, plaques and scales. Apart from the impaired appearance and intense pruritus of the skin lesions, various comorbidities have a significant impact on the quality of life in patients with psoriasis. Among the comorbidities, autoimmune thyroid disease (AITD) has been characterised in patients with psoriasis. For patients with psoriasis who also develop complications, their management requires extra attention. Therefore, understanding the risk of other diseases on psoriasis has important clinical significance.

AITD is an inflammatory disease of the thyroid gland with the presence of thyroid autoantibodies, lymphocytic infiltration of thyroid parenchyma and even thyroid dysfunction. Graves’ disease (GD) and Hashimoto’s thyroiditis (HT) are the two main clinical subtypes of AITD. GD is characterised by hyperthyroidism and the presence of thyroid-stimulating hormone receptor antibodies (TRAb) in serum, while HT is characterised by hypothyroidism and the presence of thyroid peroxidase antibodies (TPOAb) or thyroglobulin antibodies (TgAb) in serum.

Psoriasis and AITD share some common pathophysiological features, such as Th1-predominant adaptive immune reaction.
Hence, the relationship between AITD and psoriasis has been hypothesised and studied. Antonelli et al first reported that the prevalence of AITD in patients with psoriatic arthritis was significantly higher than in the general population. However, the study reported by Tsai et al pointed that the association between psoriasis and AITD was limited. In recent years, several observational studies regarding the association between psoriasis and AITD were published in succession, but the results of the studies were inconsistent. In addition, Karadag et al reported that the commonly administered acitretin treatment for psoriasis system treatment affects the levels of free T4 (thyroid hormone). To address this discrepancy, we designed and performed a meta-analysis with the existing evidence to assess the relationship between psoriasis and AITD and provide guidance on the clinical management of psoriasis.

METHODS

Search strategy
The literature search was conducted through PubMed, EMBASE, Scopus and the Cochrane Library for relevant studies published before 1 November 2021. Detailed literature-search strategies of the databases are presented in Appendix 1.

Inclusion and exclusion criteria
The inclusion criteria for the studies included in our analysis were the following: (1) The prevalence of AITD in patients with psoriasis/psoriatic arthritis and non-psoriasis was studied; (2) The study was a cohort study, case–control study or cross-sectional study; (3) The observed indicators were at least one of the following outcomes: the prevalence of hypothyroidism, hyperthyroidism, HT, GD or the positive rate of TPOAb, TgAb or TRAb; (4) The number of patients with psoriasis and the control group should be over 50. Drug-related studies, animal studies, reviews and conference abstracts were excluded from our analysis.

Data extraction
The specific process for analysing the studies generated from the search was as follows: record screening and data extraction were performed by two independent authors (XZ and SZ), and checked by the third author (RW). We used ORs and 95% CIs to describe the differences ware. We used ORs and 95% CIs to describe the differences between patients with and without psoriasis. Differences were considered statistically significant when p<0.05. The prediction interval was used to explore the prevalence of AITD in individuals with psoriasis. The I² statistic was used to evaluate heterogeneity as follows: I² ≤25%, no heterogeneity; 25% ≤I²≤50%, mild heterogeneity; 50% <I²≤75%, moderate heterogeneity; I² >75%, severe heterogeneity.

Quality assessment
The Newcastle-Ottawa Scale (NOS) was used to assess the quality of the included cohort and case–control studies. The quality of the study was scored on three dimensions: selection, comparability and exposure/outcome. Studies that achieved 0–3, 4–6, 7–9 scores were considered low, moderate and high quality respectively. Additionally, the tools recommended by the Agency for Healthcare Research and Quality (AHRQ) were used for the cross-sectional studies. Eleven items were included in AHRQ. The study was assigned one point if the answer ‘yes’, otherwise no points were assigned. Studies that achieved 0–3, 4–7 and 8–11 points were considered of low, moderate and high quality, respectively. Moreover, the ROBINS-I (Risk Of Bias In Non-randomised Studies-of Interventions) was used to assess the risk of bias. The assessments were carried by two authors (XZ and SZ), and checked by the third author (RW).

The meta-analysis was performed using Stata V.16.0 software. We used ORs and 95% CIs to describe the differences between patients with and without psoriasis. Differences were considered statistically significant when p<0.05. The prediction interval was used to explore the prevalence of AITD in individuals with psoriasis. The I² statistic was used to evaluate heterogeneity as follows: I² ≤25%, no heterogeneity; 25% ≤I²≤50%, mild heterogeneity; 50% <I²≤75%, moderate heterogeneity; I² >75%, severe heterogeneity.
heterogeneity. The random effects model was applied throughout the analyses. Publication bias was assessed by funnel plot and Egger’s test (publication bias was considered when \( p<0.1 \)). Sensitivity analysis was performed to assess the stability of the meta-analysis by omitting one study in each turn. Univariate meta-regression analysis was used to investigate the sources of heterogeneity. The flow chart was drawn in Adobe Illustrator, and the forest plots, funnel plots, and Egger’s test charts were drawn by Stata V.16.0 software.

**Patient and public involvement**

No patients or members of the public were involved in this review.

**RESULTS**

**Search results**

After removing duplicate results, we identified 6380 published studies in the initial search: 6377 studies were included by searching through databases and three studies were harvested by manually searching the references of relevant studies. After screening the titles and abstracts, the remaining 42 studies underwent further full-text screening. Eventually, 11 studies that met the inclusion criteria were included in the final analysis (figure 1).

**Study characteristics**

The basic characteristics of the included studies are shown in (tables 2 and 3). A total of 253313 patients with psoriasis and 1376533 control patients were included in the analysis. Two of the studies were cohort studies, eight were case-controlled studies and one was a cross-sectional study.

**Quality of studies**

Overall, five studies were of high quality and six of moderate ones (table 3). In the studies checked with NOS (n=10), five studies were considered of moderate quality because the control groups were not from the same community. The only cross-sectional study checked

![Flow chart for study screening.](image-url)
with AHRQ was a moderate quality study as the method for control of confounding was not clear. Based on ROBINS-I, all included studies had moderate risk in overall bias (table 4).

Prevalence of AITD in patients with psoriasis

Eleven studies provided available data on the prevalence of AITD in patients with psoriasis. The meta-analysis showed that patients with psoriasis had a higher prevalence of AITD than the controls (OR 1.76, 95% CI 1.35 to 2.28, Z=4.25, p<0.01). The prediction interval ranged from 0.79 to 2.73, and the heterogeneity was severe (I²=92.72%).

Heterogeneity analysis

To investigate potential sources of heterogeneity, we first performed a subgroup analysis by types of study design. The high rate of comorbidity between psoriasis and AITD was also observed in the cross-sectional study strata (OR 2.12, 95% CI 1.55 to 2.89), and in the case–control study strata (OR 1.75, 95% CI 1.23 to 2.48, Z=3.14, p<0.01) but with heterogeneity remaining severe (figure 2), which indicated that inconsistency of the study designs was not the source of high heterogeneity.

We further conducted a meta-regression analysis to explore the reason for between-study heterogeneity. Seven variables were included in the regression model, covering

Table 2 Characteristics of the included studies

<table>
<thead>
<tr>
<th>Study (author)</th>
<th>Year</th>
<th>Country</th>
<th>Study design</th>
<th>No patients</th>
<th>No controls</th>
<th>Patients, % female</th>
<th>Patients, mean age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antonelli et al</td>
<td>2006</td>
<td>Italy</td>
<td>Case–control</td>
<td>80</td>
<td>400</td>
<td>45</td>
<td>57</td>
</tr>
<tr>
<td>Tsai et al</td>
<td>2011</td>
<td>China</td>
<td>Case–control</td>
<td>51800</td>
<td>207200</td>
<td>38.5</td>
<td>46.4</td>
</tr>
<tr>
<td>Peluso et al</td>
<td>2011</td>
<td>Italy</td>
<td>Case–control</td>
<td>108</td>
<td>318</td>
<td>52.8</td>
<td>39.9</td>
</tr>
<tr>
<td>Wu et al</td>
<td>2012</td>
<td>American</td>
<td>Case–control</td>
<td>25341</td>
<td>126705</td>
<td>48.4</td>
<td>48.9</td>
</tr>
<tr>
<td>Vassilatou et al</td>
<td>2017</td>
<td>Greece</td>
<td>Case–control</td>
<td>114</td>
<td>286</td>
<td>49.1</td>
<td>52.7</td>
</tr>
<tr>
<td>Kiguradze et al</td>
<td>2017</td>
<td>Greece</td>
<td>Cross-sectional</td>
<td>9654</td>
<td>846961</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Haddad et al</td>
<td>2017</td>
<td>Israel</td>
<td>Case–control</td>
<td>3161</td>
<td>31610</td>
<td>53.4</td>
<td>58.4</td>
</tr>
<tr>
<td>Fallahi et al</td>
<td>2017</td>
<td>Italy</td>
<td>Cohort</td>
<td>97</td>
<td>97</td>
<td>47.4</td>
<td>56</td>
</tr>
<tr>
<td>Alidrisi et al</td>
<td>2019</td>
<td>Iraq</td>
<td>Case–control</td>
<td>56</td>
<td>54</td>
<td>58.9</td>
<td>43.05</td>
</tr>
<tr>
<td>Wang et al</td>
<td>2019</td>
<td>China</td>
<td>Cohort</td>
<td>162842</td>
<td>162842</td>
<td>45.5</td>
<td>45</td>
</tr>
<tr>
<td>Valduga et al</td>
<td>2021</td>
<td>Valduga</td>
<td>Case–control</td>
<td>60</td>
<td>60</td>
<td>66.7</td>
<td>54.5</td>
</tr>
</tbody>
</table>

*This was a score based on the AHRQ evaluation.

AHRQ, Agency for Healthcare Research and Quality; AITD, autoimmune thyroid disease; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; NOS, Newcastle–Ottawa Scale; TgAb, thyroglobulin antibodies; TPOAb, thyroid peroxidase antibodies.

Table 3 Characteristics of the included studies (2)

<table>
<thead>
<tr>
<th>Study (Author)</th>
<th>Definition of psoriasis</th>
<th>Definition of AITD</th>
<th>NOS score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antonelli et al</td>
<td>The criteria of Vasey and Espinoza</td>
<td>Serum levels of thyroid stimulating hormone and TgAb and TPOAb</td>
<td>7</td>
</tr>
<tr>
<td>Tsai et al</td>
<td>ICD-9-CM code 696.0</td>
<td>ICD-9-CM codes 242.9 x, 244.9 x</td>
<td>6</td>
</tr>
<tr>
<td>Peluso et al</td>
<td>Classification of Psoriatic Arthritis study group criteria</td>
<td>Serum levels of TgAb &gt; 115 IU/mL or TPOAb &gt; 34 IU/mL, and Thyroid ultrasonography</td>
<td>7</td>
</tr>
<tr>
<td>Wu et al</td>
<td>ICD-9-CM code 696.0</td>
<td>ICD-9-CM codes 242.0, 245.2</td>
<td>7</td>
</tr>
<tr>
<td>Vassilatou et al</td>
<td>Moll and Wright criteria</td>
<td>Serum levels of TgAb &gt; 115 IU/mL or TPOAb &gt; 34 IU/mL</td>
<td>7</td>
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<tr>
<td>Kiguradze et al</td>
<td>ICD-9-CM code 696.0</td>
<td>ICD-9-CM codes 245.2</td>
<td>6*</td>
</tr>
<tr>
<td>Haddad et al</td>
<td>Clinical diagnosis from Clalit Health Services</td>
<td>Clinical diagnosis from Clalit Health Services</td>
<td>6</td>
</tr>
<tr>
<td>Fallahi et al</td>
<td>Criteria of Vasey and Espinoza</td>
<td>Serum levels of TgAb or TPOAb &gt; 100 IU/mL</td>
<td>6</td>
</tr>
<tr>
<td>Alidrisi et al</td>
<td>Clinical diagnosis from Endocrine and Metabolism Centre</td>
<td>Serum levels of TgAb &gt; 115 IU/mL or TPOAb &gt; 34 IU/mL</td>
<td>6</td>
</tr>
<tr>
<td>Wang et al</td>
<td>ICD-9-CM code 696.0</td>
<td>ICD-9-CM code 242, 242.0, 244, 246</td>
<td>8</td>
</tr>
<tr>
<td>Valduga et al</td>
<td>Clinical diagnosis and measured by Psoriasis Area and Severity Index</td>
<td>Hypothyroidism was detected, or when they need for thyroid hormone replacement therapy or positive of TPOAb with or without TgAb</td>
<td>6</td>
</tr>
</tbody>
</table>

AHRQ, Agency for Healthcare Research and Quality; AITD, autoimmune thyroid disease; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; NOS, Newcastle–Ottawa Scale; TgAb, thyroglobulin antibodies; TPOAb, thyroid peroxidase antibodies.
<table>
<thead>
<tr>
<th>Study (author)</th>
<th>Year</th>
<th>Bias due to confounding</th>
<th>Bias in selection of participants into the study</th>
<th>Bias in classification of interventions</th>
<th>Bias due to deviations from intended interventions</th>
<th>Bias due to missing data</th>
<th>Bias in measurement of outcomes</th>
<th>Bias in selection of the reported result</th>
<th>Overall bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antonelli et al&lt;sup&gt;8&lt;/sup&gt;</td>
<td>2006</td>
<td>Moderate risk</td>
<td>Low risk</td>
<td>Low risk</td>
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<tr>
<td>Tsai et al&lt;sup&gt;9&lt;/sup&gt;</td>
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<td>Moderate risk</td>
<td>Low risk</td>
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<td>Low risk</td>
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<tr>
<td>Peluso et al&lt;sup&gt;10&lt;/sup&gt;</td>
<td>2011</td>
<td>Moderate risk</td>
<td>Low risk</td>
<td>Low risk</td>
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<tr>
<td>Wu et al&lt;sup&gt;11&lt;/sup&gt;</td>
<td>2012</td>
<td>Moderate risk</td>
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<td>Kiguradze et al&lt;sup&gt;13&lt;/sup&gt;</td>
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<td>Haddad et al&lt;sup&gt;12&lt;/sup&gt;</td>
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<td>Low risk</td>
<td>Low risk</td>
<td>Low risk</td>
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</tr>
<tr>
<td>Fallahi et al&lt;sup&gt;11&lt;/sup&gt;</td>
<td>2017</td>
<td>Moderate risk</td>
<td>Low risk</td>
<td>Low risk</td>
<td>Moderate risk</td>
<td>Low risk</td>
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</tr>
<tr>
<td>Aliabadi et al&lt;sup&gt;10&lt;/sup&gt;</td>
<td>2019</td>
<td>Moderate risk</td>
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<tr>
<td>Wang et al&lt;sup&gt;16&lt;/sup&gt;</td>
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<tr>
<td>Valduga et al&lt;sup&gt;14&lt;/sup&gt;</td>
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<td>Moderate risk</td>
<td>Low risk</td>
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<td>Moderate risk</td>
<td>Low risk</td>
<td>Low risk</td>
<td>Low risk</td>
<td>Moderate risk</td>
</tr>
</tbody>
</table>

ROBINS-I, Risk Of Bias In Non-randomised Studies-of Interventions.
Psoriasis and specific AITD

The prevalence of HT in patients with psoriasis and the controls was 0.215% and 0.199%, respectively. In comparison, the prevalence of GD in patients with psoriasis and the controls was 0.443% and 0.405%, respectively. The prevalence of HT was significantly higher in patients with psoriasis than the controls (OR 1.88, 95% CI 1.50 to 2.35, Z=5.47, p<0.01) and the heterogeneity was moderate (I²=55.98%). The prevalence of GD was also higher in patients with psoriasis than the controls (OR 1.02, 95% CI 0.65 to 1.60, Z=0.07, p=0.94) and the heterogeneity was severe (I²=92.78%). However, the difference was not statistically significant (figures 4C and 5A).

Psoriasis and thyroid serological antibodies

No studies provided data on the positive rate of TRAb in patients with psoriasis, so we only included TgAb and TPOAb in the meta-analysis (figure 5B,C). The positive rate of TgAb was significantly higher in patients with psoriasis than the controls (OR 1.98, 95% CI 1.50 to 2.53, Z=3.90, p<0.01) and the heterogeneity was moderate (I²=55.55%). The positive rate of TPOAb was significantly higher in patients with psoriasis than the controls (OR 2.15, 95% CI 1.31 to 3.52, Z=3.05, p<0.01) and the heterogeneity was moderate (I²=56.27%).

DISCUSSION

To our knowledge, this is the first meta-analysis focusing on the risk of AITD for psoriasis patients. The study by Khan et al is the first meta-analysis of studies on the association between AITD and the incidence risk of psoriasis.24 By summarising all available evidence on the association between psoriasis and AITD, we found that the prevalence of AITD, particularly HT, was higher in patients with psoriasis than the control individuals. Additionally, elevated positive rates of TgAb and TPOAb were also observed in patients with psoriasis. As psoriasis is a type of discometic dermatosis and therefore likely to be of concern, patients with psoriasis are more likely to be active about seeing a doctor regarding their condition than patients with AITD. As such, we recommend that patients with psoriasis receive a thyroid-related examination when they have suspicious AITD-related symptoms. By promoting early diagnosis and treatment of AITD, patients may be able to avoid thyroid dysfunction.

Main findings

The primary finding of this meta-analysis is that the prevalence of AITD is increased in patients with psoriasis compared with the general population. However, severe heterogeneity was observed. In order to determine whether or not the inconsistency of the study designs...
was the primary source of heterogeneity, the subgroup analysis based on different study designs was conducted. However, the heterogeneity was not limited by subgroup analysis; hence the heterogeneity in this meta-analysis was not caused by inconsistency of the study design. Through further meta-regression analysis, we found that the differences in sample size and scope of research onAITD among these studies might explain the high level of between-study heterogeneity. Furthermore, the heterogeneity was improved when we focused on the link of psoriasis with specific clinical characters ofAITD, such as hypothyroidism, hyperthyroidism and the positivity rate of autoantibodies.

According to the definition of the study designs, an accurate cause–effect relationship can only be demonstrated in cohort studies. This study included three types of study designs, including cohort, case-controlled and cross-sectional studies. Therefore, the results should be interpreted with caution. Additionally, it has been demonstrated that the prevalence of HT in patients with psoriasis is elevated compared with the controls. HT, a main clinical subtype ofAITD, is generally accompanied by hypothyroidism. An elevated frequency of hypothyroidism was also observed in patients with psoriasis. Taken together, the current data indicates that psoriasis may be closely associated with the loss-of-function disorder of the thyroid gland.

Common pathogenesis of psoriasis andAITD

Both abnormal immunological reactions and underlying genetic risk can contribute to the pathogenesis of psoriasis andAITD. These two diseases share some autoimmune processes and susceptibility genes, which may explain the concurrence of psoriasis andAITD. The predominant Th1 immune reaction has been observed in patients with psoriasis, such as Th1 infiltration in involved tissues, and high serum levels of Th1-prototype chemokines and cytokines (TNF-α, IFN-γ and CXCL10), all of which are present inAITD. Additionally, Th17-mediated immune disorder has also been observed in psoriasis andAITD. The two diseases share several predisposing genetic alleles or regions. For example, the genetic data from 265 families with two or more autoimmune disorders have shown that the PTPN22-R620W allele has a remarkable association with HT and a mild association with psoriasis. Additionally, other SNP variations in the PTPN22 gene have been demonstrated to be indicators for evaluating the risk of psoriasis. IL12B has been generally recognised as a psoriasis susceptibility gene, an upstream variation of which affects the phenotype ofAITD in men.
Implications for practice

As information relating to patient medications was not provided by in the original research, drug exposure may be a source of residual confounding in this study and a potential risk factor for concurrence of psoriasis and AITD, apart from the reasons mentioned above. β-blocker, used to control thyrotoxicosis-related symptoms, has been implicated in induction or exacerbation of psoriasis.40 41 In addition, it has been reported that the administration of acitretin, a common drug for the treatment of psoriasis, can lead to the reduction of free T4 (thyroid hormone) levels in patients with psoriasis.17 Therefore, once the patients develop suspicious symptoms after these treatments, diagnostic investigation and intervention should be considered as early as possible to avoid the exacerbation. On the other hand, the treatment for AITD and psoriasis can be mutually beneficial. For example, propylthiouracil, a drug used to inhibit thyroid hormone synthesis, has been effective in the treatment of psoriasis.42 Based on the above findings, it is recommended that the treatment options be adjusted once patients with psoriasis are diagnosed with comorbid AITD.

Limitations

There are several limitations to this meta-analysis. First, the meta-analysis included studies with different study designs. Given this, we conducted a subgroup analysis of each study design, which also showed that the patients with psoriasis had an increased prevalence of AITD in the cross-sectional study strata and the case–control study strata. Second, there is considerable heterogeneity in this study. Subgroup analysis and meta-regression analysis
helped us to identify the potential sources of the heterogeneity. However, there are likely to be other unknown reasons responsible for the heterogeneity. Third, the lack of information on drug application made drug exposure a confounding factor. Therefore, further large-scale and high-quality prospective studies are still required to validate our findings.

**CONCLUSIONS**

The present meta-analysis revealed that AITD was more prevalent in patients with psoriasis than in the general population, especially loss-of-function disorder of the thyroid gland. Moreover, patients with psoriasis were found to have elevated positive rates of TPOAb and TgAb compared with the control individuals. Accordingly, we recommend that every dermatologist be conscious of this association and suggest necessary examinations and intervention be considered as soon as possible when patients with psoriasis have suspicious AITD-related symptoms.

**Correction notice** This article has been corrected since it was published. PZ has been added as co-corresponding author.

**Contributors** XZ and SZ carried out the extraction of reference data, meta-analysis and wrote manuscripts, RW and PZ supported and assisted the manuscripts, YS and SL reviewed and suggested the manuscripts. YS and PZ were responsible for the work and the conduct of the study, controlled the decision to publish. All authors were involved in finalising the manuscript.
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Patient consent for publication Not applicable.

Ethics approval This study does not involve human participants.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as online supplemental information.

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ORCID iD
Yuwen Su http://orcid.org/0000-0001-9918-1830

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