BMJ Open

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

Xiaochao Zhang, Suhan Zhang, Ruifang Wu, Siying Li, Yuwen Su ![ORCID] , Peng Zhang

![Check for updates]

Dermatology, The Second Xiangya Hospital of Central South University, Changsha, Hunan, China

Correspondence to
Dr Yuwen Su;
suyuwen1963@csu.edu.cn and
Dr Peng Zhang;
zhangpeng@csu.edu.cn

ABSTRACT

Objective Psoriasis is a chronic inflammatory disease with autoimmune aetiology. 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 I^2 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 253 313 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 3.10, 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.

Strengths and limitations of this study

► This is the first meta-analysis focusing on the risk of autoimmune thyroid disease (AITD) for psoriasis patients, which included hypothyroidism, hyperthyroidism, subclinical hypothyroidism, subclinical hyperthyroidism, Hashimoto's thyroiditis, Graves' disease, thyroglobulin antibodies positivity and thyroid peroxidase antibodies positivity.

► All studies included were of moderate to high quality and were representative. All studies were published in recent years.

► The heterogeneity in the pooled data cannot be ignored, and was not improved by subgroup analysis. However, meta-regression analysis identified the differences of sample size and scope of research on AITD among these studies as the potential sources of heterogeneity.

appearance and intense pruritus of the skin lesions, various comorbidities have a significant impact on the quality of life in patients with psoriasis.[3] [4] 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.[5] 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.[6] 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.[7]

Psoriasis and AITD share some common pathophysiological features, such as Th1-predominant adaptive immune reaction.[6]

INTRODUCTION

Psoriasis is a chronic inflammatory disease with autoimmune aetiology, affecting approximately 125 million people around the world.[1] The skin lesions of psoriasis occur mainly on the scalp, trunk and exterior surfaces of the limbs, and manifest as erythema, plaques and scales.[2] Apart from the impaired

Table 1	Database source and retrieval strategy
Database	**Retrieval strategy**
PubMed	((((((((((Thyroid(Title/Abstract)) OR (Thyroiditis(Title/Abstract))) OR (Hashimoto Thyroiditis(Title/Abstract))) OR (Graves Disease(Title/Abstract))) OR (Hyperthyroidism(Title/Abstract))) OR (Hypothyroidism(Title/Abstract))) OR (TgAb(Title/Abstract))) OR (TPOAb(Title/Abstract))) OR (TRAb(Title/Abstract))) OR (Endocrine Comorbidities(Title/Abstract))) OR (Autoimmune diseases(Title/Abstract))) AND ((psoriasis(Title/Abstract)) OR (psoriatic(Title/Abstract)))
Embase	(thyroid:ab,ti OR thyroiditis:ab,ti OR 'hashimoto thyroiditis':ab,ti OR 'graves disease':ab,ti OR hyperthyroidism:ab,ti OR hypothyroidism:ab,ti OR tgab:ab,ti OR tpoab:ab,ti OR trab:ab,ti OR 'endocrine comorbidities':ab,ti OR 'autoimmune diseases':ab,ti) AND (psoriasis:ab,ti OR psoriatic:ab,ti)
Scopus	((TITLE-ABS-KEY (thyroiditis) OR TITLE-ABS-KEY (hashimoto AND thyroiditis) OR TITLE-ABS-KEY (graves AND disease) OR TITLE-ABS-KEY (hyperthyroidism) OR TITLE-ABS-KEY (hypothyroidism) OR TITLE-ABS-KEY (tgab) OR TITLE-ABS-KEY (tpoab) OR TITLE-ABS-KEY (trab))) AND (TITLE-ABS-KEY (psoriasis) OR TITLE-ABS-KEY (psoriatic))
Cochrane	(((Psoriasis) OR psoriatic) OR Pustulosis of Palms) AND (((((((Thyroid) OR Thyroiditis) OR Thyroiditides) OR Hashimoto Disease) OR Graves Disease) OR Hyperthyroidism) OR Hypothyroidism)). And chose literature published up to "2021/11/01". Then chose "Trials"

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.[8] However, the study reported by Tsai *et al*[9] 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.[10–16] In addition, Karadag *et al* reported that the commonly administered acitretin treatment for psoriasis system treatment affects the levels of free T4 (thyroid hormone).[17] 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 table 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 were 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) according to the above retrieval strategy. When disagreements could not be resolved through consensus by the two authors, these were referred to the third author (RW) and resolved through discussion. The following information in the included studies was extracted: the name of the first author, year of publication, country of origin, study design, sample size, the definition of psoriasis and AITD, gender ratio and mean age.

Quality assessment
The Newcastle-Ottawa Scale (NOS)[18] 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 of low, moderate and high quality respectively. Additionally, the tools recommended by the Agency for Healthcare Research and Quality (AHRQ)[19] 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.[20] 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 I^2 statistic was used to evaluate heterogeneity as follows: $I^2 \leq 25\%$, no heterogeneity; $25\% \leq I^2 \leq 50\%$, mild heterogeneity; $50\% < I^2 \leq 75\%$, moderate heterogeneity; $I^2 > 75\%$, severe

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[8–16 21 22] 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 253 313 patients with psoriasis and 1 376 533 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
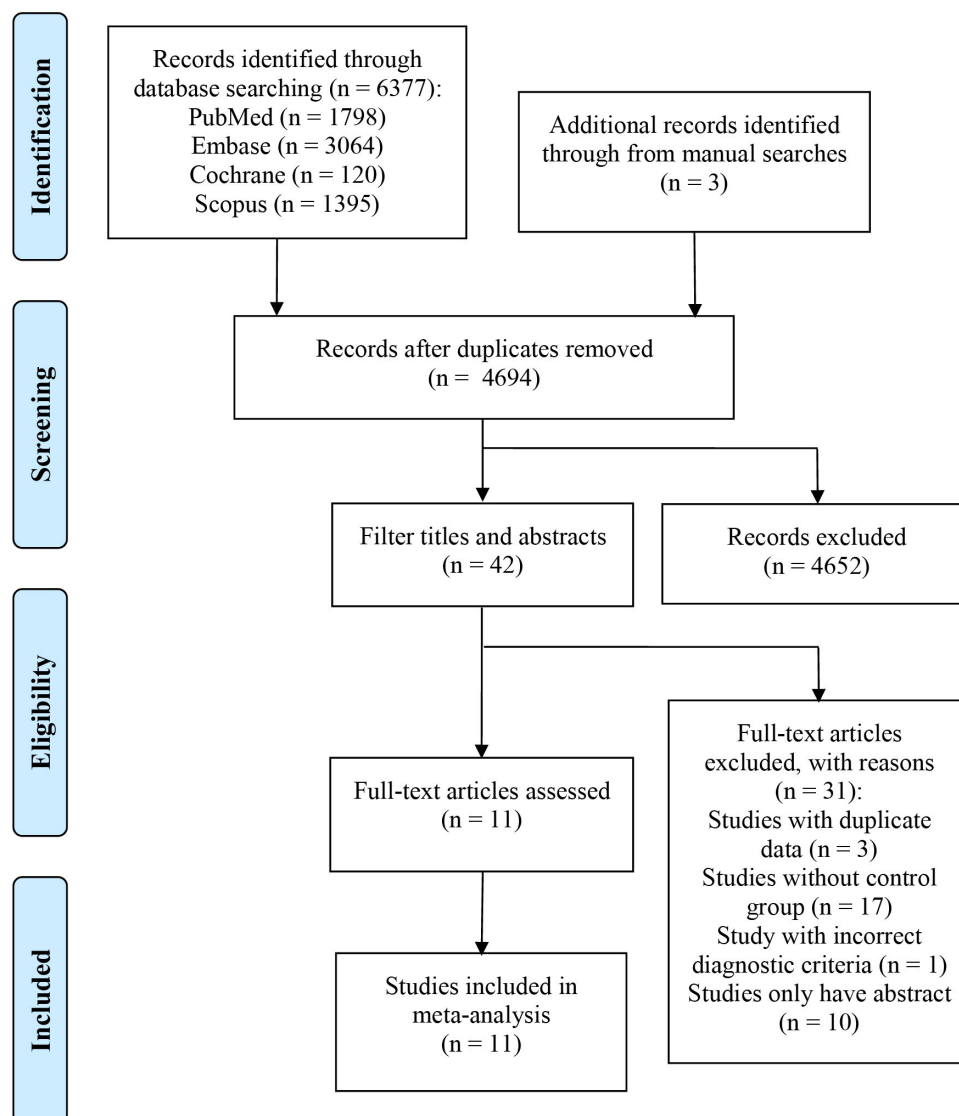
Figure 1 Flow chart for study screening.

Table 2 Characteristics of the included studies

Study (author)	Year	Country	Study design	No patients	No controls	Patients, % female	Patients, mean age
Antonelli et al[8]	2006	Italy	Case–control	80	400	45	57
Tsai et al[9]	2011	China	Case–control	51 800	207 200	38.5	46.4
Peluso et al[21]	2011	Italy	Case–control	108	318	52.8	39.9
Wu et al[22]	2012	American	Case–control	25 341	126 705	48.4	48.9
Vassilatou et al[15]	2017	Greece	Case–control	114	286	49.1	52.7
Kiguradze et al[13]	2017	Greece	Cross-sectional	9654	846 961	NA	NA
Haddad et al[12]	2017	Israel	Case–control	3161	31 610	53.4	58.4
Fallahi et al[11]	2017	Italy	Cohort	97	97	47.4	56
Alidrisi et al[10]	2019	Iraq	Case–control	56	54	58.9	43.05
Wang et al[16]	2019	China	Cohort	162 842	162 842	45.5	45
Valduga et al[14]	2021	Valduga	Case–control	60	60	66.7	54.5

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 (I^2=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 3 Characteristics of the included studies (2)

Study (Author)	Definition of psoriasis	Definition of AITD	NOS score
Antonelli et al[8]	The criteria of Vasey and Espinoza	Serum levels of thyroid stimulating hormone and TgAb and TPOAb	7
Tsai et al[9]	ICD-9-CM code 696.0	ICD-9-CM codes 242.9 x, 244.9 x	6
Peluso et al[21]	Classification of Psoriatic Arthritis study group criteria	Serum levels of TgAb > 115 IU/mL or TPOAb > 34 IU/mL, and Thyroid ultrasonography	7
Wu et al[22]	ICD-9-CM code 696.0	ICD-9-CM codes 242.0, 245.2	7
Vassilatou et al[15]	Moll and Wright criteria	Serum levels of TgAb > 115 IU/mL or TPOAb > 34 IU/mL	7
Kiguradze et al[13]	ICD-9-CM code 696.0	ICD-9-CM codes 245.2	6*
Haddad et al[12]	Clinical diagnosis from Clalit Health Services	Clinical diagnosis from Clalit Health Services	6
Fallahi et al[11]	Criteria of Vasey and Espinoza	Serum levels of TgAb or TPOAb > 100 IU/mL	6
Alidrisi et al[10]	Clinical diagnosis from Endocrine and Metabolism Centre	Serum levels of TgAb > 115 IU/mL or TPOAb > 34 IU/mL	6
Wang et al[16]	ICD-9-CM code 696.0	ICD-9-CM code 242, 242.0, 244, 246	8
Valduga et al[14]	Clinical diagnosis and measured by Psoriasis Area and Severity Index	Hypothyroidism was detected, or when they need for thyroid hormone replacement therapy or positive of TPOAb with or without TgAb	6

*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 4 Risk of bias for the 11 included studies based on the ROBINS-I tool

Study (author)	Year	Bias due to confounding	Bias in selection of participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall bias
Antonelli et al[8]	2006	Moderate risk	Low risk	Low risk	Moderate risk	Low risk	Low risk	Low risk	Moderate risk
Tsai et al[9]	2011	Moderate risk	Low risk	Low risk	Moderate risk	Low risk	Low risk	Low risk	Moderate risk
Peluso et al[21]	2011	Moderate risk	Low risk	Low risk	Moderate risk	Low risk	Low risk	Low risk	Moderate risk
Wu et al[22]	2012	Moderate risk	Low risk	Low risk	Moderate risk	Low risk	Low risk	Moderate risk	Moderate risk
Vassilatou et al[15]	2017	Moderate risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate risk
Kiguradze et al[13]	2017	Moderate risk	Low risk	Low risk	Moderate risk	Low risk	Low risk	Moderate risk	Moderate risk
Haddad et al[12]	2017	Moderate risk	Low risk	Low risk	Moderate risk	Low risk	Low risk	Low risk	Moderate risk
Fallahi et al[11]	2017	Moderate risk	Low risk	Low risk	Moderate risk	Low risk	Low risk	Low risk	Moderate risk
Alidrisi et al[10]	2019	Moderate risk	Low risk	Low risk	Moderate risk	Low risk	Low risk	Low risk	Moderate risk
Wang et al[16]	2019	Moderate risk	Low risk	Low risk	Moderate risk	Low risk	Low risk	Low risk	Moderate risk
Valduga et al[14]	2021	Moderate risk	Low risk	Low risk	Moderate risk	Low risk	Low risk	Moderate risk	Moderate risk

ROBINS-I, Risk Of Bias In Non-randomised Studies-of Interventions.

average age, sex ratio, nation (China or other counties), race (Caucasian or non-Caucasian), sample size, clinical types of psoriasis (psoriasis vulgaris or psoriatic arthritis), and scope of research on AITD (all studies were divided into two categories: one focusing on the loss-of-function disorder of the thyroid gland alone and the other focusing on both the loss-of-function disorder and hyperfunction disorder of the thyroid gland). When the statistical significance was set as p<0.1, sample size ($\beta=-0.40$, SE=0.20, p=0.07) and scope of research on AITD ($\beta=0.45$, SE=0.15, p=0.02) were the potential sources of high heterogeneity.

We removed three studies[8 13 21] outside the funnel plot and then conducted the meta-analysis again. The results of the reanalysis also showed that patients with psoriasis had a higher prevalence of AITD than the controls (OR 1.34, 95% CI 1.20 to 1.50, Z=5.07, p<0.01), but with moderate heterogeneity ($I^2=57.30\%$). The results indicated that these three studies may have contributed to severe heterogeneity in the previous analysis. The source of heterogeneity in the study of Antonelli et al was that all the patients were patients with psoriatic arthritis,[8] and the prevalence of AITD in patients with psoriatic arthritis may be higher than that of patients with psoriasis.[23] The source of heterogeneity in the study by Peluso et al may have been due to the control group being comprised of hospital staff rather than the general population.[21] The source of heterogeneity in the study of Kiguradze et al may lie in the fact that it was a cross-sectional study.[13] These three studies were not excluded because they had little effect on the final results of the analysis.

Sensitivity analysis and publication bias

Omission of either of the included studies did not significantly change the CI of the combined effect (figure 3A). Therefore, the results of the analysis were considered reliable and stable. The funnel plot for the publication bias is shown in figure 3B. The results of Egger's test showed significant publication bias (p=0.036, figure 3C). There was a possibility of exaggerating the association between psoriasis and AITD.

Psoriasis and thyroid function status

Patients with psoriasis had a higher prevalence of hypothyroidism than the controls (OR 1.21, 95% CI 1.12 to 1.30, Z=4.80, p<0.01) and no significant heterogeneity was observed ($I^2=0.00\%$). Patients with psoriasis had a higher prevalence of hyperthyroidism than the controls (OR 1.20, 95% CI 1.12 to 1.30, Z=4.78, p<0.01) and no significant heterogeneity was observed ($I^2=0.00\%$, figure 4A,B).

Additionally, a higher prevalence of subclinical hypothyroidism and subclinical hyperthyroidism was observed in patients with psoriasis compared with the controls (Subclinical hypothyroidism: OR 2.24, 95% CI 0.26 to 19.13, Z=0.74, p=0.46. Subclinical hyperthyroidism: OR 2.66, 95% CI 0.70 to 10.07, Z=1.44, p=0.15). However, the difference was not statistically significant (online supplemental figure 1A,B).
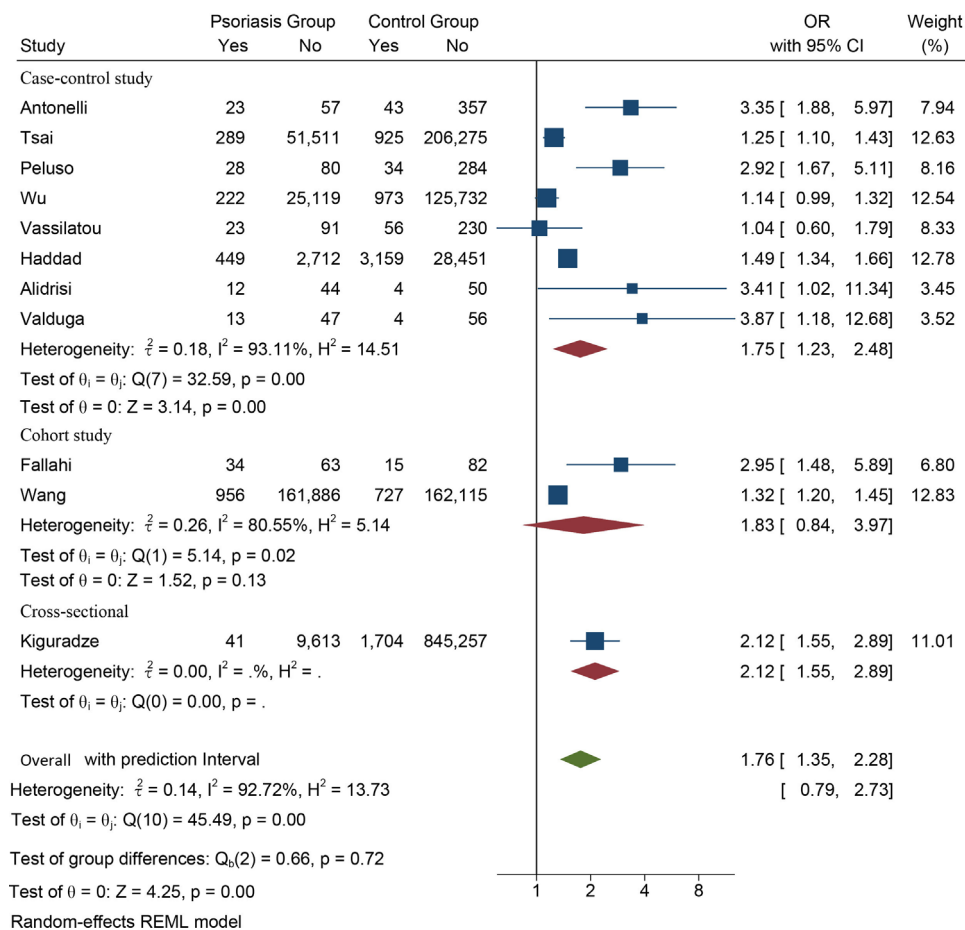
Figure 2 Forest plot of the association between psoriasis and autoimmune thyroid disease.

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 (I^2=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 (I^2=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 1.27 to 3.10, Z=3.00, p<0.01) and the heterogeneity was mild (I^2=41.54%). 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 (I^2=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 discosmetic 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
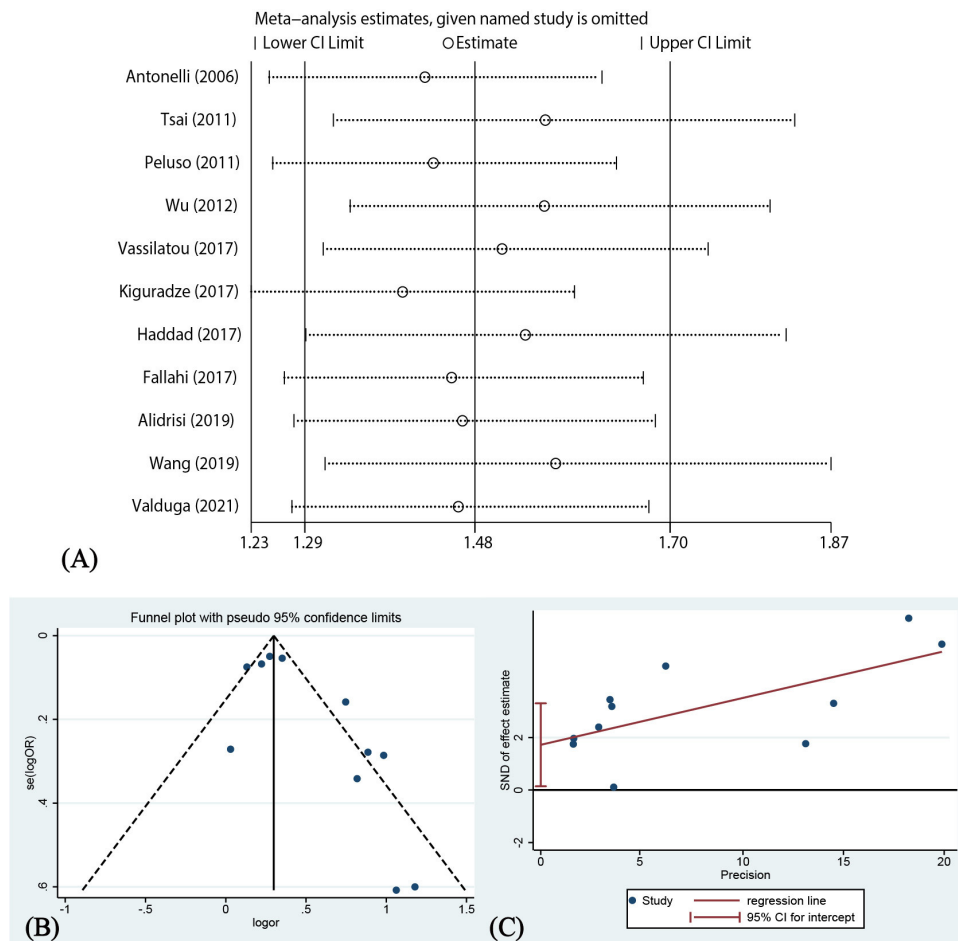
Figure 3 Sensitivity analysis and publication bias. SND, standard normal deviate.

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 on AITD 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 of AITD, 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 of AITD, 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 and AITD

Both abnormal immunological reactions and underlying genetic risk can contribute to the pathogenesis of psoriasis and AITD.[25 26] These two diseases share some autoimmune processes and susceptibility genes, which may explain the concurrence of psoriasis and AITD. The predominant Th1 immune reaction has been observed in patients with psoriasis,[27 28] 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 in AITD.[29–32] Additionally, Th17-mediated immune disorder has also been observed in psoriasis and AITD.[33 34] 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.[35] Additionally, other SNP variations in the PTPN22 gene have been demonstrated to be indicators for evaluating the risk of psoriasis.[36 37] IL12B has been generally recognised as a psoriasis susceptibility gene,[38] an upstream variation of which affects the phenotype of AITD in men.[39]
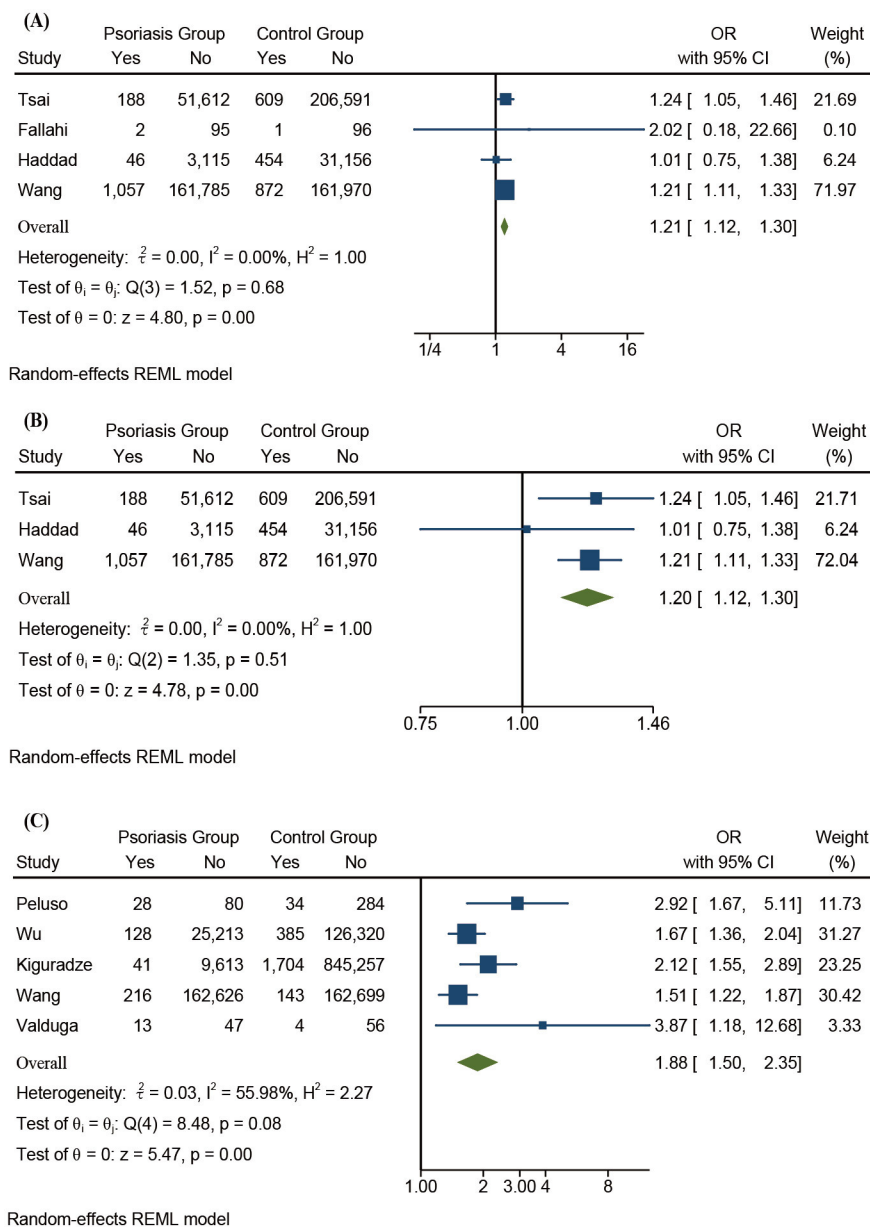
Figure 4 (A) Forest plots of psoriasis and hypothyroidism. (B) Forest plots of psoriasis and hyperthyroidism. (C) Forest plots of psoriasis and HT. HT, Hashimoto's thyroiditis; REML, restricted maximum-likelihood.
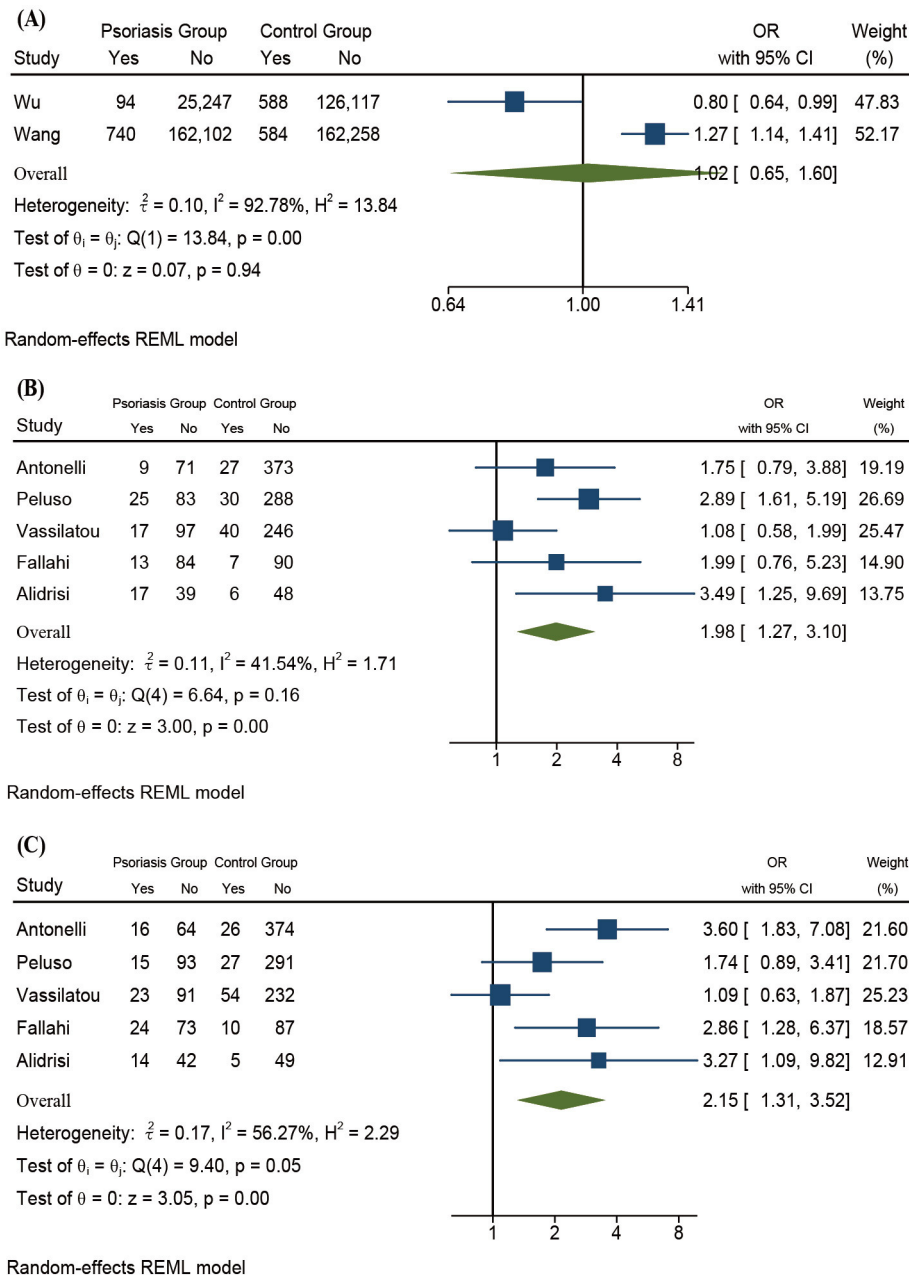
Implications for practice

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

(A)

Study	Psoriasis Group Yes	No	Control Group Yes	No	OR with 95% CI	Weight (%)
Wu	94	25,247	588	126,117	0.80 [0.64, 0.99]	47.83
Wang	740	162,102	584	162,258	1.27 [1.14, 1.41]	52.17
Overall					1.02 [0.65, 1.60]	

Heterogeneity: $\tau^2 = 0.10$, $I^2 = 92.78\%$, $H^2 = 13.84$

Test of $\theta_i = \theta_j$: Q(1) = 13.84, p = 0.00

Test of $\theta = 0$: z = 0.07, p = 0.94

0.64   1.00   1.41

Random-effects REML model

(B)

Study	Psoriasis Group Yes	No	Control Group Yes	No	OR with 95% CI	Weight (%)
Antonelli	9	71	27	373	1.75 [0.79, 3.88]	19.19
Peluso	25	83	30	288	2.89 [1.61, 5.19]	26.69
Vassilatou	17	97	40	246	1.08 [0.58, 1.99]	25.47
Fallahi	13	84	7	90	1.99 [0.76, 5.23]	14.90
Alidrisi	17	39	6	48	3.49 [1.25, 9.69]	13.75
Overall					1.98 [1.27, 3.10]	

Heterogeneity: $\tau^2 = 0.11$, $I^2 = 41.54\%$, $H^2 = 1.71$

Test of $\theta_i = \theta_j$: Q(4) = 6.64, p = 0.16

Test of $\theta = 0$: z = 3.00, p = 0.00

1   2   4   8

Random-effects REML model

(C)

Study	Psoriasis Group Yes	No	Control Group Yes	No	OR with 95% CI	Weight (%)
Antonelli	16	64	26	374	3.60 [1.83, 7.08]	21.60
Peluso	15	93	27	291	1.74 [0.89, 3.41]	21.70
Vassilatou	23	91	54	232	1.09 [0.63, 1.87]	25.23
Fallahi	24	73	10	87	2.86 [1.28, 6.37]	18.57
Alidrisi	14	42	5	49	3.27 [1.09, 9.82]	12.91
Overall					2.15 [1.31, 3.52]	

Heterogeneity: $\tau^2 = 0.17$, $I^2 = 56.27\%$, $H^2 = 2.29$

Test of $\theta_i = \theta_j$: Q(4) = 9.40, p = 0.05

Test of $\theta = 0$: z = 3.05, p = 0.00

1   2   4   8

Random-effects REML model

Figure 5 (A) Forest plots of psoriasis and GD. (B) Forest plots of psoriasis and TgAb. (C) Forest plots of psoriasis and TPOAb. GD, Graves' disease; REML, restricted maximum-likelihood; TgAb, thyroglobulin antibodies; TPOAb, thyroid peroxidase antibodies.

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.

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

REFERENCES

1 Griffiths CEM, van der Walt JM, Ashcroft DM, *et al*. The global state of psoriasis disease epidemiology: a workshop report. *Br J Dermatol* 2017;177:e4–7.
2 Langley RGB, Krueger GG, Griffiths CEM. Psoriasis: epidemiology, clinical features, and quality of life. *Ann Rheum Dis* 2005;64 Suppl 2:ii18–23.
3 Daudén E, Castañeda S, Suárez C, *et al*. Clinical practice guideline for an integrated approach to comorbidity in patients with psoriasis. *J Eur Acad Dermatol Venereol* 2013;27:1387–404.
4 Schaefer CP, Cappelleri JC, Cheng R, *et al*. Health care resource use, productivity, and costs among patients with moderate to severe plaque psoriasis in the United States. *J Am Acad Dermatol* 2015;73:585–93.
5 Kaushik SB, Lebwohl MG. Psoriasis: which therapy for which patient: psoriasis comorbidities and preferred systemic agents. *J Am Acad Dermatol* 2019;80:27–40.
6 Antonelli A, Ferrari SM, Corrado A, *et al*. Autoimmune thyroid disorders. *Autoimmun Rev* 2015;14:174–80.
7 Hesarghatta Shyamasunder A, Abraham P. Measuring TSH receptor antibody to influence treatment choices in Graves' disease. *Clin Endocrinol* 2017;86:652–7.
8 Antonelli A, Delle Sedie A, Fallahi P, *et al*. High prevalence of thyroid autoimmunity and hypothyroidism in patients with psoriatic arthritis. *J Rheumatol* 2006;33:2026–8.
9 Tsai T-F, Wang T-S, Hung S-T, *et al*. Epidemiology and comorbidities of psoriasis patients in a national database in Taiwan. *J Dermatol Sci* 2011;63:40–6.
10 Alidrisi HA, Al Hamdi K, Mansour AA. Is there any association between psoriasis and Hashimoto's thyroiditis? *Cureus* 2019;11:e4269.
11 Fallahi P, Ferrari SM, Ruffilli I, *et al*. Increased incidence of autoimmune thyroid disorders in patients with psoriatic arthritis: a longitudinal follow-up study. *Immunol Res* 2017;65:681–6.
12 Haddad A, Ashkenazi RI, Bitterman H, *et al*. Endocrine comorbidities in patients with psoriatic arthritis: a population-based case-controlled study. *J Rheumatol* 2017;44:786–90.
13 Kiguradze T, Bruins FM, Guido N, *et al*. Evidence for the association of Hashimoto's thyroiditis with psoriasis: a cross-sectional retrospective study. *Int J Dermatol* 2017;56:553–6.
14 Valduga JAG, Rebeiko LB, Skare TL. Prevalence of Hashimoto's thyroiditis in psoriasis patients. *Rev Assoc Med Bras* 2021;67:52–7.
15 Vassilatou E, Papadavid E, Papastamatakis P, *et al*. No association of psoriasis with autoimmune thyroiditis. *J Eur Acad Dermatol Venereol* 2017;31:102–6.
16 Wang S-H, Wang J, Lin Y-S, *et al*. Increased risk for incident thyroid diseases in people with psoriatic disease: a cohort study. *J Am Acad Dermatol* 2019;80:1006–12.
17 Karadag AS, Ozlu E, Kostek O, *et al*. Effect of low-dose acitretin treatment on pituitary hormones in psoriasis vulgaris: a retrospective study. *Indian J Dermatol Venereol Leprol* 2019;85:300–4.
18 Wells G, Shea B, O'connell D. The Newcastle-Ottawa scale (NOS) for assessing the quality of nonrandomised studies in Newcastle-analyses, 2019. Available: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp
19 Rostom A, Dubé C, Cranney A. AHRQ evidence reports, 2004. Available: https://www.ncbi.nlm.nih.gov/books/NBK35156/
20 Sterne JA, Hernán MA, Reeves BC, *et al*. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ* 2016;355:i4919.
21 Peluso R, Lupoli GA, Del Puente A, *et al*. Prevalence of thyroid autoimmunity in patients with spondyloarthropathies. *J Rheumatol* 2011;38:1371–7.
22 Wu JJ, Nguyen TU, Poon K-YT, *et al*. The association of psoriasis with autoimmune diseases. *J Am Acad Dermatol* 2012;67:924–30.
23 Vastarella M, Megna M, Lupoli GA, *et al*. Is there any association between psoriasis, psoriatic arthritis and thyroid autoimmunity? *Australas J Dermatol* 2021;62:e207-e211.
24 Khan SR, Bano A, Wakkee M, *et al*. The association of autoimmune thyroid disease (AITD) with psoriatic disease: a prospective cohort study, systematic review and meta-analysis. *Eur J Endocrinol* 2017;177:347–59.
25 Perera GK, Di Meglio P, Nestle FO. Psoriasis. *Annu Rev Pathol* 2012;7:385–422.
26 Simmonds MJ. Gwas in autoimmune thyroid disease: redefining our understanding of pathogenesis. *Nat Rev Endocrinol* 2013;9:277–87.
27 Cai Y, Fleming C, Yan J. New insights of T cells in the pathogenesis of psoriasis. *Cell Mol Immunol* 2012;9:302–9.
28 Lowes MA, Suárez-Fariñas M, Krueger JG. Immunology of psoriasis. *Annu Rev Immunol* 2014;32:227–55.
29 Antonelli A, Ferrari SM, Giuggioli D, *et al*. Chemokine (C-X-C motif) ligand (CXCL)10 in autoimmune diseases. *Autoimmun Rev* 2014;13:272–80.
30 Ruffilli I, Ragusa F, Benvenga S, *et al*. Psoriasis, psoriatic arthritis, and thyroid autoimmunity. *Front Endocrinol* 2017;8:139.
31 Nanba T, Watanabe M, Inoue N, *et al*. Increases of the Th1/Th2 cell ratio in severe Hashimoto's disease and in the proportion of Th17 cells in intractable Graves' disease. *Thyroid* 2009;19:495–501.
32 Peng S, Li C, Wang X, *et al*. Increased Toll-like receptors activity and TLR ligands in patients with autoimmune thyroid diseases. *Front Immunol* 2016;7:578.
33 Hänsel A, Günther C, Ingwersen J, *et al*. Human slan (6-sulfo lacNAc) dendritic cells are inflammatory dermal dendritic cells in psoriasis and drive strong TH17/TH1 T-cell responses. *J Allergy Clin Immunol* 2011;127:787–94.
34 Vitales-Noyola M, Ramos-Levi AM, Martínez-Hernández R, *et al*. Pathogenic Th17 and Th22 cells are increased in patients with autoimmune thyroid disorders. *Endocrine* 2017;57:409–17.
35 Criswell LA, Pfeiffer KA, Lum RF, *et al*. Analysis of families in the multiple autoimmune disease genetics Consortium (MADGC) collection: the PTPN22 620W allele associates with multiple autoimmune phenotypes. *Am J Hum Genet* 2005;76:561–71.
36 Li Y, Liao W, Chang M, *et al*. Further genetic evidence for three psoriasis-risk genes: ADAM33, CDKAL1, and PTPN22. *J Invest Dermatol* 2009;129:629–34.
37 Wang H, Wang Z, Rani PL, *et al*. Identification of PTPN22, ST6GAL1 and Jazf1 as psoriasis risk genes demonstrates shared pathogenesis between psoriasis and diabetes. *Exp Dermatol* 2017;26:1112–7.
38 Cargill M, Schrodi SJ, Chang M, *et al*. A large-scale genetic association study confirms IL12B and leads to the identification of IL23R as psoriasis-risk genes. *Am J Hum Genet* 2007;80:273–90.
39 Walsh JP, Berry J, Liu S, *et al*. The clinical presentation of autoimmune thyroid disease in men is associated with IL12B genotype. *Clin Endocrinol* 2011;74:508–12.
40 Balak DM, Hajdarbegovic E. Drug-Induced psoriasis: clinical perspectives. *Psoriasis* 2017;7:87–94.
41 McDermott MT. Hyperthyroidism. *Ann Intern Med* 2020;172:ITC49.
42 Gnanaraj P, Malligarjunan H, Dayalan H, *et al*. Therapeutic efficacy and safety of propylthiouracil in psoriasis: an open-label study. *Indian J Dermatol Venereol Leprol* 2011;77:673–6.