SYSTEMATIC REVIEW



Association Between Psoriasis and Vitiligo: A Systematic Review and Meta-Analysis

Hsi Yen¹ · Ching-Chi Chi^{1,2}

Published online: 13 October 2018 © Springer Nature Switzerland AG 2018

Abstract

Background The relationship between psoriasis and vitiligo has not been previously confirmed, and we therefore aimed to investigate this association.

Methods We conducted a search of the MEDLINE and EMBASE electronic databases on 22 January 2018 for case–control, cross-sectional, and cohort studies examining the association between psoriasis and vitiligo. A customized Newcastle–Ottawa Scale was used to assess the risk of bias of the included studies. We performed a random effects meta-analysis to calculate pooled odds ratios (ORs) with 95% confidence intervals (CIs) for case–control and cross-sectional studies.

Results Of 2453 citations identified from the literature search, 10 case–control/cross-sectional studies with a total of 120,866 psoriasis cases and 79,907 vitiligo cases were included in our study. Four of these studies were rated as high risk of bias. We found a significantly increased odds for vitiligo in psoriasis patients (summary OR 2.29, 95% CI 1.56–3.37, studies = 7), as well as a significantly elevated odds for psoriasis in vitiligo patients (summary OR 3.43, 95% CI 1.86–6.33, studies = 4). **Conclusions** Our meta-analysis showed that psoriasis and vitiligo are associated with each other. Several studies had a high risk of bias, and further investigation is needed to confirm this association and amplify treatment options.

Key Points

This meta-analysis found a statistically positive association between psoriasis and vitiligo; psoriatic patients had a twofold odds of vitiligo while vitiligo patients had a threefold odds of psoriasis.

A shared genetic basis and common cellular immune pathway may explain this association, implying a potential for overlap in disease management.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s40257-018-0394-1) contains supplementary material, which is available to authorized users.

Ching-Chi Chi chingchi@cgmh.org.tw

- ¹ Department of Dermatology, Chang Gung Memorial Hospital, Linkou, 5, Fuxing St, Guishan District, Taoyuan 33305, Taiwan
- ² College of Medicine, Chang Gung University, Taoyuan, Taiwan

1 Introduction

Psoriasis is a chronic systemic inflammatory disease that typically presents on the skin as erythematous plaques with silver scales. It is a relatively common disease with an estimated prevalence ranging from 0.51 to 11.43% in adults [1]. Current evidence supports an immune-related cytokine and chemokine dysfunction as the main pathogenesis for psoriasis [2], with stem cell abnormalities potentially contributing to the immune imbalance [3].

Vitiligo is a pigmentary dermatosis where destruction of epidermal melanocytes causes macular or patchy depigmentation of the skin. A systematic review reported a prevalence of vitiligo that ranges from 0.06 to 2.28% in the general population [4]. Many causes, including autoimmunity, have been implicated in the etiology of vitiligo [5].

Currently, there are limited observational studies evaluating the association between psoriasis and vitiligo, and results are inconsistent [6–15]. While the association between the two diseases could simply be coincidental, it has been proposed that patients with one immune-mediated inflammatory disorder are more likely than controls to have another immune-mediated inflammatory disorder, raising the possibility of a shared etiology [16]. Psoriasis patients were reported to have a higher frequency of concomitant autoimmune diseases than the general population, including rheumatoid arthritis, inflammatory bowel diseases, and multiple sclerosis [17]. Similarly, vitiligo has been associated with other autoimmune diseases, such as thyroid diseases, pernicious anemia, diabetes mellitus, and alopecia areata [5]. Shared cell-mediated immune pathogenesis, including T-helper (Th) 1 and Th17 pathways, may contribute to similar patterns of overactive cellular response in both diseases [17]. The objective of this study was to systematically evaluate the evidence and quantify the association between psoriasis and vitiligo.

2 Materials and Methods

We conducted a systematic review and meta-analysis of observational studies on the association between psoriasis and vitiligo. The reporting of this study was in accordance with the Meta-Analysis of Observational Studies in Epidemiology (MOOSE) guidelines [18]. The two authors (HY and CC) independently conducted study selection, data extraction, and risk of bias assessment, and disagreement was resolved by discussion.

2.1 Inclusion and Exclusion Criteria

Observational case–control, cross-sectional, or cohort studies written in English that examined the association between psoriasis and vitiligo were included in our study. Studies must have provided odds ratios (ORs) or sufficient raw data to calculate ORs. The exclusion criteria included abstractonly articles, conference proceedings, and articles that were not peer-reviewed.

2.2 Literature Search and Study Selection

We conducted a search of the MEDLINE and EMBASE electronic databases on 22 January 2018 for relevant observational studies (a detailed search strategy is presented in electronic supplementary Table S1). Titles and abstracts were first screened from the initial literature search result. After screening the titles and abstracts, we obtained the full text of potential articles and examined them for relevance. Finally, the bibliographies of all included articles were reviewed to screen for potential relevant studies.

2.3 Data Extraction

After identifying relevant studies, the following information was extracted: author, publication year, country of study, study design, number in the case and control groups, method of defining cases and controls, method for selection of controls, how exposure was ascertained for cases and controls, demographic characteristics of cases and controls, nonresponse rates, risk estimates on the association between psoriasis and vitiligo, and whether any additional confounders were adjusted or matched for in the analysis.

2.4 Risk of Bias Evaluation

The risk of bias of included observational studies was assessed by using a customized Newcastle–Ottawa Scale (NOS) for case–control studies [19]. A green, yellow, and red light scoring system was designed by the two authors to interpret the NOS results (see details in electronic supplementary Table S2). A study with one or more red lights indicated a lower-quality study, while a study with no red lights suggested a higher-quality study. Specifically, a study was considered low risk of bias for comparability if it controlled for additional confounding factors in the analysis in addition to age and sex, such as healthcare consumption or comorbid diseases.

2.5 Statistical Analysis

Two meta-analyses were performed separately to examine the association between psoriasis and vitiligo. The first meta-analysis assessed the OR of vitiligo in psoriasis patients, while the second meta-analysis assessed the OR of psoriasis in vitiligo patients. The most fully adjusted OR was used whenever provided. If OR estimates were not presented in the study, then crude ORs were calculated by using the reported raw data. Taking into account potential betweenstudy variability, the DerSimonian and Laird random-effects model was used to obtain summary ORs and 95% confidence intervals (CIs) [20]. The chi-square test was used to assess heterogeneity, and was quantified using the I^2 statistic [21]. An I^2 of <25% was considered lower heterogeneity, while more than 75% considered higher heterogeneity [22].

Assessment for heterogeneity was explored by subgroup analysis on adjustment for other potential confounding variables and study quality. Funnel plots were used to examine potential publication bias [23]. All statistical analyses were performed using Review Manager version 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). All statistical tests were two-sided, and a *p* value < 0.05 was considered statistically significant.

3 Results

3.1 Study Characteristics

Our systematic literature search identified 2453 articles, and a total of 10 studies were ultimately included in our study. flow diagram

Seven studies investigated the association of vitiligo in psoriasis patients [6-12], including three case-control studies and four cross-sectional studies. Four studies looked at the association of psoriasis in vitiligo patients, including three case-control studies and one cross-sectional study [11, 13–15]. One overlapping case–control study looked at both associations [11]. We found no relevant cohort studies. The selection process and reasons for exclusion are summarized in Fig. 1. A total of 120,866 psoriasis cases and 79,907 vitiligo cases were included in the statistical analyses.

The main characteristics of the included studies are summarized in Table 1. Risk of bias assessment revealed four studies of lower quality [8, 10, 14, 15] and six studies of higher quality (electronic supplementary Fig. S1) [6, 7, 9, 11-13].

3.2 Meta-Analysis of the Association between Psoriasis and Vitiligo

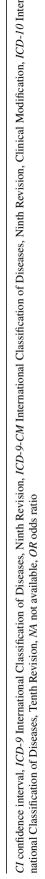
A meta-analysis of seven studies [6-12] that provided the odds of vitiligo in psoriasis patients revealed a twofold increase of vitiligo in psoriasis patients (summary OR 2.29, 95% CI 1.56-3.37) (Fig. 2). There was high statistical heterogeneity across the included studies (p < 0.00001, $I^2 = 84\%$).

Conversely, a meta-analysis of four studies that provided the odds of psoriasis in vitiligo patients [11, 13-15] found a threefold increase of psoriasis in vitiligo patients (summary OR 3.43, 95% CI 1.86-6.33) [Fig. 3]. There was also high statistical heterogeneity across the four studies (p < 0.00001, $I^2 = 97\%$).

Fig. 1 The systematic search Records identified through Additional records identified database searching through other sources (n = 2453)(n = 0)Records after duplicates removed (n = 1877) **Records screened** Records excluded (n = 1877) (n = 1841) Full-text articles assessed Full-text articles excluded: for eligibility Abstract only (n = 9)(n = 36)Non-English (n = 3) No relevant data (n = 10) Irrelevant comparison groups (n = 4)Studies included in qualitative synthesis (n = 10) Studies included in quantitative synthesis (meta-analysis) (n = 10) Psoriasis versus nonpsoriasis (n = 7)Vitiligo versus non-vitiligo (n=4)

First author, year,	Study design	Cases (% female and mean	Controls (% female and mean	Case definition and sampling	Results	
country		age)	age)	population/outcome definition	Crude OR (95% CI)	Adjusted OR (95% CI)
Studies investigating th	Studies investigating the odds of vitiligo in psoriasis patients	ients				
Tsai et al. 2011, Taiwan [6]	Case-control (1:4 ratio, matched by age, sex, and urbanization level of resi- dential areas)	51,800 psoriasis cases (38%, 46.4 years)	207,200 controls (38%, 46.3 years)	ICD-9-CM psoriasis code from national health insurance data- base in 2006, validation carried out more than once/ICD-9-CM code for vitiligo, diagnosis confirmed by specialist at least two consecutive times	4.77 (3.16-7.18)	ΝΑ
Wu et al. 2012, USA [7]	Case-control (1:5 ratio, matched by age, sex, and length of enrollment)	25,341 psoriasis cases (52%, 48.7 years)	126,705 controls (52%, 48.9 years)	ICD-9 psoriasis code from Kaiser 1.75 (1.45–2.12) Permanente, Southern Califor- nia, database from 1 January 2004 to 28 February 2011/ ICD-9 vitiligo code, validation carried out more than once	1.75 (1.45-2.12)	ΝΑ
Augustin et al. 2015, Germany [8]	Cross-sectional	1313 childhood psoriasis cases (52%, NA)	291,868 children without psoriasis (49%, NA)	ICD-10 psoriasis code from Ger- man health insurance company database in 2009/ICD-10 vitiligo code	2.08 (0.67–6.49)	NA
Blegvad et al. 2017, Denmark [9]	Cross-sectional	1925 children and adoles- cents with psoriasis (55%, 13.8 years)	1,194,712 children and ado- lescents without psoriasis (49%, 9.2 years)	ICD-10 psoriasis code from Dan- ish registries on 31 December 2012/ICD-10 vitiligo code	18.77 (8.32–42.33)	4.76 (1.71–13.20) adjusting for age, sex, and number of dermatology visits
Radtke et al. 2017, Germany [10]	Cross-sectional	37,456 adults with psoriasis (NA)	1,305,215 adults without psoriasis (NA)	ICD-10 psoriasis code from Ger- man health insurance company database in 2009/ICD-10 vitiligo code	2.44 (2.07–2.87)	NA
Sharquie et al. 2017, Iraq [11]	Case-control (1:2 ratio, hospi- tal controls were visiting for other reasons and matched by age and sex)	250 psoriasis cases between 14 and 68 years of age (64%, 26.6 years)	500 controls (58%, 28.0 years)	Diagnosis from documented dermatology clinic visit with physical examination at a single hospital/clinical diagnosis on documented visit	3.38 (0.80–14.26)	ΝΑ

First author, year,	Study design	Cases (% female and mean	Controls (% female and mean	Case definition and sampling	Results	
country		age)	age)	population/outcome definition	Crude OR (95% CI)	Adjusted OR (95% CI)
Zander et al. 2017, Germany [12]	Cross-sectional	2781 psoriasis cases between 16 and 70 years of age (38%, 46.2 years)	136,137 participants without psoriasis (44%, 43.1 years)	Diagnosis by board-certified dermatologist who conducted physical examination and standardized interviews for employees undergoing occu- pational skin cancer screening from 2001 to 2014/clinical diagnosis on documented visit	0.87 (0.52–1.45)	0.82 (0.49–1.38) adjusting for age and sex
Studies investigating th	Studies investigating the odds of psoriasis in vitiligo patients	ients				
Chen et al. 2015, Taiwan [13]	Case-control (1:4 ratio, matched by age and sex)	14,883 adult vitiligo cases (57%, 44 years)	59,532 adult controls (57%, 44 years)	ICD-9-CM vitiligo code from national health insurance data- base from 1 January 1997 to 31 December 2011, diagnosis confirmed by dermatologist at least three consecutive times/ ICD-9-CM psoriasis code	4.16 (3.62-4.78)	3.15 (2.72–3.64), adjusting for age, sex, other comorbid diseases, visit times, annual income, and area
Lee et al. 2015, South Korea [14]	Cross-sectional	63,467 average vitiligo cases over 3 years (NA)	General population: average 50,131,632 over 3 years (57%, NA)	ICD-10 vitiligo code from nation- wide health insurance database from 2009 to 2011/ICD-10 psoriasis code	5.83 (5.50–6.19)	NA
Teulings et al. 2015, The Netherlands [15]	Case-control (cases were asked to invite a genetically non-related person of the same age group without vitiligo to fill in the ques- tionnaire)	1307 non-segmental vitiligo cases aged ≥ 50 years (63%, 61 years)	788 controls (44%, 60 years)	Clinical diagnoses made during a visit to the Netherlands Institute of Pigment Disorders from January 1996 to September 2010/diagnoses by written self- report via postal survey	1.10 (0.71–1.70)	ΝΑ
Sharquie et al. 2017, Iraq [11]	Case-control (1:2 ratio, hos- pital controls were visiting for other reasons and were matched by age and sex)	250 vitiligo cases between 14 and 68 years of age (63%, 27.1 years)	500 controls (58%, 28.0 years)	Diagnosis from documented dermatology clinic visit with physical examination at a single hospital/clinical diagnosis on documented visit	15.89 (3.61–70.06)	ΝΑ



Study or Subgroup	log[Odds Ratio]		Psoriasis Total	Control Total	Weight	Odds Ratio IV, Random, 95% C	I	Odds Ra IV, Random,		
Augustin 2015	0.7323	0.5807	1313	291868	7.6%	2.08 [0.67, 6.49]				
Blegvad 2017	1.5598	0.5208	1925	1194712	8.8%	4.76 [1.71, 13.20]				_
Radtke 2017	0.8914	0.0835	37456	1305215	22.0%	2.44 [2.07, 2.87]			-	
Sharquie 2017	1.2182	0.7345	250	500	5.4%	3.38 [0.80, 14.26]				
Tsai 2011	1.5614	0.2094	51800	207200	18.2%	4.77 [3.16, 7.18]				
Wu 2012	0.5624	0.0961	22653	126705	21.7%	1.75 [1.45, 2.12]		-	-	
Zander 2017	-0.1985	0.2627	2781	136137	16.2%	0.82 [0.49, 1.37]				
Total (95% CI)			118178	3262337	100.0%	2.29 [1.56, 3.37]			◆	
Heterogeneity: Tau ² =	0.17; Chi ² = 37.31,	df = 6 (P	< 0.00001)	; I² = 84%					<u> </u>	<u> </u>
Test for overall effect:	Z = 4.22 (P < 0.000	1)					0.05 0.2		5 oriasis	20

Fig. 2 The odds of vitiligo in psoriasis patients. CI confidence interval, df degrees of freedom, IV inverse variance, SE standard error

Study or Subgroup	log[Odds Ratio]	SE Weight	Odds Ratio IV, Random, 95% Cl	Odds Ratio IV, Random, 95% Cl
Chen 2015	1.1463 0.07	43 30.8%	3.15 [2.72, 3.64]	•
Lee 2015	1.7638 0.03	01 31.2%	5.83 [5.50, 6.19]	•
Sharquie 2017	2.7659 0.75	69 11.0%	15.89 [3.61, 70.06]	
Teulings 2016	0.0961 0.22	16 27.0%	1.10 [0.71, 1.70]	+
Total (95% CI)		100.0%	3.43 [1.86, 6.33]	•
Heterogeneity: Tau ² = Test for overall effect:	0.31; Chi ² = 111.58, df = Z = 3.96 (P < 0.0001)	L L L L L L L L L L L L L L L L L L L		

Fig. 3 The odds of psoriasis in vitiligo patients. CI confidence interval, df degrees of freedom, IV inverse variance, SE standard error

3.3 Exploration of Heterogeneity and Publication Bias

Stratified analysis was carried out to assess heterogeneity, and no significant between-subgroup heterogeneity by adjustment for potential confounding variables or study quality was identified (p > 0.47 for all subgroup differences). There remained a largely positive association and high heterogeneity for both adjusted and unadjusted subgroups in the two meta-analyses, although the summary estimate was not statistically significant for adjusted odds of vitiligo in psoriasis patients (Figs. 4 and 5). With regard to study quality, stratified estimates remained similar for studies on psoriasis patients; lower-quality studies had minimal heterogeneity, while higher-quality studies had high heterogeneity (Fig. 6). For studies on vitiligo patients, there was positive association for psoriasis that was statistically significant only in higher-quality studies, and heterogeneity remained high regardless of study quality (Fig. 7). Finally, no obvious publication bias was detected on funnel plots for both meta-analyses, but interpretation was difficult due to the low number of studies.

4 Discussion

Although there have been reports of patients who had concomitant psoriasis and vitiligo, including cases where the psoriatic plaques were confined to vitiligo patches [24], it has been argued that this may be due to chance alone [25]. However, our meta-analyses found significant associations between psoriasis and vitiligo that were consistent in both directions: compared with controls, psoriasis patients were 2.29-fold more likely to have vitiligo, while vitiligo patients were 3.43-fold more likely to be diagnosed with psoriasis.

The most common reason for studies to have a higher risk of bias was lack of adjustment for additional variables in addition to sex and age, limiting the comparability between cases and controls. However, the similar effect estimates regardless of study quality suggest that the positive association between the two diseases is consistent even after adjusting for potential confounders, such as comorbid diseases and healthcare consumption. However, stratified results should be interpreted with caution as some of the CIs were very wide, resulting in imprecise effect estimates.

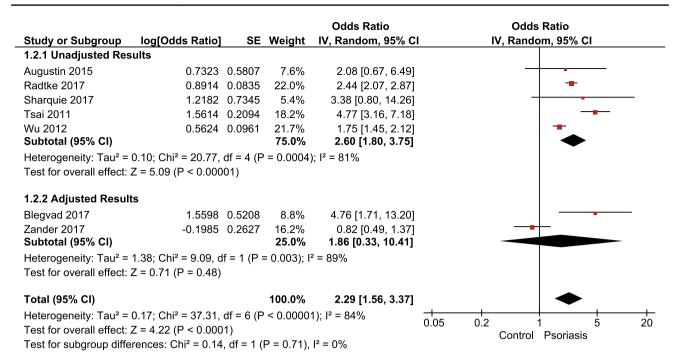


Fig. 4 The odds of vitiligo in psoriasis patients, stratified by adjustment. CI confidence interval, df degrees of freedom, IV inverse variance, SE standard error

Study or Subgroup	log[Odds Ratio]	SE Wei	ght i	Odds Ratio IV, Random, 95% Cl	I	Odds Ratio IV, Random, 95% Cl	
2.2.1 Unadjusted Res	sults		2				
Lee 2015	1.7638 0.	0301 31.	2%	5.83 [5.50, 6.19]		•	
Sharquie 2017	2.7659 0.	7569 11.	0%	15.89 [3.61, 70.06]			-
Teulings 2016 Subtotal (95% CI)	0.0961 0.		0% . 2%	1.10 [0.71, 1.70] 4.13 [1.06, 16.11]			
Heterogeneity: Tau ² =	1.28; Chi ² = 57.47, df	= 2 (P < 0.0	0001);	; I² = 97%			
Test for overall effect:	Z = 2.04 (P = 0.04)						
2.2.2 Adjusted Resul	ts						
Chen 2015 Subtotal (95% CI)	1.1463 0.		8% . 8%	3.15 [2.72, 3.64] 3.15 [2.72, 3.64]		•	
Heterogeneity: Not ap	plicable						
Test for overall effect:	Z = 15.43 (P < 0.0000	1)					
Total (95% CI)		100.	0%	3.43 [1.86, 6.33]		•	
Heterogeneity: Tau ² = Test for overall effect: Test for subgroup diffe	Z = 3.96 (P < 0.0001)	,		,,	0.01 0.1	1 10 1 Control Vitiligo	00

Fig. 5 The odds of psoriasis in vitiligo patients, stratified by adjustment. CI confidence interval, df degrees of freedom, IV inverse variance, SE standard error

One explanation for the association between psoriasis and vitiligo is the common genetic basis for increased autoimmunity and inflammation. Genome-wide association studies have found increasing evidence of genetic predisposition to multiple autoimmune diseases [26]. Inflammasomes, multiprotein complexes in the cytoplasm that activate pro-inflammatory cytokines, may play an important role [27, 28]. Inflammasome-related genetic sequence variants have been found to be associated with psoriasis in generalized vitiligo patients and play a role in psoriasis susceptibility [29, 30]. Inflammasome markers in the skin have been identified in both vitiligo and psoriasis [31–33]. Both diseases

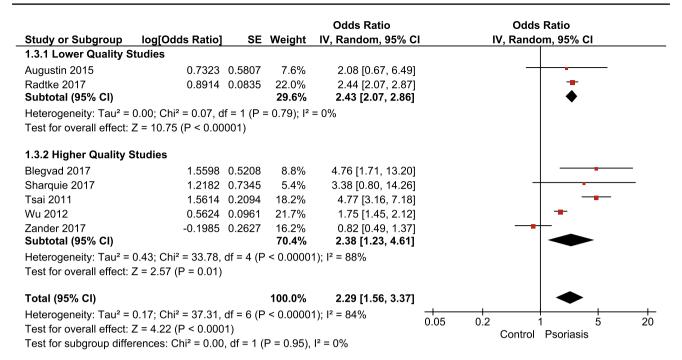


Fig. 6 The odds of vitiligo in psoriasis patients, stratified by study quality. CI confidence interval, df degrees of freedom, IV inverse variance, SE standard error

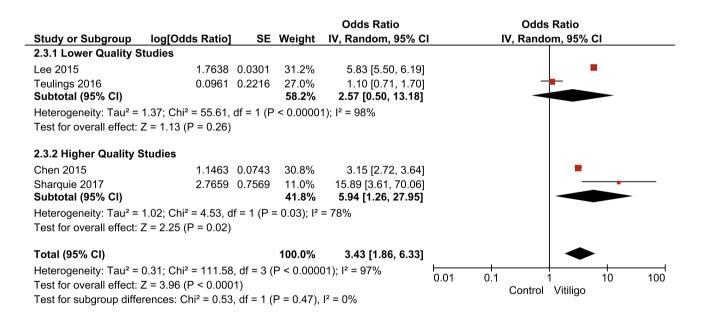


Fig. 7 The odds of psoriasis in vitiligo patients, stratified by study quality. CI confidence interval, df degrees of freedom, IV inverse variance, SE standard error

also share a common genetic locus in major histocompatibility complex [34].

A second explanation is a shared importance of cellular immune pathways, including Th1 and Th17 [35–40]. Additionally, interferon (IFN)- α has been recognized to potentially induce both psoriasis and vitiligo when used to treat

hepatitis C infection [41–44]. One patient treated with IFN α for hepatitis B infection developed vitiligo and psoriasis lesions concurrently [45]. IFN α produced by plasmacytoid dendritic cells may play a role in the pathogenesis of both diseases via Th1- and Th17-mediated autoimmune inflammation of the skin [43, 46, 47].

Interestingly, the Janus kinase (JAK) inhibitor tofacitinib has been used to treat both psoriasis and vitiligo [48, 49]. In psoriasis patients, tofacitinib inhibits JAK/signal transducers and activators of transcription (JAK/STAT)-dependent cytokines, blocking stimulation of Th17 cells and reducing the production of IL-17. For vitiligo, tofacitinib reduces the targeted destruction of melanocytes by T cells, which is mediated by IFNy and the JAK-STAT pathway. While evidence is still limited, there have been promising initial results for the effect of tofacitinib in both diseases. Furthermore, narrow-band ultraviolet B phototherapy treatment has been shown to simultaneously improve psoriasis and vitiligo in the same patient [50]. The potential effectiveness of tofacitinib and narrow-band ultraviolet B phototherapy at managing both diseases lends support to the argument of a shared cellular immune pathway.

This study has several limitations. First, all the included studies were either cross-sectional or case–control studies, with potential for recall bias. However, most of the included studies used data from claims databases and would thus mitigate such bias. Second, there is a risk of language bias as the search was limited to English-language studies only. This bias may be minimized as studies from Taiwan, Germany, Denmark, Iraq, and South Korea were also included. Additionally, few studies presented ORs after adjustment for potential confounders. Finally, we were unable to further explore heterogeneity due to the small number of included studies. The strengths of this study include the use of two meta-analyses to establish a significant and consistent association between psoriasis and vitiligo, as well as the relatively large number of cases for both psoriasis and vitiligo.

5 Conclusion

This study found that psoriasis patients have a significantly higher odds of vitiligo, and vice versa. These results remained consistent for both low- and high-quality studies. While an understanding of this association may have future therapeutic implications for both diseases, more investigation is necessary to test this hypothesis.

Compliance with Ethical Standards

Funding No funding was received for the conduct of this study or the preparation of this article.

Conflict of interest Hsi Yen and Ching-Chi Chi have no conflicts of interest directly relevant to the content of this article.

References

- Michalek I, Loring B, John S. A systematic review of worldwide epidemiology of psoriasis. J Eur Acad Dermatol Venereol. 2017;31(2):205–12.
- Lowes MA, Bowcock AM, Krueger JG. Pathogenesis and therapy of psoriasis. Nature. 2007;445(7130):866–73.
- Damiani G, Berti E, Pigatto P, Franchi C, Asa'ad F. Benchmarking stem cells and transplantation in psoriasis. J Stem Cell Res Ther. 2018;8(3):416.
- Krüger C, Schallreuter KU. A review of the worldwide prevalence of vitiligo in children/adolescents and adults. Int J Dermatol. 2012;51(10):1206–12.
- Alikhan A, Felsten LM, Daly M, Petronic-Rosic V. Vitiligo: a comprehensive overview: part I. Introduction, epidemiology, quality of life, diagnosis, differential diagnosis, associations, histopathology, etiology, and work-up. J Am Acad Dermatol. 2011;65(3):473–91.
- Tsai TF, Wang TS, Hung ST, Tsai PI, Schenkel B, Zhang M, et al. Epidemiology and comorbidities of psoriasis patients in a national database in Taiwan. J Dermatol Sci. 2011;63(1):40–6.
- Wu JJ, Nguyen TU, Poon KYT, Herrinton LJ. The association of psoriasis with autoimmune diseases. J Am Acad Dermatol. 2012;67(5):924–30.
- Augustin M, Radtke MA, Glaeske G, Reich K, Christophers E, Schaefer I, et al. Epidemiology and comorbidity in children with psoriasis and atopic eczema. Dermatology. 2015;231(1):35–40.
- Blegvad C, Egeberg A, Tind Nielsen TE, Gislason GH, Zachariae C, Nybo Andersen AM, et al. Autoimmune disease in children and adolescents with psoriasis: A cross-sectional study in Denmark. Acta Derm Venereol. 2017;97(10):1225–9.
- Radtke MA, Schäfer I, Glaeske G, Jacobi A, Augustin M. Prevalence and comorbidities in adults with psoriasis compared to atopic eczema. J Eur Acad Dermatol Venereol. 2017;31(1):151–7.
- Sharquie KE, Salman HA, Yaseen AK. Psoriasis and vitiligo are close relatives. Clin Cosmet Investig Dermatol. 2017;10:341–5.
- Zander N, Schäfer I, Radtke M, Jacobi A, Heigel H, Augustin M. Dermatological comorbidity in psoriasis: results from a large-scale cohort of employees. Arch Dermatol Res. 2017;309(5):349–56.
- Chen YT, Chen YJ, Hwang CY, Lin MW, Chen TJ, Chen CC, et al. Comorbidity profiles in association with vitiligo: a nationwide population-based study in Taiwan. J Eur Acad Dermatol Venereol. 2015;29(7):1362–9.
- Lee H, Lee MH, Lee DY, Kang HY, Kim KH, Choi GS, et al. Prevalence of vitiligo and associated comorbidities in Korea. Yonsei Med J. 2015;56(3):719–25.
- 15. Teulings HE, Ceylan E, Overkamp M, Vrijman C, Bos JD, Nijsten TE, et al. Nonsegmental vitiligo disease duration and female sex are associated with comorbidity and disease extent: a retrospective analysis in 1307 patients aged ≥ 50 years. Br J Dermatol. 2016;175(4):821–4.
- Robinson D Jr, Hackett M, Wong J, Kimball AB, Cohen R, Bala M, et al. Co-occurrence and comorbidities in patients with immune-mediated inflammatory disorders: an exploration using US healthcare claims data, 2001–2002. Curr Med Res Opin. 2006;22(5):989–1000.
- Ayala-Fontánez N, Soler DC, McCormick TS. Current knowledge on psoriasis and autoimmune diseases. Psoriasis (Auckl). 2016;6:7–32.
- Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. JAMA. 2000;283(15):2008–12.
- Wells G, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle–Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. 2006. http://www.

ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed 6 Feb 2018.

- DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials. 1986;7(3):177–88.
- 21. Higgins J, Thompson SG. Quantifying heterogeneity in a metaanalysis. Stat Med. 2002;21(11):1539–58.
- Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003;327(7414):557–60.
- Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997;315(7109):629–34.
- 24. Sawchuk M, Spano F, Loo WJ, Guenther L. The coexistence of psoriasis and vitiligo: a review. J Cutan Med Surg. 2012;16(5):300-5.
- 25. Sandhu K, Kaur I, Kumar B. Psoriasis and vitiligo. J Am Acad Dermatol. 2004;51(1):149–50.
- Zhernakova A, Van Diemen CC, Wijmenga C. Detecting shared pathogenesis from the shared genetics of immune-related diseases. Nat Rev Genet. 2009;10(1):43–55.
- Kummer JA, Broekhuizen R, Everett H, Agostini L, Kuijk L, Martinon F, et al. Inflammasome components NALP 1 and 3 show distinct but separate expression profiles in human tissues suggesting a site-specific role in the inflammatory response. J Histochem Cytochem. 2007;55(5):443–52.
- Martinon F, Gaide O, Pétrilli V, Mayor A, Tschopp J. NALP inflammasomes: a central role in innate immunity. Semin Immunopathol. 2007;29(3):213–29.
- Jin Y, Mailloux CM, Gowan K, Riccardi SL, LaBerge G, Bennett DC, et al. NALP1 in vitiligo-associated multiple autoimmune disease. N Engl J Med. 2007;356(12):1216–25.
- Carlström M, Ekman AK, Petersson S, Söderkvist P, Enerbäck C. Genetic support for the role of the NLRP3 inflammasome in psoriasis susceptibility. Exp Dermatol. 2012;21(12):932–7.
- Johansen C, Moeller K, Kragballe K, Iversen L. The activity of caspase-1 is increased in lesional psoriatic epidermis. J Invest Dermatol. 2007;127(12):2857–64.
- Salskov-Iversen ML, Johansen C, Kragballe K, Iversen L. Caspase-5 expression is upregulated in lesional psoriatic skin. J Invest Dermatol. 2011;131(3):670–6.
- Marie J, Kovacs D, Pain C, Jouary T, Cota C, Vergier B, et al. Inflammasome activation and vitiligo/nonsegmental vitiligo progression. Br J Dermatol. 2014;170(4):816–23.
- Zhu K-J, Lv Y-M, Yin X-Y, Wang Z-X, Sun L-D, He S-M, et al. Psoriasis regression analysis of MHC loci identifies shared genetic variants with vitiligo. PLoS One. 2011;6(11):e23089.
- Griffiths CE, Barker JN. Pathogenesis and clinical features of psoriasis. Lancet. 2007;370(9583):263–71.

- Taher Z, Lauzon G, Maguiness S, Dytoc M. Analysis of interleukin-10 levels in lesions of vitiligo following treatment with topical tacrolimus. Br J Dermatol. 2009;161(3):654–9.
- Di Cesare A, Di Meglio P, Nestle FO. The IL-23/Th17 axis in the immunopathogenesis of psoriasis. J Invest Dermatol. 2009;129(6):1339–50.
- Singh RK, Lee KM, Vujkovic-Cvijin I, Ucmak D, Farahnik B, Abrouk M, et al. The role of IL-17 in vitiligo: a review. Autoimmun Rev. 2016;15(4):397–404.
- Basak PY, Adiloglu AK, Ceyhan AM, Tas T, Akkaya VB. The role of helper and regulatory T cells in the pathogenesis of vitiligo. J Am Acad Dermatol. 2009;60(2):256–60.
- 40. Bassiouny D, Shaker O. Role of interleukin-17 in the pathogenesis of vitiligo. Clin Exp Dermatol. 2011;36(3):292–7.
- Simsek H, Savas C, Akkiz H, Telatar H. Interferon-induced vitiligo in a patient with chronic viral hepatitis C infection. Dermatology. 1996;193(1):65–6.
- Hamadah I, Binamer Y, Sanai FM, Abdo AA, Alajlan A. Interferon-induced vitiligo in hepatitis C patients: a case series. Int J Dermatol. 2010;49(7):829–33.
- Afshar M, Martinez A, Gallo R, Hata T. Induction and exacerbation of psoriasis with Interferon-alpha therapy for hepatitis C: a review and analysis of 36 cases. J Eur Acad Dermatol Venereol. 2013;27(6):771–8.
- Fattovich G, Giustina G, Favarato S, Ruol A. A survey of adverse events in 11 241 patients with chronic viral hepatitis treated with alfa interferon. J Hepatol. 1996;24(1):38–47.
- Seçkin D, Durusoy Ç, Şahin S. Concomitant vitiligo and psoriasis in a patient treated with interferon alfa-2a for chronic hepatitis B infection. Pediatr Dermatol. 2004;21(5):577–9.
- Gilliet M, Lande R. Antimicrobial peptides and self-DNA in autoimmune skin inflammation. Curr Opin Immunol. 2008;20(4):401–7.
- Bertolotti A, Boniface K, Vergier B, Mossalayi D, Taieb A, Ezzedine K, et al. Type I interferon signature in the initiation of the immune response in vitiligo. Pigment Cell Melanoma Res. 2014;27(3):398–407.
- Damsky W, King BA. JAK inhibitors in dermatology: the promise of a new drug class. J Am Acad Dermatol. 2017;76(4):736–44.
- Kuo CM, Tung TH, Wang SH, Chi CC. Efficacy and safety of tofacitinib for moderate-to-severe plaque psoriasis: a systematic review and meta-analysis of randomized controlled trials. J Eur Acad Dermatol Venereol. 2018;32(3):355–62.
- Malerba M, Damiani G, Radaeli A, Ragnoli B, Olivini A, Calzavara-Pinton P. Narrowband ultraviolet B phototherapy in psoriasis reduces proinflammatory cytokine levels and improves vitiligo and neutrophilic asthma. Br J Dermatol. 2015;173(6):1544–5.