Association of psoriasis with asthma: A systematic review and meta-analysis of observational studies

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Abstract

Background: Psoriasis is a chronic inflammatory skin disease that has been associated with various inflammatory comorbidities such as cardiovascular disease and uveitis. Asthma involves inflammation of the airway. The two diseases share cytokine-mediated inflammatory mechanisms. Objectives: The main objective of the study was to examine the association of psoriasis with asthma. Methods: We conducted a systematic review and meta-analysis of observational studies that examined the association of psoriasis with asthma. We searched MEDLINE, Embase, and CENTRAL from inception to May 2, 2019 for relevant case–control, cross-sectional, or cohort studies. The risk of bias of included studies was assessed by using the Newcastle–Ottawa Scale. The random-effects model meta-analysis was used to calculate the odds ratio (OR) for case–control/cross-sectional studies and hazard ratio (HR) for cohort studies. Results: We included six case–control/cross-sectional (one case–control and five cross-sectional studies) and one cohort studies. Three studies were rated with a high risk of bias in case definition, representativeness of the cases, selection of controls, definition of controls, and ascertainment of exposure. Psoriasis was associated with significantly increased odds (OR 1.29; 95% confidence interval [CI] 1.20–1.37) and risk (HR 1.38; 95% CI 1.23–1.54) for asthma. A subgroup analysis revealed increased odds for asthma in both pediatric and adult patients with psoriasis (pooled OR being 1.24 [95% CI 1.10–1.41] and OR 1.38 [95% CI 1.27–1.50], respectively). Conclusion: The current evidence indicates a significant association of psoriasis with asthma. When psoriasis patients present with respiratory symptoms for shortness of breath, wheezing, and chest tightness, referral to pulmonologist may be considered.

Keywords: Asthma, meta-analysis, psoriasis, systematic review

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Psoriasis is no longer considered just a skin disease. Recent studies have demonstrated that psoriasis which has been associated with various inflammatory and immunologic comorbidities such as cardiovascular disease,[9] chronic kidney disease,[10] uveitis,[10] thyroid diseases,[11] inflammatory bowel disease,[12] vitiligo,[13] and multiple sclerosis.[14]

Asthma is a worldwide public health problem associated with chronic inflammation of the airways and characterized with airway hyperresponsiveness.[15] Both psoriasis and asthma have shared inflammatory cytokine-mediated mechanisms.[16] In addition, involvement of T-helper 17 (Th17) cells and Th17-associated cytokines, such as interleukin (IL)-17A and IL-17 receptor A, has been proposed as the common pathway in both psoriasis and asthma.[18][17][18] Psoriasis is a prototypic Th17-mediated disease with skin-infiltrating Th17 cells as the central players in the pathogenesis of psoriasis.[19] One previous Scottish population-based cross-sectional study found an increased prevalence of psoriasis in patients with asthma.[20]

The objective of this study was to examine whether psoriasis is associated with asthma.

**Materials and Methods**

**Literature search**

We conducted a systematic search of MEDLINE, Embase, and Cochrane Central Register of Controlled Trials from inception to May 2, 2019 for relevant studies. The search strategy is shown in Table 1. No language limitations were imposed. Case–control, cross-sectional, and cohort studies that examined the association of psoriasis with asthma were eligible for inclusion.

**Study selection**

Our inclusion criteria were: (1) study design being case–control, cross-sectional, or cohort study; (2) the case/exposure group comprised people diagnosed with psoriasis and the control group comprised individuals without psoriasis; and (3) the outcomes of interest was the odds of prevalent asthma or the risk of incident asthma. Two authors scanned the titles and abstracts of the search results and selected potentially eligible studies. We examined the full text to determine whether a study met our inclusion criteria. We excluded studies that employed the same data source or did not provide usable data for assessing the association of psoriasis with asthma. Disagreement was resolved by discussion.

**Data extraction**

For each included study, we extracted the following data determined *a priori*: first author, publication year, country, study design, case/exposure group, control group, characteristics of study participants (including age), and measures of association.

**Risk of bias assessment**

The risk of bias was assessed by using the Newcastle–Ottawa Scale (NOS).[21] The NOS applies three domains (selection of study groups, comparability, and outcome assessment) to evaluate the risk of bias of observational studies.

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**Table 1: Search strategy**

| MEDLINE search strategy |
|-------------------------|
| 1. exp Psoriasis/ |
| 2. psoriasis.mp |
| 3. 1 or 2 |
| 4. exp Asthma/ |
| 5. asthma.mp |
| 6. 4 or 5 |
| 7. 3 and 6 |

**CENTRAL search strategy**

#1. MeSH descriptor: [Psoriasis] explode all trees
#2. Psoriasis:ti, ab, kw (Word variations have been searched)
#3. #1 or #2
#4. MeSH descriptor: [Asthma] explode all trees
#5. Asthma: ti, ab, kw (Word variations have been searched)
#6. #4 or #5
#7. #3 and #6

**Embase search strategy**

#1. psoriasis:ti
#2. psoriatic:ti
#3. #1 or #2
#4. asthma*
#5. #3 and #4

**CENTRAL: Cochrane Central Register of Controlled Trials**

**Statistical analysis**

The association of psoriasis with asthma was expressed as odds ratio (OR) with 95% confidence interval (CI) in case–control and cross-sectional studies, and as hazard ratio (HR) with 95% CI in cohort studies. The Review Manager Version 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) was used for conducting meta-analysis. Using the inverse variance method, we performed a random-effects model meta-analysis because we expected considerable clinical heterogeneity.

We also performed subgroup analyses according to the severity of psoriasis and age groups of study participants, i.e., those with severe psoriasis versus mild psoriasis and below 18 years (pediatric group) versus equal or above 18 years (adult group). The $I^2$ statistic was calculated for assessing the statistical heterogeneity across the included studies. An $I^2$ value of ≥ 50% represents substantial heterogeneity.[22]

**Results**

**Characteristics of included studies**

As illustrated in Figure 1, 802 records were identified from our search and 2 records were obtained from other sources (1 from a relevant review and 1 provided by an author [CC]). After removing duplicates, 651 records were available for screening. We excluded 642 records that did not meet our inclusion criteria. We included six case–control/cross-sectional (one case–control and five cross-sectional studies) and one cohort studies, with six providing usable data for meta-analyses. Two studies used overlapped study subjects, with one using data from March 1995 to the end of 2008 of the National
Health Insurance Research Database\textsuperscript{[7]} and the other using data between January 1, 2006 and December 31, 2007 of the same database.\textsuperscript{[23]} Therefore, we excluded the latter study.\textsuperscript{[23]}

The characteristics of the included studies are summarized in Table 2. These studies were published between 2011 and 2017. The study subjects in five included studies were Caucasians,\textsuperscript{[1,24-27]} while the study subjects of the other two studies were Asian populations.\textsuperscript{[3,8]} Two included studies reported data on pediatric populations,\textsuperscript{[1,27]} and three studies provided data on adults.\textsuperscript{[24-26]} Three studies were rated with

| First author, year, country | Study design | Case/exposed group | Control group | Age of study subjects | Prevalence/incidence of asthma in case/exposed group (%) | Prevalence/incidence of asthma in control group (%) | Results |
|-----------------------------|--------------|--------------------|---------------|-----------------------|--------------------------------------------------------|-----------------------------------------------------|---------|
| Augustin, 2015, Germany      | Population-based cross-sectional study | 1313 children with psoriasis | 291,868 children without psoriasis | <18 years | 12.19 | 9.36 | Calculated OR (95% CI): 1.34 (1.14‒1.59) |
| Galili, 2017, Israel         | Population-based cross-sectional study | 3122 adolescents with psoriasis | 884,653 healthy adolescents | Between 16 and 18 years | 11.05 | 7.95 | All psoriasis: adjusted OR (95% CI): 1.18 (1.04–1.34) Mild psoriasis: adjusted OR (95% CI): 0.95 (0.79–1.15); Moderate-to-severe psoriasis: adjusted OR (95% CI): 1.83 (1.20–2.81) adjusted for age, sex, country of origin, socioeconomic status, and body mass index |
| Andersen, 2017, Denmark      | Population-based cross-sectional study | 24,505 patients with diagnosed psoriasis | 79,370 general population | ≥18 years | 2.80 | 2.00 | Calculated OR (95% CI): 1.41 (1.29–1.55) |
| Hajdarbegovic, 2013, Netherlands | Cross-sectional study | 133 patients with psoriasis | 147 patients with varicose veins but did not have psoriasis | All ages; mean age in the case: 49±15.5 years; control: 54±15.6 years | 9.80 | 9.50 | Adjusted OR (95% CI): 0.96 (0.43–2.15), after adjustment for age, sex, methotrexate use, and current smoking |
| Lonnberg, 2015, Denmark      | Population-based cross-sectional study | 1385 adults with psoriasis | 31,993 adults without psoriasis | 20-71 years | 10.90 | 8.50 | Adjusted OR (95% CI): 1.27 (1.06–1.54), after adjustment for sex, age, smoking, body mass index, and hospital-diagnosed chronic obstructive pulmonary disease |
| Tsai, 2011, Taiwan           | Population-based case-control study | 51,800 patients with psoriasis | 207,200 controls matched by age, gender, and urbanisation level of residential areas | Mean age 46±18.6 years | 1.66 | 1.35 | Calculated OR (95% CI): 1.24 (1.15-1.34) |
| Fang, 2015, Taiwan           | Retrospective population-based cohort study | 10,288 adults with psoriasis | 41,152 adults without psoriasis matched by sex, age (within 5 years), and index year | ≥20 years | 6.41/1000 person-years | 4.38/1000 person-years | HR (95% CI): 1.38 (1.23–1.54) after adjustment for age, sex, and comorbidities |

CI: Confidence interval, OR: Odds ratio, HR: Hazard ratio
a high risk of bias in case definition, representativeness of the cases, selection of controls, definition of controls, and ascertainment of exposure [Figure 2a]. The one included cohort study was rated low risk of bias for all domains except for “adequacy of follow-up” where no relevant descriptions were provided [Figure 2b]. Asthma was identified by the use of ICD codes in five studies\(^1,7,8,26,27\) and self-report in two studies.\(^{24,25}\)

**Association of psoriasis with asthma**

As illustrated in Table 2, the prevalence of asthma in the psoriasis group ranged from 1.66% to 12.19% while that of the control group was 1.35%–9.50%. Only one cohort study examined the risk of asthma and the incidence of asthma was 6.41/1000 person-years in the psoriasis group and 4.38/1000 person-years in the control group.\(^{[8]}\) As shown in Figure 3, all six included case–control and cross-sectional studies found that people with psoriasis were associated with significantly increased odds of asthma (pooled OR 1.29; 95% CI 1.20–1.37; studies = 6). The statistical heterogeneity was low (\(I^2 = 33\%\)). Consistently, the included cohort study showed an increased risk of asthma in people with psoriasis (HR 1.38; 95% CI 1.23–1.54; study = 1).\(^{[8]}\)

As illustrated in Figure 4, the subgroup analysis based on age groups found increased odds of asthma in both the pediatric (pooled OR 1.24; 95% CI 1.10–1.41; studies = 2) and adult populations (pooled OR 1.38; 95% CI 1.27–1.50; studies = 3). No significant difference between the pediatric and adult subgroups in the odds of asthma was found (\(P = 0.180\)).

**Discussion**

Our study found a significant association of psoriasis with asthma. Compared to nonpsoriatic controls, psoriasis patients had 1.29-fold odds for prevalent asthma and 1.38-fold risk for incident asthma. Our stratified analysis based on age found significantly increased odds for asthma in both pediatric and adult psoriasis patients, with no significant difference between the two age groups.

Two case–control studies examined the respective OR for asthma in patients with mild and moderate-to-severe psoriasis.\(^7,27\) The Galili et al. 2017 study did not report the methods of classifying severity of psoriasis,\(^{27}\) while the Tsai et al. 2011 study employed treatment pattern to
identify the severity of psoriasis. Therefore, we did not perform a meta-analysis based on the severity of psoriasis as the stratified data from the two studies might have not been comparable.

The exact mechanism of association of psoriasis with asthma is unclear but may be related to chronic inflammation. Pro-inflammatory cytokines, for example, IL-17 are released from active psoriatic plaques through the bloodstream and trigger inflammation of other organs. The “psoriatic march” has been proposed to explain the association of psoriasis and cardiovascular comorbidities driven by systemic inflammation. The same mechanism may be applied to the respiratory comorbidities of psoriasis, including asthma found in this study. Genetic factors may be another explanation for the association between psoriasis and asthma. A previous twin study indicated that the association between psoriasis and asthma may be explained in part by a shared genetic factor between the two diseases.

There has been one similar systematic review that examined the association between psoriasis and asthma by Wang et al. Both the studies of ours and Wang et al. found a significant association of psoriasis with asthma. However, our study has the following strengths compared to the study by Wang et al. First, we excluded the study by Yang et al. because they used data overlapped with another study. Therefore, our study avoids double counting of the same data and resultant overestimation of the association between psoriasis and asthma. Second, we reclassified the study of Tsai et al. as a case–control study after reading its full text. We recalculated the OR values and improved the accuracy of effect estimates on the association of psoriasis with asthma. Third, we included one new study and conducted a updated meta-analysis on the association of psoriasis with asthma.

**CONCLUSION**

The current evidence indicates a significant association of psoriasis with asthma. Patients with psoriasis should be educated of potentially comorbid asthma. When psoriasis patients present with respiratory symptoms for example shortness of breath, wheezing, and chest tightness, referred to pulmonologist may be considered. On the other hand, further studies that provide specific data for groups of different ages, genders, or population are needed to clarify which subgroups of patients with psoriasis have an increased risk of asthma. Furthermore, additional prospective cohort studies are required to evaluate the causal relationship between psoriasis and asthma.

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**Conflicts of interest**

There are no conflicts of interest.

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