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Association of psoriasis with allergic multimorbidity of asthma, rhinitis, and eczema among adolescents: a cross-sectional study

Ali H. Ziyab^{1*} , Yaser Ali², Dina Zein³, Manal Al-Kandari¹, John W. Holloway⁴ and Wilfried Karmaus⁵

Abstract

Background Associations between psoriasis and allergic diseases (asthma, rhinitis, and eczema) in children have been reported in a limited number of studies, and the association between psoriasis and multimorbidity (co-occurrence) of allergic diseases remains unclear. Hence, this study aimed to assess the association between psoriasis and the co-occurrence of asthma, rhinitis, and eczema in adolescents.

Methods This school-based cross-sectional study enrolled adolescents ($n=3,864$) aged 11–14 years. Parents completed a questionnaire on doctor-diagnosed psoriasis as well as symptoms and clinical history of asthma, rhinitis, and eczema. Eight nonoverlapping groups comprising single and co-occurring current (past 12 months) asthma, rhinitis, and eczema were identified. A multinomial logistic regression model was used to estimate the adjusted odds ratios (aOR) and 95% confidence intervals (CI).

Results In the analytical sample ($n=3,710$; 1,641 male and 2,069 female participants), 3.5% reported doctor-diagnosed psoriasis, and 15.7%, 15.0%, and 10.3% had current asthma, rhinitis, and eczema symptoms, respectively. Doctor-diagnosed psoriasis was associated with “asthma only” (aOR = 2.11, 95% CI: 1.15–3.89), “eczema only” (6.65, 4.11–10.74), “asthma + eczema” (5.25, 2.36–11.65), “rhinitis + eczema” (3.60, 1.07–12.15), and “asthma + rhinitis + eczema” (7.38, 2.93–18.58). Doctor-diagnosed psoriasis was not statistically significantly associated with “rhinitis only” (1.42, 0.71–2.84) and “asthma + rhinitis” (1.78, 0.69–4.56).

Conclusion Our findings indicate that psoriasis is associated with the co-occurrence of allergic diseases among adolescents. However, further studies are required to investigate which biological mechanisms may be shared between psoriasis and allergic diseases.

Keywords Psoriasis, Eczema, Asthma, Rhinitis, Multimorbidity, Adolescents

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Introduction

Psoriasis is a chronic, immune-mediated inflammatory skin disease that affects over 60 million people worldwide, with varying prevalence estimates across regions [1]. The systemic impact of psoriasis-related inflammation causes long-term damage to multiple tissues and organs [2]. Patients with psoriasis may present different comorbidities, including psoriatic arthritis, metabolic syndrome (obesity, hypertension, type 2 diabetes, and dyslipidemia), cardiovascular disease (stroke and myocardial infarction), chronic obstructive pulmonary disease, chronic kidney disease, and inflammatory bowel disease [1, 2]. In addition, mental disorders, including depression and anxiety, have been reported as common comorbidities in patients with psoriasis [1, 2]. Hence, psoriasis impairs the physical and psychosocial well-being of affected individuals.

Although the pathophysiology of psoriasis remains unclear, cross-talk between innate and adaptive immune systems underlies the inflammatory infiltrate observed in psoriasis [3]. Activated myeloid dendritic cells release interleukin-12 (IL-12) and IL-23, which induce the proliferation of T-helper type 1 (Th1), Th17, and Th22 cells that subsequently produce pro-inflammatory cytokines (e.g., IL-17, IL-122, interferon gamma [IFN- γ], and tumor necrosis factor-alpha [TNF- α]) that characterize psoriasis, with the IL-23/Th17 pathway being the most predominant [2]. In contrast, allergic diseases, such as asthma, rhinitis, and eczema (atopic dermatitis), mainly involve skewed Th2-cells response to foreign bodies (allergens), which can lead to over-expression of IL-4 and IL-13, and subsequently increased production of immunoglobulin E, thereby causing an allergic reaction [4]. Although up-regulation of Th1 cells has been hypothesized to correlate with down-regulation of Th2 cells and vice versa, this paradigm has been challenged as the coexistence of autoimmune diseases caused by Th1 immune responses and allergic diseases caused by Th2 immune responses is not rare [5, 6]. Furthermore, genetic studies on allergic and autoimmune diseases have demonstrated considerable commonality in susceptibility loci [7], especially between eczema and psoriasis as inflammatory diseases of the skin [8], while others have reported opposing genetic susceptibility at the same loci [9].

The association between psoriasis and allergic diseases has been assessed in a limited number of studies. Majority of the studies that have assessed the association between psoriasis and allergic diseases have reported positive associations and suggested that psoriasis and allergic diseases have a common pathogenesis [10–15], while few reports found no or inverse association between psoriasis and allergic diseases [16, 17]. Given that the multimorbidity (co-occurrence) of allergic disease is not rare [18], the association between psoriasis

and multimorbidity of allergic diseases requires further investigations. Hence, we aimed to evaluate the association of psoriasis with asthma, rhinitis, and eczema both as single and co-occurring conditions in adolescents.

Methods

Study design, setting, and population

This school-based cross-sectional study enrolled adolescents ($n=3,864$) aged 11–14 years resident in Kuwait. As previously described [19], a representative sample of middle school students attending public schools was obtained using stratified two-stage cluster sampling. The study questionnaire was sent home with the adolescents for parental/guardian completion and return. Ethical approval for the current study was obtained from the Standing Committee for the Coordination of Health and Medical Research, Ministry of Health, Kuwait (No. 2016/451). Written informed consent was obtained from the parents or legal guardians of the adolescents participating in this study, which was conducted following the principles and guidelines of the Declaration of Helsinki for medical research involving human participants.

Ascertainment of study variables

Ever doctor-diagnosed psoriasis was determined by an affirmative response by the parent/guardian to the following question: “Has this child ever been diagnosed with psoriasis by a doctor?” [20]. The International Study of Asthma and Allergies in Childhood (ISAAC) methodology was applied to ascertain allergic diseases [21]. Current (past 12 months) eczema was defined as “ever doctor-diagnosed eczema” and/or “having ever had a recurrent itchy rash for at least 6 months” plus “having an itchy rash at any time in the past 12 months that affected the folds of the elbows or the areas behind the knees, in front of the ankles, under the buttocks, or around the neck, ears, or eyes” [22, 23]. Current asthma was defined by an affirmative response to the items “history of physician-diagnosed asthma” and “wheezing in the past 12 months” and/or “asthma treatment in the past 12 months” [19, 24]. Current rhinitis was defined as “ever doctor-diagnosed rhinitis” and “having problems with a sneezing, runny, or blocked nose in the absence of a cold or flu in the past 12 months” [25]. Combinations of current asthma, rhinitis, and eczema resulted in eight nonoverlapping groups of single and coexisting allergic diseases: “no allergic disease,” “asthma only,” “rhinitis only,” “eczema only,” “asthma+rhinitis,” “asthma+eczema,” “rhinitis+eczema,” and “asthma+rhinitis+eczema” groups.

Covariates

The parent/guardian reported the mode of participant birth (vaginal or cesarean section) and whether

the participant was ever directly fed at the breast during infancy. Household exposure to secondhand smoke was assessed by asking whether any household member smoked cigarettes or tobacco-related products inside the

home. To ascertain exposure to household cats and dogs during infancy, two separate questions were asked: “Did you have a cat/dog in your home during the first year of this child life?”

Table 1 Characteristics of the total study sample and the analytical study sample

Variables	Total study sample (n = 3864)	Analytical study sample* (n = 3710)
Sex, n (%)		
Male	1695 (43.9)	1641 (44.2)
Female	2169 (56.1)	2069 (55.8)
Age (years), n (%)		
≤ 11	1065 (27.6)	1026 (27.6)
12	1170 (30.3)	1125 (30.3)
13	964 (24.9)	919 (24.8)
≥ 14	665 (17.2)	640 (17.3)
BMI-for-age groups, n (%)		
Thinness (< -2 SD)	219 (5.8)	209 (5.8)
Normal (-2 to 1 SD)	1517 (40.1)	1457 (40.1)
Overweight (> 1 to 2 SD)	961 (25.3)	921 (25.3)
Obese (> 2 SD)	1089 (28.8)	1048 (28.8)
Missing, n	78	75
Mode of birth, n (%)		
Vaginal	3106 (81.8)	2998 (81.7)
Cesarean section	692 (18.2)	673 (18.3)
Missing, n	66	39
Breastfeeding ever, n (%)		
Yes	2894 (76.3)	2796 (76.3)
Missing, n	72	45
Secondhand smoke exposure, n (%)		
Yes	1755 (45.8)	1694 (45.8)
Missing, n	28	8
Cat exposure in infancy, n (%)		
Yes	232 (6.1)	224 (6.1)
Missing, n	35	15
Dog exposure in infancy, n (%)		
Yes	85 (2.2)	84 (2.3)
Missing, n	32	10
Ever doctor-diagnosed psoriasis		
Yes	136 (3.6)	131 (3.5)
Missing, n	58	0
Current eczema, n (%)		
Yes	388 (10.2)	381 (10.3)
Missing, n	73	0
Current asthma, n (%)		
Yes	600 (15.7)	581 (15.7)
Missing, n	35	0
Current rhinitis, n (%)		
Yes	566 (15.1)	558 (15.0)
Missing, n	105	0

BMI: body mass index; SD: standard deviation

* Refers to the sample of participants with complete information on psoriasis status, current eczema status, current, asthma status, and current rhinitis status

Statistical analysis

Analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC, USA). The statistical significance level was set at $\alpha=0.05$. Descriptive analyses were performed to calculate frequencies and proportions of categorical variables. Chi-square (X^2) test was used to assess associations between categorical variables. The association between psoriasis status (exposure variable) and allergic diseases (outcome variable) was assessed using: (i) binary logistic regression when evaluating the association with each allergic disease (non-mutually exclusive), and (ii) multinomial logistic regression when evaluating the association with the single/co-occurring allergic disease(s) [mutually exclusive; nominal outcome variable, with the “no allergic disease” category set as the reference]. Adjusted odds ratios (aOR) and their 95% confidence intervals (CI) were estimated. In addition to age and sex, individual characteristics that demonstrated possible association (p -value < 0.2) with psoriasis were included in the multivariable models as potential confounders.

Results

A total of 5,228 schoolchildren (2,483 male and 2,745 female adolescents) were invited to participate, of whom 3,864 (1,695 male and 2,169 female adolescents) agreed to participate (response proportion: 73.9%). The analytical sample ($n=3,710$; restricted to participants with complete information on ever doctor-diagnosed psoriasis, current asthma, rhinitis, and eczema) and the total study sample ($n=3,864$) were similar regarding the studied characteristics (Table 1). Of the total analytical sample, 3.5% of the adolescents reported having doctor-diagnosed psoriasis. The prevalence of current (past 12 months) asthma, rhinitis, and eczema were estimated to be 15.7%, 15.0, and 10.3%, respectively (Table 1).

Table 2 shows the prevalence of ever doctor-diagnosed psoriasis according to individual characteristics. The prevalence of psoriasis was similar in male and female participants (3.4% vs. 3.7%, $p=0.598$). The prevalence of ever doctor-diagnosed psoriasis was higher among adolescents who were exposed to secondhand smoke in their households than among those who were not exposed (4.3% vs. 2.9%, $p=0.019$). Similarly, having cats during infancy was associated with an increased prevalence of ever doctor-diagnosed psoriasis (7.6% vs. 3.3%, $p<0.001$). Breastfed during infancy was associated with a lower prevalence of ever doctor-diagnosed psoriasis compared with those who were never breastfed (3.1% vs. 4.8%, $p=0.014$).

Table 2 Prevalence of ever-doctor diagnosed psoriasis according to individual characteristics

Variables	n	Ever doctor-diagnosed psoriasis, % (n)	P-value*
Sex			
Male	1641	3.4 (55)	0.598
Female	2069	3.7 (76)	
Age (years)			
≤ 11	1026	3.7 (38)	0.245
12	1125	2.7 (30)	
13	919	4.2 (39)	
≥ 14	640	3.8 (24)	
BMI-for-age groups			
Thinness (< -2 SD)	209	6.2 (13)	0.145
Normal (-2 to 1 SD)	1457	3.4 (50)	
Overweight (> 1 to 2 SD)	921	3.9 (36)	
Obese (> 2 SD)	1048	3.1 (32)	
Mode of birth			
Vaginal	2998	3.6 (107)	0.848
Cesarean section	673	3.4 (23)	
Breastfeeding ever			
Yes	2796	3.1 (86)	0.014
No	869	4.8 (42)	
Secondhand smoke exposure			
Yes	1694	4.3 (73)	0.019
No	2008	2.9 (58)	
Cat exposure in infancy			
Yes	224	7.6 (17)	<0.001
No	3471	3.3 (114)	
Dog exposure in infancy			
Yes	84	6.0 (5)	0.226
No	3616	3.5 (126)	

BMI: body mass index; SD: standard deviation

* Calculated using chi-square (χ^2) test**Table 3** Adjusted associations between ever doctor-diagnosed psoriasis and allergic diseases

Allergic disease	Ever doctor-diagnosed psoriasis		aOR [‡] (95% CI)	P-value
	Yes (n = 131)	No (n = 3579)		
Asthma	26.0 (34)	15.3 (547)	1.93 (1.28–2.91)	0.002
Rhinitis	18.3 (24)	14.9 (534)	1.31 (0.83–2.07)	0.253
Eczema	36.6 (48)	9.3 (333)	5.36 (3.68–7.82)	<0.001

aOR: Adjusted odds ratio; CI: Confidence interval

[‡] Adjusted for sex, age, BMI-for-age groups, breastfeeding, secondhand smoke exposure, and cat exposure in infancy**Table 4** Adjusted associations between ever doctor-diagnosed psoriasis and single and co-occurring allergic diseases

Allergic disease	Ever doctor-diagnosed psoriasis			aOR [‡] (95% CI)	P-value
	Total (n = 3710)	Yes (n = 131)	No (n = 3579)		
None	68.1 (2526)	40.5 (53)	69.1 (2473)	1.00 (Reference)	–
Asthma only	8.9 (328)	11.5 (15)	8.8 (313)	2.11 (1.15–3.89)	0.016
Rhinitis only	9.0 (334)	7.6 (10)	9.1 (324)	1.42 (0.71–2.84)	0.316
Eczema only	6.1 (227)	23.7 (31)	5.5 (196)	6.65 (4.11–10.74)	<0.001
Asthma + Rhinitis	3.8 (141)	3.8 (5)	3.8 (136)	1.78 (0.69–4.56)	0.232
Asthma + Eczema	1.9 (71)	6.1 (8)	1.8 (63)	5.25 (2.36–11.65)	<0.001
Rhinitis + Eczema	1.1 (42)	2.3 (3)	1.1 (39)	3.60 (1.07–12.15)	0.039
Asthma + Rhinitis + Eczema	1.1 (41)	4.6 (6)	1.0 (35)	7.38 (2.93–18.58)	<0.001

aOR: Adjusted odds ratio; CI: Confidence interval

[‡] Adjusted for sex, age, BMI-for-age groups, breastfeeding, secondhand smoke exposure, and cat exposure in infancy

Associations between ever doctor-diagnosed psoriasis and non-mutually exclusive occurrence of current asthma, rhinitis, and eczema are shown in Table 3. Ever doctor-diagnosed psoriasis was associated with increased prevalence of current asthma (aOR=1.93, 95% CI: 1.28–2.91) and current eczema (aOR=5.36, 95% CI: 3.68–7.82), but not current rhinitis (aOR=1.31, 95% CI: 0.83–2.07; Table 3).

Associations between ever doctor-diagnosed psoriasis and single and co-occurring allergic diseases are shown in Table 4. The prevalence of “asthma only” (aOR=2.11, 95% CI: 1.15–3.89) and “eczema only” (aOR=6.65, 95% CI: 4.11–10.74), but not the prevalence of “rhinitis only” (aOR=1.42, 95% CI: 0.71–2.84), was increased in children with ever doctor-diagnosed psoriasis compared to those without prior diagnosis of psoriasis. Moreover, ever doctor-diagnosed psoriasis was associated with the co-occurrence of “asthma+eczema” (aOR=5.25, 95% CI: 2.36–11.65), “rhinitis+eczema” (aOR=3.60, 95% CI: 1.07–12.15), and “asthma+rhinitis+eczema” (aOR=7.38, 95% CI: 2.93–18.58; Table 4).

Discussion

In this study, we demonstrated that doctor-diagnosed psoriasis was associated with an increased prevalence of current asthma and eczema, but not with rhinitis. Moreover, when assessing the mutually exclusive occurrence (nonoverlapping groups) of allergic diseases, psoriasis was associated with “asthma only” and “eczema only,” and the co-occurrence of “asthma+eczema,” “rhinitis+eczema,” and “asthma+rhinitis+eczema”. These findings suggest that the association between psoriasis and asthma is not dependent on the coexistence of other allergic diseases (i.e., eczema and rhinitis). Moreover, we demonstrated that psoriasis increased the odds of co-occurring allergic diseases.

In agreement with our findings, previous studies have found associations between psoriasis and asthma [10–14, 26]. Moreover, the association observed between psoriasis and eczema is supported by previous reports, as summarized in a meta-analysis [27]. To the best of our knowledge, only two prior studies have investigated such associations among children and reported increased odds of asthma [13, 15] and eczema [15] in relation to psoriasis. Although we observed an increased odds of rhinitis in relation to psoriasis (aOR=1.31, 95% CI: 0.83–2.07), this association was not statistically significant, contradicting previous findings that observed increased risk of rhinitis related to psoriasis in children [13, 15]. Our analysis adds to the literature by investigating associations between psoriasis and the coexistence of asthma, rhinitis, and eczema. This investigation showed that psoriasis was associated with increased odds of single and co-occurrence of allergic diseases, with the odds of the co-occurrence of “asthma, rhinitis, and eczema” being noticeably increased. Hence, our findings suggest that psoriasis and allergic diseases are not mutually exclusive and may share certain biological mechanisms.

Classically, psoriasis and allergic diseases are considered Th1- and Th2-driven diseases, respectively. Nonetheless, the role of the IL-23/Th17 pathway leading to IL-17 secretion has emerged as dominant in the pathophysiology of psoriasis [1, 2]. Moreover, a recent study has shown that a group of patients with asthma had high IL-17 levels and demonstrated psoriasis-like immunophenotypic features [28]. A study using murine models has shown that psoriatic inflammation enhanced airway inflammation through the IL-23/Th17 axis [29]. Similarly, IL-17 reportedly contributes to the immune dysregulation observed in patients with eczema [30]. Therefore, Th17-cell activation leading to IL-17 production could be a common link between psoriasis and allergic diseases. In addition, a genome-wide association study demonstrated overlapping loci between eczema, asthma, and psoriasis, further indicating a shared genetic background [8].

Moreover, in terms of risk factors, genetic predisposition is the major contributor to the development of psoriasis, with few environmental and behavioral/lifestyle factors being implicated in the etiology of psoriasis [31, 32]. Alcohol use, smoking, and obesity have been shown to be risk factors for psoriasis [33–35]. To investigate possible causal effects of the identified risk factors, Mendelian Randomization studies have reported potential causal effects of smoking and obesity on psoriasis, but not alcohol consumption [36–38]. Similarly, smoking and obesity have been shown to be risk factors for the development of allergic diseases [39–41]. Moreover, breastfeeding has been shown to be associated with allergic diseases [42, 43], and more recently few studies have reported the association between breastfeeding and psoriasis [20, 44]. Collectively, the aforementioned factors have been speculated to alter immune development and responses, hence altering the risk of immune mediated diseases such as psoriasis and allergic diseases.

The population-based design (capturing the spectrum of diseases) and large sample size are the strengths of our study. Although the reliability (Cohen’s kappa: 0.7558) [45] and validity (sensitivity: 56%; specificity: 99%; positive predictive value: 78%; negative predictive value: 96%) [46] of self-reported psoriasis diagnoses are reportedly high, misclassification of the disease status cannot be eliminated, which can bias the estimated measures of association. Our assessment focused on doctor-diagnosed psoriasis reported by parent/guardian. A prior study showed that the inclusion of “self-reported doctor-diagnosed psoriasis” compared to only “self-reported psoriasis” yielded increased validity [46]. Moreover, we have previously shown that the majority of individuals who reported a doctor-diagnosed psoriasis in our study sample have reported the involvement of typical psoriasis anatomical sites (scalp [47.6%], and extensor surfaces of the knees [50%] and elbows [38.1%]) [20], which further supports the validity of our definition of psoriasis. Similarly, the misclassification of asthma, rhinitis, and eczema symptoms cannot be excluded. Nonetheless, we have used the standardized ISAAC questionnaire to ascertain allergic diseases, which has been shown to have good validity [21]. For instance, a prior study showed that the ISAAC criteria for ascertaining asthma symptoms as compared to physician diagnosis of asthma had a sensitivity of 85% and specificity of 81% [47]. Similarly, among children in the UK, using GP-recorded asthma as the gold standard, parental-reported ever doctor-diagnosed asthma had a sensitivity of 88.5% and a specificity of 95.7% [48]. Moreover, prior studies that defined asthma in a similar manner to our “current asthma” variable showed that their defined asthma to be associated with reduced lung function parameters [24, 49]. Compared to prior studies that defined asthma in a similar manner

to our study, the estimated prevalence of current asthma (15.7%) in this report is similar to the prevalence estimate of current asthma (16.1%) in a preceding study conducted among adolescents aged in 16–19 years in Kuwait [50], and comparable to current asthma prevalence estimate among 18-year old Isle of Wight birth cohort participants (17.7%) in the UK [51]. Such observations further support the used asthma definition. Furthermore, given that the magnitude and direction of the estimated measures of association (ORs) in our study are similar to that in previous studies [10, 13–15, 26], we speculate that the effect of misclassification, if any, should be minimal on our results. It is essential to also indicate that our reported cross-sectional (concurrent) associations do not implicate any causal associations.

Conclusions

This study demonstrated associations between psoriasis and the single- and co-occurrence of allergic diseases in a sample of adolescents, and these findings add new knowledge into the limited literature in this area. Such associations further suggest that the coexistence of psoriasis and allergic diseases is not rare, and the paradigm of their nonoverlapping existence requires reexamination. Further studies are needed to investigate the biological mechanisms and genetic polymorphisms shared by psoriasis and allergic diseases that may result in their coexistence. The elucidation of these mechanisms may improve the clinical management of patients with coexisting psoriasis and allergic diseases.

Abbreviations

IL	interleukin
Th	T-helper type cells
IFN- γ	interferon gamma
TNF- α	tumor necrosis factor-alpha
aOR	adjusted odds ratio
CI	confidence interval

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Author contributions

AHZ conceived, designed, and planned the study, obtained funding, supervised the research conduct, analyzed and interpreted the data, and drafted the manuscript. YA, DZ, MA, JWH, and WK contributed to the study conception, design and planning, contributed to data interpretation, and critically revised the manuscript. All authors critically revised the manuscript for important intellectual content. The manuscript has been read and approved by all authors.

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Data availability

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Ethical approval for the current study was obtained from the Standing Committee for the Coordination of Health and Medical Research, Ministry of Health, Kuwait (No. 2016/451). Written informed consent was obtained from the parents or legal guardians of the adolescents participating in this study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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