Psoriasis Among Adolescents in Kuwait and the Role of Siblings, Breastfeeding, and Household Cat and Secondhand Smoke Exposure: A Cross-Sectional Study

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ABSTRACT

Introduction: Globally, the epidemiology of psoriasis is poorly understood, and most countries lack essential epidemiologic data regarding disease burden and its determinants. This study sought to estimate the prevalence of psoriasis among adolescents in Kuwait and assess its association with different risk factors, including obesity, sibship size, breastfeeding, and exposure to household secondhand smoke (SHS) and pets.

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Methods: Schoolchildren aged 11–14 years ($n = 3864$) were enrolled in a cross-sectional study. Lifetime and current (past 12 months) prevalence of psoriasis were ascertained according to ever having a history of doctor-diagnosis plus current active lesion(s) and/or current use of treatment of psoriasis. Associations were assessed using Poisson regression with robust variance estimation, and adjusted prevalence ratios (aPR) and 95% confidence intervals (CI) were estimated.

Results: The lifetime and current prevalence of psoriasis were estimated to be 3.6% (136/3806) and 1.1% (42/3806), respectively. Commonly reported anatomical sites affected by psoriasis included scalp (47.6%) and the extensor surface of the knees (50%) and elbows (38.1%). Household SHS exposure was associated with increased lifetime psoriasis (aPR = 1.41, 95% CI 1.07–1.98), and showed a trend for association with current psoriasis (1.77, 0.89–3.53). Similarly, cat-keeping during infancy was associated with lifetime psoriasis (1.96, 1.14–3.37), and demonstrated a trend for association with current psoriasis (1.49, 0.52–1.98). In contrast, breastfeeding was associated with a decreased lifetime psoriasis (0.62, 0.44–0.89), but was not associated with current psoriasis. Trend analyses showed that the prevalence of lifetime and current psoriasis increased with increasing numbers of total, older, and younger siblings.

Conclusions: Psoriasis affects a considerable proportion of schoolchildren in Kuwait.

Interestingly, psoriasis prevalence was related to risk factors also found in allergic diseases, such as exposure to SHS, cat-keeping in infancy, breastfeeding, and sibship size, possibly suggesting a role of immune dysregulation.

Keywords: Adolescents; Breastfeeding; Epidemiology; Kuwait; Prevalence; Psoriasis; Risk factors; Secondhand smoke; Siblings

Key Summary Points

Why carry out this study?

Globally, the epidemiology of psoriasis is poorly understood, and most countries lack essential epidemiologic data regarding the disease burden and risk factors

This study sought to estimate the prevalence of psoriasis among adolescents in Kuwait and assess its association with different risk factors for the first time

What was learned from the study?

The findings of this study indicated that psoriasis is a common condition among adolescents in Kuwait, with lifetime and current prevalence estimates being 3.6% and 1.1%, respectively

Exposure to household secondhand smoke and cat-keeping during infancy and having siblings were associated with an increased psoriasis prevalence, whereas direct breastfeeding was linked with a decreased lifetime prevalence of psoriasis

These observed associations highlight the potential role of prenatal and postnatal exposures in psoriasis development

INTRODUCTION

Psoriasis is a chronic inflammatory skin disease that affects both children and adults. The main hallmarks of this disease are epidermal hyperproliferation (scaling) and systemic inflammation that lead to skin redness, itching, soreness, and bleeding [1, 2]. Psoriasis commonly affects the scalp, elbows, knees, trunk, buttocks, and genitals and may extend to the nails, palms, and soles of the feet [2, 3]. Although most patients suffer from a mild form of the disease, the physical, social, and psychological burden can be substantial because of visible disfiguration and associated disability [4]. Moreover, the clinical burden of psoriasis is increased by numerous comorbid diseases, such as psoriatic arthritis, cardiometabolic diseases, and psychological disorders (e.g., depression and anxiety) [5–7].

The dysregulation of innate and adaptive immune responses and their cross-talk underlie the pathogenesis of psoriasis [4, 8]. Although a full understanding of the etiology of psoriasis is lacking, a complex interplay among genetic, environmental, and immune factors is involved in the disease pathophysiology [9]. In genetically susceptible individuals, psoriasis may be triggered or aggravated by mild skin trauma (scratching, piercing, tattoos, sunburn, and chemical irritants), infections (streptococcal pharyngitis), and the use of medications (β-blockers, lithium, and nonsteroidal anti-inflammatory drugs) [2, 4, 9]. Other risk factors that have been linked to psoriasis development include smoking, exposure to secondhand smoke (SHS), alcohol consumption, emotional stress, and obesity [9–12].

Globally, psoriasis is estimated to affect 1–3% of the general population, and wide variations in the prevalence exist across different age groups (more common in adults than in children), geographical regions (more frequent in nations farther from the equator), and ethnicities (Caucasians are more susceptible) [13–15]. Population-based studies have shown that the prevalence estimates of psoriasis range from 0% (Taiwan) to 2.1% (Italy) among children and 0.5% (USA) to 11.4% (Norway) among adults [14, 15]. Time trend investigations indicate that the incidence and prevalence of psoriasis have increased over the past 3 to 4 decades [16–20]. Accordingly, the World Health Organization (WHO) has recently recognized

psoriasis as a major public health problem, and requested Member States to increase awareness of the disease and highlighted the need for further research [21].

Systematic reviews of the literature indicate that globally the epidemiology of psoriasis is poorly understood and up to 81% of countries worldwide lack essential epidemiologic data regarding the disease burden and risk factors [14, 15, 21–23]. Furthermore, most previous studies were conducted in Europe, North America, and Asia. Therefore, to narrow the geographic gaps in knowledge, this cross-sectional study is the first to estimate the prevalence of psoriasis among schoolchildren in Kuwait. Moreover, since psoriasis is an immune-mediated inflammatory disease, we sought to specifically assess associations of psoriasis with factors that have the potential to influence immune responses and maturation, such as obesity, sibship size, breastfeeding, and exposure to household SHS and pets.

METHODS

Study Setting, Design, and Participants

Geographically, Kuwait is divided into six governorates, and the school districts follow a similar geographic division. Education in Kuwait is mainly provided by free public schools funded by the state and, to a lesser extent, by private schools. The education system can be divided into four stages, namely kindergarten, elementary school (1st–5th grade), middle school (6th–9th grade), and high school (10th–12th grade); the last three stages are sex segregated. Schooling is compulsory in Kuwait for all children aged 6–14 years.

This cross-sectional study enrolled schoolchildren ($n = 3864$) attending public middle schools throughout the State of Kuwait, which mostly include individuals aged between 11 and 14 years. The schoolchildren were enrolled in the study during the 2016/2017 school year (September 2016 to May 2017) and the first semester of the 2017/2018 school year (September to December 2017). A stratified two-stage cluster sampling method was used to select a representative study sample of schoolchildren from a random sample of schools. The sampling methodology is described in detail elsewhere [24]. Ethical approval for the current study was obtained from the Standing Committee for Coordination of Health and Medical Research, Ministry of Health, Kuwait (no. 2016/451). The study was conducted in accordance with principles and guidelines of the Declaration of Helsinki for medical research involving human subjects. Written informed consent for each enrolled child was obtained from the parents or legal guardians.

Children were asked to take the study-specific questionnaires home for parental/guardian completion and return them to school. The questionnaires gathered information on demographic data, lifestyle factors, environmental exposures, and the health status of the children, including clinical history and symptoms of psoriasis.

Ascertainment of Psoriasis and Affected Body Areas

Parents were asked the following questions, which were used to ascertained psoriasis status:

1. Has this child ever been diagnosed with psoriasis by a doctor? If parents answered this question affirmatively, they were asked the following subset of questions:

    1.1 Has the child had active psoriasis lesion(s) in the past 12 months?
    1.2 Has the child used any treatments for his/her psoriasis at any time in the past 12 months? (Answer options: did not used any treatments, topical treatments, phototherapy, biologics, and other treatments.)

An affirmative response to "lifetime history of doctor-diagnosed psoriasis" (question 1) was used to define lifetime parent-reported doctor-diagnosed psoriasis. Current (past 12 months) parent-reported doctor-diagnosed psoriasis was ascertained by an affirmative response to the items: "lifetime history of doctor-diagnosed psoriasis" (question 1) and "current active

psoriasis lesion(s)" (question 1.1) and/or "current use of psoriasis treatment" (question 1.2). Moreover, anatomical sites (e.g., extensor surfaces of the elbows and knees) affected by psoriasis in the past 12 months were reported by parents. Also, parents were asked to report who diagnosed their child's psoriasis, with answer options including dermatologist, pediatrician, general practitioner, and other health care provider.

Ascertainment of Exposure and Covariate Variables

Information regarding exposures and covariates was obtained from questionnaires self-completed by the parents/guardians. Since body mass index (BMI), which is a measure of general adiposity, markedly changes in children with growth, we estimated the BMI-for-age z scores (standard deviation [SD] scores) using the WHO growth reference for those aged between 5 and 19 years [25]. The BMI-for-age score was categorized as follows: thin, < -2 SD; normal, -2 to 1 SD; overweight, > 1 to 2 SD; and obese, > 2 SD [25]. Exposure to secondhand smoke (SHS) was assessed by inquiring whether any member of the household smokes cigarettes or tobacco-related products inside the home. To ascertain exposure to household cats and dogs during infancy, the following two separate questions were asked: "Did you have a cat/dog in your home during the first year of this child's life?" The breastfeeding status was determined by asking whether the child was ever directly fed at the breast during infancy. The questionnaire also asked about the child's total number of siblings and number of older and younger siblings. To avoid potential confusion with eczema but also investigate the overlap, following the Hanifin and Rajka criteria [26], current 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 last 12 months that affected the folds of the elbows, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears, or eyes."

Statistical Analysis

All statistical analyses were conducted using SAS 9.4 (SAS Institute, Cary, North Carolina, USA). The statistical significance level was set to $\alpha = 0.05$ for all association analyses. Descriptive analyses were conducted to determine the frequencies and proportions of the categorical variables and the medians and 5th and 95th percentiles of the quantitative variables. To assess whether the analytical study sample ($n = 3806$; sample of participants with complete information on status of psoriasis) was representative of the total enrolled study sample ($n = 3864$), we compared proportions of categorical variables across these two samples using chi-square (χ^2) tests. The lifetime and current prevalence of parent-reported doctor-diagnosed psoriasis were estimated along with their binomial 95% confidence interval.

The number of total siblings was initially categorized into six groups (0, 1, 2, 3, 4, and ≥ 5); however, since only one child with no (zero) siblings had psoriasis (1/39; 2.6%), we combined the no siblings and one sibling groups (reported as: 0/1) to avoid small cell sizes in the statistical testing. Hence, the number of total siblings was analyzed in the following five groups: 0/1, 2, 3, 4, and ≥ 5. The numbers of older and younger siblings were analyzed using the following categories: 0, 1, 2, 3, and ≥ 4. Two analytical approaches were applied to assess the associations between the numbers of total, older, and younger siblings and psoriasis prevalence: the variables were treated as (1) categorical (0 or 0/1 siblings serving as the reference group) and (2) quantitative to infer the trends per additional sibling. Moreover, the statistical interaction between the numbers of older and younger siblings was evaluated on a multiplicative scale by including a product term (number of older siblings $\times$ number of younger siblings) in the regression model to test for the homogeneity of the effects on psoriasis.

Adjusted associations were assessed by applying a modified Poisson regression with robust variance estimation using the GENMOD procedure in SAS 9.4 to estimate and infer prevalence ratios (PR) and their 95% confidence intervals (CI) [27]. Associations of personal

attributes and risk factors with two outcome variables, i.e., lifetime and current parent-reported doctor-diagnosed psoriasis, were assessed. The following variables were simultaneously entered into the multivariable regression models: sex age, BMI-for-age, mode of birth, breastfeeding ever, current eczema, SHS exposure, cat exposure in infancy, dog exposures in infancy, and total number of siblings. Additionally, while assessing the association between the number of older siblings and psoriasis, the number of younger siblings was included as a covariate in the regression model, and vice versa.

RESULTS

Description of Study Sample

In total, 5228 schoolchildren (2483 male and 2745 female) were invited to participate, and 3864 schoolchildren (1695 male and 2169 female) were enrolled in the study (response proportion 73.9%). The analytical study sample ($n = 3806$; restricted to participants with information regarding psoriasis status) and total study sample ($n = 3864$) were similar in all characteristics investigated (Table 1). The median (5th, 95th percentile) age of the study participants was 12.0 (11.0, 14.0) years. The BMI-for-age groups indicated that 25.3% (946/3729) and 28.8% (1072/2729) of the schoolchildren were overweight and obese, respectively. In total, 2863 (76.3%) children were reported to have ever been directly breastfed during infancy. The prevalence of current eczema was estimated to be 10.2% (385/3761; Table 1).

Lifetime and Current Prevalence of Psoriasis

The lifetime prevalence of parent-reported doctor-diagnosed psoriasis in the total study sample was estimated to be 3.6% (136/3806, 95% CI 3.0–4.2), with no difference between male (3.3%, 55/1672) and female subjects (3.8%, 81/2134, $P = 0.404$; Fig. 1). The estimated current prevalence of parent-reported

doctor-diagnosed psoriasis was 1.1% (42/3806, 95% CI 0.8–1.5), with a slightly higher estimate in female (1.4%, 29/2134) than in male subjects (0.8%, 13/1672, $P = 0.088$; Fig. 1).

Body Areas Affected by Psoriasis

Figure 2 shows the reported body areas affected by psoriasis lesions among subjects with current parent-reported doctor-diagnosed psoriasis ($n = 42$). The most frequently reported affected body areas were the extensor surface of the knees (50.0%), scalp (47.6%), extensor surface of the elbows (38.1%), lower leg (33.3%), buttocks (31.0%), and hands (31.0%; Fig. 2).

Factors Associated with Lifetime and Current Psoriasis

Associations of personal characteristics and risk factors with lifetime and current prevalence of parent-reported doctor-diagnosed psoriasis are presented in Table 2. The lifetime prevalence of psoriasis was similar in female and male subjects (aPR = 0.92, 95% CI 0.65–1.30), whereas the current prevalence of psoriasis was higher, though not statistically significant, in female compared to male subjects (aPR = 1.24, 95% CI 0.64–2.42). Although older subjects had increased current psoriasis prevalence compared to younger subjects (age ≥ 14 vs. ≤ 11: aPR = 1.53, 95% CI 0.60–3.88), this difference was not statistically significant. Overweight and obesity were not associated with lifetime or current psoriasis prevalence; however, subjects in the thin BMI-for-age group exhibited statistically non-significant elevated prevalence of lifetime (aPR = 1.47, 95% CI 0.79–2.73) and current (aPR = 2.16, 95% CI 0.75–6.25; Table 2) psoriasis compared to the normal weight group. Current eczema was strongly associated with both lifetime (aPR = 4.86, 95% CI 3.40–6.96) and current (aPR = 4.27, 95% CI 2.10–8.69) psoriasis prevalence. Exposure to household SHS was positively associated with lifetime psoriasis prevalence (aPR = 1.41, 95% CI 1.07–1.98) and showed a trend for association with current psoriasis prevalence (aPR = 1.77, 95% CI 0.89–3.53). Similarly, having cats during

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

Variables	Total study sample ($n = 3864$)	Analytical study sample ($n = 3806$)[a]
Sex, n (%)		
Male	1695 (43.9)	1672 (43.9)
Female	2169 (56.1)	2134 (56.1)
Age (years), n (%)		
≤ 11	1065 (27.5)	1052 (27.6)
12	1170 (30.3)	1151 (30.2)
13	964 (17.2)	946 (24.9)
≥ 14	665 (17.2)	657 (17.3)
BMI-for-age groups, n (%)		
Thin (< -2 SD)	219 (5.8)	215 (5.8)
Normal (-2 to 1 SD)	1517 (40.1)	1496 (40.1)
Overweight (> 1 to 2 SD)	961 (25.3)	946 (25.3)
Obese (> 2 SD)	1089 (28.8)	1072 (28.8)
Missing, n	78	77
Mode of birth, n (%)		
Vaginal	3106 (81.8)	3072 (81.8)
Cesarean section	692 (18.2)	685 (18.2)
Missing, n	66	49
Breastfeeding ever, n (%)		
Yes	2894 (76.3)	2863 (76.3)
Missing, n	72	54
Current eczema, n (%)		
Yes	388 (10.2)	385 (10.2)
Missing, n	73	45
Secondhand smoke exposure, n (%)		
Yes	1755 (45.8)	1740 (45.8)
Missing, n	28	10
Cat exposure in infancy, n (%)		
Yes	232 (6.1)	231 (6.1)
Missing, n	35	17
Dog exposure in infancy, n (%)		
Yes	85 (2.2)	85 (2.2)
Missing, n	32	11

Table 1 continued

Variables	Total study sample (*n* = 3864)	Analytical study sample (*n* = 3806)[a]
Total number of siblings, *n* (%)		
0	40 (1.1)	39 (1.0)
1	206 (5.4)	205 (5.5)
2	396 (10.5)	394 (10.5)
3	707 (18.6)	704 (18.8)
4	835 (22.0)	816 (21.8)
≥ 5	1609 (42.4)	1589 (42.4)
Missing, *n*	71	59
Number of older siblings, *n* (%)		
0	1103 (28.7)	1092 (28.8)
1	801 (20.8)	791 (20.8)
2	638 (16.6)	630 (16.6)
3	519 (13.5)	508 (13.4)
≥ 4	783 (20.4)	774 (20.4)
Missing, *n*	20	11
Number of younger siblings, *n* (%)		
0	544 (14.4)	538 (14.4)
1	757 (20.1)	751 (20.2)
2	798 (21.1)	787 (21.1)
3	802 (21.3)	791 (21.2)
≥ 4	872 (23.1)	861 (23.1)
Missing, *n*	91	78

BMI body mass index, *SD* standard deviation

[a] Refers to the sample of participants with complete information regarding psoriasis status (i.e., excludes 58 subjects with no information regarding psoriasis status)

infancy was associated with lifetime psoriasis prevalence (aPR = 1.96, 95% CI 1.14–3.37), but not with current psoriasis prevalence (aPR = 1.49, 95% CI 0.52–4.23). Dog-keeping during infancy showed a non-statistically significant trend for association with higher prevalence of lifetime psoriasis (aPR = 1.31, 95% CI 0.54–3.14) and showed no effect on current psoriasis prevalence (aPR = 0.92, 95% CI 0.15–5.63). Being ever directly breastfed was associated with reduced prevalence of lifetime psoriasis (aPR = 0.62, 95% CI 0.44–0.89); however, this association was not evident for current psoriasis (aPR = 0.95, 95% CI 0.45–1.99; Table 2).

Results of the association analyses of the numbers of total, older, and younger siblings with lifetime and current psoriasis prevalence are shown in Table 3. Trend analyses (per additional sibling) showed that the prevalence of
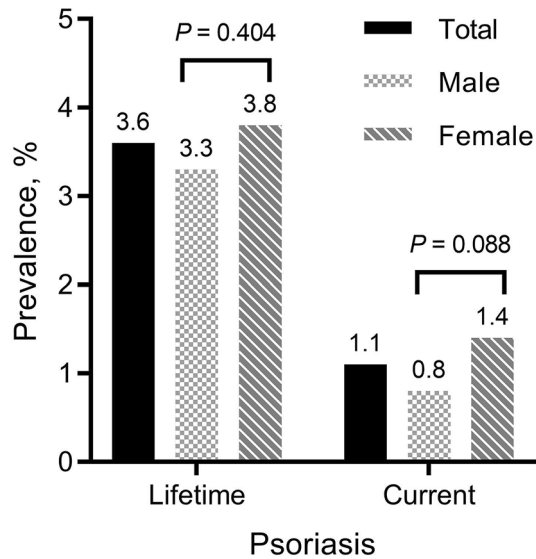
Fig. 1 Prevalence of lifetime and current parent-reported doctor-diagnosed psoriasis in the total study sample and by sex
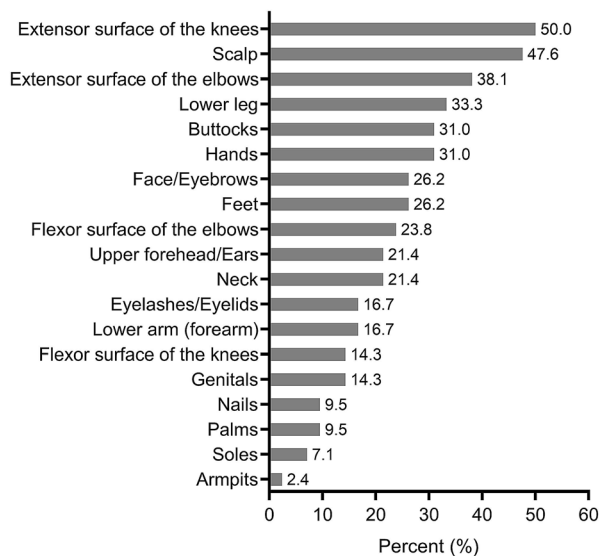

Fig. 2 Reported body areas affected by psoriasis lesions among subjects with current parent-reported doctor-diagnosed psoriasis ($n = 42$)

lifetime and current psoriasis increased with increasing numbers of total siblings, older siblings, and younger siblings (Table 3). There was no significant difference between the effects of older and younger siblings on psoriasis prevalence ($P_{interaction} > 0.05$). Increased number of

older siblings was associated with elevated prevalence of lifetime (≥ 4 vs. 0 older siblings: aPR = 1.83, 95% CI 1.13–2.98) and current (≥ 4 vs. 0 older siblings: aPR = 2.17, 95% CI 0.95–4.97) psoriasis. Moreover, compared to having no (zero) younger siblings, having any number of younger siblings (i.e., one or more) was strongly associated with a higher lifetime psoriasis prevalence (e.g., ≥ 4 vs. 0 younger siblings: aPR = 2.85, 95% CI 1.30–6.24). Although increased number of younger siblings was associated with elevated current psoriasis prevalence, these effects did not demonstrate statistical significance (e.g., ≥ 4 vs. 0 younger siblings: aPR = 2.31, 95% CI 0.60–8.94; Table 3).

DISCUSSION

The current study estimated the lifetime and current prevalence of psoriasis in a large school-based sample of adolescents in Kuwait for the first time and assessed the role of early life risk factors. This investigation showed that 3.6% of the enrolled adolescents have ever had psoriasis and 1.1% have had active psoriasis in the past 12 months, with the scalp and extensor surfaces of the knees and elbows reported as the most commonly affected body areas by psoriasis lesions. Currently having eczema was strongly associated with elevated lifetime and current psoriasis prevalence. Exposure to household SHS and cat during infancy were associated with an elevated lifetime psoriasis prevalence, and showed a trend for association with current psoriasis prevalence. Direct breastfeeding was associated with a significantly reduced lifetime prevalence of psoriasis but was not related to current psoriasis prevalence. Overall, prevalence of both lifetime and current psoriasis demonstrated increasing trends with higher numbers of total, older, and younger siblings. These observed associations highlight the potential role of environmental exposures and sibship size (a marker of prenatal and/or postnatal exposures) in psoriasis development.

Globally, the prevalence of psoriasis is scarcely investigated, with around 81% of countries around the world lacking epidemiologic data on psoriasis [23]. Moreover, existing studies

Table 2 Adjusted associations of personal attributes and risk factors with psoriasis among adolescents in Kuwait

	Lifetime parent-reported doctor-diagnosed psoriasis		Current parent-reported doctor-diagnosed psoriasis	
	% (*n*/total)	Adjusted PR[a] (95% CI)	% (*n*/total)	Adjusted PR[a] (95% CI)
Sex				
Male	3.3 (55/1672)	1.00 (reference)	0.8 (13/1672)	1.00 (Reference)
Female	3.8 (81/2134)	0.92 (0.65–1.30)	1.4 (29/2134)	1.24 (0.64–2.42)
Age (years)				
≤ 11	3.6 (38/1052)	1.00 (reference)	1.1 (11/1052)	1.00 (reference)
12	2.9 (33/1151)	0.90 (0.52–1.43)	0.8 (9/1151)	0.90 (0.35–2.32)
13	4.2 (40/946)	1.26 (0.80–1.99)	1.2 (11/946)	1.14 (0.45–2.87)
≥ 14	3.8 (25/657)	1.02 (0.61–1.70)	1.7 (11/657)	1.53 (0.60–3.88)
BMI-for-age groups				
Thin (< −2 SD)	6.1 (13/215)	1.47 (0.79–2.73)	2.3 (5/215)	2.16 (0.75–6.25)
Normal (−2 to 1 SD)	3.5 (53/1496)	1.00 (reference)	1.1 (16/1496)	1.00 (reference)
Overweight (> 1 to 2 SD)	3.9 (37/946)	1.10 (0.73–1.65)	1.1 (10/946)	1.11 (0.50–2.47)
Obese (> 2 SD)	3.1 (33/1072)	0.86 (0.55–1.33)	1.0 (11/1072)	0.93 (0.41–2.09)
Mode of birth				
Vaginal	3.7 (112/3072)	1.00 (reference)	1.2 (37/3072)	1.00 (reference)
Cesarean section	3.4 (23/685)	0.85 (0.55–1.30)	0.7 (5/685)	0.64 (0.25–1.64)
Breastfeeding ever				
No	4.8 (43/889)	1.00 (reference)	1.0 (9/889)	1.00 (reference)
Yes	3.1 (90/2863)	0.62 (0.44–0.89)[‡]	1.1 (31/2863)	0.95 (0.45–1.99)
Current eczema				
No	2.5 (84/3376)	1.00 (reference)	0.8 (26/3376)	1.00 (reference)
Yes	13.0 (50/385)	4.86 (3.40–6.96)[‡]	3.6 (14/385)	4.27 (2.10–8.69)[‡]
Secondhand smoke exposure				
No	2.9 (59/2056)	1.00 (reference)	0.7 (15/2056)	1.00 (reference)
Yes	4.4 (77/1740)	1.41 (1.07–1.98)[†]	1.6 (27/1740)	1.77 (0.89–3.53)
Cat exposure in infancy				
No	3.3 (119/3558)	1.00 (reference)	1.1 (38/3558)	1.00 (reference)
Yes	7.4 (17/231)	1.96 (1.14–3.37)[†]	1.7 (4/231)	1.49 (0.52–4.23)
Dog exposure in infancy				
No	3.5 (131/3710)	1.00 (reference)	1.1 (41/3710)	1.00 (reference)

Table 2 continued

	Lifetime parent-reported doctor-diagnosed psoriasis		Current parent-reported doctor-diagnosed psoriasis	
	% (*n*/total)	Adjusted PR[a] (95% CI)	% (*n*/total)	Adjusted PR[a] (95% CI)
Yes	5.9 (5/85)	1.31 (0.54–3.14)	1.2 (1/85)	0.92 (0.15–5.63)

PR prevalence ratio, *CI* confidence interval, *BMI* body mass index, *SD* standard deviation

[†] $P < 0.05$; [‡]$P < 0.01$

[a] Simultaneously adjusted for all variables shown in the table plus total number of siblings was included in the multivariable model

reporting on psoriasis prevalence are difficult to compare due to different methodologies, types of reported prevalence estimate (point, period, or lifetime), methods of ascertaining psoriasis (self-reported or physician/dermatologist diagnosed), population age (children, adults, or total population), and study settings (population-based, existing electronic health records, clinical settings) [21, 28]. In the current study, the lifetime prevalence of parent-reported doctor-diagnosed psoriasis was estimated to be 3.6%, which is higher than the most extreme estimate reported in the literature among children, i.e., 2.1% in Italy [14]. Moreover, the prevalence of current parent-reported doctor-diagnosed psoriasis was estimated to be 1.1% among the enrolled adolescents in our study, which is twice as high as the most extreme period prevalence of 0.45% reported among children in Germany [15, 29]. At the regional level, a study conducted among Saudi schoolchildren (average age 10.3 years) estimated the prevalence of psoriasis to be 0.6% [30], which is comparable to our findings of a current prevalence of 1.1%. Given that genetic factors are the largest contributor to psoriasis development [2, 3, 31], a plausible explanation of the observed elevated prevalence of psoriasis in our sample is the high prevalence of consanguinity (inbreeding) in Kuwait, which was previously estimated to be between 22.6 and 42.1% [32]. Consanguineous marriages are associated with higher rates of genetically determined diseases due to increased homozygosity of recessive alleles [33]. For instance, a meta-analysis demonstrated that offspring of consanguineous marriages were more likely to suffer from primary immunodeficiency diseases with autosomal recessive pattern of inheritance than children with no parental consanguinity [34]. In our sample of adolescents with current psoriasis, 50% reported family history of psoriasis (i.e., grandparents, parents, and/or siblings), where 24.4% reported history in grandparents, 33.3% reported history in siblings, 7.1% reported history in father, and 11.9% reported history in mother (the prior proportions are not mutually exclusive). Our estimate of positive family history (50%) is consistent with prior studies showing 47% of psoriasis patients in Spain [35] and 45.9% of psoriasis patients in Italy [36] reported a positive family history. Moreover, out of the 42 subjects with current psoriasis, 42.9% were born to couples related as second cousins or closer (data not shown). Hence, such factors may underlie the elevated prevalence estimates in our study sample. Moreover, our study might have included more mild cases of psoriasis due to the population-based sample, where such cases are usually less likely to be included in clinical-based samples. Also, parents' inability to differentiate between psoriasis and eczema (atopic dermatitis)/seborrheic dermatitis may have contributed to a higher prevalence of psoriasis in our report. However, eczema and psoriasis show clear difference in their anatomical location (flexor vs. extensor surfaces, e.g., of the elbows and knees).

Table 3 Adjusted associations of the total number of siblings, number of older siblings, and number of younger siblings with psoriasis among adolescents in Kuwait

	Lifetime parent-reported doctor-diagnosed psoriasis		Current parent-reported doctor-diagnosed psoriasis	
	% (*n*/total)	Adjusted PR[a] (95% CI)	% (*n*/total)	Adjusted PR[a] (95% CI)
Total siblings				
0/1[b]	2.5 (6/244)	1.00 (reference)	0.8 (2/244)	1.00 (reference)
2	2.3 (9/394)	0.86 (0.31–2.35)	0.5 (2/394)	0.62 (0.09–4.47)
3	2.6 (18/704)	0.94 (0.38–2.33)	0.7 (5/704)	0.80 (0.16–4.13)
4	4.2 (34/816)	1.69 (0.72–3.98)	1.0 (8/816)	1.05 (0.22–5.03)
≥ 5	4.3 (68/1589)	1.60 (0.71–3.64)	1.6 (25/1589)	1.47 (0.34–6.25)
Per additional sibling	–	1.15 (1.06–1.24)	–	1.17 (1.01–1.36)
P_{trend}	–	< 0.001	–	0.033
Older siblings				
0	3.5 (38/1092)	1.00 (reference)	1.2 (13/1092)	1.00 (reference)
1	3.7 (29/791)	1.25 (0.78–2.01)	0.8 (6/791)	0.78 (0.30–2.03)
2	2.5 (16/630)	0.75 (0.41–1.38)	0.8 (5/630)	0.50 (0.14–1.74)
3	3.7 (19/508)	1.38 (0.79–2.41)	0.6 (3/508)	0.63 (0.18–2.19)
≥ 4	4.4 (34/774)	1.83 (1.13–2.98)[†]	1.9 (15/774)	2.17 (0.95–4.97)
Per additional older sibling	–	1.12 (1.03–1.23)	–	1.16 (0.99–1.36)
P_{trend}	–	0.011	–	0.068
Younger siblings				
0	1.9 (10/538)	1.00 (reference)	0.7 (4/538)	1.00 (reference)
1	3.2 (24/751)	2.00 (0.95–4.21)	0.9 (7/751)	1.40 (0.41–4.78)
2	4.2 (33/787)	2.61 (1.26–5.43)[†]	1.1 (9/787)	1.75 (0.51–6.08)
3	4.1 (32/791)	2.99 (1.43–6.27)[‡]	0.9 (7/791)	1.45 (0.40–5.33)
≥ 4	4.2 (36/861)	2.85 (1.30–6.24)[‡]	1.7 (15/861)	2.31 (0.60–8.94)
Per additional younger sibling	–	1.19 (1.07–1.32)	–	1.20 (0.98–1.46)
P_{trend}	–	0.001	–	0.075

PR prevalence ratio, *CI* confidence interval

[†] $P < 0.05$; [‡] $P < 0.01$

[a] Adjusted for sex, age, BMI-for-age, mode of birth, breastfeeding ever, current eczema, secondhand smoke exposure, cat exposure in infancy, and dog exposure in infancy. Additionally, PRs of older siblings were simultaneously adjusted for younger siblings, and PRs of younger siblings were simultaneously adjusted for older siblings

[b] Since only one child with no (zero) siblings had psoriasis (1/39; 2.6%), we combined the no siblings and one sibling groups (reported as: 0/1) to avoid small cell sizes

Prior investigations have reported conflicting findings regarding sex distribution in psoriasis, with reports suggesting that psoriasis affects males and females equally [14, 15, 21], psoriasis is slightly more common in males than females [20], and psoriasis is slightly more prevalent in females than males [37, 38]. Our findings showed that the lifetime prevalence of psoriasis did not differ between males (3.3%) and females (3.8%). However, current psoriasis prevalence was more common among females (1.4%) compared to males (0.8%). Hence, indicating that the type of prevalence measure (lifetime, point, or period) might explain the inconsistencies in the reported sex disparities. Another possible explanation for the marginal female predominance is that females experience, on average, an earlier age of onset of psoriasis compared to males [23]. Several studies have shown consistent positive associations between adiposity and psoriasis [10, 39–41]. However, our analysis did not show any such association, rather a statistically non-significant increase in lifetime and current psoriasis prevalence among thin (underweight) subjects compared to those with normal weight was observed. This finding contradicts the current literature and should be corroborated in future investigations. Exposure to household SHS was associated with increased prevalence of lifetime and current psoriasis in our report, which is consistent with the existing scientific literature [11, 12, 42]. Moreover, the observed strong association between current eczema and both lifetime and current psoriasis prevalence is in agreement with prior investigations [29, 43], and is further supported by the shared genetic predisposition [44, 45].

We have specifically investigated the association of breastfeeding, household pet (cat/dog) exposure during infancy, and sibship size with psoriasis due to the ability of these factors to influence the development of the immune system (i.e., immune maturation and response). Breastfeeding was strongly associated with reduced prevalence of lifetime psoriasis, but not current psoriasis prevalence. Hence, indicating that the protective effect of breastfeeding is limited to psoriasis that develops early in childhood. We identified only one prior study

that showed *no* exclusive breastfeeding for at least 3 months was associated with increased odds of psoriasis (odds ratio = 1.46, 95% CI 1.09–1.95) [42]. This finding further supports our observation that breastfeeding might provide early life protection for children susceptible to psoriasis. In contrast, we observed positive associations between family ownership of a household cat during a child's first year of life and lifetime and current psoriasis prevalence, though the association with current psoriasis did not gain statistical significance. Dog-keeping during child's infancy showed a trend for association with lifetime psoriasis and showed no effect on current psoriasis. This observation might have been obscured by the fact that a very limited proportion (2.2%) of families in our study sample reported having dogs (i.e., lack of statistical power). Moreover, we showed that increased numbers of total, older, and younger siblings are associated with an elevated lifetime and current psoriasis prevalence. In particular, an elevated prevalence of lifetime and current psoriasis was observed in the groups with a large total number of siblings (e.g., 4 or $\geq$ 5) and a large number of older siblings (e.g., $\geq$ 4). Whereas, having at least one younger sibling was associated with an increased lifetime and current psoriasis prevalence. Overall, when analyzed as quantitative variables to infer trends per additional sibling, numbers of total, older, and younger siblings demonstrated statistically significant positive associations with lifetime and current psoriasis. These reported associations of household cat-keeping in infancy and sibship characteristics with psoriasis are novel and are exclusively based on empirical findings. Since immune dysregulation, specifically the stimulation of T helper type 1 and type 17 (Th1 and Th17) cells, in addition to resident skin cells (e.g., keratinocytes and dendritic cells), in response to external triggers/insults [3, 4, 46], characterize psoriasis development, we speculate that immune-mediated mechanisms might underlie the aforementioned observed associations. For instance, breastfeeding has been shown to support the proper maturation of an infant's immune system, which might explain

the observed protective effect of breastfeeding on psoriasis in early life [47].

The observed positive association between household cat exposure during infancy and psoriasis could be explained by the fact that keeping pets, including cats, has been linked to increased endotoxins and microbial exposures in homes; such exposures in early life may promote exaggerated Th1 immune responses and, in turn, possibly increase the risk of psoriasis in susceptible individuals [48, 49]. In general, sibship is a marker of unknown exposure; however, the effects of older siblings could reflect prenatal and/or postnatal programming, whereas associations with younger siblings are likely explained by postnatal mechanisms [50]. An investigation demonstrated that immune priming occurs in utero and depends on the number of previous maternal pregnancies [51]. Moreover, a study demonstrated that the presence of siblings is associated with in utero programming of exaggerated Th1 and Th17 immune responses in the airways of asymptomatic neonates [52]. Such findings support the observed elevated psoriasis prevalence with increased numbers of total, older, and younger siblings. In addition, the association observed between sibship characteristics and psoriasis prevalence is opposite from what has been reported for eczema and allergic diseases, namely a decreasing risk with increasing number of siblings has been widely reported [53, 54]. Given that the pathophysiology of psoriasis involves Th1/Th17 pathways and allergic diseases are driven by Th2 activation, the opposite effects of siblings on psoriasis (more siblings is associated with higher risk) and allergies (more siblings is associated with lower risk) can be speculatively explained by different Th1/Th17 and Th2 patterns. However, more studies are needed to corroborate our findings.

A major strength of the current study is the large and representative study sample that allowed for the estimation of psoriasis prevalence among schoolchildren throughout Kuwait. A potential limitation to our study is the inaccuracy of parent/guardian-reported weight and height of their children, which could have led to misclassification of children into the BMI-for-age groups. However, the estimated prevalence of overweight (25.3%) and obesity (28.8%) in the current report did not substantially differ from that in a previous investigation conducted among schoolchildren aged 6–18 years in Kuwait that used objective weight and height measurements (overweight, 21.6%; and obesity, 30.5%) [55]. Moreover, the possibility of misclassification of the psoriasis status cannot be excluded because it was parent-reported. However, to increase the validity of parent-reporting, we asked whether psoriasis was *doctor*-diagnosed. A prior study has shown that the validity of self-reported psoriasis increases when asking if the condition was physician-diagnosed [56]. To minimize the effect of recall bias, when defining current psoriasis, we incorporated having had active psoriasis lesion(s) and/or used psoriasis treatment in the past 12-month, in addition to lifetime history of doctor-diagnosed psoriasis. The validity of the current psoriasis definition used in this study is supported by the fact that a high proportion of subjects with current psoriasis showed typical manifestation of psoriasis in usual anatomical sites (scalp [47.6%] and extensor surfaces of the knees [50%] and elbows [38.1%]), which is supported by previous studies [3, 57]. A prior validation study showed that compared to the gold standard (i.e., clinical skin examination performed by a dermatologist), self-reported psoriasis had an estimated sensitivity of 56%, specificity of 99%, positive predictive value of 78%, and negative predictive value of 96%. [56]. These results indicate that self-reporting is a valid method for ascertaining psoriasis in population-based studies that may underestimate rather than overestimate the true prevalence. Similarly, another study found that self-reporting of psoriasis tends to underestimate the prevalence of cases identified in clinical settings [38]. However, the generalizability of the aforementioned validation study results to our study population should be cautiously interpreted since those studies were conducted in different settings and populations (i.e., Norwegian and Danish adults). Another issue is that differential diagnosis of psoriasis with eczema is common and may lead to misclassification. However, of the 42 children classified as currently having psoriasis in our report, 35 (83.3%)

reported that their diagnosis was made by a dermatologist, and 4 (9.5%) and 3 (7.2%) were diagnosed by general practitioner and pediatrician, respectively. Hence, given that the majority were diagnosed by dermatologists, the effect of misdiagnoses on results of this report should be minimal. Given that 0.8% of the children with no current eczema had a diagnosis of psoriasis and 3.6% of children had current eczema, there may be a small overlap in the diagnoses of the two diseases. A further limitation to our study is the lack of statistical power to detect statistically significant effects when assessing associations with current psoriasis prevalence (e.g., effect of SHS: aPR = 1.77, 95% CI 0.89–3.53); this is due to the limited number of subjects ($n = 42$) with current psoriasis. Moreover, family history of psoriasis was only sought from subjects who reported current psoriasis; hence, we were not able to adjust for its effects in our association analyses. Given that psoriasis and eczema share, to some extent, similar clinical and pathologic features, including immune dysregulation and epidermal barrier defects [58], our association analyses adjusted for the effect of current eczema. Hence, the reported associations were independent of eczema effect. Moreover, it is essential to indicate that our analysis aimed to assess associations between different exposures and psoriasis rather than to infer causal relationships.

CONCLUSIONS

Our study estimated the lifetime (3.6%) and current (1.1%) prevalence of parent-reported doctor-diagnosed psoriasis among adolescents in Kuwait for the first time. Also, we demonstrated that exposure to household SHS and cats during infancy and having siblings are associated with an increased psoriasis prevalence, whereas direct breastfeeding is linked with a decreased lifetime prevalence. These empirical findings suggest that different prenatal and postnatal factors are associated with psoriasis, speculatively, through immune-mediated mechanisms. Future investigations are needed to corroborate our findings and explore the possible underlying etiological mechanisms.

Moreover, there is a need for more population-based studies among children to better understand the role of early life risk factors.

the Declaration of Helsinki for medical research involving human subjects. The authors have no ethical conflicts to disclose.

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

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