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Cardiovascular comorbidities of pediatric psoriasis in United States hospitalized children

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Abstract

Background—Psoriasis has been shown to be associated with cardiovascular disease in adults.

Little is known about cardiovascular risk in pediatric psoriasis.

Objective—To determine if there is an association between pediatric psoriasis and cardiovascular comorbidities.

Study Design—Data were analyzed from the 2002–2012 National Inpatient Sample including 4,884,448 hospitalized children age 0–17 years. Bivariate and multivariate survey logistic regression models were created to calculate the odds of psoriasis on cardiovascular comorbidities.

Results—In multivariate survey logistic regression models adjusting for age, sex and race/ethnicity, pediatric psoriasis was significantly associated with 5 of 10 cardiovascular comorbidities, including obesity (adjusted odds ratio [95% confidence interval]: 3.15 [2.46–4.05]), hypertension (2.63 [1.93–3.59]), diabetes (2.90 [1.0–4.42]), arrhythmia (1.39 [1.02–1.88]), and valvular heart disease (1.90 [1.07–3.37]). The highest odds of cardiovascular risk factors occurred in blacks and Hispanics, and children ages 0–9 years, but there were no sex-differences.

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JI Silverberg had full access to all the data in the study and take responsibility for the integrity of the data and accuracy of the data analysis.

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Limitations—The study was limited to hospitalized children. We were unable to assess the impact of psoriasis treatment or family history on cardiovascular risk.

Conclusions—Pediatric psoriasis is associated with higher odds of multiple cardiovascular comorbidities in hospitalized patients. Strategies for mitigating excess cardiovascular risk in pediatric psoriasis may need to be determined.

Keywords

psoriasis; cardiovascular risk factors; hypertension; diabetes; obesity; hyperlipidemia; arrhythmia; comorbidities; racial differences

Introduction

Psoriasis affects between 0–2.15% of children in Europe and Asia¹. Previous studies demonstrate a consistently increased risk for cardiovascular comorbidities in adults with psoriasis, including ischemic heart disease, peripheral vascular disease, atherosclerosis, diabetes, hypertension, dyslipidemia, obesity and metabolic syndrome². Less is known about cardiovascular risk factors and/or events in childhood psoriasis.

A recent meta-analysis found 7 studies, with a total of 965 children, that assessed metabolic and/or cardiovascular risk in children with psoriasis³. It found significantly higher rates of metabolic syndrome in 3 studies (with only 60 children), lower high-density lipoprotein cholesterol levels in 6 of 7 studies, and higher fasting glucose levels in 4 studies (with only 40 children), but no significant differences in triglyceride levels, waist circumference or blood pressure³. These studies were limited by insufficient power to detect metabolic and cardiovascular risk.

We hypothesized that children with psoriasis are at higher risk for cardiovascular risk factors and even cardiovascular disease. Demographic factors, e.g. age, sex and race/ethnicity, are associated with differential risk of both psoriasis and cardiovascular disease. We hypothesized that cardiovascular risk in childhood psoriasis is influenced by demographic factors. In this study, we examined the association between psoriasis and cardiovascular risk factors and disease in a nationwide cohort of hospitalized children.

Methods

We analyzed data from the 2002–2012 Nationwide Inpatient Sample (NIS) provided by the Healthcare Cost and Utilization Project (HCUP) from the Agency for Healthcare Research and Quality. Each year of NIS contains an approximately 20% stratified representative sample of all hospitalizations in the United States (US). Sample weights were created by NIS that factored the complex sampling design and were used to provide representative estimates of discharges across the US. Data were de-identified and no attempts were made to identify individuals in the database. Patient consent was not obtained as the databases were received de-identified. All parties with access were compliant to HCUP's formal data use agreement. The study was approved by the Institutional Review Board at Northwestern University.

Identification of psoriasis and comorbidities

Psoriasis and comorbidities were determined through the use of the International Classification of Disease 9th Clinical Modification (ICD-9-CM) and Clinical Classification Software (CCS) codes provided by the NIS for each patient discharge (Supplemental Table 1). A previous study validated the use of the discharge diagnosis code 696.1 in the inpatient setting for the study of psoriasis^{4, 5}. The control group included all pediatric patients without a diagnosis of psoriasis, yielding a representative cohort of hospitalized children in the US. Newborn infants were excluded from the cohort.

Statistics

All data analyses and statistical processes were performed using SURVEY procedures in SAS version 9.4 (SAS Institute, Cary, NC). Analyses were limited to ages 0–17 years. Summary statistics were generated. Adjusted P values are presented, with values ≤ 0.05 considered significant.

Survey weighted binary logistic regression models with strata and cluster analysis were constructed to determine the association of psoriasis (independent variable) with various comorbidities (dependent variable). Crude odds ratios (OR) and 95% confidence intervals (CI) are presented. Multivariate logistic regression models included age (continuous), sex (male/female), and race/ethnicity (white/non-white) as covariates. Regression models were also stratified by race/ethnicity (white/black/Hispanic/multiracial-other), sex (male/female), and age (0–9/10–17 years). In models stratified by race/ethnicity, covariates included age and gender. In models stratified by sex, covariates included age and race/ethnicity. In models stratified by age, covariates included sex and race/ethnicity. Multivariate regression models were also constructed that included age (continuous), sex (male/female), race/ethnicity (white/non-white) as above, as well as obesity (yes/no), hypertension (yes/no), and diabetes (yes/no). Adjusted OR (aOR) and 95% CI are presented.

Results

Overall, there were 4,884,448 hospital discharges captured in the NIS between the years 2002 and 2012 for children (ages 0–17 years). There were 126 and 1380 admissions with a primary or secondary diagnosis of pediatric psoriasis, which was equivalent to a weighted prevalence of 25.8 and 287.4 per-million persons, respectively. Pediatric inpatients with a diagnosis of psoriasis were 47.5% male, 64.9% white, 11.9% black, and 14.2% Hispanic.

Cardiovascular comorbidities

In bivariate survey logistic regression models, 6 of 10 cardiovascular comorbidities analyzed were significantly associated with pediatric psoriasis (Table 2). Obesity was the most common comorbidity in childhood psoriasis, occurring in 7.5% compared with only 1.4% of those without psoriasis (survey logistic regression). Psoriasis was associated with higher rates of hypertension, diabetes, arrhythmia, heart conduction disorders, and composite lipid abnormality.

In multivariate regression models adjusting for age, sex and race/ethnicity, the associations with pediatric psoriasis remained significant in 4 of 6 comorbidities, including obesity, hypertension, and diabetes, arrhythmia. In addition, psoriasis was significantly associated with valvular heart disease in multivariate models, despite no association in bivariate analyses (Table 2).

Several disorders had no or too infrequent occurrences in children to allow for analysis of association with psoriasis: congestive heart failure, pulmonary circulatory disorder, diabetes mellitus with chronic complications, atrial fibrillation, peripheral vascular disease, pulmonary hypertension, myocardial infarction (MI), coronary artery disease, cardiomyopathy, supraventricular arrhythmia, sinoatrial node dysfunction, ventricular tachycardia, myocarditis, endocardial fibroelastosis, history of unspecified circulatory disease, personal history of transient ischemic attack (TIA) and cerebral infarction, chronic ischemic heart disease, other cerebrovascular disorders, subendocardial infarction, carotid artery occlusion, cardiac arrest, and peripheral and visceral atherosclerosis.

Stratified models by socio-demographics

To determine which subsets of hospitalized psoriasis patients are at highest risk of cardiovascular comorbidities, stratified analyses were performed by demographics for comorbidities that were significant in either bivariate or multivariate analyses and had sufficient frequencies (Table 3).

The association between obesity and psoriasis was significant in Hispanics, blacks, whites, and marginally significant in multiracial/other. The association between diabetes and psoriasis was strongest in blacks, followed by Hispanics, and whites. Similarly, the association between psoriasis and hypertension was strongest in blacks, followed by Hispanics, and whites. Arrhythmia was only significantly associated with psoriasis in races/ethnicities categorized as “other”, but not in whites or Hispanics. Valvular heart disease was significantly associated with psoriasis only in whites. Heart conduction disorder was marginally significantly associated with psoriasis in whites. Composite lipid abnormalities were associated with psoriasis in Hispanics.

Males with psoriasis were significantly more likely to have obesity, diabetes, and hypertension, but not arrhythmia. Females with psoriasis had higher odds of obesity, diabetes, hypertension, and arrhythmia.

The associations of obesity, diabetes and hypertension with psoriasis were stronger in children ages 0–9 vs. 10–17 years. Psoriasis was marginally associated with arrhythmia and significantly associated with valvular heart disease only in ages 10–17, but not 0–9 years. Psoriasis was associated with heart conduction disorder, but not composite lipid abnormality in ages 10–17 years.

The associations of obesity, diabetes and hypertension with psoriasis were significant in children living in areas with household incomes both below and above the national median and in children with health insurance. There was insufficient powering to stratify models in the uninsured.

Overlap of cardiovascular comorbidities

The majority of pediatric psoriasis patients who had arrhythmia, valvular heart disease, heart conduction disorder, and composite lipid abnormality did not have obesity, hypertension, or diabetes (Table 4).

Discussion

This study found higher odds of multiple cardiovascular comorbidities among pediatric inpatients with psoriasis. Pediatric psoriasis was associated with higher odds of cardiovascular risk factors, including obesity, diabetes, hypertension, and lipid abnormalities, as well as arrhythmias, valvular heart disease, and heart conduction disorder. The cardiovascular comorbidities occurred at greatest frequency in adolescents aged 10–17 years. However, the relative increase of odds of cardiovascular comorbidities was highest in children ages 0–9 years. This is likely due to lower rates of cardiovascular comorbidities in younger children without psoriasis (controls). There were significantly increased odds of cardiovascular risk factors across racial/ethnic groups. The strongest effect sizes for cardiovascular risk were observed in black and Hispanic children. Black and Hispanic patients may have higher cardiovascular risk, even in the absence of psoriasis. However, psoriasis was associated with increased cardiovascular risk in multivariate models controlling for race/ethnicity, as well as in bivariate models stratified by race/ethnicity. There were no apparent sex differences for any comorbidity.

These data may have important clinical ramifications. Children with psoriasis could benefit from early and more frequent surveillance for cardiovascular risk, in order to initiate lifestyle interventions and/or pharmacologic treatment to reduce cardiovascular events in adulthood. Educational interventions potentially include improving diet, increasing physical activity, and preventing poor health behaviors, e.g., smoking and excess alcohol consumption. Improved long-term control of psoriatic skin disease could mitigate the observed excess cardiovascular risk.

Our results are consistent with previous studies^{6–8}. A German study of 1.3 million non-selected individuals from a health insurance database found that children with a diagnosis of psoriasis had increased rates of hyperlipidemia, obesity, hypertension, and diabetes⁶. A case-control study of adolescents age 10–18 years found that psoriasis was associated with higher body mass index, waist circumference, systolic blood pressure, plasma glucose, and higher levels of high-sensitivity C-reactive protein than controls⁷. A pediatric case-control study (age 5–15 years) found that psoriasis was associated with higher body mass index, waist circumference, waist-to-height ratio and high blood pressure, and higher prevalence of metabolic syndrome⁸.

The highest odds of obesity, diabetes and hypertension occurred in black and/or Hispanic children with psoriasis. Obesity, diabetes and hypertension, were increased in children ages 0–9 and 10–17 years, with highest odds at ages 0–9 years. Psoriasis was marginally associated with arrhythmia and significantly associated with valvular heart disease, and heart conduction disorder at ages 10–17 years. These stratified analyses require careful interpretation. While 1506 cases of pediatric psoriasis were included in these analyses, many

of the cardiovascular comorbidities are rare outcomes. Thus, there was reduced statistical power for the subset analyses. There was little overlap of obesity, hypertension and diabetes with arrhythmia, valvular heart disease, heart conduction disorder and composite lipid abnormality. Children with psoriasis may be more likely to have only one cardiovascular comorbidity, but not multimorbidity. Phenotypical differences of psoriasis and/or patient characteristics may differentially impact risk and type of cardiovascular comorbidity. Finally, traditional cardiovascular risk factors may not account for the excess risk of other cardiovascular comorbidities observed.

The mechanism of increased cardiovascular risk in pediatric psoriasis has not been thoroughly explored. Adult studies showed that systemic inflammatory responses are activated in both mild and severe psoriasis, resulting in imbalances of “neutrophil activation products and their inhibitors”⁹. Others suggest that abnormal C-reactive protein and alpha2-macroglobulin plasma activity in people with psoriasis may confer increased cardiovascular risk¹⁰. Elevated levels of plasma osteopontin are associated with psoriasis, as well as hypertension, diabetes, and severity of coronary artery disease¹¹. Adolescents with psoriasis had higher blood levels of lipids, including mean total cholesterol, triglycerides, and low density lipoproteins¹². Abnormal changes in plasma lipid composition, in conjunction with increased oxidative stress and decreased antioxidant capacity, are linked to increased cardiovascular disease in patients with psoriasis¹³. Regardless of the mechanism, there is biologic plausibility for a direct relationship between having psoriasis and cardiovascular risk.

Strengths of this study include analysis of a large-scale, nationally representative, all-payer dataset of all hospitalizations over a period of 11 years. The use of ICD-9-CM codes for identifying psoriasis in the inpatient setting was previously validated⁵. Despite the large sample size overall, there were low frequencies of children with psoriasis and some comorbidities. Patients analyzed were from an inpatient setting, which may not be generalizable to all children with psoriasis. Hospitalized children with psoriasis likely have more severe disease, receive more intensive treatment, and do not represent the entire spectrum of psoriasis. It may be that children with mild psoriasis seen as outpatients have minimal or no increased cardiovascular risk. On the other hand, cardiovascular comorbidities may be greater than observed, as underreporting of dermatologic conditions has been observed in adults when patients are admitted for acute comorbidities, e.g., MI¹⁴. All entries within NIS were single inpatient admissions rather than complete health records for individual patients. Dates of diagnosis of psoriasis and comorbidities were not available, precluding assessment of temporal relationships between psoriasis and comorbidities. Family history, psoriasis treatment and their effects on comorbidities were unavailable in NIS.

Early onset cardiovascular risk factors may predispose to cardiovascular events in adulthood. However, one study showed that childhood-onset psoriasis was not associated with increased cardiovascular comorbidities in adulthood¹⁵. Some studies show that systemic therapy for psoriasis decreased biomarkers of cardiovascular risk¹⁶, suggesting that excess cardiovascular risk may be modifiable with improved control of the skin-disease and/or

other strategies. Further study is required to determine the effect of cardiovascular comorbidities on the lifetime course of pediatric psoriasis.

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Abbreviations used

aOR	adjusted odds ratio
CI	confidence interval
NIS	National Inpatient Sample
OR	odds ratio

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Table 1

Associations of pediatric psoriasis in the inpatient setting.

Variable	Diagnosis of psoriasis					
	No			Yes		
	Raw freq	Weighted prevalence [95% CI]	Raw freq	Weighted prevalence [95% CI]	p#	
Age (yr)						
0–5	2632880	55.0 [54.3–55.6]	192	13.0 [11.1–14.9]		
6–10	710969	14.9 [14.7–15.1]	311	20.8 [18.5–23.1]		<0.0001*
11–17	1439650	30.2 [29.5–30.9]	976	66.2 [63.5–68.9]		
Sex						
Male	2577438	54.1 [54.0–54.3]	709	47.5 [44.8–50.3]		<0.0001*
Female	2183595	45.9 [45.7–46.0]	781	52.5 [49.7–55.2]		
Race						
White	1924377	51.6 [49.6–53.5]	758	64.9 [60.9–68.9]		
Black	630232	16.8 [15.5–18.1]	137	11.9 [9.7–14.2]		
Hispanic	843000	22.5 [20.5–24.5]	166	14.2 [11.3–17.1]		<0.0001*
Asian	102098	2.7 [2.1–3.4]	27	2.3 [1.1–3.4]		
Multiracial/Other	237081	6.4 [5.8–7.0]	78	6.8 [5.1–8.4]		
Income Quartile						
1 st	1370714	31.9 [30.2–33.6]	393	28.5 [25.5–31.5]		
2 nd	1080448	25.2 [24.2–26.1]	354	25.6 [22.7–28.4]		0.08
3 rd	963220	22.4 [21.6–23.2]	351	25.2 [22.7–27.7]		
4 th	878547	20.6 [18.8–22.3]	283	20.8 [17.9–23.7]		
Insured						
Yes	4470673	92.2 [91.7–92.8]	1392	92.7 [91.3–94.2]		
No	179508	3.7 [3.3–4.2]	53	3.5 [2.5–4.5]		0.76
Other/no charge	198595	4.1 [3.7–4.4]	58	3.8 [2.7–4.8]		

[#] Rao-Scott chi square test

* Significant at level p=0.05.

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Missing values were encountered in 74,202 (1.53%) for age, 96,657 (1.99%) for sex, 1,121,226 (23.1%) for race/ethnicity, 564,870 (11.6%) for median household income, 8,901 (0.18%) for type of insurance.

Table 2

Association between pediatric psoriasis and cardiovascular comorbidities in US children.

Comorbidity	Diagnosis of psoriasis					
	No (n=4,857,674)			Yes (n=1,506)		
	Freq (%)	Freq (%)	Crude OR (95% CI)	P	Adjusted OR (95% CI)	P
Obesity	65,259 (1.4%)	113 (7.5%)	5.90 (4.79–7.27)	<0.0001	3.15 (2.46–4.05)	<0.0001
Diabetes	24,167 (0.5%)	39 (2.6%)	5.35 (3.72–7.70)	<0.0001	2.90 (1.90–4.42)	<0.0001
Hypertension	59,621 (1.2%)	62 (4.2%)	3.50 (2.63–4.66)	<0.0001	2.63 (1.93–3.59)	<0.0001
Arrhythmia	112,002 (2.3%)	50 (3.3%)	1.46 (1.10–1.94)	0.009	1.39 (1.02–1.88)	0.04
Valvular heart disease	46,973 (1.0%)	22 (1.5%)	1.54 (0.93–2.54)	0.09	1.90 (1.07–3.37)	0.03
Heart conduction disorder	16,685 (0.3%)	10 (0.7%)	1.92 (1.03–3.56)	0.04	1.78 (0.93–3.39)	0.08
Composite lipid abnormality	10,026 (0.2%)	<10 (0.6%)	2.96 (1.58–5.54)	0.0007	1.41 (0.60–3.30)	0.43
Cerebrovascular accident	13,311 (0.3%)	<10 (0.3%)	1.23 (0.46–3.31)	0.69	1.71 (0.64–4.54)	0.28
Chest pain	5,484 (0.1%)	<10 (0.3%)	2.39 (0.90–6.38)	0.08	1.30 (0.42–4.08)	0.65
Late effects of cerebrovascular disease	5,243 (0.1%)	<10 (0.3%)	2.36 (0.89–6.24)	0.09	1.05 (0.27–4.14)	0.94

Table 3

Stratified models of pediatric psoriasis and cardiovascular risk by race/ethnicity, sex, age, household income and insurance status.

Socio-demographic subset	Comorbidity (aOR [95% CI])					
	Obesity	Diabetes	Hypertension	Arrhythmia	Valvular heart disease	Heart conduction disorder
Race/ethnicity						
White	2.85 [2.04–3.98]	2.01 [1.19–3.40]	2.15 [1.32–3.49]	1.317 [0.88–1.97]	2.23 [1.12–4.45]	2.05 [0.99–4.28]
Black	3.76 [1.97–7.19]	6.68 [2.50–17.84]	4.30 [2.47–7.49]	NE	NE3	NE3
Hispanic	4.19 [2.50–7.02]	5.26 [1.71–16.20]	4.11 [1.80–9.35]	1.54 [0.69–3.40]	NE3	7.11 [2.90–17.40]
Multiracial/other	2.40 [0.99–5.81]	NE	NE	2.79 [1.10–7.09]	NE3	NE
Sex						
Male	3.30 [2.29–4.74]	2.99 [1.64–5.47]	2.81 [1.90–4.14]	1.21 [0.76–1.95]	1.63 [0.72–3.69]	NE3
Female	3.11 [2.18–4.44]	2.90 [1.67–5.05]	2.53 [1.53–4.20]	1.51 [1.01–2.27]	2.19 [0.97–4.94]	NE3
Age						
0–9	6.25 [3.11–12.58]	8.51 [3.55–20.43]	4.35 [2.43–7.79]	1.36 [0.75–2.47]	0.99 [0.38–2.59]	NE3
10–17	3.15 [2.42–4.08]	2.86 [1.86–4.40]	2.78 [1.96–3.95]	1.42 [0.99–2.02]	2.24 [1.16–4.33]	2.06 [1.02–4.13]
Household income						
Below median	3.33 (2.39–4.64)	2.85 (1.59–5.13)	2.63 (1.60–4.32)	1.27 (0.81–1.97)	1.25 (0.55–2.84)	NE
Above median	2.64 (1.76–3.98)	3.08 (1.50–6.31)	2.45 (1.55–3.87)	1.48 (0.95–2.29)	2.78 (1.24–6.22)	NE
Insured	3.04 (2.33–3.98)	3.09 (2.02–4.73)	2.74 (1.99–3.78)	1.34 (0.97–1.87)	2.06 (1.16–3.65)	1.68 (0.84–3.35)
						1.50 (0.65–3.48)

Table 4

Association between cardiovascular comorbidities and obesity, hypertension, and diabetes in US children.

Comorbidity	Obesity	Hypertension	Diabetes
Arrhythmia (n=50)	14%	12%	0%
Valvular heart disease (n=22)	4.5%	4.5%	4.5%
Heart conduction disorder (n=10)	10%	20%	10%
Composite lipid abnormality (n=9)	33.3%	11.1%	11.1%