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Clinically diagnosed urticaria and risk of systemic lupus erythematosus in children: A nationwide population-based case-control study

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Abstract

Background: Urticaria is one of the most common diseases seen in clinical practice, whereas several reports have proposed that urticaria may have a link with autoimmune disorders. Few studies have examined the clinical association between urticaria with systemic lupus erythematosus (SLE). By conducting a nationwide population-based case-control study in Taiwan, we evaluated the risk of SLE in children with a prior clinical diagnosis of urticaria.

Methods: Using 2000-2011 claims data from the Taiwanese National Health Insurance Research Database, we identified 2105 SLE children during 2004-2011 as the study group, along with randomly selected 8420 non-SLE patients matched (1:4) for age, sex, and first diagnosis date as the control group. The correlation between urticaria and SLE risk was estimated using conditional logistic regression analysis.

Results: The prevalence rates of clinically diagnosed acute and chronic urticaria in SLE patients were 22.09% and 18.24%, respectively. A significant association was found between clinically diagnosed urticaria and childhood SLE, with a stronger risk associated with more episodes of urticaria (≥3 visits, OR: 2.33, 95% CI 1.91-2.84). The risk was higher with chronic urticaria (OR: 2.21, 95% CI 1.85-2.64) than with acute urticaria (OR: 1.54, 95% CI 1.34-1.76). Subgroup analysis stratified by sex or age indicated that the risk associated with SLE was significantly greater among female children and adolescents with urticaria.

Conclusions: Our results suggest that children with urticaria have a significantly higher risk of SLE, with the risk increasing further among those with more episodes of urticaria or chronic urticaria.

KEYWORDS

children, claims data, systemic lupus erythematosus, urticaria

1 | INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic and persistent autoimmune disorder with diverse clinical presentations affecting multiple organ systems.[1] Early diagnosis and appropriate treatment are crucial to prevent further morbidity and obtain favorable long-term outcome.[2] Approximately 10%-20% of affected individuals have childhood-onset SLE.[3] Most children with SLE have a more

aggressive disease activity than adults; therefore, highlighting optimal care for pediatric SLE patients is necessary.[4]

Several SLE patients may present with cutaneous involvement and a variety of skin lesions including urticaria.[5,6] Cutaneous manifestations were reported to occur in up to 70% of such patients during the disease course.[7] Mucocutaneous manifestations such as malar rash and oral mucosal lesions are more common in pediatric SLE patients than in adult SLE patients.[8]The cutaneous features of SLE could be categorized as lupus erythematosus (LE)-specific and non-LE-specific lesions based on histopathological findings according to the Gilliam and Sontheimer classification.[9] Specific skin lesions include malar rash and discoid rash, which are crucial for diagnosing SLE. Nonspecific skin lesions include Raynaud's phenomenon, cutaneous vasculitis, alopecia, and urticaria. Although they are not included in the diagnostic criteria of SLE, they are related to the underlying SLE process and systemic involvement.

Urticaria is common in children and often prompts patients to make hospital visits in the outpatient or emergency department. Urticaria affects 15%-25% of people at some time during their lives.[10] It is characterized by sudden-onset erythematous and edematous wheals in the superficial layers of the skin and is associated with an itching or burning sensation. In general, urticaria is classified as acute or chronic. Acute urticaria in children can be induced by various factors such as infections, medications, and foods; the most frequent cause is infection.[11,12] Chronic urticaria is defined as the persistence of wheals for at least 6 weeks with a frustrating condition. Chronic urticaria-like lesions may appear in LE tumidus, which is an uncommon but distinct subtype of cutaneous LE.[13] The manifestation of chronic urticaria is diverse and often characterized by flares and remissions, and there may be an overlap between clinical features of chronic urticaria and SLE. The prevalence of chronic urticaria is 4.5%-12% in children with SLE, but there is little information on the prevalence of SLE in children with urticaria.[14]

Although patients with acute or chronic urticaria usually do not exhibit LE-specific skin lesions and do not meet the diagnostic criteria for SLE, urticaria may represent the first complaint in these patients before the more classical form of SLE manifests.[15] Urticaria and SLE may have similar cutaneous manifestations, and both are related to immunopathological conditions; however, few studies have examined the effects on SLE of a history of urticaria. In this nationwide population-based case-control study, we investigated whether a significant association exists between SLE and clinically diagnosed urticaria in children.

2 | METHODS

2.1 | Data source

The National Health Insurance Research Database (NHIRD), which contains outpatient and inpatient claims for all beneficiaries enrolled in Taiwan's mandatory National Health Insurance (NHI) program.[16] For analysis, we collected claims data for approximately 23 million beneficiaries representing approximately 99% of the total population in Taiwan from January 1, 2000, to December 31, 2011. The study protocol was approved by the Research Ethics Committee of Ditmanson Medical Foundation Chia-Yi Christian Hospital (CYCH-IRB-106072).

2.2 | Sample collection

Patients with a history of urticaria and newly diagnosed with SLE using the International Classification of Diseases, 9th Revision, Clinical Modification codes (ICD-9-CM; code 710), and concurrent catastrophic illness certificate were included. Finally, 2105 patients with new-onset SLE were selected, and 8420 random non-SLE patients matched (1:4) for age, sex, and first diagnosis date were considered as the control group.

2.3 | Definition of urticaria

Urticaria was defined by ICD-9-CM (708.0-708.9). We used three types of urticaria for data analysis based on different definitions: visiting the hospital for any urticaria (the number of visits was categorized as 0, 1, 2, and ≥3 visits), infection-caused urticaria or not, and classifications of urticaria as acute or chronic. Chronic urticaria was classified by at least two claims of ICD (708.0-708.9) and at least 6 weeks apart. Patients with urticaria who did not fulfill the definition of chronic urticaria were classified as having acute urticaria. They were given a diagnosis of acute infections as causes for urticaria: acute airway infection (ICD-9-CM: 460-466), acute gastrointestinal infection (001-009), pneumonia and influenza (480-487), urinary tract infection (590, 599.0), otitis media (381, 382), and cellulitis (528.3, 681.0-681.1, 681.9, or 682.0-682.9) at the time of their urticarial attack or within 7 days before or after the attack. Both acute urticaria and chronic urticaria were included in the data of patients with infection-caused urticaria if they had a diagnosis of these ICD codes.

2.4 | Potential confounders

Because correlations might exist between comorbid diseases, we also adjusted for the different atopic diseases and autoimmune or autoinflammatory diseases in the multivariable conditional logistic regression analyses. If these diagnostic codes were used in two or more ambulatory claims 6 months before and after the index date, they were recorded as comorbidities. Atopic diseases comprised asthma (ICD9-CM: 493), atopic dermatitis (691.8), and allergic rhinitis (477.9). Autoimmune diseases comprised autoimmune thyroiditis (245.2), lupus erythematosus (695.4), juvenile idiopathic arthritis (714), and ankylosing spondylitis (720). Autoinflammatory diseases involved Behçet's disease (136.1), periodic fever syndromes (277.31), and Sweet's syndrome (695.89).

2.5 | Statistical analysis

The demographic data and types of urticaria between cases and controls were compared using Pearson's chi-squared tests. We used conditional logistic regression analyses to calculate the odds ratio (OR) and 95% confidence interval (CI) for having been previously

diagnosed with urticaria between the two groups. Further adjustments were conducted to evaluate the associations of urticaria with SLE through two other conditional logistic regression models. In the first model, variables adjusted were the number of hospital visits, infection-caused urticaria or not, and different comorbidities between the two groups. In the second model, variables adjusted were infection-caused urticaria or not, classifications of urticaria, and different comorbidities between the two groups. A two-tailed *P* value of <0.05 was considered statistically significant. We conducted all statistical analyses using SAS statistical software (version 9.3; SAS Institute Inc., Cary, NC, USA).

3 | RESULTS

3.1 | Demographic data of children with SLE and controls

A total of 68 877 patients fulfilled the diagnosis of SLE between 2004 and 2011; of them, 2105 children (<18 years) with SLE were included as the case group (Figure 1). Demographic and clinical data of the cases and controls are shown in Table 1.

Among the 2105 patients, 1608 (76.39%) were female individuals; 1526 (72.49%) were adolescents (13-18 years). Patients with SLE had a significantly higher rate of urticaria than the controls (40.33% vs 26.90%), in addition to having a significantly higher number of hospital visits for urticaria. Infection-caused urticaria was relatively common in patients with SLE compared with the controls (19.57% vs 12.23%). In total, 384 SLE patients had chronic urticaria and 465 had acute urticaria; the prevalence of either type was higher than that in the control group.

3.2 | Associations of childhood SLE with urticaria

Compared with those with no hospital visits for urticaria, the ORs associated with childhood SLE for those with 1, 2, and ≥3 hospital visits for urticaria were 1.51 (95% CI: 1.32-1.73), 1.98 (95% CI: 1.66-2.37), and 2.49 (95% CI: 2.13-2.90) (Table 2). Compared with those who did not have infection-caused urticaria, the OR associated with childhood SLE for those with infection-caused urticaria was 1.78 (95% CI: 1.56-2.02). Moreover, compared with those without urticaria, the OR associated with childhood SLE for those with acute urticaria was 1.60 (95% CI: 1.42-1.80) and that for those with chronic urticaria was 2.34 (95% CI: 2.04-2.69). Patients with atopic dermatitis and allergic rhinitis tended to have a higher risk of associated SLE (OR: 1.65, 95% CI: 1.44-1.89 and OR: 1.24, 95% CI: 1.12-1.37, respectively). Patients with autoimmune or autoinflammatory diseases had a significantly higher risk of associated SLE (OR: 6.53, 95% CI: 5.14-8.30).

3.3 | Association of SLE risk with urticaria according to sex stratification

Table 3 reveals a consistently significant association between SLE risk and urticaria. Patients with ≥3 hospital visits for urticaria were associated with a significant risk of SLE (OR: 2.33, 95% CI: 1.91-2.84). Patients with acute or chronic urticaria were associated with a higher risk of SLE (OR: 1.54, 95% CI: 1.34-1.76 and OR: 2.21, 95% CI: 1.85-2.64, respectively) than the controls. However, after adjustments, the risk in patients with infection-caused urticaria was not significantly higher than that in those without infection-caused urticaria.

Analysis of data stratified by sex revealed that the risk of SLE was significantly higher in female patients with acute urticaria (OR: 1.71, 95% CI: 1.46-1.99) than in male patients. Nevertheless, the OR of SLE was significantly higher in patients with chronic urticaria, both in female (OR: 2.40, 95% CI: 1.96-2.95) and in male (OR: 1.62, 95% CI: 1.10-2.39) patients. The overall risk of SLE increased in female patients as the number of hospital visits for urticaria increased, with the highest risk being observed in the group with ≥3 hospital visits compared with individuals without urticaria (OR: 2.54, 95% CI: 2.05-3.17). In male patients, the OR of SLE was significantly higher in the group with ≥3 hospital visits for urticaria (OR: 1.71, 95% CI: 1.11-2.64). These results emphasize that the risk of SLE was significantly associated with the frequency of hospital visits for urticaria. Additionally, we found that both female and male patients with atopic dermatitis had a higher risk of SLE.

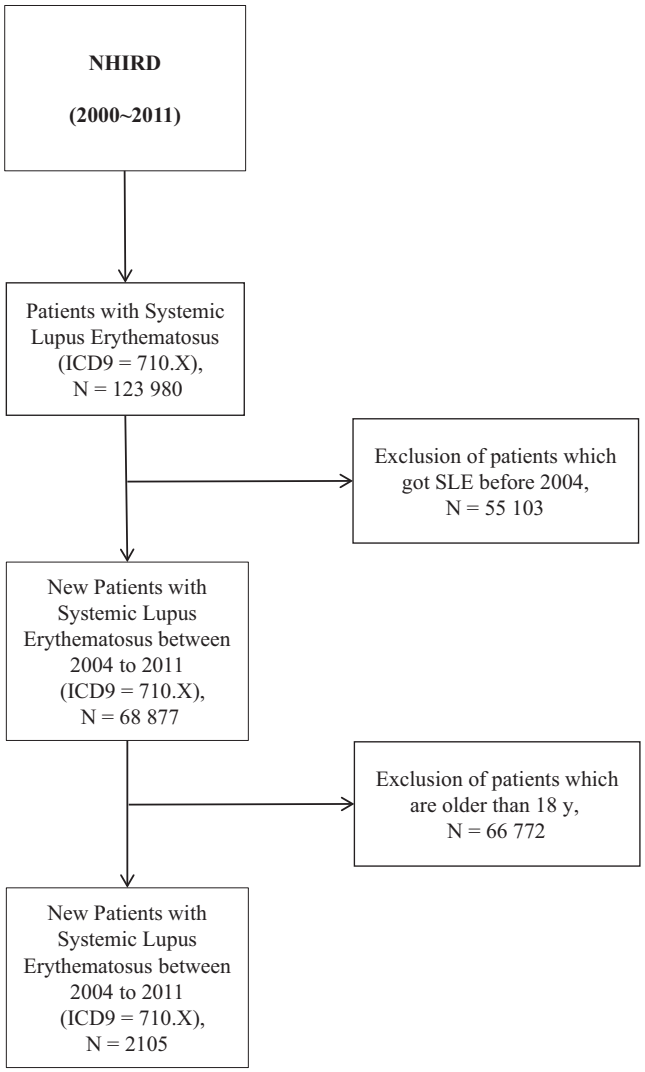

FIGURE 1 Flow chart showing selection of study subjects

3.4 | Association of SLE risk with urticaria according to age stratification

To elucidate the association between urticaria and age of onset of SLE, we performed multiple logistic regression stratified by age: preschool-aged (≤6 years), school-aged (7-12 years), and adolescent (13-18 years). As shown in Table 4, a significant association was observed between urticaria and SLE in school-aged and adolescent patients, although the trend was not significant in the younger group (0-6 years). In school-aged patients, the risk of SLE increased with the number of hospital visits for urticaria up to twice (OR: 1.94, 95% CI: 1.29-2.90) and ≥3 times (OR: 2.67, 95% CI: 1.72-4.14). Increased OR was found in both acute and chronic urticaria, with the risk of SLE being higher in chronic (OR: 2.37, 95% CI: 1.60-3.52) than in acute urticaria (OR: 1.38, 95% CI: 1.02-1.87). Notably, in adolescent patients, even one hospital visit for urticaria could increase the risk (OR: 1.53, 95% CI: 1.29-1.82), and the risk became higher with the increase in the number of hospital visits (2 visits: OR: 2.01, 95% CI: 1.59-2.54) and (≥3 visits: OR: 2.24, 95% CI: 1.78-2.82). Similarly, increased OR was found both in acute urticaria and chronic urticaria, with the risk of SLE being higher in chronic (OR: 2.18, 95% CI: 1.78-2.69) than in acute urticaria (OR: 1.60, 95% CI: 1.36-1.87).

TABLE 1 Demographic data of patients with childhood systemic lupus erythematosus (SLE) and controls

Variables	Case (n = 2105) N (%)	Control (n = 8420) N(%)	*P* value[a]
Age			
≦6 y	106 (5.04)	424 (5.04)	-
7~12 y	473 (22.47)	1892 (22.47)	
13~18 y	1526 (72.49)	6104 (72.49)	
Gender			
Female	1608 (76.39)	6432 (76.39)	-
Male	497 (23.61)	1988 (23.61)	
Urticaria	849 (40.33)	2265 (26.90)	<0.0001
Number of hospital visits			
0	1256 (59.67)	6155 (73.10)	<0.0001
1	363 (17.24)	1189 (14.12)	
2	194 (9.22)	486 (5.77)	
≧3	292 (13.87)	590 (7.01)	
Infection caused urticaria			
No	1693 (80.43)	7390 (87.77)	<0.0001
Yes	412 (19.57)	1030 (12.23)	
Classification of urticaria			
Null	1256 (59.67)	6155 (73.10)	<0.0001
Acute urticaria	465 (22.09)	1440 (17.10)	
Chronic urticaria	384 (18.24)	825 (9.80)	
Comorbidity			
Atopic diseases			
Asthma	470 (22.33)	1791 (21.27)	0.2909
Atopic dermatitis	369 (17.53)	976 (11.59)	<0.0001
Allergic rhinitis	985 (46.79)	3531 (41.94)	<0.0001
Autoimmune or autoinflammatory diseases			
No	1922 (91.31)	8296 (98.53)	<0.0001
Yes	183 (8.69)	124 (1.47)	

[a]Pearson chi-square test.

4 | DISCUSSION

Our results reveal that compared with children without SLE, children with SLE were associated with a significantly increased rate of having a prior history of clinically diagnosed urticaria. On further stratification by sex and age, the risk associated with SLE was more likely to be found in female and adolescent patients (13-18 years) with urticaria.

The etiology of SLE includes genetic and environmental factors. Because its manifestations may evolve over time, it is crucial

TABLE 2 Logistic regression estimated odds ratio of systemic lupus erythematosus (SLE) associated with Urticaria

Type	Variables	Model (Crude) OR (95% CI)	*P* value*
I	Number of hospital visits		
	0 time	1.00	
	1 time	1.51 (1.32-1.73)	<0.0001
	2 times	1.98 (1.66-2.37)	<0.0001
	≧3 times	2.49 (2.13-2.90)	<0.0001
II	Infection caused urticaria		
	No	1.00	
	Yes	1.78 (1.56-2.02)	<0.0001
III	Classification of urticaria		
	Null	1.00	
	Acute urticaria	1.60 (1.42-1.80)	<0.0001
	Chronic urticaria	2.34 (2.04-2.69)	<0.0001
Comorbidity	Atopic diseases		
	Asthma	1.07 (0.95-1.21)	0.2707
	Atopic dermatitis	1.65 (1.44-1.89)	<0.0001
	Allergic rhinitis	1.24 (1.12-1.37)	<0.0001
	Autoimmune or autoinflammatory diseases		
	No	1.00	
	Yes	6.53 (5.14-8.30)	<0.0001

*Conditional logistic regression.

TABLE 3 Logistic regression estimated adjusted odds ratio of systemic lupus erythematosus (SLE) associated with urticaria stratified by gender

		All				Male				Female			
		Model 1		Model 2		Model 1		Model 2		Model 1		Model 2	
Type	Variables	OR (95% CI)	*P* value*	OR (95% CI)	*P* value*	OR (95% CI)	*P* value*	OR (95% CI)	*P* value *	OR (95% CI)	*P* value*	OR (95% CI)	*P* value*
I	Number of visits for urticaria												
	0	1.00				1.00				1.00			
	1	1.47 (1.27-1.70)	<0.0001			1.02 (0.74-1.40)	0.9121			1.63 (1.38-1.92)	<0.0001		
	2	1.95 (1.60-2.38)	<0.0001			1.41 (0.92-2.15)	0.1149			2.12 (1.69-2.66)	<0.0001		
	≧3	2.33 (1.91-2.84)	<0.0001			1.71 (1.11-2.64)	0.0149			2.54 (2.03-3.17)	<0.0001		
II	Infection caused urticaria												
	No	1.00		1.00		1.00		1.00		1.00		1.00	
	Yes	0.97 (0.82-1.16)	0.7497	0.99 (0.83-1.18)	0.9166	1.27 (0.88-1.84)	0.2044	1.30 (0.90-1.87)	0.1668	0.90 (0.74-1.10)	0.3106	0.92 (0.76-1.12)	0.4073
III	Classification of urticaria												
	Null			1.00				1.00				1.00	
	Acute urticaria			1.54 (1.34-1.76)	<0.0001			1.07 (0.79-1.44)	0.6710			1.71 (1.46-1.99)	<0.0001
	Chronic urticaria			2.21 (1.85-2.64)	<0.0001			1.62 (1.10-2.39)	0.0149			2.40 (1.96-2.95)	<0.0001
Comorbidity	Atopic diseases												
	Asthma	0.94 (0.82-1.07)	0.3466	0.94 (0.83-1.07)	0.3536	1.01 (0.78-1.30)	0.9340	1.01 (0.78-1.30)	0.9634	0.93 (0.79-1.08)	0.3152	0.93 (0.80-1.08)	0.3346
	Atopic dermatitis	1.42 (1.24-1.64)	<0.0001	1.43 (1.25-1.65)	<0.0001	1.63 (1.25-2.11)	0.0003	1.64 (1.26-2.13)	0.0002	1.35 (1.14-1.60)	0.0004	1.36 (1.15-1.61)	0.0003
	Allergic rhinitis	1.12 (1.00-1.25)	0.0429	1.12 (1.00-1.25)	0.0424	1.19 (0.96-1.48)	0.1219	1.19 (0.95-1.48)	0.1273	1.10 (0.97-1.24)	0.1559	1.10 (0.97-1.24)	0.1520
	Autoimmune or autoinflammatory diseases												
	No	1.00		1.00		1.00		1.00		1.00		1.00	
	Yes	6.18 (4.84-7.89)	<0.0001	6.19 (4.85-7.90)	<0.0001	9.38 (5.29-16.66)	<0.0001	9.48 (5.34-16.81)	<0.0001	5.61 (4.28-7.37)	<0.0001	5.61 (4.28-7.36)	<0.0001

*Conditional logistic regression.

Model 1 were evaluated by adjusting for variables including number of hospital visits, infection/no infection and atopic diseases. Model 2 were evaluated by adjusting for variables including infection/no infection, acute/chronic urticaria and atopic diseases.

TABLE 4 Logistic regression estimated adjusted odds ratio of systemic lupus erythematosus (SLE) associated with urticaria stratified by age

		≦6 y				7~12 y				13~18 y			
		Model 1		Model 2		Model 1		Model 2		Model 1		Model 2	
Type	Variables	OR (95% CI)	*P* value*	OR (95% CI)	*P* value*	OR (95% CI)	*P* value*	OR (95% CI)	*P* value*	OR (95% CI)	*P* value*	OR (95% CI)	*P* value*
I	Number of hospital visits												
	0	1.00				1.00				1.00			
	1	1.42 (0.66-3.03)	0.3669			1.29 (0.93-1.78)	0.1228			1.53 (1.29-1.82)	<0.0001		
	2	1.07 (0.32-3.54)	0.9123			1.94 (1.29-2.90)	0.0014			2.01 (1.59-2.54)	<0.0001		
	≧3	2.03 (0.72-5.74)	0.1813			2.67 (1.72-4.14)	<0.0001			2.24 (1.78-2.82)	<0.0001		
II	Infection caused urticaria												
	No	1.00		1.00		1.00		1.00		1.00		1.00	
	Yes	1.03 (0.43-2.49)	0.9413	1.04 (0.43-2.47)	0.9379	0.98 (0.69-1.41)	0.9246	1.02 (0.72-1.45)	0.9086	0.98 (0.79-1.20)	0.8095	0.99 (0.80-1.21)	0.8950
III	Classification of urticaria												
	Null			1.00				1.00				1.00	
	Acute urticaria			1.45 (0.70-3.01)	0.3179			1.38 (1.02-1.87)	0.0361			1.60 (1.36-1.87)	<0.0001
	Chronic urticaria			1.51 (0.51-4.42)	0.4561			2.37 (1.60-3.52)	<0.0001			2.18 (1.78-2.69)	<0.0001
Comorbidity	Atopic diseases												
	Asthma	1.46 (0.86-2.46)	0.1587	1.42 (0.84-2.40)	0.1851	0.96 (0.75-1.22)	0.7231	0.96 (0.76-1.22)	0.7488	0.89 (0.76-1.05)	0.1767	0.89 (0.76-1.05)	0.1802
	Atopic dermatitis	1.49 (0.88-2.53)	0.1385	1.49 (0.88-2.52)	0.1380	1.23 (0.94-1.61)	0.1340	1.26 (0.96-1.65)	0.0905	1.50 (1.27-1.79)	<0.0001	1.51 (1.27-1.79)	<0.0001
	Allergic rhinitis	0.81 (0.49-1.33)	0.3970	0.81 (0.50-1.34)	0.4162	1.25 (0.99-1.57)	0.0595	1.24 (0.99-1.57)	0.0642	1.11 (0.97-1.26)	0.1215	1.11 (0.98-1.26)	0.1175
	Autoimmune or autoinflammatory diseases												
	No	1.00		1.00		1.00		1.00		1.00		1.00	
	Yes	9.41 (2.78-31.88)	0.0003	8.95 (2.65-30.24)	0.0004	9.58 (5.02-18.27)	<0.0001	9.66 (5.07-18.4)	<0.0001	5.54 (4.22-7.28)	<0.0001	5.55 (4.23-7.29)	<0.0001

*Conditional logistic regression.

Model 1 were evaluated by adjusting for variables including number of hospital visits, infection/no infection and atopic diseases. Model 2 were evaluated by adjusting for variables including infection/no infection, acute/chronic urticaria and atopic diseases.

to identify individuals who may eventually evolve into a defined SLE phenotype. Childhood-onset SLE has a more severe course than adult-onset SLE, with a higher rate of organ involvement.[17] Compared with adult-onset SLE patients, childhood-onset SLE patients were more likely to have mucocutaneous manifestations but may be untreated before admission.[18]

In many patients, urticaria takes a recurrent or relapsing form, for which they seek medical care. Accordingly, we evaluated the risk of SLE as per the number of hospital visits for urticaria. We found a close association between childhood SLE and urticaria and that the risk of SLE significantly increased with the number of hospital visits, particularly in female patients and adolescent patients.

In most cases, the cause of urticaria is not clear. Infection is a common etiological factor of acute urticaria, especially viral infection in children.[19] Because the most commonly identified cause is a recent infection, we examined whether infection-caused urticaria may affect the risk of SLE. The data reveal that infection-caused urticaria was relatively common in patients with SLE compared with the control group; however, logistic regression analysis indicated that the presence of infection as a trigger for urticaria was not associated with different risks of SLE. This finding implies that regardless of etiology, manifestation of urticarial disease may be independently associated with the risk of SLE.

Approximately 20%-30% of young children with acute urticaria are at risk of chronic or recurrent urticaria.[20,21] Chronic urticaria may occur at SLE onset and is associated with moderate or severe SLE activity.[22] Furthermore, chronic urticaria may be the first manifestation of SLE. We investigated whether acute or chronic urticaria was associated with the risk of SLE. Our data show that urticaria of either type was associated with the risk of SLE, but the risk was higher with chronic urticaria. Although acute urticaria is often self-limiting, we found that it may still be associated with SLE; this result is in accordance with a previous report that acute urticaria may be the first or early manifestation of SLE.[23]

Subgroup analyses of urticaria patients stratified by sex and age revealed that female patients and adolescent patients (13-18 years) were more strongly associated with the risk of SLE than male patients and younger age-groups. This result emphasizes the importance of managing and following up urticaria because most children with SLE are girls or adolescents.

Several studies have demonstrated a significant relationship between atopic diseases and the risk of SLE. Our data support the results that atopic dermatitis may be the comorbid disorders associated with SLE.[24] Additionally, our results show that some autoimmune or autoinflammatory diseases may have a close association with SLE, which has been reported by several studies.[25-27] However, even after adjustment for these comorbidities, a higher risk of SLE was significantly associated with a history of urticaria.

A recent study revealed a similarity between the pathogenesis of urticaria and SLE, with both conditions being closely linked to inflammation and autoimmunity.[28] Confino-Cohen et al[29] showed that patients with chronic urticaria had an increased risk of SLE, and a pathogenic mechanism was implied by the high prevalence of autoantibodies and may be autoimmune in origin. Our study suggests that clinicians should be aware that urticaria may be an early feature of SLE, even in the absence of SLE-specific serologic markers. These results have important implications for clinicians managing childhood urticaria for early diagnosis of a possible juvenile lupus disorder.

The strengths of this study are that it applied a nationwide population-based design involving a large group of pediatric SLE patients from the NHIRD and that it adjusted for atopy, autoimmune, and autoinflammatory diseases as comorbidities. However, the study has some limitations. Because of the retrospective design, some patients may have urticarial vasculitis or inducible urticaria, which could not be excluded. In addition, the association between the presence of urticaria and activity of SLE was not evaluated.

In conclusion, clinically diagnosed urticaria was closely associated with the risk of childhood SLE and may be the initial lupus manifestation, particularly in female patients and adolescents. Clinicians must further examine or follow up children and adolescents with cutaneous urticarial lesions for early detection of juvenile lupus disease.

CONFLICT OF INTEREST

The authors have no conflicts of interest relevant to this article.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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