ORIGINAL ARTICLE

Relationship Between Atopic Dermatitis and Wheeze in the First Year of Life: Analysis of a Prospective Cohort of Thai Children

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Abstract

Background: Patients with atopic dermatitis show increased risk of concomitant respiratory symptoms such as wheeze and cough. However, limited data is available on respiratory symptoms in atopic dermatitis patients when the disease is in remission.
Objective: The aim of this study was to investigate the relationship between atopic dermatitis and wheeze during periods of active disease and remission of atopic dermatitis.
Methods: The study formed part of the Prospective Cohort Study of Thai Children (PCTC) involving children born during the period October 2000 to September 2002. The principal caregiver in each family was identified and interviewed about socioeconomic factors, paternal health, and exposure to tobacco smoke. Data on wheeze and atopic dermatitis were collected from questionnaires administered at 6 and 12 months after birth.
Results: Of the 4245 live births included in the PCTC cohort, 4021 (94.7%) participated in the follow-up survey at age 6 months and 12 months. The prevalence of wheeze and eczema were 13.8% and 7.4%, respectively. There was also a significant association between current atopic dermatitis and wheeze in the same period (P <.01). However, no significant association was observed between previous atopic dermatitis and wheeze when atopic dermatitis was in remission.
Conclusion: There is a significant increase in the risk of wheeze in infants with current atopic dermatitis but not in those in whom the disease is in remission.

Key words: Atopic dermatitis. Wheeze. Infants.

Resumen

Antecedentes: Los pacientes con dermatitis atópica presentan un mayor riesgo de padecer síntomas respiratorios concomitantes como sibilancias y tos. No obstante, existen pocos datos disponibles sobre los síntomas respiratorios en los pacientes con dermatitis atópica, cuando la enfermedad está en remisión.
Objetivo: El propósito del estudio fue investigar la relación entre la dermatitis atópica y las sibilancias durante los periodos activos de la enfermedad y en la fase de remisión de la misma.
Métodos: El estudio formaba parte del estudio de cohortes prospectivo de niños tailandeses (PCTC) en el que participaron niños nacidos durante el mes de octubre de 2000 y septiembre de 2002. Se identificó a la persona responsable del cuidado de la familia y se la entrevistó sobre factores socioeconómicos, salud de los progenitores y exposición al humo de tabaco. Los datos sobre sibilancias y dermatitis atópica se recogieron a partir de cuestionarios realizados a los 6 y 12 meses de edad.
Resultados: De los 4.245 nacimientos vivos incluidos en el cohorte PCTC, 4.021 (94,7%) participaron en la encuesta de seguimiento a los 6 meses y a los 12 meses. La prevalencia de sibilancias y de eccema fue de un 13,8% y de un 7,4%, respectivamente. También se observó una relación significativa entre la dermatitis atópica actual y las sibilancias en el mismo periodo (P < 0,01). No obstante, no se observó una relación significativa entre la dermatitis atópica previa y las sibilancias, cuando la primera estaba en fase de remisión.
Conclusión: Existe un aumento significativo del riesgo de sibilancias en los lactantes con dermatitis atópica activa, pero no en aquellos en que la enfermedad está en remisión.

Palabras clave: Dermatitis atópica. Sibilancias. Lactantes.

Introduction

Atopic dermatitis is a chronic inflammatory skin disease occurring in young children, and in affected individuals, 80% of cases have an onset during the first year of life [1]. The major features include pruritus and the lesions display a characteristic morphology and distribution. In infancy, the face and extensor surfaces of the arms and legs are most commonly affected [2]. Patients with atopic dermatitis have an increased risk of respiratory symptoms such as wheeze and cough [3]. Eosinophilic airway inflammation and bronchial hyperresponsiveness have been observed in patients with atopic dermatitis [4]. One study showed that 43.2% of children with manifestation of atopic dermatitis in the first 2 years of life were in complete remission after their second birthday [5]. However, little data is available on respiratory symptoms in patients with atopic dermatitis when the disease is in remission.

The Prospective Cohort of Thai Children (PCTC) is a birth cohort study, making it suitable for examining the natural history of chronic problems in childhood such as atopic dermatitis and wheeze. The aim of this study, as part of the PCTC, was to investigate the relationship between atopic dermatitis and wheeze during periods of active disease and remission of atopic dermatitis.

Material and Methods

The PCTC is an observational, community-based study designed to follow different regional birth cohorts. There were 5 study sites located in different parts of the country: north, northeast, south, and central regions and Bangkok. Birth cohorts from the first 4 sites comprise a mixture of rural, semiurban, and urban communities, whereas the Bangkok cohort is a metropolitan hospital-based birth cohort. For each site, a district was selected for cohort recruitment, except in Bangkok, where the cohort was based on births in a single university teaching hospital.

Samples

From the 4 selected districts, all resident pregnant women intending to live in the study area for at least 5 years were recruited. Well-established networks of village health volunteers were employed to identify expecting mothers during the recruitment period. It was estimated that 90% of eligible mothers were included. In Bangkok, the women attending the antenatal clinic in their third trimester were recruited. Each birth cohort included births over a 1-year period. Starting dates for each cohort were staggered to spread enrollments over a 2-year period, meaning that the babies were born between October 15, 2000 and September 14, 2002.

Ethics

The National Ethics Committee of the Thai Ministry of Public Health approved the study. After explaining the study to the registered families, each family was invited to participate. Verbal permission was initially obtained followed by written informed consent.

Variables and Data Collection

The main caregiver was identified in each family and interviewed at the time of birth about socioeconomic factors, paternal health, and exposure to tobacco smoke. Data on wheeze and atopic dermatitis were collected from questionnaires administered at 6 and 12 months after birth. Identical questions were asked for both study periods. The questions were 1) "Has your baby had wheezing with whistling on his/her chest when he/she breathes in the past 6 months?", 2) "Has the baby had rashes on his/her body that look like the rash in these pictures in the past 6 months?", and 3) "Was the rash recurrent?". Atopic dermatitis was considered if a positive answer was obtained for questions 2 and 3.

Statistical Analysis

Data on categorical variables were expressed as percentages. Associations between atopic dermatitis and wheeze were assessed by logistic regression analysis. Significant effects of the explanatory variables were assessed using the likelihood ratio test. The analyses were performed using R software (The R Foundation for Statistical Computing). Statistical significance was established at $P < .05$

Results

Of the 4245 live births included in the PCTC cohort, 4021 (94.7%) participated in the follow-up survey at age 6 months and 12 months. The demographic characteristics of study subjects including missing data are shown in Table 1. For various reasons, such as the main caregiver not being a parent or because the family moved from the area, background information could not be completed for some of the variables. The rate of missing information was less than 7%, with the exception of the allergy history of the father.

The prevalence of wheeze was slightly higher than that of eczema in the first 6 months. While eczema decreased over time, wheeze increased by more than 20% between 6 months and 12 months (Table 2).

Table 3 shows the prevalence of wheeze according to atopic dermatitis status of the infants. When children were compared within the same period, the prevalence of wheeze was higher in children with atopic dermatitis than those without. The prevalence of wheeze increased over time except in children who had previous atopic dermatitis in the first 6 months of life. In that group, the prevalence of wheeze in the second 6 months of life was lower when atopic dermatitis was absent.

Table 4 shows the odds ratio for wheeze at age 0 to 6 and 6 to 12 months. The risk of wheeze increased significantly in boys, infants exposed to tobacco smoke, and those with atopic dermatitis during the same period. The odds ratio between atopic dermatitis and wheeze in the first 6 months was higher than that in the second 6 months of life.

Table 1. Characteristics of the Study Population in the First Year of Life (n = 4245)*

Sex	
Male	2112 (49.75)
Female	2133 (50.25)
Mother's education	
Female	2222 (52.34)
6-12 years	1554 (36.61)
>12 years	429 (10.11)
Missing	40 (0.94)
Family history of allergy	
Mother	
No	3689 (86.90)
Yes	268 (6.31)
Missing	288 (6.79)
Father	
No	3146 (74.11)
Yes	215 (5.07)
Missing	884 (20.82)
Exposure to tobacco smoke	
No	2172 (51.17)
Yes	1914 (45.09)
Missing	159 (3.74)
Wheezing	
No	3437 (80.97)
Yes	586 (13.80)
Missing	222 (5.23)
Eczema	
No	3715 (87.52)
Yes	313 (7.37)
Missing	217 (5.11)

*Data are shown as numbers (%)

Discussion

The results of this study showed that the prevalence of atopic dermatitis decreased with age whereas that of wheeze increased. We found a significant association between current atopic dermatitis and wheeze, but this association declined when atopic dermatitis was in remission. Multivariate analysis revealed that the correlation between the prevalence of atopic dermatitis and wheeze was stronger in the first 6 months than in the second 6 months of life

Our finding of decreasing prevalence of atopic dermatitis with age is consistent with that of a large population-based study undertaken in the United Kingdom, the Avon Longitudinal Study of Pregnancy and Childhood, which reported the prevalence of atopic dermatitis as 21.0%, 11.2%, and 3.8% at 0-6, 6-18, and 18-30 months of age, respectively [6]. An increase in period prevalence of wheeze in older children has been reported in many studies. Tariq et al [7] found an increase in the period prevalence of asthma from 8.7% in infancy to 14.9% at 4 years of age in a birth cohort of 1218 children. Luyt et al [8] reported an increase in the prevalence of wheeze in 1650 children (7.5% in children under 1 year compared with 15.9% in children of 4 years and over; $P < .001$). The inverse relationship between the prevalence of atopic dermatitis and that of wheeze with increasing age resulted in a progressively weaker correlation between the diseases over time. The reduced correlation also suggests that there was a reduction in the similarity of the etiology between atopic dermatitis and wheeze. Infantile eczema is usually associated with food allergy, which always declines with age [9,10], while wheeze in infants corresponds to a heterogeneous group of disorders [11].

We found a significant association between atopic dermatitis and wheeze only when considered within the same 6-month period. Many hospital-based studies have shown that children with atopic dermatitis have a high prevalence of bronchial hyperresponsiveness [4,12]. This may be explained by the correlation between IgE level, eczematous symptoms, and bronchial hyperresponsiveness. Children with visible dermatitis have higher IgE concentrations [13] and children with high IgE concentrations have been shown to develop bronchial hyperresponsiveness [14]. Thus, the increased risk of wheeze in children with atopic dermatitis may involve IgE-mediated events.

The strength of the present study lies in the large sample size, minimal loss to follow-up, and prospective design. However, one drawback is that objective measures of disease activity such as pulmonary function and bronchial challenge

Table 2. Prevalence of Atopic Dermatitis and Wheeze in the First Year of Life

Age	Atopic Dermatitis		Wheeze	
	No.	%	No.	%
0-6 months	197/4086	4.82	297/4078	7.28
6-12 months	148/4085	3.62	385/4087	9.42

Table 3. Prevalence of Wheeze According to Atopic Dermatitis Status

Atopic Dermatitis		Prevalence of Wheeze			
Age 0-6 Months	Age 6-12 Months	Age 0-6 Months		Age 6-12 Months	
		No.	%	No.	%
Absent	Absent	256/3709	6.9	333/3715	8.96
Present	Absent	23/166	13.86	19/167	11.38
Absent	Present	9/118	7.63	20/118	16.98
Present	Present	3/28	10.71	4/28	14.29

Table 4. Multiple Logistic Regression for Wheeze at 0 to 6 and 6 to12 Months*

Variables	Odds Ratio for Wheeze (95% CI)	
	Age 0-6 Months	Age 6-12 Months
Atopic dermatitis		
None	1	1
0-6 months	2.13 (1.34 − 3.38)	1.27 (0.78 − 2.09)
6-12 months	1.04 (0.52 − 2.08)	1.96 (1.19 − 3.22)
Both periods	1.54 (0.46 − 5.17)	1.59 (0.54 − 4.65)
Female	0.65 (0.51 − 0.83)	0.57 (0.46 − 0.71)
Expose to tobacco smoke	1.48 (1.15 − 1.90)	1.38 (1.10 − 1.72)
Mother's education		
Primary	1	1
Secondary	1.01 (0.78 − 1.31)	0.87 (0.69 − 1.10)
University	0.72 (0.44 − 1.17)	0.59 (0.37 − 0.92)
Family history of allergy		
Mother	1.02 (0.95 − 1.09)	0.99 (0.94 − 1.04)
Father	1.01 (0.97 − 1.05)	0.99 (0.96 − 1.02)

*CI indicates confidence interval.

test are not feasible in this age group, and different parents or guardians might perceive and interpret the question and pictures provided differently, leading to a misclassification of outcome measures. We minimized this bias through the use of the standard question for wheeze taken from the ISAAC questionnaire and pictures of rashes to identify atopic dermatitis rather than the use of questions. This misclassification bias is likely to be nondifferential, leading to reduction in the level of association. Although our study was prone to misclassification bias, we could nevertheless demonstrate a significant association between atopic dermatitis and wheeze. Consequently, we can conclude that in this cohort current atopic dermatitis was associated with a significant risk of wheeze in infants.

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