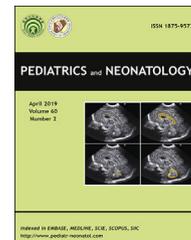




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Original Article

The prevalence and risk factors of atopic dermatitis in 6–8 year-old first graders in Taipei



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Key Words

Atopic dermatitis;
Environmental risk factors;
First graders

Abstract *Background:* Despite the advance in the understanding of etiology, pathophysiology and diagnosis of atopic dermatitis (AD), its prevalence has increased annually in Taiwan.

Purposes: The purpose of this study is to explore the prevalence, and personal and environmental risk factors of AD.

Methods: A cross-sectional survey was conducted via health centers of elementary schools in Taipei city. We used the Chinese version of ISAAC questionnaire to examine possible personal and environmental risk factors of AD. Questionnaires were completed by parents or guardians of first graders (6–8 year-old) who agreed to participate in this study. Logistic regression was conducted to examine possible personal and environmental factors related to AD (in early life and currently).

Results: The 12-month prevalence of AD (in the past 12 months) was 10.7% (2683/24,999) among 6- to 8-year-old first graders in Taipei. Forty-five percent of first graders with AD had their first episode of AD symptoms before the age of two. Children with asthma history were 1.65 times (95% CI: 1.51–1.79, $p < 0.001$) and children with rhinitis were 2.57 times (95% CI: 2.34–2.84, $p < 0.001$) more likely to have AD than those without the conditions. Compare to their counterparts, children who used antibiotics during their first year of life (OR = 1.37, 95% CI: 1.22–1.53, $p < 0.001$) and who had bronchiolitis before the age of two (OR = 1.47, 95% CI: 1.33–1.63, $p < 0.001$) had a higher chance to have AD during the last 12 months of the study. However, receiving breastfeeding for less than 4 months (OR = 0.75, 95% CI: 0.67–0.83, $p < 0.001$) and having older siblings (OR = 0.83, 95% CI: 0.76–0.92, $p < 0.001$) had 25% and 17% reduced risks for AD in the 12 months before this study, respectively.

Conclusion: Our study verified personal and environmental risk factors of AD in children in Taiwan. Based on the results, we propose that avoiding bronchiolitis before the age of two,

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using antibiotics properly in babies, and providing diet counseling for breastfeeding mothers may be good prevention strategies of AD.

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1. Introduction

Atopic dermatitis (AD) is the most common, chronic, itchy and relapsing inflammatory skin disease in children,¹ and it has a considerable amount of impact on family stress and economic burden.^{2–4} The onset of AD is relatively early in life, affecting over 20% of children.⁵ The prevalence of AD for children has increased worldwide over the past decade. In Taiwan, it increased from 1.10% in 1987 to 6.7% in 2007, and it was highest (22.4%) in the age group below 20 years old.^{6,7} To investigate the etiological factors of AD is the first step in the prevention and treatment of the problem because the mechanisms of AD are multifactorial, including personal and known environmental factors, which can lead to sensitization and later development of atopy. Most of the sensitization is directed first against food allergens and subsequently environmental allergens. The environmental factors had a stronger influence in the youngest age group and could help in the determination of effective intervention measures. A number of studies considered the personal and environmental factors of AD. However, most studies in Taiwan only paid attention to the prevalence of AD, and few large studies explored the risk factors and multiple environmental interaction of AD.

Therefore, this study aimed to explore the relationship between personal and environmental risk factors for 6- to 8-year-old school-aged children with AD in Taipei, Taiwan. The results of this study will aid in planning important policy-related prevention strategies for early intervention and treatment of AD.

2. Methods

This study method was based on questionnaires including a brief description of symptoms and signs of AD. The study was approved by the Institution Review Board of Taipei City Hospital (TCHIRB-961,007-E). The questionnaires were filled out by parents or guardians of first graders in elementary schools, after obtaining their written informed consent. The subjects were enrolled from 6- to 8-year-old children of 153 primary schools in Taipei in the period 2007 to 2008. The parents were not directly asked whether their children had AD. Instead, they were first presented with a brief description of typical signs and symptoms of those allergic diseases and then asked to fill out the questionnaires. To analyze these issues, we used questionnaires modified from the International Study of Asthma and Allergy in Childhood (ISAAC) questionnaire to evaluate the prevalence and risk factors of childhood AD in Taipei. No eligible children were excluded from the sample. Children

with incomplete data for analysis were excluded from the study. The children were as coded as positive for AD if the answers of the following questions were “yes”: “Has your child ever had an itchy rash which was coming and going for at least six months?” and “Has your child had this itchy rash at any time in the last 12 months?” Otherwise, they were coded as negative.

Questionnaires were used to provide a framework for further etiological research into personal and environmental factors affecting AD. Personal factors included gender, weight status, type of delivery, antibiotic use in the first year of life, bronchiolitis before two years old, birth weight, older siblings, younger siblings, breastfeeding, time of introducing solid food, asthma history, and rhinitis history. Details of environmental factors included having cat or dog in the first year of life or the last 12 months, as well as contact with farm animals in the first year of life. Seventeen independent variables in personal factors and environmental factors were included individually into the univariate Logistic regression analysis, and they were used to estimate odds ratios (OR) and 95% confidence intervals (CIs) for the association between personal factors, environmental factors and AD symptoms within a year. A p value < 0.05 was set to determine significance. Univariate influence was explored by comparing a logistic regression model that contains only one independent variable and one dependent variable. Next, the significant univariate relative to AD was put into multivariate consideration. Multiple regression models were used to determine whether outcome variable (AD) was associated with the significant variables. All statistical analyses were performed with SPSS version 22.0.

3. Results

The study subjects included 6- to 8-year-old children, and the questionnaires with incomplete data for analysis were excluded from the sample. A total of 24,999 subjects from 153 primary schools were included in this study, yielding a response rate of 94.6%. [Table 1](#) demonstrates the relationship between personal factors, environmental factors and AD symptoms within a year by using univariate and multivariate logistic regression analysis. Risk factors of AD required from 15 variables in the univariate logistic regression included the following: male gender, antibiotics use in the first year of life, bronchiolitis before the age of two, contact with dogs in the first year of life, exposure to farm animals in the first year of life, no older siblings, presence of younger siblings, breastfeeding more than 4 months, and introduction of solid food after 4 months. The overall prevalence of AD in the previous 12 months was 10.7% (2683/24,999), with male ($n = 1448$)

Table 1 The relationship between personal factors, environmental factors and AD symptoms in the past one year of life.

Variables (missing, %)	AD (<i>n</i> = 2683)		NO AD (<i>n</i> = 22,316)		Univariate		Multivariate (<i>n</i> = 21,255)	
	<i>n</i>	%	<i>N</i>	%	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>
Gender (24, 0.1%)								
Males	1448	(11.2)	11,467	(88.8)	1.11 (1.02–1.20)	0.012	1.05 (0.97–1.15)	0.237
Females	1234	(10.2)	10,826	(89.8)	1		1	
Weight status (4292, 17.2%)								
Overweight/obesity	516	(12.1)	3759	(87.9)	1.10 (0.99–1.22)	0.082		
Underweight/normal	1828	(11.1)	14,604	(88.9)	1			
Type of delivery (858, 3.4%)								
C/S	925	(10.7)	7684	(89.3)	0.97 (0.89–1.06)	0.507		
NSD	1712	(11.0)	13,820	(89.0)	1			
Antibiotic used in 1st year of life (1091, 4.4%)								
Yes	562	(15.2)	3129	(84.8)	1.58 (1.43–1.75)	<0.001	1.37 (1.22–1.53)	<0.001
No (including unknown)	2063	(10.2)	18,154	(89.8)	1		1	
Bronchiolitis before the age of two (1094, 4.4%)								
Yes	728	(15.2)	4053	(84.8)	1.65 (1.51–1.81)	<0.001	1.47 (1.33–1.63)	<0.001
No (including unknown)	1877	(9.8)	17,247	(90.2)	1		1	
Cats in 1st year of life (592, 2.4%)								
Yes	69	(12.6)	479	(87.4)	1.18 (0.91–1.52)	0.206		
No	2597	(10.9)	21,262	(89.1)	1			
Cats within one year (597, 2.4%)								
Yes	70	(11.0)	568	(89.0)	1.01 (0.78–1.29)	0.967		
No	2595	(10.9)	21,169	(89.1)	1			
Dogs in the first year of life (594, 2.4%)								
Yes	367	(12.2)	2639	(87.8)	1.15 (1.02–1.30)	0.018	1.04 (0.92–1.19)	0.513
No	2304	(10.8)	19,095	(89.2)	1		1	
Dogs within one year (596, 2.4%)								
Yes	260	(10.2)	2277	(89.8)	0.92 (0.81–1.06)	0.249		
No	2406	(11.0)	19,460	(89.0)	1			
Farm animals in the first year of life (598, 2.4%)								
Yes	78	(13.5)	498	(86.5)	1.28 (1.01–1.64)	0.043	1.20 (0.92–1.55)	0.180
No	2591	(10.9)	21,234	(89.1)	1		1	
Birth weight (2748, 11.0%)								
Underweight (<2500 g)	161	(10.2)	1421	(89.8)	0.89 (0.75–1.06)	0.181		
Normal (≥2500 g)	2331	(11.3)	18,338	(88.7)	1			
Older siblings (703, 2.8%)								
Yes	1182	(10.0)	10,657	(90.0)	0.83 (0.76–0.90)	<0.001	0.83 (0.76–0.92)	<0.001
No	1470	(11.8)	10,987	(88.2)	1		1	
Younger siblings (703, 2.8%)								
Yes	1006	(11.5)	7713	(88.5)	1.10 (1.02–1.20)	0.020	0.99 (0.90–1.10)	0.916
No	1646	(10.6)	13,931	(89.4)	1		1	
Breastfeeding (419, 1.7%)								
<4 months (including none)	2059	(10.2)	18,176	(89.8)	0.71 (0.65–0.78)	<0.001	0.75 (0.67–0.83)	<0.001
≥4 months	597	(13.7)	3748	(86.3)	1		1	
Time of introducing solid food after life (2561, 10.2%)								
<4 months (including none)	886	(10.6)	7483	(89.4)	0.91 (0.83–0.99)	0.033	0.93 (0.85–1.01)	0.092
≥4 months	1620	(11.5)	12,449	(88.5)	1		1	

and female patients (*n* = 1234) being accounting for 11.2% and 10.2%, respectively. The prevalence of AD in those who used antibiotics in the first year of life (*n* = 3691) was 15.2% (*n* = 562). With bronchiolitis before the age of two, 728 patients accounted for 15.2% of the total subjects answering “yes.” 367 patients (12.2%) had dogs at home in the first year of life. For regular contact with farm animals in the first year of life, 78 patients

accounted for 13.5% of the subjects answering “yes.” 1182 patients (10%) had older siblings. The patients with younger siblings were 1066 (11.5%). About 10.2% (*n* = 2059) of first graders who were breastfeeding for less than 4 months developed AD in the last 12 months. 10.6% (*n* = 886) of first graders who answered “introducing solid food after life less than 4 months” also developed AD in the previous 12 months.

Table 2 The relationship between genetic predisposition of atopy and AD symptoms in the past one year of life.

Variables (missing, %)	AD (n = 2683)		No AD (n = 22,316)		Univariate		Multivariate (n = 24,999)	
	n	%	n	%	OR (95% CI)	P	OR (95% CI)	P
Asthma history (0, 0.0%)								
Yes	1380	(15.9)	7304	(84.1)	2.18 (2.01–2.36)	<0.001	1.65 (1.51–1.79)	<0.001
No	1303	(8.0)	15,012	(92.0)	1		1	
Allergic rhinitis history (0, 0.0%)								
Yes	2041	(15.1)	11,453	(84.9)	3.02 (2.75–3.31)	<0.001	2.57 (2.34–2.84)	<0.001
No	642	(5.6)	10,863	(94.4)	1		1	

Nine significant factors were identified in the univariate analysis. To reduce significant variables of univariate model, we put these into the multivariate logistic regression analysis to verify the risk factors. The results showed significant factors in the multivariate model included antibiotics use in the first year of life (OR = 1.37, 95% CI: 1.22–1.53, $p < 0.001$), and bronchiolitis before the age of two (OR = 1.47, 95% CI: 1.33–1.63, $p < 0.001$). Compared to their counterparts, these factors had a higher chance to be associated with AD occurrence during the 12 months before the study. However, receiving breastfeeding for less than 4 months (OR = 0.75, 95% CI: 0.67–0.83, $p < 0.001$) and having older siblings (OR = 0.83, 95% CI: 0.76–0.92, $p < 0.001$) had 25% and 17% reduced risk for AD, respectively. Table 2 lists the results for the relations between endogenous variables and AD. Children with asthma history were 1.65 times (95% CI: 1.51–1.79, $p < 0.001$), and children with rhinitis were 2.75 times (95% CI: 2.34–2.84, $p < 0.001$) chance more likely to have AD than those who without the conditions.

4. Discussion

One study reported that the 12-month prevalence of AD was 1.10% in 1987, 1.88% in 1994, and 3.35% in 2002 for schoolchildren in Taichung, Taiwan.⁸ In 1992, the International Study of Asthma and Allergies in Childhood (ISAAC) was developed to gain insight into the epidemiology of allergic diseases. ISAAC is a standardized methodology and practical tool for use in different countries and languages to measure the prevalence and severity of atopic diseases in various populations. Some studies have used ISAAC questionnaires to analyze the prevalence of AD in Taiwan. In addition, another recent study, following up from age 2–6 years, reported that 7.2% of children in the 1998 birth cohort had AD, and 10.0% of children in the 2003 birth cohort had AD.⁹ In Changhua County, the prevalence of AD was 18.0% in 2002.¹⁰ In central Taiwan, the overall cumulative and 12-month prevalence of dermatitis was 7.2% in 2003.¹¹ The claims data of a nationally representative cohort of 997,729 enrolled from the National Health Insurance in Taiwan from 2000 to 2007 revealed that the overall 8-year prevalence of AD was 6.7%.⁷ The prevalence of AD (in the last 12 months) in our study was 10.7% (2683/24,999) among first graders in Taipei in 2007–2008. In summary, the above studies indicate the prevalence for children has

increased from 1.1% to 10.7% over the past decades in Taiwan.

The result of our study found an increased risk of AD from the use of antibiotics in the first year of life. It is consistent with findings from some studies.^{12–14} One study described the complex relationship between early exposure to infections, anti-infectious treatment with antibiotics, and incident AD. The risk ratio (RR) of children with early respiratory tract infections treated with macrolides or cephalosporines significantly increased the risk for AD.¹² Another study identified 17 studies and found an overall risk increase of 41% for AD in those who received at least one course of antibiotics in early life. In addition, there was a 7% increase in AD risk with each additional course of antibiotics during the first year of life. Antibiotics are usually prescribed to infants because of infections, which means that exposure to infections may result in the risk of incident AD.¹³ From nine systematic reviews, one paper provided a summary of key findings on AD from January 2012 to December 2013, suggesting that antibiotic exposure in early life was associated with increased incidence of AD.¹⁴ However, 54.0% of children received at least one course of antibiotics, mainly for acute respiratory illnesses (ARI), and 23% of ARI were treated with antibiotics.¹⁵ The antibiotic prescription rate varied between countries, ranging from 0.2 to 1.3 prescriptions per infant per year.¹⁶ Antibiotics may have an influence on the prevalence of allergic diseases through two pathways: antibiotics may remove some protective effect against allergies and the antibiotic effect on the commensal bowel may alter gut flora in atopic subjects.^{17–20} Therefore, antibiotics use in early life has a higher proportion, and reducing antibiotics use during early life is a feasible method to prevent from AD.

Bronchiolitis is the most common reason for hospitalization during infancy, being a burden for the child and family, and bearing huge costs for the healthcare systems.²¹ In Taiwan, 34.4% of children with bronchiolitis had asthma-like symptoms after joining a kindergarten.²² Although few studies put bronchiolitis into the risk factors to evaluate for AD, we considered it as a risk for AD and analyzed the relationship between AD and bronchiolitis before the age of two. The result showed that children with bronchiolitis before the age of two suffered from AD more frequently than those without bronchiolitis. The result was similar regarding bronchiolitis and asthma. For example, one study reported bronchiolitis had received particular attention as it had been suggested that an episode of

bronchiolitis in the first two years of life caused subsequent lower respiratory morbidity and that bronchiolitis identified those infants predisposed to develop asthma.²³

Since breast milk has an immunomodulatory effect that enhances the immune system and defends infants from infection, most mothers exclusively breast-feed children. However, some studies reported a different effect of breastfeeding on AD. One study indicated that children exclusively breast-fed for four months or more exhibited less AD.²⁴ One study indicated no evidence that exclusive breastfeeding for 4 months or longer protected against AD.²⁵ A meta-analysis found that exclusive breastfeeding for at least 4 months can reduce the incidence of AD in infants.²⁶ However, the results in our study are not consistent with the studies above. Receiving breastfeeding for less than 4 months had a reverse relation with AD in this study. One new study in Taiwan had the same result, also finding that increased duration of breastfeeding could increase AD risk.²⁷ The reason could be the effect of the breastfeeding policy on food limitation of mother's diet. Hence, some mothers eat foods which trigger allergic reaction and transfer it to infants. It is important to explore the role of maternal diet additives through breast-milk and how this can have impact on the infant's developing immune system. It is worth noting that the American Academy of Pediatrics suggests that breastfeeding mothers with infants at high risk of developing AD should avoid peanuts and tree nuts, and they should consider eliminating eggs, cow's milk, and fish from their diets.²⁸

The results of some studies analyzing the relationship between siblings and AD are different from ours. One study showed a significant risk factor of AD was a sibling with AD,²⁹ but our study exhibited a reverse relation between AD and children with older siblings. One study reviewed 53 different studies to examine the "protective" effects of having a higher number of siblings for the risk of asthma and allergy, revealing 9 of 11 studies reported an inverse relation with number of siblings for AD.³⁰ Another reported that two German cohort studies found no protective effect of elder siblings on eczema development.³¹ This study suggests a sibling is a protective factor against AD due to higher exposure to infections in early life. However, one study reported only 3.9% of children had at least three siblings in Taiwan,²² and the country's lower birth rate will likely persist. Therefore, creating a suitable environment for children in Taiwan which included outdoor activities is necessary to reduce AD.

Children with asthma history or allergic rhinitis were more likely to have AD in our study, and this is consistent with other studies.^{32–34} One study analyzing the claims data of a nationally representative cohort of 997,729 enrollees from the National Health Insurance from 2000 to 2007 reported the prevalences of AD, allergic rhinitis, and asthma in Taiwan.⁷ Overall, 66,446 (6.7%) patients were diagnosed with AD, and 49.8% of them had concomitant allergic rhinitis and/or asthma. Children with AD are at high risk of developing asthma and allergic rhinitis, and which is called the atopic march. Therefore, children with asthma history or allergic rhinitis have a higher chance to have AD. Therefore, early management for AD to prevent the development of the atopic march is of critical importance.

This study has several strengths, including a large sample size, a high response rate, the risk factors and the

multiple environment interaction of AD to be explored in Taiwan, and the inclusion of children from all districts in the Taipei metropolitan area. However, this study has some potential limitations. Firstly, it was based on reported symptoms that we did not confirm by clinical examination. Secondly, we did not detail items to explore the mechanism of the risk of AD, including an item for the situation of mother's diet and infant formula. However, we can use this result to design the appropriate questionnaire to explore more detailed risk factors of AD.

Increasing prevalence and severity of AD have considerable social and economic burdens on patients, families, and societies. Clarification of early environmental effects and personal factors for AD will provide a better caring strategy for predicting and preventing AD earlier. Parents and schoolteachers need to understand the risk factors at home and school in order to teach children about AD and how to avoid risk factors and to adapt to living with their difficulty.

Conflicts of interest

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

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