

Analysis of the Prevalence of and Risk Factors for Atopic Dermatitis Using an ISAAC Questionnaire in 8,750 Korean Children

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Key Words

Atopic dermatitis · Prevalence · Risk factors · Epidemiology · International Study of Asthma and Allergies in Childhood

Abstract

Background: Since 1995, epidemiologic studies of atopic disorders using the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire have been performed in many countries, including the Republic of Korea. The prevalence, burden and risk factors of atopic dermatitis were surveyed in these studies, which helped to enhance their comparability among different areas and age groups, as well as to clarify the nature of atopic dermatitis and other atopic disorders. **Methods:** From 21 facilities, 8,750 children were enrolled in this cross-sectional study. The data were collected via the Internet using a questionnaire based on the Korean-language version of the ISAAC study format. **Results:** The prevalence of atopic dermatitis over the previous 12 months was 14.4%. The prevalence in preschool children was significantly higher than in elementary school children. Family history of atopic diseases, diagnosis of allergic conjunctivitis and diagnosis of food allergy were positively as-

sociated with atopic dermatitis in both preschool and elementary school children. In addition, raising pets was positively associated with atopic dermatitis in preschool children. In elementary school children, female gender, secondhand smoking, breastfeeding, changing the parents' house to a newly built one during the first year of life, diagnosis of asthma and diagnosis of allergic rhinitis were positively associated with atopic dermatitis. **Conclusion:** The prevalence of atopic dermatitis in preschool and elementary school children in Korea is similar to that of children in other developing countries. The risk factors for atopic dermatitis are different in preschool and elementary school children. More detailed strategies will be necessary to reduce atopic dermatitis in both age groups.

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Introduction

Atopic dermatitis is a chronic inflammatory skin disease that has shown a global increase over the past few decades [1]. The precise pathomechanism of atopic dermatitis is still unknown, but genetic, environmental and

immunologic factors have been suggested. Therefore, epidemiologic studies are important to provide insight into atopic dermatitis by comparing the prevalence, geographic differences, risks and protective factors of each subject group.

Since 1995, the International Study of Asthma and Allergies in Childhood (ISAAC) has provided a cornerstone for standardized epidemiologic studies of atopic disorders, such as allergic rhinitis, asthma and atopic dermatitis [2]. The ISAAC questionnaire was developed, and an ISAAC phase one study was conducted in 56 countries worldwide, providing comparability and knowledge in studies of atopic dermatitis [1].

In the Republic of Korea, several epidemiologic studies have been performed since 1995 using the Korean-language version of the ISAAC questionnaire [3–7]. This was the first study comparing preschool and elementary school children in the Republic of Korea.

Materials and Methods

Study Population and Design

This cross-sectional study was conducted with an Atopy-Free Seoul Project foundation grant, provided by the Metropolis of Seoul in 2009. The target population consisted of preschool children (aged from 0 to 6 years) and elementary school children (aged from 7 to 12 years) in atopy-free schools in Seoul, which include kindergartens, day-care centers and elementary schools that are given support by the Seoul municipal government regarding education and the management of atopic disorders. In Seoul, a total of 83 day-care centers and primary schools participated in this project in 2009. Among these institutions, 21 facilities that agreed to participate in the survey were enrolled in this study. At the point that this Internet-based investigation began, 21 of the 83 facilities wanted to join and were enrolled in the study.

Data Collection

The survey was conducted from June to October 2009. Data were collected on the Internet (<http://www.atopyinfocenter.co.kr>). A questionnaire was created based on the Korean-language version of the ISAAC study format to obtain information on the demographic characteristics, family factors, environmental factors and status of atopic diseases. The questionnaire was answered by the subject's parents, from whom informed consent was obtained prior to completing the questionnaire. Of the 10,431 subjects enrolled, 8,780 completed the questionnaire (representing a response rate of 84.2%). Of these, 30 subjects who incorrectly completed the questionnaire (e.g. any missing values) were excluded. Therefore, a total of 8,750 children were finally enrolled in this study.

Prevalence of Atopic Disorders

The prevalence of atopic disorders over the previous 12 months was obtained based on the ISAAC criteria. Atopic dermatitis was

Table 1. General characteristics

Variables		n	%
Sex	male	4,377	50.0
	female	4,373	50.0
School attendance	preschool	1,136	13.0
	elementary school	7,614	87.0
Atopic diseases in parents	(+)	2,333	26.7
	(–)	6,417	73.3
Atopic diseases in siblings	(+)	2,456	28.1
	(–)	6,294	71.9
Secondhand smoking	(+)	3,572	40.8
	(–)	5,178	59.2
Breastfeeding	(+)	6,767	77.3
	(–)	1,983	22.7
Moving into a newly built home during the first year of life	(+)	945	10.8
	(–)	7,805	89.2
Carpet or fabric sofa	(+)	1,563	17.9
	(–)	7,187	82.1
New furniture in children's room	(+)	2,013	23.0
	(–)	6,737	77.0
Raising pets	(+)	1,037	11.9
	(–)	7,713	88.1
Diagnosis of eczema ¹	(+)	2,491	28.5
	(–)	6,259	71.5
Diagnosis of asthma ¹	(+)	797	9.1
	(–)	7,953	90.9
Diagnosis of allergic rhinitis ¹	(+)	2,510	28.7
	(–)	6,240	71.3
Diagnosis of allergic conjunctivitis ¹	(+)	1,317	15.7
	(–)	7,379	84.3
Diagnosis of food allergy ¹	(+)	537	6.1
	(–)	8,213	93.9
Diagnosis of drug allergy ¹	(+)	97	1.1
	(–)	8,653	98.9

¹ Lifelong diagnosis.

diagnosed when a subject showed positive responses to all three questions of the ISAAC questionnaire as follows: (1) an intermittent itchy rash for at least 6 months; (2) an itchy rash at any time over the past 12 months, and (3) an itchy rash at any time affecting the folds of the elbows or the areas behind the knees, in front of the ankles, under the buttocks, or around the neck, ears or eyes.

If the response to the question 'has your child ever had asthma?' was 'yes', then that child was considered to have been diagnosed with asthma. A diagnosis of another atopic disorder, including food allergies, drug allergies, allergic rhinitis and allergic conjunctivitis, was classified in the same manner.

Determination of Risk Factors

The following variables were evaluated for their associations with atopic dermatitis: age, sex, atopic diseases of the parents (any diseases in either vs. neither of the parents), atopic diseases in sib-

Table 2. Prevalence of atopic dermatitis over the past 12 months

		Preschool children	Elementary school children	Total	p value
Atopic dermatitis over the past 12 months	(-)	932 (82.0)	6,559 (86.1)	7,491 (85.6)	<0.001
	(+)	204 (18.0)	1,055 (13.9)	1,259 (14.4)	

lings (any diseases in any sibling vs. none of their siblings), secondhand smoking (at least once per week), breastfeeding, moving of the parents' household to a newly built home during the first year of life, a carpet or a sofa in the house, new furniture in the children's room (over the past 12 months), raising pets and ever having other atopic disorders, such as asthma, allergic rhinitis or allergic conjunctivitis, including food or drug allergies, in his/her life.

Statistical Analysis

The statistical analysis was performed using STATA software, version 10.0 (StataCorp, College Station, Tex., USA). The data were analyzed using χ^2 tests and forward stepwise logistic regression analysis. Odds ratios (ORs) and 95% confidence intervals (CIs) were obtained by logistic regression analysis. Stratified analysis was also applied to determine whether there were differences in the risk factors for atopic dermatitis between preschool children and elementary school children. p values <0.05 were considered significant.

Results

General Characteristics and Prevalence of Atopic Dermatitis

Table 1 lists the general characteristics of the subjects. Among the 8,750 subjects, 4,377 (50.0%) were boys and 4,373 (50.0%) were girls. Preschool children numbered 1,136 (13.0%). The prevalence of allergic rhinitis was also quite high (28.7%). The prevalence of atopic dermatitis over the past 12 months was 14.4% (table 2). The prevalence of atopic dermatitis over the past 12 months in preschool children was significantly higher than in elementary school children (18.0 vs. 13.9%, respectively; p < 0.001).

Risk Factors for Atopic Dermatitis in Preschool and Elementary School Children

Table 3 lists the variables associated with atopic dermatitis. The results were obtained with the χ^2 test. For preschool children, atopic diseases in the parents, atopic diseases in siblings, raising pets, a diagnosis of allergic conjunctivitis and a diagnosis of food allergy were significantly associated with atopic dermatitis. For elemen-

tary school children, all of the variables that were significant for preschool children, except for raising pets, were significantly associated with atopic dermatitis. In addition, secondhand smoking, breastfeeding, moving of the parents' household to a newly built home during the first year of life, a diagnosis of asthma, a diagnosis of allergic rhinitis and a diagnosis of drug allergy were significantly associated with atopic dermatitis in elementary school children.

Table 4 presents the results of unstratified and stratified multiple logistic regression (MLR) analysis. The variables in the model were selected using a stepwise selection method. According to unstratified MLR analysis, atopic dermatitis was inversely associated with age (OR = 0.95, 95% CI 0.92–0.97). More girls (1.16 times more) than boys had atopic dermatitis over the past 12 months (95% CI 1.03–1.32). Atopic diseases in the parents, atopic diseases in siblings, secondhand smoking, breastfeeding, moving of the parents' household to a newly built home during the first year of life, a diagnosis of asthma, a diagnosis of allergic conjunctivitis and a diagnosis of food allergy were significantly associated with atopic dermatitis, according to unstratified MLR analysis. In contrast, there were some differences after the data were stratified according to elementary school attendance. Age was not a significant variable in either the preschool children or elementary school children. Raising pets was a significant risk factor in preschool children (OR = 1.85, 95% CI 1.02–3.35) but not in elementary school children. Atopic diseases in the parents, atopic diseases in siblings, a diagnosis of allergic conjunctivitis and a diagnosis of food allergy were associated with atopic dermatitis in both the preschool children and elementary school children. Sex, secondhand smoking, breastfeeding, moving of the parents' household to a newly built home during the first year of life, a diagnosis of asthma and a diagnosis of allergic rhinitis were associated with atopic dermatitis in elementary school children but not in preschool children.

Table 3. Results of χ^2 tests (stratified by elementary school attendance)

		Preschool children			Elementary school children		
		AD (–)	AD (+)	p value	AD (–)	AD (+)	p value
Sex	Male	481 (82.6)	101 (17.4)	0.857	3,291 (86.7)	504 (13.3)	0.147
	Female	451 (81.4)	103 (18.6)		3,268 (85.6)	551 (14.4)	
Atopic diseases in parents	(–)	664 (85.0)	117 (15.0)	<0.001	5,027 (89.2)	609 (10.8)	<0.001
	(+)	268 (75.5)	87 (24.5)		1,532 (77.5)	446 (22.5)	
Atopic diseases in siblings	(–)	4,819 (88.9)	603 (11.1)	<0.001	4,819 (88.9)	603 (11.1)	<0.001
	(+)	1,740 (79.4)	452 (20.6)		1,740 (79.4)	452 (20.6)	
Secondhand smoking	(–)	606 (83.4)	121 (16.6)	0.124	3,867 (86.9)	584 (13.1)	0.028
	(+)	326 (79.7)	83 (20.3)		2,692 (85.1)	471 (14.9)	
Breastfeeding	(–)	126 (86.3)	20 (13.7)	0.151	1,627 (88.6)	210 (11.4)	<0.001
	(+)	806 (81.4)	184 (18.6)		4,932 (85.4)	845 (14.6)	
Moving into a newly built house ^a	(–)	810 (82.3)	174 (17.7)	0.539	5,912 (86.7)	909 (13.3)	<0.001
	(+)	122 (80.3)	30 (19.7)		647 (81.6)	146 (18.4)	
Carpet or fabric sofa	(–)	851 (82.5)	180 (17.5)	0.170	5,291 (85.9)	865 (14.1)	0.311
	(+)	81 (77.1)	24 (22.9)		1,268 (87.0)	190 (13.0)	
New furniture in children's room	(–)	773 (82.9)	160 (17.1)	0.128	5,024 (86.6)	780 (13.4)	0.059
	(+)	159 (78.3)	44 (21.7)		1,535 (84.8)	275 (15.2)	
Raising pets	(–)	888 (82.6)	187 (17.4)	0.038	5,699 (85.9)	939 (14.1)	0.056
	(+)	44 (72.1)	17 (27.9)		860 (88.1)	116 (11.9)	
Diagnosis of asthma ^b	(–)	845 (82.2)	183 (17.8)	0.672	6,024 (87.0)	901 (13.0)	<0.001
	(+)	87 (80.6)	21 (19.4)		535 (77.6)	154 (22.4)	
Diagnosis of allergic rhinitis ^b	(–)	796 (82.9)	164 (17.1)	0.073	4,685 (88.7)	595 (11.3)	<0.001
	(+)	136 (77.3)	40 (22.7)		1,874 (80.3)	460 (19.7)	
Diagnosis of allergic conjunctivitis ^b	(–)	848 (83.5)	167 (16.5)	<0.001	5,572 (87.6)	792 (12.4)	<0.001
	(+)	84 (69.4)	37 (30.6)		987 (79.0)	263 (21.0)	
Diagnosis of food allergy ^b	(–)	881 (83.1)	179 (16.9)	<0.001	6,229 (87.1)	924 (12.9)	<0.001
	(+)	51 (67.1)	25 (32.9)		330 (71.6)	131 (28.4)	
Diagnosis of drug allergy ^b	(–)	925 (82.2)	200 (17.8)	0.118 ^c	6,496 (86.3)	1,032 (13.7)	0.001
	(+)	7 (63.6)	4 (36.4)		63 (73.3)	23 (26.7)	

^a During the first year of life. ^b Lifelong diagnosis. ^c Fisher's exact test. AD = Atopic dermatitis.

Discussion

Recent studies of allergic diseases have shown that the prevalence and burden of these disorders have increased due to rapidly changing circumstances [8]. The ISAAC questionnaire is generally accepted as a reliable method to survey the epidemiology of atopic disorders. The prevalence and potential risk factors in different regions and age groups have been compared worldwide using the ISAAC questionnaire. For the ISAAC phase three study conducted between 2002 and 2003, a cross-sectional study was performed involving 193,404 children, aged 6–7 years from 66 centers in 37 countries, and of 304,679 children, aged 13–14 years from 106 centers in 56 countries [9].

The prevalence of atopic dermatitis in the Republic of Korea has increased since 1995, similar to the trends of other countries. The westernization of lifestyles, industrialization and urbanization are among the main causes. In this study, the prevalence of atopic dermatitis over the past 12 months was 14.4%. This rate is similar to those reported in other ISAAC questionnaire-based studies in the Republic of Korea and other developing countries [10, 11]. In previous ISAAC questionnaire-based studies, the reported prevalence tended to be higher than in dermatologic examination-based studies [12]. The prevalence of atopic dermatitis over the past 12 months was significantly higher in preschool children than in elementary school children. There was also a significant inverse relationship between the prevalence of atopic dermatitis and age in previous studies,

Table 4. Results of unstratified and stratified MLR analysis

	Unstratified MLR analysis ¹		Stratified MLR analysis ¹			
	OR	95% CI	preschool children		elementary school children	
			OR	95% CI	OR	95% CI
Age (continuous)	0.95	0.92–0.97	–	–	–	–
Sex (female vs. male)	1.16	1.03–1.32	–	–	1.17	1.03–1.34
Atopic diseases in parents	1.68	1.47–1.92	1.50	1.08–2.10	1.74	1.50–2.02
Atopic diseases in siblings	1.51	1.32–1.72	1.61	1.13–2.28	1.49	1.29–1.73
Secondhand smoking	1.18	1.04–1.34	–	–	1.15	1.01–1.31
Breastfeeding	1.26	1.07–1.47	–	–	1.26	1.07–1.49
Moving into a newly built house ²	1.29	1.08–1.55	–	–	1.34	1.10–1.63
Carpet or fabric sofa	–	–	–	–	–	–
New furniture in children's room	–	–	–	–	–	–
Raising pets	–	–	1.85	1.02–3.35	–	–
Diagnosis of asthma ³	1.33	1.18–1.55	–	–	1.41	1.15–1.73
Diagnosis of allergic rhinitis ³	–	–	–	–	1.41	1.22–1.63
Diagnosis of allergic conjunctivitis ³	1.41	1.20–1.65	1.74	1.12–2.71	1.36	1.15–1.61
Diagnosis of food allergy ³	2.04	1.66–2.50	2.10	1.25–3.54	2.00	1.60–2.50
Diagnosis of drug allergy ³	–	–	–	–	–	–

¹ Stepwise logistic regression was performed to select the variables. ² During the first year of life. ³ Lifelong diagnosis.

which agreed with the natural course of atopic dermatitis [3, 7, 10, 13].

The potential risk factors for atopic dermatitis were examined by logistic regression analysis. In MLR analysis, a history of other allergic disorders was placed into the model to adjust for the association with atopic dermatitis. There were some differences between the results of unstratified MLR analysis and stratified MLR analysis. Age was a significant variable in unstratified analysis but not in stratified analysis. Atopic diseases are less likely to be morbid, and they become less prevalent as children age [12]. The result of the unstratified analysis is consistent with this common knowledge. In contrast, stratified analysis suggested that the effects of age might not appear over a relatively short period of years. In the Republic of Korea, preschool children are generally aged 0–6 years, and elementary school children are aged 7–12 years. There might be no significant changes in the status of atopic dermatitis according to age within a 6-year period. Further research on this point of view, such as a cohort study, is necessary.

In children aged 0–6 years or 7–12 years, atopic diseases in the parents and siblings, a personal history of allergic conjunctivitis and food allergies were significant risk factors. In the 7- to 12-year-old age group, all kinds of allergic diseases (asthma, allergic rhinitis, allergic conjunctivitis, food allergy and drug allergy) were potential

risk factors. Among the environmental factors, secondhand smoking, breastfeeding and moving to a newly built home were significant risk factors. In the 0- to 6-year-old age group, only a history of raising pets was a significant variable among environmental factors. Environmental factors, such as secondhand smoking, curtains, carpets and moving to a newly built home before 1 year of age, were reported to be risk factors for atopic dermatitis [7, 14]. Moving to a newly built home was reported to be consistently meaningful among environmental factors in recent studies in the Republic of Korea. Sick house syndrome (sick building syndrome) consists of many diseases or symptoms, such as atopic dermatitis and asthma, caused by volatile organic compounds, aromatic hydrocarbons, etc. [15, 16]. Being a rapidly developing country, the Republic of Korea has many new houses and apartments. Therefore, sick house syndrome can be significant in South Korean settings. The reason that a history of moving into a newly built home was only significant in the 7- to 12-year-old age group and not in the 0- to 6-year-old age group is unclear. Raising pets and breastfeeding as risk factors or protective factors in atopic dermatitis remain controversial [17, 18]. In this study, both were risk factors in different age groups.

Atopic diseases in the parents and siblings were significant in both preschool and elementary school chil-

dren. Genetic factors appeared to be important in both the 0- to 6-year-old and 7- to 12-year-old age groups.

Several differences in risk factors were observed between the two age groups. In elementary school children, genetic factors, associations with other allergic diseases and environmental factors, such as secondhand smoking, breastfeeding and moving to a newly built home, were statistically significant. In preschool children, environmental factors were not significant except for raising pets. We cannot ascertain why several environmental factors (smoking, breastfeeding, sick house syndrome) were significant only in elementary school children, while other factors (raising pets) were significant in the preschool group. It is likely that genetic-environmental interactions in early life determine the development of atopy, and many factors can have effects on atopy. Several reports have shown that perinatal atopy is influenced by various prenatal causes, such as prenatal animal contact, maternal allergies and so on [7, 19, 20]. We believe that the risk factors of the younger age group were different from those of the older age group, and further extensive investigation is needed.

This study used a standardized questionnaire and a large sample with a relatively high response rate (84.2%). Nevertheless, there were several limitations with this survey. The subjects were not a representative sample of children living in Seoul. At first, 83 facilities involved in the Atopy-Free Seoul Project were recruited from the entire region of Seoul, the capital city of the Republic of Korea, without any criteria for atopic incidence. At the point at which this Internet-based investigation began, 21 of the

83 facilities wanted to enroll. We could not ascertain whether these facilities presented higher incidences of atopic disorders than other institutions. Furthermore, we presented a reasonably even regional distribution of participating facilities (data not shown). However, we believe that there is a possibility that atopy-positive families were more able to participate actively in this survey. Thus, selection bias could have been possible. Moreover, this was a cross-sectional study that could not identify any causalities from the associated factors and that was prone to recall bias.

In conclusion, the prevalence of atopic dermatitis in preschool and elementary school children in the Republic of Korea was similar to that in other developing countries. The risk factors of preschool and elementary school children were somewhat different. In elementary school children, environmental factors, such as secondhand smoking, breastfeeding and moving to a newly built home, were significant. In preschool children, only a history of raising pets was significant among the environmental factors. Genetic factors were significant in both groups. Nevertheless, more detailed and separate strategies will be necessary to reduce the prevalence of atopic dermatitis in both groups.

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