

Association of Family Histories of Atopic Disease with Childhood Atopic Diseases in Korean Children: A National Survey

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= Abstract =

영유아 및 학령전기 아동의 아토피질환과 가족의 아토피질환과의 관계: 국민건강 영양조사 결과

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목적: 본 연구는 우리나라 영유아 및 학령전기 아동의 아토피질환에 영향을 미치는 가족의 아토피질환과 사회인구학적 위험 요인을 알아보는 것을 목적으로 하고 있다.

방법: 본 연구는 2005년에 시행된 제3차 국민 건강영양 조사 결과를 이용한 횡단적 기술 연구로 6세 미만의 아동 2,559명을 대상으로 지난 12개월 동안 의사 진단을 받은 적인 있는 천식, 비염, 습진의 아토피질환에 대한 정보와 아동의 부모 및 형제의 평생 아토피 질환 유무를 이용하였다. 카이제곱 통계와 로지스틱 회귀 분석 방법을 이용하여 가족의 아토피 질환 유무와 아동의 성별과 연령, 주거형태, 어머니 교육 정도, 가족의 수입을 변수로 아토피 질환에 미치는 요인을 분석하였다.

결과: 우리나라 영유아 및 학령전기 아동의 아토피 질환 중 습진의 유병률은 23.3%, 비염은 11.4%, 그리고 천식은 3.4%이었다. 아동의 아토피 질환은 부모가 같은 아토피 질환을 가지고 있을 때 더 발병하였으며, 아토피 질환 중 가족의 천식 유무가 가장 유의하게 아동의 천식과 관련이 있었다 (아동의 모 OR=10.37, 아동의 부 OR=5.09, 아동의 형제 OR=5.05). 비염이 있는 아동은 습진(OR=1.40) 이나 천식(OR=2.45)을 함께 가지고 있을 확률이 유의하게 높았으며, 여자와이와 연령이 높은 아동에서 비염이 더 발생하였다. 음식 알러지가 있거나, 4명 이하의 가족과 함께 사는 아동은 습진이나 비염을 가지고 있을 확률이 더 높았다.

결론: 아동의 아토피 질환은 가족력, 음식 알러지, 그리고 적은 가족 수와 유의한 상관관계가 있었으므로, 아토피 질환을 가진 아동의 건강관리와 교육을 제공할 때 환경적인 요인 뿐 아니라 유전적인 요인도 함께 고려되어야 할 것이다.

Key Words: 천식, 습진, 비염, 영유아, 아동, 가족

Introduction

The prevalence of atopic diseases such as eczema, hay fever, and asthma varies worldwide (Asher et al., 2006). These diseases have historically been more prevalent in affluent Western countries than in developing countries (Asher et al., 2006; Clausen et al., 2008). However, several recent studies conducted in Western countries, for example, Switzerland and Australia have reported a divergent trend in atopic disease; the prevalence of both asthma and hay fever in children and adolescents has plateaued, or even temporarily decreased, but eczema is still on the rise, especially among girls (Duse et al., 2007; Grize et al., 2006; Ponosby et al., 2008). In Korea, the prevalence of eczema in children (6~12 years), diagnosed during lifetime or in the previous 12 months, has increased to 35~40% and 13~19%, respectively (Lee & Hwang, 2008) whereas asthma has remained at 6~10% during the last decade (Jee et al., 2009). This rapid increase in eczema exclusively in young Korean children is similar to that observed in westernized countries. A rapid increase in the number of children suffering from eczema is becoming a significant public health issue due to its effect on the child's quality of life and the health costs (Kim & Yoo, 2007). Thus, examination of the situation for young Korean children may add information on changing trends in the prevalence of atopic disease worldwide.

Given that atopic disease is influenced by genetic and environmental factors, the Korean population can provide an excellent subject to

determine the risk factors of atopic disease. Only 2% of the total population in Korea has an ethnic background other than Korean (Korea National Statistics Office, 2009). During the past three decades, Korea has undergone rapid economic development and changes in lifestyle and living environment. More than half the population is currently living in urban areas in high-rise buildings that have been constructed within the past 20 years (Korea National Statistics Office, 2009). These unique genetic and environmental characteristics of Korea may influence the development of atopic disease; however, only a few studies have investigated the contribution of both family and socio-demographic factors to the development of atopic diseases in Korean children. In the present study, we used nationally representative data to assess the relationships of childhood atopic diseases to family atopic diseases and socio-demographic factors among children under age of six years.

Materials and Methods

1. Study sample

The data used in this study were obtained from the Third Korea National Health and Nutrition Examination Survey (KNHANES III), which was conducted in 2005. The KNHSNES III used a stratified, multistage, probability sampling method. Household registries were used for selections made from sampling units based on geographical area, gender, and age groups. This stratification results in a proportional representation of the entire Korean population in

both urban and rural areas and in all types of housing. The KNHANES III consists of a basic household interview, health interview and examination, and nutritional survey. For the survey, trained interviewers visited each selected household and interviewed a member of the household using a standardized survey questionnaire. For children, the mother was interviewed regarding her child's health. Among the 12,000 households that participated in the survey in 2005, 1,864 households with at least one child under the age of six years were finally selected for the study. A total of 2,559 children under the age of six included in the study were almost evenly distributed as follows: 150 infants (5.9%) were <1 year, 344 children (13.5%) <2 years, 345 children (13.5%) <3 years, 357 children (14.0%) <4 years, 429 children (16.8%) <5 years, 475 children (18.6%) <6 years, and 459 children (17.9%) <7 years. Most children (84.2%) were residing in urban areas; however, this study investigated with only young children (≤ 6 year), only the home environment was taken into account.

2. Data

Socio-demographic factors in this study included household size, housing type (house vs. high-rise apartment), family income, and maternal education level. These were obtained from the basic household interview. Among the health interview questions, the responses to the following questions were selected to determine the atopic disease status of child and family: "Has your child been diagnosed with eczema (hay fever) by a physician in the past 12

months?" and "Has your child been diagnosed with asthma during his or her lifetime?" To represent a family history of atopic diseases, the responses of the mother, father, and siblings to the question "Have you ever been diagnosed by a physician as having any atopic disease (eczema, hay fever, and asthma) during your lifetime?" were also selected. In addition, data about child food allergies, as diagnosed by physicians, and the gender and age of the child were obtained as well.

3. Data analysis

Descriptive statistics were used to calculate the prevalence of eczema, hay fever, and asthma based on the entire sample. Chi-square test analysis was used to compare the development of an atopic disease in children from families with a history of atopic disease and children from families with no history of atopic disease. Multiple logistic regression analysis was used to identify family and socio-demographic risk factors for atopic disease development of children. All analyses were carried out using SPSS 17.0 (SPSS Inc., Chicago, IL, USA).

Results

1. Prevalence of atopic diseases

The overall prevalence of eczema, hay fever, and asthma in young Korean children was 23.3%, 11.4%, and 3.4%, respectively (Table 1). Hay fever and asthma were more likely to develop among boys than girls (12.2% versus 10.6% for hay fever and 4.0% versus 2.9% for

asthma); however, eczema was more common among girls (24.3%) than boys (22.4%). About 4.9% of children studied had more than two atopic diseases.

2. Associations of child atopic diseases with family history of atopic diseases

Chi-square tests revealed that there was a statistically significant association between atopic disease in children and atopic disease in other members of their family for all three diseases ($p < 0.001$ for all atopic diseases) (Table

2). Among children with a particular atopic disease, the percentage of children with a family history of that disease was 40.5% for eczema, 27.8% for hay fever, and 15.6% for asthma, all of which were higher than the percentage of children with an atopic disease but no family history of that disease. A positive history of eczema in a sibling (42.1%), of hay fever in both parents (40.9%), and of the mother's history of asthma (22.2%) were most frequently associated with those same diseases in the children in the sample population.

Table 1. Prevalence of Atopic Disease (N=2,559)

Variable	Eczema	Hay fever	Asthma	Any combination
Boys (n=1,306)	293 (22.4%)	159 (12.2%)	52 (4.0%)	65 (5.0%)
Girls (n=1,253)	304 (24.3%)	133 (10.6%)	36 (2.9%)	59 (4.7%)
Overall (n=2,559)	597 (23.3%)	292 (11.4%)	88 (3.4%)	124 (4.9%)

Table 2. Associations of Childhood Atopic Diseases with Familial Atopic Diseases

Family variable	Child n (%)					
	Eczema	χ^2	Hay fever	χ^2	Asthma	χ^2
No family eczema	321/1,834 (17.5)	162.4***	197/1,833 (10.7)	2.7	61/1,832 (3.3)	0.5
With family eczema	333/821 (40.5)		106/820 (12.9)		32/821 (3.9)	
Father	59/155 (38.1)		12/154 (7.8)		4/155 (2.6)	
Mother	69/176 (39.2)		25/176 (14.2)		9/176 (5.1)	
Parents	4/12 (33.3)		1/12 (8.3)		1/12 (8.3)	
Sibling	201/478 (42.1)		68/478 (14.2)		18/478 (3.8)	
No family hay fever	391/1,808 (21.6)	17.8***	117/1,808 (6.5)	237.9***	55/1,808 (3.0)	3.4
With hay fever	270/934 (28.9)		260/932 (27.8)		41/932 (4.4)	
Father	62/228 (27.2)		46/227 (20.3)		11/227 (4.8)	
Mother	94/324 (29.0)		87/323 (26.9)		12/324 (3.7)	
Parents	11/44 (25.0)		18/44 (40.9)		2/44 (4.5)	
Sibling	103/338 (30.5)		109/338 (32.2)		16/337 (4.7)	
No family asthma	560/2,412 (23.2)	0.6	268/2,411 (11.1)	4.1	68/2,412 (2.8)	59.6***
With asthma	33/124 (26.6)		21/123 (17.1)		20/128 (15.6)	
Father	7/20 (35.0)		1/19 (5.3)		3/21 (14.3)	
Mother	5/14 (35.7)		3/14 (21.4)		4/18 (22.2)	
Parents	0/0 (0.0)		0/0 (0.0)		0/0 (0.0)	
Sibling	1/90 (23.3)		17/90 (18.9)		13/89 (14.6)	

Footnote: * $p < 0.01$, ** $p < 0.05$, *** $p < 0.001$

3. Family and socio-demographic risk factors for atopic diseases

Multiple logistic regression analyses identified that children were about two times more likely to develop eczema when a sibling (OR=2.70), the father (OR=2.20), or the mother (OR=2.14) had eczema (Table 3). Children were more likely to develop hay fever when a sibling (OR=4.18), the mother (OR=3.03), or

the father (OR=1.82) had hay fever. They were more likely to develop asthma when the mother (OR=9.60), father (OR=5.78), or a sibling (OR=4.92) had asthma.

In terms of socio-demographic factors, a positive history of a diagnosed food allergy increased the possibility of a child's having eczema 4.85 times and hay fever 3.45 times, but did not increase the probability of the child's having asthma. Girls were more likely to develop hay fever than boys (OR=1.32). The possi-

Table 3. Results of Multiple Logistic Regression Analysis of Atopic Diseases in Children

Risk factor	Child					
	Eczema		Hay fever		Asthma	
	OR	95% CI	OR	95% CI	OR	95% CI
Family						
Eczema						
Father	2.26 ^{***}	1.56~3.29	0.61	0.31~1.20	0.64	0.20~2.12
Mother	2.19 ^{***}	1.54~3.11	0.81	0.47~1.37	1.26	0.56~2.79
Both parents	0.32	0.08~1.21	1.44	0.15~13.85	2.92	0.22~38.35
Sibling	2.74 ^{***}	2.18~3.43	1.11	0.79~1.56	1.13	0.64~1.98
Self			1.40 [*]	1.03~1.91	1.11	0.66~1.87
Hay Fever						
Father	1.17	0.81~1.68	1.78 [*]	1.12~2.82	1.22	0.57~2.59
Mother	1.18	0.87~1.59	2.86 ^{***}	2.03~4.05	0.74	0.35~1.55
Both parents	0.53	0.22~1.27	1.09	0.47~2.58	1.20	0.21~6.97
Sibling	1.23	0.93~1.64	4.53	3.34~6.13	1.03	0.55~1.91
Self	1.38 [*]	1.03~1.89			2.46 [*]	1.39~4.36
Asthma						
Father	1.95	0.74~5.18	0.37	0.05~2.93	5.09 [*]	1.37~18.96
Mother	2.15	0.69~6.72	1.64	0.42~6.44	10.37 ^{***}	2.96~36.34
Both parents						
Sibling	0.86	0.50~1.47	1.01	0.54~1.88	5.05 ^{***}	2.58~9.89
Self	1.12	0.67~1.87	2.45 ^{**}	1.41~4.28		
Gender (1=Girl)	0.89	0.73~1.08	1.32 [*]	1.01~1.72	1.53	0.97~2.41
Age (1=>1 year)	0.97	0.92~1.03	1.34 ^{***}	1.24~1.45	1.09	0.96~1.23
Food allergy (1=Yes)	4.76 ^{***}	2.95~7.67	3.04 ^{***}	1.74~5.33	0.87	0.26~3.08
Maternal education (1=>12 years)	0.74 [*]	0.56~0.99	2.07 ^{***}	1.49~2.87	0.80	0.42~1.52
Income (1=> median)	1.05	0.86~1.28	1.17	0.89~1.53	0.92	0.59~1.45
Family size (1=> 4)	1.26 [*]	0.10~1.61	2.08 ^{***}	1.47~3.03	0.79	0.46~1.35
Housing type (1= High-rise building)	0.92	0.62~0.98	1.16	0.88~1.54	0.98	0.61~1.56

Footnote: *p<0.05, **p<0.01, ***p<0.001

lity of developing hay fever increased with age (OR=1.34). Childhood eczema and hay fever increased in children living in larger households (OR=2.08 for hay fever and OR=1.26 for eczema). Childhood eczema decreased with higher maternal education (>12 years) (OR=0.74), but hay fever increased with higher maternal education level (OR=2.07).

Discussion

The results of this study confirm that atopic disease in children is influenced by the prevalence of atopic diseases in the family. Among family factors, the history of eczema and hay fever in a sibling is the most significant factor for the respective atopic diseases in children, whereas a history of asthma in the mother is a significant factor for asthma incidence in the children. These results are consistent with other studies reporting a stronger maternal and sibling influence in the association between parental and offspring atopy (Bener & Janahi, 2005; Bjerg et al., 2007), although an additive effect of atopic diseases in both parents was not shown in this study (Bjerg et al., 2007). Interestingly, a child's atopic disease was not affected by other atopic diseases of parents or siblings in this study. Only a strong relationship between the same atopic diseases was identified. These findings may suggest the possible presence of phenotype-specific genes, at least in the same atopic diseases.

Although this study did not demonstrate a family connection of other atopic diseases to the childhood atopic disease status, all three atopic diseases are interrelated in children.

Children with hay fever were 1.4 times more likely to have eczema and 2.45 times more likely to have asthma. This finding suggests a possible sharing of the genetic role of hay fever in the development of eczema or asthma in children (Kuyucu et al., 2006). According to the model of "atopic march," asthma often develops following hay fever and eczema in atopic children. A common genetic component among the three atopic diseases has yet to be determined (Burgess et al., 2009).

Since co-morbidity among the three atopic diseases is significantly more frequent among sensitized children, sensitization is often suggested as the mechanism that connects these diseases to each other (Kjaer et al., 2008). Although the present study did not include objective measures of sensitization to foods or aeroallergens using skin prick tests, the result of a strong association between a diagnosis of food allergies and the incidence of both eczema and hay fever may also indirectly support sensitization as a mechanism underlying the development of atopic diseases in children (Kim et al., 2008). Kim and associates (2008) reported that children born and raised in China showed higher sensitization rate to foods and aeroallergens, but lower rates of atopic disease. This is contrary to findings in Western countries, where both higher sensitization and higher prevalence of atopic diseases are observed. Growing up on a farm in China seemed to provide a protective effect from atopic disease for children. However, in westernized countries, the strength of the correlation between skin test reactivity and current wheezing increased with the economic developmental status of the coun-

try (Weinmary et al., 2007). Thus, the strong association of food allergies with eczema and hay fever shown in Korean children, which is similar to that of westernized countries, may possibly explain a divergent trend in atopic diseases of some westernized countries that is associated with the economic status of the country. On the other hand, children's asthma in this study was not associated with a history of food allergies. However, it may be that the asthma observed in these children was non-atopic rather than atopic asthma. As seen in the low prevalence rates of asthma among these children, asthma in children younger than 6 years might possibly be non-atopic asthma or asthma that has not had a chance to be triggered by environmental factors. Atopic asthma is more prevalent in school-aged children rather than preschool children (Jee et al., 2009). Further study with objective sensitization data is needed to identify patterns between sensitization and atopic diseases in young children with asthma.

Genetic factors conferring susceptibility to disease vary among ethnic groups (Sarafino, 2000). Young children with atopic disease in this study show a unique pattern of association with other atopic diseases. Among childhood atopic diseases, asthma was most strongly associated with a family history of asthma. Children with a family history of asthma were 5 times more likely to develop asthma during early childhood. Children with hay fever were more likely to have eczema or asthma. Thus, the influence of hay fever on other atopic disease development in children needs further investigation as to its mechanism for connecting the two atopic diseases.

In this study we also investigated association of socio-demographic factors with the development of childhood atopic disease. In general, eczema was more prevalent in girls (Kjaer et al., 2008); however, this study did not support that gender is a factor that influences the development of eczema in children. Rather, hay fever was more common in girls and increased in incidence as much as 1.34 times as the child aged. The finding that, as a child gets older, the possibility of developing hay fever is higher is consistent with other studies (Jee et al., 2009). Although a higher maternal education level is often related to incidence of childhood atopic disease, this study showed that higher maternal education levels decreased eczema development. This may be explained by that fact that a highly educated mother's observing her child's skin may lead to early identification of disease and preventing progression of atopic status. The probability of childhood eczema and hay fever increased when families had fewer than 4 members. This finding supports the hygiene theory that early exposure to allergen prevents the development of atopic disease (Liu, 2007) and is consistent with other studies (Ohfuki et al., 2009). In Korea, the recent very low birth rates have resulted in smaller-sized families (Korea National Statistics Office, 2009), and this may be related to the rapid increase in the number of children with eczema. Housing type was not associated with atopic diseases, although living in a newly constructed high-rise building can be hypothesized to be related to the development of eczema and asthma due to sick building syndrome (Ishibashi et al., 2007). Indoor air quality and pollution from

furniture material in a newly built apartment have been the focus in explaining the causes of atopic disease in Korea (Kim & Kim, 2005). The study's not revealing an association between housing type and atopic disease among children may be explained by the fact that the study did not assess the age of high-rise apartments, which may be a factor significantly affecting the atopic disease.

This study has several limitations. First, because the status of atopic disease was obtained from the response to asking "whether the child (or family member) had been diagnosed with any atopic diseases during the past 12 months," the validity of atopic disease cannot be confirmed. Secondly, because the severity of atopic status was not asked in the questionnaire, this study could not identify the effect of severity of atopic disease among children in the study on the development of atopic disease in childhood.

Conclusion

Atopic disease in children is influenced by both genetic and environmental factors. Children are more likely to develop atopic disease when one or both of their parents have the same atopic disease. Residing in a smaller family is related to the development of eczema and hay fever in Korean children; however, living in a high-rise building was not associated with the development of these diseases, although both factors are associated with westernization. As family history of atopic disease was found to be a relatively strong factor affecting child atopic disease, this information may be used for

parent education and development of preventive interventions for health care providers. Future study is needed with an objective measure of sensitization to further investigate the relationship of family atopic disease with child atopic disease.

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