Prevalence of Allergic Diseases among Korean School-age Children: A Nationwide Cross-Sectional Questionnaire Study

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INTRODUCTION

Asthma, allergic rhinitis and eczema have become the most common chronic diseases among children worldwide (1, 2). Many researchers have indicated an increase in the prevalence and economic burden of these diseases for the last few decades (3, 4). In developed countries, asthma accounts for 1%-2% of the total healthcare costs (5). In Korea, 663 disability-adjusted life years (DALYs) lost per 100,000 of the population is spent on asthma in men (6).

Various factors are known to be associated with the allergic diseases, which include smoking habits, age, lifestyle, obesity and environmental stimuli (e.g., exposure of allergen, air pollution, and climate) (1, 2). Among these factors, environmental factors such as outdoor or indoor air pollution are more likely than genetic factors to be explained the increasing trends. Recently, many epidemiological studies have consistently documented an association between air pollution and the prevalence of allergic diseases (7-9) and a lower prevalence of allergic diseases in subjects living in the rural areas (10-13).

In 1995 and 2000, the Korean Academy of Pediatric Allergy and Respiratory Diseases (KAPARD) has conducted in the nationwide the International Study of Asthma and Allergies in Childhood (ISAAC) survey (14, 15). The twice nationwide studies were conducted on students from elementary schools and middle schools located in Seoul and the 8 major provincial cities in Korea (Ansan, Ulsan, Suwon, Jeju, Changwon, Cheongju, Chuncheon, and Jeonju). These studies were not designed to contain a situation in non-urban area such as rural or industrial area. The other previous studies in Korea were limited by a small number of study population or region (16-18). Therefore, a nationwide prevalence was not reflected in it.

The objective of this study is to determine the prevalence of allergic diseases among Korean school-age children as well as to assess the difference between residential areas.

MATERIALS AND METHODS

Study design and subjects

We obtained the data on the geographic area and the number of students of all elementary schools (n = 6,279) in 2006 was acquired from Ministry of Education, Science and Technology (MEST) of the Republic of Korea. The clustered random sampling method was used to obtain a representative population of elementary school students in each type of residential area. Residential areas were divided into four groups: metropolitan, provincial, rural, and industrial areas. An industrial area was defined as an industrial complex harboring an elementary school. According to the definition, this study included 17 out of a total of 40 industrial complexes in Korea in the industrial area group.
Among 87 elementary schools in industrial area, 25 elementary schools (29%) were randomly selected. In each group except the industrial area, 10% of the elementary schools, of which the number of class was over 3, were randomly selected. Then, one class of each grade (among grades 3 through 5; 8-11 yr old) of each elementary school was randomly selected.

A set of letters of invitation, informed consent forms, and the questionnaires were mailed to each selected elementary school in October and November 2006. All mailing contents were addressed to the parents of the children as parents were asked to complete the questionnaire. Among 50,200 subjects of 427 elementary schools, a total of 31,026 (61.8%) of 363 elementary schools responded the survey; 10,202 (61.0%) out of 16,733 subjects in grade 3, 10,535 (63.0%) out of 16,733 subjects in grade 4, and 10,289 (61.5%) out of 16,733 subjects in grade 5.

Questionnaire
In this study, a Korean version of the ISAAC questionnaire for allergic diseases was used. Detailed characteristics of the Korean version of ISAAC questionnaire have been previously reported previously (14). Asthma prevalence was determined by lifetime and current (last 12 months) wheezing episodes. Also we asked whether they have ever been diagnosed for asthma by doctor, and treated for asthma in last 12 months. We asked similar question modules for eczema, allergic rhinitis, allergic conjunctivitis, and food allergy. In addition, questions on living conditions such as monthly electricity bill (as a proxy indicator of socio-economic status) were added.

Statistics
For the analyses, we excluded a total of 133 children with incomplete data. Nineteen children did not specify for symptoms of wheeze, allergic rhinitis and eczema; another children did not provide data for gender (n = 59), and grade (n = 55). The final study population comprised 30,893 children with complete data.

The prevalence was calculated by dividing the number of positive responses to each question. We adjusted gender-specific prevalence rates for sampling rate across the residential areas and responsible rate (PROC SURVEYFREQ in SAS). The prevalence of allergic diseases across the residential areas was calculated, as well as the weighted prevalence adjusted for response rate. For all statistical analyses the SAS 9.1 system was used. A P value of < 0.05 was considered to be significant.

Ethics statement
This study was approved by the institutional review board of Yonsei University, College of Medicine (approval number: 4-2007-0083) and informed consent was obtained from all parents and students.

RESULTS

General characteristics
A total of 30,893 children in 363 elementary schools participated in this analysis. The participants were grouped by residential area: metropolitan, provincial, rural, and industrial areas. The percentage of girls (57.1%) was slightly higher than boys (42.9%) and the proportion of grade 3 (32.9%), grade 4 (34.0%), and grade 5 (33.2%) was similar (Table 1).

Prevalence of allergic diseases by gender
The prevalence of ‘wheeze, ever’ was 12.4% (95% confidence interval [CI], 11.8-13.0) in boys and 8.7% (95% CI 8.3-9.2) in girls (Table 2). The prevalence of ‘wheezing, last 12 months’ was 5.9% (95% CI 5.5-6.3) in boys and 4.0% (95% CI 3.7-4.2) in girls. Boys showed higher prevalence than girls for both questions (P < 0.001).

The prevalence of ‘itchy rash, ever’ was 20.3% (95% CI 19.5-21.1) in boys and 22.3% (95% CI 21.6-23.0) in girls. The prevalence of allergic rhinitis and allergic conjunctivitis was higher in boys than girls (P < 0.001). Unlike other allergic symptoms, eczema had higher prevalence of girls than that of boys (P < 0.001). The prevalence of ‘symptom of food allergy, ever’ was significantly higher in girls (11.6%) than boys (10.5%), while other prev-

Table 1. Characteristic of the subjects by residential area

| Parameters                | Total       | Metropolitan area | Provincial area | Rural area | Industrial area | P value |
|---------------------------|-------------|-------------------|-----------------|------------|-----------------|---------|
| No. of subjects           | 30,893 (100.0) | 13,093 (42.4)     | 10,070 (32.6)   | 5,876 (19.0) | 1,854 (6.0)     | < 0.001 |
| Gender                    |             |                   |                 |            |                 |         |
| Boys                      | 13,254 (42.9) | 5,713 (43.6)      | 4,135 (41.1)    | 2,636 (44.9) | 770 (41.5)      | < 0.001 |
| Girls                     | 17,639 (57.1) | 7,380 (56.4)      | 5,935 (58.9)    | 3,240 (55.1) | 1,084 (58.5)    |         |
| Elementary                |             |                   |                 |            |                 |         |
| Grade 3                   | 10,148 (32.9) | 4,184 (32.0)      | 3,468 (34.4)    | 1,805 (30.7) | 691 (37.3)      | < 0.001 |
| Grade 4                   | 10,493 (34.0) | 4,503 (34.4)      | 3,365 (33.4)    | 2,007 (34.2) | 618 (33.3)      |         |
| Grade 5                   | 10,252 (33.2) | 4,406 (33.6)      | 3,237 (32.1)    | 2,064 (35.1) | 545 (29.4)      |         |
| Monthly electricity bill  |             |                   |                 |            |                 |         |
| < KRW 30,000              | 8,186 (26.9)  | 2,791 (21.6)      | 3,056 (30.8)    | 1,771 (30.8) | 568 (30.9)      | < 0.001 |
| KRW 30,000-60,000         | 16,020 (52.7) | 6,734 (52.2)      | 5,414 (54.6)    | 2,834 (50.3) | 982 (53.5)      |         |
| ≥ KRW 60,000              | 6,203 (20.4)  | 3,372 (26.2)      | 1,455 (14.7)    | 1,090 (19.0) | 286 (15.6)      |         |

KRW, Korean won; the currency of the Republic of Korea.
Prevalence in boys by residential area

In boys, the prevalence of ‘wheeze, ever’ in industrial area (13.6%, 95% CI 10.7-16.5) was the highest, which was not statistically significant (P = 0.250) (Table 3). The next highest was metropolitan area (12.9%), followed by provincial area (12.4%), and rural area (11.5%). The prevalence of ‘diagnosis of asthma, ever’ in provincial area (9.7%) was the highest, while that in industrial area (7.5%) was the lowest. It was significantly different (P = 0.021).
Children in rural area demonstrated the lowest prevalence of ‘itchy rash, ever’ at 16.9% (95% CI 15.3-18.5) compared to children from metropolitan (22.2%), provincial (20.7%), and industrial area (22.3%).

Symptoms of allergic rhinitis which included sneezing, congestion and nose itching, most frequently appeared in March, April (spring), and September, October (fall) (data not shown). For allergic rhinitis and allergic conjunctivitis, rural area showed lower prevalence than other areas. The prevalence of ‘symptom of allergic rhinitis, ever’ in metropolitan area (21.1%) was the highest, while that in rural area (16.7%) was the lowest (P < 0.001). The prevalence of ‘symptom of allergic conjunctivitis, ever’ in provincial area (21.1%) was significantly different (P < 0.001). The prevalence of ‘itchy rash, ever’ in rural area, which was lower than other areas. The prevalence of ‘itchy rash, ever’ was 19.2% (95% CI, 17.5-20.8) in rural area, which was lower than other areas. Industrial area had the highest prevalence of ‘flexural rash, last 12 months’ (22.3%) in rural area, which was lower than other areas. The prevalence of ‘symptom of allergic rhinitis, ever’ in provincial area (21.1%) was the highest, while that in rural area (16.7%) was the lowest (P < 0.001).

**Prevalence in girls by residential area**

The prevalences in boys and girls were mostly similar (Table 4). However, the highest prevalence of ‘wheeze, ever’ in girls was observed in metropolitan area (9.7%, 95% CI 9.0-10.4), which was significantly different from boys (P < 0.001). Also, no significant differences were found in other prevalences related with asthma among the four residential areas. The prevalence of ‘itchy rash, ever’ was 19.2% (95% CI, 17.5-20.8) in rural area, which was lower than other areas. Industrial area had the highest prevalence of ‘flexural rash, last 12 months’ (18.7%) while rural area showed the lowest (14.2%).

For allergic rhinitis and allergic conjunctivitis, rural area showed lower prevalence than other areas. The prevalence of ‘symptom of allergic rhinitis, ever’ in rural area (31.2%) was the lowest, and that in other areas were similar to each other (37.5% for metropolitan, 36.6% for provincial, and 36.1% for industrial areas). The prevalence of ‘diagnosis of allergic conjunctivitis, ever’ was the highest in industrial area (19.9%), while that in rural area (13.2%) was the lowest.

**DISCUSSION**

This study was a nationwide questionnaire survey to assess the prevalence of allergic diseases in elementary school-age children in Korea. Also, using random sampling and sample weight, we estimated nationally representative prevalence of allergic diseases. In 1995 and 2000, the twice nationwide studies were conducted (14, 15). These studies, which utilized the same methods to our study formulated by the ISAAC questionnaire, were conducted on students enrolled in elementary and middle schools located in Seoul and major provincial cities in Korea. While they surveyed different schools, their findings regarding the prevalences among elementary school-age children were compared with our results as all three studies used the same questionnaire.

The prevalence of ‘wheeze, ever’ was decreased from 1995 to 2006 (17.0% in 1995, 13.0% in 2000, and 10.3% in 2006), and the prevalence of “diagnosis of asthma, ever” was the highest in 2000 and dropped in 2006 (7.7% in 1995, 9.1% in 2000, and 7.6% in 2006). There was no change in the prevalence of “treatment of asthma, last 12 months” in 1995 (3.2%) and 2000 (3.3%), but the

**Table 4. Prevalence of symptoms of allergic diseases by residential area in girls**

| Clinical feature        | Metropolitan area % (95% CI) | Provincial area % (95% CI) | Rural area % (95% CI) | Industrial area % (95% CI) | P value |
|-------------------------|-----------------------------|---------------------------|-----------------------|--------------------------|--------|
| **Asthma**              |                             |                           |                       |                          |        |
| Wheeze, ever            | 9.7 (9.0-10.4)              | 8.7 (7.9-9.5)             | 7.5 (6.6-8.3)         | 8.6 (6.9-10.6)           | < 0.001|
| Wheezing, last 12 months| 4.2 (3.7-4.7)               | 3.8 (3.3-4.3)             | 3.7 (3.1-4.4)         | 4.7 (3.3-6.2)            | 0.428  |
| Diagnosis, ever         | 6.9 (6.2-7.6)               | 6.9 (6.2-7.6)             | 5.7 (4.7-6.8)         | 6.7 (4.8-8.6)            | 0.144  |
| Treatment, last 12 months| 2.2 (1.9-2.6)              | 1.8 (1.4-2.1)             | 2.0 (1.5-2.4)         | 2.1 (1.2-3.0)            | 0.284  |
| **Eczema**              |                             |                           |                       |                          |        |
| Itchy rash, ever        | 23.5 (22.4-24.7)            | 23.0 (21.9-24.1)          | 19.2 (17.5-20.8)      | 25.0 (21.1-28.8)         | < 0.001|
| Flexural rash, last 12 months| 17.5 (16.5-18.5)     | 17.0 (16.0-18.0)          | 14.2 (12.8-15.6)      | 18.7 (15.2-22.2)         | < 0.001|
| Diagnosis, ever         | 31.2 (30.0-32.4)            | 30.0 (28.7-31.3)          | 23.0 (21.2-24.9)      | 30.4 (26.4-24.5)         | < 0.001|
| Treatment, last 12 months| 15.1 (14.2-16.0)            | 15.1 (14.1-16.1)          | 12.7 (11.3-14.0)      | 14.5 (11.4-17.6)         | 0.005  |
| **Allergic rhinitis**    |                             |                           |                       |                          |        |
| Symptom, ever           | 37.5 (36.3-38.7)            | 36.6 (35.3-38.0)          | 31.2 (29.5-33.0)      | 36.1 (33.1-39.2)         | < 0.001|
| Symptom, last 12 months  | 31.7 (30.5-32.9)            | 30.6 (29.3-32.0)          | 25.6 (23.8-27.4)      | 30.0 (27.0-33.0)         | < 0.001|
| Diagnosis, ever         | 26.5 (25.3-27.6)            | 25.6 (24.2-26.9)          | 19.7 (17.9-21.5)      | 26.3 (22.5-30.1)         | < 0.001|
| Treatment, last 12 months| 19.9 (18.8-20.9)            | 19.3 (18.1-20.5)          | 14.9 (13.5-16.4)      | 19.9 (16.8-23.0)         | < 0.001|
| **Allergic conjunctivitis** |                           |                           |                       |                          |        |
| Symptom, ever           | 18.1 (17.1-19.1)            | 18.8 (17.7-19.9)          | 14.1 (12.8-15.5)      | 18.3 (16.1-20.5)         | < 0.001|
| Symptom, last 12 months  | 13.7 (12.8-14.9)            | 14.2 (13.3-15.2)          | 10.0 (9.0-11.2)       | 14.2 (12.2-16.2)         | < 0.001|
| Diagnosis, ever         | 18.1 (17.2-18.9)            | 19.6 (18.4-20.7)          | 13.2 (11.8-14.6)      | 19.9 (17.5-22.3)         | < 0.001|
| Treatment, last 12 months| 10.8 (10.1-11.5)            | 12.2 (11.3-13.1)          | 7.1 (6.0-8.2)         | 10.7 (8.6-12.8)          | < 0.001|
| **Food allergy**        |                             |                           |                       |                          |        |
| Symptom, ever           | 12.4 (11.6-13.2)            | 12.0 (11.1-12.9)          | 10.0 (8.8-11.2)       | 10.9 (8.9-12.8)          | 0.001  |
| Symptom, last 12 months  | 8.1 (7.4-8.8)               | 8.2 (7.5-9.0)             | 6.6 (5.7-7.5)         | 7.6 (5.8-9.3)            | 0.007  |
| Diagnosis, ever         | 5.4 (4.9-6.0)               | 5.1 (4.6-5.7)             | 4.5 (3.7-5.3)         | 5.7 (4.2-7.3)            | 0.206  |
| Treatment, last 12 months| 2.5 (2.2-2.9)               | 2.3 (2.0-2.7)             | 2.3 (1.7-2.8)         | 3.3 (2.3-4.2)            | 0.492  |
prevalence declined to 2.5% in 2006. The decreasing prevalence of ‘wheeze, ever’ from 1995 to 2006 might influence the recent occurrence of diagnosis and treatment of asthma. However, the prevalence of diagnosis of the other allergic diseases such as eczema, allergic rhinitis, and allergic conjunctivitis increased from 1995 to 2006. According to the ISAAC Phases One and Three repeat multi-country cross-sectional surveys, the prevalence of asthma showed an increasing trend worldwide (19). However, this trend has been halted in some countries such as Malaysia, Singapore, Mexico, Sweden, and Australia.

Only the prevalence of asthma decreased. It might reflect correct diagnosis and awareness of childhood asthma. Physicians usually diagnose asthma without methacholine challenge test in children. But using biomarkers such as blood immunoglobulin E (IgE) or allergy test, recent physician-diagnosis of asthma has been fairly correct. Moreover, the decreasing prevalence of asthma symptoms might reflect successful management. There is a possibility of recall bias on parents who answered the question about asthma; also concerned parents often misunderstand their children’s respiratory symptoms, like recurrent cough.

Using the ISAAC questionnaire, we found that all the prevalences of ‘wheeze, ever’, ‘wheezing, last 12 months’ ‘diagnosed asthma, ever’, and ‘treatment of asthma, last 12 months’ were significantly higher in boys than in girls. All prevalences regarding allergic rhinitis and allergic conjunctivitis were higher in boys than in girls, while the prevalence of eczema was higher in girls than in boys. Differences in disease susceptibility and prognosis between men and women are known to occur in the development of cardiovascular, neurodegenerative, and immunological disorders. Also, differences in allergic disease between boys and girls have been shown by other studies (20-24). Compared with girls, boys have a higher incidence of asthma in childhood, but a lower incidence after the onset of puberty (20, 25). Women exhibit higher prevalence of airway hyperresponsiveness to cholinergic challenge than men (26). This provides partial support for the hypothesis that sex hormones influence that. In our study, the higher prevalences of allergic diseases in boys could be due to the children at the pre-puberty. Also, a study by Osman et al. showed that over 15 yr (from 1989 to 2004) the gender difference in allergic diseases such as asthma, eczema, and hay fever declined (23). Further study is needed to assess the changes in the age-gender distribution.

Recently, several studies have reported associations between air pollution and allergic diseases (7-9). We expected higher prevalences of allergic diseases in industrial area, which have more point sources of air pollution than other areas. But the prevalences of allergic diseases in industrial area were similar to that in urban area including metropolitan and provincial areas. In previous Korean study, the prevalences of asthma and other allergic diseases were higher in Seoul than in other provincial cities in 1995, but became similar in 2000 (15). African studies reported on the prevalence of childhood asthma which confirmed urban-rural differences, and showed that this gap was rapidly narrowing (27). In that study, the gap may be narrowing partially because rural children were increasingly exposed to westernized lifestyle. A study by Lee et al. (14) suggests personal characteristics as more important factors than environmental pollution.

In the present study, we could not find any significant difference in the prevalence of allergic diseases among industrial, metropolitan and provincial areas, but the differences were statistically significant between rural area and other areas. Living in rural area decreased the likelihood of developing allergic diseases in other studies (11-13, 28). Also, a study in Poland showed that a fourfold higher percentage of allergic urban children were found to be sensitized to five or more allergens compared with children in rural areas (29). The type of residential area might have an important effect on allergic diseases. More study is needed to assess the lifestyle difference between urban and rural areas.

In conclusion, this study showed a gender difference in the prevalence of allergic diseases. Also there was a low prevalence of allergic diseases among school-age children in rural area compared other areas. Our results support the importance of contextual effect associated with residential area as causative agents of allergic diseases in Korean children. Therefore, further evaluations, including objective examination and prospective study, are necessary to confirm these outcomes because risk factors such as environmental and personal characteristics may be different among the types of residential area according to life style.

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Prevalence of Allergic Diseases among Korean School-age Children: A Nationwide Cross-Sectional Questionnaire Study

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The purpose of this study was to investigate the nationwide prevalence of childhood allergic diseases in Korean school-age children (8–11 yr) and to assess the difference between residential areas (metropolitan, provincial, rural, and industrial area). Among 30,893 subjects that completed a modified Korean version of a questionnaire formulated by the International Study of Asthma and Allergies in Childhood (ISAAC), the 12-month prevalence of wheeze, flexural rash, and allergic rhinitis symptoms were 4.8%, 15.3% and 32.9%, respectively. The prevalence of diagnosis of allergic diseases in boys was higher than that in girls, with the exception of eczema. In both boys and girls, the difference of the prevalence of allergic diseases among industrial, metropolitan and provincial areas was not statistically significant. In contrast, the differences between rural area and other areas were significant. Our results support the importance of contextual effect associated with residential area as causative agents of allergic diseases among Korean children.