Prevalence of Self-reported Allergic Diseases and IgE Levels: A 2010 KNHANES Analysis

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INTRODUCTION

The prevalence of allergic diseases is known to be associated with both demographic and environmental factors. Herein, we aimed to determine significant factors associated with the prevalence of allergic diseases and with total immunoglobulin E (tIgE) and specific immunoglobulin E (sIgE) levels in Korea. Methods: We analyzed unweighted data collected by the 2010 Korea National Health and Nutrition Examination Survey for 2,342 subjects who underwent serum tests for tIgE and sIgE to Dermatophagoides farinae, dog, and Blattella germanica, representing a sample of 16,003,645 citizens, by considering the sample weight and stratification. Results: The overall prevalence of self-reported allergic diseases was 37.6%. The prevalence rates of allergic rhinitis and atopic dermatitis decreased with age, whereas the asthma prevalence was not affected by the age of the subjects. When analyzed according to the type of allergic diseases, the prevalence of self-reported allergic disease was significantly associated with various factors (e.g. age, occupation, living in urban areas, and depression). The tIgE level decreased with age, but later increased. Elevation of tIgE was significantly associated with male sex, type of occupation, obesity, and smoking status. However, the risk factors for the increased sIgE levels to each allergen were quite different. Sensitization to D. farinae was more likely in young subjects, whereas the prevalence of sensitization to B. germanica was significantly higher in subjects with male sex, type of occupation, obesity, and smoking status. Finally, young age and the smoking status were significantly associated with sensitization to dog. Conclusions: Various demographic and environmental factors were significantly associated with the prevalence of self-reported allergic diseases and the levels of tIgE and sIgE to D. farinae, B. germanica, and dog in Korea.

Key Words: Allergy; demographic factors; environment; immunoglobulin E
by the Korea Centers for Disease Control and Prevention (KCDC), which collects a significant amount of demographic and environmental data. The survey sample represents the entire non-institutionalized general population of South Korea. In 2010, the survey included a questionnaire for allergic diseases and serologic tests for total immunoglobulin E (tIgE) and specific IgE (sIgE) to Dermatophagoides farinae (house dust mite), dog, and Blattella germanica (German cockroach). Thus, the KNHANES provides useful data to define and confirm significant factors associated with allergen sensitization and the prevalence of allergic diseases.

In this study, we aimed to define significant demographic and environmental factors associated with the tIgE and sIgE levels and the prevalence of allergic diseases using data from the fifth KNHANES, conducted in 2010.

MATERIALS AND METHODS

Study design and populations

This study analyzed the data from the fifth KNHANES, a national survey performed in 2010-2012. In the fifth KNHANES, all subjects were tested for tIgE. The survey used complex probability procedures to represent the entire Korean general population, including stratification and multiple stages of cluster selection using age, sex, location of residence, type of residence, education level, and other variables. In the present study, to obtain appropriate estimates, we followed the guidelines for reporting sample weight (sampling weights) and stratification designated by the KCDC; this information is available on the KNHANES website (http://knhanes.cdc.go.kr).

Among all subjects registered in 2010, a total of 2,342 subjects aged ≥10 years responded to the health survey and underwent serum IgE tests between January and December 2010. These subjects represented 16,003,645 citizens of Korea (about one-third of the total population of Korea) as obtained by complex probability sampling. In terms of the variables assessed, glucose tolerance status, body mass index (BMI), smoking history, and depression were assessed for 1,977 subjects aged ≥19 years, representing 13,762,677 citizens. The subjects’ education level, marriage status, income level, and occupation were assessed for 1,577 subjects aged ≥30 years, representing 9,624,008 citizens.

All participants provided written informed consent prior to the survey. The KCDC Institutional Review Board approved the fifth KNHANES (#KCDC-2010-02CON-21-C).

Interview items

Responses to all questionnaire items were obtained by face-to-face interviews. Allergic disease was defined as the presence of at least 1 self-reported allergic disease, including allergic rhinitis, atopic dermatitis, and bronchial asthma. Responses of “negative” for 1 or 2 allergic diseases in addition to missing responses for the remaining disease options were considered missing values. The presence of depression was assessed as previously described. Each subject’s residential district was classified as urban (“Dong” in Korea) or suburban/rural (“Eup/Myun”). The type of residence was classified as apartment or house. Income level was categorized into 4 quartiles: quartile 1, <$2,600/month; quartile 2, $2,600-$4,300/month; quartile 3, $4,300-$8,600/month; and quartile 4, >$8,600/month. Smoking history was classified as never-smoker, light smoker (<5 pack-years/entire life), or smoker (≥5 pack-years/entire life).

Measurements

BMI is measured as body weight (to the nearest 0.1 kg) divided by the square of the body weight (nearest 0.1 cm), and expressed in unit of kg/m². Glucose tolerance was tested as previously described. In brief, blood samples were obtained after ≥8 hours of fasting. Based on the fasting glucose levels, the glucose tolerance status was categorized as normal, impaired fasting glucose, or diabetes mellitus. The serum vitamin D level was categorized into 3 groups: quartile 1, <13.30 ng/mL; quartiles 2-3, 13.30-21.37 ng/mL; and quartile 4, ≥21.37 ng/mL. The 5th KNHANES included data on the tIgE and 3 types of sIgE. According to a previous Korean cohort study, the selection of these 3 types of sIgE (D. farinae, B. germanica, and dog) does not lead to large discrepancies in revealing the atopy status in Korea. We used the ImmunoCAP® system (Thermo Scientific, Uppsala, Sweden) to measure the levels of tIgE and sIgE to D. farinae, B. germanica, and dog, following the manufacturer’s instructions. Elevation of the tIgE level was defined as a tIgE level >100 kU/L. Positivity to sIgE was defined as an sIgE level >0.35 kU/L.

Statistical analysis

For data analysis of the survey, which involved a complex sample, we used the KNHANES stratification variables and sampling weight (weights). The missing data were dealt with using complete case analysis. Because the distribution of serum IgE was log-normal, the tIgE levels were logarithmically transformed for statistical analysis. Differences in the geometric mean of tIgE were tested using t tests, and differences in the prevalence of allergic diseases were tested using χ² tests. Univariate and multivariate logistic regression analyses were performed to identify factors associated with the prevalence of allergic diseases and positivity of sIgE to D. farinae, B. germanica, and dog. SPSS v.18.0 (IBM Corp., Armonk, NY, USA) was used for all analyses, and P values <0.05 were considered statistically significant.

RESULTS

Univariate analysis of factors associated with the prevalence of any allergic disease

The overall prevalence of self-reported allergic diseases was...
### Table 1. Univariate analyses of factors associated with the total and specific immunoglobulin E levels and prevalence of any allergic diseases

| Characteristics                  | No. of participants | No. of represented population (%) | Allergic disease prevalence (%) | P value | IgE (95% CI) (kU/L) | P value |
|----------------------------------|---------------------|-----------------------------------|---------------------------------|---------|---------------------|---------|
| Overall (No.)                    | 2,342               | 16,003,645 (100.0)                | 37.6                            | 0.858   | 94.8 (87.9-102.3)   | <0.001  |
| Gender                           |                     |                                   |                                 |         |                     |         |
| Male                             | 1,159               | 8,925,094 (55.8)                  | 37.8                            |         | 130.5 (117.8-144.5) |         |
| Female                           | 1,183               | 7,078,551 (44.2)                  | 37.3                            |         | 63.4 (58.0-69.3)    |         |
| Age (year)                       |                     |                                   |                                 | <0.001  |                     | 0.008   |
| 10-19                            | 395                 | 2,552,815 (16.0)                  | Not available                   |         | 104.1 (88.1-122.9)  |         |
| 20-29                            | 370                 | 3,826,822 (23.9)                  | 42.8                            |         | 90.3 (75.7-107.6)   |         |
| 30-39                            | 393                 | 2,776,446 (17.3)                  | 41.1                            |         | 84.9 (73.0-98.8)    |         |
| 40-49                            | 393                 | 3,011,436 (18.8)                  | 25.9                            |         | 81.2 (69.3-95.2)    |         |
| 50-59                            | 400                 | 2,394,115 (15.0)                  | 24.8                            |         | 114.6 (94.9-138.2)  |         |
| ≥60                              | 391                 | 1,442,012 (9.0)                   | 23.9                            |         | 114.6 (93.5-140.6)  |         |
| Residence district               |                     |                                   |                                 | 0.039   | 0.016               |         |
| Urban                            | 1,881               | 12,834,689 (80.2)                 | 39.1                            |         | 90.4 (83.2-98.2)    |         |
| Suburban/rural                   | 451                 | 3,168,956 (19.8)                  | 31.3                            |         | 115.0 (96.3-137.2)  |         |
| Type of residence                |                     |                                   |                                 | 0.719   | 0.018               |         |
| House                            | 1,258               | 10,980,539 (68.6)                 | 37.2                            |         | 100.5 (91.2-110.7)  |         |
| Apartment                        | 1,084               | 5,023,107 (31.4)                  | 38.3                            |         | 83.6 (74.3-94.0)    |         |
| Education*                       |                     |                                   |                                 | 0.002   | 0.244               |         |
| Below elementary school          | 354                 | 1,686,437 (17.7)                  | 28.0                            |         | 114.4 (91.8-142.5)  |         |
| Middle school                    | 197                 | 1,181,370 (12.4)                  | 22.5                            |         | 87.7 (69.3-111.0)   |         |
| High school                      | 524                 | 3,509,967 (36.9)                  | 25.5                            |         | 92.5 (79.7-107.4)   |         |
| Above university                 | 486                 | 3,146,779 (33.0)                  | 37.9                            |         | 89.7 (78.9-102.0)   |         |
| Marriage*                        |                     |                                   |                                 | 0.050   | 0.360               |         |
| Married                          | 1,480               | 8,801,817 (91.5)                  | 28.6                            |         | 93.2 (85.6-101.6)   |         |
| Unmarried                        | 96                  | 819,421 (8.5)                     | 41.6                            |         | 108.0 (79.6-143.4)  |         |
| Income level*                    |                     |                                   |                                 | 0.268   | 0.264               |         |
| 1 quartile                       | 411                 | 2,727,269 (28.6)                  | 32.2                            |         | 109.7 (91.0-132.1)  |         |
| 2 quartile                       | 390                 | 2,368,780 (24.9)                  | 24.9                            |         | 89.2 (76.6-103.9)   |         |
| 3 quartile                       | 379                 | 2,230,668 (23.4)                  | 32.1                            |         | 84.4 (69.2-103.0)   |         |
| 4 quartile                       | 380                 | 2,200,208 (23.1)                  | 28.8                            |         | 90.8 (77.4-106.4)   |         |
| Occupation*                      |                     |                                   |                                 | <0.001  | <0.001              |         |
| Professional job                 | 199                 | 1,353,626 (14.3)                  | 36.5                            |         | 83.9 (66.3-106.2)   |         |
| Office job                       | 147                 | 911,227 (9.5)                     | 32.9                            |         | 77.5 (61.3-97.8)    |         |
| Service, sales job               | 233                 | 1,507,708 (15.9)                  | 20.4                            |         | 82.6 (66.7-102.2)   |         |
| Agriculture and fisheries job    | 149                 | 882,398 (9.3)                     | 14.1                            |         | 179.5 (138.6-232.5) |         |
| Technician, engineer             | 136                 | 1,450,241 (15.4)                  | 35.5                            |         | 133.4 (107.7-165.1) |         |
| Labor worker                     | 127                 | 758,518 (8.0)                     | 33.1                            |         | 102.4 (71.3-147.2)  |         |
| Jobless                          | 503                 | 2,586,925 (27.4)                  | 31.9                            |         | 73.3 (63.6-84.6)    |         |
| Glucose tolerance†               |                     |                                   |                                 | 0.003   | <0.001              |         |
| Normal                           | 1,432               | 10,249,174 (77.5)                 | 36.1                            |         | 85.2 (76.8-94.4)    |         |
| Impaired fasting glucose         | 320                 | 2,036,951 (15.4)                  | 25.3                            |         | 106.2 (88.4-127.7)  |         |
| Diabetes mellitus                | 159                 | 944,641 (7.1)                     | 23.4                            |         | 142.7 (113.5-179.5) |         |
| BMI† (kg/m²)                     |                     |                                   |                                 | 0.083   | <0.001              |         |
| Low weight (<18.5)               | 86                  | 612,044 (4.5)                     | 42.0                            |         | 47.2 (35.0-63.7)    |         |
| Standard (18.5-25.0)             | 1,248               | 8,718,890 (63.7)                  | 35.5                            |         | 84.5 (76.2-93.8)    |         |
| Obesity (>25.0)                  | 628                 | 4,345,841 (31.8)                  | 29.5                            |         | 124.4 (108.5-142.5) |         |

(Continued to the next page)
37.6% (Table 1). The prevalence rates of allergic rhinitis, atopic dermatitis, and asthma were 29.0%, 7.1%, and 4.1%, respectively (Table 2). The overall prevalence of allergic diseases was inversely correlated with age (Table 1). Although the prevalence rates of allergic rhinitis ($P<0.001$) and atopic dermatitis ($P<0.001$) significantly correlated with young age, no association between the prevalence of asthma and age was observed ($P=0.882$) (Table 2). The residence district, education level, occupation, glucose tolerance, depression, elevation of tIgE, sIgE to $D. farinae$, and sIgE to dog were also identified as significant factors associated with allergic diseases in the univariate analyses (Table 1).

### Table 1. Continued

| Characteristics                  | No. of participants | No. of represented population (%) | Allergic disease prevalence (%) | $P$ value | tIgE (95% CI) (kU/L) | $P$ value |
|----------------------------------|---------------------|-----------------------------------|---------------------------------|-----------|----------------------|-----------|
| Smoking history†                 |                     |                                   |                                 | 0.226     | <0.001               |           |
| Never smoker                     | 1,051               | 6,599,290 (48.2)                  | 34.0                            |           | 66.5 (60.6-72.9)     |           |
| Light smoker (<5 pack/whole life)| 68                  | 585,990 (4.3)                     | 43.6                            |           | 103.8 (67.7-159.3)   |           |
| Smoker (≥5 pack/life)            | 845                 | 6,493,304 (47.5)                  | 32.4                            |           | 131.2 (114.4-150.4)  |           |
| Depression†                      |                     |                                   |                                 | 0.015     | 0.001                |           |
| No                               | 1,688               | 11,885,162 (86.8)                 | 32.4                            |           | 99.0 (90.4-108.5)    |           |
| Yes                              | 279                 | 1,807,876 (13.2)                  | 42.5                            |           | 64.3 (50.6-81.9)     |           |
| Serum vitamin D level            |                     |                                   |                                 | 0.199     | 0.018                |           |
| 1 quartile                       | 584                 | 4,074,877 (25.5)                  | 40.4                            |           | 84.9 (74.7-96.5)     |           |
| 2, 3 quartile                    | 1,173               | 7,862,277 (49.1)                  | 38.3                            |           | 90.7 (81.7-100.7)    |           |
| 4 quartile                       | 585                 | 4,066,492 (25.4)                  | 33.6                            |           | 115.6 (97.8-136.5)   |           |
| Elevation of tIgE (>100 kU/L)    |                     |                                   |                                 | 0.002     | -                    |           |
| Negative                         | 1,373               | 9,154,543 (57.2)                  | 33.7                            |           | 23.1 (32.3-36.0)     |           |
| Positive                         | 969                 | 6,849,102 (42.8)                  | 42.8                            |           | 372.1 (347.4-398.6)  |           |
| Positivity to sIgE to $D. farinae$|                     |                                   |                                 | <0.001    | -                    |           |
| Negative                         | 1,403               | 9,235,722 (57.7)                  | 32.4                            |           | 45.9 (42.7-49.5)     |           |
| Positive                         | 939                 | 6,767,923 (42.3)                  | 44.6                            |           | 255.0 (229.1-283.7)  |           |
| Positivity to sIgE to $B. germanica$ |                 | 12,562,395 (78.5)                 | 36.9                            | 0.387     | -                    |           |
| Negative                         | 1,878               | 3,441,250 (21.5)                  | 36.9                            |           | 67.4 (62.6-72.5)     |           |
| Positive                         | 464                 | 399 (2.4)                        | 39.9                            |           | 330.4 (291.4-374.7)  |           |
| Positivity to sIgE to dog§       |                     |                                   |                                 | 0.001     | -                    |           |
| Negative                         | 2,198               | 14,824,206 (82.6)                 | 36.0                            |           | 82.7 (76.5-89.5)     |           |
| Positive                         | 144                 | 1,179,439 (7.4)                   | 56.4                            |           | 527.8 (398.0-700.0)  |           |

$tIgE$, total immunoglobulin E; sIgE, specific immunoglobulin E; CI, confidence interval; BMI, body mass index.

*Subjects aged ≥30 years (n=1,577, representing 9,624,008 citizens); †Subjects aged ≥19 years (n=1,977, representing 13,762,677 citizens); §Data were missing for 60.3% of the participants; ‡Positivity to sIgE was defined as a level >0.35 kU/L.

### Table 2. Univariate analyses of the prevalence rates of allergic rhinitis, atopic dermatitis, and asthma according to age and sex

| Characteristics | Prevalence of allergic rhinitis (%) $P$ value | Prevalence of atopic dermatitis (%) $P$ value | Prevalence of asthma (%) $P$ value |
|-----------------|----------------------------------------------|----------------------------------------------|-----------------------------------|
| Overall         | 29.0                                         | 7.1                                          | 4.1                               |
| Gender          |                                              |                                              |                                  |
| Male            | 29.0                                         | 7.7                                          | 4.7                               |
| Female          | 29.1                                         | 6.3                                          | 3.2                               |
| Age (year)      |                                              |                                              |                                  |
| 10-19           | <0.001                                       | <0.001                                       | 0.882                             |
| 20-29           | 34.9                                         | 11.7                                         | 3.1                               |
| 30-39           | 34.8                                         | 8.6                                          | 4.6                               |
| 40-49           | 21.0                                         | 3.8                                          | 4.5                               |
| 50-59           | 20.4                                         | 4.5                                          | 3.9                               |
| ≥60             | 19.6                                         | 1.5                                          | 4.7                               |
Univariate analyses of factors associated with the tIgE level

The geometric mean tIgE level was 94.8 kU/L (95% confidence interval [CI], 87.9-102.3). The mean tIgE level was significantly higher in men than in women. The tIgE level decreased with age, but later increased. The residence district, type of residence, occupation, glucose tolerance, BMI, smoking history, depression, and serum vitamin D level were significantly associated with the tIgE level in the univariate analyses (Table 1).

Multivariate analyses for factors associated with self-reported allergic diseases

Multivariate analyses were conducted to assess the associations of the factors analyzed with each type of self-reported allergic disease (Table 2). Young age (P=0.013), the subjects’ occ-

Table 3. Multivariate analyses of potential independent risk factors for allergic rhinitis, atopic dermatitis, and asthma in subjects aged ≥30 years

| Variables                  | Allergic rhinitis |                  |                  | Allergic dermatitis |                  |                  | Asthma          |
|----------------------------|-------------------|------------------|------------------|---------------------|------------------|------------------|-----------------|
| Age (year)                 |                   |                  |                  |                     |                  |                  |                 |
| 30-39 Reference            |                   |                  |                  | 0.013               | 0.015            | 0.540            |                 |
| 40-49                      | 0.592             | 0.404-0.868      |                  | 0.472               | 0.206-1.083      | 0.996            | 0.412-2.410     |
| 50-59                      | 0.656             | 0.434-0.982      |                  | 0.608               | 0.281-1.314      | 0.523            | 0.176-1.552     |
| ≥60                        | 0.561             | 0.352-0.894      |                  | 0.162               | 0.048-0.553      | 0.637            | 0.266-1.522     |
| Residence district         |                   |                  |                  | 0.713               | 0.989            | 0.555            |                 |
| Urban Reference            |                   |                  |                  | 0.106               | 0.662            | 0.003            |                 |
| Suburban/rural             | 0.912             | 0.557-1.493      |                  | 1.068               | 0.413-2.463      | 0.757            | 0.299-1.916     |
| Education                  |                   |                  |                  |                     |                  |                  |                 |
| Below elementary school    | Reference          |                  |                  | 0.008               | 0.037            | 0.122            |                 |
| Middle school              | 0.743             | 0.405-1.365      |                  | 0.547               | 0.097-3.095      | 0.873            | 0.303-2.518     |
| High school                | 0.746             | 0.437-1.275      |                  | 0.768               | 0.288-2.047      | 0.127            | 0.041-0.392     |
| Above university           | 1.181             | 0.701-1.987      |                  | 1.155               | 0.411-3.243      | 0.430            | 0.141-1.310     |
| Occupation                 |                   |                  |                  |                     |                  |                  |                 |
| Professional job in urban  | Reference          |                  |                  | 0.023               | 0.964            | 0.298            |                 |
| Office job                 | 1.219             | 0.695-2.139      |                  | 0.552               | 0.173-1.760      | 0.537            | 0.126-2.292     |
| Service, sales job         | 0.680             | 0.396-1.168      |                  | 0.656               | 0.223-1.935      | 0.579            | 0.168-1.999     |
| Agriculture and fisheries job | 0.565             | 0.251-1.271      |                  | 0.108               | 0.016-0.746      | 0.234            | 0.046-1.203     |
| Technician, engineer       | 1.498             | 0.863-2.598      |                  | 1.030               | 0.395-2.686      | 0.842            | 0.280-2.533     |
| Labor worker               | 1.073             | 0.487-2.364      |                  | 1.700               | 0.367-7.867      | 0.247            | 0.058-1.048     |
| Jobless                    | 1.487             | 0.880-2.514      |                  | 0.425               | 0.139-1.298      | 0.349            | 0.126-0.968     |
| Glucose tolerance          |                   |                  |                  | 0.273               | 0.029            | 0.009            |                 |
| Normal                     | Reference          |                  |                  | 0.733               | 0.476-1.128      | 1.100            | 0.514-2.355     |
| Impaired fasting glucose   | 0.463             | 0.259-0.830      |                  | 1.103               | 0.222-5.470      | 1.999            | 0.666-5.999     |
| Diabetes mellitus          |                   |                  |                  |                     |                  |                  |                 |
| Depression                 |                   |                  |                  | 0.273               | 0.029            | 0.009            |                 |
| No                         | Reference          |                  |                  | 0.728               | 0.072            | 0.001            |                 |
| Yes                        | 1.247             | 0.839-1.852      |                  | 2.548               | 1.101-5.899      | 2.691            | 1.280-5.655     |
| Elevation of tIgE          |                   |                  |                  |                     |                  |                  |                 |
| Negative                   | Reference          |                  |                  | 0.064               | 0.170            | 0.078            |                 |
| Positive                   | 0.934             | 0.633-1.377      |                  | 0.505               | 0.239-1.064      | 0.264            | 0.123-0.567     |
| Positivity to sIgE to D. farinae | 0.697             | 0.475-1.021      |                  | 1.555               | 0.826-2.926      | 1.943            | 0.927-4.073     |
| Positivity to sIgE to dog  |                   |                  |                  |                     |                  |                  |                 |
| Negative                   | Reference          |                  |                  | 0.007               | 0.729            | 0.001            |                 |
| Positive                   | 0.408             | 0.213-0.784      |                  | 0.801               | 0.227-2.825      | 0.264            | 0.123-0.567     |

OR, odds ratio; CI, confidence interval; tIgE, total immunoglobulin E; sIgE, specific immunoglobulin E.
Risk factors for sensitization to D. farinae
In the univariate analysis (Table 1), male sex, age, occupation, smoking history, BMI, and the vitamin D level were significant risk factors for sensitization to D. farinae. In the multivariate analysis, smoking history, BMI, and the vitamin D level were significant and independently associated with allergic diseases, when compared with those aged 30-39 years as the reference group (OR, 0.611 in those aged 40-49 years; OR, 0.765 in those aged 50-59 years; OR, 0.644 in those aged ≥60 years; P=0.036). Although the vitamin D level was significantly associated with sensitization to D. farinae, the effects on the sensitization were not consistent (OR, 0.731 for quartiles 2-3, P=0.030; OR, 1.072 for quartile 4) (Table 5).

Risk factors for sensitization to B. germanica
In the univariate analysis, male sex, residential district, type of residence, occupation, glucose tolerance status, BMI, and smoking history were significant risk factors for sensitization to B. germanica. In the multivariate analysis, male sex was found to be a significant independent risk factor of sensitization to B. germanica (OR, 0.307 in women; 95% CI, 0.193-0.489; P<0.001), whereas subjects living in apartments had a reduced risk (OR, 0.307 in women; 95% CI, 0.193-0.489; P=0.004) (Table 7).

Risk factors for sensitization to dog
In the univariate analysis, male sex, age, and smoking status were significant risk factors for sensitization to dog. In the multivariate analysis, older age was found to be associated with a low risk for sensitization to dog (P=0.014), whereas smokers were associated with a high risk, as compared with never smokers (OR, 2.423; 95% CI, 1.416-4.145; P=0.004) (Table 7).
DISCUSSION

This large cross-sectional study aimed to identify demographic and environmental factors associated with the prevalence of allergic diseases and allergen sensitization in the non-institutionalized Korean general population. As a result, we found that allergic diseases and allergen sensitization were significantly associated with various demographic factors.

First, age was a significant risk factor for self-reported allergic diseases. Specifically, the prevalence of allergic rhinitis and atopic dermatitis decreased with increasing age, supporting the findings of previous studies. Aging-related immunomodulation and immune tolerance induced by long-term exposure to allergens could be responsible for these associations. In contrast, the asthma prevalence was not associated with age in this study. A previous large-scale cohort study also showed that age was not significantly associated with the prevalence of asthma. However, some previous Korean cohort studies conversely showed that the prevalence of asthma increased with age. Thus, further studies should be performed to confirm the association between the prevalence of asthma and age in Korea.

Second, occupation was a significant contributing factor for allergic diseases. The prevalence of at least 1 allergic disease for subjects in agriculture and fishery occupations was higher than for subjects in other occupations. This finding is consistent with previous studies which showed that exposure to allergens in agricultural and fishery occupations is associated with an increased risk of allergy.

In conclusion, our study identified several risk factors for allergic diseases and allergen sensitization in the Korean population. Further research is needed to understand the mechanisms underlying these associations and to develop strategies to prevent allergic diseases.

Table 5. Univariate and multivariate analyses for positivity of specific immunoglobulin E to D. farinae

| Variables | Univariate analysis | Multivariate analysis* |
|-----------|---------------------|------------------------|
|          | OR 95% CI           | Pvalue  | OR 95% CI | Pvalue  |
| Sex       |                     |         |           |         |
| Male      | 1.000 -              | <0.001  | 1.000 -   | 0.141   |
| Female    | 0.535 0.437-0.654    | 0.720 0.465-1.116    |
| Age (year)|                     |         |           |         |
| 10-19     | 1.000 -              | <0.001  | -         | 0.036   |
| 20-29     | 1.169 0.814-1.679    | -       | -         |         |
| 30-39     | 0.779 0.562-1.079    | 1.000   | -         |         |
| 40-49     | 0.529 0.372-0.751    | 0.611 0.431-0.867    |
| 50-59     | 0.685 0.469-1.001    | 0.785 0.561-1.119    |
| ≥60       | 0.591 0.391-0.892    | 0.644 0.432-0.960    |
| Occupation*|                    |         |           |         |
| Professional job | 1.000 -   | 1.000 -   | 1.000 -   | 0.104   |
| Office job | 0.725 0.451-1.165   | 0.618 0.373-1.025    |
| Service, sales job | 0.655 0.413-1.038 | 0.718 0.426-1.210    |
| Agriculture and fisheries job | 1.666 0.996-2.785 | 1.663 0.919-3.008   |
| Technician, engineer | 1.075 0.713-1.621 | 0.828 0.526-1.302   |
| Labor worker | 0.836 0.498-1.404 | 0.957 0.545-1.681   |
| Jobless    | 0.618 0.409-0.933    | 0.788 0.484-1.282    |
| BMI†       |                     | 0.016   | 0.056     |         |
| Normal    | 1.000 -              | 1.000   | 1.000     |         |
| Low weight| 0.493 0.290-0.838    | 0.377 0.154-0.921    |
| Obesity   | 1.182 0.926-1.509    | 1.146 0.855-1.537    |
| Smoking history†|              | <0.001  | 0.093     |         |
| Never smoker | 1.000 -               | 1.000   | 1.000     |         |
| Light smoker | 0.593 0.468-0.753    | 1.102 0.460-2.643    |
| Smoker    | 0.594 0.315-1.120    | 1.576 1.045-2.377    |
| Serum vitamin D level |               | 0.029   | 0.030     |         |
| Low level (Q1) | 1.000 -             | 1.000   | 1.000     |         |
| Mod level (Q2-Q3) | 0.827 0.858-1.535 | 0.731 0.524-1.020   |
| High level (Q4) | 1.148 0.658-1.040 | 1.072 0.692-1.662   |

Positivity to sIgE was defined as sIgE levels >0.35 kU/L. OR, odds ratio; CI, confidence interval; BMI, body mass index.
*Analysis included subjects aged ≥30 years (n=1,577, representing 9,624,008 citizens ≥30 years); †Analysis included subjects aged ≥19 years (n=1,977, representing 13,762,677 citizens ≥19 years).
vice and sales occupations (20.4%) was significantly lower than that for those in other occupations (31.9%-36.5%; data not shown). Especially, an occupation related to agriculture and fisheries was a protective factor for allergic rhinitis in the multivariate analysis, whereas it was an independent risk factor for the elevation of tIgE. Exposure to a farm environment has been considered protective against allergic diseases, whereas exposure to chemical agents in some occupations, including among technicians and labor workers, is a risk factor for allergic diseases. Thus, different occupational environments may affect the development of allergic disease.

Third, depression was significantly associated with allergic diseases, especially self-reported asthma (OR, 2.691; 95% CI, 1.280-5.655; \( P=0.009 \)) and self-reported atopic dermatitis (OR, 2.549; 95% CI, 1.101-5.899; \( P=0.029 \)). However, in contrast to the other factors described above, depression may not be a direct cause of allergic disease. The adverse effect of self-reported allergic disease on depression has already been well demonstrated in previous studies, and it is likely that depression may be induced or aggravated by allergic diseases rather than being a cause.

Lastly, glucose intolerance was found to be a significant risk factor for allergic rhinitis, whereas a higher level of education was protective for self-reported asthma. Previous studies have reported a significant correlation between diabetes and allergic diseases. However, evidence to confirm a significant causal re-

### Table 6. Univariate and multivariate analyses for positivity of specific immunoglobulin E to B. germanica

| Variables                        | Univariate analysis | Multivariate analysis* |
|----------------------------------|---------------------|------------------------|
|                                  | OR      | 95% CI       | \( P \) value | OR      | 95% CI       | \( P \) value |
| Sex                              |         |              |               |         |              |               |
| Male                             | 1.000   | -            | <0.001        | 1.000   | -            | <0.001        |
| Female                           | 0.365   | 0.262-0.473  | 0.307         | 0.193-0.489 |
| Residence district               |         |              | 0.040         |         |              | 0.230         |
| Urban                            | 1.000   | -            |               | 1.000   | -            |               |
| Suburban/rural                   | 1.458   | 1.017-2.090  | 1.293         | 0.849-1.970 |
| Type of residence                |         |              | <0.001        |         |              | 0.028         |
| House                            | 1.000   | -            |               | 1.000   | -            |               |
| Apartment                        | 0.583   | 0.446-0.761  | 0.682         | 0.484-0.959 |
| Occupation*                      |         |              | <0.001        |         |              | 0.221         |
| Professional job                 | 1.000   | -            |               | 1.000   | -            |               |
| Office job                       | 1.340   | 0.758-2.369  | 1.317         | 0.693-2.501 |
| Service, sales job               | 1.107   | 0.616-1.988  | 1.359         | 0.701-2.635 |
| Agriculture and fisheries job    | 2.256   | 1.272-4.03  | 1.761         | 0.902-3.437 |
| Technician, engineer             | 1.823   | 1.058-3.240  | 1.341         | 0.720-2.469 |
| Labor worker                     | 2.114   | 1.084-4.121  | 2.500         | 1.219-5.127 |
| Jobless                          | 0.843   | 0.512-1.389  | 1.297         | 0.763-2.205 |
| Glucose tolerance†               |         |              | <0.001        |         |              | 0.012         |
| Normal                           | 1.000   | -            |               | 1.000   | -            |               |
| Impaired fasting glucose         | 1.748   | 1.237-2.470  | 1.413         | 0.568-2.084 |
| Diabetes mellitus                | 2.418   | 1.555-3.761  | 1.928         | 1.182-3.147 |
| BMI†                             |         |              | <0.001        |         |              | 0.225         |
| Normal                           | 1.000   | -            |               | 1.000   | -            |               |
| Low weight                       | 0.346   | 0.128-0.935  | 0.274         | 0.055-1.363 |
| Obesity                          | 1.611   | 1.224-2.122  | 1.126         | 0.804-1.577 |
| Smoking history†                 |         |              | <0.001        |         |              | 0.972         |
| Smoker                           | 1.000   | -            |               | 1.000   | -            |               |
| Light smoker                     | 0.869   | 0.413-1.828  | 0.958         | 0.387-2.374 |
| Never smoker                     | 0.496   | 0.384-0.676  | 0.945         | 0.589-1.517 |

Positivity to sIgE was defined as IgE levels >0.35 kU/L.
OR, odds ratio; CI, confidence interval; BMI, body mass index.
*Analysis included subjects aged ≥30 years (n=1,577, representing 9,624,008 citizens ≥30 years); †Analysis included subjects aged ≥19 years (n=1,977, representing 13,762,677 citizens ≥19 years).
The factors associated with positivity of sIgE differed according to the type of allergen. Male sex and house residence were significant factors associated with positivity of sIgE to B. germanica. These factors are associated with household hygiene and have been previously reported as significant factors for sensitization to B. germanica. In addition, smoking was significantly associated with positivity of sIgE to dog; this result is also supported by other studies.

Some of the associated factors identified in the present study are modifiable, and exposure or avoidance of these factors may help prevent allergen sensitization and development of allergic diseases. For example, early exposure to a farm-like environment may help prevent allergic diseases. Hygiene-related factors, including residing in an apartment, and glucose intolerance should be improved to avoid sensitization to cockroaches. In addition, avoidance of smoking and obesity may help prevent the development of allergic diseases.

The major strength of this study is that the data were obtained from a well-designed national program with complex, multi-stage probability sample extraction, and that we used complex sample analysis, resulting in the representation of 16,003,645 citizens, which is one-third of the total population of Korea. Although the KNHANES provides specific guidelines to ensure appropriate estimates and results due to the inherent nature of a multiple complex survey design, almost all research articles published on the basis of the data from the KNHANES used standard statistical analyses. We followed the KNHANES guidelines concerning the statistical analysis; this provided valuable information that can be generalized to the entire Kore-

### Table 7. Univariate and multivariate analyses for positivity of specific immunoglobulin E to dog

| Variables                  | Univariate analysis          | Multivariate analysis*          |
|----------------------------|------------------------------|---------------------------------|
|                            | OR   | 95% CI | *P value* | OR   | 95% CI | *P value* |
| Sex                        |      |        |          |      |        |          |
| Male                       | 1.000| -      | <0.001   | 1.000| -      | 0.249    |
| Female                     | 0.407| 0.278-0.596 | 0.750   | 0.459-1.226 | 0.492 | 0.069-0.814 | 0.162 | 0.043-0.610 | 0.271 | 0.076-0.971 | 0.186 | 0.050-0.685 | 0.001 | 0.004 |
| Age (year)                 |      |        |          |      |        |          |
| 10-19                      | 1.000| -      |          | 1.000| -      |          |
| 20-29                      | 0.575| 0.316-1.045 | 0.492   | 0.150-1.617 | 0.237 | 0.069-0.814 | 0.162 | 0.043-0.610 | 0.271 | 0.076-0.971 | 0.186 | 0.050-0.685 | 0.001 | 0.004 |
| 30-39                      | 0.373| 0.184-0.757 | 0.271   | 0.076-0.971 | 0.186 | 0.050-0.685 | 0.001 | 0.004 |
| 40-49                      | 0.644| 0.335-1.236 | 0.271   | 0.076-0.971 | 0.186 | 0.050-0.685 | 0.001 | 0.004 |
| 50-59                      | 0.411| 0.200-0.846 | 0.271   | 0.076-0.971 | 0.186 | 0.050-0.685 | 0.001 | 0.004 |
| ≥60                        |      |        |          |      |        |          |
| Smoking history*           |      |        |          |      |        |          |
| Never smoker               | 1.000| -      |          | 1.000| -      |          |
| Light smoker               | 0.941| 0.157-1.533 | 1.024   | 0.293-3.576 | 1.243 | 0.234-6.363 | 2.423 | 1.416-4.145 | 0.001 | 0.004 |
| Smoker                     | 0.385| 0.234-0.636 | 2.423   | 1.416-4.145 | 0.001 | 0.004 |

Positivity to sIgE was defined as sIgE levels > 0.35 kU/L.
OR, odds ratio; CI, confidence interval.
*Analysis included subjects aged ≥ 19 years (n = 1,977, representing 13,762,677 citizens ≥ 19 years).

The relationship between these conditions is still lacking. Similarly, while data regarding the effects of education level on self-reported asthma have been accumulated, the evidence is still insufficient.

Interestingly, in the present study, we observed significant gaps between the tIgE level and the prevalence of allergic disease. Male sex, obesity, and smoking were identified as significant risk factors for tIgE. The higher frequency of elevated tIgE in men supports the findings of previous studies. This result may be secondary to the correlations of alcohol consumption and/or parasitic infections with IgE, as heavy alcoholics and asymptomatic parasite-infected subjects are frequently observed in Korea, especially among men.

Although the data are not shown, the positivity rate of tIgE increased with increasing alcohol consumption amount in this study (37.1%, 50.5%, and 70.5% for subjects with ≤ 1, 2-3, and ≥ 4 events of alcohol consumption/week, respectively P < 0.001). However, male sex was still a significant risk factor for positivity of tIgE even after adjusting for the alcohol consumption amount in the multivariate analysis, indicating that male sex is an independent risk factor for positivity of tIgE regardless of alcohol consumption. The effects of obesity and smoking on the tIgE level are also widely accepted, based on sufficient evidence. Of note, recent studies have revealed that the sIgE/tIgE ratio is more accurate than sIgE alone in predicting outcomes in food allergy, suggesting a protective effect of tIgE against allergic symptoms. However, this topic remains controversial, with varying opinions, and some studies have suggested that the serum tIgE level is positively correlated with allergic disease.
an general population.

However, an important limitation of the present study is its cross-sectional design; because it was not a longitudinal study, the temporal relationship of the associated factors could not be evaluated. For example, we could not determine if smoking was a significant risk factor for allergic diseases or if subjects with allergic disease were at risk for smoking. Another limitation of this study is that the data in the multivariate analysis were assessed only for subjects who were older than 30 years. This was because we considered that the assessment of the subjects’ education level, marriage status, income level, and occupation at that age was reliable. Third, most parameters, including allergic disease, occupation, and income level, were obtained using a self-reported survey. The prevalence of physician-diagnosed allergic disease may differ from that of self-reported allergic disease. Similarly, self-reported occupation and income level may be affected by the respondent’s judgment. Moreover, the residence district and occupation may also be affected by various parameters. For example, people who moved to a rural area recently after living in an urban area or who had a recent change in occupation might result in confusion. Lastly, although we could not conduct further analysis due to limited provided information, dividing the subjects into those with allergic asthma and non-allergic asthma might provide interesting results, as the pathogeneses and treatments differ between these entities.47

In conclusion, demographic and environmental risk factors associated with the tIgE and sIgE levels, as well as with self-reported allergic diseases, differ according to the type of allergens and allergic diseases. The results of the present study suggest that appropriate management of numerous modifiable factors might help prevent allergic sensitization and development of allergic diseases. Further studies are warranted to confirm our findings and identify any causal relationships.

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REFERENCES

1. Larsen FS, Holm NV, Henningsen K. Atopic dermatitis. A genetic-epidemiologic study in a population-based twin sample. J Am Acad Dermatol 1986;15:487-94.
2. Sicherer SH, Furlong TJ, Maes HH, Desnick RJ, Sampson HA, Gelb BD. Genetics of peanut allergy: a twin study. J Allergy Clin Immunol 2000;106:53-6.
3. Liu X, Zhang S, Tsai HJ, Hong X, Wang B, Fang Y, et al. Genetic and environmental contributions to allergen sensitization in a Chinese twin study. Clin Exp Allergy 2009;39:991-8.
4. Campbell DE, Boyle RJ, Thornton CA, Prescott SL. Mechanisms of allergic disease - environmental and genetic determinants for the development of allergy. Clin Exp Allergy 2015;45:844-58.
5. Ariano R, Berra D, Chiodini E, Ortolani V, Cremoni LG, Mazzarello MG, et al. Ragweed allergy: pollen count and sensitization and allergy prevalence in two Italian allergy centers. Allergy Rhinol (Providence) 2015;6:177-83.
6. Park HJ, Lee JH, Park KH, Kim KR, Han MJ, Choe H, et al. A six-year study on the changes in airborne pollen counts and skin positivity rates in Korea: 2008-2013. Yonsei Med J 2016;57:714-20.
7. Song Y, Wang M, Xie J, Li W, Zhang X, Wang T, et al. Prevalence of allergic rhinitis among elementary and middle school students in Changsha city and its impact on quality of life. J Laryngol Otol 2015;129:1108-14.
8. Lusi EA, Di Ciommo VM, Patrissi T, Guarascio P. High prevalence of nickel allergy in an overweight female population: a pilot observational analysis. PLoS One 2015;10:e0123265.
9. Han YY, Forno E, Gogna M, Celedón JC. Obesity and rhinitis in a nationwide study of children and adults in the United States. J Allergy Clin Immunol 2016;137:1460-5.
10. Niruban SJ, Aliagakrishnan K, Beach J, Senthilselvan A. Association between vitamin D and respiratory outcomes in Canadian adolescents and adults. J Asthma 2015;52:653-61.
11. Kim Y. The Korea National Health and Nutrition Examination Survey (KNHANES): current status and challenges. Epidemiol Health 2014;36:e2014002.
12. Chun YH, Han K, Park YG, Yoon JS, Kim HH, Kim JT, et al. Examining impacts of allergic diseases on psychological problems and tobacco use in Korean adolescents: the 2008-2011 Korean National Health and Nutrition Examination Survey. PLoS One 2015;10:e0125172.
13. Lu Y, Mak KK, van Bever HP, Ng TP, Mak A, Ho RC. Prevalence of anxiety and depressive symptoms in adolescents with asthma: a meta-analysis and meta-regression. Pediatr Allergy Immunol 2012;23:707-15.
14. Kim DH, Han K, Kim SW. Relationship between allergic rhinitis and mental health in the general Korean adult population. Allergy Asthma Immunol Res 2016;8:49-54.
15. Fukui M, Tanaka M, Hamaguchi M, Senmaru T, Sakabe K, Shiraishi E, et al. Eosinophil count is positively correlated with albumin excretion rate in men with type 2 diabetes. Clin J Am Soc Nephrol 2009;4:1761-5.
16. Park HJ, Lim HS, Park KH, Lee JH, Park JW, Hong CS. Changes in allergen sensitization over the last 30 years in Korea respiratory allergic patients: a single-center. Allergy Asthma Immunol Res 2014;6:434-43.
17. Salo PM, Arbes SJ Jr, Jaramillos R, Calatroni A, Weir CH, Sever ML, et al. Prevalence of allergic sensitization in the United States: results from the National Health and Nutrition Examination Survey (NHANES) 2005-2006. J Allergy Clin Immunol 2014;134:350-9.
18. Hwang CY, Chen YJ, Lin MW, Chen TJ, Chu SY, Chen CC, et al. Prevalence of atopic dermatitis, allergic rhinitis and asthma in Taiwan: a national study 2000 to 2007. Acta Derm Venereol 2010;90:589-94.
19. Vasto S, Malavolta M, Pawelec G. Age and immunity. Immun Ageing 2006;3:2.
20. Yao CW, Shen TC, Lu CR, Wang YC, Lin CL, Tu CY, et al. Asthma is
associated with a subsequent risk of peripheral artery disease: a longitudinal population-based study. Medicine (Baltimore) 2016; 95:e2546.

21. Kim S, Kim J, Kim K, Kim Y, Park Y, Baek S, et al. Healthcare use and prescription patterns associated with adult asthma in Korea: analysis of the NHI claims database. Allergy 2013;68:1435-42.

22. Kim CY, Park HW, Ko SK, Chang SI, Moon HB, Kim YY, et al. The financial burden of asthma: a nationwide comprehensive survey conducted in the republic of Korea. Allergy Asthma Immunol Res 2011;3:34-8.

23. von Mutius E, Vercelli D. Farm living: effects on childhood asthma and allergy. Nat Rev Immunol 2010;10:861-8.

24. Smit LA, Heederik D, Lammers JW, Wouters IM. Occupational endotoxin exposure reduces the risk of atopic sensitization but increases the risk of bronchial hyperresponsiveness. Int Arch Allergy Immunol 2010;152:151-8.

25. Elholm G, Schlünssen V, Doekes G, Basinas I, Bibby BM, Hjort C, et al. Become a farmer and avoid new allergic sensitization: adult farming exposures protect against new-onset atopic sensitization. J Allergy Clin Immunol 2013;132:1239-41.

26. Prodi A, Rui F, Fortina AB, Corradin MT, Filon FL. Occupational sensitization to epoxy resins in Northeastern Italy (1996-2010). Int J Occup Environ Health 2015;21:82-7.

27. Zhao HJ, Cai SX, Tong WC, Li WJ, Fu L. Influence of education level on self-evaluation and control of patients with bronchial asthma. Nan Fang Yi Ke Da Xue Xue Bao 2008;28:715-7.

28. Lee KS, Rha YH, Oh IH, Choi YS, Choi SH. Socioeconomic and sociodemographic factors related to allergic diseases in Korean adolescents based on the Seventh Korea Youth Risk Behavior Web-based Survey: a cross-sectional study. BMC Pediatr 2016;16:19.

29. Ezeamuzie CI, Al-Ali SF, Al-Dowaisan A, Khan M, Hilaji Z, Thomson MS. Reference values of total serum IgE and their significance in the diagnosis of allergy among the young adult Kuwaiti population. Clin Exp Allergy 1999;29:375-81.

30. Paula Couto TA, Falsarella N, Mattos Cde C, Mattos LC. Total IgE plasma levels vary according to gender and age in Brazilian patients with allergic rhinitis. Clinics (Sao Paulo) 2014;69:740-6.

31. Linneberg A, Petersen J, Nielsen NH, Madsen F, Frølund L, Dirksen R. Serum total IgE levels vary according to gender and age in Brazilian patients with allergic rhinitis. Clinics (Sao Paulo) 2014;69:740-6.

32. Song WJ, Chang YS, Lim MK, Yun EH, Kim SH, Kang HK, et al. The relationship of alcohol consumption to total immunoglobulin E and the development of immunoglobulin E sensitization: the Copenhagen Allergy Study. Clin Exp Allergy 2003;33:192-8.

33. Song WJ, Chang YS, Lim MK, Yun EH, Kim SH, Kang HK, et al. Staphylococcal enterotoxin sensitization in a community-based population: a potential role in adult-onset asthma. Clin Exp Allergy 2014;44:553-62.

34. Visness CM, London SJ, Daniels JL, Kaufman JS, Yeatts KB, Sieg-Riz AM, et al. Association of obesity with IgE levels and allergy symptoms in children and adolescents: results from the National Health and Nutrition Examination Survey 2005-2006. J Allergy Clin Immunol 2009;123:1163-9, 1169.e1-4

35. Schachter LM, Peat JK, Salome CM. Asthma and atopy in overweight children. Thorax 2003;58:1031-5.

36. Holford-Strevens V, Warren P, Wong C, Manfreda J. Serum total immunoglobulin E levels in Canadian adults. J Allergy Clin Immunol 1984;73:516-22.

37. Barbee RA, Halonen M, Kaltenborn W, Lebowitz M, Burrows B. A longitudinal study of serum IgE in a community cohort: correlations with age, sex, smoking, and atopic status. J Allergy Clin Immunol 1987;79:919-27.

38. Gupta RS, Lau CH, Hamilton RG, Donnell A, Newhall KK. Predicting outcomes of oral food challenges by using the allergen-specific IgE-total IgE ratio. J Allergy Clin Immunol Pract 2014;2:300-5.

39. Grabenhenrich L, Lange L, Härtl M, Kalb B, Ziegert M, Finger A, et al. The component-specific to total IgE ratios do not improve peanut and hazelnut allergy diagnoses. J Allergy Clin Immunol 2016;137:1751-1760.e8.

40. Daniluk U, Allifier M, Kaczmarski M, Stasiak-Barmuta A, Lebszcztejo D. Longitudinal observation of children with enhanced total serum IgE. Ann Allergy Asthma Immunol 2015;114:404-410.e4.

41. Benício MH, Ferreira MJ, Cardoso MR, Konno SC, Monteiro CA. Wheezing conditions in early childhood: prevalence and risk factors in the city of São Paulo, Brazil. Bull World Health Organ 2004;82:516-22.

42. Satwani H, Rehman A, Ashraf S, Hassan A. Is serum total IgE levels a good predictor of allergies in children? J Pak Med Assoc 2009;59:698-702.

43. Kim SH, Yang SY, You J, Lee SB, You J, Chang YS, et al. Association of specific immunoglobulin E to staphylococcal enterotoxin with airway hyperresponsiveness in asthma patients. Tuberc Respir Dis (Seoul) 2016;79:295-301.

44. Adisesh A, Gruszka L, Robinson E, Evans G. Smoking status and immunoglobulin E seropositivity to workplace allergens. Occup Med (Lond) 2011;61:62-4.

45. Shargorodsky J, Garcia-Esquinas E, Navas-Acien A, Lin SY. Allergic sensitization, rhinitis, and tobacco smoke exposure in U.S. children and adolescents. Int Forum Allergy Rhinol 2015;5:471-6.

46. Kim Y, Park S, Kim NS, Lee BK. Inappropriate survey design analysis of the Korean National Health and Nutrition Examination Survey may produce biased results. J Prev Med Public Health 2013;46:96-104.

47. Kim DK, Park YB, Oh YM, Jung KS, Yoo JH, Yoo KH, et al. Korean Asthma Guideline 2014: summary of major updates to the Korean Asthma Guideline 2014. Tuberc Respir Dis (Seoul) 2016;79:111-20.