



Regional Difference of Causative Pollen in Children with Allergic Rhinitis

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The aim of this study was to investigate role of common pollen in Korean school-aged children with allergic rhinitis (AR) in 5 provinces (Incheon Metropolitan City-Gyeonggi Province, Chungcheongbuk-do, Gwangju Metropolitan City, Busan Metropolitan City, and Jeju Special Self-Governing Province), using a questionnaire and skin prick test, and to assess the differences among the residential regions. Among the enrolled 14,678 total children, 1,641 (22.0%) had AR. The sensitization rate to pollen (38.7%) was the second highest among examined allergens and significant differences were in the sensitization rates to trees, weeds, and grasses among the 5 provinces ($P < 0.05$). The sensitization to trees (25.2%) was the highest common among the pollen types and significant differences also were observed in the sensitization rates to alder, birch, Japanese cedar, oak, and elm among the 5 provinces. The sensitization rate to weeds (19.9%) was the second highest and significant differences were observed in the sensitization rate to Japanese hop, mugwort, and ragweed among the 5 provinces. The sensitization rate to house dust mite was 86.8%, the highest among examined allergens and that to *Dermatophagoides farinae* exhibited regional differences ($P = 0.003$) but not to *D. farinae* ($P = 0.584$). The sensitization rate to mold (13.5%) was the highest in Jeju and lowest in Busan, and a statistically significant difference was detected among the 5 provinces. These results support that examined pollen allergens are strongly associated with residential region due to regional causative pollen differences among children with AR within Korea to investigate the main pollen allergens.

Keywords: Rhinitis; Pollen; Children; Region

INTRODUCTION

Allergic rhinitis (AR) is one of the most common allergic diseases worldwide. The symptoms of which interrupt the daily and school lives of children and the disease may create an economic burden (1-3). Therefore, the accurate diagnosis and appropriate treatment of AR are becoming very important. For these reasons, the Korean Academy of Pediatric Allergy and Respiratory Diseases (KAPARD) completed the International Study of Asthma and Allergies in Childhood (ISAAC) survey in 1995 and 2000 (4,5).

However, these studies of AR were solely conducted using questionnaires and did not obtain any information about AR common allergens. Other studies have also investigated children who visited clinics or hospitals with AR symptoms including coughing, rhinorrhea, and nasal stiffness and these studies were limited to small populations in special regions (6-8). Because of the global warming, pollen reactivity of AR has increased in Korea (9-11). In the recent study, tree pollen sensitization in the 2010s sharply increased among pollen types but this study had been conducted in a single-center (15). Owing to such lim-

itations of the previous studies, common allergens including pollen could not be ascertained in school-aged children with AR within Korea.

Therefore, the aim of this study was to investigate the causative pollen in Korean school-aged children with AR in 5 provinces (Incheon Metropolitan City-Gyeonggi Province [Gyeonggi], Chungcheongbuk-do [Chungbuk], Gwangju Metropolitan City [Gwangju], Busan Metropolitan City [Busan], and Jeju Special Self-Governing Province [Jeju]) by using questionnaire and skin prick test (SPT) and to assess the differences of popular pollen among residential regions.

MATERIALS AND METHODS

Study design and subjects

A total of 14,678 school-aged children (from the first grade of elementary school to the second grade of high school) were randomly enrolled in the Inha University School of Medicine and Environmental Health Center for Allergic Rhinitis. They were enrolled for a cross-sectional study based on the general population in 5 provinces between March 2010 and December

2015. Pediatricians and trained field technicians visited 5 provinces of schools that were 52 elementary, 27 middle, and 23 high schools. The students' parents completed a modified Korean version of a questionnaire formulated by the ISAAC prior to their visiting. The students underwent the physical examinations and SPT in their respective schools by trained field technicians. In the present study, AR was defined as having current symptoms of AR with at least one or more positive allergens in SPT.

Questionnaire

The Korean ISAAC questionnaire, a standardized method to evaluate AR in Korean epidemiologic studies, was used (4). The prevalence of AR was identified through a comprehensive evaluation of clinical history, including: 1) lifetime symptoms of AR—Has your child ever had a problem with sneezing, a runny, or a blocked nose when he/she DID NOT have a cold or the flu?; and 2) 12-month symptoms of AR—During the past 12 months, has your child had a problem of sneezing, a runny, or a blocked nose when he/she DID NOT have a cold or the flu? Age, gender, birth date, and schools were considered confounding factors.

Measurement of atopy

The SPTs were performed on the volar skin surface of both arms with normal appearance. The positive and negative controls and all the allergens were manufactured by Allergopharma (Reinbek, Germany) except *Chenopodiaceae*. The reagents for *Chenopodiaceae* were manufactured by Shin Kwang New Drugs Company (Seoul, Korea). Subjects were tested for sensitivity to the following 27 common allergens including pollen (tree: *Cryptomeria* [Japanese cedar], *Pinus* [pine], *Salix* [willow], *Acer* [maple], *Betula* [birch], *Quercus* [oak], *Alnus* [alder], *Ulmus* [elm]; weed: *Ambrosia* [ragweed], *Artemisia* [mugwort], *Humulus* [Japanese hop], *Chenopodiaceae* [fathen], *Plantago* [plantain]; grass: *Cynodon* [Bermuda grass], *Phleum* [timothy grass], *Lolium* [rye grass], *Dactylis* [orchard grass], *Poa* [meadow grass], *Anthoxanthum* [vernal grass]), house-dust mites (HDM: *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*), mold (*Penicilla*

tum, *Aspergillus*, *Cladosporium*, and *Alternaria*), and pet (dog hair and cat fur) (9-12).

In the present study, the pollen name was allowed by the scientific name based on the internationally accepted notation of the International Code of Botanical Nomenclature, and the English name was written in parentheses to facilitate comprehension of the scientific name. Generic names that were difficult to classify morphologically were written as the family name. A positive SPT was defined as a mean wheal diameter ≥ 3 mm and greater than that of the positive control (12). Allergic sensitization was defined as the presence of one or more positive reactions to the SPT.

Statistical analysis

All of the statistical analyses were performed using SAS (ver. 9.4; SAS Institute Inc., Cary, NC, USA). The experimental results are presented as arithmetic mean \pm standard deviation (SD). One-way analysis of variance (ANOVA) was used to assess intergroup differences in continuous variables, while the frequencies were compared using the ANOVA. A *P* value < 0.05 was considered significant.

Ethics statement

This study was approved by the Institutional Review Board (IRB) at Inha University in Incheon (IRB approval number: 12-05). Written informed consent was confirmed by the IRB and was obtained from all parents prior to participation.

RESULTS

General characteristics

Subject characteristics are shown in Table 1. School-aged children from 5 provinces (Gyeongin, Chungbuk, Gwangju, Busan, and Jeju) participated in the present study. A total of 14,678 participants were recruited from Gyeongin (7,622; 52.2%), Chungbuk (2,212; 15.1%), Gwangju (1,224; 8.3%), Busan (2,213; 15.1%), and Jeju (1,407; 9.6%).

Table 1. Demographic characteristics of the study population

Characteristics	GG & IC	CB	GJ	BS	JJ	Total	<i>P</i> value
No. (%)	7,622 (100.0)	2,212 (100.0)	1,224 (100.0)	2,213 (100.0)	1,407 (100.0)	14,678 (100.0)	
Gender							< 0.001
Boy	3,746 (49.1)	1,006 (45.5)	571 (46.7)	1,254 (56.7)	715 (50.8)	7,292 (49.7)	
Girl	3,876 (50.9)	1,206 (54.5)	653 (53.3)	959 (43.3)	692 (49.2)	7,386 (50.3)	
Schools							< 0.001
Elementary	2,985 (39.2)	1,026 (46.4)	390 (31.9)	991 (44.8)	569 (40.4)	5,961 (40.6)	
Middle	2,555 (33.5)	704 (31.8)	360 (29.4)	649 (29.3)	486 (34.5)	4,754 (32.4)	
High	2,082 (27.3)	482 (21.8)	474 (38.7)	573 (25.9)	352 (25.0)	3,963 (27.0)	
Age, yr	12.55 \pm 3.46	13.32 \pm 9.07	13.57 \pm 2.87	12.35 \pm 2.93	12.65 \pm 2.44	12.73 \pm 4.61	< 0.001
Duration	2010 Mar–2015 Nov	2010 Sep–2010 Nov	2013 Apr–2013 Aug	2014 Mar–2014 Jun	2010 Mar	2010 Mar–2015 Nov	

Values are presented as number (%) and mean \pm SD.

GG & IC = Incheon Metropolitan City-Gyeonggi Province, CB = Chungcheongbuk-do, GJ = Gwangju Metropolitan City, BS = Busan Metropolitan City, JJ = Jeju Special Self-Governing Province, SD = standard deviation.

Significant differences were observed in gender, the proportion of schools, and mean age among the 5 provinces. The study sample included 7,292 (49.7%) boys and 7,386 (50.3%) girls, and 5,961 (40.6%) from elementary schools, 4,754 (32.4%) from middle schools, and 3,963 (27.0%) from high schools. Gwangju exhibited the highest proportion of high schools, whereas the other provinces exhibited the highest proportion of elementary schools. The mean ages \pm SDs of the total population was 12.73 ± 4.61 years; that of Gwangju was 13.57 ± 2.87 years, the oldest, while that of Busan was 12.35 ± 2.93 years, the youngest.

Characteristics of the subjects with AR in the 5 provinces

The characteristics of children with AR are shown in Table 2. A total of 3,236 children had AR; 1,651 from Gyeongin, 477 from Chungbuk, 304 from Gwangju, 452 from Busan, and 1,407 from Jeju. The overall prevalence of AR was 22.0%, and Jeju exhibited the highest prevalence of AR among the 5 provinces, whereas Busan exhibited the lowest. Of the 3,236 children, boys (1,927; 59.6%) were more likely to have AR compared to girls (1,309; 40.4%). The proportion of schools was 20.0% elementary, 23.0% middle, and 24.0% high schools. The highest proportion of elementary schools was detected in Chungbuk and Busan. Gyeongin and Jeju exhibited the highest proportion of middle schools, whereas Gwangju exhibited the highest proportion of high schools.

Allergen sensitization rate of AR in school children in the 5 provinces

The sensitization rate to pollen (38.7%) was the second highest among the examined allergens. Sensitization rate to pollen was the highest in Jeju (50.6%) and lowest in Gyeongin (35.3%). A statistically significant difference was detected among the 5 provinces ($P < 0.001$) (Fig. 1A).

Pollen was divided into 3 types (tree, weed, grass) in the present study. The sensitization rate to trees (25.2%) was the highest

among pollen types. Concerning region, sensitization rate to trees was the highest in Jeju (42.3%) and lowest in Gyeongin (19.0%) and, a statistically significant difference was detected among the 5 provinces ($P < 0.001$). Significant differences also were observed in the sensitization rates to alder, birch, Japanese cedar, oak, and elm in children with AR among the 5 provinces. The sensitization rate to birch (10.3%) was the highest among the tree pollens. According to regions, the sensitization rate to birch was as follows: 23.9%, Busan; 14.8%, Gwangju; 12.8%, Chungbuk; 6.4%, Gyeongin; 4.0%, Jeju. The sensitization rate to alder (8.8%) was the second among the tree pollens. The sensitization rate to alder was the highest in Busan (21.0%) among the 5 provinces, while that to alder in other provinces was as follows: 11.8%, Gwangju; 10.7%, Chungbuk; 6.0%, Gyeongin; 1.4%, Jeju. The sensitization rate to oak was 6.7%, the third among the tree pollens, highest in Busan (11.5%) and lowest in Jeju (2.8%) (Fig. 1B).

The sensitization rate to weeds was 19.9%, the second highest among the pollen type. The sensitization rate to weeds was the highest in Chungbuk (28.9%) and lowest in Busan (10.4%) and, there was a statistically significant difference among the 5 provinces. Significant differences also were observed in the sensitization rate to Japanese hop, mugwort, and ragweed among the 5 provinces. The sensitization rate to Japanese hop (10.1%) was the highest among the weeds and, in Chungbuk (16.4%), and the lowest in Jeju (4.6%). The sensitization rate to mugwort (8.4%) was the second highest among the weeds and, in Chungbuk (11.7%), and the lowest in Busan (2.4%). The sensitization rate to ragweed was the highest in Gwangju (3.6%) and, the lowest in Busan (0.2%) (Fig. 1C).

The sensitization rate to grass was 7.6%, the third highest among the pollen types. The sensitization rate to grass was the highest in Jeju (12.5%), and the lowest in Busan (5.3%). There was a statistically significant difference among the 5 provinces ($P < 0.001$) (Fig. 1D).

Table 2. Demographic characteristics of the students with AR

Characteristics	GG & IC	CB	GJ	BS	JJ	Total	P value
No. (%)	1,651 (100.0)	477 (100.0)	304 (100.0)	452 (100.0)	352 (100.0)	3,236 (100.0)	
Gender							< 0.001
Boy	1,035 (62.7)	239 (50.1)	156 (51.3)	284 (62.8)	213 (60.5)	1,927 (59.6)	
Girl	616 (37.3)	238 (49.9)	148 (48.7)	168 (37.2)	139 (39.5)	1,309 (40.4)	
School							< 0.001
Elementary	530 (32.1)	245 (51.4)	100 (32.9)	205 (45.4)	113 (32.1)	1,193 (36.9)	
Middle	602 (36.5)	139 (29.1)	81 (26.6)	144 (31.9)	127 (36.1)	1,093 (33.8)	
High	519 (31.4)	93 (19.5)	123 (40.5)	103 (22.8)	112 (31.8)	950 (29.4)	
Age, yr	12.92 ± 2.88	13.08 ± 8.77	13.61 ± 2.97	12.36 ± 2.75	13.13 ± 2.46	12.95 ± 4.26	0.002
Prevalence, %	21.7	21.6	24.8	20.4	25.0	22.0	
Elementary	17.8	23.9	25.6	20.7	19.9	20.0	
Middle	23.6	19.7	22.5	22.2	26.1	23.0	
High	24.9	19.3	25.9	18.0	31.8	24.0	

Values are presented as number (%) and mean \pm SD.

AR = allergic rhinitis, GG & IC = Incheon Metropolitan City-Gyeonggi Province, CB = Chungcheongbuk-do, GJ = Gwangju Metropolitan City, BS = Busan Metropolitan City, JJ = Jeju Special Self-Governing Province, SD = standard deviation.

The sensitization rate to HDM, *D. pteronyssinus* and *D. farinae*, was the highest (86.8%) among the examined allergens. The sensitization rate to HDM was the highest in Gwangju (89.5%) and, lowest in Jeju (83.5%), and a statistically significant difference was detected among the 5 provinces ($P = 0.048$). The sensitization rate to *D. pteronyssinus* (77.3%) was higher than that to *D. farinae* (68.1%). Concerning region, the sensitization rate to *D. pteronyssinus* was the highest in Busan (79.4%) and the lowest in Chungbuk (76.1%). No statistically significant differ-

ence was detected among the 5 provinces ($P = 0.584$). Sensitization rate to *D. farinae* was the highest in Gwangju (73.4%) and, that to *D. farinae* in other provinces was as follows: 73.0%, Busan; 69.4%, Chungbuk; 66.6%, Gyeongin; 62.5%, Jeju. Significant differences were observed in the sensitization rate *D. farinae* in the 5 provinces ($P = 0.003$) (Fig. 1E).

The sensitization rate to mold was 13.5%, the highest in Jeju (19.3%) and lowest in Busan (7.1%). A statistically significant difference was detected among the 5 provinces. Significant dif-

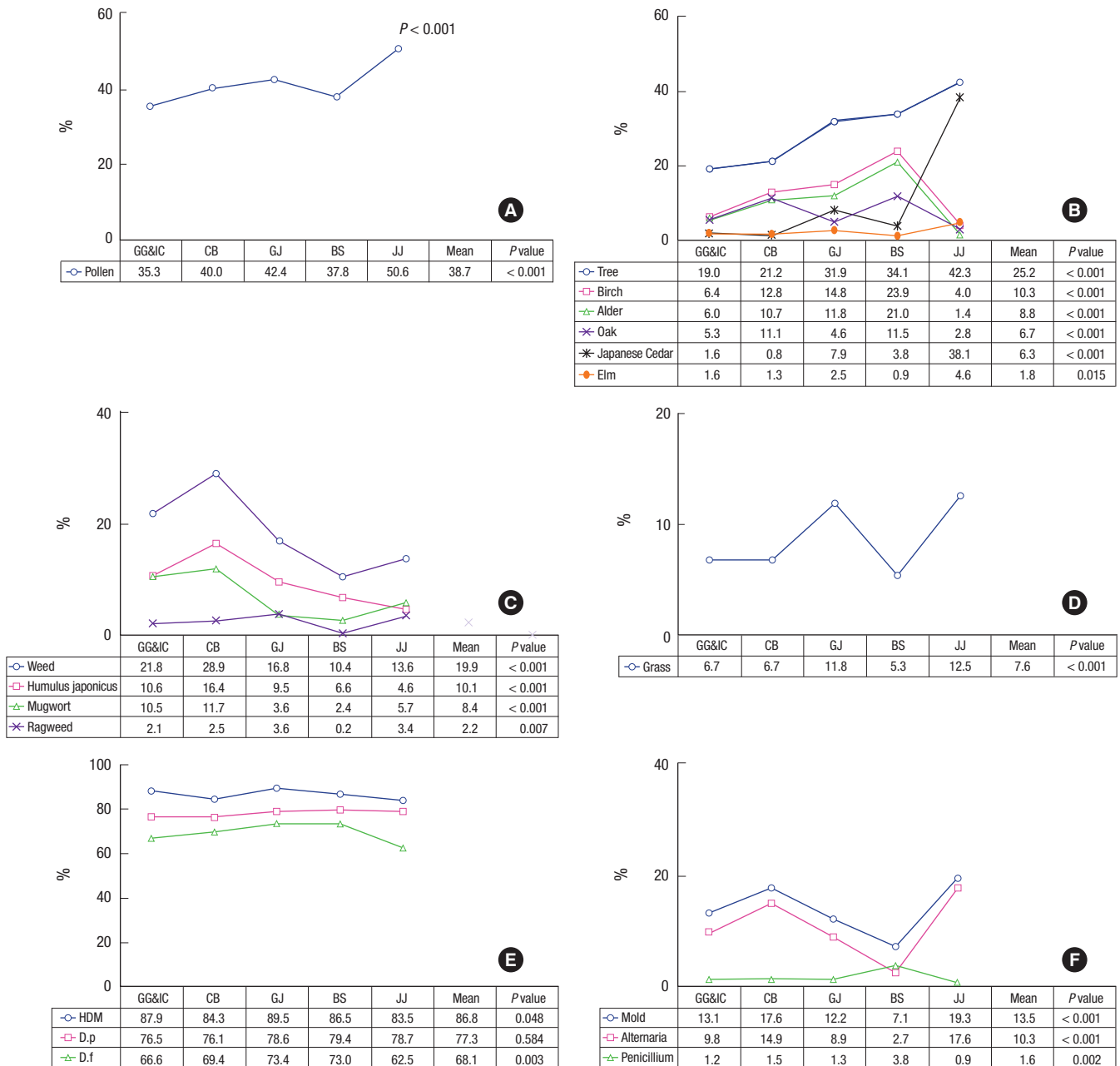


Fig. 1. Sensitization rate of causative allergen in school-aged children with AR in 5 provinces, within Korea. (A) Pollen, (B) Tree, (C) Weed, (D) Grass, (E) House dust mite, and (F) Mold. AR = allergic rhinitis, GG & IC = Incheon Metropolitan City-Gyeonggi Province, CB = Chungcheongbuk-do, GJ = Gwangju Metropolitan City, BS = Busan Metropolitan City, JJ = Jeju Special Self-Governing Province.

ferences also were observed in the sensitization rates to *Alternaria* and *Penicillium* among the 5 provinces ($P < 0.001$). In Jeju, in particular, the sensitization rate to *Alternaria* (10.3%) was the lowest, while that to *Penicillium* (1.6%) was the highest among the 5 provinces (Fig. 1F).

DISCUSSION

In the present article, we have described a multi-center cross-sectional study that was conducted in the 5 provinces, including a questionnaire and SPT to investigate the common allergen including pollen, HDM, and mold of AR in school-aged children who did not visit clinics or the hospital to complain of rhinitis symptoms. According to the respective region, notable differences in the common pollen were detected in the present study. Because of climate change, the sensitization rate to pollen continues to increase (9-11). The allergen sensitization rate to pollen was 38.7%, which was the second highest among examined allergens in the present study and, higher than reported in previous studies (10,13,14). The ecological landscape differs among residential regions: as such, the primary pollen sensitization rate may vary among the geographical locations of the 5 provinces in the present study.

The sensitization rate to a few trees was similar to or higher than that in previous studies (10,13,14) and, birch and alder were the most common pollen allergens in 4 of 5 provinces all but Jeju. However, Japanese cedar pollen was the most common pollen allergen in Jeju that is similar to that of previous studies, because Jeju has a high proportion of Japanese cedar in mandarin orange farms to protect against the wind (15-17). The present study also demonstrated that the sensitization rates to Japanese cedar pollen in Gwangju (7.9%) and Busan (3.8%) may have resulted from the fact that regions in the south and north of Chungbuk, south of Chungnam, and the northern and southern coasts of Gyeongsang had Japanese cedar (17). This result is a good example of how environmental change is followed by allergic sensation rate change. The sensitization rate to oak was 6.7% that was lower than birch or alder in the present study. This result is different to a previous study that oak is the most common tree pollen (10). However, the previous study has limitation in exact comparison owing to its retrospective study design such as small sample size and prevalence of allergic disease, so the more study is needed to.

The sensitization rate to weeds was 19.9%, the second highest among the pollen type, and the highest sensitization rates were for Japanese cedar and, mugwort, followed by ragweed. The current sensitization rate of 19.9% is the lowest of the studies, having decreased from 10.9% in 1990s, to 27.0% in 2010s, respectively (10). However, according to other recent studies, the sensitization rate to weed pollens was significantly increased in Croatia and Sweden (18,19). The collected amount and sen-

sitization rate of Japanese cedar have increased among weeds pollen since 2008 in Busan (20), similar to current study result. Through these differences, we assume that environment change happened for the past 3 decades within Korea. Therefore, further study is needed to determine why sensitization rate to weed pollens has decreased and the primary weed pollen type has changed in Korea.

The sensitization rate to grass, known as a major pollen allergen in European with its expansive plains (21), is lower than that to trees or weeds in Korea, which has plenty of mountains. We may confirm this fact again in the present study.

The most common allergen was HDM, which is consistent with the finding of previous studies in Korea (13,14), Chinese, and Turkey (22,23). However, the present study indicated a geographical difference in the sensitization rate to HMD allergens, although it was within Korea. *D. pteronyssinus* (77.3%) was the dominant species of HDM, followed by *D. farinae* (68.1%) in the present study, but in another nationwide survey, *D. farinae* is the dominant species of HDM, followed by *D. pteronyssinus* in Seoul, Gyeongin, Daejeon, Gwangju, and Jeonju but not in Daegu and Busan (24). This difference may have originated from differences in the subjects' ages, as the mean age in the previous study was the late 30s years vs. in the late teens in the present study. The prominent HDM also differs in that *D. farinae* was the causative organism in 6 to 7 year aged children versus *D. pteronyssinus* in 12 to 13 year aged children in another nationwide survey in 2010 (12). From these results, we may assume that sensitization type to HMD varies by age in Korea.

The HMD type differs among countries, and it is known that *D. pteronyssinus* is prominent in Europe and Australia versus *D. farinae* in Asia (25,26). Surveys of HDM have been conducted by Cho and Houh in Korea since 1977, who revealed that *D. pteronyssinus* is prominent in the humanized regions whereas *D. farinae* is prominent in dry inland regions (27,28). However, in the present study, the sensitization rate to *D. farinae* was the lowest in Jeju, the most humid of 5 studied provinces. This difference originates from that in previous studies based on visiting house and collecting the HMD number, and not the allergic sensitization rate with the allergic disease. Therefore, true evaluation of *D. farinae* sensitization according to region will require the further examination of additional region within Korea.

The sensitization rate to molds was the highest in Jeju and higher than that to weed and grass in the present study. Jeju is an island separated from the Korean peninsula and, owing to its warm and wet climate, the sensitization to mold was assumed to be the highest (29). Among molds, *Alternaria* was the most common in 4 of 5 provinces (all but Busan), and the sensitization rate to *Alternaria* was markedly higher than that to *Penicillium*. As with pollens, the sensitization rates to mold could differ among regions. Therefore, future studies are required to evaluate sensitization rate to molds in various other regions within

Korea.

The current study had a few limitations. First, the investigator period was from March 2010 to November 2015, we must consider the 6-year period bias. The sensitization rates could differ among seasons, but this study was conducted from spring to autumn we should also consider the potential seasonal bias. Second, only school-aged children with AR who lived in 5 provinces were included and further studies in other provinces are needed in the future. However, the strengths of the present study include the large sample size and the use of a comprehensive and stringent questionnaire and SPT, which yields accurate and objective data. The present study identified the characteristics of common allergens including pollen, HDM, and mold in school-aged children with AR in 5 provinces within Korea.

In conclusion, we found that the most common allergen is HDM, but the primary pollen type is tree and there are notable differences in the main pollen allergens according to respective regions. Therefore, these results support that examined pollen allergens strongly associated with residential region due to regional common pollen differences among children with AR within Korea to investigate the main pollen allergens.

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DISCLOSURE

The authors have no potential conflicts of interest to disclose.

AUTHOR CONTRIBUTION

Conceptualization: Lim DH. Data curation: Sung M, Kim SW, Kim JH, Lim DH. Investigation: Sung M, Kim JH, Lim DH. Writing - original draft: Sung M, Lim DH. Writing - review & editing: Sung M, Lim DH.

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