

# Inhalant allergen sensitization in early life predicts development of respiratory allergic diseases in Korean children

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**Purpose:** Inhalant allergen sensitization is a well-known risk factor for asthma and allergic rhinitis (AR). However, there are few recent data on the prevalence of allergic sensitization in the general population of preschool Korean children. This study assessed the association between early-life sensitization and respiratory allergic diseases.

**Methods:** This study analyzed data from the COCOA (COhort for Childhood Origin of Asthma and allergic diseases) cohort including 1,925 children at age 3 and 988 children at age 7. New-onset allergic diseases were defined as those not diagnosed before age 6 and diagnosed after age 7. Skin prick tests and serum specific IgE tests were performed at ages 3 and 7. Provocative challenge test was performed at age 7.

**Results:** House dust mite (HDM) was the most frequently sensitized allergen at both ages 3 and 7 (*Dermatophagoides pteronyssinus* 13.1%, *Dermatophagoides farina* 14.4%; 33.8%, 39.3%, respectively). Sensitization to indoor allergens at ages 3 and 7 increased risks for new-onset AR (adjusted odds ratio [aOR], 2.80; 95% confidence interval [CI], 2.05–3.84 and aOR, 5.70; 95% CI, 3.13–10.29), asthma (aOR, 2.89; 95% CI, 1.65–5.03 and aOR, 2.68; 95% CI, 1.10–6.51) and bronchial hyperresponsiveness (BHR) (aOR, 2.14; 95% CI, 1.45–3.14 and aOR, 1.69; 95% CI, 1.25–2.30). Early persistent sensitization to HDM was a risk factor for new-onset AR (aOR, 5.25; 95% CI, 1.69–16.30), asthma (aOR, 4.07; 95% CI, 1.19–13.87) and BHR (aOR, 2.82; 95% CI, 1.80–4.43).

**Conclusion:** Early persistent sensitization to HDM is associated with increased risk of new-onset AR, asthma and BHR. Early-life assessment of sensitization is important in predicting future respiratory allergic disease development. (*Allergy Asthma Respir Dis* 2025; 13:114-122)

**Keywords:** Sensitization, Inhalant allergen, Early life, Asthma, Allergic rhinitis

## INTRODUCTION

Allergic diseases such as asthma and rhinitis represent some of the most prevalent chronic condition affecting children.<sup>1,2</sup> These diseases are multifactorial, arising from complex interactions be-

tween genetic predisposition and environmental exposures and their prevalence has been increasing steadily over the past 3 decades.<sup>3</sup> The age of onset for allergic rhinitis (AR) and asthma has become progressively younger and studies have indicated that these conditions negatively impact sleep quality, academic achieve-

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ment and mental health.<sup>4,5</sup> Therefore, the identification of risk factors contributing to the development of allergic diseases in childhood is critical for the effective management and prevention of these conditions.

Allergic sensitization plays an important role in the pathogenesis of asthma and AR.<sup>6-8</sup> The patterns of allergic sensitization vary by ethnicity, geographic region and age.<sup>9</sup> Furthermore, previous studies have also demonstrated that both the age at onset and the extent of sensitization are associated with long-term prognosis. In the German Multicenter Allergy Study, allergen sensitization emerged as the most significant risk factor for the development of asthma and its persistence through the school years.<sup>10</sup> Similarly, findings from the Childhood Asthma Management Program indicated that both inhalant allergen sensitization and environmental exposure to inhalant allergens were associated with asthma development.<sup>11</sup> Notably, previous studies have shown that inhalant allergen sensitization during early life is linked to the subsequent development of AR and asthma during the school-age years.<sup>12-14</sup> However, recent data on the prevalence of allergic sensitization among preschool children in the general Korean population are lacking. Moreover, there are few studies in Korea that investigated the association between sensitization among children in the general population and allergic diseases, but all of these studies were aimed at school-aged children.<sup>14-16</sup>

In this study, we examined the prevalence of allergic sensitization in Korean children from the COhort for Childhood Origin of Asthma and allergic diseases (COCO) cohort, a population-based birth cohort study. We further assessed how the onset of sensitization during the preschool years, as well as its persistence and degree, is associated with the subsequent development of respiratory allergic diseases. By focusing on the trajectory of early-life sensitization, this study provides a novel perspective on the long-term implications of allergic sensitization in early childhood.

## MATERIALS AND METHODS

### 1. Study population

Data were analyzed from the COCO, a longitudinal prospective population-based birth cohort study conducted in South Korea.<sup>17,18</sup> Recruitment of mother-infant pairs was initiated on 19 November, 2007 and concluded on 31 December, 2015. Enrollment was performed at 5 medical centers and 8 public-health centers providing antenatal care in Seoul and Gyeonggi-do. Following de-

livery, all infants, excluding those who met predefined exclusion criteria, underwent 11 scheduled follow-up assessments: at 6 months, 1 year and annually thereafter. This study included 1,925 children aged 3 years and 988 children aged 7 years for whom complete skin prick test (SPT) results were available at each respective time points, and whose AR and asthma status had been determined by physicians (Supplementary Fig. 1). The study protocol received approval from the Institutional Review Boards of Asan Medical Center (IRB No. 2008-0616), Samsung Medical Center (IRB No. 2009-02-021), Severance Medical Center (IRB No. 4-2008-0588), CHA Gangnam Medical Center (IRB No. 2010-010) and Seoul National University Hospital (IRB No. H-1401-086-550) prior to initiation. Written informed consent was obtained from the parents or legal guardians of all participants before interview was conducted, in accordance with IRB guidelines.

### 2. Definitions of AR and asthma

AR was suspected in participants reporting characteristic rhinitis symptoms (i.e., watery rhinorrhea, nasal obstruction, sneezing or itching). A diagnosis of AR was confirmed when a physician-documented history revealed allergic sensitization and typical rhinitis symptoms persisting for 2 or more consecutive days lasting longer than 1 hour on most days.<sup>19</sup> Asthma diagnosis was based on multiple outcome measures. The diagnosis of asthma was established when participants exhibited a history of relevant symptoms in combination with bronchial hyperresponsiveness (BHR) or reversible airway obstruction.<sup>20</sup> Additionally, new-onset AR and asthma were defined as cases in which diagnoses were not made before the age of 6 years but were made after the age of 7.

### 3. Allergic sensitization

SPTs were performed for 18 common allergens in children at age 3 and 7 (Allergopharma GmbH & Co. KG, Germany). The test panel comprised 14 inhalant allergens (i.e., *Dermatophagoides pteronyssinus* [Der. p], *Dermatophagoides farinae* [Der. f], dog dander, cat epithelium, German cockroach, *Alternaria alternata*, *Aspergillus fumigatus*, grasses mixture, Japanese hop, birch, oak, ragweed, mugwort, and alder) and 4 food allergens (i.e., egg white, peanut, cow's milk, and soybean).<sup>17</sup> Histamine (10 mg/mL) and normal saline were used as positive and negative controls, respectively. A mean wheal diameter of  $\geq 3$  mm for allergens and histamine after 15 minutes was considered as a positive result. Positive sensitization was defined as at least one positive test result to any

of the 18 allergens tested by SPT.

Serum specific IgE levels to *Der. f* and birch were measured using the ImmunoCAP (Thermo Fisher Scientific Inc., Sweden) in a subset of the study population.<sup>17</sup> Serum specific IgE concentrations exceeding 0.35 IU/mL were considered positive for allergic sensitization.

To assess associations between sensitization patterns and allergic disease development, the 14 inhalant allergens were categorized as indoor or outdoor allergens. Indoor allergens included *Der. p*, *Der. f*, cockroach, dog dander and cat epithelium, whereas outdoor allergens included Japanese hop, alder, birch, oak, mugwort, ragweed, grasses mixture, *Alternaria alternata* and *Aspergillus fumigatus*.

#### 4. Bronchial hyperresponsiveness

BHR was assessed using a provocholine bronchial challenge test at age 7.<sup>21</sup> A modified 5-breath dosimeter method was employed. Normal saline was administered as a baseline, followed by stepwise concentrations of provocholine (0.0625, 0.25, 1, 4, and 16 mg/mL). The cumulative dose of provocholine required to produce a 20% reduction in forced expiratory volume in 1 second (PC<sub>20</sub>), in accordance with the American Thoracic Society guidelines, was recorded. Participants with PC<sub>20</sub> ≤ 8 mg/mL were classified as having BHR to provocholine.

#### 5. Allergic sensitization trajectories

Allergic sensitization trajectories were classified based on SPT results at ages 3 and 7 as follows: no sensitization (negative results at both time points), late sensitization (negative results at age 3 and positive results at age 7), early transient sensitization (positive results at age 3 and negative results at age 7) and early persistent sensitization (positive results at both time points). A total of 820 children received SPT at both ages 3 and 7 and these participants were included in the analysis of allergic sensitization trajectories. 168 children who lacked SPT results at either age 3 or 7 were excluded from the analysis.

#### 6. Statistical analysis

Statistical analysis were performed using IBM SPSS Statistics ver. 26.0 (IBM Co., USA). Associations between sensitization and allergic diseases were examined using multivariable-adjusted logistic regression and expressed as odds ratios (ORs) with 95% confidence interval (CI). The same method was used to analyze associations between sensitization and its potential risk factors. Ad-

justment variables included sex, parental history of allergic diseases, maternal education level and exclusive breastfeeding during the first 6 months of life. For comparisons between characteristics of the age 3 and age 7 groups, continuous variables were presented as mean ± standard deviation and categorical variables were expressed as percentages (%). Comparisons between groups classified according to the onset of sensitization were analyzed using 1-way analysis of variance. A *P*-value of < 0.05 was considered statistically significant.

## RESULTS

### 1. Characteristics of the study population

This study included 1,925 children aged 3 years and 988 children aged 7 years. Baseline characteristics are presented in Supplementary Table 1.

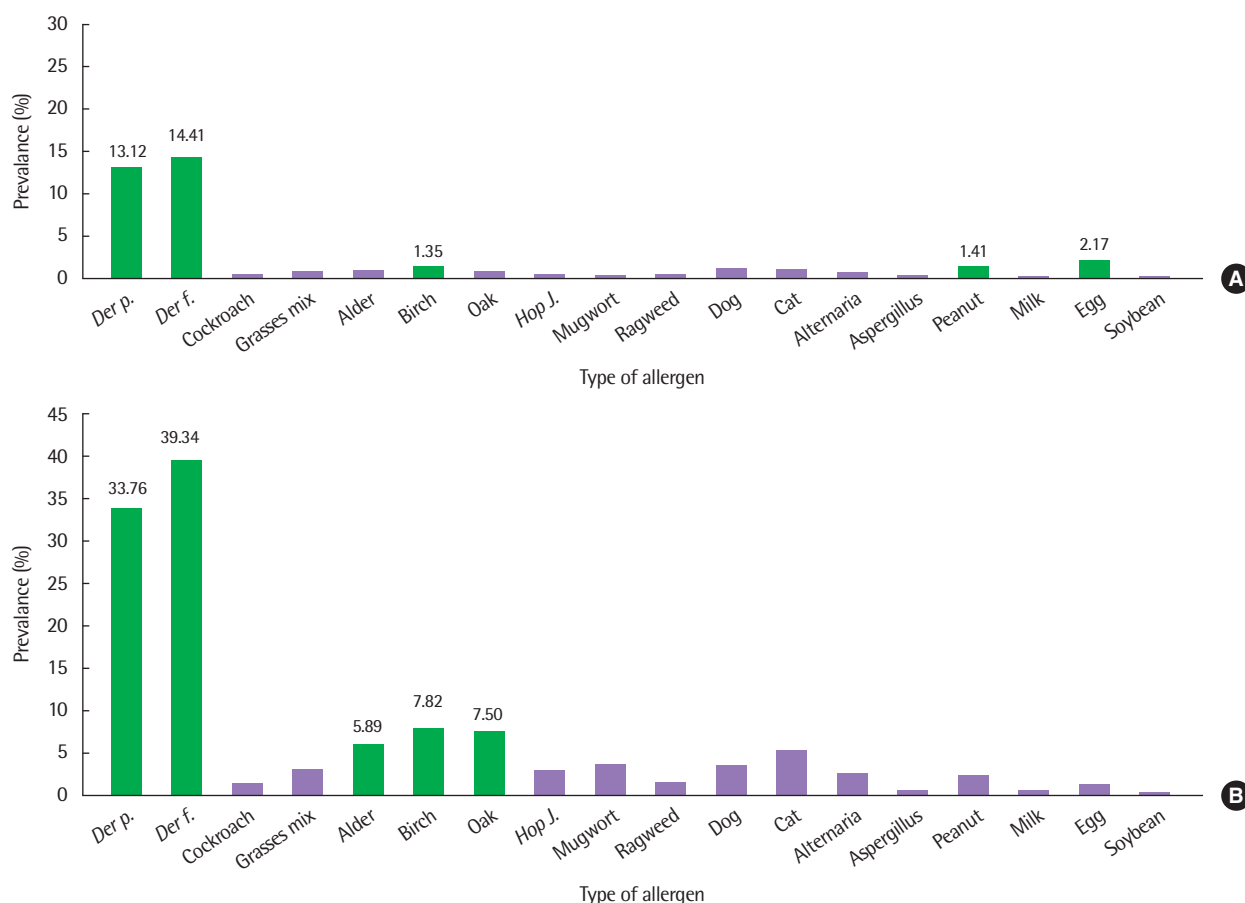
### 2. Prevalence of allergic sensitization by age and risk factors

Among Korean children, the prevalence of allergic sensitization increased with age (Fig. 1). At 3 years of age, the most common allergens were house dust mite (HDM) *Der. p* (13.1%) and *Der. f* (14.4%). At 7 years of age, HDM remained the most frequently detected allergen, with sensitization rates increasing to 33.8% for *Der. p* and 39.3% for *Der. f*. At 3 years of age, the sensitization rates to birch and oak were 1.35% and 0.88%, respectively. By age 7, birch (7.8%) and oak (7.5%) had the second and third highest sensitization rates.

At age 3, having older siblings was associated with increased risk of inhalant allergen sensitization, based on both SPT and ImmunoCAP results (Supplementary Figs. 2 and 3).

### 3. Association between allergic sensitization and AR, asthma and BHR

Cross-sectional analysis at age 3 showed that inhalant allergen sensitization was associated with increased risks of new-onset AR (adjusted OR [aOR], 1.98; 95% CI, 0.95–4.13), asthma (aOR, 3.14; 95% CI, 1.42–6.98) and BHR (aOR, 1.97; 95% CI, 1.36–2.85) (Fig. 2). New-onset AR was associated with sensitization to indoor allergens, particularly to HDM (aOR, 2.27; 95% CI, 1.01–5.12). New-onset asthma was associated with sensitization to both indoor (aOR, 2.89; 95% CI, 1.65–5.03) and outdoor (aOR, 3.55; 95% CI, 1.40–9.00) allergens. Sensitization to tree pollen allergens among outdoor allergens was significantly associated with new-onset asthma (aOR,



**Fig. 1.** Prevalence (%) of allergic sensitization by skin prick test at age 3 (A), age 7 (B). *Der p*, *Dermatophagoides pteronyssinus*; *Der f*, *Dermatophagoides farinae*; Hop J, Japanese hop; *Alternaria*, *Alternaria alternata*; *Aspergillus*, *Aspergillus fumigatus*.

5.52; 95% CI, 1.06–28.80). BHR was associated with sensitization to indoor allergens, particularly HDM (aOR, 2.17; 95% CI, 1.46–3.24).

At age 7, sensitization to indoor allergens remained a significant risk factor for new-onset AR (aOR, 5.68; 95% CI, 3.13–10.29), asthma (aOR, 2.68; 95% CI, 1.10–6.51) and BHR (aOR, 1.69; 95% CI, 1.25–2.30) (Fig. 3). Sensitization to HDM was significantly associated with new-onset AR (aOR, 5.79; 95% CI, 3.19–10.53), asthma (aOR, 2.84; 95% CI, 1.17–6.91) and BHR (aOR, 1.68; 95% CI, 1.23–2.28). In contrast, sensitization to outdoor allergens at age 7 was only associated with an increased risk of new-onset AR (aOR, 3.48; 95% CI, 1.23–9.85).

#### 4. Effect of polysensitizations and the degree of sensitization by ImmunoCAP on allergic diseases

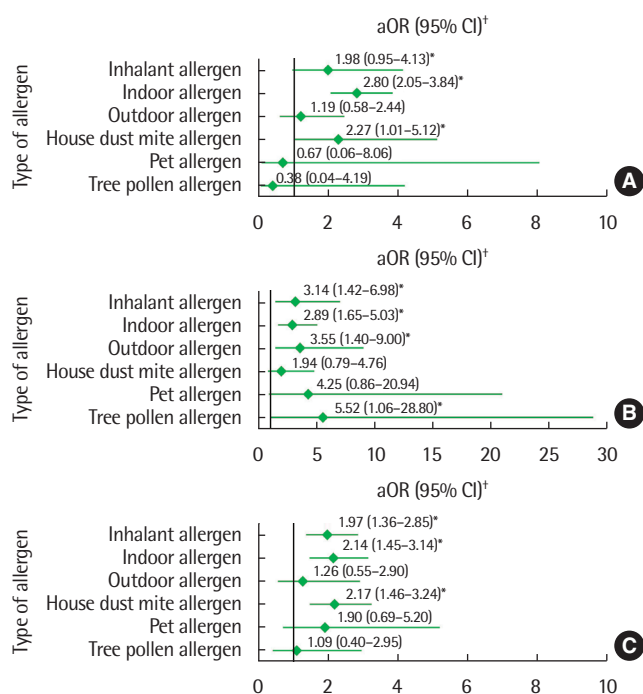
The degree of *Der. f* sensitization was classified by ImmunoCAP values. Values were stratified into tertiles based on a normal distri-

bution at ages 3 and 7. At age 3, no statistically significant associations were observed. However, at age 7, higher ImmunoCAP values were significantly associated with an increased risk of new-onset AR and asthma (Fig. 4).

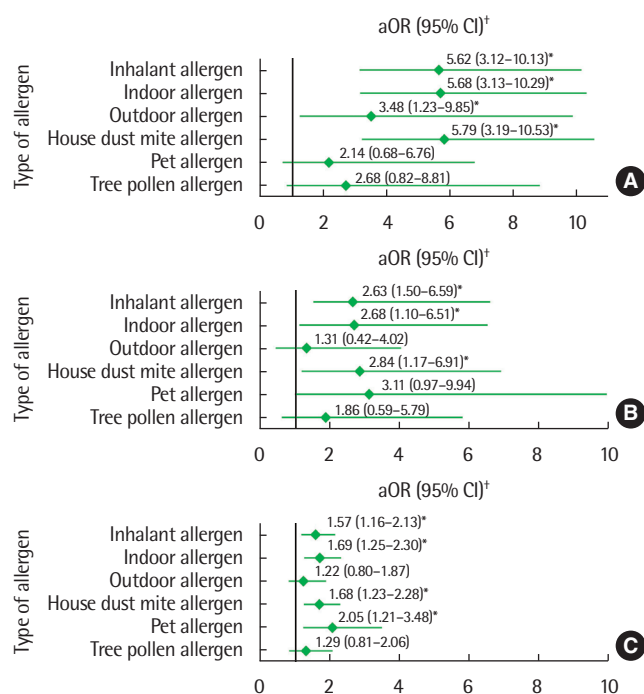
Furthermore, at age 7, children who tested positive for both *Der. f* and birch allergens exhibited a significantly elevated risk of new-onset AR (aOR, 7.53; 95% CI, 1.68–33.72) and asthma (aOR, 5.68; 95% CI, 1.64–19.74) compared to those sensitized to *Der. f* alone (aOR, 2.91; 95% CI, 1.69–5.03 for AR; aOR, 3.18; 95% CI, 1.20–8.40 for asthma). Similarly, the risk of BHR was significantly higher among children sensitized to both allergens (aOR, 2.21; 95% CI, 1.07–4.56) than in those sensitized to *Der. f* alone (aOR, 1.80; 95% CI, 1.29–2.50) (Fig. 5).

#### 5. Effect of allergic sensitization trajectories on allergic diseases

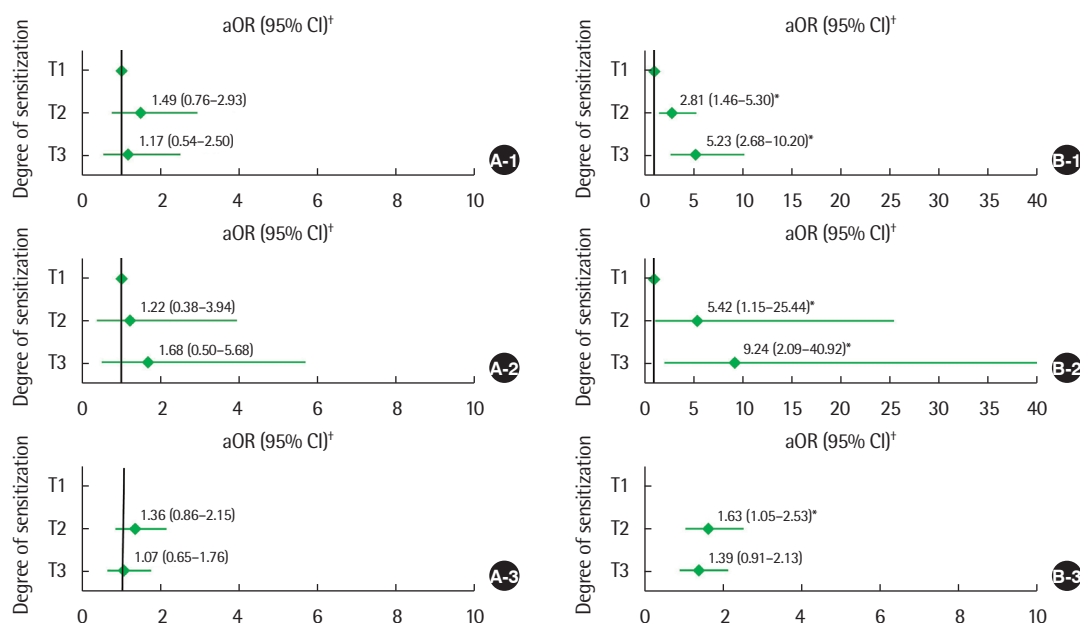
The study population was categorized into 4 trajectories: no



**Fig. 2.** Adjusted odds ratio of new-onset allergic rhinitis, asthma and bronchial hyperresponsiveness after age 7 according to inhalant sensitization by skin prick test at age 3. (A) New-onset allergic rhinitis. (B) New-onset asthma. (C) Bronchial hyperresponsiveness. aOR, adjusted odds ratio; CI, confidence interval. \* $P < 0.05$ . <sup>†</sup>Adjusted by maternal education status, sex, family history of allergic disease and type of feeding for the first 6 months.

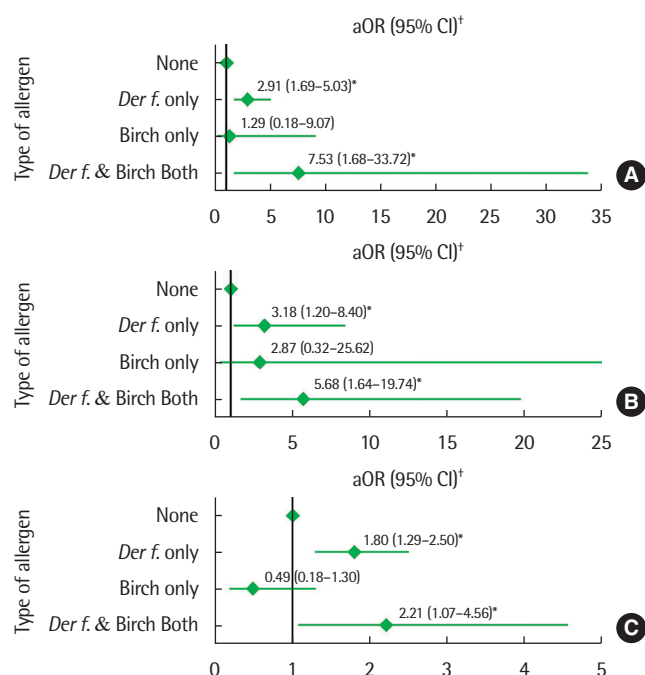


**Fig. 3.** Adjusted odds ratio of new-onset allergic rhinitis, asthma and bronchial hyperresponsiveness after age 7 according to inhalant sensitization by skin prick test at age 7. (A) New-onset allergic rhinitis. (B) New-onset asthma. (C) Bronchial hyperresponsiveness. aOR, adjusted odds ratio; CI, confidence interval. \* $P < 0.05$ . <sup>†</sup>Adjusted by maternal education status, sex, family history of allergic disease and type of feeding for the first 6 months.



**Fig. 4.** Adjusted odds ratio of new-onset allergic rhinitis, asthma after age 7 according to degree of sensitization of *Der f* by ImmunoCAP at age 3 (A) and at age 7 (B). In a normal distribution, the lower 1/3, middle 1/3 and upper 1/3 of specific IgE values were defined as T1, T2 and T3, respectively. *Der f*, *Dermatophagoides farinae*. (A-1) New-onset allergic rhinitis. (A-2) New-onset asthma. (A-3) Bronchial hyperresponsiveness. (B-1) New-onset allergic rhinitis. (B-2) New-onset asthma. (B-3) Bronchial hyperresponsiveness. aOR, adjusted odds ratio; CI, confidence interval. \* $P < 0.05$ . <sup>†</sup>Adjusted by maternal education status, sex, family history of allergic disease and type of feeding for the first 6 months.





**Fig. 5.** Adjusted odds ratio of new-onset allergic rhinitis, asthma and bronchial hyperresponsiveness after age 7 according to monosensitization and polysensitization at age 7 by ImmunoCAP. (A) New-onset allergic rhinitis. (B) New-onset asthma. (C) Bronchial hyperresponsiveness. aOR, adjusted odds ratio; CI, confidence interval; Der f, *Dermatophagoides farinae*. \* $P < 0.05$ . †Adjusted by maternal education status, sex, family history of allergic disease and type of feeding for the first 6 months.

sensitization (N = 422, 51.5%), late sensitization (N = 248, 30.2%), early transient sensitization (N = 9, 1.1%) and early persistent sensitization (N = 141, 17.2%) (Table 1).

Trajectory characteristics are presented in Supplementary Table 2.

Regarding indoor allergens, early persistent sensitization trajectory was associated with the highest risk for new-onset AR (aOR, 5.79; 95% CI, 2.01–16.00), asthma (aOR, 4.34; 95% CI, 1.34–13.97) and BHR (aOR, 2.66; 95% CI, 1.72–4.13), compared with other trajectories. The same pattern was observed in participants sensitized to HDM. Within the early persistent HDM sensitization trajectory, the risks for new-onset AR, asthma and BHR were highest, with aOR of 5.25 (95% CI, 1.69–16.30), 4.07 (95% CI, 1.19–13.87) and 2.82 (95% CI, 1.80–4.42), respectively.

In contrast, among outdoor allergens, specifically tree pollens, only late onset sensitization trajectory was significantly associated with an increased risk of new-onset AR with aOR of 4.48 (95% CI, 1.43–14.00) and 3.48 (95% CI, 1.01–12.00), respectively.

**Table 1.** Risk of new-onset allergic rhinitis, asthma and bronchial hyperresponsiveness after age 7 according to sensitization trajectories by skin prick test at age 3 and 7

| Variable          | New-onset allergic rhinitis | New-onset asthma  | Bronchial hyperresponsiveness |
|-------------------|-----------------------------|-------------------|-------------------------------|
| Inhalant allergen |                             |                   |                               |
| None              | 1 (Reference)               | 1 (Reference)     | 1 (Reference)                 |
| Late              | 4.94 (2.55–9.60)            | 2.35 (0.79–6.96)  | 1.28 (0.88–1.85)              |
| Early transient   | -                           | -                 | 0.37 (0.04–3.05)              |
| Early persistent  | 5.02 (1.80–14.00)           | 4.50 (1.45–13.96) | 2.47 (1.61–3.81)              |
| Indoor allergen*  |                             |                   |                               |
| None              | 1 (Reference)               | 1 (Reference)     | 1 (Reference)                 |
| Late              | 4.97 (2.51–9.83)            | 3.32 (1.14–9.64)  | 1.39 (0.95–2.02)              |
| Early transient   | -                           | -                 | 0.68 (0.08–6.22)              |
| Early persistent  | 5.79 (2.01–16.70)           | 4.34 (1.34–13.98) | 2.66 (1.72–4.13)              |
| Outdoor allergen† |                             |                   |                               |
| None              | 1 (Reference)               | 1 (Reference)     | 1 (Reference)                 |
| Late              | 4.48 (1.43–14.00)           | 0.80 (0.18–3.48)  | 1.26 (0.78–2.03)              |
| Early transient   | 1.22 (0.09–16.65)           | -                 | 1.11 (0.20–6.11)              |
| Early persistent  | -                           | 5.41 (0.55–53.12) | 1.28 (0.41–4.01)              |
| HDM allergen      |                             |                   |                               |
| None              | 1 (Reference)               | 1 (Reference)     | 1 (Reference)                 |
| Late              | 5.31 (2.69–10.20)           | 3.79 (1.33–10.79) | 1.39 (0.96–2.03)              |
| Early transient   | -                           | -                 | 0.91 (0.09–8.94)              |
| Early persistent  | 5.25 (1.69–16.30)           | 4.07 (1.19–13.87) | 2.82 (1.80–4.43)              |
| Pet allergen      |                             |                   |                               |
| None              | 1 (Reference)               | 1 (Reference)     | 1 (Reference)                 |
| Late              | 2.01 (0.54–7.48)            | 2.93 (0.79–10.92) | 2.01 (1.10–3.69)              |
| Early transient   | -                           | -                 | 2.24 (0.14–36.39)             |
| Early persistent  | 1.97 (0.11–36.20)           | 6.59 (0.68–63.57) | 1.63 (0.51–5.21)              |
| Tree allergen     |                             |                   |                               |
| None              | 1 (Reference)               | 1 (Reference)     | 1 (Reference)                 |
| Late              | 3.48 (1.01–12.00)           | 1.65 (0.46–5.91)  | 1.43 (0.85–2.39)              |
| Early transient   | -                           | -                 | 0.93 (0.08–11.03)             |
| Early persistent  | -                           | -                 | 1.03 (0.25–4.25)              |

Values are presented as aOR† (95% CI).

aOR, adjusted odds ratio; CI, confidence interval; HDM, house dust mite.

\*Indoor allergens included *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, cockroach, dog dander, and cat epithelium. †Outdoor allergens included alder, birch, oak, Japanese hop, mugwort, ragweed, grasses mix, *Alternaria alternata* and *Aspergillus fumigatus*. ‡Adjusted by maternal education status, sex, family history of allergic disease and type of feeding for the first 6 months.

## DISCUSSION

This study analyzed the characteristics of early life sensitization and its association with the development of respiratory allergic diseases in the general pediatric population of Korea. HDM was the most prevalent allergen among children aged 3 and 7 years and the frequency of sensitization increased with age. Inhalant al-

lergen sensitization was associated with new-onset respiratory allergic diseases. In particular, sensitization to indoor allergens, especially HDM, at age 3 was associated with an increased risk of new-onset AR, asthma and BHR, whereas sensitization to tree pollen at age 3 was linked to new-onset asthma.

The degree of sensitization was also correlated with the risk of new-onset allergic diseases. Moreover, children with polysensitizations to both *Der. f* and birch by ImmunoCAP at age 7 had a higher risk of AR and asthma compared to those with monosensitization to *Der. f*. The timing of sensitization was also associated with allergic diseases. Early persistent sensitization to indoor allergens, particularly HDMs, was linked to increased risk of new-onset AR, asthma and BHR. These findings underscore the importance of identifying children sensitized to common major inhalant allergens based on degree and multiplicity particularly at age 3 and with persistent sensitization at age 7. Regular monitoring for allergic sensitization and the development of respiratory allergic diseases from preschool children onward, along with the implementation of inhalant allergen avoidance strategies in this population may contribute to preventing long-term disease progression.

Previous studies have demonstrated that sensitization patterns to inhalant allergens vary according to geographic region and climatic conditions.<sup>22</sup> In Asian countries, HDMs are the most prevalent inhalant allergens.<sup>23</sup> Although the age groups examined differ across studies, the reported sensitization rates to HDMs among children in the general population are 32.3% in Singapore, 30% in Taiwan, 54.3% in Japan and 33.76% in Korea.<sup>24–26</sup> Consistent with these findings, our study identified *Der. p* and *Der. f* as the most predominant allergens among Korean children aged 3 and 7 years. Notably, Japan exhibits a distinct sensitization profile among Asian countries, with a higher prevalence of sensitization to pollen. According to the JECS (Japan Environment and Children's Study) study, the sensitization rates to HDMs and Japanese cedar in t2-year-old children, were 10% and 2.4%, respectively.<sup>3</sup> Moreover, the T-Child (Tokyo Children's Health, Illness and Development study) study reported sensitization rates to Japanese cedar of 32.8% at age 5 and 57.8% at age 9, while the corresponding rates for *Der. f* were 42.1% and 54.3%, respectively, indicating that sensitization frequency increases with age.<sup>26</sup> Similarly, our findings demonstrated an age-related increase in inhalant allergen sensitization from age 3 to age 7. Specifically, the sensitization rate to *Der. p* increased from 13.1% to 33.8% and *Der. f* from 14.4% to 39.3%. Sensitization

to birch pollen also increased from 1.35% to 7.82%. Although previous studies in Korea have focused on school-aged children,<sup>16,27</sup> the present study extends this research to include children as young as 3 years old within a population-based cohort.

Previous investigations have reported that sensitization patterns influence the development of respiratory allergic diseases, including AR, asthma and BHR.<sup>16</sup> In Western countries, sensitization to pollen has been strongly associated with the exacerbation of respiratory allergic diseases. Conversely, in Asian populations, sensitization to HDMs has been more closely linked to the pathogenesis of AR and asthma than pollen sensitization.<sup>23</sup> In this study, sensitization to tree pollen at the age of 3 increased the risk of new-onset asthma (aOR, 5.52; 95% CI, 1.06–28.80). Furthermore, sensitization to HDMs at the age of 3 increased the risk of new-onset AR (aOR, 2.27; 95% CI, 1.01–5.12) and BHR (aOR, 2.17; 95% CI, 1.46–3.24).

Furthermore, studies have shown that early-life sensitization increases the risk of developing asthma and AR by the age of 19.<sup>28</sup> Ongoing research aims to elucidate the mechanisms by which early sensitization heightens this risk. Individuals with defects in epithelial barrier surfaces, such as those of the skin, gastrointestinal tract and respiratory tract exhibit increased permeability to allergens, facilitating IgE-mediated sensitization.<sup>29</sup> A compromised epidermal epithelium promotes environmental allergen absorption, initiating a systemic T-helper type 2 response and leading to a immune dysregulation.<sup>29</sup> This process has been reported to elevate the risk of future allergic disease development.<sup>29</sup> Additionally, it has been reported that prolonged duration of sensitization correlates with increased specific IgE levels, molecular spreading and polysensitization, all of which contribute to increased risks of asthma and AR.<sup>30</sup> The findings of this study align with the previously proposed hypothesis, as similar patterns were observed in cases of early sensitization, multiple sensitizations, severe sensitizations.

This study also confirmed that early persistent sensitization to indoor allergens, particularly HDMs, increases the risk of new-onset AR, asthma and BHR. However, whereas most previous studies have primarily investigated sensitization patterns in school-aged children,<sup>16,28</sup> this study emphasizes an earlier developmental window, specifically at age 3, to assess the influence of early-life sensitization on the subsequent development of allergic respiratory diseases. Another German birth cohort study has similarly analyzed sensitization at age 3 and demonstrated that inhalant allergen sensitization most significantly increases the risk of develop-

ment of asthma during the school years, which is consistent with the results of this study.<sup>10</sup> However, the previous study focused on an allergy high risk population, distinguishing it from this study based on the general population. Therefore, the current findings of this study emphasizes the importance of early detection and proper management of sensitization in young children from the general population.

This study has certain limitations. The study population was limited to children residing in Seoul and Gyeonggi-do, Korea. As sensitization patterns may differ between urban and rural settings, this geographic constraint should be considered when interpreting the results. However, according to previous reports from Korea, although there may be some minor differences, the overall nationwide pattern remains highly similar and thus this is not of significant concern. Furthermore, as this study focused on children from the general population, it offers the advantage of allowing broader generalization of the findings.

This study reported age-specific sensitization rates within a general population of Korean children. It also demonstrated that the risk of respiratory allergic diseases varies according to the specific type of sensitized inhalant allergen, degree of sensitization, presence of polysensitization and the timing and persistence of early sensitization. These findings underscore the importance of identifying early-life sensitization to indoor or outdoor inhalant allergens in clinical practice to facilitate prediction of subsequent allergic disease development. Regular monitoring of sensitized children may enable early diagnosis and timely intervention. Most importantly, efforts should focus on minimizing inhalant allergen exposure to prevent early sensitization and further research on the pathogenesis and identification of predictive biomarkers should be prioritized.

## SUPPLEMENTARY MATERIALS

Supplementary Tables 1-2 and Supplementary Figs. 1-3 are available at <http://www.aard.or.kr/src/sm/aard-13-114-s002.pdf>.

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