

ORIGINAL ARTICLE

WILEY

Food allergy in early childhood increases the risk of oral allergy syndrome in schoolchildren: A birth cohort study

Kun-Baek Song¹ | Min Jee Park² | Eom Ji Choi¹ | Sungsu Jung³ | Jisun Yoon⁴ |
 Hyun-Ju Cho⁵ | Bong-Seong Kim⁶ | Kangmo Ahn⁷ | Kyung Won Kim⁸ |
 Youn Ho Shin⁹ | Dong In Suh¹⁰ | Soo-Jong Hong¹ | So-Yeon Lee¹

¹Department of Pediatrics, Childhood Asthma Atopy Center, Humidifier Disinfectant Health Center, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

²Department of Pediatrics, Uijeongbu Eulji Medical Center, Eulji University School of Medicine, Uijeongbu, Korea

³Department of Pediatrics, Pusan National University Yangsan Hospital, Yangsan, Korea

⁴Department of Pediatrics, Chung-Ang University Hospital, Chung-Ang University College of Medicine, Seoul, Korea

⁵Department of Pediatrics, International St. Mary's Hospital, Catholic Kwandong University College of Medicine, Incheon, Korea

⁶Department of Pediatrics, Gangneung Asan Hospital, University of Ulsan College of Medicine, Gangneung, Korea

⁷Department of Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

⁸Department of Pediatrics, Severance Children's Hospital, Yonsei University College of Medicine, Seoul, Korea

⁹Department of Pediatrics, CHA Gangnam Medical Center, CHA University School of Medicine, Seoul, Korea

¹⁰Department of Pediatrics, Seoul National University College of Medicine, Seoul, Korea

Correspondence

So-Yeon Lee and Soo-Jong Hong,
 Department of Pediatrics, Asan Medical
 Center, 88 Olympic-ro 43-gil, Songpa-gu,
 Seoul 05505, Korea.
 Email: imipenem@hanmail.net

Funding information

This work was supported by the
 Research Program funded Korea National
 Institute of Health (2008-E33030-00,
 2009-E33033-00, 2011-E33021-00,
 2012-E33012-00, 2013-E51003-00,
 2014-E51004-00, 2014-E51004-01,
 2014-E51004-02, 2017-E67002-00,
 2017-E67002-01, 2017-E67002-02).
 This work was supported by the National
 Research Foundation of Korea (NRF)
 grant funded by the Korea government
 (Ministry of Science and ICT) (NRF-
 2020R1A2C2012822).

Editor: Motohiro Ebisawa

Abstract

Background: The level of pollen in Korea has increased over recent decades. Research suggests that oral allergy syndrome (OAS) may be more frequent in childhood than previously recognized. We aimed to investigate the prevalence and characteristics of OAS in children aged 6–10 years from a general-population-based birth cohort.

Methods: We analyzed 930 children from the cohort for childhood origin of asthma and allergic diseases (COCOA). Allergic diseases were diagnosed annually by pediatric allergists. The skin prick tests were performed with 14 common inhalant allergens and four food allergens for the general population of children aged 3 and 7 years.

Results: Of the 930 eligible children, 44 (4.7%) aged 6–10 years were diagnosed with OAS. The mean age at onset was 6.74 years. OAS prevalence was 7.2% among children with allergic rhinitis (AR) and 19.1% among those with pollinosis, depending on comorbidity. OAS was more prevalent in schoolchildren with atopic dermatitis, food allergy, and sensitization to food allergens and grass pollen in early childhood. In schoolchildren with AR, only a history of food allergy until the age of 3 years increased the risk of OAS (aOR 2.971, 95% CI: 1.159–7.615).

This article is commented on by Motohiro Ebisawa & Philippe A. Eigenmann. To view this editorial comment visit <https://onlinelibrary.wiley.com/doi/10.1111/pai.13788>

Abbreviations: AC, allergic conjunctivitis; AD, atopic dermatitis; aOR, adjusted odds ratio; AR, allergic rhinitis; CI, confidence interval; COCOA, cohort for childhood origin of asthma and allergic diseases; *Der f*, *Dermatophagoides farinae*; *Der p*, *Dermatophagoides pteronyssinus*; Hop J, *Japanese hop*; IgE, immunoglobulin E; OAS, oral allergy syndrome; OR, odds ratio; SD, standard deviation; sIgE, specific immunoglobulin E; SPT, skin prick test.

© 2022 EAACI and John Wiley and Sons A/S. Published by John Wiley and Sons Ltd.

Conclusion: Food allergy and food sensitization in early childhood were associated with OAS in schoolchildren with AR. Further study is required to elucidate the mechanism by which food allergy in early childhood affects the development of OAS.

KEYWORDS

allergic rhinitis, birth cohort, children, food allergy, food sensitization, oral allergy syndrome, prevalence

1 | INTRODUCTION

Oral allergy syndrome (OAS) is a hypersensitivity reaction to specific foods caused by prior sensitization to inhalant pollen allergens. OAS is triggered by certain fresh (uncooked) fruits and vegetables that cross-react with pollen.¹ Global warming has increased the levels of carbon dioxide, nitric oxide, and ozone, increasing the abundance of and sensitization to pollen.^{2–6} Moreover, the prevalence of asthma, rhinitis, and OAS is also increasing globally.^{2,3,5} In Korea, tree pollens such as pine, alder, oak, and birch produce higher pollen concentrations than grass or weed pollens.⁵

The prevalence of OAS in patients with pollinosis is approximately 8%–63.3% in adults and 5%–12.4% in children.^{1,7,8} A single-center study noted a prevalence of 12.4% in Korean children with pollinosis, while multicenter studies noted a prevalence of 42.7% in patients with allergic rhinitis (AR), allergic conjunctivitis (AC), or asthma.^{9–11} Studies on the prevalence of OAS typically investigated populations with AR or inhalant allergen sensitization, which may have caused an overestimation of the prevalence.¹² However, there are few studies on the prevalence of OAS in the general population, with only two cross-sectional cohort studies in Danish adults¹³ and Japanese adolescents.¹⁴

Allergic rhinitis patients with OAS had a higher prevalence of additional allergic comorbidities, especially anaphylaxis, urticaria, asthma, and atopic dermatitis (AD), compared with those without.¹⁵ Additionally, atopic adults with OAS had a higher prevalence of rhinoconjunctivitis, asthma, and chronic urticaria than atopic adults without OAS.¹⁶ Although these studies investigated comorbidities in high-risk patients, few have assessed the general population or analyzed the relationship between OAS and allergic diseases longitudinally.^{13,14}

Therefore, we aimed to investigate the prevalence of OAS in the general population aged 6–10 years.

2 | MATERIALS AND METHODS

2.1 | Study population

The cohort for childhood origin of asthma and allergic diseases (COCOA) is a prospective, general-population-based birth cohort study designed to investigate the individual and interactive effects of genetics, perinatal environment, maternal lifestyle, and

Key Message

The prevalence of OAS in 6–10-year-old Korean children was 4.7%. Food allergy and food sensitization in early childhood was positively associated with OAS in schoolchildren with allergic rhinitis. Careful monitoring for OAS symptoms before the age of 6 years is necessary for children with a history of food allergy in early childhood.

psychosocial stress of mother and child on pediatric susceptibility to allergic diseases.¹⁷ The eligibility of the women is identified before recruitment.¹⁷ A woman is recruited if she lacks high-risk conditions that could affect the development of allergic disease in the child (e.g., diabetes, preeclampsia, anemia, and severe infections), plans to deliver at an affiliated medical center, and is a resident of Seoul.¹⁷ The eligibility of the baby is determined by the collaborating obstetrician and pediatrician soon after delivery.¹⁷ Babies are excluded at birth if their gestational age is <37 weeks or they have any oxygen supplementation.¹⁷ Regular follow-up visits involving physician examination and self-report questionnaires concerning the environment were conducted at a minimum of 26 weeks of gestation, at birth, 6 months, 1 year, and then annually.¹⁸ We collected information on the allergic symptoms, diagnosis, and prescribed treatment from yearly follow-ups of pediatric allergists. The average age of the patients was 8.02 years, and 52.7% were male patients. Significant differences in birthweight, breastfeeding rates, and antibiotic use before 1 year of age were observed between the included and excluded groups (Table S1). The study was approved by 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) before initiation. Written informed consent was obtained from each patient's parents or guardians before the interview and confirmed by each IRB.

2.2 | Definition of allergic diseases

Oral allergy syndrome was diagnosed by a physician or on the basis of typical symptoms (itching, sore throat, or swelling) in the

lips, mouth, and throat immediately after eating fresh fruits or vegetables using a parental questionnaire. If OAS was suspected, its trigger was also investigated. Food allergy was assessed at every scheduled visit via a questionnaire asking whether a doctor had ever diagnosed food allergy, whether food was suspicious, and whether medications had been prescribed for the condition.¹⁷ If there was a positive response, the diagnosis of food allergy was then confirmed by a pediatric allergy specialist during follow-up at each hospital.¹⁷ AD was assessed at every scheduled visit by asking, via a questionnaire, whether a doctor had ever diagnosed atopic dermatitis and whether medications had been prescribed for the condition.¹⁷ When the children were followed-up at the hospital, the presence of AD was clinically diagnosed by pediatric allergy specialists on the basis of the criteria of Hanifin and Rajka.¹⁷ AR was suspected when the subject complained of relevant rhinitis symptoms (i.e., watery rhinorrhea, nasal obstruction, sneezing, or itching).¹⁷ If a detailed history taken by doctors revealed that the subject had had allergic sensitization and presented with typical rhinitis symptoms for a sufficient period of time (for two or more consecutive days and for more than 1 h on most days), the subject was diagnosed with allergic rhinitis.¹⁷ Asthma was assessed by various outcome measures.¹⁷ Typical asthma symptoms (i.e., wheezing, dyspnea, exercise-induced wheezing, or nocturnal cough) were assessed by questionnaires during regular visits at the ages of 6 months, 1 year, and then yearly thereafter when pediatric allergists also evaluated each subject on the basis of their detailed history and the physical examination.¹⁷ Asthma was diagnosed when the subjects presented a history of relevant asthma symptoms plus bronchial hyperresponsiveness or reversible airway obstruction.¹⁷ For preschool children who could not give reliable results in lung function tests, the subjects who had had three or more episodes of wheezing were deemed to have asthma based on confirmation by the pediatric allergists.¹⁷

2.3 | Specific IgE to egg white and milk

Serum levels of specific IgE to egg white and milk at 1 and 3 years of age were determined using the Immuno-CAP (Thermo Fisher Scientific) system.

2.4 | Skin prick tests (SPTs)

SPTs were performed for the 14 most common inhalant allergens (Allergopharma GmbH & Co), including *Dermatophagoides pteronyssinus* (Der p), *Dermatophagoides farina* (Der f), dog dander, cat epithelium, cockroach, *Alternaria alternata*, *Aspergillus fumigatus*, grass pollen mixture, alder, birch, oak, ragweed, mugwort, alder, and four food allergens, including peanuts, egg whites, cow's milk, and soybeans at 3 and 7 years of age.^{19,20} Histamine (10 mg/ml) was used as the positive control, and normal saline was used as the negative control. A mean wheal size of 3 mm or larger for allergens and histamine after 15 min was considered a positive result. Atopy was defined as

the presence of one or more positive test results to any of the 18 allergens assessed using SPTs.^{19,20}

2.5 | Statistical analysis

Data are presented as means and standard deviations or numbers and percentages. Data were analyzed using IBM SPSS Statistics ver. 23.0 (IBM Co.). Comparisons between the OAS and non-OAS groups were calculated using the Pearson's chi-square test or independent t-test, as appropriate. Unadjusted and multivariable-adjusted logistic regression models examined associations between OAS and allergic disease in early childhood. Statistical procedures excluded cases with missing variable values from the analysis. Candidate variables for adjustment, including sex, delivery mode, gestational age, parental history of allergic diseases, maternal education level, exclusive breastfeeding during the first 6 months of life, and antibiotic treatment during the first 1 year of life, were used to calculate the odds ratios and 95% confidence intervals. A *p*-value of <.05 was considered statistically significant. To assess whether allergic disease status mediated the association between other allergic disease and OAS, the method proposed by Iacobucci²¹ was adopted for binary mediators. The mediation effect was calculated as the ratio of the indirect effect to its standard error by performing a Z test under the null hypothesis to show that the indirect effect was equal to zero.

3 | RESULTS

3.1 | Clinical characteristics of the study population and prevalence of OAS

Among the 3102 pairs enrolled in the COCOA cohort, 1636 children were aged over 6 years. Of these 1636 children, 706 patients lacking clinical and laboratory data were excluded, leaving 930 patients to be analyzed (Figure S1). Of the 930 children, 44 (4.7%) had OAS, and the mean age of onset was 6.74 years (Table 1). The mean age of the OAS group was higher than that of the non-OAS group, whereas the rate of breastfeeding was significantly higher in the non-OAS group than the OAS group. The prevalence of AR and AC in the study population was 48.9% and 16.5%, respectively (Figure 1). The prevalence of pollen sensitization in the study population was 11% (Figure 1), commonly observed for birch, oak, and alder (in order of frequency). Depending on comorbidity, the prevalence of OAS was 7.2% among children with AR and 19.1% among children with pollen sensitization (Figure S2).

3.2 | Causative foods

Foods triggering OAS in Korean children in the order of prevalence were fruits (47.7%), vegetables (27.3%), and nuts (9.1%) (Table 2). Among fruits, kiwi (22.7%) and peach (11.4%) were the most common causes of OAS.

	OAS (n = 44, 4.7%)	Non-OAS (n = 886, 95.3%)	p-Value
Age, year	8.48 ± 1.3	8.00 ± 1.3	.016
Sex (% male)	50.0	52.8	.758
Age at onset, years	6.74 ± 1.6	NA	NA
Parental history of allergic disease	58.1%	47.8%	.212
Gestational age, weeks	39.1 ± 1.3	39.1 ± 1.2	.746
Birthweight, g	3197.2 ± 341.0	3166.4 ± 415.2	.632
Breastfeeding	45.5%	61.8%	.038
Delivery type (cesarean section)	34.1%	34.0%	1.000
Antibiotics before 1 year of age	77.3%	72.0%	.495
Comorbidities (6–10 years of age)			
Asthma	7.3%	5.0%	.461
Atopic dermatitis	31.7%	15.9%	.016
Allergic rhinitis	75.6%	47.6%	.001
Food allergy	72.7%	14.4%	<.001
Atopy at 7 years of age	65.6%	46.8%	.045

TABLE 1 Clinical characteristics of all children

Note: Data presented as mean ± SD (range) or number (%). p-Values for comparing the OAS and non-OAS groups were calculated using the Pearson's chi-square test or independent t-test, as appropriate.

Abbreviations: IgE, immunoglobulin E; OAS, oral allergy syndrome; SD, standard deviation.

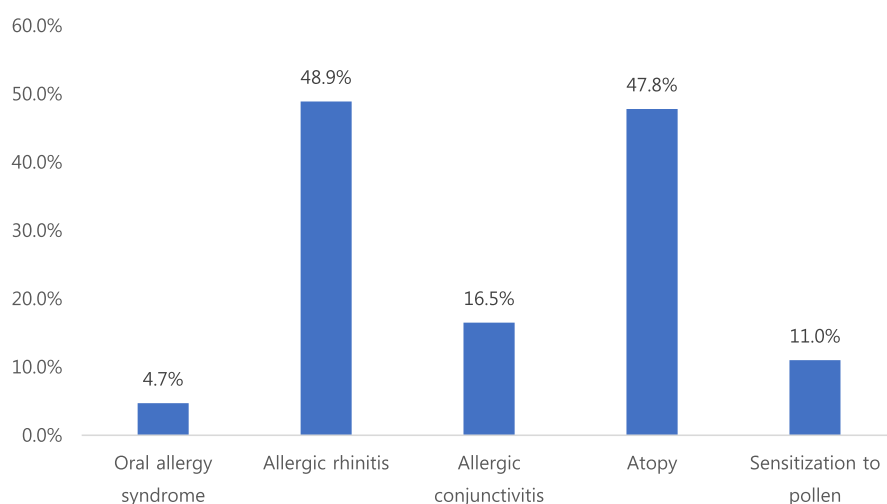


FIGURE 1 Prevalence of allergic disease and characteristics of study participants aged 6–10 years

3.3 | Comorbidity of allergic diseases and sensitization in schoolchildren with OAS

Children with OAS were more likely to be diagnosed with AR and AD than those without OAS (75.6% vs. 47.6%, $p = .001$; 31.7% vs. 15.9%, $p = .016$) (Table 1). There was no significant difference in the prevalence of asthma between the OAS group and non-OAS group (7.3% vs. 5.0%, $p = .461$).

Subjects with OAS showed a significantly higher sensitization rate at 6–7 years of age to birch (34.4%), alder (12.5%), Hop J (12.5%), oak (18.8%), and ragweed (6.3%) than those without OAS (Figure 2). However, there was no significant difference between the two

groups in the sensitization to food allergens (data not shown), indoor allergens such as *Der f*, *Der p*, and dogs, or other outdoor allergens, such as *Alternaria*.

3.4 | Association between OAS and allergic diseases or sensitization in early childhood

OAS was associated with food allergy (adjusted odds ratio [aOR], 3.803; 95% confidence interval [CI]: 1.795–8.057) and AD at age 1–3 years (aOR, 2.393; 95% CI: 1.243–4.609) (Table S2). Sensitization to milk or egg white with respect to serum-specific IgE

at 1 year and sensitization to food allergens in the SPT performed at age 3 years were risk factors in the development of OAS in schoolchildren (Table S2). However, there was no significant association between OAS and AR or recurrent wheeze between children aged 1–3 years (Table S2).

At 1 year of age, the sensitization rates to egg white and milk were 36.4% and 33.3% in the OAS group and 25.3 and 23.4% in the non-OAS group, respectively. The food allergen sensitization rate was 54.5% in the OAS group, which was significantly higher than 36.8% in the non-OAS group (data not shown). Among children with OAS, the sensitization rates to egg (14.3%), milk (5.6%), peanut (5.6%), and grass (5.6%) at age 3 years were higher in children with OAS than in those without OAS (Table S3).

TABLE 2 Food triggers of oral allergy syndrome

	Food	N	%
Fruits	Kiwi	10	22.7
	Peach	5	11.4
	Pineapple	3	6.8
	Orange	2	4.6
	Mango	1	2.3
	Others	1	2.3
Nuts	Peanut	3	6.8
	Hazelnut	1	2.3
	Pine nut	1	2.3
Vegetables	Tomato	8	18.2
	Watermelon	4	9.1
	Oriental melon	1	2.3
	Paprika	1	2.3
	Cucumber	1	2.3

3.5 | Association between OAS and allergic diseases or sensitization in early childhood among school children with AR

The mean and gestational ages of the AR group were higher than those of the non-AR group, and the prevalence of parental history of allergic disease and the prevalence of comorbid atopy, asthma, AD, and OAS were significantly higher in the AR group than in the non-AR group (Table S4). Among children with AR, OAS was significantly associated with food allergy in early childhood (aOR, 2.971; 95% CI: 1.159–7.615) but not associated with AD, AR, or recurrent wheeze (Table 3). Sensitization to milk or egg white with respect to serum-specific IgE at 1 year of age, as well as atopy and sensitization to milk, egg, or peanut at age 3 years, were risk factors in the development of OAS in schoolchildren with AR (Table 3).

3.6 | Mediation analysis in children with AR

Both AD and food allergy may be risk factors of OAS. We therefore evaluated the potential indirect effect of food allergy on OAS mediated through AD. In schoolchildren with AR, there was a significant direct effect of food allergy on OAS (direct effect: estimate = 1.10, 95% CI 0.21 to 1.99, $p = .015$; Figure 3), while the indirect effect through AD was not significant.

4 | DISCUSSION

The prevalence of OAS in 6–10-year-old Korean children was 4.7%, and the mean age of onset was 6.74 years. Kiwi, tomato, and peach were the most common triggers of OAS. Food allergy, AD, and sensitization to foods in early childhood were associated with the

FIGURE 2 Comparison of sensitization to inhalant allergens at 6–7 years of age between OAS group and controls. p -Values for the comparison between the OAS and non-OAS groups were calculated using the Pearson's chi-square test. OAS, oral allergy syndrome. * $p < .05$

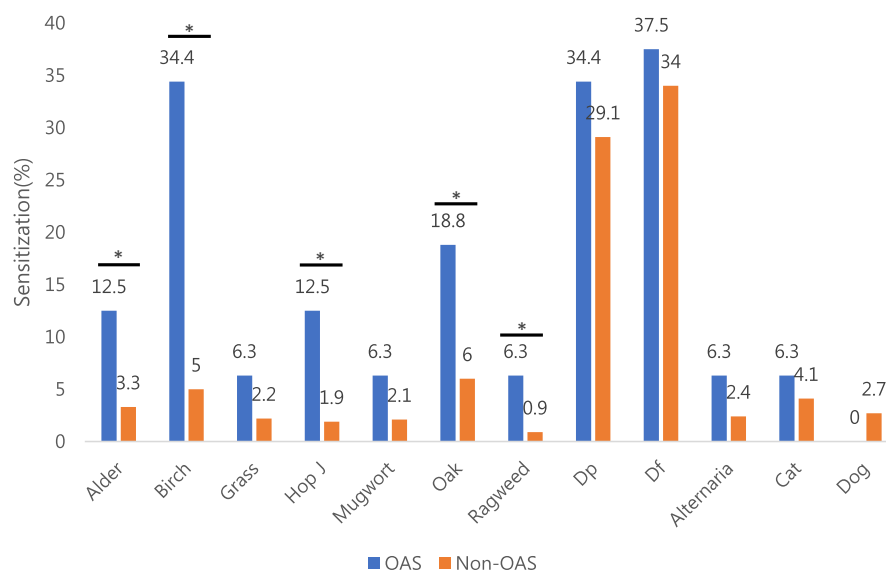


TABLE 3 Effect of allergic diseases and sensitization in early childhood on oral allergy syndrome in children with allergic rhinitis

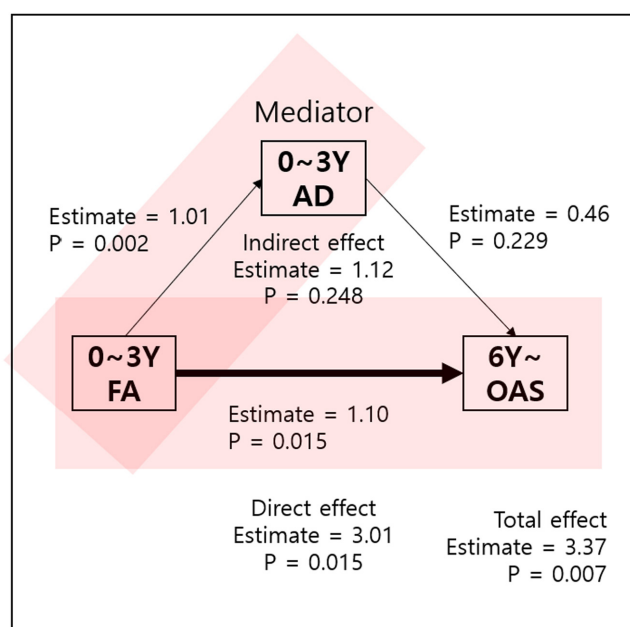
	OR	95% CI	aOR	95% CI
Allergic rhinitis	0.608	0.179–2.066	0.539	0.153–1.899
Atopic dermatitis	1.832	0.880–3.815	1.594	0.716–3.549
Food allergy	3.356	1.402–8.033	2.971	1.159–7.615
Recurrent wheeze	1.129	0.378–3.376	1.348	0.427–4.253
Sensitization ^a to milk or egg white (specific IgE) at age 1 year	2.536	1.065–6.041	3.164	1.006–9.957
Sensitization ^b to food allergens (SPT) at age 3 years	23.114	3.669–145.598	26.342	1.768–392.555
Sensitization ^b to inhalant allergens (SPT) at age 3 years	1.300	0.500–3.380	1.458	0.430–4.943
Atopy	2.327	1.151–4.703	2.377	1.170–4.832

Note: aORs and 95% CIs obtained from logistic regression analysis adjusted for sex, parental history of allergic disease, maternal education level, delivery type, breastfeeding.

Abbreviations: aORs, adjusted odds ratios; CIs, confidence intervals.

^aSpecific IgE ≥ 0.35 IU/ml.

^bAllergen histamine ratio ≥ 1 .

**FIGURE 3** Mediation by atopic dermatitis in schoolchildren with AR. AD, atopic dermatitis; FA, food allergy; OAS, oral allergy syndrome

development of OAS in schoolchildren. Sensitization to inhalant allergens at 3 years did not increase the risk of school-age OAS. Thus, the sensitization to food antigens and food allergy in early childhood was related to OAS in schoolchildren, particularly in those with AR. To the best of our knowledge, this is the first general-population-based cohort study that demonstrates the association between allergic diseases in early childhood and OAS.

Most studies on the prevalence of OAS have focused on high-risk patients who visited hospitals for treatment or suffered from allergic diseases, recording a prevalence of 4.7% to more than 20% in children and 13%–58% in adults.^{12,22,23} In Korea, a multicenter,

cross-sectional study reported an OAS prevalence of 42.7% in children with pollinosis.⁹ However, there is a possibility that prevalence in high-risk populations is overestimated compared with that in the general population. In addition, because the diversity of risk factors directly affects the prevalence, these results are difficult to generalize or compare with findings of other studies. Only two cross-sectional studies were conducted to investigate OAS in the general population cohort. A Danish study reported an OAS prevalence of 16.7% in young adults, which was lower than 20.5% in adolescents and adults with AR in other European studies, or 23.0% in children with risk factors.^{13,15} A Japanese study in the general population also reported that 11.7% of adolescents had OAS and that 22.9% with pollen allergy had OAS.¹⁴ Thus, the lower prevalence of OAS (4.7%) in this study probably results from the examination of the general population and the younger age of the participants compared with other studies.

Most studies on OAS were cross-sectional observational studies intending to identify an association between OAS and other risk factors. In an Italian study on pollen-induced AR, a longer AR duration was associated with OAS.²² Additionally, the prevalence of asthma was significantly higher in patients with birch-sensitization and OAS than in those without OAS. There was also no significant difference in the prevalence of other allergic diseases such as AD and rhinoconjunctivitis according to the presence of OAS.¹⁶ As these studies analyzed the comorbidities at the time of investigation, it is difficult to determine the relationship between OAS and sensitization or allergic diseases in early childhood. In this study, children were followed-up longitudinally from birth so that the association between the development of OAS and allergic conditions could be thoroughly assessed. There were significant differences in AD, food sensitization, and food allergy in early childhood between the OAS and non-OAS groups. In particular, food sensitization and food allergy in younger schoolchildren with AR remained significant risk factors for OAS. In addition,

mediation analysis showed that the effect of food allergy on OAS was direct in children with AR and AD did not mediate the association between food allergy and OAS (Figure 3). These findings suggest that AR children with food allergy in early childhood are more susceptible to OAS than AR children without any history of food allergy. Therefore, monitoring OAS symptoms is necessary in children with a history of food allergy or sensitization in early childhood.

Class II food allergens are the primary concern in children with OAS. Unlike class I food allergens, class II food allergens are typically not the primary sensitizers.¹² In general, class I food allergens are stable in heat and during digestion,¹² allowing them to retain their immunoglobulin E (IgE)-binding conformation, potentially leading to an increased ability to sensitize and a higher incidence of severe systemic reactions.¹² In this study, sensitization to class I food allergens in early childhood and a history of food allergy were proven risk factors for school-age OAS. Additionally, despite the varying characteristics of food antigens and sensitization pathways, mucosal immunity defects may be associated with food allergy and OAS. Further research is needed to elucidate the mechanisms of OAS.

A single study conducted on adults using questionnaires in the United Kingdom reported 25 years as the age at which food reactions begin, including OAS.²⁴ In this study, the mean age of onset of OAS was 6.74 years (3–10 years). Therefore, monitoring for OAS is necessary in children under 6 years of age.

Kiwi, peach, tomato, and watermelon were the common causative foods in this study, which are associated with birch antigens (Bet V1 and Bet V2), the most common cause of pollen sensitization.²⁵ Another Korean study revealed that apple, peach, and kiwi were common causative foods for children aged 2–6 years with AD and birch sensitization.²⁶ In Western countries, 60%–90% of patients with pollinosis exhibit OAS symptoms^{27,28}; however, OAS symptoms were observed in only 41.7% of patients with pollinosis in a Korean multicenter study⁹ and in 19.1% of the children in this study. In Western countries, pollinosis from *Poaceae*, such as birch and timothy grass, and *Asteraceae*, such as ragweed and mugwort, are common, given their cross-reactions with many foods. The incidence of OAS varies depending on the environment, plant cultivation practices, ethnic groups, and regional differences,⁷ explaining the difference in prevalence between Korea and western countries.

This study has several limitations. First, the number of children with OAS in this general-population-based birth cohort study was lower than those in other high-risk population studies. Second, OAS was diagnosed using a questionnaire and physician's diagnosis, and a food provocation test was not performed. However, OAS was diagnosed by referring to the detailed medical history noted by pediatric allergists. Third, the causative food antigens of OAS should be confirmed by prick-to-prick tests or antigen-specific IgE tests. However, in this study, the lack of confirmation of the causative food is a limitation for the accurate diagnosis of OAS. Despite these limitations, this study is the first to investigate OAS prevalence in

young children in the general population. Moreover, as a birth cohort study, longitudinal analysis was possible based on the acquisition of various clinical data before the development of OAS. Novel associations between OAS and food allergy or food sensitization have been revealed, and further studies are warranted to expand on this new perspective on OAS.

In conclusion, OAS occurs in 4.73% of children aged 6–10 years, and the most common causative food is fruit, especially kiwi. The risk of developing OAS in schoolchildren with AR increased in the presence of food allergy or food sensitization in early childhood. Further studies are required to investigate the association of food allergy in early childhood with the development of OAS.

AUTHOR CONTRIBUTION

Kun-Baek Song: Data curation (lead); Formal analysis (lead); Investigation (equal); Visualization (lead); Writing – original draft (lead). **Min Jee Park:** Validation (supporting); Writing – review & editing (supporting). **Eom Ji Choi:** Validation (supporting); Writing – review & editing (supporting). **Sungsu Jung:** Validation (supporting); Writing – review & editing (supporting). **Ji-Sun Yoon:** Validation (supporting); Writing – review & editing (supporting). **Hyun-Ju Cho:** Validation (supporting); Writing – review & editing (supporting). **Bong-Seong Kim:** Conceptualization (equal); Investigation (equal); Resources (equal). **Kangmo Ahn:** Investigation (equal). **Kyung Won Kim:** Conceptualization (equal); Investigation (equal); Resources (equal). **Youn Ho Shin:** Conceptualization (equal); Investigation (equal); Resources (equal). **Dong In Suh:** Conceptualization (equal); Investigation (equal); Resources (equal). **Soo-Jong Hong:** Conceptualization (equal); Funding acquisition (lead); Investigation (equal); Resources (equal); Supervision (equal); Writing – review & editing (equal). **So-Yeon Lee:** Conceptualization (equal); Funding acquisition (supporting); Investigation (equal); Resources (equal); Supervision (equal); Writing – review & editing (equal).

CONFLICT OF INTEREST

The authors have no financial or non-financial conflicts of interests to declare.

PEER REVIEW

The peer review history for this article is available at <https://publons.com/publon/10.1111/pai.13786>.

DATA AVAILABILITY STATEMENT

The data used in this study is expected to be made public next year by the Korea National Institute of Health, which funded it, but it is not currently published.

ORCID

Kun-Baek Song  <https://orcid.org/0000-0001-6981-6292>

Min Jee Park  <https://orcid.org/0000-0003-0891-1311>

Eom Ji Choi  <https://orcid.org/0000-0002-1122-1592>

Sungsu Jung  <https://orcid.org/0000-0002-0559-4982>

Bong-Seong Kim  <https://orcid.org/0000-0002-3562-3916>

Kangmo Ahn  <https://orcid.org/0000-0001-7751-9829>
 Kyung Won Kim  <https://orcid.org/0000-0003-4529-6135>
 Youn Ho Shin  <https://orcid.org/0000-0003-3227-5511>
 Dong In Suh  <https://orcid.org/0000-0002-7817-8728>
 Soo-Jong Hong  <https://orcid.org/0000-0003-1409-2113>
 So-Yeon Lee  <https://orcid.org/0000-0002-2499-0702>

REFERENCES

- Ma S, Sicherer SH, Nowak-Wegrzyn A. A survey on the management of pollen-food allergy syndrome in allergy practices. *J Allergy Clin Immunol*. 2003;112:784-788.
- Ziska LH, Makra L, Harry SK, et al. Temperature-related changes in airborne allergenic pollen abundance and seasonality across the northern hemisphere: a retrospective data analysis. *Lancet Planet Health*. 2019;3:e124-e131.
- Loraud C, de Ménerville CT, Bourgoignie Heck M, Cottel N, Wanin S, Just J. Emergence of pollen food allergy syndrome in asthmatic children in Paris. *Pediatr Allergy Immunol*. 2021;32:702-708.
- Beck I, Jochner S, Gilles S, et al. High environmental ozone levels lead to enhanced allergenicity of birch pollen. *PLoS One*. 2013;8:e80147.
- Oh JW, Lee HB, Kang IJ, et al. The revised edition of Korean calendar for allergenic pollens. *Allergy Asthma Immunol Res*. 2012;4:5-11.
- Cassia R, Nocioni M, Correa-Aragunde N, Lamattina L. Climate change and the impact of greenhouse gases: CO₂ and NO_x, friends and foes of plant oxidative stress. *Front Plant Sci*. 2018;9:273.
- Bircher A, Van Melle G, Haller E, Curty B, Frei P. IgE to food allergens are highly prevalent in patients allergic to pollens, with and without symptoms of food allergy. *Clin Exp Allergy*. 1994;24:367-374.
- Eriksson NE, Formgren H, Svenonius E. Food hypersensitivity in patients with pollen allergy. *Allergy*. 1982;37:437-443.
- Kim M-A, Kim D-K, Yang H-J, et al. Pollen-food allergy syndrome in Korean pollinosis patients: a nationwide survey. *Allergy Asthma Immunol Res*. 2018;10:648.
- Choi J, Kim D, Yang H, et al. Oral allergy syndrome in patients with pollen allergies in Korea: a multicenter cross-sectional study. *Allergy*. 2018;73:650.
- Park YA, Jeong KU, Kim YH, et al. Etiology and clinical feature of oral allergy syndrome in children. *Allergy Asthma Respir Dis*. 2018;6:219-224.
- Carlson G, Coop C. Pollen food allergy syndrome (PFAS): a review of current available literature. *Ann Allergy Asthma Immunol*. 2019;123:359-365.
- Osterballe M, Mortz CG, Hansen TK, Andersen KE, Bindslev-Jensen C. The prevalence of food hypersensitivity in young adults. *Pediatr Allergy Immunol*. 2009;20:686-692.
- Kiguchi T, Yamamoto-Hanada K, Saito-Abe M, et al. Pollen-food allergy syndrome and component sensitization in adolescents: a Japanese population-based study. *PLoS One*. 2021;16:e0249649.
- Lipp T, Acar Sahin A, Aggelidis X, et al. Heterogeneity of pollen food allergy syndrome in seven Southern European countries: The @IT.2020 multicenter study. *Allergy*. 2021.
- Kim JH, Kim SH, Park HW, Cho SH, Chang YS. Oral allergy syndrome in birch pollen-sensitized patients from a Korean University Hospital. *J Korean Med Sci*. 2018;33:e218.
- Yang H-J, Lee S-Y, Suh DI, et al. The Cohort for Childhood Origin of Asthma and Allergic Diseases (COCOA) study: design, rationale and methods. *BMC Pulm Med*. 2014;14:1-12.
- Beasley R. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. *Lancet*. 1998;351:1225-1232.
- Broide DH. Immunologic and inflammatory mechanisms that drive asthma progression to remodeling. *J Allergy Clin Immunol*. 2008;121:560-570.
- Lang A, Carlsen K, Haaland G, et al. Severe asthma in childhood: assessed in 10 year olds in a birth cohort study. *Allergy*. 2008;63:1054-1060.
- Iacobucci D. Mediation analysis and categorical variables: the final frontier. *J Consum Psychol*. 2012;22:582-594.
- Dondi A, Tripodi S, Panetta V, et al. Pollen-induced allergic rhinitis in 1360 Italian children: comorbidities and determinants of severity. *Pediatr Allergy Immunol*. 2013;24:742-751.
- Ivkovic-Jurekovic I. Oral allergy syndrome in children. *Int Dent J*. 2015;65:164-168.
- Skypala I, Bull S, Deegan K, et al. The prevalence of PFS and prevalence and characteristics of reported food allergy; a survey of UK adults aged 18-75 incorporating a validated PFS diagnostic questionnaire. *Clin Exp Allergy*. 2013;43:928-940.
- Faber MA, Van Gasse AL, Decuyper II, et al. Cross-reactive aeroallergens: which need to cross our mind in food allergy diagnosis? *J Allergy Clin Immunol Pract*. 2018;6:1813-1823.
- Kim KI, Lee B, Min TK, Lee J, Pyun BY, Jeon YH. Clinical characteristics of oral allergy syndrome in children with atopic dermatitis and birch sensitization: a single center study. *J Korean Med Sci*. 2019;34:e11.
- Osawa Y, Ito Y, Takahashi N, et al. Epidemiological study of oral allergy syndrome in birch pollen dispersal-free regions. *Allergol Int*. 2020;69:246-252.
- Amlot P, Kemeny D, Zachary C, Parkes P, Lessof M. Oral allergy syndrome (OAS): symptoms of IgE-mediated hypersensitivity to foods. *Clin Exp Allergy*. 1987;17:33-42.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

How to cite this article: Song K-B, Park MJ, Choi EJ, et al. Food allergy in early childhood increases the risk of oral allergy syndrome in schoolchildren: A birth cohort study. *Pediatr Allergy Immunol*. 2022;33:e13786. doi:[10.1111/pai.13786](https://doi.org/10.1111/pai.13786)