

Original Article





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Prevalence and Comorbidities of Atopic Dermatitis in Korean Children and Adolescents From 1995 to 2022: A Population-Based Study

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ABSTRACT

Purpose: We aimed to investigate the prevalence of atopic dermatitis (AD) and its associated risk factors in Korean children in 2022, and to compare to our findings with previous results to identify changes or trends over time.

Methods: A nationwide, cross-sectional study of randomly selected schoolchildren aged 6-7, 9-10, and 12-13 years, respectively, was completed. Information was obtained through the International Study of Asthma and Allergies in Childhood questionnaire, and comparisons between the current and prior surveys performed in 1995, 2000, and 2010 were conducted using a trend test.

Results: In the 2022 survey, the prevalence of "itchy eczema, ever" was 18.3% in 6- to 7-year-olds, 21.6% in 9- to 10-year-olds, and 18.8% in 12- to 13-year-olds. The prevalence of "AD diagnosis, ever" in 6- to 7-year-olds rose from 20.9% in 1995 to 35.4% in 2010, then dropped to 13.6% in 2022 (P < 0.001), while in 12- to 13-year-olds, it increased from 7.1% in 1995 to 23.7% in 2010, then declined to 17.5% in 2022 (P < 0.001). In 6- to 7-year-olds, the prevalence of "AD only" and "AD and asthma" decreased between 1995 and 2022 (all P < 0.001). In 12- to 13-year-olds, the prevalence of "AD only," "AD and rhinitis," and "AD and asthma and rhinitis" all increased during the same period (all P < 0.001).

Conclusions: The prevalence of AD decreased in Korean children aged 6-7 years and

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Disclosure

There are no financial or other issues that might lead to conflict of interest.

increased in those aged 12-13 years, respectively, between 1995 and 2022, with a concomitant rise in allergic comorbidities among adolescents, suggesting age-dependent trends influenced by diverse AD phenotypes.

Keywords: Adolescents; atopic dermatitis; allergic rhinitis; antibiotics; asthma; prevalence

INTRODUCTION

Atopic dermatitis (AD) is a prevalent chronic inflammatory skin disease in children and adolescents, characterized by pruritus and eczematous skin lesions. The diverse symptoms and chronicity of AD significantly compromise the quality of life and place a psychosocial burden on patients and their caregivers. The complex interplay of genetic and environmental factors, including climate, air pollution, and altered skin microbiome, contributes to the development of AD. Over the past decades, the global prevalence of AD has shown an increasing trend, with substantial variations among different populations. A recent Korean study reported a decrease in the prevalence of very-early-onset AD between 2003 and 2018, with an increase in childhood-onset AD, indicating the considerable phenotypic heterogeneity of AD. This underscores the necessity for a comprehensive understanding of AD prevalence and associated risk factors in pediatric and adolescent populations for effective public health interventions.

To address this, many researchers have conducted epidemiologic studies in Korea, primarily based on data from the National Health Insurance Service (NHIS) and a nationwide questionnaire survey through the International Study of Asthma and Allergies in Childhood (ISAAC).³⁻⁶ The NHIS, as a comprehensive database, enables researchers to conduct large-scale analyses of real-world clinical data with high statistical power. A recent study using NHIS data demonstrated that the estimated prevalence of AD in patients < 19 years of age increased from 4.0% in 2003 to 4.5% in 2018.³ However, the NHIS data focus on health care usage, potentially leading to an underestimation of milder or subclinical cases of AD. Additionally, reliance on diagnostic codes may introduce misclassification bias, skewing prevalence estimates.

In contrast, the ISAAC study uses standardized questionnaires to collect data on AD prevalence and associated risk factors, allowing cross-national comparisons and the identification of potential environmental factors, such as urbanization, indoor environment, and early-life antibiotic use. Moreover, the longitudinal administration of the ISAAC questionnaire at regular intervals over several decades offers the advantage of tracking changes in AD prevalence with the same tool in each region in the world. In Korea, nationwide surveys using the ISAAC questionnaire were conducted in 1995, 2000, and 2010, respectively, with the fourth nationwide survey on childhood AD performed in 2022. ^{5,6} The objective of this study was to investigate the prevalence of AD and its associated risk factors in Korean children and adolescents in 2022, comparing these findings with results of previous analyses to identify any significant changes or trends over time.



MATERIALS AND METHODS

Study design and subjects

A cross-sectional survey was conducted in 4,144 children aged 6-7 years, 4,321 children aged 9-10 years, and 4,387 students aged 12-13 years. Participants were selected from a random sample of 213 elementary and 103 middle schools located nationwide. The sampling frame was based on a comprehensive national list of schools in Korea. A stratified 2-stage cluster sampling design was employed, where schools were stratified by geographic regions, school location type (metropolitan, urban, or rural areas), and the proportion of households residing in apartment complexes. During the first stage of sampling, schools were stratified, and sample schools were selected using a systematic probability proportional to the sizesampling procedure, with the number of classes in the school serving as the measure of size. The school frame was ordered by region, zip code, and school enrollment before sample selection. Participation rates for originally sampled schools were 100% for both elementary and middle schools. In the second stage, 2 classes were randomly selected within each sample school, and all children in those classes were asked to take part in the survey. Parents provided demographic information, including age, sex, region, urbanization, and monthly family income. The survey was conducted between September and November 2022, aligning with previous surveys in 1995, 2000, and 2010. School locations were classified into 3 groups (metropolitan, urban, or rural area) based on population size and density.

The study survey was conducted using a combination of field survey and online methods. In elementary schools, most data were collected via field surveys, with a response rate of 96.6%, while 3.4% of surveys were administered online. A similar strategy was applied in middle schools, where field surveys were predominantly deployed, with a response rate of 97.6%, while 2.4% were administered online. This study was approved by the Institutional Review Board of Inje University in Seoul (PAIK 2022-01-006). Written informed consent was obtained from parents before their children participated in the study.

Assessment of risk factors by questionnaire

The Korean version of the ISAAC questionnaire was used to assess risk factors in this study. A detailed description of the questionnaire was reported previously. The prevalence of AD was assessed using the following definitions: "itchy eczema, ever" referred to those who had experienced itchy eczema episodes in their lifetime; "itchy eczema, lasting for 12 months" included those who had experienced itchy eczema episodes within 12 months of the survey; "AD diagnosis, ever" applied to those who had been diagnosed with AD by a physician in their lifetime; and "AD treatment, last 12 months" referred to those who had received treatment for AD within 12 months of the survey. Current AD was defined by the presence of an intermittent itchy skin rash that came and went for ≥ 6 months among those who experienced itchy eczema episodes in their lifetime and reported the rash within the past 12 months. The core questionnaire also included basic socio-demographic information and potential risk factors influencing the development or exacerbation of AD. For elementary school students, parents completed the entire questionnaire, including questions on risk factors and the prevalence of AD. For middle school students, parents completed questions on risk factors, while students answered questions related to the prevalence of AD.

Previous epidemiological investigations for comparative analysis

Previous epidemiological investigations for comparative analysis were conducted by a research team with continuity in many of the senior researchers and clinical supervisors,



while the field survey teams responsible for data collection differed across surveys. The survey methodology in our study closely follows the approach of earlier investigations, which used the Korean version of the ISAAC questionnaire in 1995, 2000, and 2010, as previously described. ^{5,6} During the initial phase of our study in 1995, a cross-sectional survey of 3,985 children aged 6-7 years and 5,010 students aged 12-13 years was conducted, with an overall response rate of 94.9%. Similarly, in 2000, our cross-sectional survey targeted 4,650 children aged 6-7 years and 5,109 students aged 12-13 years (response rate, 97.8%), with exclusive reliance on field surveys to collect information from these age groups. Using the same random sampling and stratified 2-stage cluster sampling design, we analyzed data from 4,003 children aged 6-7 years and 4,112 students aged 12-13 years from 45 elementary and 40 middle schools, with final response rates of 92.1% and 93.8%, respectively, in 2010.

Statistical analysis

Because the survey participants were selected in 2010 and 2022 using a stratified 2-stage cluster sampling design, we constructed the sampling weights for this study to account for differential selection probabilities, non-response, and post-stratification. Categorical variables are presented as frequencies and weighted percentages. Prevalence rates of AD were calculated using the SURVEYFREQ procedure in SAS, a statistical software widely used for complex survey data analysis. This procedure accounts for complex multistage survey designs by incorporating stratification, clustering, and unequal weighting to compute estimates. Comparisons between current and previous surveys were conducted using a Cochran-Armitage trend test to assess changes in prevalence rates over time. Somers' delta and Pearson's correlation coefficients were used to assess the direction of the trend. Additionally, we conducted logistic regression analysis to examine the association between potential risk factors and the prevalence of AD. The results were presented as adjusted odds ratios (aORs) with 95% confidence intervals (CIs). Potential risk factors included sex, a family history of allergic diseases, birth-related variables (delivery mode, birth weight, gestational age, breastmilk feeding, antibiotics use during infancy, household pets during the perinatal period), and residential area. The SURVEYLOGISTIC procedure in SAS was used for logistic regression, incorporating complex survey design features such as stratification and weighting. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA). P < 0.05 was considered statistically significant.

RESULTS

A total of 4,038 children aged 6-7 years, 4,251 children aged 9-10 years, and 4,269 aged 12-13 years, respectively, participated in 2022 survey (**Table 1**). Among them, 2,037 (51.2%) boys aged 6-7 years, 2,120 (51.3%) boys aged 9-10 years, and 2,143 (51.5%) boys aged 12-13 years were included. The prevalence rates of "itchy eczema, ever" among children aged 6-7 years, 9-10 years, and 12-13 years were 18.3%, 21.6%, and 18.8%, respectively (**Fig. 1A**), while the prevalence rates of "itchy eczema, lasting for 12 months" for each age group were 12.9%, 14.0%, and 11.1%. In children aged 6-7 years, the lifetime prevalence of AD diagnosis was 13.6%, while the prevalence of AD treatment in the last 12 months was 6.2%. On the other hand, in the 9- to 10-year-olds and 12- to 13-year-olds, the lifetime prevalence rates of AD diagnosis were 17.0% and 17.5%, with corresponding prevalence rates of AD treatment in the last 12 months of 6.4% and 6.6%, respectively (**Fig. 1A**).



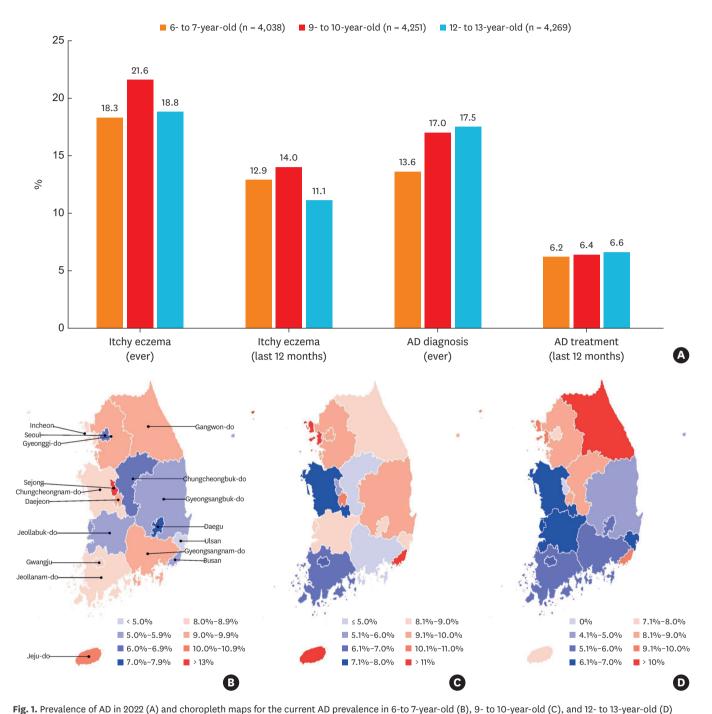
Table 1. Characteristics of the study population in 2022 (n = 12,558)

Characteristics	6- to 7-year-olds	9- to 10-year-olds	12- to 13-year-olds	
	(n = 4,038)	(n = 4,251)	(n = 4,269)	
Sex				
Male	2,037 (51.2)	2,120 (51.3)	2,143 (51.5)	
Female	2,001 (48.8)	2,131 (48.7)	2,126 (48.5)	
Family history of allergic				
diseases				
None	1,401 (34.5)	1,625 (37.9)	1,957 (46.0)	
Father alone	730 (17.9)	746 (17.6)	707 (17.3)	
Mother alone	854 (21.3)	883 (20.5)	831 (19.0)	
Both parents	1,051 (26.3)	996 (66.1)	769 (17.6)	
Birth type				
Vaginal delivery	2,332 (57.9)	2,655 (61.8)	2,667 (62.3)	
Cesarean section	1,706 (42.1)	1,596 (38.2)	1,602 (37.7)	
Gestational period				
≤ 36 weeks	523 (12.5)	538 (12.8)	561 (12.3)	
37-42 weeks	3,434 (85.5)	3,618 (85.3)	3,584 (84.8)	
≥ 43 weeks	80 (1.9)	94 (1.9)	124 (2.9)	
Birth weight				
< 3.1 kg	1,475 (36.5)	1,488 (35.2)	1,492 (35.0)	
3.1-3.5 kg	1,802 (44.8)	1,927 (45.1)	1,928 (44.7)	
≥ 3.6 kg	758 (18.7)	835 (19.8)	849 (20.3)	
Breastfeeding				
Yes	3,764 (93.3)	3,993 (94.2)	4,001 (93.8)	
No	274 (6.7)	258 (5.8)	267 (6.2)	
Antibiotics use during infancy				
Yes	1,539 (37.1)	1,553 (35.3)	1,242 (29.1)	
No	2,498 (62.9)	2,698 (64.7)	3,027 (70.9)	
Household pets during the perinatal period				
Yes	361 (9.4)	268 (6.7)	234 (5.3)	
No	3,677 (90.6)	3,983 (93.3)	4,035 (94.7)	
Residential area				
Metropolitan	1,803 (40.8)	1,949 (40.6)	1,914 (41.0)	
Urban	2,039 (54.5)	2,115 (54.8)	2,153 (54.1)	
Rural	196 (4.7)	187 (4.6)	202 (4.9)	

Values are presented as number (%).

For 6- to 7-year-olds, the prevalence of AD was highest in Sejong (13.9%), followed by Jeju-do (10.3%), and Daejeon (9.6%), while the lowest rates were recorded in Ulsan (3.1%), Busan (5.1%), and Jeollabuk-do (5.0%) (**Fig. 1B**). Among 9- to 10-year-olds, Incheon had the highest prevalence (12.2%), followed by Jeju-do (11.9%), and Busan (11.6%), whereas the lowest rates were documented in Chungcheongbuk-do (3.2%), Gyeongsangnam-do (4.8%), and Sejong (5.3%) (**Fig. 1C**). Among 12- to 13-year-olds, Gangwon-do (11.0%), Busan (9.9%), and Incheon (9.6%) reported the highest rates, while Sejong (0.0%), Gyeongsangbuk-do (4.2%), and Daegu (5.2%) reported the lowest rates (**Fig. 1D**).

Among 6- to 7-year-olds, the prevalence of itchy eczema within the last 12 months changed from 15.1% in 1995 to 12.5% in 2000, and 20.5% in 2010, respectively, then tapered off to 12.9% in 2022 (*P* for trend = 0.020) (**Fig. 2A**). When the AD characteristic "diagnosis, ever" was considered, the prevalence of AD in 6- to 7-year-olds rose from 20.9% in 1995 to 29.3% in 2000 and further to 35.4% in 2010, then declined to 13.6% in 2022 (*P* for trend < 0.001) (**Fig. 2A**). When the AD characteristic "treatment, last 12 months" was considered, it gradually increased to 9.7%, 14.3%, and 15.7% in 1995, 2000, and 2010, respectively, with a subsequent decrease to 6.2% in 2022 (*P* for trend < 0.001) (**Fig. 2A**). In contrast, the lifetime prevalence of eczema symptoms and current AD, respectively, did not show a statistical significance from 1995



children in 2022. (A) and choropleth maps for the current AD prevalence in 6-to 7-year-old (B), 9- to 10-year-old (C), and 12- to 13-year-old (D). AD, atopic dermatitis.

to 2022 (*P* for trend = 0.846 and 0.137). Among the 12 to 13-year-olds, the prevalence of "AD diagnosis, ever" increased from 7.1% in 1995 to 23.7% in 2010, while that of "AD treatment, last 12 months" rose from 4.2% in 1995 to 8.5% in 2010. Thereafter, however, the prevalence as determined in 2022 dropped slightly to 17.5% for "AD diagnosis, ever" and 6.6% for "AD treatment, last 12 months," respectively (*P* for trend < 0.001) (**Fig. 2B**). Meanwhile, the respective changes in the prevalence rates of "itchy eczema, ever"; "itchy eczema, last 12

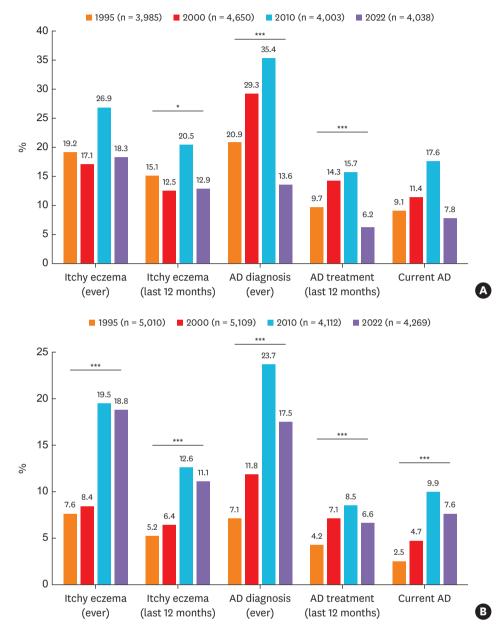


Fig. 2. Prevalence of AD in 6- to 7-year-old (A) and 12- to 13-year-old (B) children from 1995 to 2022. The prevalence rates of "itchy eczema, last 12 months"; "AD diagnosis, ever"; and "AD treatment, last 12 months" in 6- to 7-year-old children significantly decreased between 1995 and 2022 (all P for trend < 0.05), whereas those of AD of any definition in 12- to 13-year-old children significantly increased during the same period (all P for trend < 0.01). The Cochran-Armitage trend test was used to evaluate trends in prevalence changes. AD, atopic dermatitis. "P < 0.05; ""P < 0.001.

months"; and "current AD" between 1995 and 2010 showed similar patterns to those of AD with the other definitions (all P for trend < 0.001) (**Fig. 2B**).

Because we found that the prevalence rate of AD significantly decreased in 6- to 7-year-olds but increased 12- to 13-year-olds over time, we tried to analyze whether the distribution of risk factors had changed since 2010. Among 6- to 7-year-olds, the analysis of 2010 data identified a family history of allergic diseases as a significant risk factor for AD, with aORs of 1.3 (95%)



Table 2. Comparison of risk factor analysis findings for atopic dermatitis between 2010 and 2022 in 6- to 7-year-old children

Characteristics		2010 (n = 3,167)			2022 (n = 4,031)		
	No. (%)	aOR (95% CI)	P value	No. (%)	aOR (95% CI)	P value	
Sex							
Female	1,601 (48.3)			1,998 (48.8)			
Male	1,629 (51.7)	0.9 (0.7-1.1)	0.204	2,033 (51.2)	1.2 (0.9-1.6)	0.302	
Family history of allergic diseases							
No	1,403 (43.1)			1,396 (34.4)			
Paternal allergy (only)	590 (18.5)	1.3 (1.0-1.6)	0.019	730 (17.9)	2.5 (1.6-3.8)	< 0.001	
Maternal allergy (only)	683 (21.0)	1.5 (1.1-2.0)	0.008	854 (21.3)	2.2 (1.5-3.2)	< 0.001	
Parental allergy (both)	554 (17.4)	1.6 (1.2-2.1)	0.001	1,051 (26.4)	3.4 (2.4-4.9)	< 0.001	
Delivery modes							
Vaginal delivery	2,036 (62.3)			2,329 (57.9)			
Cesarean section	1,194 (37.7)	1.0 (0.9-1.2)	0.775	1,702 (42.1)	0.8 (0.6-1.0)	0.054	
Gestational age							
37-42 weeks	2,620 (81.6)			3,430 (85.5)			
Preterm	447 (13.8)	1.0 (0.8-1.3)	0.840	521 (12.5)	0.7 (0.4-1.1)	0.137	
Postterm	163 (4.6)	0.7 (0.4-1.2)	0.217	80 (1.9)	1.2 (0.6-2.6)	0.587	
Birth weight							
3.1-3.5 kg	1,550 (48.0)			1,801 (44.8)			
< 3.1 kg	995 (30.9)	1.0 (0.7-1.3)	0.797	1,473 (36.5)	1.0 (0.7-1.4)	0.885	
≥ 3.6 kg	685 (21.1)	0.9 (0.7-1.2)	0.650	757 (18.7)	0.9 (0.6-1.2)	0.502	
Breastmilk feeding							
Yes	2,392 (73.9)			3,757 (93.3)			
No	838 (26.1)	0.9 (0.7-1.2)	0.440	274 (6.7)	0.6 (0.3-1.1)	0.094	
Antibiotics use during infancy							
No	2,048 (63.2)			2,495 (62.9)			
Yes	1,182 (36.8)	1.3 (1.1-1.6)	0.010	1,536 (37.1)	1.4 (1.0-1.8)	0.041	
Household pets during perinatal period							
No	3,036 (94.0)			3,671 (90.6)			
Yes	194 (6.0)	1.0 (0.6-1.5)	0.890	360 (9.4)	1.1 (0.7-1.7)	0.744	
Residential area							
Metropolitan	1,498 (41.7)			1,800 (40.9)			
Rural	168 (4.7)	1.0 (0.7-1.5)	0.843	195 (4.7)	1.1 (0.6-1.8)	0.823	
Urban	1,564 (53.6)	1.0 (0.8-1.3)	0.704	2,036 (54.5)	1.3 (1.0-1.6)	0.048	

Bold-styled values denote statistically significant.

aOR, adjusted odds ratio; CI, confidence interval.

CI, 1.0-1.6; P = 0.019) for paternal allergy, 1.5 (95% CI, 1.1-2.0; P = 0.008) for maternal allergy, and 1.6 (95% CI, 1.2-2.1; P = 0.001) for allergies in both parents (**Table 2**), respectively. Additionally, the use of antibiotics during infancy was associated with an increased risk of AD (aOR, 1.3; 95% CI, 1.1-1.6; P = 0.010). In 2022, a family history of allergic diseases was related to an increased risk for AD, with elevated aORs of 2.5 (95% CI, 1.6-3.8) for paternal allergy, 2.2 (95% CI, 1.5-3.2) for maternal allergy, and 3.4 (95% CI, 2.4-4.9) for allergies in both parents (all P < 0.001). Additionally, the risk for AD associated with antibiotic use during infancy was higher compared to those who had not received antibiotics treatment (aOR, 1.4; 95% CI, 1.0-1.8; P = 0.041). In 2022, residential areas were identified as a risk factor, with residency in urban areas leading to an increased risk compared to residency in metropolitan areas (aOR, 1.3; 95% CI, 1.0-1.6; P = 0.048).

Among 12- to 13-year-olds, a family history of allergic diseases was a consistent risk factor for AD in both 2010 and 2022. In 2010, children with only a paternal allergy (aOR, 1.5; 95% CI, 1.1-2.1; P = 0.008), only a maternal allergy (aOR, 1.7; 95% CI, 1.2-2.3; P = 0.001), or allergies in both parents (aOR, 2.4; 95% CI, 1.9-3.1; P < 0.001) showed increased risks of developing AD (**Table 3**). This phenomenon was also documented in 2022, with aORs of 1.7 (95% CI, 1.1-2.4; P = 0.011) for paternal allergy, 1.8 (95% CI, 1.2-2.7; P = 0.002) for maternal allergy, and 2.4 (95% CI, 1.7-3.5; P < 0.001) for allergies in both parents. In 2010, living in rural areas



Table 3. Comparison of risk factor analysis findings for atopic dermatitis between 2010 and 2022 in 12- to 13-year-old children

Characteristics	2010 (n = 3,019)			2022 (n = 4,263)		
	No. (%)	aOR (95% CI)	P value	No. (%)	aOR (95% CI)	P value
Sex						
Female	1,587 (49.3)			2,125 (48.5)		
Male	1,481 (50.7)	0.9 (0.7-1.2)	0.570	2,138 (51.5)	1.0 (0.8-1.3)	0.888
Family history of allergic diseases						
No	1,875 (61.1)			1,956 (46.1)		
Paternal allergy (only)	398 (12.8)	1.5 (1.1-2.1)	0.008	707 (17.4)	1.7 (1.1-2.4)	0.011
Maternal allergy (only)	519 (17.0)	1.7 (1.2-2.3)	0.001	831 (19.0)	1.8 (1.2-2.7)	0.002
Parental allergy (both)	276 (9.0)	2.4 (1.9-3.1)	< 0.001	769 (17.6)	2.4 (1.7-3.5)	< 0.001
Delivery modes						
Vaginal delivery	1,898 (61.9)			2,662 (62.2)		
Cesarean section	1,170 (38.1)	0.8 (0.6-1.1)	0.231	1,601 (37.8)	0.8 (0.6-1.1)	0.154
Birth weight						
3.1-3.5 kg	1,025 (32.8)			1,927 (44.7)		
< 3.1 kg	1,436 (47.2)	1.1 (0.9-1.4)	0.482	1,488 (34.9)	1.2 (0.9-1.7)	0.161
≥ 3.6 kg	607 (20.0)	0.8 (0.5-1.1)	0.138	848 (20.4)	1.2 (0.8-1.7)	0.330
Gestational age						
37-42 weeks	2,329 (76.0)			3,579 (84.8)		
Preterm	465 (15.0)	0.8 (0.6-1.1)	0.153	560 (12.4)	0.8 (0.5-1.2)	0.209
Postterm	274 (9.0)	1.0 (0.7-1.6)	0.827	124 (2.9)	1.8 (1.0-3.3)	0.050
Breastmilk feeding						
Yes	2,024 (66.1)			3,997 (93.8)		
No	1,044 (33.9)	0.9 (0.8-1.1)	0.398	266 (6.2)	1.1 (0.6-1.8)	0.825
Antibiotics use during infancy						
No	2,346 (76.4)			3,021 (70.9)		
Yes	722 (23.6)	1.3 (1.0-1.7)	0.063	1,242 (29.1)	1.2 (0.9-1.6)	0.284
Household pets during perinatal period						
No	2,918 (95.6)			4,029 (94.7)		
Yes	150 (4.4)	1.1 (0.6-2.1)	0.735	234 (5.3)	0.8 (0.5-1.3)	0.298
Residential area						
Metropolitan	1,361 (41.5)			1,911 (41.0)		
Rural	76 (2.3)	0.2 (0.1-0.8)	0.021	199 (4.9)	0.4 (0.1-1.0)	0.056
Urban	1,631 (56.2)	1.0 (0.8-1.3)	0.778	2,153 (54.1)	1.0 (0.8-1.4)	0.808

Bold-styled values denote statistically significant.

aOR, adjusted odds ratio; CI, confidence interval.

was more protective against AD compared to living in metropolitan areas (aOR, 0.2; 95% CI, 0.1-0.8; P = 0.021), whereas this association was not statistically significant in 2022.

In this study, time trends in AD and allergic comorbidities were analyzed between 1995 and 2022. In children aged 6-7 years, the prevalence rates of "AD, only" and "AD and asthma" declined, while that of "AD and rhinitis" increased (all *P* for trend < 0.001) (**Fig. 3A**). Meanwhile, the prevalence of "AD and asthma and rhinitis" did not change over time (*P* for trend = 0.102) (**Fig. 3A**). In contrast, the prevalence rates of "AD, only"; "AD and rhinitis"; and "AD and asthma and rhinitis" increased among 12- to 13-year-old children during the same period (all *P* for trend < 0.001) (**Fig. 3B**).

DISCUSSION

Prevalence surveys using questionnaires in cross-sectional studies can investigate a large number of subjects in a short period of time. However, challenges persist when using this method, including diagnostic inaccuracies and the risk of recall bias. Although the exact prevalence figures derived from such surveys may not be correct, comparing prevalence rates over time is feasible if the same questionnaires are consistently used. Thus, the present



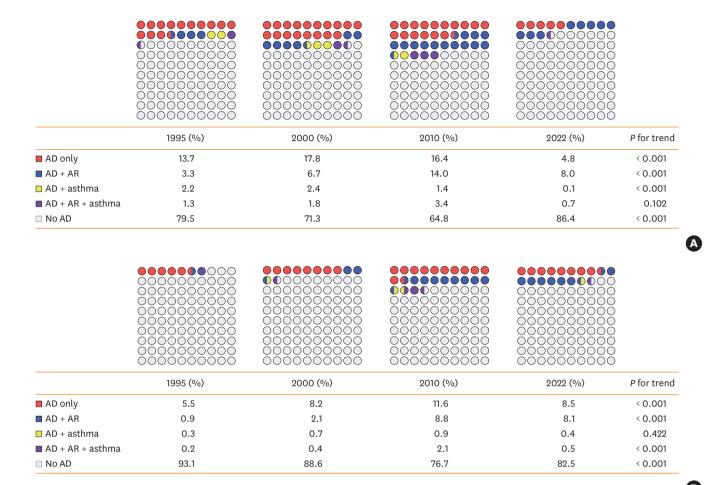


Fig. 3. Time trends in the prevalence rates of AD and allergic comorbidities among 6- to 7-year-old (A) and 12- to 13-year-old (B) children from 1995 to 2022. The presence of allergic diseases was defined as children who had ever been diagnosed with AD, AR, or asthma by a physician. The Cochran-Armitage trend test was used to evaluate trends in prevalence changes.

AD, atopic dermatitis; AR, allergic rhinitis.

study contributes meaningful insights by analyzing the time trend in AD prevalence among Korean children and adolescents over a 27-year timespan based on the same ISAAC protocol. When observing longitudinal trends in AD prevalence, we need to consider that AD is a heterogeneous disease with a multifactorial etiology and complex pathophysiology. In clinical practice, the AD phenotype is defined by stratification in various ways depending on the clinical characteristics of AD.¹⁰ For example, depending on the onset age, AD patients show either very-early-onset (between 3 months and 2 years), early-onset (2-6 years), childhood-onset (6-14 years), adolescent-onset (14-18 years), adult-onset (20-60 years), or very-late-onset (> 60 years) patterns.¹¹ These diverse phenotypes account for different trajectories.^{12,13} Therefore, it is necessary to longitudinally assess our cross-sectional studies on AD epidemiology from 1995 according to different disease phenotypes or trajectories.

In 6- to 7-year-old children, significant trends in itchy eczema within the last 12 months, the lifetime prevalence of AD diagnosis, and AD treatment in the last 12 months were detected. These prevalence rates increased from 1995 to 2010, but it significantly reduced in 2022. Meanwhile, a previous study in Korea that analyzed data from the Korean NHIS and Statistics Korea for children aged \leq 18 years between 2003 and 2018 found a slight rise in the overall



annual AD prevalence from 4.0% in 2003 to 4.5% in 2018.³ Among children aged \leq 5 years, the prevalence increased from 9.1% in 2003 to 11.6% in 2008, then dropped to 8.1% in 2018. A particular increase in AD prevalence among 6- to 7-year-olds was noted from 2003 to 2013, followed by a slight decrease in 2018. Thus, our longitudinal assessment of AD prevalence through questionnaire surveys aligns with the results from NHIS data. Specifically, it suggests that the prevalence of very-early-onset AD or early-onset AD, which can be seen in 6-to 7-year-olds, gradually increased in Korea until around 2010 and then decreased thereafter. However, the present study indicated that the 2022 prevalence rate was lower than that of 1995, whereas NHIS data suggested a higher prevalence in 2018 compared to 2003. This discrepancy likely comes from methodological differences in estimating prevalence rates, the specific time points compared (2022 vs. 2018), and the reduced availability of medical services during the coronavirus disease 2019 (COVID-19) pandemic era.

In children aged 12-13 years, there was a statistically significant increase in the prevalence rates of the lifetime prevalence of AD symptoms, AD symptoms in the last 12 months, the lifetime prevalence of AD diagnosis, AD treatment in the last 12 months, and current AD diagnosis between 1995 and 2010. These observations made in 12- to 13-year-olds in 2022 suggest that there may be an increase in early-onset AD that persists into later childhood or a more frequent incidence of childhood-onset AD. Our prior study using NHIS data demonstrated that the AD prevalence in 12- to 13-year-olds increased from 2002 to 2016 and remained unchanged at a plateau until 2018, just before the COVID-19 pandemic began.³ This also suggests that there has been a change in the distribution of AD phenotypes in 2022 compared to 1995. Genetic predisposition, social circumstances, and microbiome composition may contribute to the distinct trends observed in adolescents.^{14,15} These findings underscore the necessity for a shift in AD management strategies among Korean children and adolescents from those used in the past.

In the present study, the prevalence of AD in both the 6- to 7- and 12- to 13-year-olds increased from 1995, reaching a plateau in 2010. In the ISAAC phase 1 and phase 3 repeat multi-country cross-sectional surveys conducted between 2002 and 2003, the prevalence of eczema symptoms increased in 6- to 7-year-olds in most countries and in 12- to 13-yearolds in low-prevalence countries. 16 Thereafter, in Western developed countries, the time trend of AD prevalence was reported to maintain the plateau. The prevalence of AD in schoolchildren was maintained without any further increase in Norway between 1985 and 2008 and the Netherlands between 2001 and 2010. 14,17 The incidence of AD remained largely unchanged between 2013 and 2021 in annual cohorts of 0- to 17-year-old German children and adolescents. 18 Stable incidence rates of AD were also observed in a cross-sectional, populationbased cohort study involving children born in Denmark from 1997 to 2011 or born in Sweden from 2006 to 2010. 19 In contrast, in the Asia-Pacific region, which includes many developing countries, the prevalence rates of asthma and allergies are changing rapidly, probably due to environmental pollution, rapid urbanization, and Westernization.²⁰ A recent systematic review of studies using ISAAC questionnaires revealed that the lifetime-ever eczema prevalence in children aged 0-18 years showed an increasing trend between 1985 and 2015 in mainland China, whereas decreasing trends were found for Hong Kong as well as Taiwan. 21 AD prevalence is influenced by ethnicity and socioeconomic status,²² and this fact explains the time trend of AD prevalence in Korean children and adolescents over the past 27 years.

In the present study, we sought to discern the causes of the change in AD prevalence between 2010 and 2022. In 6- to 7-year-olds, the parental history of allergic diseases and antibiotic



use during the perinatal period were important risk factors for AD development in both 2010 and 2022. The decreasing trend in AD prevalence among this age group may reflect improved public awareness and preventive practices, such as the widespread use of moisturizers and breastfeeding. The presence of allergic diseases in the family also contributed to the development of AD among 12- to 13-year-olds in both 2010 and 2022. In 2010, the AD prevalence decreased among 12- to 13-year-old children living in rural areas compared to those living in metropolitan areas. However, this protective effect lost statistical significance in the 2022 survey, possibly due to urbanization and its associated environmental changes. Additionally, the increasing prevalence of AD in this age group may be influenced by exposure to environmental pollutants and psychological stress.^{23,24}

While our study used standardized methodology across different survey years, it is important to acknowledge certain limitations in interpreting temporal trends. First, the surveys were not conducted in identical regions across all study years, which may have introduced regional variations affecting AD prevalence. However, as the sampling strategy was designed to ensure national representativeness, this effect is expected to be minimal. Secondly, as this study is based on cross-sectional surveys rather than a longitudinal cohort, individual-level disease trajectories were not assessed. Therefore, observed prevalence changes reflect differences between independent populations at each time point rather than true longitudinal changes within the same individuals. Additional research is needed to determine whether this time trend in AD prevalence will continue or what environmental factors may have caused this change.

From 1995 to 2022, trends in allergic comorbidities among children with AD differed depending on age group. Of note, there was a statistically significant increase in the prevalence rates of "AD and allergic rhinitis (AR)" and "AD and AR and asthma" among 12- to 13-year-olds. That is, in Korean children aged 12-13 years, allergic comorbidities became more common as the prevalence of AD increased, suggesting that earlier and more proactive management of AD should be started before the age of 12-13 years. The trend of combined AD, asthma, and AR showed an upward trajectory, and it remains unclear whether this is a manifestation of the allergic march or if AR is increasing independently.^{25,26} Moreover, the involvement of diverse asthma phenotypes could contribute to these trends, underscoring the complexity of asthma as a comorbidity.²⁷ In contrast, the prevalence of AD in 6- to 7-year-olds decreased and the prevalence of asthma among those with AD also declined. This possibly reflects a good prognosis in this age group, in which very-early-onset or early-onset AD mainly occurs. However, a key distinction is that, while younger children displayed a significant downward trend in "AD and asthma," no such trend was observed among the 12- to 13-year-olds. This could suggest that the etiology of asthma in younger children may primarily be related to viral infections commonly found in early childhood, whereas, among 12- to 13-year-olds, different factors could be at play, potentially including the allergic march. 26,28 Nevertheless, despite the reduced prevalence of asthma during the COVID-19 pandemic—likely due to the significant decrease in other respiratory viral infections—the increase in rhinitis complicates interpretations of trends of allergic comorbidities in 6- to 7-year-old children.

In conclusion, from 1995 to 2022, the prevalence of AD decreased over time in Korean children aged 6-7 years and increased over time in those aged 12-13 years, respectively. This study also determined that allergic comorbidities have also increased over time in 12- to 13-year-old Korean patients with AD. These time trends appear differently depending on the age group due to the diversity of AD phenotypes, but the cause of changes in AD and allergic comorbidity prevalence over time remains unclear.



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