

# Original Article



# Trends in the Prevalence of Asthma in Korean Children: A Population-Based Study From 1995 to 2022

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# OPEN ACCESS

Received: Aug 2, 2024
Revised: Oct 30, 2024
Accepted: Dec 21, 2024
Published online: Feb 11, 2025

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# **ABSTRACT**

**Purpose:** We investigated the prevalence of asthma and its risk factors in Korean children in 2022, comparing the prevalence with previous data to identify trends in the prevalence of childhood asthma over time.

Methods: This nationwide cross-sectional study enrolled 4,038 children aged 6–7 years and

4,269 children aged 12–13 years from 213 randomly selected elementary schools in 2022. The prevalence of asthma in 2022 was compared with those in 1995, 2000, and 2010, with subgroup comparisons classified by gender. A modified International Study of Asthma and Allergies in Childhood questionnaire assessed asthma prevalence with environmental factors. **Results:** The prevalence of "asthma diagnosis ever" in children aged 6–7 years was 9.1%, 9.4%, and 10.4% in 1995, 2000, and 2010, respectively, which was decreased in 2022 (2.1%, P < 0.001). The prevalence of 'current asthma' in children aged 6–7 years showed fluctuations (3.5%, 2.0%, 4.2%, and 0.6% in 1995, 2000, 2010, and 2022, respectively) without showing a significant trend. The prevalence of 'asthma diagnosis ever' and 'current asthma' in children aged 6–7 years was significantly higher in males than in females. The prevalence of 'asthma diagnosis ever' in children aged 12–13 years was 3.1% in 1995, with a significant increasing trend in 2000 (5.8%) and 2010 (7.5%), followed by a decrease in 2022 (3.4%). Male sex, a history of bronchiolitis in early life, allergic rhinitis diagnosis ever, and atopic dermatitis diagnosis ever were associated with 'asthma diagnosis ever' in children aged 6–7



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#### Disclosure

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

years. For children aged 12–13 years, male sex and history of bronchiolitis in early life were independently associated with 'asthma diagnosis ever.'

**Conclusions:** Childhood asthma prevalence has decreased, varying by asthma definition. The study's findings provide important information for establishing prevention and management strategies of childhood asthma.

**Keywords:** Asthma; children; epidemiology; prevalence; risk factor

#### INTRODUCTION

Asthma is one of the most common chronic lung diseases in children, with a considerable disease burden. The complex interactions between host factors (*e.g.*, genetic susceptibility) and environmental factors (*e.g.*, exposure to air pollution and microbial dysbiosis) contribute to the development of asthma. Changes in environmental factors related to climate and lifestyle changes over time might affect the epidemiology of childhood asthma and control status of asthma. Therefore, to develop a comprehensive approach and establish appropriate management strategies for childhood asthma in line with changes in environmental factors over time, research on changes in the epidemiology and risk factors for childhood asthma is essential.

In the early to mid-1990s, global studies on childhood asthma prevalence showed that the prevalence of asthma during childhood varied depending on the study period and geographic region. Subsequent studies reported that childhood asthma prevalence showed an increasing or stationary trend over time with geographic variations, suggesting that changes in environmental factors can affect the development of asthma in children and its prevalence. In addition, the emergence of new respiratory infections can affect the epidemiology of allergic diseases, especially asthma. Children with asthma have an increased susceptibility to respiratory infections and therefore the emergence of new respiratory viruses and strategies to mitigate their spread, such as social distancing and school closure, can alter the epidemiology of respiratory allergic diseases. As social distancing and school closure, can alter the epidemiology of respiratory allergic diseases.

To provide insight into the changes of the epidemiology of childhood asthma, which are the key factors in the establishment of prevention and management strategies of childhood asthma, identification of trends in the epidemiology of asthma over time and their risk factors is essential. Therefore, in the present study, we investigated the prevalence of asthma in children aged 6–7 years and 12–13 years in 1995, 2000, 2010, and 2022 in the general population-based cohort in Korea. In addition, we identified the risk factors for asthma in children aged 6–7 years and those aged 12–13 years in 2022.

#### MATERIALS AND METHODS

#### **Study population**

This nationwide cross-sectional study enrolled 4,038 children aged 6–7 years and 4,269 children aged 12–13 years from 213 randomly selected elementary schools across the country using probability sampling methods in 2022. A survey on the epidemiology of allergic diseases was conducted using a modified International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire from September to November 2022. To increase the



response rate, the survey was conducted in person, by mail, or on an online platform. From September to November in 1995, 2000, and 2010, investigations using the ISAAC questionnaire were also conducted to determine the prevalence of asthma and its risk factors. This study was approved by the Institutional Review Board (IRB) of Inje University Seoul Paik Hospital (IRB approval number: PAIK 2022-01-006). Written informed consent was confirmed by the IRB and obtained from all parents before participation in this study.

# Sampling of participants

We applied sample weighting to ensure the representativeness of the population at the national level in Korea using a combination of stratification, clustering, and multi-stage sampling methods for the selection of participants in the present study. The stratification variables considered in the study included geographic regions based on cities, provinces, and counties. In a sample school, one class from each grade was selected as the sample class. All students in the selected classes participated in this survey.

#### Questionnaire

The questionnaire was completed by the parents or caregivers of the study participants. To investigate the prevalence of asthma, we used a modified ISAAC questionnaire, which included 3 items as follows: 1) general characteristics, including age, gender, height, weight, and residential area, 2) environmental factors related to allergic diseases, and 3) presence of allergic diseases including asthma, allergic rhinitis, and atopic dermatitis. Asthma prevalence was investigated with the following questionnaire: 1) "has your child ever had wheezing symptoms (wheeze ever)?", "has your child ever been diagnosed with asthma by doctors (asthma diagnosis ever)?", "has your child had wheezing in the preceding 12 months (wheeze in the last 12 months)?", and "has your child ever been treated for asthma in the preceding 12 months (asthma treatment in the last 12 months)?". 'Current asthma' was defined as the presence of wheezing in the preceding 12 months in children diagnosed with asthma ever. The questionnaire was completed by parents or guardian.

#### Statistical analysis

Trends in the prevalence of asthma outcomes during the study period were compared using a trend test. In addition, the prevalence of asthma in the participants was investigated according to gender. Logistic regression analysis was used to examine risk factors for 'asthma diagnosis ever' and 'wheeze ever' with adjustment for potential confounding factors, including gender, family history of allergic diseases, maternal education level, history of bronchiolitis, mode of birth delivery, antibiotic use during infancy, birth weight, and other allergic diseases (allergic rhinitis and atopic dermatitis). The SURVEYLOGISTIC procedure was applied for the logistic regression analysis and trend test. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA). A *P* value < 0.05 was considered to be significant.

#### **RESULTS**

#### Baseline characteristics of the study population

The baseline characteristics of the study population are presented in **Table 1**. The percentages of male and female participants were 50.4% and 49.6%, respectively, for children aged 6–7 years and 50.2% and 49.8%, respectively, for children aged 12–13 years in 2022. A parental history of allergic diseases was reported for 62.1% of children aged 6–7 years and 51.7% of



Table 1. Characteristics of the study population

Variables		022
	6-7 yr	12-13 yr
No. of subjects	4,038	4,269
Age (yr)	$6.95 \pm 0.07$	$13.34 \pm 0.14$
Male	2,037 (50.4)	2,143 (50.2)
BMI (kg/m²)	$16.41 \pm 0.05$	20.13 ± 0.07
Parental history of allergic diseases	2,506 (62.1)	2,205 (51.7)
Current exposure to environmental tobacco smoking	1,668 (40.7)	1,794 (42.3)
Maternal education level		
≤ High school	759 (18.8)	1,175 (27.5)
≥ University	3,078 (76.2)	2,829 (66.3)
No response	201 (5.0)	265 (6.2)
History of bronchiolitis (yes)	1,232 (30.5)	864 (20.2)
Gestational age (wk)		
≤ 36	523 (13.6)	561 (13.2)
37-42	3,434 (89.5)	3,584 (84.0)
≥ 43	80 (2.1)	124 (2.9)
Birth weight (kg)		
< 3.1	1,475 (36.6)	1,492 (34.9)
3.1 ≤ birth weight < 3.6	1,802 (44.7)	1,928 (45.2)
≥ 3.6	758 (18.7)	849 (19.9)
Breast milk feeding (mon)		
None	274 (6.8)	267 (6.3)
1-6	2,185 (54.1)	1,947 (45.6)
≥ 7	1,579 (39.1)	2,054 (48.1)
Delivery mode, vaginal delivery	2,332 (57.8)	2,667 (62.5)
Antibiotic use during infancy (yes)	1,539 (38.1)	1,242 (29.1)
Exposure to cats or dogs during pregnancy or in the first year (yes)	361 (8.9)	234 (5.5)
Allergic rhinitis diagnosis ever	1,832 (45.4)	1,390 (32.6)
Food allergy diagnosis ever	251 (6.2)	178 (4.2)
Atopic dermatitis diagnosis ever	535 (13.2)	734 (17.2)

Values are presented as mean ± standard deviation or number (%). BMI, body mass index.

children aged 12–13 years. The prevalence of 'allergic rhinitis ever' was 45.4% of children aged 6–7 years and 32.6% of children aged 12–13 years. The prevalence of 'food allergy ever' was 6.2% of children aged 6–7 years and 4.2% of children aged 12–13 years. In addition, the prevalence of 'atopic dermatitis ever' was 13.2% in children aged 6–7 years and 17.2% in children aged 12–13 years, respectively.

#### Prevalence of asthma in the 2022 survey

The prevalence of 'wheeze ever,' 'wheeze in the last 12 months,' 'asthma diagnosis ever,' 'asthma treatment in the last 12 months,' and 'current asthma' in the 2022 survey was 13.9%, 2.9%, 2.1%, 0.6% and 0.6%, respectively, among children aged 6–7 years (**Fig. 1A**). Among children aged 12–13 years, the prevalence of 'wheeze ever,' 'wheeze in the last 12 months,' 'asthma diagnosis ever,' 'asthma treatment in the last 12 months,' and 'current asthma' was in 2022 survey was 16.4%, 5.6%, 3.4%, 0.7% and 1.0%, respectively.

There were regional differences in asthma prevalence: the prevalence of 'wheeze in the last 12 months' in children aged 6–7 years was highest in the Sejong province and lowest in the Gyeongsangbuk-do (**Fig. 1B**), whereas that in children aged 12–13 years was highest in Sejong province and lowest in Busan (**Fig. 1C**).



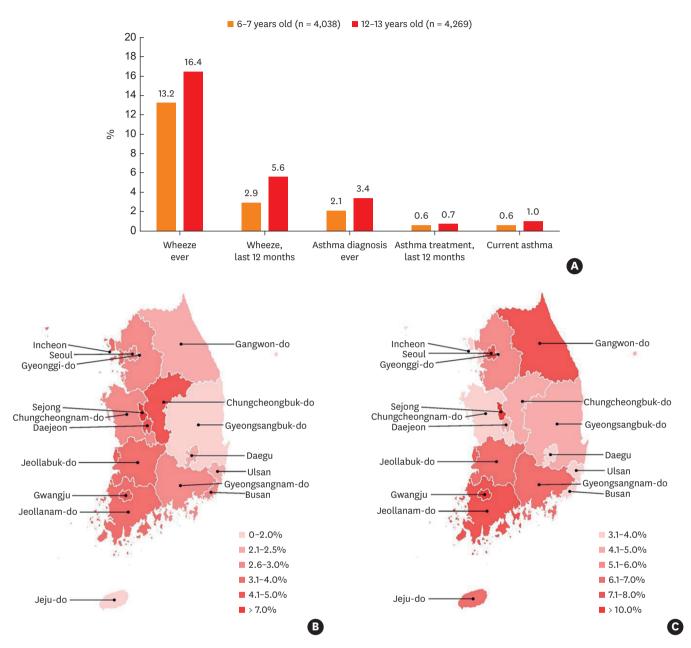


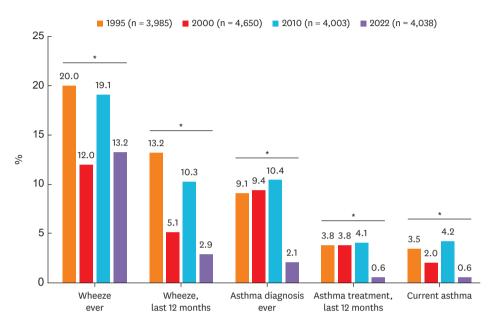
Fig. 1. Prevalence of asthma in 2022 (A) and choropleth map of the prevalence of 'wheeze in the last 12 months' in children aged 6–7 years (B) and 12–13 years (C) in 2022.

# Trends in the prevalence of asthma in children aged 6-7 years

The prevalence of 'asthma diagnosis ever' in children aged 6–7 years was 9.1% in 1995 with no significant change in 2000 (9.4%) and 2010 (10.4%), followed by a decrease in 2022 (2.1%, P < 0.001) (**Table 2, Fig. 2**). The prevalence of 'wheeze ever' showed fluctuations (20.0% in 1995, 12.0% in 2000, 19.1% in 2010, and 13.2% in 2022) with a significant decreasing trend (P for trend during the study period < 0.001). The prevalence of 'current asthma' in children aged 6–7 years showed fluctuations (3.5% in 1995, 2.0% in 2000, and 4.2% in 2010) with a significant decrease in 2022 (0.6%) (P for trend during the study period < 0.001).



The prevalence of 'wheeze ever,' 'wheeze in the last 12 months,' 'asthma diagnosis ever,' and 'current asthma' in children aged 6–7 years was significantly higher in males than in females in all years of study (**Table 2**).



**Fig. 2.** Temporal trend of the prevalence of asthma in children aged 6–7 years from 1995 to 2022. \*One asterisk indicates that trend P is < 0.001.

Table 2. Trajectories in the prevalence of asthma at 6-7 years of age according to sex

Variables		19	995			20	000			20	010			20	)22	
	М	F	Total	P value	М	F	Total	P value	М	F	Total	P value	М	F	Total	P value
Total	2,071	1,914	3,985		2,441	2,209	4,650		2,021	1,982	4,003		2,037	2,001	4,038	
Wheeze ever	443 (21.4)	354 (18.5)	797 (20.0)	0.035	321 (13,2)	238 (10.8)	559 (12.0)	0.009	444 (22.2)	314 (15.6)	758 (19.1)	< 0.001	326 (14.2)	273 (12.1)	599 (13.2)	0.046
Wheeze, last 12 mon	280 (13.5)	247 (12.9)	527 (13.2)	0.659	130 (5.3)	106 (4.8)	236 (5.1)	0.370	242 (12.4)	160 (8.0)	402 (10.3)	0.001	72 (3.4)	50 (2.3)	122 (2.9)	0.064
Asthma diagnosis ever	214 (10.3)	149 (7.8)	363 (9.1)	0.004	280 (11.5)	157 (7.1)	437 (9.4)	< 0.001	260 (12.8)	148 (7.9)	408 (10.4)	< 0.001	69 (2.9)	33 (1.2)	102 (2.1)	< 0.001
Asthma treatment, last 12 mon	82 (4.0)	68 (3.6)	150 (3.8)	0.475	105 (4.3)	73 (3.3)	178 (3.8)	0.075	104 (5.6)	50 (2.6)	154 (4.1)	< 0.001	19 (0.8)	10 (0.4)	29 (0.6)	0.886
Current asthma	76 (3.7)	64 (3.3)	140 (3.5)	0.565	59 (2.4)	34 (1.5)	93 (2.0)	0.029	106 (5.6)	50 (2.6)	156 (4.2)	0.001	20 (0.8)	10 (0.4)	30 (0.6)	0.078
Frequency of wheeze in the last 12 mon				0.628				0.366				0.198				0.131
1-3	116 (5.6)	89 (4.7)	205 (5.1)		94 (3.9)	89 (4.0)	183 (3.9)		167 (8.7)	119 (6.0)	286 (7.4)		57 (2.8)	44 (2.0)	101 (2.4)	
4-12	22 (1.1)	18 (0.9)	40 (1.0)		25 (1.0)	16 (0.7)	41 (0.9)		47 (2.4)	22 (1.2)	69 (1.8)		13 (0.5)	3 (0.2)	16 (0.4)	
≥ 13	19 (0.9)	10 (0.5)	29 (0.7)		15 (0.6)	9 (0.4)	24 (0.5)		13 (0.6)	5 (0.3)	18 (0.5)		2 (0.0)	3 (0.1)	5 (0.1)	
Sleep disturbance due to wheezing in the last 12 mon	189 (9.1)	172 (9.0)	361 (9.1)	0.766	77 (3.2)	64 (2.9)	141 (3.0)	0.470	NA	NA	NA	NA	22 (1.2)	13 (0.5)	35 (0.8)	0.026
Exercise-induced wheeze in the last 12 mon	93 (4.5)	78 (4.1)	171 (4.3)	0.512	99 (4.1)	79 (3.6)	178 (3.8)	0.394	73 (3.8)	42 (2.2)	115 (3.0)	0.013	16 (0.6)	15 (0.7)	31 (0.7)	0.712
Nocturnal dry cough	391 (18.9)	315 (16.5)	706 (17.7)	0.032	449 (18.4)	389 (17.6)	838 (18.0)	0.522	436 (20.9)	320 (16.7)	756 (18.9)	< 0.001	320 (16.2)	238 (11.5)	558 (13.9)	< 0.001

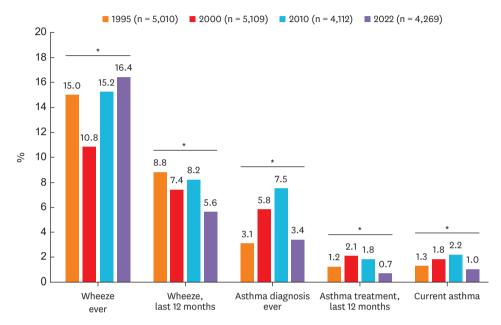
Values are presented as number (%).

M, male; F, female; NA, not applicable.



# Trends in the prevalence of asthma in children aged 12-13 years

The prevalence of 'asthma diagnosis ever' in children aged 12–13 years was 3.1% in 1995 with significant increases in 2000 (5.8%, P < 0.001) and 2010 (7.5%, P < 0.001), followed by a decrease in 2022 (3.4%, P < 0.001); however, the trend during the study period did not show statistical significance (**Table 3**, **Fig. 3**). The prevalence of 'wheeze ever' showed an increasing



**Fig. 3.** Temporal trend of the prevalence of asthma in children aged 12–13 years from 1995 to 2022. \*One asterisk indicates that trend P is < 0.001.

Table 3. Trajectories in the prevalence of asthma at 12–13 years of age according to sex

Variables		19	995			20	000			20	10			20	022	
	М	F	Total	P value	М	F	Total	P value	М	F	Total	P value	М	F	Total	P value
Total	2,712	2,298	5,010		2,820	2,289	5,109		2,029	2,083	4,112		2,143	2,126	4,269	
Wheeze ever	419 (15.5)	332 (14.5)	751 (15.0)	0.329	299 (10.6)	251 (11.0)	550 (10.8)	0.986	325 (16.3)	309 (14.0)	634 (15.2)	0.059	396 (18.2)	347 (14.5)	743 (16.4)	0.033
Wheeze, last 12 mon	234 (8.6)	209 (9.1)	443 (8.8)	0.578	206 (7.3)	173 (7.6)	379 (7.4)	0.981	175 (8.7)	170 (7.6)	345 (8.2)	0.175	118 (5.6)	121 (5.7)	239 (5.6)	0.866
Asthma diagnosis ever	92 (3.4)	64 (2.8)	156 (3.1)	0.206	186 (6.6)	109 (4.8)	295 (5.8)	0.003	193 (10.0)	108 (4.8)	301 (7.5)	< 0.0001	91 (4.6)	46 (2.1)	137 (3.4)	< 0.0001
Asthma treatment, last 12 mon	37 (1.4)	25 (1.1)	62 (1.2)	0.373	68 (2.4)	37 (1.6)	105 (2.1)	0.040	43 (2.4)	26 (1.1)	69 (1.8)	0.029	20 (1.0)	9 (0.4)	29 (0.7)	0.818
Current asthma	34 (1.3)	30 (1.3)	64 (1.3)	0.872	56 (2.0)	37 (1.6)	93 (1.8)	0.325	65 (3.2)	29 (1.1)	94 (2.2)	< 0.0001	24 (1.2)	17 (0.8)	41 (1.0)	0.305
Frequency of wheeze in the last 12 mon				0.393				0.248				0.111				0.130
1-3	171 (6.3)	151 (6.6)	322 (6.4)		126 (4.5)	116 (5.1)	242 (4.7)		100 (5.0)	112 (5.0)	212 (5.0)		80 (3.8)	78 (3.4)	158 (3.6)	
4-12	40 (1.5)	34 (1.5)	74 (1.5)		50 (1.8)	46 (2.0)	96 (1.9)		44 (2.3)	34 (1.5)	78 (1.9)		24 (1.0)	31 (1.8)	55 (1.4)	
≥ 13	8 (0.3)	13 (0.6)	21 (0.4)		24 (0.9)	12 (0.5)	36 (0.7)		25 (1.1)	12 (0.5)	37 (0.8)		14 (0.7)	11 (0.5)	25 (0.6)	
Sleep disturbance due to wheeze in the last 12 mon	190 (7.0)	163 (7.1)	353 (7.1)	0.994	157 (5.6)	112 (4.9)	269 (5.3)	0.178					18 (0.9)	28 (1.0)	46 (0.9)	0.957
Exercise-induced wheeze in the last 12 mon	376 (13.9)	358 (15.6)	734 (14.7)	0.090	365 (12.9)	353 (15.4)	718 (14.1)	0.017	149 (7.5)	162 (7.0)	311 (7.3)	0.610	119 (6.6)	154 (7.2)	273 (6.9)	0.431
Nocturnal dry cough	220 (8.1)	274 (11.9)	494 (9.9)	< 0.0001	273 (9.7)	362 (15.8)	635 (12.4)	< 0.0001	239 (12.0)	286 (14.4)	525 (13.2)	0.016	225 (11.6)	350 (16.3)	575 (13.9)	< 0.0001

Values are presented as number (%).

M, male; F, female.



trend (15.0% in 1995, 10.8% in 2000, 15.2% in 2010, and 16.4% in 2022) during the study period (P < 0.001). The prevalence of 'current asthma' in children aged 12–13 years showed an increasing trend from 1995 to 2010 (1.3% in 1995, 1.8% in 2000, and 2.2% in 2010) with a decrease in 2022 (1.0%); however, the trend was not statistically significant during the study period. The prevalence of 'wheeze ever' in 2000 and 'wheeze in the last 12 months' in 1995, 2000, and 2022 was higher in females than in males among children aged 12–13 years; however, the result was not statistically significant.

#### Risk factors for 'asthma diagnosis ever' in children

Male sex, a history of bronchiolitis in early life, an allergic rhinitis diagnosis ever, and an atopic dermatitis diagnosis ever were significantly associated with an increased risk of 'asthma diagnosis ever' in children aged 6–7 years (**Table 4**). The risk of 'asthma diagnosis ever' was higher with an odds ratio of 23.55 (95% confidence interval, 9.11–60.85) in children with a history of bronchiolitis in early life and an allergic rhinitis diagnosis ever compared to children without a history of bronchiolitis in early life and an allergic rhinitis diagnosis ever as the reference group. There was no difference in the risk factors for 'asthma diagnosis ever' between males and females among children aged 6–7 years.

Among children aged 12–13 years, male sex and a history of bronchiolitis in early life were independently associated with an increased risk of 'asthma diagnosis ever.' A history of bronchiolitis in early life and an allergic rhinitis diagnosis ever did not show a significant interaction effect with 'asthma diagnosis ever' in children aged 12–13 years.

#### Risk factors for 'wheeze ever' in children

A high level of maternal education, a history of bronchiolitis in early life, an allergic rhinitis diagnosis ever, and an atopic dermatitis diagnosis ever were significantly associated with an increased risk of 'wheeze ever' in children aged 6–7 years (**Supplementary Table S1**). A combination of a history of bronchiolitis in early life and an allergic rhinitis diagnosis ever increased the risk of 'wheeze ever' in children aged 6–7 years compared with those without the two factors. There was no difference in the risk factors for 'wheeze ever' in children aged 6–7 years between males and females, except for maternal educational level.

Among children aged 12–13 years, a history of bronchiolitis was commonly associated with 'wheeze ever' in both males and females. Exposure to antibiotics in infancy was associated with an increased risk of 'wheeze ever' in males, whereas vaginal delivery was associated with a decreased risk of 'wheeze ever' in females.

# **DISCUSSION**

In the present study, we examined trends in the asthma prevalence of children aged 6–7 years and 12–13 years from 1995 to 2022, with the identification of risk factors for 'asthma diagnosis ever.' In children aged 6–7 years, the prevalence of asthma showed no changes or fluctuations from 1995 to 2010 with a decrease in 2022; however, the prevalence of asthma showed an increasing pattern from 1995 to 2010 with a decrease in 2022 in children aged 12–13 years. Male sex and a history of bronchiolitis in early life were independent risk factors of asthma for both children aged 6–7 years and those aged 12–13 years. Children with a history of bronchiolitis in early life had an increased risk of asthma if they were ever diagnosed with allergic rhinitis in the age group of 6–7 years. When the participants were classified according



 Table 4. Risk factors for asthma diagnosis ever in children aged 6-7 years and 12-13 years in 2022

Variables	)		6-7 vr of age	200					19-13 vr of age	of ago		
	Male		Female	0	Total		Male		Female	- O	Total	
	aOR (95% CI)	<i>P</i> value	aOR (95% CI)	<i>P</i> value	aOR (95% CI)	P value	aOR (95% CI)	P value	aOR (95% CI)	P value	aOR (95% CI)	<i>P</i> value
Model 1: Individual effects on asthma diagnosis ever	,		,						,		,	
Sex (male)					1.98	900.0					1.76	0.006
	0		L C		(2.5. 3.1.)		6	0	0		(20.5)	
Parental history of allergic diseases	0.67 (0.34–1.29)	0.228	(0.74-8.85)	0.136	0.86 $(0.48-1.54)$	0.612	1.28 (0.64–2.55)	0.482	1.26 (0.49–3.23)	0.638	L.29 (0.81–2.05)	0.289
Maternal education level												
≤ High school	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
≥ University	2.70	0.066	0.88	0.804	1.80	0.112	1.16	0.661	0.76	0.565	0.99	0.987
	(0.94-7.75)		(0.32-2.42)		(0.87 - 3.73)		(0.61-2.20)		(0.30-1.93)		(0.52-1.90)	
History of bronchiolitis	4.51 (2.57-7.92)	< 0.0001	5.09 (2.39–10.83)	< 0.0001	4.61 (2.89-7.36)	< 0.0001	3.67 (2.30–5.86)	< 0.0001	2.72 (1.31–5.63)	0.007	3.34 (2.22–5.04)	< 0.0001
Delivery mode												
Cesarean section	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
Vaginal delivery	0.72	0.208	1.26	0.556	0.83	0.364	1.06	0.852	0.71	0.353	0.91	0.704
	(0.43 - 1.20)		(0.58 - 2.75)		(0.55 - 1.25)		(0.56 - 2.03)		(0.34-T.47)		(0.54 - 1.51)	
Antibiotic use during infancy	1.24 (0.73–2.12)	0.426	1.44 (0.66–3.14)	0.354	1.34 (0.87-2.07)	0.191	1.56 (0.89-2.72)	0.118	1.89 (0.90-3.93)	0.091	1.68 $(1.11-2.55)$	0.015
Birth weight (kg)												
3.1 ≤ birth weight < 3.6	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
< 3.1	1.26	0.472	1.16	0.717	1.26	0.373	1.19	0.614	1.31	0.433	1.20	0.517
	(0.67 - 2.35)		(0.51-2.65)		(0.76-2.12)		(0.60-2.36)		(0.67-2.58)		(0.69-2.10)	
≥ 3.6	1.29	0.510	0.61	0.481	1.12	0.734	1.58	0.189	0.78	0.665	1.36	0.299
	(0.60-2.77)		(0.15-2.44)		(0.58 - 2.19)		(0.80 - 3.13)		(0.26 - 2.38)		(0.76 - 2.40)	
Exposure to pets during pregnancy or in the first	1.02	0.963	0.448	0.303	0.83	0.618	0.33	0.138	1.87	0.227	0.89	0.796
year	(0.43-2.42)		(0.03/-2.07)		(0.41-1.70)		(0.00-1.43)		(0.60-3.10)	0	(0.33-2.23)	1
AK diagnosis ever	3.40 (1.41-8.22)	0.007	5.68 (2.09-15.43)	0.001	3.97 $(1.97-8.01)$	0.000	1.45 (0.69-3.03)	0.328	0.57	0.207	L.13 (0.59–2.15)	0.713
Atopic dermatitis diagnosis ever	2.54 (1.32-4.87)	0.005	2.38 (1.00-5.66)	0.050	2.47 (1.46-4.18)	0.001	1.09 (0.52-2.30)	0.825	3.78 (1.73-8.25)	0.001	1.68 (0.90-3.12)	0.102
Model 2: Combined effects of history of bronchiolitis and allergic rhinitis diagnosis ever												
History of bronchiolitis (-) & AR diagnosis ever (-)	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
History of bronchiolitis (-) & AR diagnosis ever (+)	6.28	0.006	3.80	0.150	5.70	0.005	1.57	0.31	0.34	0.065	0.97	0.928
	(1.70-23.20)		(0.62-23.40)		(1.95-16.63)		(0.66 - 3.78)		(0.11-1.07)		(0.47-1.99)	
History of bronchiolitis (+) & AR diagnosis ever (-)	9.24 (2.50–34.18)	0.001	2.84 (0.36–22.59)	0.323	7.14 (2.38–21.48)	0.001	3.98 (2.06-7.71)	< 0.0001	1.92 (0.68–5.44)	0.219	2.92 (1.66–5.13)	< 0.0001
History of bronchiolitis (+) & AR diagnosis ever (+)	23.59	< 0.0001	21.75	< 0.0001	23.55	< 0.0001	5.38	< 0.0001	1.87	0.310	3.79	0.005
	(7.01-79.39)		(4.50-105.17)		(9.11-60.85)		(2.11-13.73)		(0.56-6.25)		(1.64-8.74)	

Values in bold indicate statistical significance. aOR, adjusted odds ratio; CI, confidence interval; AR, allergic rhinitis.



to gender, similar patterns were observed in terms of the prevalence of asthma and risk factors. The results of the present study provide fundamental information for management and prevention strategies for asthma in children.

Studies on the epidemiology of asthma in children have shown inconclusive results. Some studies reported an increasing trend in asthma prevalence, <sup>10,11</sup> whereas, other studies showed a constant or decreasing trend. <sup>12</sup> The inconclusive results on the epidemiology of asthma might be attributed to differences in the study population, geographic region, investigation methods, and definition of asthma as well as environmental changes over time that can affect the development of asthma. <sup>7, 13,14</sup> In the cross-sectional Global Asthma Network (GAN) Phase I study conducted from 2015 to 2020 using the ISAAC questionnaire, the worldwide prevalence of asthma in children aged 6–7 years and 13–14 years was 7.6% and 10.5%, respectively. <sup>15</sup> In comparison with the results of the GAN Phase I study over the same period, <sup>15</sup> the prevalence of 'asthma diagnosis ever' was slightly higher in children aged 6–7 years (10.4% in 2010) and 12–13 years (7.5% in 2010) in the present study.

In our present study, trends in the prevalence of asthma differed according to age. The prevalence of 'asthma diagnosis ever' in children aged 6–7 years remained constant from 1995 to 2010 with a decrease in 2022, which was during the coronavirus disease 2019 (COVID-19) pandemic; however, it was increased from 1995 to 2010 with a significant decrease in 2022, in children aged 12–13 years. Differences in the patterns of asthma prevalence between the two groups might be explained by the difficulties in differentiating between virus-induced wheezing in early life and asthma during preschool ages due to a lack of cooperation and the unavailability of pulmonary function data. <sup>16,17</sup> The significant decrease in the prevalence of 'wheeze in the last 12 months,' 'asthma treatment in the last 12 months,' and 'current asthma' in 2022 in both groups might be attributed to social distancing, school closure, and facial mask wearing for the prevention of COVID-19.<sup>7</sup> This finding suggests that the epidemiology of asthma may be affected by the emergence of unexpected respiratory viral epidemics along with the implementation of health and social strategies for epidemic prevention.

When the prevalence of asthma was classified according to gender, the prevalence of 'wheeze ever,' 'wheeze in the last 12 months,' 'asthma diagnosis ever,' and 'asthma treatment in the last 12 months' in children aged 6–7 years was higher in males than in females. Among young children, the higher prevalence of asthma in males might be explained by a smaller airway diameter relative to lung volume.¹8 Some studies indicated that males may have higher allergen sensitization; however, this finding is limited to certain cases.¹9,20 Among children aged 12–13 years, the prevalence of 'wheeze ever' in 2020 and 'wheeze in the last 12 months' in 1995, 2000, and 2022 seemed higher in females than in males; however, the results were not statistically significant. The shift in the female predominance in asthma prevalence among older children might be attributed to hormonal changes, gender differences in environmental exposure, and more cases of undiagnosed wheezing in females, especially among adolescents.¹8,21</sup> Awareness of gender differences in the epidemiology of childhood asthma according to age is necessary to establish age-specific management and prevention strategies for childhood asthma.

Male sex and a bronchiolitis history in early life were risk factors for 'asthma diagnosis ever' in children aged 6–7 years and 12–13 years. Although there are some debates, <sup>22</sup> higher rates of asthma and wheeze have been observed in males than in females. <sup>18</sup> A history of bronchiolitis



in early life is known as a risk factor for asthma.<sup>23</sup> However, the association of bronchiolitis with asthma may be dependent on the heterogeneity of bronchiolitis.<sup>2,24</sup> In our study, bronchiolitis history in early life was investigated using a questionnaire; thus, we could not determine the phenotypic association of bronchiolitis with later development of asthma in children. Although it is well known that allergic comorbidities, such as atopic dermatitis and allergic rhinitis, are associated with an increased risk of asthma,<sup>25</sup> these associations were observed only in children aged 6–7 years in the present study. However, the association of asthma with other allergic diseases was not identified in children aged 12–13 years. Allergic diseases were investigated using a questionnaire; thus, remote memory bias might have partially influenced the results.

As the interactions of various factors can affect the development of asthma,<sup>2</sup> we investigated the combined effects of independent risk factors on childhood asthma. We observed increased associations with 'asthma diagnosis ever' in children aged 6–7 years with a history of bronchiolitis in early life and an allergic rhinitis, which were not observed in children aged 12–13 years. These findings suggest that allergic rhinitis, as a respiratory allergic disease, may be a predictive factor for the development of asthma in children if they had a history of bronchiolitis in early life, as indicated by the original asthma predictive index.<sup>26,27</sup> The lack of a significant combined effect of a history of bronchiolitis in early life and 'allergic rhinitis ever' on the 'asthma diagnosis ever' in children aged 12–13 years may be related to changes of the epidemiology of childhood allergic diseases during the COVID-19 pandemic or other factors.

Some limitations should be noted. We investigated the prevalence of allergic diseases using a questionnaire instead of physical examination or one-on-one detailed medical history taking. Therefore, there might be discrepancies between the actual prevalence and results of the present study. This study adopted a cross-sectional design; thus, the identified risk factors for asthma do not determine the cause-and-effect relationship. Nevertheless, by applying probability sampling methods, we could obtain nationwide representative data on the epidemiology of asthma in children.

In conclusion, we observed the trends in asthma prevalence in children aged 6–7 years and 12–13 years from 1995 to 2022, who were classified according to gender. The trends differed depending on the age group and definition of asthma. In both age groups, the prevalence of asthma was decreased in 2022, which might be attributed to health and social strategies for preventing COVID-19. The results of the present study provide fundamental information for the establishment of management and prevention strategies for childhood asthma.

#### **ACKNOWLEDGMENTS**

This research was supported by the Research Program funded by the Korea Centers for Disease Control and Prevention (2021-11-034).

#### SUPPLEMENTARY MATERIAL

#### **Supplementary Table S1**

Risk factors of wheeze ever in children aged 6-7 years and 12-13 years in 2022



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