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Association between early childhood infections and adolescent chronic diseases: a nationwide cohort analysis

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Abstract

Background Early childhood infections remain major contributors to the global disease burden in children under five years of age. Beyond their acute effects, such infections may influence susceptibility to non-communicable diseases later in life. It was hypothesized that common early childhood infections are associated with an increased risk of chronic diseases during adolescence.

Methods A 18-year, nationwide, population-based cohort study was conducted using the Korean National Health Information Database (2002–2019), including 3,942,947 children aged 0–4 years (2002-2006) at baseline who were followed until ages 13–17 years (2016-2019). Cox proportional hazards models were used to estimate associations between early childhood infections and subsequent adolescent chronic diseases, adjusting for age and gender.

Results Acute upper respiratory tract infections (URTI) at multiple sites (9.7%) and acute nasopharyngitis (9.2%) were the most prevalent infections in early childhood. In adolescence, allergic rhinitis (2.6%) and chronic sinusitis (0.9%) were most frequent. Early-life acute URTI at multiple sites was modestly associated with adolescent allergic rhinitis (HR: 1.03, 95% CI: 1.00–1.06), while acute laryngitis and tracheitis was associated with chronic bronchitis (HR: 1.09, 95% CI: 1.00–1.20) and acute enteritis was associated with chronic noninfective gastroenteritis and colitis (HR: 1.21, 95% CI: 1.06–1.40). Stratified analyses demonstrated slightly stronger associations among boys for allergic rhinitis and urticaria and among girls for chronic noninfective gastroenteritis and colitis.

Conclusion In this nationwide cohort, early childhood respiratory and gastrointestinal infections were consistently associated with chronic conditions such as allergic rhinitis, bronchitis, and gastroenteritis and colitis in adolescents. These findings suggest potential early-life origins of chronic disease and highlight the need for targeted prevention strategies to reduce the long-term burden of chronic illnesses in children.

Keywords Adolescent, Children, Chronic diseases, Disease transition, Early-life infections

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Introduction

Infectious diseases in early childhood remain among the top five causes of childhood morbidity worldwide, including in South Korea [1]. Despite advances in medical care and public health, the incidence of infectious diseases in children under five continues to rise due to increased global mobility, the resurgence of vaccine-preventable diseases such as measles, and the emergence of novel pathogens [2]. Although global under-five mortality has declined, current projections indicate that more than 48 million deaths among children under five will occur between 2020 and 2030 [3]. Findings from the 2023 Global Burden of Disease (GBD) study demonstrate a decline in neonatal disorders and respiratory infections; however, these conditions remain among the leading causes of childhood morbidity globally [4]. National Disease Surveillance Data from the Korea Disease Control and Prevention Agency (KDCA) also show increasing rates of respiratory, enteric, and skin infections among children under five years of age [5, 6]. Infectious diseases during infancy and early childhood are common and have the potential for long-term health consequences throughout the life course.

Chronic diseases account for one in five deaths among adolescents and more than half of the disability-adjusted life years in this age group globally [7]. In South Korea, the prevalence of chronic conditions such as asthma, allergic rhinitis, and atopic dermatitis has steadily increased among adolescents [8]. The World Health Organization emphasizes that chronic diseases in adolescence not only impair immediate health but also set the stage for morbidity and mortality in adulthood. While lifestyle-related factors such as diet, physical inactivity, and substance use are well-recognized contributors, growing evidence suggests that early-life biological exposures, including infectious diseases, are important determinants of chronic disease risk [9].

Biologically, early-life infections can disrupt immune maturation, alter microbiome development, and modulate inflammatory regulatory pathways, potentially increasing susceptibility to noncommunicable diseases later in life [10]. Disruptions of immune homeostasis during critical developmental windows may lead to immune imprinting and persistent low-grade inflammation, promoting aberrant tissue repair and metabolic dysregulation. Frequent viral infections in childhood have been linked to asthma development through chronic airway inflammation and immune remodeling [11, 12], and acute pyelonephritis in children can cause renal scarring that predisposes to secondary hypertension and chronic kidney disease [13]. Recurrent viral or bacterial gastrointestinal infections may cause long-term gut microbiome dysbiosis, leading to chronic gastrointestinal symptoms or functional bowel disorders during adolescence [14, 15]. Collectively, these biological pathways suggest that early infectious exposures may reprogram immune and metabolic systems, forming the foundation for chronic disease susceptibility in later life.

However, research evaluating the relationship between infectious diseases in early childhood and chronic disease development in adolescence remains limited, largely due to the lack of large-scale, longitudinal cohorts that initiate follow-up during early life. Children represent a particularly vulnerable population because of their immature immune systems and high exposure to environmental infectious risk factors, yet the long-term health effects of early infections remain underexplored.

Therefore, the objective of this study was to identify the most prevalent infectious diseases in early childhood and chronic diseases in adolescence and to assess the association between early-life infections and subsequent chronic disease risk using a nationwide, population-based cohort from South Korea.

Methods

Study population

This nationwide population-based cohort study utilized data from the Korean National Health Information Database (NHID), which is maintained by the Korean National Health Insurance Service (NHIS) and covers approximately 98% of the South Korean population. As a universal health coverage system, the NHIS provides comprehensive public data on healthcare utilization. The NHID includes detailed information on demographics, healthcare use, diagnostic records, health screenings, and mortality, based on pseudonymized insurance claims collected through the national health insurance system [16]. The cohort was constructed using demographic characteristics, diagnosis codes, and healthcare institution records. Children aged 0–4 years from 2002 to 2006 with at least one recorded infectious disease diagnosis were eligible for inclusion. Individuals with pre-existing chronic diseases or missing demographic or diagnostic data were excluded. After applying all exclusion criteria, the baseline cohort consisted of 4,701,467 children aged 0–4 years, of whom 3,942,947 were successfully followed until ages 13–17 years between 2016 and 2019 (Fig. 1).

This study was approved by the Institutional Review Board of Ewha Womans University Seoul Hospital (SEUMC2024-01-034). Approval to access the NHID was granted by the NHIS (NHIS-2024-10-1-029), and data access was restricted to authorized users. Informed consent was not required because all data were anonymized and de-identified by the NHIS prior to analysis.

Early childhood infectious disease definition

Early childhood infections were defined as conditions with sudden onset and short duration, typically lasting

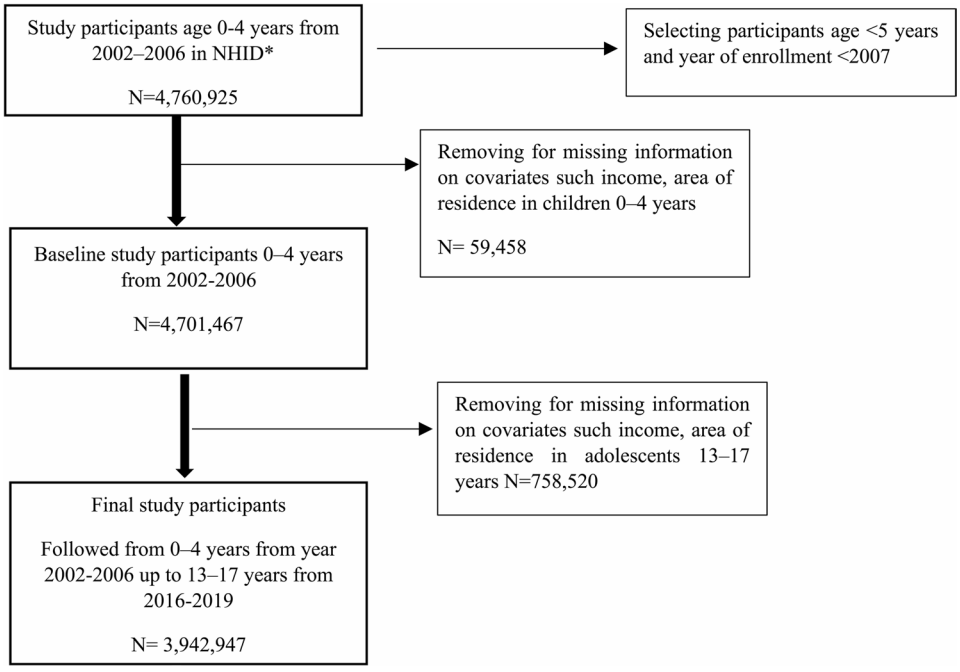


Fig. 1 Selection of study participants aged 0 to 4 years from 2002 to 2006
*NHID: National Health Information Database

days to weeks. The analysis focused on children aged 0–4 years, a critical period characterized by heightened susceptibility to infections and rapid immune system development [17]. Infections were classified based on the first recorded diagnosis within this age range. To ensure standardization and clinical relevance, acute infections were grouped into six categories: respiratory, ear, gastrointestinal, cardiac, renal, and viral. In total, 132 acute diseases and syndromes were identified using International Classification of Diseases, 10th revision (ICD-10) codes (Supplementary Table 1). These classifications reflect organ system involvement and allow reproducible identification of infectious disease diagnoses in the NHID.

Chronic diseases definition

Chronic diseases were defined as conditions lasting longer than 3 months and requiring ongoing medical management. Chronic adolescent disease outcomes were classified based on the first diagnosis between ages 13 and 17 years. Ten categories of chronic conditions were identified, including allergic, pulmonary, ear, gastrointestinal, renal, endocrine, metabolic, cardiovascular, neurological, and neoplastic diseases. A total of 105 chronic diseases were captured using ICD-10 diagnostic codes (Supplementary Table 2).

Covariates

Covariates were selected based on variable availability in the database and previous literature [18]. Gender, area of residence, income level, age, and season of infection were included as covariates. Area of residence at birth was classified as cities or provinces. Income level was determined using insurance premium percentiles and categorized into four groups: 16–20th percentile (highest), 11–15th percentile (upper middle), 6–10th percentile (lower middle), and 0–5th percentile (lowest). Higher insurance premiums reflect higher income levels. Age was calculated as the difference between the birth year and the year of enrollment in the NHID. Season of infection was based on the month of acute infection diagnosis among children aged 0–4 years. Potential confounders such as vaccination status, parental education, preterm birth, birth weight, and other perinatal or environmental factors were not available in the NHID, which may have contributed to residual confounding.

Statistical analysis

Descriptive statistics were generated using the t test for continuous variables and the chi square test for categorical variables. The period prevalence of early-life infections (age 0–4 years) from 2002 to 2006 was calculated using the number of children diagnosed with infectious diseases as the numerator and the number of children assessed as the denominator. The prevalence of chronic diseases in adolescence from 2016 to 2019 was calculated similarly, using the number of adolescents diagnosed with chronic diseases as the numerator and the number assessed as the denominator. The most prevalent infectious diseases and chronic conditions were identified using these estimates.

Time-to-event for chronic disease development was measured, and participants without chronic disease diagnoses during follow-up were treated as censored cases. Cox proportional hazards regression models were applied to estimate hazard ratios (HR) and 95% confidence intervals (CI) for the association between early childhood infectious diseases (age 0–4 years) and subsequent chronic disease outcomes in adolescence (age 13–17 years). All models were adjusted for age, gender, income level, area of residence, and season of infection. The proportional hazards assumption was evaluated using Schoenfeld residuals and log minus log survival plots, with no significant violations observed. Sensitivity analyses were conducted by excluding participants with early indicators of chronic disease at baseline and by modifying the follow-up period to assess the robustness of the findings. Stratified analyses were performed by gender, income level, area of residence, and treatment department to further explore variations in association patterns.

All analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) and R version 4.3.1 (R Core Team): package "*survival*" and *"survminer"*. Statistical significance was defined as a two sided p value < 0.05.

Results

At baseline, the mean ± standard deviation (SD) age of children under five years was 1.0 ± 1.14 years, and the mean age at the end of follow-up (13–17 years) was 14.4 ± 1.53 years. Approximately 48% of participants were girls. A total of 51% resided in cities, and 67% were within the middle-income category (Table 1).

The most prevalent early childhood infection was acute upper respiratory tract infection (URTI) at multiple sites, a syndrome (9.74%), followed by acute nasopharyngitis (9.24%) and acute bronchitis (9.20%) (Table 2). During adolescence, allergic rhinitis was the most common diagnosis (2.58%), followed by chronic sinusitis (0.89%) and chronic conjunctivitis (0.88%). Differences in infection prevalence by gender are presented in Fig. 2, showing generally higher acute infection rates among boys, although these differences were not statistically significant. Supplementary Tables 1–6 provide definitions, prevalence, and incidence rates of early childhood infectious diseases and chronic adolescent conditions according to ICD-10 codes.

Cox proportional hazards analyses demonstrated that several early childhood infections were modestly but significantly associated with subsequent chronic diseases in adolescence (Table 3). Acute URTI at multiple sites was associated with an increased risk of allergic rhinitis (HR: 1.03, 95% CI: 1.00–1.06), and acute nasopharyngitis was associated with chronic rhinits nasopharyngitis and pharyngitis (HR: 1.07, 95% CI: 1.00–1.14). Acute bronchitis increased the risk of noninfective gastroenteritis and colitis (HR: 1.05, 95% CI: 1.01–1.09), and acute bronchiolitis and laryngitis and tracheitis increased the risk of chronic bronchitis (HR: 1.06, 95% CI: 1.00–1.13 and HR: 1.09, 95% CI: 1.00–1.20, respectively). Acute enteritis showed the strongest association, particularly with noninfective gastroenteritis and colitis (HR: 1.21, 95% CI: 1.06–1.40). Although the effect sizes were modest, the consistent associations across multiple outcomes support potential long-term immune or inflammatory pathways that may have clinical relevance at the population level.

Table 1 General characteristics of the study participants among children (0–4 years) and adolescents (13–17 years) in the NHID cohort

	All **Mean ± SD / %** ***N* = 3,942,947**	**Boys** **Mean ± SD / %** ***N* = 2,053,817**	**Girls** **Mean ± SD / %** ***N* = 1,889,130**	***p*-value[#]**
Age at baseline (years)[a]	1.0 ± 1.14	1.1 ± 1.10	1.0 ± 1.12	0.092
Age at endpoint (years)[b]	14.4 ± 1.53	14.5 ± 1.50	14.4 ± 1.55	0.585
Area of residence				
Cities[c]	50.88	26.47	24.41	< 0.001
Provinces[d]	49.12	25.62	23.50	
Income category [r]				
1 (Lowest)	10.46	5.42	5.04	< 0.001
2 (Lower Middle)	28.46	14.74	13.71	
3 (Upper Middle)	38.51	20.06	18.45	
4 (Highest)	22.57	11.86	22.35	

Abbreviations: *NHID* National Health Information Database, *SD* Standard deviation

Notes: [#]*p*-value by t-test and chi-square test; [r]Income category shows quartiles according to the Korean annual income percentiles with 1 being lowest and 4 highest

[a]Baseline participants: Children age 0-4 years in year 2002 to 2006

[b]Endpoint participants: Adolescents age 13-17 years in year 2016 to 2019

[c]Cities include: Seoul, Busan, Daegu, Incheon, Gyeongju, Daejon, and Ulsan

[d]Provinces include: Gyeongi-do, Gangwan-do, Chungcheongbuk-do, Chungcheongnam-do, Jeollabuk-do, Jeollanam-do, Gyeongsangbuk-do, Gyeongsangnam-do, and Jeju-do

Table 2 Top 10 prevalent acute infections in children (0–4 years) and chronic diseases in adolescents (13–17 years) in the NHID cohort

Sr. No. ⌜	Acute infections in children (0–4 years)	*N* (%)	Chronic diseases in adolescents (13–17 years)	*N* (%)
1	Acute upper respiratory tract infections at multiple sites		Allergic rhinitis	
	0	3,558,732 (90.26)	0	3,841,218 (97.42)
	≥ 1	384,215 (9.74)	≥ 1	101,729 (2.58)
2	Acute nasopharyngitis		Chronic sinusitis	
	0	3,578,432 (90.76)	0	3,907,684 (99.11)
	≥ 1	364,515 (9.24)	≥ 1	35,263 (0.89)
3	Acute bronchitis		Chronic conjunctivitis	
	0	3,580,272 (90.80)	0	3,908,446 (99.12)
	≥ 1	362,675 (9.20)	≥ 1	34,501 (0.88)
4	Acute pharyngitis		Chronic bronchitis	
	0	3,737,554 (94.79)	0	3,910,170 (99.17)
	≥ 1	205,393 (5.21)	≥ 1	32,777 (0.83)
5	Acute bronchiolitis		Atopic dermatitis	
	0	3,774,712 (95.73)	0	3,915,481 (99.3)
	≥ 1	168,235 (4.27)	≥ 1	27,466 (0.70)
6	Acute tonsillitis		Noninfective gastroenteritis and colitis	
	0	3,781,652 (95.91)	0	3,917,867 (99.36)
	≥ 1	161,295 (4.09)	≥ 1	25,080 (0.64)
7	Gastroenteritis and colitis infections		Chronic gastritis	
	0	3,819,905 (96.88)	0	3,918,642 (99.38)
	≥ 1	123,042 (3.12)	≥ 1	24,305 (0.62)
8	Acute laryngitis and tracheitis		Urticaria	
	0	3,879,460 (98.39)	0	3,921,977 (99.47)
	≥ 1	63,487 (1.61)	≥ 1	20,970 (0.53)
9	Acute pneumonia		Chronic rhinitis nasopharyngitis and pharyngitis	
	0	3,902,047 (98.96)	0	3,926,365 (99.58)
	≥ 1	40,900 (1.04)	≥ 1	16,582 (0.42)
10	Acute enteritis		Irritable bowel syndrome	
	0	3,907,434 (99.10)	0	3,929,965 (99.67)
	≥ 1	35,513 (0.90)	≥ 1	12,982 (0.33)

Abbreviation: *NHID* National Health Information Database

Note: ⌜ Sr.No.: represent the top 10 prevalent diseases in the NHID cohort

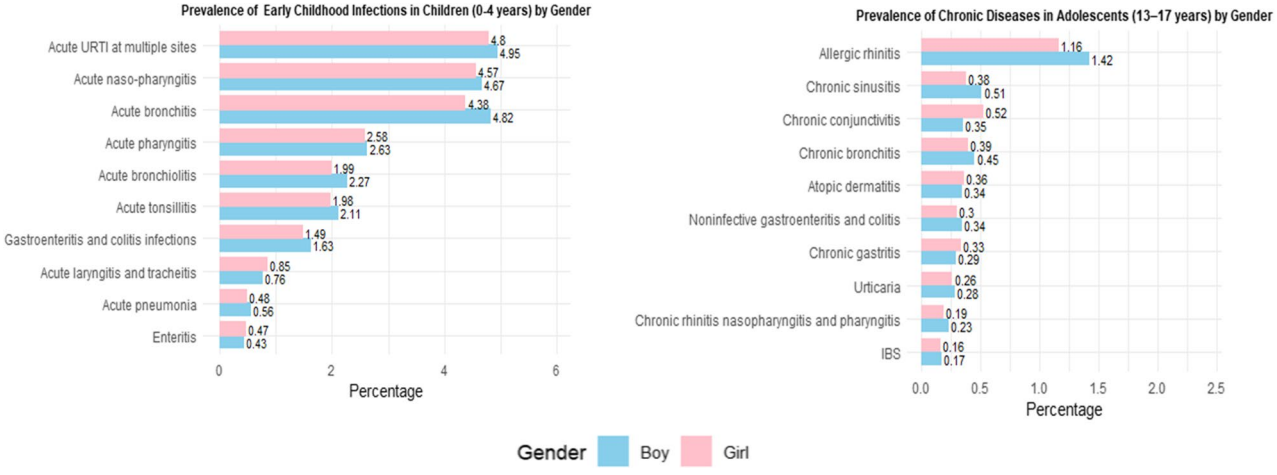


Fig. 2 Prevalence of early childhood infectious diseases in children (0–4 years) and chronic diseases in adolescents (13–17 years) by gender
URTI: Upper Respiratory Tract Infection; IBS: Irritable Bowel Syndrome

Table 3 Cox regression analysis for infectious diseases in early childhood affecting chronic diseases in adolescence

Chronic diseases ➡	Allergic rhinitis (*N* = 101,729)	Chronic sinusitis (*N* = 35,263)	Chronic conjunctivitis (*N* = 34,501)	Chronic bronchitis (*N* = 32,777)	Atopic dermatitis (*N* = 27,466)	Noninfective gastroenteritis and colitis (*N* = 25,080)	Chronic gastritis (*N* = 24,305)	Urticaria (*N* = 20,970)	Chronic rhinitis nasopharyngitis and pharyngitis (*N* = 16,582)	IBS (*N* = 12,982)
Infectious diseases⬇	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**	**HR (95% CI)**
Acute URTI at multiple sites	1.03 (1.00,1.06)*	0.98 (0.94,1.03)	1.00 (0.96,1.05)	0.95 (0.91,0.99)	0.92 (0.88,0.97)	0.98 (0.93,1.03)	0.98 (0.93,1.04)	1.05 (0.99,1.10)	1.04 (0.97,1.10)	1.00 (0.93,1.07)
Acute naso-pharyngitis	1.03 (0.99,1.05)	0.97 (0.92,1.01)	0.98 (0.93,1.03)	1.01 (0.97,107)	0.95 (0.90,1.01)	0.97 (0.92,1.03)	0.96 (0.91,1.02)	1.00 (0.94,1.06)	1.07 (1.00,1.14)*	0.98 (0.90,1.06)
Acute bronchitis	0.99 (0.96,1.01)	1.01 (0.97,1.05)	0.96 (0.92,1.00)	1.04 (0.99,1.09)	0.91 (0.87,0.96)	1.05 (1.01,1.09)*	1.01 (0.96,1.06)	1.02 (0.97,1.07)	0.97 (0.92,1.04)	1.02 (0.96,1.09)
Acute pharyngitis	1.09 (0.99,1.05)	1.04 (0.98,1.10)	0.94 (0.89,0.99)	0.98 (0.92,1.04)	0.94 (0.88,0.99)	0.99 (0.93,1.06)	1.02 (0.96,1.08)	1.00 (0.93,1.07)	1.04 (0.96,1.12)	1.01 (0.93,1.10)
Acute bronchiolitis	0.99 (0.95, 1.03)	0.96 (0.90,1.02)	1.03 (0.96,1.09)	1.06 (1.00,1.13)*	0.98 (0.91,1.05)	1.06 (0.99,1.13)	1.00 (0.93,1.07)	0.97 (0.90,1.06)	0.99 (0.91,109)	1.06 (0.97,1.16)
Acute tonsillitis	0.99 (0.95,1.04)	0.99 (0.91,1.07)	1.02 (0.96,1.08)	1.04 (0.98,1.10)	0.98 (0.92,1.05)	0.97 (0.90,1.04)	1.00 (0.93,1.07)	0.99 (0.92,1.07)	0.94 (0.86,1.03)	1.06 (0.97,1.16)
Gastroenteritis and colitis infections	0.99 (0.95,1.04)	0.99 (0.91,1.07)	1.00 (0.93,1.09)	0.97 (0.89,1.05)	1.00 (0.92,1.09)	1.02 (0.93,1.11)	1.01 (0.92,1.11)	1.00 (0.90,1.10)	1.04 (0.93,1.17)	0.99 (0.87,1.13)
Acute laryngitis and tracheitis	0.99 (0.94,1.05)	1.04 (0.95,1.13)	1.00 (0.91,1.09)	1.09 (1.00,1.20)*	1.02 (0.92,1.06)	0.96 (0.86,1.07)	0.89 (0.79,1.01)	0.89 (0.79,1.01)	0.92 (0.81,1.06)	1.03 (0.90,1.18)
Acute pneumonia	0.97 (0.90,1.04)	1.02 (0.90,1.14)	1.01 (0.89,1.14)	1.07 (0.96,1.20)	1.09 (0.96,1.07)	0.93 (0.81,1.07)	0.57 (0.75,1.01)	0.96 (0.85,1.15)	0.87 (0.73,1.05)	1.02 (0.85,1.22)
Acute enteritis	1.02 (0.95,1.10)	0.98 (0.86,1.12)	0.96 (0.84,1.10)	0.99 (0.87,1.14)	0.89 (0.76,1.04)	1.21 (1.06,1.40)*	1.03 (0.89,1.20)	1.01 (0.86,1.20)	0.87 (0.71,1.07)	0.97 (0.79,1.20)

Abbreviations: *IBS* Irritable bowel syndrome, *HR* Hazard ratio, *CI* Confidence interval, *URTI* Upper respiratory tract infections; **p*-value <0.05

Stratified analyses by gender, area of residence, and treatment department are summarized in Supplementary Tables 7–9. Among boys, acute URTI at multiple sites, nasopharyngitis, tonsillitis, pneumonia, and laryngitis and tracheitis were associated with increased risks of urticaria (HR: 1.08, 95% CI: 1.00–1.17), allergic rhinitis (HR: 1.03, 95% CI: 1.00–1.07), chronic bronchitis (HR: 1.09, 95% CI: 1.01–1.17 and HR: 1.25, 95% CI: 1.09–1.44), and chronic gastritis (HR: 1.20, 95% CI: 1.04–1.36), respectively. Among girls, acute laryngitis and tracheitis, bronchitis, bronchiolitis, and enteritis were associated with chronic bronchitis (HR:1.13, 95% CI: 1.00–1.29) and noninfective gastroenteritis and colitis (HR: 1.07, 95% CI:1.00–1.15; HR: 1.14, 95% CI: 1.03–1.26; HR: 1.34, 95% CI: 1.10–1.63), respectively (Supplementary Tables 7 A and 7B).

Treatment department served as a proxy for infection severity. Among children treated in outpatient settings, acute pharyngitis, acute gastroenteritis, and acute enteritis were associated with elevated risks of chronic conjunctivitis (HR: 1.09, 95% CI: 1.04–1.16) and irritable bowel syndrome (HR: 1.23, 95% CI: 1.00–1.52). In contrast, among those treated in inpatient settings, the same infections were linked to substantially higher risks of allergic rhinitis (HR: 3.17, 95% CI: 1.03–9.80), chronic bronchitis (HR: 3.93, 95% CI: 1.17–13.25), and chronic sinusitis (HR: 6.16, 95% CI: 1.35–28.02) (Supplementary Tables 8 A and 8B).

Geographical variation analyses showed that in cities, acute URTI at multiple sites and tonsillitis were associated with allergic rhinitis (HR: 1.05, 95% CI: 1.01–1.11) and chronic bronchitis (HR: 1.20, 95% CI: 1.03–1.21), respectively. In provinces, acute nasopharyngitis, bronchitis, and enteritis were associated with allergic rhinitis (HR: 1.06, 95% CI: 1.02–1.09), chronic bronchitis (HR: 1.06, 95% CI: 1.00–1.12), and noninfective gastroenteritis and colitis (HR: 1.25, 95% CI: 1.04–1.51), respectively (Supplementary Tables 9 A and 9B).

Discussion

This study demonstrates that early childhood infections, particularly acute URTI at multiple sites, nasopharyngitis, laryngitis, bronchiolitis, and enteritis, were associated with increased hazards of chronic allergic rhinitis, chronic nasopharyngitis, chronic bronchitis, and noninfective gastroenteritis and colitis, respectively, during adolescence. These associations were consistent across both boys and girls.

Previous research has similarly shown that infections in early life may predispose individuals to chronic diseases later in life. Early respiratory infections have been linked to asthma and chronic obstructive pulmonary disease in adulthood [19, 20]. A British birth cohort study reported that childhood lower respiratory tract infections doubled

the risk of premature adult mortality due to respiratory diseases. Mansell et al. found that early childhood infections in an Australian cohort were associated with altered metabolomic and lipid profiles, indicating potential long-term metabolic disturbances [21]. A nationwide Taiwanese study demonstrated an association between early-life infections and later development of atopic dermatitis [22]. In addition, Llorente Pelayo et al. identified a higher risk of celiac disease among children with a history of early respiratory infections [23]. Collectively, these studies from different populations suggest that early-life infections may exert long-term systemic effects through immune, inflammatory, and metabolic reprogramming. Despite variations in ethnicity, environment, and healthcare systems across countries, the direction of associations has been largely consistent, reinforcing the biological plausibility of early infection as a developmental determinant of chronic disease. Our findings extend this evidence to an East Asian population, highlighting that similar patterns are observed in Korean children within a nationwide cohort, and emphasizing the need for preventive strategies tailored to early childhood infection control.

Our results align with environmental and hygiene studies [24] indicating that exposures such as contaminated urban environments, inadequate sanitation systems, and air pollution from industrial and biomass fuel sources contribute not only to acute respiratory and enteric infections but also to later chronic respiratory conditions including asthma and chronic bronchitis. These converging lines of evidence underscore the potential influence of environmental determinants on the long-term health effects of early-life infections and reinforce the need for future studies to incorporate detailed exposure assessments.

Several host-related mechanisms may explain how acute infections evolve into chronic disease states. Immune maturation, genetic susceptibility, and microbiome composition can modulate individual vulnerability to chronic sequelae. Infections may drive chronic disease development through persistent inflammation, immune-mediated organ impairment, or structural tissue damage [25]. Prolonged inflammatory responses initiated by pathogens can result in sustained immune activation, cellular remodeling, and fibrosis, ultimately contributing to long-term functional decline [26]. Dysregulated immune responses may also induce autoreactivity, whereby immune cells target host tissues and generate enduring inflammatory injury.

Early-life respiratory infections may interfere with the establishment of a healthy airway microbiota. Interactions between infectious pathogens and resident respiratory microbes can alter immune signaling and tolerance, potentially increasing susceptibility to asthma or other chronic pulmonary disorders later in life. Disruption of the gut–lung axis has also been implicated, as respiratory infections can alter gut microbiota composition, reduce short-chain fatty acid production, and increase intestinal permeability, thereby contributing to chronic gastritis and irritable bowel syndrome [27]. Neural crosstalk along the vagus nerve may further propagate systemic inflammation and connect respiratory and gastrointestinal disease processes. Together, these mechanisms suggest that early infections may reprogram immune and metabolic pathways, predisposing children to long-term chronic disease trajectories.

Stratified analyses revealed no major gender-specific differences for most associations. However, acute laryngitis and acute pneumonia were significantly associated with chronic gastritis and chronic bronchitis, respectively, while acute enteritis and acute pneumonia were associated with noninfective gastroenteritis and chronic conjunctivitis, respectively. The absence of substantial sex-based variation across many infection-related chronic outcomes suggests that gender may not play a primary role in modifying long-term disease risk. Although sex chromosome–linked immune response differences have been reported [28], the chronic sequelae of early-life infections may be similar across genders in certain populations.

This study has several strengths, including the use of the largest population-based cohort to date with 18 years of follow-up. To our knowledge, most previous investigations have been hospital-based, creating a significant gap in population-level research, and only a limited number of nationwide studies worldwide have explored these associations. The present study leveraged the NHID of the NHIS, a large-scale, nationally representative database that captures comprehensive healthcare utilization data from public and private medical institutions across South Korea. From a public health perspective, these findings emphasize the importance of strengthening early infection prevention and management programs. Existing national initiatives, including the National Health Screening Program for Infants and Children and the National Immunization Program, provide essential infrastructure for monitoring and reducing infection burden in early life. Integrating infection surveillance with long-term monitoring of growth and chronic disease outcomes may enhance understanding of early-life determinants of health. Preventive strategies such as timely vaccination, breastfeeding promotion, improving indoor air quality, and parental education on infection control could collectively reduce future chronic disease burdens linked to early infections. To the best of our knowledge, this is the first epidemiological nationwide study in Asia to investigate the association between early-life infectious diseases and chronic disease development in adolescence.

The study has several limitations. First, disease identification was based on ICD-10 diagnostic codes recorded in the NHID, which may be subject to diagnostic variability or misclassification [29]. Because information on treatment procedures and prescribed medications was not incorporated, case definitions may have been broader and less specific than clinical diagnostic standards. Second, although multiple covariates were included in the analyses, residual confounding from unmeasured factors such as nutritional status, concurrent infections, environmental exposures (including crowding, ventilation, sanitation, and biomass fuel use), and socioeconomic circumstances cannot be excluded [30]. Third, reliance on administrative claims data may introduce healthcare-seeking bias, as children with more frequent medical encounters may have higher detection rates for both infectious and chronic conditions [31]. Fourth, generalizability is limited because all study participants were Korean. Potential differences in disease pathogenesis across racial, ethnic, and geographic groups should therefore be considered when extrapolating our findings. Additionally, the infectious syndromes and chronic diseases analyzed represent broad clinical categories with variable underlying etiologies and effect modifiers. Thus, considering the observational study design, the findings should be interpreted as high-level indicators that can guide more detailed future investigations focused on specific risk exposures and targeted prevention strategies.

Conclusion

This large nationwide population-based study identified the most prevalent infectious diseases in early childhood and their associations with chronic conditions manifesting in adolescence. Respiratory infections such as acute URTI at multiple sites, nasopharyngitis, laryngitis, and bronchiolitis, as well as enteritis, were associated with increased risks of chronic allergic rhinitis, chronic nasopharyngitis, chronic bronchitis, and noninfective gastroenteritis and colitis, respectively. These results reinforce early childhood as a critical period for shaping long-term health trajectories. Although causality cannot be established from this observational design, the findings underscore the importance of strengthening infection prevention and pediatric health programs during early life. Future research should elucidate the biological mechanisms linking early infectious exposures with immune programming and chronic disease development, and interventional studies are warranted to clarify causal pathways and inform effective public health strategies.

Abbreviations

NHID	National Health Information Database
NHIS	National Health Insurance Service
KDCA	Korea Disease Control and Prevention Agency
ICD-10	International Classification of Diseases-10
GBD	Global Burden of Disease
URTI	Upper Respiratory Tract Infection
IBS	Irritable Bowel Syndrome
HR	Hazard Ratio
CI	Confidence Interval

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-025-26058-w.

Supplementary Material 1.

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Not applicable.

Authors' contributions

JO: Methodology, Formal analysis, Data curation, Data Analysis, Writing—original draft. JHL: Data curation, Writing original draft. YB: Methodology, Writing—original draft. JL: Conceptualization, Methodology, Writing—original draft. EH: Conceptualization, Methodology, Supervision, Writing—original draft. SS: Conceptualization, Methodology, Data Curation, Data Analysis, Writing—original draft. All authors reviewed the manuscript.

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Data availability

The data that support the findings of this study are available from National Health Information Database of Korea but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Ewha Womans University Seoul Hospital (SEUMC2024-01-034). With the approval by the Institutional Review Board of principal investigator's affiliation, we applied for the access to the Korean National Health Information database (NHID) approved by the Korean National Health Insurance Service (NHIS) (NHIS-2024-10-1-029) in accordance with the ethical principles outlined in the Declaration of Helsinki. Informed consent was not obtained because the data was already anonymized and de-identified by the NHIS before analysis.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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