ORIGINAL ARTICLE

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The effects of *Helicobacter pylori* eradication and development of immune-mediated disorder in children: a nationwide population-based study in Korea

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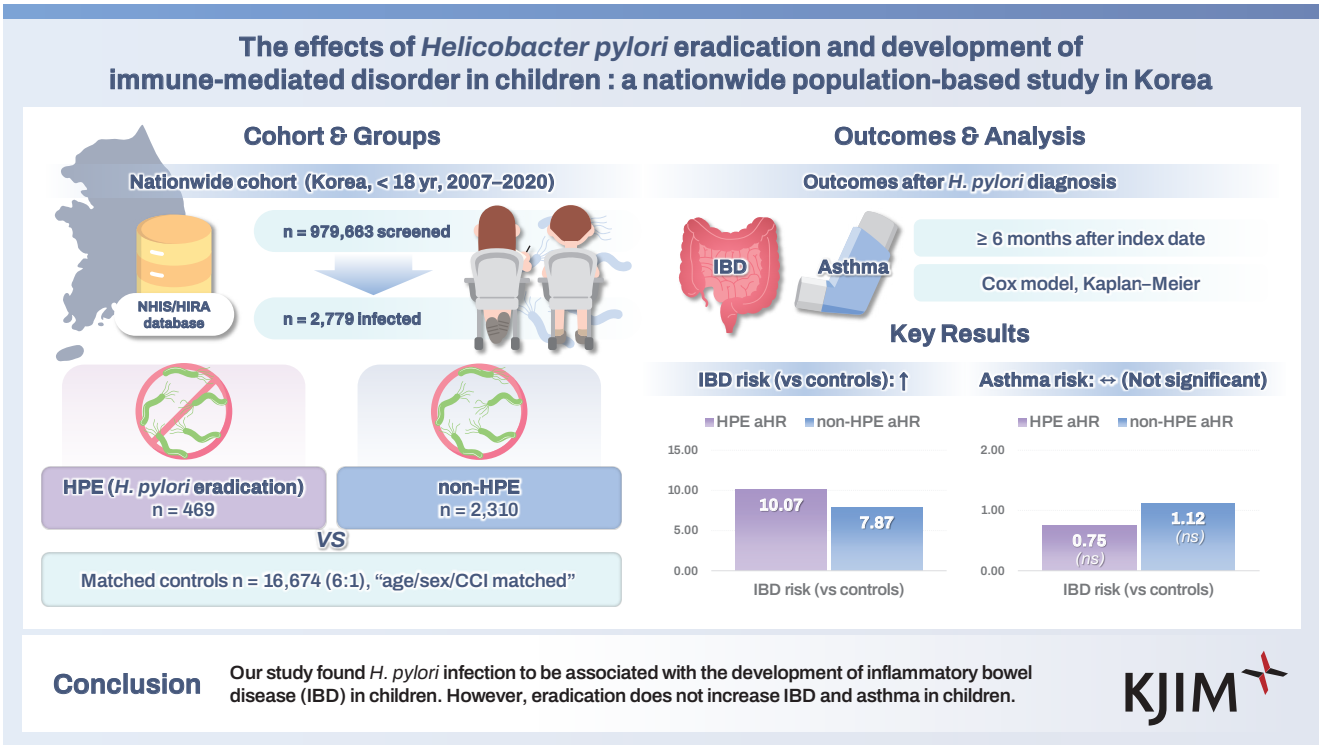

Background/Aims: *Helicobacter pylori* may protect against immune-mediated disorders such as inflammatory bowel disease (IBD) and asthma. This study evaluated whether eradication was associated with IBD and asthma in Korean children.

Methods: Data were collected from the Korean National Health Insurance information on patients younger than 18 years and without a prior diagnosis of IBD or asthma from January 2007 to September 2020. Patients confirmed with *H. pylori* infection were divided into the eradication and non-eradication group. We compared the incidence of IBD and asthma in infected patients with an age, and sex-matched control group.

Results: In total, 979,663 patients were selected based on the inclusion criteria and 2,779 patients were included based on

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the exclusion criteria. The occurrence of IBD in infected patients was statistically significant ($p < 0.05$) but there was no association of infection with asthma. There was no association with eradication and the development of IBD and asthma. The infected group had a shorter duration till diagnosis of IBD than the control group.
Conclusions: Our study found *H. pylori* infection to be associated with the development of IBD in children. However, eradication does not increase IBD and asthma in children.

Keywords: *Helicobacter pylori*; Inflammatory bowel disease; Asthma; Child

INTRODUCTION

Helicobacter pylori is a gram-negative bacterium that [1,2] is observed in half of the world's population. 10–15% of those infected develop peptic ulcer disease (PUD), and 3% develop gastric cancer [3]. The diagnostic and therapeutic strategies for *H. pylori* in pediatric patients differ from those in the corresponding adults [4]. Recent guidelines report that *H. pylori* always induces gastritis, and eradication is recommended in areas with a high risk of gastric cancer [5,6]. However, the eradication of *H. pylori* in asymptomatic children is controversial and must be individualized [7]. Recent pediatric guidelines recommend that eradication should be performed only after endoscopic diagnosis in patients with symptoms related to *H. pylori* infection [8].

Inflammatory bowel disease (IBD) is an immunological disorder with a diverse and multifactorial etiologies, including host genetic and immunological factors, environmental factors, and microbiota. Various immune cells, such as T lymphocytes, are involved in the pathogenesis of IBD. In general, T helper 1 (Th1) cells mediate the immunological reactions related to infection, while T helper 2 (Th2) cells induce the production of cytokines that mediate allergic reactions [9,10]. The imbalance between these two immune responses plays a vital role in the development of IBD and allergic diseases. *H. pylori* infection activates the T cell-mediated pathways. Recent studies have reported that *H. pylori* increases the expression of regulatory T cells, which may prevent the development of IBD [11]. Other studies have reported that *H. pylori* induces a strong Th1 response and is associated with the development of allergy [12-18].

Asthma is also an immunological disorder of the respiratory tract, which is one of the most common chronic respiratory diseases in children, and its incidence and associated mortality rates have increased recently [19]. Although several studies have reported an inverse correlation between asthma and *H. pylori* infection, there have been no reports on the prevalence of asthma after *H. pylori* eradication [12,17,20-24]. Similarly, the prevalence of IBD has also increased in recent years, but there is limited research on the role of *H. pylori* eradication in the onset of IBD [25]. Therefore, we examined whether *H. pylori* infection and eradication were associated with the incidence of autoimmune diseases such as IBD and asthma using nationwide cohort data.

METHODS

Database

Data were extracted from the publicly available Healthcare Bigdata Hub of the Health Insurance Review & Assessement Service (HIRA) provided by the National Health Insurance Service (NHIS). The NHIS is a national single insurer that covers the entire population of Korea, and this dataset includes information on demographics, diagnoses, medications, procedures, medical costs, and mortality of patients. Diagnoses were coded according to the International Classification of Disease – 10th revision. Data were extracted using the following research methods.

Study design

Patients who were younger than 18 years and diagnosed with *H. pylori* were selected from January 2007 to September 2020. Those who had only an allergic disease other than asthma, or who had been diagnosed with IBD or asthma before the diagnosis of *H. pylori* were excluded. These patients were divided into the *H. pylori* eradication group (HPE) and the non-*H. pylori* eradication group (non-HPE). Patients diagnosed with IBD, including Crohn's disease (CD) or ulcerative colitis (UC), as well as asthma, after the diagnosis of *H. pylori* infection were examined. The period between the diagnosis of *H. pylori* and the diagnosis of these autoimmune

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diseases was examined. The control group comprised six times the number of patients with *H. pylori* infection (Fig. 1).

Definition of subjects

Patients with *H. pylori* infection were defined by a diagnosis code of *H. pylori* and if the patient received a laboratory test or endoscopic procedure prior to diagnosis. Laboratory tests included antibody test, stool antigen test, and urease breath tests, whereas endoscopic procedures included Warthin–Starry silver staining, urease test, and cultures. The HPE group consisted of patients prescribed a standard triple or bismuth quadruple therapy regimen. The non-HPE group comprised patients who did not prescribed with either therapy. Standard triple therapy consisted of a proton pump inhibitor (PPI), amoxicillin (AMO) and either clarithromycin (CLA) or metronidazole (MET). Bismuth quadruple therapy consisted of PPI, AMO, CAL or MET and bismuth.

To confirm eradication therapy, the presence of diagnostic codes for stool antigen test, urea breath test, *H. pylori* polymerase chain reaction, urease test, and Giemsa staining were used as evidence for confirmation testing. These tests were required to have occurred at least 21 days after the eradication therapy. Successful eradication was defined as the presence of a confirmation test within six months after the eradication therapy and the absence of a second eradication therapy within one year.

Asthma was defined as the presence of at least one of the following prescriptions for at least 3 months, along with a diagnosis code for asthma; 1) inhalants such as ciclesonide, fluticasone, budesonide, 2) leukotriene receptor antagonist, 3) long acting β2-adrenergic agonist, and 4) anti-immunoglobulin E. CD and UC are legally classified and managed as rare intractable diseases in Korea and diagnosis is managed and supervised by the NHIS. Therefore, diagnostic code alone were deemed to be sufficient for the diagnosis of these two diseases [26]. Patients with allergic diseases other than asthma such as allergic rhinitis and atopic dermatitis were excluded. In addition, patients with IBD or asthma before *H. pylori* diagnosis were also excluded. Diagnosis of IBD and asthma were defined as cases diagnosed at least six months after the definition of *H. pylori* infection.

The control group was matched for age, sex, and Charlson's comorbidity index score with the case group and was six folds the size of the case group. To exclude the impact of antimicrobial therapy on the development of autoimmune diseases, we defined the control group as patients with prescription codes for AMO, MET, or CLA for more than 1 week. In order to exclude diagnoses that could influence the development of IBD and asthma, the control group consisted of patients who were prescribed antibiotics for diseases

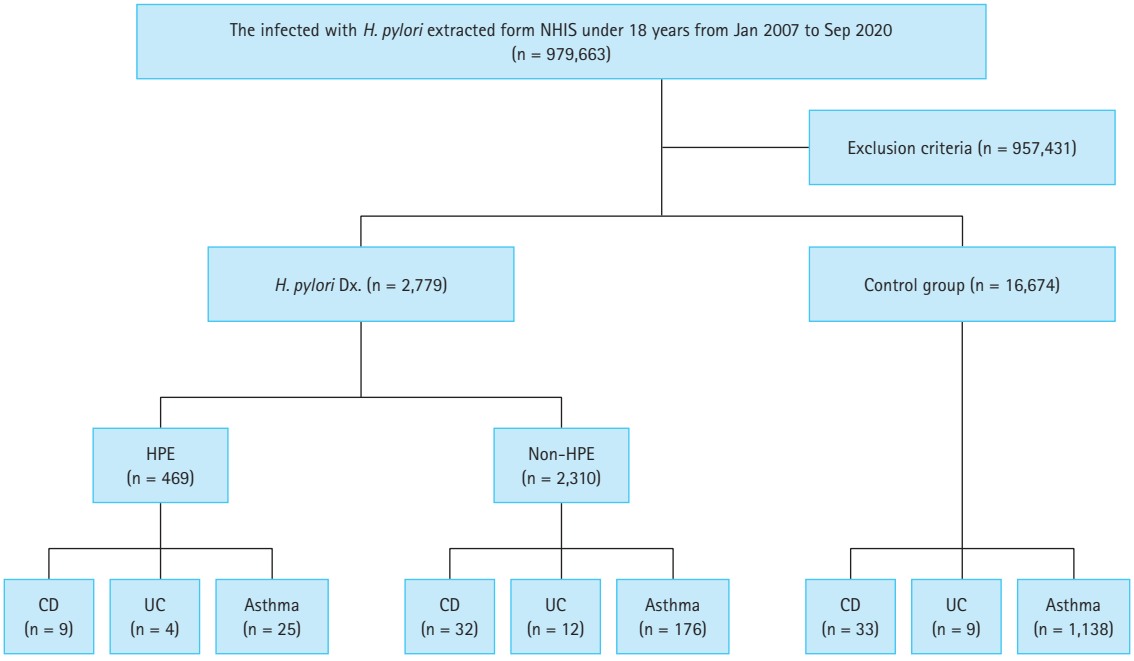

Figure 1. The process of study with inclusion and exclusion criteria. HPE, *Helicobacter pylori* eradication; CD, Crohn's disease; UC, ulcerative colitis.

such as dental caries, cellulitis or chronic sinusitis, mycoplasma pneumonia, or skin infections. This study was approved by the Institutional Review Board of Incheon St. Mary's hospital (No. OC21ZISI0039).

Statistical analysis

All statistical analyses were performed using R version 3.5.1 (R Foundation for Statistical Computing). Continuous variables are presented as mean ± standard deviation or median (range) and were analyzed using the Student t-test or Mann–Whitney test. Categorical variables are described as numbers (%) and were analyzed using the chi-squared test or Fisher's exact test. The cumulative events of asthma, CD, and UC were estimated using the Kaplan–Meier curve and analyzed using the log-rank test. The relative risks of IBD and asthma after *H. pylori* eradication were analyzed using Cox proportional hazards regression analysis, and are presented as adjusted hazard ratios (aHR) with 95% confidence intervals. A $p < 0.05$ was considered statistically significant in all analyses.

RESULTS

Basic characteristics

The total number of patients treated from January 2007 to September 2020 was 2,779. Patients with *H. pylori* infection (n = 2,779) were classified into HPE (n = 469) and non-HPE (n = 2,310) groups. The control group consisted of 16,674 individuals who matched the patients with *H. pylori* infection in terms of age, sex, and Charlson's comorbidity index score (Fig. 1).

The baseline characteristics of the patients are shown in Table 1. In the HPE group, the average age was 12.5 ± 3.7 years and 48.6% (n = 228) of the patients were male. In the non-HPE group, the average age was 12.2 ± 4.2 years, and 50.4% (n = 1,165) were male. In the control group, the average age was 12.3 ± 4.2 years, and 49.9% (n = 8,321) were male. The median follow-up duration was 5.7, 5.2, and 5.1 years in the HPE, non-HPE, and control groups, respectively (Table 1).

Development of IBD and asthma related to *H. pylori* infection

The prevalence of IBD in the HPE, non-HPE and control groups were 2.8%, 1.9%, and 0.3%, respectively. The prevalence rate of CD were 1.9%, 1.4%, and 0.2%, respectively. The prevalence rates of UC in each group were 0.9%, 0.5%, and 0.1%, respectively ($p < 0.001$). The prevalence of asthma was 5.3%, 7.6%, and 6.8%, respectively ($p = 0.149$). The HPE group exhibited a shorter duration form the diagnosis of *H. pylori* to the onset of IBD compared to the control group. This duration was also decreased in the HPE group compared with that in the control group in the

Table 1. Comparison of the basal characteristics between *Helicobacter pylori* eradication and non-eradication group

Variable	HPE (n = 469)	Non-HPE (n = 2,310)	Control (n = 16,674)	*p* value
Age (yr)	12.5 ± 3.7	12.2 ± 4.2	12.3 ± 4.2	0.332
Male	228 (48.6)	1,165 (50.4)	8,321 (49.9)	0.755
FU duration (yr)	5.7 (3.4–7.2)	5.2 (2.9–7.1)	5.1 (2.8–7.2)	0.101
IBD	13 (2.8)	44 (1.9)	42 (0.3)	< 0.001
Crohn's disease	9 (1.9)	32 (1.4)	33 (0.2)	< 0.001
Ulcerative colitis	4 (0.9)	12 (0.5)	9 (0.1)	< 0.001
Asthma	25 (5.3)	176 (7.6)	1,138 (6.8)	0.149
Time to onset of disease (d)				
IBD	227 ± 307	234 ± 491	1,210 ± 1,144	< 0.001
Crohn's disease	267 ± 328	200 ± 430	1,069 ± 1,150	< 0.001
Ulcerative colitis	275 ± 471	470 ± 814	1,527 ± 1,051	< 0.001
Asthma	580 ± 581	620 ± 599	658 ± 737	< 0.001

Values are presented as mean ± standard deviation, number (%), or median (range).
HPE, *Helicobacter pylori* eradication; FU, follow-up; IBD, inflammatory bowel disease.

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Table 2. aHR of IBD and subtypes of IBD

Variable	aHR	95% CI	*p* value
IBD			
Control	ref		
Non-HPE	7.85	5.06–12.20	< 0.001
HPE	10.07	5.15–19.69	< 0.001
CD			
Control	ref		
Non-HPE	7.48	4.57–12.23	< 0.001
HPE	10.07	4.80–21.13	< 0.001
UC			
Control	ref		
Non-HPE	9.73	4.10–23.10	< 0.001
HPE	15.39	4.74–49.99	< 0.001
Asthma			
Control	ref		
Non-HPE	1.12	0.96–1.32	0.147
HPE	0.75	0.50–1.11	0.155

Cox proportional hazards regression anlaysis was performe.
aHR, adjusted hazard ratio; CI, confidence interval; IBD, inflammatory bowel disease; HPE, *Helicobacter pylori* eradication; CD, Crohn's disease; UC, ulcerative colitis.

context of asthma (Table 1).

Risk of IBD and asthma after eradication of *H. pylori*

Cox proportional hazard regression analysis was performed to evaluate the effect of eradication on the occurrence of IBD and asthma (Table 2). The aHR for IBD in the HPE and non-HPE group were 10.07 and 7.85, respectively. The aHR for CD in the HPE and non-HPE group were 10.07 and 7.48, respectively. The aHR for UC in the HPE and non-HPE groups were 15.39 and 9.73, respectively. However, aHR did not show a statistically significant difference in asthma. Eradication of *H. pylori* itself did not increase the risk of developing CD or UC (Fig. 2A, B). There were no statistically significant differences in *H. pylori* infection or eradication in patients with asthma (Fig. 2C).

Comparison of IBD and asthma onset according to period after *H. pylori* eradication

We examined the duration utill diagnosis of IBD and asthma after *H. pylori* eradication (Table 3). Most cases of IBD occurred within 5 years after the diagnosis of *H. pylori*, the diagnosis of CD occurred within 5 years after diagnosis of *H. pylori* in all cases. The diagnosis of UC occurred after 5 years in two cases and within 5 years in 14 cases. In the HPE group, 7 (77.8%) patients were diagnosed with CD within 1 year, and 2 (22.2%) were diagnosed after 1 year. Three (75.0%) patients were diagnosed with UC within 1 year and one (25.0%) patient was diagnosed after 1 year. No statistically significant differences were observed in the time from *H. pylori* diagnosis to onset of IBD between the HPE and non-HPE groups.

Twelve (48.0%) patients were diagnosed with asthma within one year and 13 (52.0%) were diagnosed after one year in the HPE group. In the non-HPE group, 79 cases (44.9%) were diagnosed within one year, and 84 cases (55.1%) were diagnosed after one years. No statistically significant differences were observed in the time from *H. pylori* diagnosis to onset of asthma between the HPE and non-HPE groups.

DISCUSSION

This study examined whether *H. pylori* infection and eradication are associated with immunological disorders such as IBD and asthma in children. Several recent studies have reported that *H. pylori* infection may have a protective role in the development of immunological diseases [12,13,22,27,28]. However, few studies have examined whether eradication is associated with immunological disease in children [25,29]. To our knowledge, this study is the first to examine whether eradication is associated with IBD and asthma in pediatric patients. We found that IBD was increased in *H. pylori*-infected patients, but eradication did not increase the risk of IBD. Meanwhile, asthma was not associated with *H. pylori* infection or eradication.

In our study, only the presence of *H. pylori* infection, and not eradication, was shown to increase the new onset of both CD and UC. However, recent studies have mainly stated that *H. pylori* infection has a protective effect against IBD [29-31]. In addition, the prevalence of *H. pylori* infection has decreased significantly in Korea from 10.8% in 2008 to 6.5% in 2014 [32,33]. Meanwhile, the prevalence of IBD in children in Korea is increasing [34]. The reduction in the prevalence of *H. pylori* is commonly attributed to the hygiene hypothesis. Although the incidence of IBD has increased, this increase cannot be solely attributed to the de-

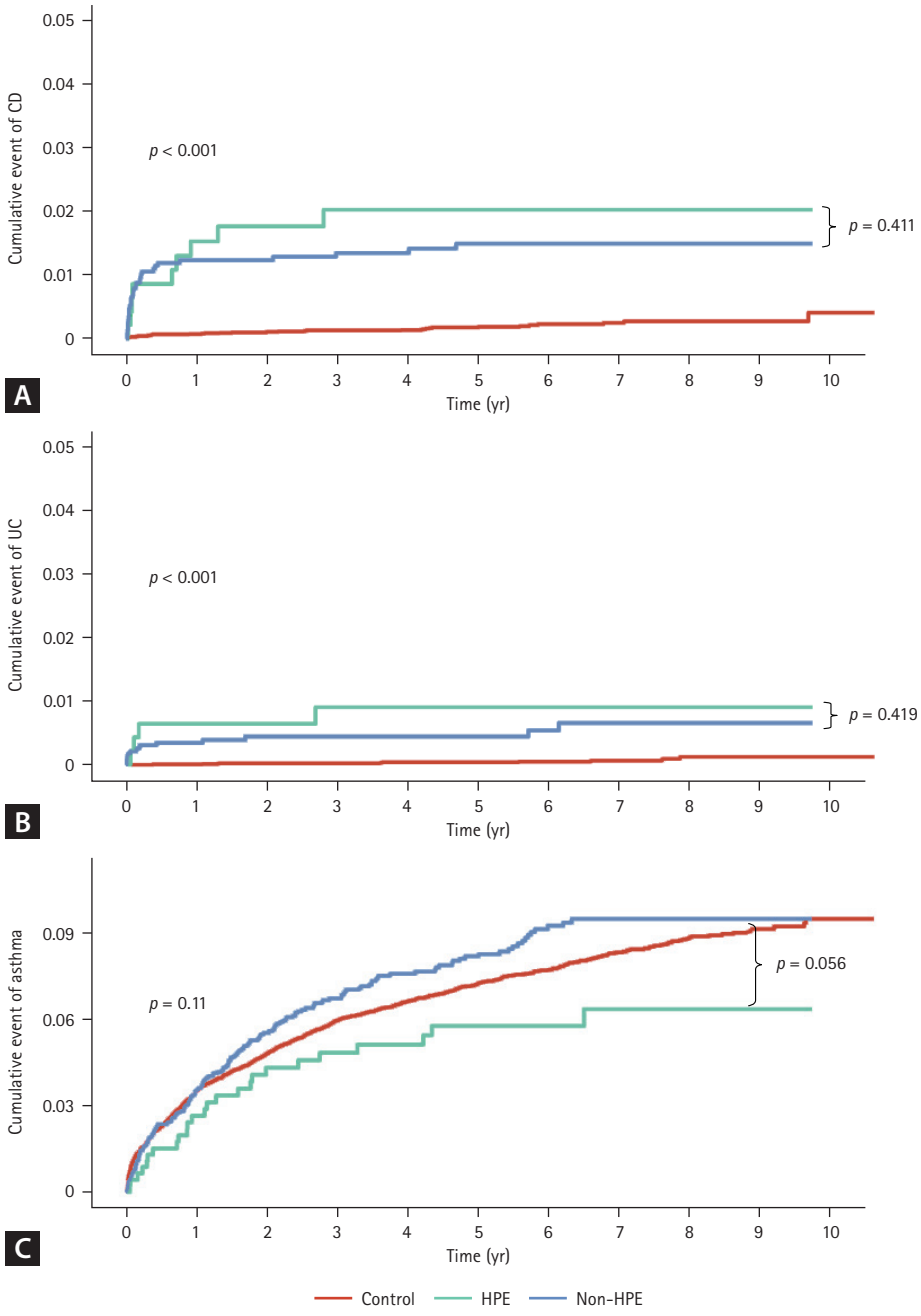

Figure 2. Cumulative event rate of inflammatory bowel disease (IBD) and asthma in *Helicobacter pylori* infection, eradication and control group. Kaplan–Meier plots estimated the cumulative event of IBD and asthma, and the log-rank test was used for analysis. (A) Crohn's disease. (B) Ulcerative colitis. (C) Asthma. HPE, *Helicobacter pylori* eradication.

cline in *H. pylori* infection. Instead, environmental factors, such as adoption of Westernized diets, may contribute to the pathogenesis of IBD. This study, however, concluded that *H. pylori* infection might increase the risk of developing IBD, which could be explained by several mechanisms. First, from an immunological perspective, *H. pylori* infection induces the production of neutrophil activating proteins, which trigger Th1 activation. Given that Th1 cells play a crucial role in IBD pathogenesis, this pathway may contribute to the development of IBD. Second, recent pediatric studies have reported that *H. pylori* infection exacerbates dysbiosis [35], which is a key factor in IBD pathogenesis. Since *H. py-*

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Table 3. Comparison of prevalence and characteristics according to the period after *Helicobacter pylori* infection

Variable	0–1 yr				1–5 yr			
	HPE (n = 469)	Non-HPE (n = 2,310)	Control (n = 16,674)	*p* value	HPE (n = 435)	Non-HPE (n = 2,127)	Control (n = 15,385)	*p* value
Age (yr)	14.0 (1.0–17.0)	13.0 (0.9–17.0)	13.0 (0.2–17.0)	0.399	14.0 (1.0–17.0)	13.0 (0.9–71.0)	14.0 (0.2–17.0)	0.103
Male	228 (48.6)	1,165 (50.4)	8,321 (49.9)	0.755	210 (48.3)	1,073 (50.4)	7,666 (49.8)	0.692
IBD	10 (2.1)	36 (1.6)	13 (0.1)	< 0.001	3 (0.7)	6 (0.3)	18 (0.1)	0.040
Crohn's disease	7 (1.6)	28 (1.2)	12 (0.1)	< 0.001	2 (0.5)	4 (0.2)	14 (0.1)	0.040
Ulcerative colitis	3 (0.6)	8 (0.3)	1 (0.0)	< 0.001	1 (0.2)	2 (0.1)	4 (0.0)	0.041
Asthma	12 (2.6)	79 (3.4)	565 (3.4)	0.612	12 (2.8)	84 (3.9)	473 (3.1)	0.086

Values are presented as median (range) or number (%).
HPE, *Helicobacter pylori* eradication; IBD, inflammatory bowel disease.

lori infection can independently cause dysbiosis, it may act as a risk factor for IBD. Another possible reason for this result is that endoscopies were performed when patients had gastrointestinal symptoms, which could lead to the confirmation of *H. pylori* infection. Most cases of IBD occurred within five years after the diagnosis of *H. pylori*. Therefore, symptomatic patients in the preclinical stage of IBD may be diagnosed with *H. pylori* infection.

In asthma, most studies have reported that *H. pylori* infection exerts protective effects through not only innate immune cells but also adaptive immunity, but in this study, *H. pylori* infection showed no significant association with developing asthma, and eradication of *H. pylori* did not increase the risk. The peak incidence of asthma in children typically occurs between 5 and 14 years of age [36]. However, in this study, the mean age at the diagnosis of *H. pylori* infection was 12 years. Since the development of asthma was evaluated after the diagnosis of *H. pylori* infection, it may be challenging to fully assess the impact of *H. pylori* infection on pediatric asthma.

This study found that *H. pylori* infection increases the risk of IBD, but is not associated with asthma. This difference may arise from the fact that gastrointestinal tract is the primary site of *H. pylori* infection, making its impact on intestinal diseases such as IBD more significant than respiratory tract disorders such as asthma. However, many recent studies have reported an inverse correlation between *H. pylori* infection and both IBD and asthma, emphasizing the need for further investigation of the underlying mechanisms.

It is also important to consider that the clinical manifestations of *H. pylori* infections differ between children and adults. In adults, *H. pylori* infection is primarily associated with PUD and gastric cancer, whereas pediatric infections are often asymptomatic. Symptomatic infections in children are more commonly observed when they develop later in life. One recent adult study reported that *H. pylori* eradication increased the risk of autoimmune diseases, including IBD [25], and our findings similarly suggest that eradication might elevate the risk in pediatric populations. Regarding asthma, early exposure to *H. pylori* in children has been reported to have a protective effect [24], whereas in adults, some studies have suggested that *H. pylori* infection may increase the prevalence of asthma [37]. These discrepancies may reflect differences in immune responses, as pediatric immune systems are still maturing, leading to distinct immunological reactions compared to those in adults.

This study had several limitations. Our study is based on public claims data, and the inherent limitations of such studies are also presented. Diagnosis and prescription of procedures and medications were based on diagnostic codes. However, we believe that the diagnosis of *H. pylori* infection and IBD is correct, as it is based on objective examinations. In addition, the diagnosis of IBD is regulated by the Korean NHIS. It is also the possible that the control group included asymptomatic patients with *H. pylori* infection. Moreover, subtype classification, such as IBD-unclassified, is an important subtype in children, and may not have independent diagnostic codes in the database, posing limitations for subtype analysis. Laboratory findings, such as test results for asthma-related strains of *H. pylori*, were not available in the databases, as only information about whether the test was performed was recorded. Finally, we could not investigate whether the eradication effects differed between male and female children. Despite these limitations, this study is significant as it is a large-scale investigation of the impact of *H. pylori* infection and eradication on the development of IBD and asthma in pediatric patients.

In conclusion, we found that *H. pylori* infection is positively correlated with the developing IBD, but eradication has no relation with IBD occurrence. The diagnosis of IBD was made within the first year of *H. pylori* infection, suggesting that symptomatic patients were investigated and diagnosed more often in *H. pylori* infected patients. There was no relationship between *H. pylori* infection and eradication with asthma. Therefore, this study suggests that the eradication of *H. pylori* itself does not increase the development of IBD and asthma in children. Further prospective studies are needed to evaluate the correlation between *H. pylori* infection and autoimmune disease.

KEY MESSAGE

1. *H. pylori* infection has been associated with a risk of IBD in children.
2. Our nationwide study found that *H. pylori* eradication itself does not increase the development of IBD and asthma in children.

REFERENCES

1. Malaty HM, El-Kasabany A, Graham DY, et al. Age at acquisition of Helicobacter pylori infection: a follow-up study from infancy to adulthood. Lancet 2002;359:931-935.
2. Sugano K, Tack J, Kuipers EJ, et al.; faculty members of Kyoto Global Consensus Conference. Kyoto global consensus report on Helicobacter pylori gastritis. Gut 2015;64:1353-1367.
3. Forman D, Newell DG, Fullerton F, et al. Association between infection with Helicobacter pylori and risk of gastric cancer: evidence from a prospective investigation. BMJ 1991;302:1302-1305.
4. Mišak Z, Hojsak I, Homan M. Review: Helicobacter pylori in pediatrics. Helicobacter 2019;24 Suppl 1:e12639.
5. Malfertheiner P, Megraud F, Rokkas T, et al.; European Helicobacter and Microbiota Study group. Management of *Helicobacter pylori* infection: the Maastricht VI/Florence consensus report. Gut 2022:gutjnl-2022-327745.
6. Liou JM, Malfertheiner P, Lee YC, et al.; Asian Pacific Alliance on Helicobacter and Microbiota (APAHAM). Screening and eradication of *Helicobacter pylori* for gastric cancer prevention: the Taipei global consensus. Gut 2020;69:2093-2112.
7. Desai T, Edhi AI, Hakim S. Eradicating H. pylori. Am J Gastroenterol 2019;114:1827-1828.
8. Jones NL, Koletzko S, Goodman K, et al.; ESPGHAN, NASPGHAN. Joint ESPGHAN/NASPGHAN guidelines for the management of Helicobacter pylori in children and adolescents (update 2016). J Pediatr Gastroenterol Nutr 2017;64:991-1003.
9. Wang SK, Zhu HF, He BS, et al. CagA+ H pylori infection is associated with polarization of T helper cell immune responses in gastric carcinogenesis. World J Gastroenterol 2007;13:2923-2931.
10. Reibman J, Marmor M, Filner J, et al. Asthma is inversely associated with Helicobacter pylori status in an urban population. PLoS One 2008;3:e4060.
11. Lundgren A, Suri-Payer E, Enarsson K, Svennerholm AM, Lundin BS. Helicobacter pylori-specific CD4+ CD25high regulatory T cells suppress memory T-cell responses to H. pylori in infected individuals. Infect Immun 2003;71:1755-1762.
12. Zuo ZT, Ma Y, Sun Y, Bai CQ, Ling CH, Yuan FL. The protective effects of Helicobacter pylori infection on allergic asthma. Int Arch Allergy Immunol 2021;182:53-64.
13. Chen Y, Zhan X, Wang D. Association between *Helicobacter pylori* and risk of childhood asthma: a meta-analysis of 18 observational studies. J Asthma 2022;59:890-900.

https://doi.org/10.3904/kjim.2024.065

14. Chen CM, Huang WT, Chang LJ, Hsu CC, Hsu YH. Peptic ulcer disease is associated with increased risk of chronic urticaria independent of Helicobacter pylori infection: a population-based cohort study. Am J Clin Dermatol 2021;22:129-137.
15. Elias N, Nasrallah E, Khoury C, et al. Associations of Helicobacter pylori seropositivity and gastric inflammation with pediatric asthma. Pediatr Pulmonol 2020;55:2236-2245.
16. Kim HJ, Kim YJ, Lee HJ, et al. Systematic review and meta-analysis: effect of Helicobacter pylori eradication on chronic spontaneous urticaria. Helicobacter 2019;24:e12661.
17. Zhou X, Wu J, Zhang G. Association between Helicobacter pylori and asthma: a meta-analysis. Eur J Gastroenterol Hepatol 2013;25:460-468.
18. Wang Q, Yu C, Sun Y. The association between asthma and Helicobacter pylori: a meta-analysis. Helicobacter 2013;18:41-53.
19. Serebrisky D, Wiznia A. Pediatric asthma: a global epidemic. Ann Glob Health 2019;85:6.
20. Lee SP, Lee SY, Kim JH, et al. Correlation between Helicobacter pylori infection, IgE hypersensitivity, and allergic disease in Korean adults. Helicobacter 2015;20:49-55.
21. den Hollander WJ, Sonnenschein-van der Voort AM, Holster IL, et al. Helicobacter pylori in children with asthmatic conditions at school age, and their mothers. Aliment Pharmacol Ther 2016;43:933-943.
22. Tsigalou C, Konstantinidis TG, Cassimos D, et al. Inverse association between *Helicobacter pylori* infection and childhood asthma in Greece: a case-control study. Germs 2019;9:182-187.
23. Akiner U, Yener HM, Gozen ED, Kuzu SB, Canakcioglu S. Helicobacter pylori in allergic and non-allergic rhinitis does play a protective or causative role? Eur Arch Otorhinolaryngol 2020;277:141-145.
24. Melby KK, Carlsen KL, Håland G, Samdal HH, Carlsen KH. Helicobacter pylori in early childhood and asthma in adolescence. BMC Res Notes 2020;13:79.
25. Lin KD, Chiu GF, Waljee AK, et al. Effects of anti-Helicobacter pylori therapy on incidence of autoimmune diseases, including inflammatory bowel diseases. Clin Gastroenterol Hepatol 2019;17:1991-1999.
26. Kim JA, Yoon S, Kim LY, Kim DS. Towards actualizing the value potential of Korea Health Insurance Review and Assessment (HIRA) data as a resource for health research: strengths, limitations, applications, and strategies for optimal use of HIRA data. J Korean Med Sci 2017;32:718-728.
27. Yoo S, Kim DW, Kim YE, et al. Data resource profile: the allergic disease database of the Korean National Health Insurance Service. Epidemiol Health 2021;43:e2021010.
28. Miftahussurur M, Nusi IA, Graham DY, Yamaoka Y. *Helicobacter*, hygiene, atopy, and asthma. Front Microbiol 2017;8:1034.
29. Rosania R, Von Arnim U, Link A, et al. Helicobacter pylori eradication therapy is not associated with the onset of inflammatory bowel diseases. A case-control study. J Gastrointestin Liver Dis 2018;27:119-125.
30. Zhong Y, Zhang Z, Lin Y, Wu L. The relationship between *Helicobacter pylori* and inflammatory bowel disease. Arch Iran Med 2021;24:317-325.
31. Chiba M, Tsuji T, Takahashi K, Komatsu M, Sugawara T, Ono I. Onset of ulcerative colitis after *Helicobacter pylori* eradication therapy: a case report. Perm J 2016;20:e115-e118.
32. Park JS, Jun JS, Seo JH, Youn HS, Rhee KH. Changing prevalence of Helicobacter pylori infection in children and adolescents. Clin Exp Pediatr 2021;64:21-25.
33. Weyermann M, Rothenbacher D, Brenner H. Acquisition of Helicobacter pylori infection in early childhood: independent contributions of infected mothers, fathers, and siblings. Am J Gastroenterol 2009;104:182-189.
34. Choe JY, Choi S, Song KH, et al. Incidence and Prevalence Trends of Pediatric Inflammatory Bowel disease in the Daegu-Kyungpook Province from 2017 to 2020. Front Pediatr 2022;9:810173.
35. Yang L, Zhang J, Xu J, et al. *Helicobacter pylori* infection aggravates dysbiosis of gut microbiome in children with gastritis. Front Cell Infect Microbiol 2019;9:375.
36. Johnson CC, Chandran A, Havstad S, et al.; Environmental Influences on Child Health Outcomes (ECHO) collaborators. US childhood asthma incidence rate patterns from the ECHO consortium to identify high-risk groups for primary prevention. JAMA Pediatr 2021;175:919-927.
37. Wang YC, Lin TY, Shang ST, et al. Helicobacter pylori infection increases the risk of adult-onset asthma: a nationwide cohort study. Eur J Clin Microbiol Infect Dis 2017;36:1587-1594.

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