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Trend of *Helicobacter pylori* Infection in Childhood: A Single-Center Experience

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What is already known on this topic?

- *Helicobacter pylori (HP) is still the most common infectious agent worldwide. Many studies have been conducted on its incidence in children. When socioeconomic status increases, the infection is seen less frequently. Based on this point, we examined the course of HP in children in our center over the years.*

What this study adds on this topic?

- *Our study is important in terms of conveying the 16-year experience of a single center. There was no change in the presenting symptoms, endoscopy findings, and histopathologic findings of HP infection. We observed that the incidence of HP in our center has gradually decreased over the years. This may be attributed to the increase in socioeconomic welfare and hygiene conditions.*

ABSTRACT

Objective: *Helicobacter pylori* (HP) is the most common bacterial infection in humans. *Helicobacter pylori* infection, which frequently increases with age, is seen in 30%-56.6% of children in Türkiye, although it varies by region. In this study, we aimed to determine the frequency of HP in children and adolescents who underwent upper gastrointestinal endoscopy and gastric biopsy in our region and to compare the changes over the years.

Materials and Methods: Cases who underwent upper gastrointestinal endoscopy for various indications between 2007 and 2022 in our pediatric gastroenterology unit were included in the study. The clinical and endoscopic characteristics of 1737 cases whose histopathologic specimens were obtained, have been retrospectively analyzed from their records. The diagnosis of HP infection was based on the presence of HP on histopathologic examination of gastric biopsy specimens.

Results: Of 1737 cases, 504 (29%) were HP positive. The HP positive case rates were 14.5%, 26.9%, and 33.6% in the 0-6, 7-12, and 13-18 age groups, respectively. *H. pylori* positivity was detected in 65.7% of patients with duodenal ulcers, and the relationship between duodenal ulcers and HP positivity was significant ($P < .001$). The average HP positivity rates were 44%, 28.6%, and 24.2% in 2007-2012 (group 1), 2013-2017 (group 2), and 2018-2022 (group 3). *H. pylori* positivity rates significantly decreased in years ($P = .001/P = .056/P < .001$).

Conclusion: We found that the frequency of HP infection in children decreased in our region over the years. *Helicobacter pylori* positivity was higher in older than younger children. A decrease in HP frequency prevalence may be possible in parallel with awareness and socioeconomic development.

Keywords: Endoscopy, *Helicobacter pylori*, duodenal ulcer, child, frequency, trend

INTRODUCTION

The prevalence of *Helicobacter pylori* (HP), a gram-negative, catalase and urease-positive, spiral bacterium, one of the most common bacterial infectious agents in humans, increases with age worldwide.[1] It is thought that 30%-56.6% of the pediatric age group is infected in our country.[2,3]

Helicobacter pylori causes acute nodular gastritis, chronic active gastritis, peptic ulcer, duodenal ulcer, and intestinal metaplasia in children. Exposure to the microorganism at a young age may lead to gastric atrophy, gastric adenocarcinoma secondary to chronic inflammation, and mucosa-associated lymphoid tissue lymphoma in adulthood.[4] Therefore, early diagnosis and treatment impact the morbidity of the disease in the following years. According to current guidelines, non-invasive tests such as urea breath tests, serologic tests, and invasive tests such as histopathologic examination of endoscopic biopsy, polymerase chain reaction,

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and urease tests are used for diagnosis. Currently, the gold standard diagnostic test is endoscopic biopsy.[5] Nodular gastritis is antral gastritis characterized endoscopically by a miliary pattern resembling goose flesh and pathologically by infiltration of prominent lymphoid follicles and mononuclear cells.[6]

As countries develop socioeconomically, the incidence of HP decreases.[7] In addition, a crowded environment at home, the number of children, having an infected parent, living in places such as boarding schools and dormitories, consuming raw vegetables, and swimming in freshwater sources such as streams can be counted among the conditions that increase the prevalence.[8]

Studies conducted in various countries have shown that the prevalence of HP is between 25% and 82% in the childhood age group.[9] It is curious how the prevalence has changed over time. In Argentina, the prevalence was 41.2% between 2002 and 2004, dropping to 26% between 2007 and 2009.[10] In a Brazilian study, the prevalence decreased from 48.2% to 27.7% over 10 years.[11] This change is thought to result from socioeconomic developments, drop in children, hygiene, and easy access to clean drinking water. We could not find a study showing the change over time in our country.

In this study, we aimed to contribute to the literature about the situation in our country by finding the frequency of HP in children and adolescents who underwent upper gastrointestinal endoscopy and gastric biopsy in our unit and its change over 15 years.

MATERIALS AND METHODS

Study Design

This is a retrospective study conducted in the pediatric gastroenterology unit of Süleyman Demirel University Research and Education Hospital. This unit is a center providing tertiary health care services in the West Mediterranean region of Türkiye, covering a population of approximately 2.5 million, including the surrounding provinces. Between January 1, 2007, and December 31, 2022, 2984 patients underwent upper gastrointestinal tract (GI) endoscopy for different indications in the unit. In total, 1247 patients who had corrosive substance ingestion, foreign body removal, patients who did not undergo biopsy, dilatation for esophageal stenosis, and gastrostomy catheter were not included in the study. The study was carried out retrospectively in 1737 cases whose endoscopy and pathology reports were examined.

Diagnostic Procedures

In each patient, biopsy specimens were taken from the body (2 pieces), antrum (2 pieces), esophagus (1 piece), and duodenal bulb. Endoscopic views of the patients were recorded and then compared with the histopathological results. In the histopathologic examination, the preparations were stained with hematoxylin–eosin, modified Giemsa stains and examined for pathology under light microscopy.

The trials were evaluated according to the Sydney classification. Accordingly, they were classified as high (++++), moderate (+++), low (+), and absent (−).

Patients Groups

Patients were divided into 3 age groups (0-6, 7-12, and 13-18 years) for comparison with previous studies. While evaluating the course of HP (+) according to years, our study was divided into 3 periods: the first 6 years (group 1: 2007-2012), the middle 5 years (group 2: 2013-2017), and the last 5 years (group 3: 2018-2022). The change in the 3 periods was compared statistically. Age-appropriate eradication treatment was applied to patients with a histopathological diagnosis of HP. Control endoscopy data after eradication treatment were not included in the study.

This study used the principles of the Declaration of Helsinki 2008. The ethics committee approval for this study was obtained from the Süleyman Demirel University Ethics Committee (date: September 21, 2023; number: 178). Verbal informed consent was obtained from the patients who agreed to take part in the study.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS, version 27.0) (IBM Corp., Armonk, NY, USA) was used for statistical analysis. Continuous variables were expressed in mean ± SD, and categorical variables were expressed in number (n) and percentage (%). Categorical variables were compared between groups using the chi-square test (or Fisher's exact test when necessary). *P*-values ≤ .05 were considered statistically significant.

RESULTS

Patients and Clinical Findings

Of the 1737 patients included in the study, 1107 were girls (63.7%) and the mean age was 12.2 ± 4.49 years (0-18 years). Of the cases, 242, 502, and 993 cases were between 0 and 6, 7 and 12, and 13 and 18 years old, respectively. The overall infection rate of HP infection was 29% (95% CI, 26.9%-31.2%) (n = 504). Of these cases, 163 were boys (32.3%) and 341 were girls (67.7%). When the patients were analyzed according to age groups, 14.5% of the cases between 0 and 6 years, 26.9% between 7 and 12 years, and 33.6% between 13 and 18 years were HP-positive (Table 1).

Table 1. *Helicobacter pylori* Rate According to Sex and Age Groups

	Number of Cases		*H. pylori* Positive		
Age Group	**n**	**%**	**n**	**%**	***P****
Sex					**.029**
Boys	630	36.3	163	32.3	
Girls	1107	63.7	341	67.7	
Total	1737		504	29	
0-6 ages	242	13.9	35	14.5	.08
Boys	109	45	11	31.4	
Girls	133	55	24	68.6	
7-12 ages	502	28.9	135	26.9	.494
Boys	232	46.2	59	43.7	
Girls	270	53.8	76	56.3	
13-17 ages	993	57.1	334	33.6	.534
Boys	289	29.1	93	27.8	
Girls	704	70.9	241	72.2	

The value in bold indicates statistical significance.
*Chi-square test.

Turk Arch Pediatr 2024; 59(3): 264-269

Table 2. Clinical Characteristics of the Cases

Complaint	*H. pylori* Positive n	*H. pylori* Positive %	*H. pylori* Negative n	*H. pylori* Negative %	*P**
Vomiting					
Yes	29	19.2	122	80.8	**.005**
No	475	29.9	1111	70.1	
Abdominal pain					
Yes	159	27.7	414	72.3	.414
No	345	29.6	819	70.4	
Dyspepsia					
Yes	104	35.6	188	64.4	**.006**
No	400	27.7	1045	72.3	
Epigastric pain					
Yes	16	38.1	26	61.9	.189
No	488	28.8	1207	71.2	
Bleeding					
Yes	38	29.2	92	70.8	.955
No	466	29	1141	71	

Values in bold indicate statistical significance.
*Chi-square test.

The clinical characteristics of the cases are shown in Table 2. The most common indications for endoscopy were abdominal pain (n = 573) and dyspeptic complaints (n = 292). *Helicobacter pylori* positivity was most frequently detected in cases with epigastric pain (38.1%), dyspepsia (35.6%), and bleeding (29.2%).

Endoscopic and Histopathologic Findings

Helicobacter pylori positivity was found in 65.7%, 34.6%, and 28.9% of cases with macroscopic duodenal ulcer, gastritis, and gastric ulcer, respectively. There was a statistically significant correlation between duodenal ulcers, gastritis, oesophagitis, and HP positivity (Table 3).

Inflammation and activation were found most frequently according to the Sydney classification, while atrophy was not observed on histopathologic examination. There was a statistically significant correlation between HP positivity and the presence of inflammation and activation (*P* < .001) (Table 3).

Table 3. Endoscopic and Histopathologic Findings of All Cases

Endoscopic and Histopathologic Findings	*H. pylori* Positive n	*H. pylori* Positive %	*H. pylori* Negative n	*H. pylori* Negative %	*P**
Esophagitis					
Yes	40	19.1	169	80.9	**<.001**
No	464	30.4	1064	69.6	
Gastritis					
Yes	294	34.6	556	65.4	**<.001**
No	210	23.7	677	76.3	
Duodenitis					
Yes	123	28.1	315	71.9	**.67****
No	381	29.3	918	70.7	
Gastric ulcer					
Yes	11	28.9	27	71.1	.991
No	501	29	1225	71	
Duodenal ulcer					
Yes	23	65.7	12	34.2	**<.001**
No	481	28.3	1221	71.7	
Inflammation					
Yes	500	41.4	709	58.6	**<.001****
No	4	0.8	524	99.2	
Activation					
Yes	267	79.2	70	20.8	**<.001**
No	237	16.9	1163	83.1	
Atrophy					
Yes	0	0	3	100	.561**
No	504	29.7	1230	70.9	
Metaplasia					
Yes	10	27.8	26	72.2	.869
No	494	29	1207	71	

Values in bold indicate statistical significance.
*Chi-square test.
**Fisher's exact test.

Comparison of *Helicobacter pylori* Positivity According to Years

When HP positivity was analyzed by years, the highest rate was observed in the first 6-year period of the study (group 1) with

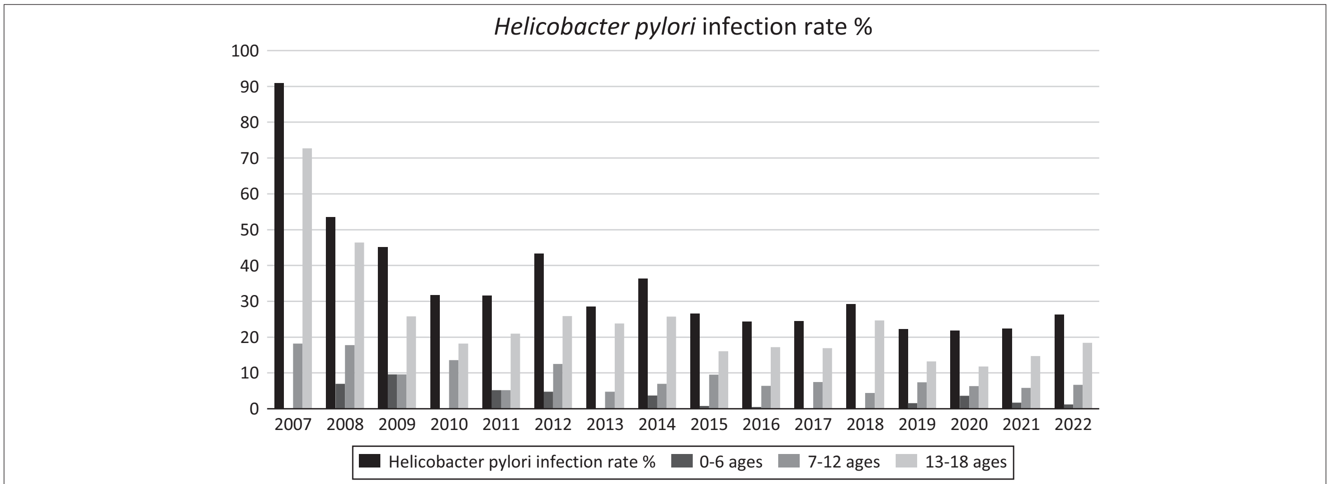

Figure 1. The rate of *Helicobacter pylori* infection by years and age groups (%).

Table 4. The Rates of *Helicobacter pylori* (+) Cases According to Years and Age Groups

	Total		*H. pylori* (+)		
Age and Date Groups	**n**	**%**	**n**	**%**	***P*** *
0-6 ages	242		35	14.5	
7-12 ages	502		135	26.9	
13-18 ages	993		334	33.6	
0-6 ages vs. 7-12 ages					**<.001**
7-12 ages vs. 13-18 ages					**.008**
0-6 ages vs. 13-18 ages					**<.001**
2007-2012 (group 1)	234		103	44	
Boys	85		36	42.4	.699
Girls	149		67	45	
2013-2017 (group 2)	850		243	28.6	
Boys	307		79	25.7	.166
Girls	543		164	30.2	
2018-2022 (group 3)	653		158	24.2	
Boys	238		48	20.2	.069
Girls	415		110	26.5	
Group 1 vs. 2					**<.001**
Group 1 vs. 3					**<.001**
Group 2 vs. 3					.056

Values in bold indicate statistical significance.
*Chi-square test.

44% (Figure 1). *Helicobacter pylori* positivity was 28.6% between 2013 and 2017 (group 2) and 24.2% between 2018 and 2022 (group 3). When the groups were compared with each other, a statistically significant decrease was observed (groups 1 and 2, $P = .001$; groups 1 and 3, $P < .001$) (Table 4).

DISCUSSION

Our study is valuable in showing the frequency of HP infection in our region over many years. While the rate was 44% in the first years, it decreased to 24.2% in recent years. This study is very important in showing the course of HP frequency in the same region over time. In our country, there are similar studies showing the trend of HP in the same region over a period of time.[12] However, our study is valuable in terms of showing the continuous trend in a single center over a long period of time. Therefore, our study will contribute to the literature.

In studies conducted in various countries, HP positivity was observed between 20% and 40% in developed countries and 30% and 70% in developing countries.[13,14] Low rates in western provinces and high rates in eastern regions were generally observed in our country. In studies conducted in the pediatric age group in our country, 97.1% in Afyonkarahisar, 59.8% and 35% in 2 separate studies in Istanbul, 63.2% in Elazığ, 67.1% in Şanlıurfa.[15-19] In a study involving 408 cases in Antalya, HP positivity was 38.7%.[20] In the study conducted by Sag et al[21] in 2022, *Helicobacter pylori* gastritis was found in 11 (16.9%) of 65 patients with severe anemia in children. In a cross-sectional study conducted in Istanbul between 2019 and 2021, HP antigen positivity in feces was 11.8% in 543 children.[22] Our research found HP (+) in 29% of 1737 patients who underwent endoscopy. The result in our study may be explained by the fact that HP was histopathologically confirmed only by endoscopic biopsy, and endoscopy was performed cross-sectionally only in cases with dyspeptic complaints and not in all children. In addition, the region where the study was conducted may have a better socioeconomic status and a lower household population than the east of the country.

In the literature, similar HP (+) rates have been reported among boys and girls.[13] When the cases were analyzed according to sex, 67.7% of HP (+) patients were girls. This result was explained by the fact that 63.7% of the cases included in the study group were girls. When analyzed by sex, 25.8% (163/630) of all boys and 30.8% (341/1107) of all girls were HP (+).

When the frequency of HP is analyzed according to age groups, it is reported to increase with age.[23-25] In our study, the rate of HP positivity was 14.5%, 26.9%, and 33.6% in the 0-6, 7-12, and 13-18 age groups, respectively, and it was determined that the HP frequency increased with age. This result was consistent with the reported studies.[15,26-28]

In this study, the most common indications for endoscopy were abdominal pain, dyspeptic complaints, and epigastric pain. While the association of dyspeptic complaints with HP (+) was statistically significant, the association with abdominal pain and epigastric pain was not significant. No statistically significant correlation was found between abdominal pain and HP (+) in the study by Özbey et al.[18] Similar studies observed that endoscopy was performed most frequently with the complaint of abdominal pain.[21,29,30]

Helicobacter pylori positivity was found in 65.7%, 34.6%, and 28.9% of cases with duodenal ulcers, gastritis, and gastric ulcers, respectively. The association of duodenal ulcer with HP positivity was significant ($P < .001$). In previous studies, HP positivity was found to be 33%-92% in cases with duodenal ulcers and 20%-75% in patients with gastric ulcers.[31-34] In our country, in a study conducted in Elazığ, the relationship between gastritis and HP positivity was significant. At the same time, 66.7% of patients with duodenal ulcers were HP positive, but it was not statistically significant.[15] In the study by Koca et al[35] HP was found in 71.5% of patients with duodenal ulcers and 40% with gastric ulcers. In the study by Tang et al[25] study, no statistically significant difference was found between HP (+) and gastritis and peptic ulcer. The fact that the studies are not homogeneous, the number of cases is different, and different diagnostic methods and classifications are used in other age groups may explain the differences between the rates.

According to current guidelines, upper gastrointestinal endoscopy and histopathologic examination are the gold standards for diagnosing HP. In addition to the presence of HP, histologic changes such as inflammation, activation, atrophy, and metaplasia can also be identified by evaluating the material obtained. In previous studies, a statistically significant correlation was found between HP positivity and the presence of inflammation and activation.[23,24,20] In our study, consistent with the literature, the presence of inflammation and activation in HP-positive cases was significant compared to the HP-negative group ($P < .001$). Among the patients with activation, 79.2% were HP (+). *Helicobacter pylori* was negative in 58.6% of 1209 cases with inflammation. This result may be explained by insufficient pathogen detection, hopping distribution of the pathogen on the mucosa, or other causes of gastritis (viral, bacterial, autoimmune, drug-antibiotic use, etc.).[36]

The rates of atrophy and intestinal metaplasia in gastric endoscopic biopsy specimens vary in studies. In the study by Erdoğan Durmuş et al,[37] atrophy and intestinal metaplasia were not observed. In contrast, in the study by Marginean et al,[38] atrophy was observed in 3 and intestinal metaplasia in 4 of 462 cases.[24,38] Domşa et al[23] observed atrophy in 36 and intestinal metaplasia in 3 of 248 points and found a statistically significant correlation between atrophy and HP positivity. Irak et al[39] found 33% and 15.1% atrophy rates in another study conducted in İzmir. Our research showed atrophy in only 3 cases (0.17%) and intestinal metaplasia in 36 patients (2.07%). Atrophy and intestinal metaplasia may not have been detected in biopsy specimens performed in childhood because they may develop especially after long years of HP exposure. In addition, biopsy specimens not taken from the correct location may lead to false negative results. The "The H. pylori Genome Project" study conducted worldwide found that the risk of developing disease from *Helicobacter pylori* infection varies significantly by geography.[40]

When the HP rate was analyzed by years in our study, a gradual decrease was observed from 2007 to 2022. The highest rate (44%) of HP positivity was observed in the first 6-year period of the study (group 1). *Helicobacter pylori* positivity was 28.6% between 2013 and 2017 (group 2) and 24.2% between 2018 and 2022 (group 3). When the groups were compared, a statistically significant decrease was observed (groups 1 and 2, P = .001; groups 1 and 3, P < .001). In prevalence studies conducted worldwide, it is observed that HP positivity has decreased in recent years, especially in developed and developing countries.[11] A study conducted by Tang et al[25] in children showed that HP positivity decreased from 25.6% in 2005 to 12.8% in 2018.[25] In a study conducted in Ankara, while the prevalence of HP was 48.1% in 2002-2003, it was found to be 23.1% in 2012-2013 in the same center and was statistically significant (P < .001).[12] In a meta-analysis published in 2022 and including 198 articles, the global prevalence of HP in children was 32.3%. In the same meta-analysis, the association of HP positivity with low economic status, having more children, sharing the same room, having no sewage system, having an infected family member, and drinking untreated water was statistically significant.[41] As a result, improved hygiene conditions, socioeconomic improvement, a decrease in the number of children in families due to the decline in fertility rate, an increase in the level of welfare, or widespread use of antibiotics may explain the reduction in the prevalence of HP.

Our retrospectively designed study had some limitations. Information such as the absence of a control group, comorbidities of the cases, medication use, whether they received eradication treatment or not, and socioeconomic status of the families was missing. In addition, the frequency found cannot be generalized to the pediatric population since the study was not a community screening but only in symptomatic cases presenting to the hospital. Nevertheless, our study, which was conducted in a single center covering an extended period, was thought to contribute to the literature examining the course of HP over the years.

In conclusion, the current study showed a decreasing frequency of HP in our region compared to previous years. This suggests that, similar to other developing countries, the frequency of HP is decreasing over time in our country. This improvement may indicate that the awareness and sociocultural development of our country toward this infection has increased.

Ethics Committee Approval: This study was approved by the Ethics Committee of Süleyman Demirel University (approval no: 178; date: October 21, 2023).

Informed Consent: Verbal informed consent was obtained from the patients who agreed to take part in the study.

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