

Prevalence of *Helicobacter pylori* among children in a training and research hospital clinic in Istanbul and comparison with Updated Sydney Classification Criteria

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ABSTRACT

OBJECTIVE: *Helicobacter pylori* (*H. pylori*) is a gram-negative bacterium and one of the reasons for gastritis, peptic and duodenal ulcers. It is a crucial public health problem for both children and adults, especially in developing countries. This study aims to investigate the prevalence of *Helicobacter pylori* positivity in children and to compare with updated Sydney classification criteria.

METHODS: This study was conducted from January 2015 to June 2017. This study included 885 children aged 0-17 year(s). Endoscopic biopsies were evaluated for the diagnosis of infection due to *H. pylori*.

RESULTS: The findings showed that 418 (47.2%) of 885 children were positive for *H. pylori*, and this positivity had a significantly increasing correlation with the presence of chronic inflammation, neutrophilic activity, lymphoid aggregates, and follicles. Erythematous pangastritis and antral nodularity on endoscopic findings had a correlation with *H. pylori* positivity.

CONCLUSION: In this hospital-based study, the findings suggest that *H. pylori* infection is a problem for children and more extensive studies are needed to determine the prevalence of *H. pylori* positivity among children.

Keywords: *H. pylori* among children; Sydney classification.

Cite this article as: Calim Gurbuz B, Inceman HN, Aydemir M, Celtik C, Gerenli N, Zemheri E. Prevalence of *Helicobacter pylori* among children in a training and research hospital clinic in Istanbul and comparison with Updated Sydney Classification Criteria. *North Clin Istanbul* 2020;7(5):499–505.

Helicobacter pylori is a gram-negative microorganism that is commonly seen worldwide. Robin Warren and Barry Marshall discovered it as the causative agent of gastritis and peptic ulcer in 1982 [1]. More than 50% of the world's population is infected with *H. pylori* [2]. It is also more common in developing countries and the prevalence of *H. pylori* is approximately 90% in these countries [3].

H. pylori-associated infection can be either clinically silent or non-specific. Specific signs or symptoms are

including esophagitis, gastroesophageal reflux, and various motility disorders. Older children with peptic complaints may have symptoms more than younger children, and diagnosis of *H. pylori* infection is more difficult in early childhood. Childhood, early adult years, living in developing or poor countries have an apparent risk for infection [4].

Although *H. pylori*-associated infection in our country has limited data for the epidemiology, in Turkey, the prevalence of *H. pylori* infection in children has been

Received: May 09, 2019 Accepted: February 06, 2020 Online: August 17, 2020



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reported as different rates, from 23.6% to 78.5% [4, 5]. Therefore, this study was conducted to evaluate the prevalence of *H. pylori* in children in Western Turkey and also to investigate the association between *H. pylori*, updated Sydney classification criteria and endoscopic findings.

MATERIALS AND METHODS

In total, 885 children's endoscopic biopsies, which were taken from the Department of Pediatric Gastroenterology, from January 2015 to June 2017, were evaluated for endoscopic and histologic findings. According to endoscopic findings and preliminary diagnosis, the patients clarified to erythematous pangastritis, antral nodularity, erosion/ulcer on gastric mucosa, esophagitis, celiac disease, duodenitis, and inflammatory bowel disease. One patient may have more than one endoscopic findings and preliminary diagnosis.

Patients who were less than 18 years old were included in our study. The patients were divided into four groups considering their age. Group 1 included patients who were 0–5 year(s), Group 2 included patients who were 6–10 years, Group 3 included patients who were 11–15 years, and Group 4 included patients who were 16–17 years.

The biopsies were placed on the filter paper, fixed in 10% neutral buffered formalin, and embedded in paraffin. Serial sections of 5 µm were prepared for each fragment and stained with hematoxylin-eosin, modified Giemsa for evaluating *H. pylori*, and periodic acid Schiff and alcian blue (PAS-AB) for evaluating intestinal metaplasia. Histomorphological evaluation was performed according to the Updated Sydney System criteria [6]. *H. pylori* positivity, chronic inflammation and neutrophilic activity were reported as none (0), mild (1), moderate (2) and severe (3). Lymphoid aggregates, lymphoid follicles, intestinal metaplasia and atrophy were defined as absent (0) or present (1).

Ethical clearance for this study was provided by the Medical Ethics Committee of Health Sciences University with B.10.1.TKH.4.34.H.GP.0.01/195 number on 23 October 2019.

Statistical Methods

IBM SPSS Statistics 22 was used for the statistical analysis. The suitability of the parameters to the normal distribution was evaluated by the Shapiro Wilks test for less

TABLE 1. Findings of the total patients

Demographic features	%
Sex	
Female	58.3
Male	41.7
Age groups	
0–5 year(s) (Group 1)	11.6
6–10 years (Group 2)	22.2
11–15 years (Group 3)	44.4
16–17 years (Group 4)	21.8
Endoscopic findings	
Erythematous pangastritis	74.8
Antral nodularity	15.1
Erosion and ulcer on gastric mucosa	2.1
Preliminary diagnosis	
Celiac	6.4
Esophagitis	6.2
Duodenitis	3.2
Inflammatory bowel disease	0.8
<i>H. pylori</i>	
Negative	52.8
Positive	47.2

than 50 samples and Konglomorov test for more than 50 samples. Descriptive statistical methods (mean, standard deviation, frequency) were used as well as the Chi-square test, Fisher Freeman Halton test, and Continuity (Yates) Correction for comparison of qualitative data. Significance was evaluated as $p < 0.05$.

RESULTS

According to the demographic evaluation of the patients who underwent endoscopic biopsy, there were 885 children—516 females (58.3%) and 369 males (41.7%). The most crowded group was Group 3, with 393 children (44.4%) aged 11–15 years. Erythematous pangastritis was the most common endoscopic finding with 662 children (74.8%). 418 of 885 patients was positive for *H. pylori* (47.2%) (Table 1).

Females were 60.3%, and males were 39.7% of *H. pylori*-positive group. 11–15 years old, group 3, had the highest rate (46.4%) of all *H. pylori* positive age groups. Erythematous pangastritis (82%) was the most common endoscopic finding in the patients who were *H. pylori* in-

fect. The grading of *H. pylori* positivity was 50.2% for mild infection, 30.9% for moderate infection, 18.9% for severe infection. Histologically, moderate neutrophilic activity (40.7%) and moderate chronic inflammation (40.4%) were the highest part of *H. pylori* positive patients. Lymphoid aggregates were found as 77.5% and lymphoid follicles were found as 45.4% in *H. pylori*-positive patients (Table 2).

According to Updated Sydney Classification System criteria and *H. pylori*-positive, the absence of neutrophilic activity and chronic inflammation were found statistically more significant in *H. pylori* negative patients (68.3%, 7.1%) than the absence of neutrophilic activity and chronic inflammation in mild *H. pylori*-positive patients (24.3%, 0.9%) ($p=0.001$; $p<0.05$). In mild *H. pylori*-positive patients, mild neutrophilic activity was 55.2% and mild chronic inflammation was 71.9%. These rates were 18.1% for moderate neutrophilic activity, 22.4% for moderate chronic inflammation, 2.4% for severe neutrophilic activity, and 4.8% for severe chronic inflammation. Mild neutrophilic activity and chronic inflammation were found statistically significant compared to moderate and severe neutrophilic activity and chronic inflammation in mild *H. pylori*-positive patients ($p=0.001$; $p<0.05$). In addition, there was a statistically significant difference between the severity of *H. pylori* and the presence of lymphoid aggregates and follicles. As a result of binary comparisons made for the determination of difference, the presence of lymphoid aggregates was statistically lower in *H. pylori* negative patients (52.5%) compared to mild (68.1%), moderate (83.7%) and severe (92.4%) *H. pylori*-positive patients ($p=0.001$; $p<0.05$). Same way, the presence of lymphoid follicles was statistically lower in *H. pylori* negative patients (10.3%) compared to mild (26.2%), moderate (60.5%) and severe (72.2%) *H. pylori*-positive patients ($p=0.001$; $p<0.05$). The rate of the presence of lymphoid aggregates and follicles in moderate *H. pylori*-positive children (83.7%, 60.5%) and in severe *H. pylori* positive children (92.4%, 72.2%) also had a higher incidence than mild *H. pylori* positive children (68.1%, 26.2%) ($p=0.001$; $p<0.05$). Intestinal metaplasia and atrophy was 0.5% in the total patient group. There was no statistically significant difference between *H. pylori*, atrophy, and intestinal metaplasia ($p>0.05$) (Table 3).

Different endoscopic findings and preliminary diagnosis were existing in *H. pylori*-positive patients. The rate of erythematous pangastritis was statistically lower in *H. pylori* negative patients (68.3%) compared to mild

TABLE 2. Findings of the *H. pylori*-positive patient

Demographic features	%
Sex	
Female	60.3
Male	39.7
Age groups	
0-5 year(s) (Group 1)	6.7
6-10 years (Group 2)	20.6
11-15 years (Group 3)	46.4
16-17 years (Group 4)	26.3
Endoscopic findings	
Erythematous pangastritis	82
Antral nodularity	26.5
Erosion and ulcer on gastric mucosa	2.1
Preliminary diagnosis	
Esophagitis	5.2
Celiac	5.02
Duodenitis	3.3
Inflammatory bowel disease	1.1
<i>H. pylori</i> grading	
Mild	50.2
Moderate	30.9
Severe	18.9
None	12.4
Neutrophilic activity	
Mild	30.4
Moderate	40.7
Severe	16.5
None	0.5
Chronic inflammation	
Mild	39
Moderate	40.4
Severe	20.1
Lymphoid aggregates	
Absent	22.5
Present	77.5
Lymphoid follicles	
Absent	54.6
Present	45.4

(76.2%), moderate (89.1%) and severe (86.1%) *H. pylori*-positive patients ($p=0.037$, $p=0.001$, $p=0.002$; $p<0.05$, respectively). The rate of antral nodularity was statistically higher in mild (12.4%), moderate (37.2%) and severe (46.8%) *H. pylori*-positive patients compared to *H. pylori* negative patients (4.9%) ($p=0.001$; $p<0.05$) (Table 4).

TABLE 3. Grading of *H. pylori* positivity and the Updated Sydney System criteria comparison

	<i>Helicobacter pylori</i>								Total		p
	None		Mild		Moderate		Severe		n	%	
	n	%	n	%	n	%	n	%			
Neutrophilic activity											
None	319	68.3	51	24.3	1	0.8	0	0	371	41.9	0.001¹
Mild	136	29.1	116	55.2	11	8.5	0	0	263	29.7	
Moderate	8	1.7	38	18.1	97	75.2	35	44.3	178	20.1	
Severe	4	0.9	5	2.4	20	15.5	44	55.7	73	8.3	
Chronic inflammation											
None	33	7.1	2	0.9	0	0	0	0	35	4	0.001¹
Mild	400	85.7	151	71.9	8	6.2	4	5.1	563	63.6	
Moderate	30	6.4	47	22.4	94	72.9	28	35.4	199	22.5	
Severe	4	0.8	10	4.8	27	20.9	47	59.5	88	9.9	
Lymphoid aggregates											
Absent	222	47.5	67	31.9	21	16.3	6	7.6	316	35.7	0.001²
Present	245	52.5	143	68.1	108	83.7	73	92.4	569	64.3	
Lymphoid follicle											
Absent	419	89.7	155	73.8	51	39.5	22	27.8	647	73.1	0.001²
Present	48	10.3	55	26.2	78	60.5	57	72.2	238	26.9	
Atrophy											
Absent	465	99.6	209	99.5	129	100	78	98.7	881	99.5	0.488 ¹
Present	2	0.4	1	0.5	0	0	1	1.3	4	0.5	
Intestinal metaplasia											
Absent	478	99.8	202	96.2	126	97.7	75	94.9	881	99.5	0.503 ¹
Present	2	0.4	1	0.5	0	0	1	1.3	4	0.5	

1: Fisher Freeman Halton Test; 2: Chi-square Test; *: p<0.05.

DISCUSSION

H. pylori is the most common chronic bacterial infection in developing countries [7]. The prevalence of the disease is 90% in developing countries and higher than the developed countries (40%), except in Japan [6, 8]. Generally, in the first five years of life, *H. pylori* infection is presented more than half of the world's population [9, 10]. The proportion of *H. pylori* infection during adulthood is over 90% in developing countries, whereas the *H. pylori* infection rate is from 30% to 50% of children in the same countries [11]. The prevalence of the infection is low (1.2–12.2%) in children of developed countries [12]. In our study, we found the prevalence of *H. pylori* in children as 47.2%, similar to developing countries.

The prevalence of *H. pylori* infection may differ from developing countries to other developing countries.

Highest prevalence belongs to Bangladeshi children (80%) and after Indian children (57%) [13, 14]. Prevalence of *H. pylori* in Turkey is different in many studies. Ozden et al. [5] evaluated the patients aged between 7–14 years in 1990 and 2000 separately by serological tests. They found the prevalence of *H. pylori* infection as 78.5% in 1990, and as 66.3% in 2000. The conclusion was *H. pylori* infection has decreased over 10 years. Yilmaz et al. [15] found the seropositivity of *H. pylori* as 43.9% of 346 children, and Selimoglu et al. [16] reported the seropositivity of *H. pylori* as 64.4% in 466 children aged 6–17 years in eastern Turkey. These findings suggest that the results can be different even in the same country.

In eastern Turkey, the prevalence of *H. pylori* is found 30.7% with culture, 66.3% with PCR and 63.2% with a histological examination in children from ages 4 to 18

TABLE 4. Grading of *H. pylori* positivity and endoscopic findings/preliminary diagnosis comparison

	<i>Helicobacter pylori</i>								Total		p
	None		Mild		Moderate		Severe		n	%	
	n	%	n	%	n	%	n	%			
Endoscopic findings											
Erythematous pangastritis	319	68.3	160	76.2	115	89.1	68	86.1	662	74.8	0.001 ¹
Antral nodularity	23	4.9	26	12.4	48	37.2	37	46.8	134	15.1	0.001 ¹
Erosion/ulcer on gastric mucosa	10	2.1	5	2.4	2	1.6	2	2.5	19	2.1	0.955 ²
Preliminary diagnosis											
Celiac	36	7.7	15	7.1	3	2.3	3	3.8	57	6.4	0.114 ²
Esophagitis	33	7.1	13	6.2	3	2.3	6	7.6	55	6.2	0.248 ²
Duodenitis	14	3	4	1.9	7	5.5	3	3.8	28	3.2	0.328 ²
Inflammatory bowel disease	2	0.4	2	1	3	2.3	0	0	7	0.8	0.148 ²

1: Chi-square Test; 2: Fisher Freeman Halton Test; *: p<0.05.

years From March 2011 to September 2012 by Ozbey et al. [17]. In that study, patients 13 to 18 years old show the highest prevalence (75.8%), while 4 to 6 years old have the lowest prevalence (40%). In our study, *H. pylori* was presented in all age groups, but children aged 11–15 years, had the highest rate.

Ozbey et al. [17] analyzed *H. pylori* via culture, polymerase chain reaction and histopathological diagnosis in 101 children in 2015. They observed antral nodularity in 55 children (54.5%) of which 76.4% were *H. pylori*-positive. Relationship between *H. pylori* and endoscopic nodular gastritis was shown by Bahu et al. also [18]. 27% of their patients was positive for *H. Pylori*, and 22 of 50 children, 44% of all patients, had antral nodularity. Their rate of antral nodularity in *H. pylori* positive patients was lower compared to the rate of Dogan et al. [19] (73.6% antral nodularity), and Ozcay et al. [20] (64.7% antral nodularity). Association of *H. pylori* and antral nodularity was higher, as 98.5% in a Japanese study [21]. Peptic ulcer prevalence differs in children from country to country between 1.8% and 19.5% [20, 22]. The prevalence of peptic ulcer was 8.6% in European children in 2005 and 13.2% in Turkish children in 2011 [23, 24]. In our study, we observed that erythematous pangastritis and antral nodularity were the most common endoscopic findings, and the relation with *H. pylori* infection was statistically significant.

Two techniques for detecting *H. pylori* infection can be used. These techniques are grouped as noninvasive

and invasive tests. They are microbiological culture, rapid urease test (RUT), histological test and polymerase chain reaction (PCR). For histological examination, esophagogastroduodenoscopy (EGD) and biopsies are necessary [7, 25]. Histological testing has an advantage of evaluating pathologic changes, such as the severity of chronic inflammation, the grade of atrophy, intestinal metaplasia, and malignancy [26, 27]. However, we should keep in mind that using some medications, such as proton pump inhibitors (PPIs), antibiotics and bismuth, may decrease the sensitivity and specificity of the histological test [26]. Cohen et al. [28] studied 79 gastric biopsies from pediatric patients. Thirty-five biopsies were mild for neutrophilic infiltration, and 38 biopsies were mild for mononuclear infiltrates. Langner et al. evaluated 132 biopsies from symptomatic children infected with *H. pylori*. In their study, mononuclear infiltrate was observed in 98.5%, and polymorphonuclear cell infiltrate was observed in 93.9% of the biopsies [29, 30]. Lymphoid aggregates were observed 13.6% and lymphoid follicles were observed 31.8% of the patients in the study [29]. In our study, *H. pylori* negativity correlated with the absence of neutrophilic activity and chronic inflammation. Mild *H. pylori* positivity was related with a mild degree of neutrophilic activity and chronic inflammation as well. Lymphoid aggregates and lymphoid follicles were present in *H. pylori* infected children. Especially, moderate and severe *H. pylori* infection correlated with the presence of lymphoid aggregates and lymphoid follicles.

The ratio of gastric atrophy and intestinal metaplasia influences from geography/genetics and environmental factors [17]. In one study, intestinal metaplasia was found in four children, who are infected by *H. pylori*. In two of them, atrophy was present [30]. In one Japanese study, 4.6% of children had both intestinal metaplasia and *H. pylori* positivity [31]. The proportion of gastric atrophy was high in Columbian children (16%) and also higher in Japanese children (51.9%) [31, 32]. In our study, there was no correlation between intestinal metaplasia, atrophy, and *H. pylori*.

In conclusion, it can be seen that the studies conducted concerning *H. pylori* for pediatric patients in Turkey are generally from eastern regions, while mid- and western regions have relatively little research for the topic. Since this paper is western-based, it can be said that it will be an important contribution to the literature. Besides that, in completed research where serological tests are widely used, to our knowledge, there is no Turkish research that evaluates *H. Pylori* positivity with histopathological evidences to our knowledge. Based on this, this study can be seen as an initial step that will lead to further investigations. During our research, we found that the results of *H. pylori* positivity and endoscopic findings are similar to the ratios in the mid- and eastern regions of Turkey. When the results are compared to worldwide studies, similarities to developing countries have been noticed. In addition, it is also observed that early detection of *H. pylori* infection among children is important and may reduce the complications later in life.

Ethics Committee Approval: The Umraniye Training and Research Hospital Clinical Research Ethics Committee granted approval for this study (date: 23.10.2019, number: 205).

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

Authorship Contributions: Concept – BCG, HNI, MA, CC, NG, EZ; Design – BCG, HNI, MA, CC, NG, EZ; Supervision – BCG, HNI, MA, CC, NG, EZ; Materials – BCG, HNI, MA, CC, NG; Data collection and/or processing – BCG, CC, NG; Analysis and/or interpretation – BCG, HNI, MA; Literature review – BCG, EZ; Writing – BCG, EZ; Critical review – BCG, EZ.

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