DOI: 10.4274/buchd.galenos.2023.75875
J Dr Behcet Uz Child Hosp 2023;13(2):101-107

Original Article

Complaints, Endoscopic and Histopathological Findings in Children with *Helicobacter pylori* Infection: Are There Any Correlations with Each Other?

Helicobacter pylori Enfeksiyonu Olan Çocuklarda Şikayetler, Endoskopik ve Histopatolojik Bulgular: Birbirleriyle Korelasyon Var Mı?

Günsel Kutluk[1], Esra Polat[2], Muharrem Çiçek[3], Tuğçe Kalaycı Oral[3], Şeyma Murtezaoğlu Karatekin[3], Nermin Gündüz[4]

[1]University of Health Sciences Turkey, Başakşehir Çam and Sakura City Hospital, Clinic of Pediatric Gastroenterology, İstanbul, Turkey
[2]University of Health Sciences Turkey, Şehit Prof. Dr. İlhan Varank Sancaktepe Training and Research Hospital, Clinic of Pediatric Gastroenterology, İstanbul, Turkey
[3]University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospital, Clinic of Pediatrics, İstanbul, Turkey
[4]University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospital, Clinic of Pathology, İstanbul, Turkey

ABSTRACT

Objective: There is no significant clinical manifestations indicating *Helicobacter pylori* (*H. pylori*) infection in pediatric population. In this study, the most common complaints, endoscopic and histopathological findings in children with *H. pylori* infection were evaluated and their correlation with each other was explicated.

Method: Patients between 3-18 years, who had documented *H. pylori* infection, were enrolled in this study. Gastric biopsies were taken in all patients for rapid urease test (RUT) and histopathological examination, activity of gastritis, chronic inflammation, and Sydney classification was used to evaluate intensity of *H. pylori*, grade of atrophy, and intestinal metaplasia. Demographic characteristics, complaints, endoscopic findings and Sydney scores of the patients were recorded.

Results: A total of 339 patients (183 females) were enrolled in the study. The most common complaints were dyspepsia and epigastric pain. Ninety percent of the patients had antral pathology, including antral nodularity in 78% of the cases. Relation between dyspepsia, epigastric pain, and antral nodularity was found to be statistically significant. In histopathological examination, intensity of *H. pylori* is found to be increasing with age. RUT was positive in 89.4% of the patients and relation between RUT results and the intensity of *H. pylori* was statistically significant. Highly significant correlations were detected between macroscopic changes in the antrum, the intensity of *H. pylori* and gastritis activity ($p \leq 0.0001$, $p=0.01$, respectively).

Conclusion: The most common complaints of children with *H. pylori* infection were epigastric pain and dyspepsia. There were significant relations with these complaints, antral macroscopic changes and intensity of *H. pylori*, which increases with age. As a result, dyspepsia and epigastric pain are related with antral changes. Considering that antral changes are also associated with *H. pylori* intensity, gastritis activity and chronic inflammation, early eradication of the *H. pylori* infection can be recommended to prevent long-term complications in children with *H. pylori* infection.

Keywords: Children, endoscopic findings, *Helicobacter pylori*, histopathological findings

ÖZ

Amaç: Pediatrik popülasyonda *Helicobacter pylori* (*H. pylori*) enfeksiyonunu gösteren önemli bir klinik durum yoktur. Bu çalışmada, *H. pylori* enfeksiyonu olan çocuklarda en sık görülen şikayetler, endoskopik ve histopatolojik bulgular değerlendirilmiş ve birbirleri ile korelasyonu ortaya konmuştur.

Yöntem: Bu çalışmaya 3-18 yaş arası, belgelenmiş *H. pylori* enfeksiyonu olan hastalar alındı. Tüm hastalardan hızlı üreaz testi (RUT) ve histopatolojik inceleme için mide biyopsisi alındı. *H. pylori* yoğunluğunu, gastrit aktivitesini, kronik enflamasyonu, atrofiyi ve intestinal metaplaziyi değerlendirmek için Sydney sınıflandırması kullanıldı. Hastaların demografik özellikleri, şikayetleri, endoskopik bulguları ve Sydney skorları kaydedildi.

Bulgular: Çalışmaya toplam 339 hasta (183 kadın) alındı. En sık şikayetler dispepsi ve epigastrik ağrı idi. Hastaların %90'ında antral patoloji mevcuttu ve bunların %78'i nodülarite idi. Dispepsi, epigastrik ağrı ve antral nodülarite arasındaki ilişki istatistiksel olarak anlamlı bulunmuştur. Histopatolojik incelemede yaşla birlikte *H. pylori* yoğunluğunun arttığı tespit edildi. Hastaların %89,4'ünde RUT pozitifti ve RUT ile *H. pylori* şiddeti arasındaki ilişki

Received: 23.08.2022
Accepted: 19.02.2023

Corresponding Author
Günsel Kutluk,
University of Health Sciences Turkey, Başakşehir Çam and Sakura City Hospital, Clinic of Pediatric Gastroenterology, İstanbul, Turkey
gekutluk@gmail.com
ORCID: 0000-0002-9719-4352

Cite as: Kutluk G, Polat E, Çiçek M, Kalaycı Oral T, Murtezaoğlu Karatekin Ş, Gündüz N. Complaints, Endoscopic and Histopathological Findings in Children with *Helicobacter pylori* Infection: Are There Any Correlations with Each Other?. J Dr Behcet Uz Child Hosp. 2023;13(2):101-107

istatistiksel olarak anlamlıydı. Antrumdaki makroskopik değişiklikler ile *H. pylori* yoğunluğu ve gastrit aktivitesi arasındaki ilişkiler oldukça anlamlıydı (sırasıyla p≤0,0001, p=0,01).

Sonuç: *H. pylori* enfeksiyonu olan çocukların en sık şikayetleri epigastrik ağrı ve dispepsi idi. Bu şikayetler, antral makroskopik değişiklikler ve *H. pylori*'nin şiddeti ile anlamlı ilişkiler vardı ve yaşla birlikte *H. pylori*'nin şiddeti artmaktaydı. Bu şikayetler antral değişikliklerle ilişkili olduğundan ve bu değişiklikler gastrit aktivitesi, kronik enflamasyon ve artan *H. pylori* yoğunluğu ile ilişkili olduğundan, bu çocuklarda uzun dönemli komplikasyonlardan korunmak için erken eradikasyon önerilebilir.

Anahtar kelimeler: Çocuklar, endoskopik bulgular, *Helicobacter pylori*, histopatolojik bulgular

INTRODUCTION

Helicobacter pylori (*H. pylori*) is a microorganism associated with serious gastric diseases such as chronic gastritis, peptic ulcer, gastric mucosa-associated lymphoid tissue (MALT) lymphoma, adenocarcinoma of the stomach and considered as a great health problem especially in developing countries due to its high prevalence rates[1,2]. Bacteria are commonly acquired in the first years of life by inter-family transmittance and cause a lifelong chronic infection[3,4]. The prevalence of *H. pylori* was 20% to 79% in children in cohort studies using non-invasive direct detection methods and prevalence estimates appear to increase with age and in developing countries[5]. *H. pylori* infection may be asymptomatic in most of the patients in pediatric population[6]. Recent studies have shown that children infected with *H. pylori* have gastrointestinal complaints such as, chronic or recurrent abdominal pain, epigastric pain, anorexia, weight loss, dyspepsia, vomiting, gastrointestinal bleeding demonstrated as hematemesis or melena[5,7]. Although recurrent abdominal pain is a common symptom among children at school age, it cannot definitely be associated with *H. pylori* infection[6].

Although *H. pylori* infection commonly causes diffuse antral gastritis and pangastritis in pediatric age group, endoscopic findings may be normal in 50% of the patients, Nonetheless, antral nodularity, believed to appear due to lymphoid hyperplasia caused by *H. pylori* infection, is more commonly seen as a specific endoscopic finding[8]. Guarner et al.[9] reported in their 10 years long compilation of diagnostic methods, that endoscopy with histopathological assessment is the only and the most effective diagnostic method for *H. pylori* infection and its associated lesions. Although some studies have shown that *H. pylori* infection may not alter the normal histopathology in children, children colonized with *H. pylori* most commonly develop chronic gastritis[8,10]. Histological findings include infiltration of gastric mucosa with domination of plasma cells and lymphocyte. The organism can be identified with Giemsa, Diff-Quick, periodic acid Schiff-Alcian blue or hematoxylin and eosin dyes[11,12]. In Sydney classification *H. pylori* gastritis is defined, and the intensity of *H. pylori,* gastric activity, and severity of inflammation, antral atrophy and intestinal metaplasia are graded[12]. In this study, the most common complaints, endoscopic and histopathological findings in children with *H. pylori* infection were evaluated and their correlation with each other was explicated.

MATERIALS and METHODS

The study was conducted according to the principles of World Medical Association Declaration of Helsinki (ethical principles for medical research involving human subjects) and approved by the University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospitals Clinical Research Ethics Committee (decision no: 4, date: 22.08.2014). Children between 3-18 years of age, applied to pediatric gastroenterology outpatient clinic within the last two years who had not used any antibiotics, non-steroid anti-inflammatory drugs or gastric acid inhibitors within the last three months and underwent upper gastrointestinal tract endoscopy due to different complaints including dyspepsia, epigastric pain, reflux symptoms, growth retardation, malabsorption findings, resistant iron and/or vitamin B12 deficiency and suspicion of gastrointestinal bleeding were enrolled in the study. Patients' informed consent was obtained from their parents and under the deep sedation applied by anesthesiologist, esophagogastroduodenoscopy was performed with age- appropriate size Fujinon video endoscope (Alternup Medical, France). Macroscopic findings seen at esophagus, stomach or duodenum were noted by performing endoscopist.

During the endoscopy procedure, four tissue biopsy specimens were obtained both from gastric corpus and antrum. One biopsy specimen from both sites were used for rapid urease test (RUT), other three biopsy specimens from each region were sent to pathology laboratory in 10% neutral buffered formalin solution. Tissue samples were prepared in the laboratory and stained with hematoxylin-eosin and May Guenwald-Giemsa staining solutions and evaluated by an experienced specialist. Findings of *H. pylori* gastritis revealed in histopathologic evaluation were scored by Sydney classification[12]. Intensity of *H. pylori,* gastric activity, severity of inflammation,

antral atrophy, and intestinal metaplasia were graded based on Sydney classification system. Accordingly, 1) intensity of *H. pylori* defined by the percentage of bacteria on mucosa, 2) gastric activity defined by the quantity of polymorphonuclear leukocytes, 3) severity of inflammation indicated by the increase in the number of mononuclear cells (lymphocytes, plasma cells, monocytes, mast cells, and eosinophils) on the mucosa were graded as absent, mild (grade 1), moderate (grade 2), and severe (grade 3). Intestinal metaplasia was graded as absent, complete (type 1; 1+), incomplete (type 2 and type 3; 2+) and all findings were recorded[13].

Statistical Analysis

Statistical analyses of the study data were performed by using SPSS (Statistical Package for Social Sciences, Chicago, IL, USA) for Windows v.16.0 program. Besides supplemental statistical methods as frequency, percentage, mean and standard deviation, Student's t-test was used for group median comparison of quantitative data and chi-square test and Fisher's Exact test were used for comparison of qualitative data. Results were evaluated within 95% confidence interval and at a statistical significance level of $p<0.05$.

RESULTS

A total of 339 patients, 183 girls (54%) and 156 boys (46%), who underwent endoscopy for any gastrointestinal complaint and were diagnosed with *H. pylori* infection, were included in the study. Mean age of cases was 12.18±3.51 years (range: 3-17.7 years).

Epigastric pain was the most common complaint in 61.9% of the cases. Dyspeptic symptoms like bloating, early satiety, abdominal distension, and belching were seen in 45.1% of the patients. Both of these complaints were present in 42% of the patients. The other commonly seen symptoms were failure to thrive in 34.5%, reflux symptoms as nausea, vomiting, regurgitation, retrosternal pain, and swallowing difficulty in 21.2%, anemia in 20.4% of the patients. Also 14% of the patients had other complaints such as loss of appetite and diarrhea (Figure 1).

In endoscopic evaluation, esophageal findings were in normal physiological ranges in 182 (53.6%) out of 339 patients. Hyperemia was present in 152 (44.8%) and erosion in 53 (15.6%) patients. Nodularity and ulcer were other esophageal findings. Gastric corpus was normal in appearance in 198 patients (58.4%). Hyperemia was present in 143 (42.2%) and antral nodularity in 36 (10.6%) patients. All of the patients with antral nodularity also had hyperemia.

Antral pathology was present in 308 (90.8%) of 339, hyperemia in 284 (83.7%), gastric erosion in 16 (4.7%), and gastric ulcer in 4 (1.2%) patients. Antral nodularity, mostly accepted as a finding of *H. pylori* infection, was present in 268 (79%) patients. Hyperemia and antral nodularity were seen together in 246 (72.5%) patients. Duodenum was found to be normal in 76% (258) of the patients. Nodularity was present in 10.3% (35) and erosion in 9% (30) patients. Ulcer was found in 24 (7.1%) patients and 4 of these patients had both erosion and ulcer.

Biopsies taken from gastric corpus and antral region have been evaluated histopathologically and *H. pylori* gastritis was scored by Sydney classification. In 74% (251) of the patients lymphoid aggregates or follicles were detected. Lymphoid aggregates were found in 134 (53.3%) and lymphoid follicles in 117 (46.6%) patients. In 51 of these patients both lymphoid aggregates and lymphoid follicles were present. Histopathological findings, especially intensity of *H. pylori* was found to increase with age. When patients were divided into three groups according to age, intensity of *H. pylori* was mild in 83% of 0-6 years group, decreased to 28.2% in 6-12 years group and it was 20.6% in patients aged 12 years and over. Severe *H. pylori* intensity was found to be 17% in 0-6 years group, 30.8% in 6-12 years group and 33.8% in patients aged 12 years and over. Intensity of *H. pylori* differed statistically significantly between age groups ($p=0.021$).

RUT was positive in 303 (89.4%) and negative in 36 (10.6%) patients. A strong statistically significant relationship existed between positive RUT and intensity of *H. pylori* ($p<0.001$).

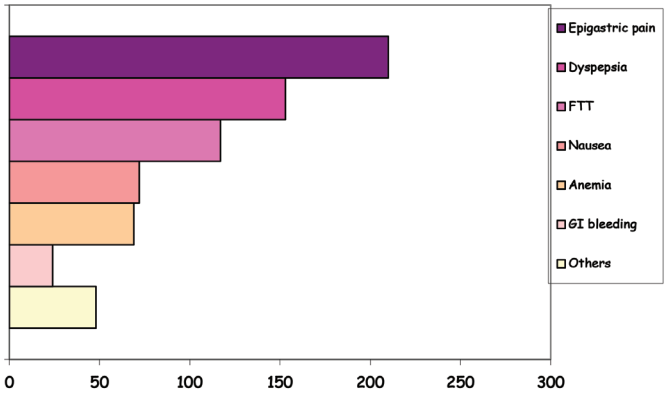

Figure 1. Complaints of patients

GI: Gastrointestinal, FTT: Failure to thrive

Intestinal metaplasia was seen in 8.2% and gastric atrophy in 6.8% of the patients in the study group, without any statistically significant correlation between gastric atrophy or intestinal metaplasia and *H. pylori* intensity, endoscopic findings and complaints.

Complaints and their relations with endoscopic findings were assessed, and extremely, and statistically significant correlations were detected between epigastric pain and antral pathologies (hyperemia, nodularity, erosion and ulcer) (p≤0.0001) (Table 1). There was no significant relationship between epigastric pain and other endoscopic findings. There was also extremely significant relationship between dyspeptic complaints and antral nodularity (p≤0.0001) (Table 2). We did not find any relation between other complaints and endoscopic findings.

When the pathologic or normal appearance of the antrum and histopathological findings were compared; there was statistically significant difference between the group of patients with normal antrum and antral pathologies (hyperemia and/or nodularity, erosion/ulcer); and *H. pylori* intensity and activity (p≤0.0001 and p=0.01, respectively) (Table 3). The relationship between antral nodularity observed in endoscopy and *H. pylori* intensity and chronic inflammation scores was statistically significant (p=0.001 and p=0.001, respectively) (Table 3). The relationship between lymphoid aggregates or lymphoid follicles and antral nodularity was not statistically significant.

Table 1. Association between epigastric pain and antral pathologies

Epigastric pain	Antral pathologies (hyperemia and/or nodularity)		F x^2
	+	-	
+	201 (59.3%)	9 (2.7%)	p≤0.0001
-	104 (30.7%)	25 (7.3%)	
Total	305 (90%)	34 (10%)	

F x^2: Fisher's Exact test

Table 2. Association between dyspepsia and antral nodularity

Dyspepsia	Antral nodularity		F x^2
	+	-	
+	135 (39.8%)	18 (5.3%)	p≤0.0001
-	129 (38.1%)	57 (16.8%)	
Total	264 (77.9%)	75 (22.1%)	

F x^2: Fisher's Exact test

Table 3. Association between antral endoscopic and histopathological findings

Histo-pathological findings	Antral endoscopic findings (hyperemia and/or nodularity)	Sydney scores				
		0	1	2	3	X^2
***H. pylori* intensity**	+	0 (0%)	72 (21.2%)	140 (41.3%)	93 (27.4%)	p≤0.0001
	-	0 (0%)	18 (5.3%)	1 (0.3%)	15 (4.4%)	
Activity	+	1 (0.3%)	159 (46.9%)	126 (37.2%)	18 (5.3%)	p=0.01
	-	2 (0.6%)	15 (4.4%)	15 (4.4%)	3 (0.9%)	
	Antral nodularity	**Sydney scores**				
		0	**1**	**2**	**3**	**X^2**
***H. pylori* intensity**	+	0 (0%)	54 (15.9%)	120 (35.4%)	90 (26.5%)	p=0.0001
	_	0 (0%)	36 (10.6%)	21 (6.2%)	18 (5.3%)	
Inflammation	+	2 (0.6%)	64 (19.5%)	150 (44.2%)	46 (13.5%)	p=0.001
	_	1 (0.3%)	32 (9.7%)	42 (12.4%)	2 (0.5%)	

0= Negative, 1= Mild, 2= Moderate, 3= Severe, X^2: Chi-square test

DISCUSSION

H. pylori infection is one of the most commonly seen infections in the world, thus it is a great public health problem for developing countries. It has been accepted that nearly half of the world's population will be infected with *H. pylori* sometime during their life[5,14] *H. pylori* infection is seen more commonly in some age and ethnic groups but without any gender predominance[15]. In our study, 54% of female and 46% of male patients were infected with *H. pylori* without any significant gender difference.

Studies have shown that the children acquired the bacteria mostly by inter-familial transmission during early childhood, prevalence of the disease increased with age and it may become a lifelong infection if *H. pylori* infection is not eradicated[2,3,15]. Ertem et al.[15] reported that the rate of *H. pylori* infection is 18.2% in children under 4 years of age, and its prevalence increases with age even up to 65% in adolescence group in our country. Similar to these findings, in our study on pediatric patients infected with *H. pylori* between the years of 3 and 18, only 5.5% of the patients were under the age of 6 and 60% were above the age of 12.

H. pylori infection in pediatric population has no characteristic clinical manifestations, and the infection is mostly asymptomatic. On the other hand, gastrointestinal symptoms such as epigastric pain, dyspeptic symptoms (early satiety, bloating, abdominal distension and belching), nausea, lack of appetite, weight loss, treatment-resistance iron deficiency anemia, upper gastrointestinal bleedings described as hematemesis or melena may be manifestations of *H. pylori* infection and may be also associated with organic diseases such as peptic ulcer. It is recommended to perform esophagogastroduodenoscopy to those patients[2,7,16]. In our study, the most common complaint, in correlation with literature findings, was epigastric pain (61.9%), and dyspepsia (45.1%) at indicated rates. Failure to thrive, reflux symptoms like nausea, vomiting, regurgitation, retrosternal pain, dysphagia and anemia were the other common complaints.

In a pediatric study reviewing topographic settlement of *H. pylori* in stomach, bacteria colonization and gastritis findings were specifically observed in antral region[4,17]. In our study, antral pathology was detected in 90% of the patients, where *H. pylori* is localized mostly. Especially in patients with epigastric pain, antral pathology was observed at higher rates during endoscopic examination. Antral nodularity have been reported at varying rates in the study of Koh et al.[18] (50.6%; total n=328) and, Tomić et al.[19] (67.5%). In our study antral nodularity was found in 77.9% of the patients which was at a higher in patients undergoing endoscopy with dyspeptic complaints.

Gastric ulcer in children usually occurs due to etiologic factors unrelated to *H. pylori* and *H. pylori* associated ulcers are seen very rarely[10]. In our patient group, gastric erosion was present in 16 (4.7%) patients and only four patients (1.2%) had gastric ulcer. On the other hand, *H. pylori* infection is the primary etiologic factor in bulbar and duodenal ulcers in pediatric age group. In the study of Rick et al.[20] duodenal ulcer was present in 11 patients out of 51 and all of these patients had *H. pylori* infection. In our study population of 339 patients, 30 (9%) had gastric erosion and 24 (7.1%) had bulbar or duodenal ulcer.

Sensitivity and specificity of RUT in the detection of *H. pylori* in gastric mucosa were found to be 83.4% and 99%, respectively[21]. Madani et al.[22] found that positive RUT correlated with *H. pylori* intensity in gastric mucosa and activity of gastritis. In our study, RUT was positive in 89.4% and negative in 10.6% of the patients and the relation between the positivity of the test and intensity of *H. pylori* was statistically significant.

Histopathologic features of *H. pylori* gastritis were scored by the Sydney classification[12] based on intensity of bacteria, neutrophil activity showing active gastritis, chronic mononuclear inflammation, glandular atrophy and intestinal metaplasia. Tutar et al.[8] showed that *H. pylori* infection may also appear with normal gastric histopathology, but in our study almost all of the patients had *H. pylori*-related chronic active gastritis except three patients had not active gastritis; and about half of our patients had moderate gastritis and chronic inflammation. In the study of Kamada et al.[23] with young adult patients, mostly moderate activity of gastritis and chronic inflammation were detected as in our study (67.9%, and 46.4%, respectively).

In our study group, when all patients were evaluated independent of age, *H. pylori* intensity was mild in 26.5%, moderate in 41.6%, and severe in 31.9% of the patients. When patients were divided into three age groups and evaluated, 17% of 6 years and below group and 33.8% of 12 and above group had severe (3+) *H. pylori* intensity. This increase with age was found to be significant. These findings also support the study of Domşa et al.[24] which stated that the prevalence of *H. pylori* increased gradually with age.

Atrophic gastritis and intestinal metaplasia are primary histopathologic changes which may lead to gastric cancer in years to come[25]. The relationship

between *H. pylori* infection acquired in childhood and development of gastric cancer in adulthood is still unclear. However, the study by Yörgüç et al.[26] on tissue immune markers have shown that the pathogenicity of *H. pylori* in children is higher than in adults. Although the prevalence of intestinal metaplasia is reportedly very low in pediatric studies[8,18]; according to the findings of Kato et al.[27] atrophic gastritis, a precursor of gastric cancer, is significantly more common in children infected with *H. pylori* compared to the uninfected group. Ethnicity-associated genetic factors, environmental factors like nutritional habits or virulence of *H. pylori* seen in some geographic regions may be the reason of high rates of atrophic gastritis especially reported in Far Eastern studies[18,23,27]. In our study group, intestinal metaplasia and gastric atrophy rates were 8.2% and 6.8%, respectively and we could not find any correlation among *H. pylori* intensity, endoscopic findings and complaints.

There are many studies analyzing the coexistence and relation between antral nodular gastritis and *H. pylori* infection in pediatric population[18,27-29]. These studies support the association of antral nodular gastritis with *H. pylori* intensity, increased activity of gastritis and chronic inflammation. Correspondingly, our study has shown that antral nodularity is especially associated with *H. pylori* intensity and chronic inflammation. In addition to these findings, Yang's[30] recent study has also revealed that nodular gastritis may indicate gastric MALT in children with *H. pylori* infection and that the degree of antral nodularity is also correlated with severity of MALT.

In their study, Kato et al.[27] determined that the intensity of *H. pylori* was significantly higher in patients with duodenal ulcer relative to the patients with gastric ulcer. In our study group, only four patients had gastric ulcer and severe (grade 3) *H. pylori* intensity. Besides, gastric activity and inflammation according to Sydney classification system of gastritis 7.1% of the patients had duodenal ulcer and no significant correlation was found between duodenal ulcer and *H. pylori* intensity in this group.

Study Limitations

Based on literature findings, the relation between complaints and histopathologic findings in pediatric or adult age group with *H. pylori* gastritis has not been investigated so far. Although retrospective design and limited number of patients were the limitations of our study; we found some significant correlations between the endoscopic and histopathological findings and the complaints of the patients. According to the findings of our study; epigastric pain was significantly related with antral pathologies such as hyperemia, nodularity, erosion and ulcer. There was also statistically significant relationship between dyspeptic complaints and antral nodularity. Other complaints such as heartburn, failure to thrive, gastrointestinal bleeding or anemia were not correlated with endoscopic findings.

CONCLUSION

Especially in regions with relatively higher *H. pylori* prevalence, children may acquire *H. pylori* infection at an early age and most of them develop gastritis. The most common complaints of these children with *H. pylori* infection are epigastric pain and dyspepsia. According to our findings there is a significant relation with these complaints and morphological changes in antrum such as hyperemia, nodularity, erosion or ulcer. These antral pathologies are also significantly related to *H. pylori* intensity, activity of gastritis and chronic inflammation scores determined at histopathological evaluation.

As a result; since these complaints are related with antral morphological changes and these changes are related with intensity of *H. pylori,* which is increasing with age, early eradication of *H. pylori* infection can be recommended in these children in order to prevent from its long- term complications, such as peptic ulcer, gastric atrophy and even possibly gastric cancer, and MALT lymphoma later in life.

Ethics

Ethics Committee Approval: The study approved by the University of Health Sciences Turkey, Kanuni Sultan Süleyman Training and Research Hospitals Clinical Research Ethics Committee (decision no: 4, date: 22.08.2014).

Informed Consent: Patients' informed consent was obtained.

Peer-review: Externally and internally peer reviewed.

Author Contributions

Surgical and Medical Practices: G.K., E.P., M.Ç., T.K.O., Ş.M.K., N.G., Concept: G.K., E.P., M.Ç., T.K.O., Ş.M.K., N.G., Design: G.K., E.P., M.Ç., T.K.O., Ş.M.K., N.G., Data Collection and/or Processing: G.K., E.P., T.K.O., Ş.M.K., N.G., Analysis or Interpretation: G.K., E.P., T.K.O., Ş.M.K., N.G., Literature Search: G.K., E.P., M.Ç., T.K.O., Ş.M.K., N.G., Writing: G.K., E.P., M.Ç., T.K.O., Ş.M.K., N.G.

Conflict of Interest: The authors have no conflict of interest to declare.

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

REFERENCES

1. Infection with Helicobacter pylori. IARC Monogr Eval Carcinog Risks Hum. 1994;61:177-240.
2. Cho J, Prashar A, Jones NL, Moss SF. Helicobacter pylori Infection. Gastroenterol Clin North Am. 2021;50(2):261-82. doi: 10.1016/j.gtc.2021.02.001.
3. Ashorn M, Miettinen A, Ruuska T, Laippala P, Mäki M. Seroepidemiological study of Helicobacter pylori infection in infancy. Arch Dis Child Fetal Neonatal Ed. 1996;74(2):F141-2. doi: 10.1136/fn.74.2.f141.
4. Lucero Y, Lagomarcino AJ, Torres JP, Roessler P, Mamani N, George S, et al. Corrigendum to 'Corrigendum Helicobacter pylori, clinical, laboratory and noninvasive biomarkers suggestive of gastric damage in healthy school-aged children: a case-control study'. Int J Infect Dis. 2022;122:442. doi: 10.1016/j.ijid.2022.05.063.
5. Zabala Torrres B, Lucero Y, Lagomarcino AJ, Orellana-Manzano A, George S, Torres JP, et al. Review: Prevalence and dynamics of Helicobacter pylori infection during childhood. Helicobacter. 2017;22(5). doi: 10.1111/hel.12399.
6. Tindberg Y, Nyrén O, Blennow M, Granström M. Helicobacter pylori infection and abdominal symptoms among Swedish school children. J Pediatr Gastroenterol Nutr. 2005;41(1):33-8. doi: 10.1097/01.mpg.0000163734.84518.9e.
7. Spee LA, Madderom MB, Pijpers M, van Leeuwen Y, Berger MY. Association between helicobacter pylori and gastrointestinal symptoms in children. Pediatrics. 2010;125(3):e651-69. doi: 10.1542/peds.2010-0941.
8. Tutar E, Ertem D, Kotiloglu Karaa E, Pehlivanoglu E. Endoscopic and histopathologic findings associated with H. pylori infection in very young children. Dig Dis Sci. 2009;54(1):111-7. doi: 10.1007/s10620-008-0334-7.
9. Guarner J, Kalach N, Elitsur Y, Koletzko S. Helicobacter pylori diagnostic tests in children: review of the literature from 1999 to 2009. Eur J Pediatr. 2010;169(1):15-25. doi: 10.1007/s00431-009-1033-x.
10. Drumm B. Helicobacter pylori in the pediatric patient. Gastroenterol Clin North Am. 1993;22(1):169-82.
11. Alkhamiss AS. Evaluation of Better Staining Method among Hematoxylin and Eosin, Giemsa and Periodic Acid Schiff-Alcian Blue for the Detection of Helicobacter pylori in Gastric Biopsies. Malays J Med Sci. 2020;27(5):53-61. doi: 10.21315/mjms2020.27.5.6.
12. Dixon MF, Genta RM, Yardley JH, Correa P. Classification and grading of gastritis. The updated Sydney System. International Workshop on the Histopathology of Gastritis, Houston 1994. Am J Surg Pathol. 1996;20(10):1161-81. doi: 10.1097/00000478-199610000-00001.
13. Filipe MI, Muñoz N, Matko I, Kato I, Pompe-Kirn V, Jutersek A, et al. Intestinal metaplasia types and the risk of gastric cancer: a cohort study in Slovenia. Int J Cancer. 1994;57(3):324-9. doi: 10.1002/ijc.2910570306.
14. Suerbaum S, Michetti P. Helicobacter pylori infection. N Engl J Med. 2002;347(15):1175-86. doi: 10.1056/NEJMra020542.
15. Ertem D, Harmanci H, Pehlivanoğlu E. Helicobacter pylori infection in Turkish preschool and school children: role of socioeconomic factors and breast feeding. Turk J Pediatr. 2003;45(2):114-22.
16. Malfertheiner P, Megraud F, O'Morain CA, Gisbert JP, Kuipers EJ, Axon AT, et al. Management of Helicobacter pylori infection-the Maastricht V/Florence Consensus Report. Gut. 2017;66(1):6-30. doi: 10.1136/gutjnl-2016-312288.
17. Mărginean CO, Cotoi OS, Pitea AM, Mocanu S, Mărginean C. Assessment of the relationship between Helicobacter pylori infection, endoscopic appearance and histological changes of the gastric mucosa in children with gastritis (a single center experience). Rom J Morphol Embryol. 2013;54(3 Suppl):709-15.
18. Koh H, Noh TW, Baek SY, Chung KS. Nodular gastritis and pathologic findings in children and young adults with Helicobacter pylori infection. Yonsei Med J. 2007;48(2):240-6. doi: 10.3349/ymj.2007.48.2.240.
19. Tomić T, Persić M, Rajić B, Tomić Z. Endoscopic features of gastric mucosa in children having pathohistological evidence of Helicobacter pylori infection. Coll Antropol. 2009;33 Suppl 2:53-7.
20. Rick JR, Goldman M, Semino-Mora C, Liu H, Olsen C, Rueda-Pedraza E, et al. In situ expression of cagA and risk of gastroduodenal disease in Helicobacter pylori-infected children. J Pediatr Gastroenterol Nutr. 2010;50(2):167-72. doi: 10.1097/MPG.0b013e3181bab326.
21. Roma-Giannikou E, Roubani A, Sgouras DN, Panayiotou J, van-Vliet C, Polyzos A, et al. Endoscopic tests for the diagnosis of Helicobacter pylori infection in children: Validation of rapid urease test. Helicobacter. 2010;15(3):227-32. doi: 10.1111/j.1523-5378.2010.00756.x.
22. Madani S, Rabah R, Tolia V. Diagnosis of Helicobacter pylori infection from antral biopsies in pediatric patients is urease test that reliable? Dig Dis Sci. 2000;45(6):1233-7. doi: 10.1023/a:1005574608074.
23. Kamada T, Sugiu K, Hata J, Kusunoki H, Hamada H, Kido S, et al. Evaluation of endoscopic and histological findings in Helicobacter pylori-positive Japanese young adults. J Gastroenterol Hepatol. 2006;21(1 Pt 2):258-61. doi: 10.1111/j.1440-1746.2006.04128.x.
24. Domșa AT, Lupușoru R, Gheban D, Șerban R, Borzan CM. Helicobacter pylori Gastritis in Children-The Link between Endoscopy and Histology. J Clin Med. 2020;9(3):784. doi: 10.3390/jcm9030784.
25. Uemura N, Okamoto S, Yamamoto S, Matsumura N, Yamaguchi S, Yamakido M, Tet al. Helicobacter pylori infection and the development of gastric cancer. N Engl J Med. 2001;345(11):784-9. doi: 10.1056/NEJMoa001999.
26. Yörgüç E, Gülerman HF, Kalkan İH, Güven B, Balcı M, Yörgüç MÇ. Comparison of clinical outcomes and FOXP3, IL-17A responses in Helicobacter pylori infection in children versus adults. Helicobacter. 2021;26(3):e12795. doi: 10.1111/hel.12795.
27. Kato S, Nakajima S, Nishino Y, Ozawa K, Minoura T, Konno M, et al. Association between gastric atrophy and Helicobacter pylori infection in Japanese children: a retrospective multicenter study. Dig Dis Sci. 2006;51(1):99-104. doi: 10.1007/s10620-006-3091-5.
28. Jaramillo-Rodríguez Y, Nares-Cisneros J, Martínez-Ordaz VA, Velasco-Rodríguez VM, Márquez FC, Manríquez-Covarrubias LE. Chronic gastritis associated with Helicobacter pylori in Mexican children: histopathological patterns. Pediatr Dev Pathol. 2011;14(2):93-8. doi: 10.2350/09-12-0754-OA.1.
29. Yang HR, Choi HS, Paik JH, Lee HS. Endoscopic and histologic analysis of gastric mucosa-associated lymphoid tissue in children with Helicobacter pylori infection. J Pediatr Gastroenterol Nutr. 2013;57(3):298-304. doi: 10.1097/MPG.0b013e318298020a.
30. Yang HR. Updates on the Diagnosis of Helicobacter pylori Infection in Children: What Are the Differences between Adults and Children? Pediatr Gastroenterol Hepatol Nutr. 2016;19(2):96-103. doi: 10.5223/pghn.2016.19.2.96.