Helicobacter pylori infection and peptic ulcer in eastern Turkish children: is it more common than known?

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***Helicobacter pylori (H. pylori)* infection is mainly acquired in childhood and is frequent in developing countries. The infection is associated with chronic gastritis in all infected children, but peptic ulcer disease develops in a small number of them. In our country, *H. pylori* infection and associated peptic ulcer disease are common. In eastern Turkey, we found peptic ulcer disease in 13.2% of children who underwent endoscopic examination. Peptic ulcers were mostly gastric ulcers and *H. pylori*-positive in the studied population, and most of the children were admitted due to abdominal pain. As there are no well-established criteria leading directly to diagnosis, pediatricians should include *H. pylori* infection and peptic ulcer disease in the differential diagnosis list when evaluating children with abdominal pain, failure to thrive and upper gastrointestinal system bleeding.**

Key words: peptic ulcer disease, Helicobacter pylori, children.

Helicobacter pylori (*H. pylori)* infection is mainly acquired in childhood, and family is the main source of the infection[1]. It mainly occurs among children living in developing countries and in children living in poor socioeconomic circumstances in developed countries. *H. pylori* infection is associated with chronic gastritis in all infected children, but peptic ulcer disease (PUD) develops in a small number of children[2]. Peptic ulcers (PUs) are thought to be uncommon in children when compared with adults[3,4]. Environmental factors are the major defining factors for *H. pylori*-associated PUD. However, recent reports about childhood PUD show that *H. pylori*-negative PUD is increasing[5]. The aim of this study was to describe the prevalence and characteristics of PUD among children in the eastern part of Turkey.

Material and Methods

The records of children admitted to Malatya State Hospital Pediatric Gastroenterology, Hepatology and Nutrition Clinic between November 2007 and January 2010 were evaluated retrospectively. Children admitted with gastrointestinal symptoms were enrolled in this study. *H. pylori* infection was diagnosed when urea breath test (UBT) and histology were positive. All children underwent upper gastrointestinal system endoscopy (UGE) because of abdominal pain, failure to thrive and upper gastrointestinal bleeding. UGE was performed after informed consent was taken from the families. Among patients undergoing endoscopy, macroscopical findings were noted, and antral and/or body biopsies were taken from all cases unexceptionally. Histological diagnosis was made in accordance with the modified Sydney system[6]. Patients with *H. pylori*-positive peptic disease were treated with triple therapy consisting of omeprazole, clarithromycin and amoxicillin for 10 days, and patients with *H. pylori*-negative peptic disease were treated with omeprazole. Follow-up UBT was performed eight weeks after beginning the triple therapy. None of the children in the study used non-steroidal antiinflammatory drugs (NSAIDs), and none was diagnosed with a chronic disease.

Statistical Analysis

Patient demographics were analyzed using the Statistical Package for the Social Sciences (SPSS) 13.0.

Results

A total of 357 children (149 boys, 208 girls) with a mean age of 11.5±2.6 years were included in the study. The major complaints of the children were abdominal pain, epigastric pain, heartburn, pyrosis and/or belching, failure to thrive, and upper gastrointestinal system bleeding. One hundred eighty-six (52.1%) of them had family members with gastrointestinal complaints. All children underwent UGE.

H. pylori status of the children: UBT was performed in 340 children (17 could not do the test due to technical problems), and was negative in 33 children. After Sydney classification, 9 of these children were found to have *H. pylori*-positive gastritis. Among the UBT-positive children, 14 were found to be *H. pylori*-negative with Sydney classification.

The most common symptom was abdominal pain. There were only 4 children with upper gastrointestinal system bleeding, and all of them had nodular gastritis and gastric ulcers with positive *H. pylori*.

The most common finding on endoscopy was nodular gastritis (59.6%). The other endoscopic findings were esophagitis (10.6%), pangastritis (10.6%), flask lower esophageal sphincter (6.4%), and flat duodenal folds (4.2%).

Ulcers were detected in 47 patients (13.2%) (29 girls [61.7%], 18 boys [38.3%]; median age: 14 years, range: 8-17 years). Twenty-seven patients had gastric (57.4%) and 13 had duodenal (27.7%) ulcers, and 7 (14.9%) had both gastric and duodenal ulcers. Among 27 children with gastric ulcers, 23 (85.2%) were *H. pylori*-positive and 4 (14.8%) were *H. pylori*-negative. Of 13 patients with duodenal ulcers, 10 (76.9%) were *H. pylori*-positive and 3 (23.1%) were *H. pylori*- negative. In 7 children having both gastric and duodenal ulcers, 5 (71.4%) were *H. pylori*-positive and 2 (28.6%) were *H. pylori*-negative. *H. pylori*-negative ulcers were seen in 9 (19.1%) children (5 boys, 4 girls). *H. pylori* status of the children and ulcer distribution are shown in Table I and Table II.

All patients with PUD were planned to undergo a follow-up UGE, but only 12 families approved the procedure. The rest of the *H. pylori*-positive ulcer patients were followed with UBT and symptoms. Two patients had normal endoscopic findings, but pathology revealed that *H. pylori* gastritis was not eradicated. Family screening with UBT showed that the mother, father and older sister were *H. pylori*-positive. The family members were consulted to the Gastroenterology Department and the whole family including our patients took *H. pylori* eradication treatment at the same time. The remaining 10 patients undergoing follow-up UGE had normal endoscopic and histological results.

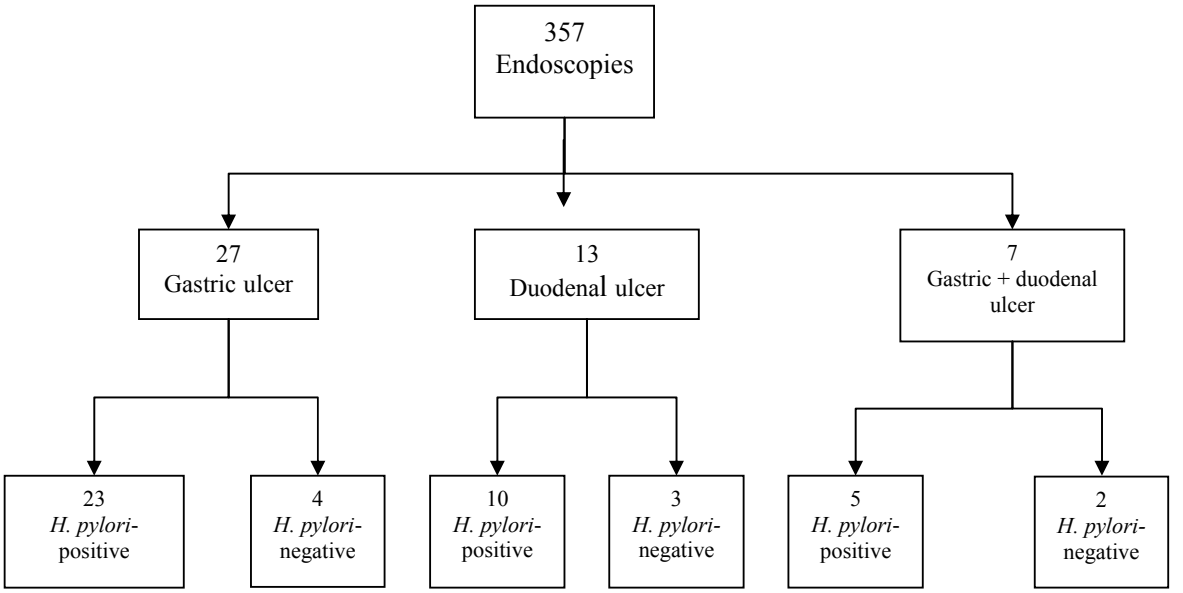
Among *H. pylori*-positive children, all but 4 were eradicated after triple therapy regimen. Thus, a second regimen with additive metronidazole and switch to esomeprazole was administered to the cases with positive follow-up UBT. The follow-up was made by endoscopy in 2 patients and UBT in the other 2 patients. Two children were found to be *H. pylori*-negative with UBT. The 2 children undergoing UGE had no ulcers macroscopically but were not eradicated. *H. pylori*-negative children with PUs were succesfully treated with proton pump inhibitor (PPI) treatment.

Pathological examination showed that 2 children had intestinal metaplasia; both of

Table I. *H. pylori* Status among Children with Peptic Ulcer

	n	Age mean±SD	H. pylori-positive n (%)	H.pylori-negative n (%)
Gastric ulcer	27	12.5±2.4 (8-16)	23 (85.2%)	4 (14.8%)
Duodenal ulcer	13	12.1±2.1 (8-15)	10 (76.9%)	3 (23.1%)
Gastric+duodenal ulcers	7	12.1±2.0 (9-15)	5 (71.4%)	2 (28.6%)

Table II. Overall Results of the Study



them were *H. pylori*-positive and had gastritis as well. Follow-up endoscopies were found to be normal. No patient had gastric atrophy.

There were 47 PUD cases in the study, and 9 of those were *H. pylori*-negative. Among these children, none had celiac disease, inflammatory bowel disease, NSAID or steroid use, or any chronic illness. We suggest these cases remain as idiopathic ulcer.

Discussion

This study revealed a considerably high ratio of PU among children in a developing country. Almost three-fourths of PUD cases were *H. pylori*-positive. The prevalence of *H. pylori* among asymptomatic Japanese children was reported between 7.6% and 19.5%[7]. The prevalence of *H. pylori* in Turkish children is shown to be higher than in industrialized countries. The seroprevalence of *H. pylori* among children was reported to be 53% in western[8] and 64.4% in eastern Turkey[9]. In a recent study, the seroprevalence of *H. pylori* among students in the capital city of Turkey was reported as 78.5% in 1990 and 66.3% in 2000[10]. According to factors such as crowded living, large sibship size and low socioeconomic lifestyles, *H. pylori* infection is highly seen among Turkish children. These factors and results are compatible with the high incidence of *H. pylori*-positive ulcers in our study population.

There are different reports about PUD in children from different parts of the world (Table III)[11-20]. These reports are discussed in this paragraph. The PUD ratio varies between countries from 1.8% to 19.5%[13,16]. Tam et al.[18] analyzed the differences between *H. pylori*-positive and *H. pylori*-negative ulcers among Chinese children. They overviewed 43 primary PU cases retrospectively and observed that boys and older children were more likely to have *H. pylori*-positive ulcers. Ulcer recurrence was more common among the *H. pylori*-negative group. Egbaria et al.[17] retrospectively studied 751 children undergoing UGE. They detected 51 children (6.8%) with ulcer and 118 children (15.7%) with erosions. PUD distribution was 21 gastric (11 *H. pylori*-positive), 26 duodenal (14 *H. pylori*-positive) and 4 gastric+duodenal (3 *H. pylori*-positive). The authors showed that non-*H. pylori* ulcer and erosions were secondary to systemic diseases, and the rest of the group remained idiopathic.

A multicentric European study (PERTH study) provided information on the prevalence of PU in *H. pylori*–infected European children[21]. Among 518 children from different European countries, 12.1% had PUD. This rather high ratio is attributed to the fact that 102 children were added from Russia, where a high prevalence of PU is reported. The highest PUD ratio in children is reported from Japan, as 19.5%[16].

Table III. Studies Reporting Peptic Ulcer in Children

Country, year	No. of endoscopies	Gastric ulcer and ratio	Duodenal ulcer and ratio	Gastric and duodenal ulcer/ ratio	PUD number and ratio	Ref. no
Australia, 1993	227	3	9	0	12 / 5.3%	11
Greece, 2001	2550	10	42		52 / 2.0%	12
USA, 2001	622	3	10		11 / 1.8%	13
Turkey, 2002	324	*	*		8 / 2.5%	14
Saudi Arabia, 2004	521	4	20		24 / 4.6%	15
Japan, 2004	732	43	100	0	143 / 19.5%	16
Israel, 2008	751	21	26	4	51 / 6.8%	17
China, 2009	619	6	37	0	43 / 6.9%	18
Taiwan, 2010	1234	27	40	0	67 / 5.4%	19
USA, 2010	805	8	11	*	19 / NA	20

*: not mentioned

In that study, one-third of patients with PUD had duodenal ulcers. The authors suggested *H. pylori* as the most important causal factor for the development of duodenal ulcer in childhood. In a very recent study made among 51 children, 6 had gastric ulcer and 11 had duodenal ulcers. All children with gastric ulcer and 10 of 11 duodenal ulcer patients were *H. pylori*-positive. *H. pylori* by 16S rDNA and cagA polymerase chain reaction (PCR) was found significantly higher in children with ulcer compared with normal children[20]. In our study, the PUD ratio was 13.2%, and most of children with gastric or duodenal ulcers were *H. pylori*-positive. The non-*H. pylori* ulcer patients in our population did not have chronic systemic diseases or NSAID use. This is not consistent with the other studies explained above.

Nodularity seen endoscopically is a reflection of the presence of lymphoid follicles in the gastric antrum. In a study from Turkey, antral nodularity was detected in 64.7% of symptomatic *H. pylori*-positive children[22]. Bahú Mda et al.[23] reported the specificity of antral nodularity as 98.5% and positive predictive value as 91.5% in the diagnosis of *H. pylori* infection. Antral nodularity was found in 68.3% of the patients undergoing UGE in the present study. The present study is consistent with the notion that the formation of these lymphoid follicles is a specific reaction to *H. pylori* infection in the stomach and that nodular gastritis is the most common presentation of *H. pylori* gastritis in childhood.

There is no established clinical presentation of patients, but most children with PUD have abdominal pain. It is known that in non-ulcer-dyspeptic *H. pylori*-infected children, there is no specific characteristic symptom[24]. In a recent prospective multicentric study from Europe, the frequency of ulcers or erosions among children referred for upper endoscopy was investigated[25]. The most common complaints of the children were epigastric tenderness, pain awakening the child at night, hematemesis, melena, and weight stagnation, so these can be considered as significant risk factors for ulcers or erosions. In the present study, the most common complaint was abdominal pain and failure to thrive.

H. pylori-positive ulcers in children share some features with those in adults - they occur more frequently in older children and in males, and the recurrence rate is low if the infection is eradicated[18]. The present study produced different results, in that the *H. pylori*-positive children were younger and dominantly female and the male/female ratio was 0.88. *H. pylori*-negative ulcers are reported in younger children with a similar male-female prevalence. The female dominance and younger age of *H. pylori*-positive ulcers may be attributed to some factors: a) The mean age range was narrow, so the groups had a close age range, and b) most of the children undergoing UGE were female, which may have had a negative influence on the gender distribution of ulcer diseases.

Large case series of PU were reported from Japan and Israel. Kato et al.[16] and Egbaria et

al.[17] reported 19.5% and 6.8% PUD among 732 and 751 UGEs, respectively. In the presented study, we performed 357 UGEs, and found PUD as 13.2%. The number of patients with erosions was not included in the number of ulcers in our study, which would increase the ratio. Although the number of endoscopies was almost half of both the other studies, the PU prevalence was similar. Accordingly, we may suggest that PUD is more common than in the other countries.

The present study has some limitations. The population studied was not a general pediatric population, but rather patients referred for upper endoscopy to the pediatric gastroenterology division, and most of them had positive UBT results. This may have influenced the high PU ratio. The children who underwent upper endoscopy were generally adolescents and females, so this affects the age and sex distribution. Generally, as children with abdominal pain are referred to our division, this caused the majority of patient complaints as well.

In conclusion, the results of this study indicate a high frequency of PUD among children from a developing country. *H. pylori*-positive ulcers are seen among children in the second decade of their lives. The authors suggest that the high incidence of *H. pylori* infection in Turkey may affect the frequency of PUD. Thus, proper eradication and follow-up are very important in childhood PUD for clinical improvement and preventing long-term complications.

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