

## Helicobacter Pylori Infection: Clinical, Endoscopic and Pathological Findings in Iranian Children

Farzaneh Motamed<sup>1,\*</sup>, Rana Doroudian<sup>2</sup>, Mehri Najafi<sup>1</sup>, Maryam Monajemzade<sup>3</sup>,  
Sayed Mahdi Marashi<sup>4</sup>, Leila Arastoo<sup>2</sup>, Fatemeh Farahmand<sup>1</sup>, Ahmad Khodadad<sup>1</sup>,  
Golamhosein Fallahi<sup>1</sup>

<sup>1</sup>Department of Pediatric Gastroenterology, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran.

<sup>2</sup>Department of Pediatrics, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran.

<sup>3</sup>Department of Pediatric Pathology, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran.

<sup>4</sup>Legal Medicine Research Center, Legal Medicine Organization, Tehran, Iran.

### Abstract

#### **Background:**

Helicobacter pylori (H.pylori) infection has an important role in promoting gastrointestinal disease in human. It may be acquired early in life, particularly in developing countries. The aim of this study is to evaluate the association between H.pylori infection and clinical manifestations in Iranian children.

#### **Materials and Methods:**

In this retrospective, cross-sectional study, H. pylori status was assessed by pathological examination of gastric biopsy in symptomatic children. A total of 266 patients were diagnosed as infected by H. pylori, compared with 268 uninfected patients matched by age and sex. Reported symptoms, endoscopic and pathological findings in the two groups were analyzed using chi-square test. The limit of statistical significance was set at (P<0.05).

#### **Results:**

The prevalence of H. pylori infection in children suffering from gastrointestinal symptoms was 9% and rised with age (54.9% of infected children were older than 8 years old). Recurrent abdominal pain was the most common symptom in 62.5% of infected children. With regard to gastric endoscopy, a statistically significant correlation was observed between antral nodularity and H. pylori Infection (P=0.000). Gastritis was the most common seen pathology (91.5%) with mostly mild (30.9%) or moderate (34.9%) inactive inflammation.

#### **Conclusion:**

This study demonstrated that emphasis on clinical manifestations rather than paraclinical testing is not suitable to predict H. pylori infection. However, existence of antral nodularity can be assigned as an endoscopic sign of infection in children.

**Keywords:** Children, Clinical manifestations, Diagnosis, Helicobacter pylori, Nodularity.

#### **\*Corresponding Author:**

Rana Doroudian, MD, Department of Pediatrics, Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran.

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## Introduction

Helicobacter pylori (H.pylori) is a Gram-negative bacterium that discovered for the first time in (1983) by Warren and Marshall. This bacterium is found in the mucous membrane of gastrointestinal tract and because of the high level of urease activity, it can be survived in the highly acidic environment of the stomach and cause chronic inflammation on mucous membrane (1). (chronic gastritis) H.pylori infection is the most common bacterial infection in human (1-3).

However, the most common age of incidence of H. Pylori it is unknown and the range varies between developed and developing countries (4,5). Though, some studies showed that in developing countries H.pylori is more common and is often seen in lower age (6). The most reliable method for diagnosis of H. pylori is endoscopic biopsy (6). Today, H.pylori has been identified as causative agent for infectious diseases such as chronic gastritis, peptic ulcer, gastric adenocarcinoma, and mucosa-associated lymphoid tissue lymphoma (MALT) (1-8). Various studies have shown that H. pylori eradication is effectively reducing recurrence of peptic ulcer and remissions of MALT lymphoma (7,9,10).

However, it is believed that humans are the only definitive source of H. pylori infection (7). The ways of transmission of infection is still unknown; however, H. pylori was found in dental plaque and saliva. Therefore, fecal –oral or oral - oral transmission is probable (7,9).

Symptoms of H.pylori infection may be appeared by loss of appetite, abdominal pain (at night or with eating), weight loss, pallor, and any other abdominal symptoms (11). However, it should be considered that clinical symptoms in patients with H. pylori can vary in range (12). Antrum gastritis is associated with increased gastric acid secretion, in patients with increased risk for gastro esophageal

reflux disease (GERD) and duodenal ulcer, and both conditions improve with H. pylori eradication. In pangastritis or corpus gastritis associated with increased gastrin level and reduced acid secretion, H.pylori eradication, predisposes patients to GERD by increasing acid secretion (13).

Several studies have been done on children with H. pylori infection all around the world. These studies indicate that the appropriate treatment in children can eradicate gastrointestinal symptoms. According to the fact that most physicians prefer an experimental treatment (eradicating infection before doing further diagnostic investigations in suspected H. pylori patients) (14), and knowing that early diagnosis and treatment can prevent serious complications in these patients, we performed this study to assess demographic characteristics and the association between symptoms and endoscopic and pathologic findings in patients referred to our tertiary Center from (2007-2012) in Iranian population.

## Materials and Methods

In this study, all patients who visited the department or medical center of pediatric gastroenterology clinic from the beginning of 2007 until the end of 2012 were evaluated. The present study has been approved by the ethics committee of Tehran University of Medical Sciences.

In the present study, 3031 patients were evaluated. Data about H. pylori infection was gathered from the results of pathology samples. All information (age, sex, clinical symptoms, laboratory findings, endoscopic findings, pathological findings and other information), were collected by questionnaire. Children of Parents who did not consent to participate in this study, as well as 8 cases who had defects in documentation, were excluded from the study. All collected data was analyzed by SPSS<sub>19</sub>. Quantitative data was reported by Mean  $\pm$  SD and qualitative data was reported by frequency and percentage.

In our study, Chi-square test was used to assess the relationship between qualitative variables and its' comparison. Significance was defined as ( $P < 0.05$ ).

## Results

In this retrospective study, 3031 patients (whom underwent endoscopy for gastrointestinal symptoms), were evaluated. Among these cases, 274 patients had evidence of *H. pylori* infection. The prevalence of *H. pylori* infection in pediatric patients suffering from digestive symptoms was 9%. This study showed the *H. pylori* infection is 1.21 times more common in boys compared to girls. The mean age of diagnosis was  $8.33 \pm 3.22$  (1 to 16 years) and  $7.81 \pm 3.54$  (7 months to 15 years) for girls and boys, respectively, mean age in general was  $7.91 \pm 3.93$  years. Most of boys (40.4%) and girls (46.7 %) with infection of *H. pylori* were 4 to 8 years and 8 to 12 years, respectively. However, this difference was not statistically significant. ( $P = 0.135$ ).

This study showed there is a significant difference in prevalence of infection among different age groups, 45.1% of patients less than or equal to 8 years and 54.9% of patients older than 8 years was infected ( $P = 0.001$ ). The study also showed the risk of gastrointestinal complications in patients were approximately 1.09 times

more in male than female. Abdominal pain was the most common symptom of *H. pylori* infection (62.5%). On the other hand, gastrointestinal bleeding (9.8%), and vomiting (8.3%) and failure to thrive (FTT) (8.7%), anemia (3.4%) and GERD (3%) were seen in this study.

Based on our results, normal esophagus or mild esophagitis were seen in 88.8% of *H. pylori* negative and 83.4% of *H. pylori* positive cases.

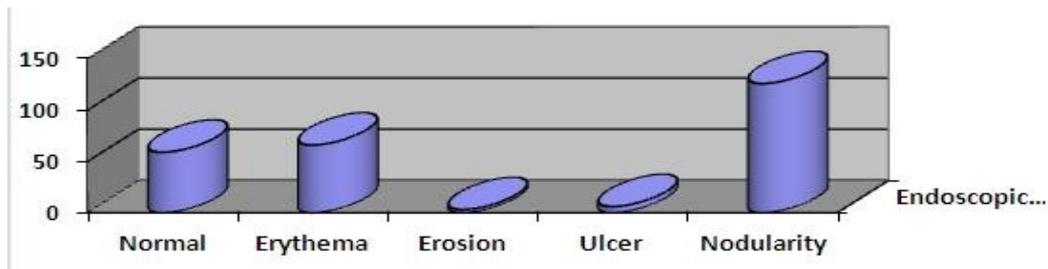
Esophagitis at grade 2 or higher was less than 5% in both groups (*H. pylori* positive and negative) in endoscopic examination.

Most *H. pylori* negative patients had normal stomach endoscopic findings (64.9 %), or mucosal erythema (21.6%) at endoscopic examination. Nodularity was seen in stomach of 10.1% of cases (as the third most common endoscopic finding in *H. pylori* negative patients). On the other hand, among *H. pylori* positive patients, erosion and mucosal ulcers were seen in less than 5 % of the cases. In endoscopic examination, 22.2% of *H. pylori* positive patients had normal findings (or had mucosal erythema (24.8%). The most common stomach endoscopic finding was reported as nodularity (47.4%). ( $P = 0.000$ ). (Table. 1 and Figure 1 illustrate Prevalence of gastric endoscopic findings in patients with *H. pylori* infection).

**Table 1:** Endoscopy of gastric findings between two groups (*Helicobacter pylori* positive and *Helicobacter* negative)

Gastric endoscopic		Helicobacter pylori( <i>H. pylori</i> ) result		Total
		<i>H. pylori</i> -	<i>H. pylori</i> +	
Normal	N	174	59	233
	%	64.9%	22.2%	43.6%
Erythematic membrane	N	58	66	124
	%	21.6%	24.8%	23.2%
Erosion	N	5	3	8
	%	1.9%	1.1%	1.5%
Ulcer	N	3	6	9
	%	1.1%	2.3%	1.7%
Nodularity	N	27	126	153
	%	10.1%	47.4%	28.7%
Sample not exist	N	1	6	7
	%	.4%	2.3%	1.3%
Total	N	268	266	534
	%	100%	100.0%	100.0%

$P = 0.000$  *Helicobacter pylori* (*H. pylori*)



**Fig 1:** Gastric endoscopic findings in patients with H.pylori infection.

In H.pylori negative patients with complains of gastrointestinal problems, pathological examination was normal or showed only mildly inactive gastritis (92.2%). While, pathology finding in H.pylori positive patients was normal or mild inactive gastritis (34.2%), moderate inactive gastritis (30.9%), mild active

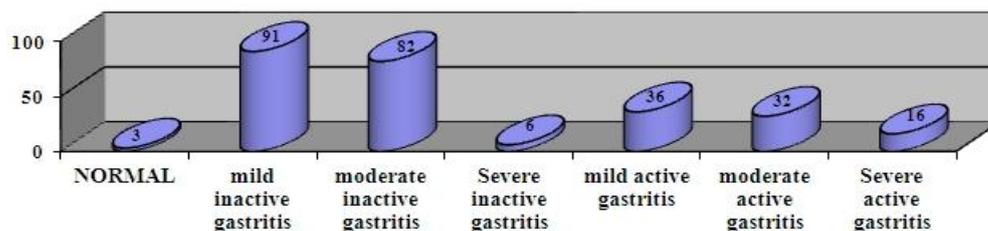
gastritis (13.6 %) or moderate active gastritis (12.1 %).

Severe active gastritis was seen in less than 10 % of H.pylori positive patients, so a significant differences was observed between pathological findings in both groups (P=0.000) (Table and Figure 2).

**Table2:** pathology of gastric findings between the two groups(Helicobacter pyloriP positive and Helicobacter pylori negative)

Pathological findings	H.pylori result		Total	
	H.pylori-	H.pylori+		
Normal	N	94	3	97
	%	35.1%	1.1%	18.2%
Mild inactive gastritis	N	153	91	244
	%	57.1%	34.2%	45.7%
Moderate inactive gastritis	N	14	82	96
	%	5.2%	30.9%	18.0%
Severe inactive gastritis	N	2	6	8
	%	.7%	2.3%	1.5%
Mild active gastritis	N	1	36	37
	%	.4%	13.6%	6.9%
Moderate active gastritis	N	1	32	33
	%	.4%	12.1%	6.2%
Severe active gastritis	N	2	16	18
	%	.7%	6.0%	3.4%
Not exist	N	1	0	1
	%	.4%	.0%	.2%
Total	N	268	266	534
	%	100.0%	100.0%	100.0%

P=0.000 Helicobacter pylori (H.pylori)



**Fig 2:** Gastric pathological findings in patients with H.pylori infection.

Most of patients in both groups had normal duodenal endoscopic finding for H.pylori (96.3 % and 78.6% in H.pylori positive and negative patients, respectively). The most common abnormal finding in patients with H.pylori positive were duodenal ulcer (7.1%), erythema and mucosal erosion (4.5%).

However, the difference in symptoms and duodenal endoscopic findings in H.pylori positive and negative patients wasn't significant ( $P=0.095$ ). According to the pathological findings of deoudenom, normal pathology was seen in 89.6% of patients with negative H.pylori and 80.1 % of positive H.pylori children. Duodenitis was seen in 6.4% of H.pylori positive patients.

Therefore, only one-fifth of patients were hospitalized for further diagnostic evaluation. By blood test results (only available in 129 cases), we found that, 76.2 % of H .pylori positive patients and 78.8% of H.pylori negative patients, had no laboratory sings of anemia ( $P=0.72$ ).

## Discussion

For the first time in 1982, Marshall and Warren reported the associations between H. pylori infection and peptic ulcer (15). there is controversy among researchers about relation between abdominal pain and H.pylori infection (16).

In the present study, 3031 patients were examined by endoscopy and biopsy for gastrointestinal symptoms. Among them, 274 patients (9%) had evidence of H. pylori infection. Jacobson reported the prevalence of H. pylori infection in Canadian children in gastrointestinal endoscopy was reduced from 49% in 1994 to 5% in 2005 (17). Tkachenko and coworkers reported the risk of infection in Russians children and showed that this incidence was reduced from 44% in 1995 to 13% in 2005 (18). Sykora et al estimated H.pylori infection prevalence by positive

ELISA test (Enzyme-linked immunosorbent assay) on stool, 5.5% and 9.4% in urban and rural children, respectively in the Czech Republic (19).

It should be noted that in our study, the diagnosis was made based on the endoscopy findings; which indicates that, some patients did not undergo endoscopy (thus no biopsy) or had not multiple biopsies from different parts of stomach; that is why our report may defer from previous studies.

Our study showed the H. pylori infection was seen more than 1.21 times in boys . The average age of the patients in our study was similar with age of diagnosis reported by Haghi-Ashtiani (20). According to the study by Sykora et al, the risk of infection in boys was 1.42 times more compared to girls (19).

Mahalanabis and colleagues also showed that H. pylori infection in boys was 1.03 times more common than girls (21). However, Martel and Parsonnet in their meta-analysis on 10 studies, showed that there is no significant relationship between sex and incidence of H. pylori infection (22).

Our study showed, with increasing age, the risk of H. pylori infection increased. The finding of study by Rowland (18) and Sykora (19) were consistence on increasing age parallel increasing the risk of H. pylori infection. However, Alborzi reported a significant reduction in incidence of H. pylori infection in children at 15 years old than lower ages (23).

In this study Clinical examination of H.pylori positive infection abdominal pain was identified in 62.5%. According to the study Tindberg, abdominal pain was seen in 63 % of cases, and a positive association was found between infection and abdominal pain (24). However, the study by Kalach is demonstrated that only 26 % of children with dyspepsia were affected by H. pylori infection (25).

In the present study, other symptoms were seen in less than 10% of the cases (such as gastrointestinal bleeding, FTT and frequent vomiting). According to the studies by Sood and colleagues (26) and Sherman and Lin (27), there is no significant association between H. pylori infection and FTT.

1. This study showed that GERD is less associated with H. pylori infection. It seems that clinical criteria do not have acceptable predictive value for diagnosing H. pylori infection in children. Endoscopic findings of esophagus in two groups of Helicobacter Pylori (HP) positive and negative patients, showed normal or grade 1 esophagitis. The percentage of patients with grade 2 or higher esophagitis in both HP positive and negative groups was less than 5% of cases; Thus our results is consistent with the results of the study by Raghunath (28) and Newton (29). The study by Luzza demonstrated that in H.pylori positive patients, erythema and erosion were seen in 13% and 3% of patients, respectively (30,31). Based on pathology findings in this study, half of the patients with complaint of digestive symptoms whom were negative for H.pylori infection, had mild esophagitis.

Koike et al showed erosive esophagitis was seen in 76.2% of H.pylori negative patients (32). In our study, 49.6% of H.pylori positive patients had normal esophageal pathology and mild esophagitis have been reported as the second most common pathology in only 33.8 % of the patients. In study by Koike, it was shown that erosive esophagitis is present in 34.3 % of H.pylori positive patients (32). The study of Varanasi showed H.pylori infection was present in 30.7% of patients with esophagitis and in 42% of patients without esophagitis (33). Thus, our results are consistent with the result of study by Ashktorab (34). According to our results, most H.pylori negative patients had

normal findings or only erythema of mucosa in gastric endoscopic examination. The study by Luzza reported that erythema of mucosa was present in 21% of H.pylori negative patients (as the most common finding) and only in one H.pylori negative patient, erosion was seen (30).

In our study, 10.1% of negative H.pylori patients had nodularity in the stomach (as the third most common endoscopic findings). Prasad et al showed, nodularity was seen in 11.4% of H.pylori negative patients (35). However, in the study by Luzza et al, nodularity was not seen in any H.pylori negative patient (30).

On the other hand, in this study nodularity was observed in 47.4 % of H.pylori positive patients (as the most common endoscopic finding) and, mucosal erythema was seen in 24.8% of H.pylori positive patients (as the second endoscopic finding).

According Prasad et al's study (35), nodularity was seen in 42.4% of H.pylori positive patients. At Luzza's study (30), nodularity was the most common symptom and was present in 40% of H.pylori positive patients, and erythema as the second finding was seen in 13% of H.pylori positive patients. In luzza's study (30) erosion and ulcer were present in 1% of H.pylori positive patients, while in our study erosion and ulcer were seen in 5% of H.pylori positive patients.

Loffeld (36) showed the sensitivity, specificity, positive predictive and negative predictive value for presence of nodularity in endoscopy for diagnosing H. pylori infection were 19.6% ,98.6% ,93.9%, 53.3%, respectively. In fact, we can conclude that presence of nodularity in endoscopy has a strong association with H. pylori infection in children.

In this study, most of the patients who had complained of digestive symptoms and were H.pylori negative in pathologic study, had inactive mild gastritis or normal

stomach (most pathologic findings). Inactive moderate gastritis was seen in 5% of H.pylori negative patients.

Cardenas-Mondragon et al (37) demonstrated that H.pylori and EBV infection might be associated with the occurrence of abnormal pathology in the stomach, but none of the patients in their study had symptoms of inactive severe gastritis.

In the study by Luzza (30) it was reported that erosive gastritis was seen in only one H.pylori negative patients.

In our study 1.1% of H.pylori positive patients had normal gastric endoscopic findings. Mild inactive gastritis, moderate inactive gastritis and severe inactive gastritis were seen in 34.2%, 30.9%, 2.3% of H.pylori positive patients, respectively. Whereas mild active gastritis, moderate active gastritis and severe active gastritis were seen in 13.6%, 12.1%, 6% of H.pylori positive patients, respectively. (Table 2 and figure 2 shows pathologic findings).

However, the study by Cardenas-Mondragon et al showed that none of the H.pylori positive patients had normal gastric pathology findings, 31% of the total had mild gastritis, 14.9 % of the total had moderated active gastritis and 4% had severe gastritis in evaluation of biopsy specimen's examination (37).

In Cardenas-Mondragon et al's study the biopsy findings of H.pylori positive patients illustrated mild active gastritis in 17.8% and moderate and severe active gastritis in 2.9% of the patients (37).

According to our results, most of the patients in both groups (H.pylori positive and H.pylori negative) had normal duodenum in endoscopic examination. The most common abnormal findings in H.pylori positive patients were duodenal ulcer, erythema and erosion, respectively ( $P>0.05$ ). The study by Luzza, were consistent with our results (30).

In the present study, most H.pylori positive and negative patients had normal duodenal pathology. However, deoudenitis was seen in 6.4% of H.pylori positive patients (as the most common pathology finding).

Luzza et al (30) demonstrated that 10.7% of H.pylori positive cases and 2.2% of H.pylori negative cases had some degrees of duodenal inflammation. In study by Kori et al, it was shown that mild and chronic duodenal inflammation is present in 6.5% of H.pylori positive cases. And also, 4.9 % of H.pylori positive children had giardiasis infection (38).

This study showed that only 23.8% of H.pylori positive patients and 21.2% of H.pylori negative patients, had anemia; but, this difference was not statistically significant ( $P=0.72$ ).

In study by Haghi-Ashtiani et al (20), it was demonstrated that the prevalence of anemia in H. pylori positive and negative patients was almost equal (in H.pylori positive 36% and in H.pylori negative patients 42.2%). However, according to study by Seo (39) a positive relationship between H. pylori infection and anemia was suggested. It seems that clinical criteria are not exact enough for diagnosing H. pylori infection in children.

### Conclusion

Due to high prevalence of this infection among Iranian children with gastrointestinal symptoms, appropriate diagnostic evaluations should be considered for these patients. Nodularity in endoscopy is strongly related with H.pylori infection; however absence of nodularity does not rule out H.pylori infection.

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