

# Helicobacter Pylori Infection in Jordanian Children: Prevalence, Endoscopic Findings, and Relationship with Dyspepsia

*Abdallah Majed Ghanma, MD\*; Mohammad Salem Shatnawi, MD\*; Mohammad Mu'azi Alrwalah, MD\*; Mohammad Lutfi Alqura'an, MD\*; Backer Nayel Rawashdeh, MD\*\*; Sana' Khaza'leh, MD\*; Sura Mohammad Alrawabdeh, MD\**

## ABSTRACT

**Objectives:** To evaluate the prevalence of *Helicobacter pylori* (*H. pylori*) infection in Jordanian children who underwent esophagogastroduodenoscopy (EGD) for different indications, and to study the correlation between *H. pylori* status in dyspeptic and non-dyspeptic children.

**Methods:** This was a retrospective study conducted between January 2017 and December 2017 at Queen Rania Hospital for Children in Amman, Jordan. 312 children under the age of fourteen years who underwent EGD for different indications and in whom gastric biopsies were taken have been included in the study. Data collected included age, gender, EGD indications and findings, histopathological results and other related variables. The patients were divided into two groups based on the presence of dyspepsia (Group A: 178 patients) and other indications (Group B: 134 patients). Their *H. pylori* status was assessed through both histopathological examination and rapid urease test, and CLO test was done for all patients.

**Results:** *H. pylori* was found in 79% of all patients, without any significant difference between both groups (81% in Group A and 75% in Group B). Normal EGD was the most common gastric endoscopic finding and was associated with 40% positive *H. pylori*. Gastric nodularity was observed in 49% of positive *H. pylori* (so nodularity was more common than normal) with high specificity (90%) and positive predictive value (94%). Peptic ulcer disease was observed in 8% of positive *H. pylori* and only in 2% of *H. pylori*-negative patients.

**Conclusion:** *H. pylori* infection is very common in Jordanian children who need EGD for different reasons. Gastric nodularity and peptic ulcer disease are specific to *H. pylori* infection. Although dyspepsia is the most common indication for EGD in our study, the prevalence of *H. pylori* infection is not significantly different from non-dyspeptic children, which might make *H. pylori* less responsible for their dyspeptic symptoms.

**Keywords:** children, *H. pylori*, EGD, Jordan, dyspepsia.

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## Background

*Helicobacter pylori* (*H. pylori*) infection is the most common bacterial infection worldwide in both adults and children (1). It is acquired during childhood and remains the most common cause of peptic ulcer and gastritis in all age groups (2).

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From the departments of

\*Pediatric Gastroenterology.

\*\*Hepatology and nutrition.

Correspondence should be addressed to: Dr. Mohammad Salem Shatnawi, email: shatnawi.mohd@yahoo.com

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It plays an important causative role in gastric adenocarcinoma and mucosa-associated lymphoid tissue (MALT) lymphoma (3,4) and is linked to many extra-intestinal diseases (5,6).

*H. pylori* is a gram-negative and spiral or curved microaerophilic bacillus that has been isolated in humans and other primates. Epidemiological evidence indicate that *H. pylori* is transmitted by fecal-oral, oral-oral or gastro-oral routs (7). It has a wide range of geographic, ethnic and racial differences throughout the world and the prevalence of *H. pylori* infection among developing countries is higher than in developed nations with wide variations (8,9). Many risk factors can probably explain those variations, including low socioeconomic status and high-density living conditions (10).

Dyspepsia in clinical practice is one of the most common referral symptoms that need evaluation in the pediatric gastroenterology clinic. The term has been used inconsistently by healthcare professionals to describe symptoms related to the upper gastrointestinal tract, including epigastric pain, nausea, vomiting, fullness, early satiety, bloating, belching and retching. Most guidelines accept the Rome II definition that dyspepsia refers to pain or discomfort centered in the upper abdomen (11). Nearly all children infected with *H. pylori* have chronic gastritis which is usually asymptomatic with dyspepsia believed to be the most common symptom whether peptic ulcer is present or not (12,13). However, there is a lot of controversy on whether *H. pylori* gastritis has a direct relationship with non-ulcer dyspepsia (NUD) or recurrent abdominal pain (RAP) in children (14-18).

An esophagogastroduodenoscopy (EGD) is usually recommended to evaluate children with chronic unexplained dyspepsia and it remains the gold standard in the diagnosis and identification of *H. pylori* infection and its consequences in childhood (19,20). It allows visualization of the upper gastrointestinal tract and also facilitates the diagnosis of diseases other than those related to *H. pylori* infection. The North American Society of Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) and the European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) recommend that the diagnosis of *H. pylori* infection should be based on either positive culture or histopathology with at least one other biopsy-based test such as rapid urease test (CLO), polymerase chain reaction (PCR) or fluorescent in situ hybridization (FISH) (21).

From our practice and observations in the pediatric gastroenterology department, dyspepsia is a very common referral case in the gastrointestinal clinic and *H. pylori* gastritis is very common in children who require EGD for many indications. Therefore, we conducted this study to evaluate the prevalence of *H. pylori* infection and to study the relationship between dyspepsia and this common infection.

## Methods

This was a retrospective study conducted between 1 January 2017 and 31 December 2017 at Queen Rania Hospital for Children in Amman, Jordan. All children under the age of 14 who underwent EGD for any indication, gastric biopsies in that period were included in the study.

Our policy in the department is that all children who show dyspeptic symptoms and undergo EGD should have duodenal, gastric and esophageal biopsies taken, and to have control group, we involved children with other indications for EGD from whom gastric biopsies were obtained.

The data collected include age, gender, indications for EGD, clinical findings (including the presence of dyspepsia), EGD findings, rapid urease test results and histopathological reports.

All EGDs were done or observed by a senior pediatric gastroenterologist and at least three biopsies were taken from the gastric antrum and one from the gastric body. *H. pylori* gastritis was confirmed by both positive rapid urease test (CLO: HelicotecUT ® Plus, Strong Biotech Corporation, Taiwan, Ver.2 2015/06) and histopathology results (which were considered the most important tool of diagnosis).

Children who underwent EGD for other indications other than dyspepsia and gastric biopsies, and those who received PPI's, H2 blockers or antibiotics in the four weeks prior to EGD were excluded from the study.

A total of 312 children were included in the study. We divided them into two groups: Group A contained 178 children with dyspeptic symptoms and Group B contained 134 children with other indications for EGD (**Table I**). Changes in the prevalence of H. pylori infection was determined according to age and gender in both groups

This study was approved by the research ethics committee and institutional review board of the Jordanian Royal Medical Services (JRMS) (No. 44/3-2018).

The statistical analyses were performed using a statistical package for the social science (SPSS) software version 22 for Windows. A cut-off p-value of 0.05 for statistical significance was presumed.

## Results

Dyspepsia was one of the most common indications for EGD during our year-long study. From a total of 312 patients, 178 (57%) children underwent EGD for dyspeptic symptoms (Group A), while 134 (53%) children had other indications for EGD (Group B) (Table 1). Most other indications included a positive celiac panel, chronic diarrhea, vomiting, and failure to thrive (FTT), upper gastrointestinal bleeding (UGIB), and dysphagia.

In Group A (178 children), there was an equal number of male and female children (50% each), out of which 145 (81%) had positive H. pylori gastritis. Group B (134 children) was made up of 84 (63%) male children and 50 (37%) female children, out of which 100 children (75%) were H. pylori positive and 34 (25%) were negative for H. pylori (**Table I**).

Our study found a very high prevalence of H. pylori infection (79%) with no significant difference

Between each group (81% in Group A vs. 75% in Group B with a p-value of 0.15) (**Table II**).

**Table II:** Prevalence of H. pylori in both groups.

**Table I:** Characteristics of patients and related to gender and H. pylori status.

	Total study patients (N=312)					
	Group A (Dyspepsia)			Group B (Other indications)		
Gender	Total	Male	Female	Total	Male	Female
<b>H. pylori +ve</b>	145	75	70	100	62	38
<b>H. pylori -ve</b>	33	14	19	34	22	12
<b>Total</b>	178	89	89	134	84	50

	Total	Group A 178	Group B 134	Odds ratio (95% CL)	p-value
<b>H. pylori +ve</b>	245 (79%)	145 (81%)	100 (75%)	1.49 (0.87-2.57)	0.15
<b>H. pylori -ve</b>	67 (21%)	33 (19%)	34 (25%)	0.69 (0.39-1.15)	0.15

The study found no significant difference along age and gender lines in both groups. In Group A, the mean age was 9.4 years old in males and 9.9 in females, while in Group B, it was 7.2 years old in males and 8.4 in females. Although Group B members had younger mean age than Group A's, the difference is not significant (9.7 years vs. 7.7 years with a p-value of 0.87 and 0.66 in Groups A and B, respectively). *H. pylori*-positive patients had an older mean age than *H. pylori*-negative patients in both groups, but the difference is not significant (p-value of 0.60 and 0.31, respectively) (**Table III**).

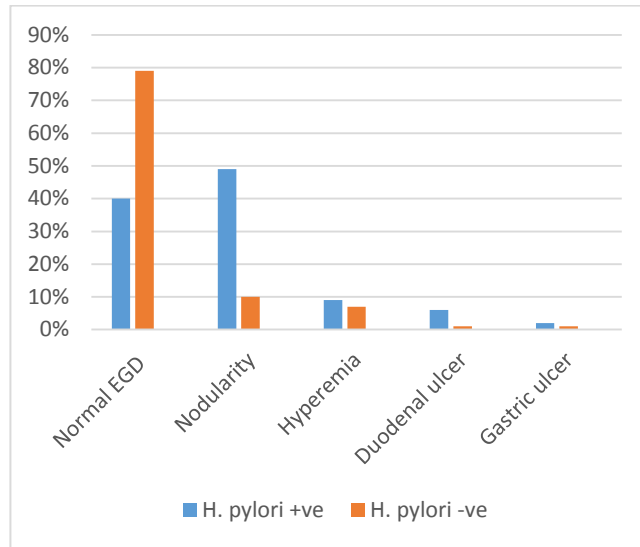
**Table III:** Characteristics of patients regarding age and gender.

	Group A			Group B			Total	p-value (age)
	Total	Male	Female	Total	Male	Female		
	Mean age (yrs.) ± SD							
<i>H. pylori</i> +ve	145 9.9 ± 3.0	75 9.7 ± 3.4	70 10.1 ± 2.6	100 8.4 ± 3.8	62 7.8 ± 3.6	38 9.3 ± 4.1	245 9.3 ± 3.4	0.60
<i>H. pylori</i> -ve	33 8.8 ± 3.0	14 7.9 ± 3.2	19 9.5 ± 2.6	34 5.9 ± 3.9	22 5.6 ± 3.5	12 6.5 ± 4.1	67 7.3 ± 3.6	0.31
<b>Total</b>	178 9.7 ± 3.0	89 9.4 ± 3.4	89 9.9 ± 2.6	134 7.7 ± 3.9	84 7.2 ± 3.7	51 8.4 ± 4.3	312 8.8 ± 3.6	
<i>p</i> -value (age)		0.87			0.66			

This study also analyzed the relationship between gross EGD findings and *H. pylori* status in all the patients. Normal EGD was observed in 40% of *H. pylori*-positive patients and in 79% of *H. pylori*-negative patients (significant p-value of < 0.0001). Normal EGD had a low negative predictive value of *H. pylori* positivity (NPV was 65%) (See **Table IV** and **Figure 1**).

**Table IV:** Relationship between *H. pylori* status and gastric endoscopic findings in all the patients.

Endoscopic gastric findings	Total N = 312		p-value	PPV	NPV	Sensitivity	Specificity
	<i>H. pylori</i> +ve N=245	<i>H. pylori</i> -ve N=67					
	N (%)	N (%)					
<i>Normal EGD</i>	98 (40)	53 (79)	<0.0001	9%	65%	40%	21%
<i>Nodularity</i>	119 (49)	7 (10)	<0.0001	94%	32%	49%	90%
<i>Hyperemia</i>	25 (9)	5 (7)	0.5	83%	22%	10%	93%
<i>Duodenal ulcer</i>	15 (6)	1 (1)	0.13	94%	22%	6%	99%
<i>Gastric ulcer</i>	4 (2)	1 (1)	0.94	80%	22%	2%	99%



**Figure 1:** relationship between gastric endoscopic findings and H.Pylori status in studied children.

Gastric nodularity was the most common abnormal EGD finding. It was observed in 49% of total H. pylori positive patients with significant difference from H. pylori negative patients (p-value < 0.0001). Gastric nodularity is associated with high positive predictive value (PPV= 94%) for H. pylori gastritis with 90% specificity and 49% sensitivity (**Table IV**).

Hyperemia in the gastric mucosa was the second most common abnormal EGD finding. It was observed in 9% of H. pylori positive patients and 7% of H. pylori negative patients with no significant difference (p-value of 0.5). Hyperemia has 83% PPV and 93% specificity for H. pylori infection (**Table IV**).

Peptic ulcer disease (PUD) was the least common abnormal EGD findings. Duodenal ulcer disease was found in 15 (6%) H. pylori positive patients and only in one child with negative H. pylori. It had significantly high PPV (94%) with 99% specificity for H. pylori infection. While gastric ulcers were observed in four H. pylori positive patients and in only one H. pylori negative patient with UGIB (**Table IV**).

There was no significant difference in endoscopic gastric findings for H. pylori positivity between the patients in Group A and Group B (**Table V**).

**Table V:** Relationship between H. pylori and gastric endoscopic findings in both groups.

Endoscopic gastric findings	Group A N = 178		Group B N = 134		p-value for H. pylori +ve
	H. pylori +ve N=145	H. pylori -ve N=33	H. pylori +ve N=100	H. pylori -ve N=34	
	N (%)	N (%)	N (%)	N (%)	
<i>Normal EGD</i>	54(37)	23(70)	44(44)	30(88)	0.29
<i>Nodularity</i>	71(49)	6(18)	48(48)	1(3)	0.88
<i>Hyperemia</i>	18(12)	3(9)	7(7)	2(6)	0.17
<i>Duodenal ulcer</i>	9(6)	0(0)	6(6)	1(3)	0.94
<i>Gastric ulcer</i>	2(1)	0(0)	2(2)	1(3)	0.71

## Discussion

The Queen Rania Hospital for Children (QRHC) is a tertiary hospital in Amman, the capital of Jordan, an underdeveloped country with limited resources. QRHC belongs to the Royal Medical Services which has many satellite hospitals distributed all over the country. All children who need advanced evaluation for their gastrointestinal symptoms are referred to the institute and we think that makes our study sample representative of the whole Jordanian population.

Pediatric EGD has many indications, and chronic dyspepsia is one of the common indications in recent decades (22,23). Our study showed that 57% of patients underwent EGD for their dyspeptic symptoms (Group A), which makes dyspepsia one of the most common indications of EGD in our patients.

In patients with dyspepsia, our study revealed no significant differences regarding age and gender. Fifty percent of the male patients had a mean age of 9.4 years while it was 9.9 years for female patients. This is similar to the findings of previous studies that also found that similar mean age of dyspeptic children and gender is not a risk factor for the majority (12,14,16-18).

The prevalence of *H. pylori* infection proved by CLO and histopathology in overall patients was very high (79%). We could only find two Jordanian published studies about *H. pylori* infection in children: one showed 82% prevalence of *H. pylori* gastritis in 163 dyspeptic children based on histopathology, which is consistent with our results (24), and the other showed 55.5% seroprevalence of *H. pylori* in healthy school children (25). Our high prevalence is also in agreement with earlier reports from adult Jordanian studies which found a prevalence between 72% and 86% based on histopathology (26-29).

Pediatric studies from neighboring countries show variable but lower prevalence rates than ours. In Saudi Arabia, an urea breath test (UBT) based study found a 27% prevalence in 314 school children and 73% in children with RAP (30). In Egypt, it was 60% in 100 children with RAP based on CLO and histopathology (31). In Sudan, seroprevalence was 40% in 312 hospitalized children (32). The prevalence from different studies in Iran was between 40-82% by serology (33) and only 9% in one study by histopathology (34). In Turkey, it was 63% in 95 symptomatic children by histopathology (35).

In comparison to global prevalence, our prevalence remains significantly high. A recent meta-analysis systematic review revealed a global *H. pylori* prevalence of 44.3%, ranging from 50.8% in developing countries to 34.7% in developed countries (36).

On the other hand, and strikingly, our study revealed statistically but insignificant differences in the prevalence of *H. pylori* between dyspeptic children (Group A) and children without dyspepsia (Group B). This result does not support the role of *H. pylori* infection in dyspepsia or RAP without peptic ulcer disease as many other studies HAVE concluded (14-17).

There was no significant difference regarding gender and *H. pylori* prevalence in dyspeptic children. While regarding age, patients with *H. pylori* had an older mean age than *H. pylori* negative patients in both groups. Although this is not significant, it is in keeping with the proven association between age and *H. pylori* infection in most studies (37).

For gross EGD findings, normal EGD was significantly more common in *H. pylori* negative patients ( $p$ -value  $<0.0001$ ), but it was not sensitive or specific for negative infection, and that emphasizes the important need of gastric biopsies to confirm *H. pylori* infection in normal EGD (21).

Antral nodularity is the most characteristic EGD finding in *H. pylori* infection and its sensitivity and specificity vary across studies (38) as found in the present study. Antral nodularity was observed in

49% of *H. pylori* positive patients with significant correlation (p-value <0.0001), and it had 90% specificity and 94% PPV for the infection with only 49% sensitivity.

Our results also support the proven relationship between *H. pylori* infection and peptic ulcer (2). Fifteen out of 16 patients with duodenal ulcers and 4 out of 5 patients with gastric ulcers had positive infections. Both duodenal and gastric ulcers had reliable PPV and specificity.

This study has some limitations. It evaluated the prevalence of *H. pylori* infection in symptomatic children who needed invasive procedures for their complaints. However, for more convenient results regarding prevalence of this very common infection in our population, we hoped for a healthy control group using non-invasive tests. To better evaluate the dyspepsia-*H. pylori* relationship, we think many other variables should be studied. These include a healthy control group, histopathological severity of *H. pylori* gastritis, and clinical response after successful eradication therapy, which will be included in a forthcoming study.

## Conclusion

The results of the current study showed a very high prevalence of *H. pylori* infection in Jordanian children. This prevalence is not significantly different between dyspeptic and non-dyspeptic children and more studies are needed to evaluate the correlation between dyspepsia and *H. pylori* infection. Gastric nodularity and peptic ulcer are highly specific for *H. pylori* infection though their absence does not rule out the infection. We suggest that consensus guidelines for *H. pylori* infection management need to be established in areas with high prevalence like Jordan and the Middle East based on local data.

## Disclosure

We declare that this paper is the original work of the authors and it has never been submitted or published by any journal, nor presented at any conference.

## Conflicts of interest

There is no conflict of interest.

## Funding

None.

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