

The Role of *Helicobacter pylori* and Gastritis in Children with Recurrent Abdominal Pain

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Abstract

Background: Recurrent abdominal pain is a common pediatric diagnostic problem. Endoscopy is sometimes performed as part of the evaluation. Although gastritis and/or *Helicobacter pylori* infection is often present, it is not known if they contribute to the symptomatology.

Objectives: To evaluate the role of either gastritis or *H. pylori* infection in the symptomatology of children with RAP.

Patients and Methods: We retrospectively studied two groups of patients, 70 children in each, who had undergone endoscopy. One group was evaluated endoscopically for RAP and the other was a heterogeneous group that underwent endoscopy for indications other than RAP. Biopsies were taken during endoscopy and Giemsa staining was performed for the presence of *H. pylori*. Triple therapy was given as indicated, and the children were followed for an average of 6 months.

Results: Microscopic gastritis was diagnosed in 39 patients (55.7%) of the RAP group and in 31 of the heterogeneous group (44.2%) (NS), and *H. pylori* was found in 32 patients of the RAP group and in 16 of the heterogeneous group (45.7% vs. 22.8%, $P < 0.01$). All children with *H. pylori*, except one in the heterogeneous group, had accompanying gastritis. On the other hand, gastritis without *H. pylori* infection was seen in 7 children in the RAP group and in 15 of the other. Endoscopy revealed macroscopic abnormalities in 52 of the 70 children with microscopic gastritis. There was a clinical improvement after triple therapy in 28 of 33 children with *H. pylori*-associated gastritis (84.85%), in 4 of 8 children with gastritis unassociated with *H. pylori* (50%), and in 8 of 15 without gastritis or *H. pylori* (53.3%) ($P < 0.01$ between the *H. pylori*-associated gastritis and each of the other groups).

Conclusions: *H. pylori* infection and gastritis may be associated with RAP in a selected subgroup of children. We recommend a complete work-up, including endoscopy and invasive or non-invasive diagnostic modalities for *H. pylori*, and treatment of the infection.

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Helicobacter pylori infection is an established cause of peptic ulcer disease and gastritis in adults. Its relationship to chronic dyspepsia is, however, controversial [1]. *H. pylori* also causes antral gastritis in children. Gastritis is often nodular in children, 30–100% compared to only 0–20% in adults [2,3], and is characterized by lymphocytic rather than neutrophilic infiltration [4]. The incidence of ulcer disease in children is low, but as in adults, 90–100% of pediatric duodenal ulcers are associated with *H. pylori* gastritis [5].

The prevalence of *H. pylori* infection varies according to age and geographic location. In Europe and North America it ranges between 6 and 16% of the pediatric population [6], while in developing countries it is usually higher [7,8].

Recurrent abdominal pain is a common problem in pediatrics, for which no organic cause is usually found [9]. Several reports have studied the relationship between RAP and *H. pylori* infection, but the results are controversial [10–12]. The aim of this study was to examine the relationship between RAP and *H. pylori* infection, the role of gastritis, and the response to treatment.

Patients and Methods

We conducted a retrospective chart review of children who underwent endoscopic evaluation at the Institute of Pediatric Gastroenterology and Nutrition, Schneider Children's Medical Center of Israel during 1994. The children were divided into two groups, 70 patients in each group. The first group had RAP, and consisted of children who met the following criteria: at least three episodes of abdominal pain during a 3 month period, with an intensity that interferes with the child's everyday life and activity. There were 25 males and 45 females in the RAP group, with a mean age of 11.5 ± 3.9 years (range 3–20), and all had an unremarkable medical history apart from their chief complaint. The second group was designated "the heterogeneous group," and consisted of children who underwent endoscopy for other indications [Table 1]. There were 42 male and 28 females in this group, with a mean age of 8.4 ± 5.2 years (range 0.7–17), and in none was abdominal pain the chief complaint or a major symptom in

RAP = recurrent abdominal pain

Table 1. Indications for endoscopy in the heterogeneous group

Diagnosis	No. of patients
Failure to thrive	28
Vomiting	15
Suspected Crohn's disease	9
Constipation	3
Diarrhea	6
GI bleeding	4
Feeding disorders	4
Portal hypertension	1

their primary disorder ($P=0.01$ between the mean ages of the two groups),

All endoscopies were performed using an Olympus PQ-20 endoscope (Japan), with midazolam or diazepam given for sedation using standard dosage. Biopsies were taken from the antrum in all babies. Occasionally, as indicated, biopsies were also taken from other sites, such as the esophagus, the body of the stomach or the duodenum. Histological samples were Giemsa stained for the detection of *H. pylori*. Evaluation of the biopsies was done by an experienced pathologist (T.D.) using established criteria. Gastritis was diagnosed when there was lymphocytic and/or neutrophilic infiltration of the lamina propria, at least superficially.

Clinical response to treatment was defined as reduction of at least 50% in the number or intensity of the abdominal pain episodes. The children were followed for an average period of 6 months (range 4–10).

Statistical evaluation was done by the statistical unit of Bar-Ilan University in Israel, using the *t*-test, Duncan grouping, or Chi-square test as appropriate.

Results

Microscopic gastritis was diagnosed in 39 patients of the RAP group (55.7%) and in 31 of the heterogeneous group (44.2%) — a not significant difference. *H. pylori* was found in 32 patients of the RAP group and in 16 of the heterogeneous group (45.7 vs. 22.8%, $P<0.01$). All children with *H. pylori*, except for one in the heterogeneous group, had accompanying gastritis. On the other hand, gastritis without *H. pylori* infection was seen in 7 children in the RAP group and in 15 of the other. In 52 of the 70 children with microscopic gastritis, endoscopy revealed macroscopic abnormalities, mostly nodularity, redness, or hyperemia.

Gastritis without the presence of *H. pylori* was diagnosed in 12% of the males and 8.8% of the females (NS). *H. pylori* was found in 64% of the males with RAP and in only 35.5% of the females ($P<0.01$).

Information about family history of peptic disease was available in 116 children. A positive family history was found in a higher number of children who had histological gastritis (20 of 29, 68%) than in those with normal histology (39 of 87, 48%) ($P<0.01$).

Additional diagnoses were found in five children of the RAP group. Two had duodenal peptic ulcer, and one each

had lactose intolerance, anorexia nervosa, and reflux esophagitis.

At the time this study was conducted, there were no clear guidelines for treatment. Triple therapy with amoxicillin, metronidazole and bismuth subcitrate for either 2 or 3 weeks was the usual protocol. Fifty-six children were given triple therapy — 37 for 2 weeks, and 19 for 3 weeks. As there was no difference in the response rate between the two groups the results were combined. Some patients were treated by their primary physician, even though there were no findings on endoscopy. Clinical improvement was found in 28 of 33 children with *H. pylori*-associated gastritis (84.85%), 4 of 8 children with gastritis unassociated with *H. pylori* (50%), and 8 of 15 without gastritis or *H. pylori* (53.3%) ($P<0.01$ between the *H. pylori*-associated gastritis and each of the other groups).

Discussion

The results of studies that have attempted to establish the role of *H. pylori* infection in RAP of children are conflicting. Early reports suggested that *H. pylori* was present in 30–60% of patients with RAP [10,13]. Evidence of *H. pylori* infection was found in 54% of Israeli children with RAP, and 85% of those became symptom free after treatment [12].

Other studies were unable to demonstrate an association between symptoms of abdominal pain and *H. pylori* infection. No difference in symptomatology between infected and non-infected children was found [14,15], and there was no relation between *H. pylori* infection and RAP in children with this entity [16–18].

In our study, a high incidence (45.7%) of *H. pylori* infection was found in children with RAP. The rate of infection in the control group was 22.8%, somewhat higher than the 6–16% incidence in other developed countries [5,6,19] but lower than the 31% incidence reported from Kuwait [20]. The high incidence of *H. pylori* infection that we found in children with RAP is similar to the 54% incidence reported in another group of Israeli children with RAP [12]. Other authors did not find any difference in the incidence of *H. pylori* infection between children with RAP and control groups [20]. This difference in incidence may be due to the fact that our group consists of highly selected children who were referred for endoscopy to a tertiary pediatric center. The fact that our control group was 3 years younger than the RAP group may have also contributed to the difference in *H. pylori* infection rate. There were more females than males in the RAP group, in contrast to more males in the heterogeneous group, but no gender difference in the incidence of *H. pylori* has been reported in the literature.

One child infected with *H. pylori* in the control group had no evidence of histological gastritis. Although gastritis is found in most cases of *H. pylori* infection, there are reports of cases with normal histology. The percentage of normal mucosal structure was reported by various authors

to be 6.64% [21], 12.5% [22], and 33% [23]. A sampling error may have contributed to these results.

An interesting finding was the presence of gastritis alone, without *H. pylori* infection, in 7 children with RAP and in 15 of the other group. Other studies have reported similar results — *H. pylori* was found in only 7 of 18 cases of gastritis [24], 18 of 48 [17], and 13 of 24 cases [20]. It is possible that *H. pylori* infection was missed in some of these children in our study, since ancillary diagnostic studies, for example the C¹³-urea breath test, were not performed. Other causes of gastritis — such as bacterial or viral infections, or irritants — may have played a role.

The different response rate to treatment between children with gastritis who were infected by or free of *H. pylori* suggests that missed *H. pylori* infection was not the cause of gastritis in those cases where *H. pylori* was not found.

The correlation between macroscopic and histological findings in our series is impressive. Macroscopic evidence of gastritis varies between 20 and 60% of children with *H. pylori*-associated gastritis [5]. Selectivity of the patient population probably explains this variation.

The higher rate of family history of peptic disease in our patients is probably also a reflection of the selected nature of our group of children, as prospective population studies did not find such a correlation [5,18].

The 85% response rate to treatment suggests that *H. pylori* infection with gastritis may be related to the symptomatology. Children with gastritis not infected with *H. pylori* respond at the same rate as those without gastritis (50–53%), suggesting a placebo effect.

In conclusion, *H. pylori* infection and gastritis may be associated with the syndrome of RAP in a selected subgroup of children. We advise a complete work-up, including diagnostic modalities for *H. pylori*. Treating patients with gastritis is probably appropriate, although no definite conclusions regarding treatment of *H. pylori* infection in patients with RAP have been reached [25].

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I have one request: may I never use my reason against the truth.

Elie Wiesel, quoting from a Hassidic prayer