

ENDOSCOPIC NODULAR GASTRITIS: AN INDICATOR OF *HELICOBACTER PYLORI* INFECTION IN CHILDREN

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ABSTRACT

Objective: To investigate the importance of endoscopic nodular gastritis associated with *Helicobacter pylori* infection in children.

Methods: In this prospective study, 220 consecutive patients (age range 2 to 15 years, mean age 9.02 ± 3.3), 118 of them males (53.6%) underwent upper endoscopy during evaluation of chronic abdominal pain. The appearance of nodular gastritis was observed during endoscopy by the author. Culture, rapid urease test and staining were carried out on gastric mucosal biopsies. With histological examination the presence of *Helicobacter pylori* and the nature of inflammation was assessed.

Results: *H. pylori* infection was identified in 110 (50%) patients. Endoscopic nodular gastritis was seen in 100 patients (45.5%), and was significantly associated with active chronic gastritis.

Nodularity in the stomach showed a sensitivity of 72.7% and a specificity of 81.8% and a ppv of 80% for the diagnosis of *H. pylori* infection and was observed in 80 (72.7% of) *H. pylori* positive cases. Antral nodularity was associated with increasing risk of infection with *H. pylori* (OR=12, 95% CI: 6.3-22.7).

Conclusion: Endoscopic findings of antral nodularity in children may suggest the presence of *H. pylori* infection.

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INTRODUCTION

Warren and Marshall first observed curved bacilli on the gastric mucosa of patients with chronic gastritis in 1983.¹ The bacterium was later named *Helicobacter pylori*. It was shown that infection with *H. pylori* can cause chronic gastritis² and peptic ulceration³ and increase the risk of gastric cancer⁴ and mucosa-associated lymphoid tissue (MALT) lymphoma.⁵ Eradication of the infection accelerates healing of peptic ulcers and prevents relapses.^{6,7} *H. pylori* infects at least 50% of the world's population.⁸ It is predominantly acquired in childhood^{7,9} and more than three-fourths

of the population in developing countries are infected during childhood.¹⁰

The inflammation that *H. pylori* causes in the gastric mucosa is not always observed macroscopically with endoscopy, but it is identified on the histologic examination of gastric biopsies.^{11,13} Endoscopic findings of nodularity can be seen in the stomach of children much more frequently than in adults. It is more often observed in the gastric antrum, and has been called antral nodular gastritis (also nodular gastritis).^{12,14} Some authors^{14,18} believe that this macroscopic change may predict *H. pylori* infection and histologic gastritis. Other authors still question the specificity of endoscopic nodular gastritis for *H. pylori* infection.¹⁹

We performed a cross-sectional study of children with chronic abdominal pain to investigate the association of *H. pylori* infection with endoscopic nodular gastritis and histologic features of gastritis.

MATERIAL AND METHODS

Patients

Chronic abdominal pain in this study was defined as recurrent abdominal pain (RAP), which persists for more than three months duration and affects normal activity.²⁰ 220 patients with recurrent abdominal pain (RAP) underwent a diagnostic upper endoscopy. These represent approximately one-third of children with RAP seen in the gastroenterology unit. The decision to perform endoscopy was based on evaluation of the severity of symptoms reflected by interference with normal daily activity.

Exclusion criteria were use of antibiotics or H₂ blockers and PPI within 3 weeks of the procedure and use of NSAIDs within 3 days of the procedure. Also patients taking immunosuppressive agents or chemotherapy drugs, and patients with immunodeficiency or chronic renal failure were excluded (24 patients).

Endoscopy was performed by one of the authors. A Pentax EG2731 videoendoscope, outer diameter=7.6 mm was used. Three gastric antral biopsy specimens were collected from each patient, one for urease rapid test, one for histologic examination and staining, and one for bacteriologic study. Patients were considered to be infected with *H. pylori* if culture or a combination of two tests (urease rapid test + histologic analysis) were positive.

Only the children whose parents gave informed consent participated in the study.

Endoscopic diagnosis

The diagnosis of endoscopic nodular gastritis was made when the mucosa had an irregular appearance resembling a cobblestone pavement. Micronodules measured 1 to 4 mm in diameter, had a smooth surface, and were the same color as the surrounding mucosa, as described by Hassal and

Dimmick.²¹

Histologic study

Biopsy specimens were fixed in 10% formalin, embedded in paraffin, and cut at 6µm. The sections were stained with hematoxylin - eosin, and the modified Giemsa technique for light microscopy. The same pathologist, who noted the presence or absence of *H. pylori*, observed all the sections. Chronic gastritis was defined according to established histologic criteria.²² Nodularity of the antral mucosa leading to a cobblestone appearance was called nodular gastritis.²¹

Bacteriologic study

Biopsy specimens were immediately placed in a transport media (Modified Campy-Thio tubes), and transported within 2 hours to the laboratory. Tubes were incubated at 37°C in an anaerobic jar. After 1-3 days, a few drops of cultured medium were transferred to the Campy-BAP plate (containing Brucella agar base, 10% sheep's blood, and antibiotics). The plates were incubated in the same conditions for 7 days.

Urease test

One biopsy was embedded into a Gastro urease test gel (Bahar Afshan, Tehran, Iran), which consists of a small portion of urea agar and a pH indicator.

Data analysis

Results were expressed as numbers, percentages, mean, range and standard deviation. Variables were assessed using χ^2 test, t -student and Odds Ratio. Significance was set at 0.05. Data were processed and analyzed with SPSS version 9.

This study was approved by the Research Ethics Committee of the Shariati Hospital, affiliated to Tehran University of Medical Sciences.

RESULTS

During a period between 1998 and 2001, 220 patients with RAP underwent a diagnostic upper endoscopy (118 male, 102 female) with a mean age of 9.02 (SD=3.3), and age range (2 to 15 years).

H. pylori was isolated in 110 (50%) patients. There were 54.5% males, age range from 2 years to 15 years.

The endoscopic appearance of nodular antritis was seen in 100 patients (45.5%). There were 60 males (54.5%).

The mean age of patients with nodular antritis were 9.8 (\pm 3.09). The mean age of patients without nodularity was 8.2 (\pm 3.3) (ANOVA, F = 7.196, $p=0.001$). An association between older age group and the prevalence of this finding was observed (OR=1.1, 95% CI: 1.06-1.26). 80/110 (72.7% of) patients with *H. pylori* infection had a nodular antritis, 30/

Table 1: Frequency of different histological patterns in 220 patients.

	Normal	Chronic gastritis	Active chronic gastritis	Follicular gastritis
HP-	19	71 (64.5%)	20 (18.2%)	0
HP+	0	39 (35.5%)	66 (60%)	5(4.5%)

110 (27.3%) had normal antrum and only 20(18.2%) of patients without *H. pylori* infection had nodular antritis. *H. pylori* infection was detected in 80 (80%) patients with nodular antritis but 30 (25%) of patients without nodular gastritis had *H. pylori* infection.

Antral nodularity was significantly associated with *H. pylori* infection (OR=12, 95% CI: 6.3-22.7). Although there was a relationship between age and *H. pylori* infection (OR=1.1, 95%CI: 1-1.18), using a regression model between *H. pylori* infection and age and nodularity revealed only a significant effect of nodularity on *H. pylori* infection (beta=-2.4, df=1 : sig=.01)

Infection with *H. pylori* was associated with the presence of chronic gastritis on histological examination of all patients. Of these 66/110 (60%) had active chronic gastritis, vs. 20/110(18.2%) in patients without infection, $\chi^2=60.04$, $p= 0.000$ (Table I).

The pathologic findings in the remaining patients with HP infection were chronic gastritis in 39 patients (35.4%) and follicular gastritis in 5 (4.5%). There is a significant correlation between nodular gastritis and active chronic gastritis, $\chi^2=55.005$ ($p=0.000$), $df=3$.

The diagnostic performance of nodular gastritis for *H. pylori* was sensitivity 72.7%, specificity 81.8%, positive predictive value 80%, and negative predictive value 75%.

There was no association with sex in the prevalence of *H. pylori* ($\chi^2 = 0.073$ $p= 0.78$, $df=1$). The mean age of the *H. pylori* positive was (9.7±3.09) vs. (8.34 ±3.4) in *H. pylori* neg, t test (t = 3.08, DF = 218, $p= 0.002$), that was significantly greater than in *H. pylori* negative cases (Fig. 1).

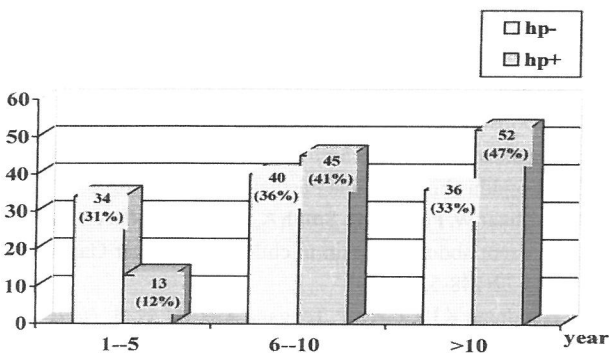


Fig. 1. Age distribution in *H. pylori* positive vs. *H. pylori* negative patients.

DISCUSSION

There are many studies describing the prevalence of *H. pylori* infection. Most epidemiologic studies have been performed in adults, who had been infected for many years before clinical symptoms appeared. There is limited data on the incidence of *H. pylori* infection in children.²³

The children included in this study had chronic abdominal pain. The decision to perform an endoscopy depends on the severity and chronicity of the symptoms in individual patients. Out of 220 patients, *H. pylori* was isolated in 110 (50%). However in six studies performed in North America, Europe, and Australia with 2715 patients, between 5% to 17% had evidence of infection with *H. pylori*.^{23,25} Prevalence of infection increases with age. This result is the same as that found in other studies.^{18,26,27}

Chronic gastritis was present in all children infected with *H. pylori* according to established histologic criteria.²⁸

In our study 66 patients (60%) had active chronic gastritis, 39(35.4%) chronic gastritis, and 5 (4.5%) follicular gastritis.

In 1982 Warren and Marshall described *H. pylori* in the gastric mucosa and reported the presence of endoscopic nodular gastritis in positive cases.¹ Later, Cadranet et al.³⁰ reported the presence of endoscopic nodular gastritis in patients with *H. pylori* infection. Nodularity was associated with lymphoid follicles in histologic examination. Prevalence of this association in different studies was between 30-100% of the cases.^{17,29,30}

An association between *H. pylori* infection and severity of inflammatory response was also found ($\chi^2=63.2$, $p= 0.000$), $df= 3$. This is the same as previous studies.^{17,27,29}

In the present study endoscopic nodular antritis was seen in 100/220 patients, and an association was found between endoscopic nodular gastritis and *H. pylori* infection (as 80% of nodular antritis cases had *H. pylori* infection and only 30(25%) of the patients with HP infection had a normal antrum ($\chi^2 = p= 0.001$, $df=1$).

In different studies this association was 67% for *H. pylori* positive versus 11.1% for *H. pylori* negative,¹⁷ and in another series of studies 43-45.3% for *H. pylori* positive and 1.5-4% for *H. pylori* negatives.^{16,17,30}

This study found a sensitivity of 72% and a specificity of 81.8%, a positive predictive value of 72.7% and a negative predictive value of 75%. It may therefore be stated that

Endoscopic Nodular Gastritis Signals *H. pylori* Infection

endoscopic nodular gastritis indicates a high probability of *H. pylori* infection.

Endoscopic nodular gastritis is not observed in all patients with *H. pylori* infection. Nodularity is probably related to the density of *H. pylori* at the beginning of infection, so that a large inoculum triggers an exaggerated immune response.^{15,16,30}

It was also found that infection with *H. pylori* was significantly associated with active chronic gastritis on histologic examination (35.4% chronic gastritis, 60% active chronic gastritis and 4.5% follicular gastritis ($\chi^2=55.005$ $p=0.000$, $df=3$).

The low rate of follicular gastritis is due to the fact that we took only one piece of biopsy from the antrum for pathologic examination, and follicles have a patchy distribution. This study establishes the importance of antral nodularity found during endoscopic examination of children. This finding is associated with *H. pylori* infection.

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