

Original Article

## Are endoscopic findings predictive for the presence of *H. pylori* infection? What about indirect histologic findings?

*Mohammad Hasan Emami\**, *Hajar Taheri\*\**, *Hamid Tavakoli\*\*\**, *Abbas Esmaeili\*\*\*\**

**Abstract**

**BACKGROUND:** It is still controversial whether certain endoscopic features can be used to diagnose *Helicobacter pylori* related gastritis. Our aim was to determine how macroscopic findings were related to histomorphological changes and the presence of *H. pylori* in patients undergoing endoscopy.

**METHODS:** The study population involved 501 consecutive gastrointestinal (GI) clinic admissions who underwent esphagogastroduodenoscopy for upper GI symptoms between October 2002 and March 2004. At least 2 antral and 2 body biopsies were obtained from each patient and were examined histologically for the presence of gastritis and were stained for *H. pylori* using modified Giemsa staining method. Endoscopic findings were reviewed retrospectively by two experts blinded to the *H. pylori* status and patients history. The endoscopic findings of gastritis, classified by a modification of the Sydney system and histological findings were determined by updated Sydney system. Statistical analysis was done using SPSS 11.

**RESULTS:** A total of 501 consecutive patients (256 females, 245males) ranging from 8 to 91 years (mean, 49.5 years) were studied. *H. pylori* was found in 326 patients (65.1%). Relative frequency of *H. pylori* in females was 53% and in males was 47%. Rugal hypertrophy, raised erosion and bleeding were observed only in patients with *H. pylori* infection (specificity = 100%). Neutrophil activity also was observed only in patients with *H. pylori* infection. Among endoscopic findings, erythema showed a high sensitivity (81.3%) and positive predictive value (87.1%) for the diagnosis of *H. pylori* infection. Gastritis was present in 84.3% of all patients and 97% (316/326) of those with *H. pylori* and 56.6% (99/175) of those without *H. pylori*. There was significant statistical correlation between *H. pylori* infection and gastritis ( $P < 0.001$ ). *H. pylori* was present in 76% (316/415) of gastritis patients and 5.1% (4/77) of patients without gastritis.

**CONCLUSIONS:** An accurate endoscopic assessment of gastritis according to the Sydney system along with the histological findings is valuable indicator of *H. pylori* infection.

**KEY WORDS:** *Helicobacter pylori*, gastritis, Sydney system, peptic ulcer.

JRMS 2007; 12(2): 80-85

**H**elicobacter pylori (*H. pylori*) infection is widespread, and it is also recognized as being strongly associated with chronic gastritis, duodenal ulceration and probably gastric carcinoma and it is a major risk factor for them<sup>1-3</sup>. But, there is no single test to be 100% accurate for its diagnosis<sup>4</sup>.

Recent studies highlighted that the presence of *H. pylori* could be assessed on the basis of the macroscopic patterns<sup>5,6</sup>, but it is still unknown how macroscopic findings are related to histomorphological changes and the presence of *H. pylori* in the gastric mucosa<sup>7,8</sup>. The Sydney system is a method for the classification of

\*Associate Professor of Gastroenterology, Isfahan University of Medical Sciences and Poursina Hakim Research Institute, Isfahan, Iran.

\*\*Medical student, Isfahan Medical Students Research Committee, IUMS and PHRI, Isfahan, Iran.

\*\*\*Assistant Professor of Gastroenterology, Isfahan University of Medical Sciences and Poursina Hakim Research Institute, Isfahan, Iran.

\*\*\*\*General Practitioner and Researcher, IUMS and PHRI, Isfahan, Iran.

Correspondence to: Hajar Taheri, Medical Student Research Committee, School of Medicine, Isfahan University of Medical Science, Isfahan, Iran. e-mail: taheri@edc.mui.ac.ir

endoscopic and histologic findings<sup>9</sup>. In 1991, an international group at the World Congress of Gastroenterology in Sydney recognized the following endoscopic features of inflammation: edema, erythema, friability, exudate formation, flat erosions, raised erosions, rugal hyperplasia, rugal atrophy, visible vessels, intramural bleeding and nodularity. Combinations of these changes were used to define seven endoscopic categories of gastric inflammation, the commonest being erythematous/exudative gastritis<sup>10,11</sup>. In relation to *H. pylori*, most studies have found that the frequency of endoscopic abnormalities is higher in infected than in non-infected patients. However, common endoscopic categories such as erythematous/exudative gastritis, atrophic gastritis, flat erosive gastritis and raised erosive gastritis show only weak associations with *H. pylori*. In contrast, stronger associations (higher positive predictive values) have been described for uncommon endoscopic manifestations such as antral nodularity and hyperplasia of folds in the body of stomach<sup>12</sup>. Since development of fibrogastroscopy techniques, endoscopic inspection without the need for biopsies would be a convenient way to diagnose such gastritis, if possible. So the patients could have the diagnosis immediately after gastroscopy and the need and costs for biopsy with histological examination would be less<sup>13,14</sup>. Our aim was to identify endoscopic and histologic features associated with *H. pylori* infections in patients undergoing endoscopy.

## Methods

### Patients

Our study population involved 501 consecutive GI clinic admissions who underwent esophagogastroduodenoscopy for upper GI symptoms between October 2002 and March 2004. Exclusion criteria were the use of antibiotics known to be effective against *H. pylori* during the last 4 weeks, anti acids, H<sub>2</sub>-receptor antagonists and non-steroidal anti-inflammatory drugs during the last 14 days. Study was approved by the local ethics com-

mittee, and informed written consent was obtained from all participants.

Endoscopic examination and detection of *H. pylori*

All participants were asked to be fast for at least 8 hours before gastroscopy and it was carried out after pharyngeal anesthesia with lidocaine spray. During endoscopy (Pentax EPM-3300, EG 2940 scope) multiple pictures were saved. At least 2 antral and 2 body sample biopsies were obtained from each patient and sent to Histopathologic Department. Samples were fixed in 10% buffered formalin, embedded in paraffin cut in 4 mm sections, and stained with Hematoxylin-Eosin for histologic examination and modified Giemsa staining method for *H. pylori* identification. *H. Pylori* was diagnosed using histology and rapid urease test (RUT).

### Endoscopic Assessment of Gastritis

Endoscopic findings were reviewed retrospectively by two experts who were blind to the *H. pylori* status and patients history. Endoscopic gastritis was diagnosed by the modified criteria of the Sydney system (15) which involves subjective assessment of presence or absence of the possible findings as of the following: erythema, exudative gastritis, raised erosive gastritis, flat erosive gastritis, hemorrhagic gastritis, rugal hypertrophy, rugal atrophy and nodularity. The gastric and duodenal mucosa was evaluated during endoscopy to find any ulcer.

### Histologic Assessment of Gastritis

Histologic diagnosis was made by a single pathologist who was blind to the endoscopic findings. Gastritis was evaluated according to the updated Sydney system<sup>15</sup>; i.e. inflammation (mononuclear cell infiltration), activity (neutrophil infiltration), atrophy and intestinal metaplasia.

### Statistical Methods

Statistical analysis was done using SPSS 11 for windows. Clinical data were analyzed by t-test (for age) and Fisher's exact test (for sex). Sensitivity, specificity, and positive and negative predictive values were

calculated. P-value less than 0.05 was considered significant. Odds ratios (OR) for endoscopic gastritis were derived by multiple conditional logistic regression analysis.

## Results

A total of 501 consecutive patients (256 females, 245 males) with a mean age of 49.5 years ranging from 8 to 91 years were studied. H. pylori was found in 326 patients (65.1%). Relative frequency of H pylori in females was 53% and in males was 47%. Frequencies of this infection among different age groups are shown in table 1. Endoscopic and histologic findings in patients with and without H. pylori are presented in table 2. Rugal hypertrophy, raised erosion, bleeding and neutrophil activity were observed only in patients with H. pylori infection. The sensitivities and specificities of various macroscopic features according to histomorphological examination are given in table 3. Among endoscopic findings, erythema showed high sensitivity (81.3%) and positive predictive value (87.1%) for diagnosis of H. pylori infection. Rugal hypertrophy,

raised erosion and bleeding showed a high specificity (100%).

**TABLE 1.** Relative frequency of H. pylori infection among different age groups.

H. pylori status	Age groups		
	<30	30-60	>60
H. pylori positive	65 (13%)	54 (10.7%)	207 (41.3%)

Gastritis was present in 84.3% of all patients and 97% (316/326) of those with H. pylori and 56.6% (99/175) of those without H. pylori. There was significant statistical correlation between H. pylori infection and gastritis ( $P < 0.001$ ). H. pylori was present in 76% (316/415) of gastritis patients and 5.1% (4/77) of patients without gastritis. H. pylori was present in 75.3% (55/73) of patients with duodenal ulcer and 73% (19/26) of those with gastric ulcer. Gastric ulcer was present in 5.8% (19/326) of patients with H. pylori and 4% (5/175) of those without H. pylori (OR = 1.48). Duodenal ulcer was found in 17% (55/326) of patients with H. pylori and 10.3% (18/175) of those without H. pylori (OR = 1.77).

**TABLE 2.** Endoscopic and histologic characteristics of patients with and without H. pylori.

Characteristics	Infected	Not infected	OR
<b>Endoscopic findings</b>			
Erythema	79.8%	20.2%	1.25
Exudates	73.7%	26.3%	1.55
Flat erosion	78.8%	21.2%	2.08
Raised erosion	100%	0%	-
Rugal hypertrophy	100%	0%	-
Rugal atrophy	42.9%	57.1%	0.39
Bleeding	100%	0%	-
Nodularity	74.4%	25.6%	1.63
<b>Histological findings</b>			
Antral Inflammation	68.8%	33.3%	1.18
Neutrophil activity	100%	0%	-
Gastric mucosal atrophy	66.7%	33.3%	1.08
Intestinal metaplasia	44.1%	55.9%	0.39

**TABLE 3.** Sensitivities and specificities of various macroscopic and histologic findings.

Characteristics	Sensitivity	Specificity	PPV	NPV
<b>Endoscopic finding</b>				
Erythema	81.3%	22.3%	87.1%	66.3%
Exudates	8.6%	94.2%	14%	3.2%
Flat erosion	8%	96%	13.4%	2.2%
Raised erosion	0.6%	100%	1.1%	0%
Rugal hypertrophy	3.7%	100%	6.4%	0%
Rugal atrophy	1.9%	95.4%	3.4%	2.4%
Bleeding	1.8%	100%	3.3%	0%
Nodularity	9.9%	93.7%	16.3%	3.6%
<b>Histological findings</b>				
Antral inflammation	3.4%	97.1%	6.1%	1.5%
Neutrophil activity	0.6%	100%	1.1%	0%
Gastric mucosal atrophy	3.1%	97.1%	5.6%	1.5%
Intestinal metaplasia	4.7%	89%	8.9%	5.8%

## Discussion

The kind and frequency of endoscopic changes associated with gastritis in subjects infected with *H. pylori* are not known in details<sup>16</sup>. This study indicates that although there are some sensitive endoscopic characteristic findings for *H. pylori* related gastropathy, they are too non-specific. On the other hand, there are some highly specific endoscopic findings which are very insensitive. We should actually look for the positive predictive value and the negative predictive value of each finding or combinations of findings to decide whether we could accurately rely on them to predict *H. pylori* positivity. Our data indicates no single finding to be highly predictive either for *H. pylori* positivity or negativity, which is compatible with some studies<sup>17,18</sup> and incompatible with some other ones<sup>16,19</sup>.

In this study, *H. pylori* infection rate was significantly higher in patients with endoscopic findings for gastritis (determined by the Sydney system) than that in subjects with normal endoscopic findings which was similar to some of the previous studies<sup>17,18</sup>. Erythema was the most frequently endoscopic abnormality seen in our study; i.e. the highest sensitivity and positive predictive value for diagnosing *H. pylori* infection. However, in some reports, erythema was found to be less frequent than before in patients infected with *H. pylori*<sup>20,21</sup>.

While Stolte et al found that raised erosion was a specific finding in *H. pylori* infection<sup>22</sup>, our study showed a high specificity of rugal hypertrophy and bleeding in addition to raised erosion for detecting *H. pylori* infection. The same results about rugal hypertrophy were shown by some other studies too<sup>23-25</sup>. Moreover, two studies have demonstrated that enlarged gastric folds improved after eradication of *H. pylori*<sup>24</sup>. Yasunaga et al also reported that increased interleukin 1B and hepatocyte growth factor production caused by *H. pylori* infection may contribute to fold thickening of the stomach by simulating epithelial cell proliferation and foveolar hyperplasia in rugal hypertrophy<sup>25</sup>. Our study confirmed the results of Laine et al study which reported antral nodularity is a fairly reproducible finding and is very specific, though not sensitive, for *H. pylori* gastritis<sup>23</sup>.

The data from this and previous studies confirm that *H. pylori* is associated with histologic gastritis<sup>26,27</sup>. *H. pylori* is believed to be the etiologic agent of this gastritis<sup>28,29</sup> and cannot be considered to be a simple commensal of the human stomach. Gastritis was more common in infected subjects adding further evidence to the contention that *H. pylori* is the cause of the histologic lesion. A small number of subjects have gastritis in the absence of *H. pylori* on gastric biopsy. Some of these indi-

viduals are noted to have an antibody response to H. pylori. It is possible that biopsies have failed to detect H. pylori in these subjects. Alternatively, the subjects might have cleared the bacterium spontaneously, while the antibody response persisted<sup>30</sup>.

We also studied the relative frequency of H pylori in patients undergoing endoscopy (65.1%). This index was >60% in Eastern European populations and <50% in Western communities<sup>31,32</sup>. The factors responsible for the differences in prevalence rates of H. pylori among different nations and different ethnic groups within the same nation are unknown<sup>33,34</sup>. There are many methods for diagnosing H. pylori infection but, there is no absolutely valid method<sup>19</sup>. Therefore, a combination of several methods is recommended to ensure accurate diagnosis. However, a combination

requires multiple biopsy specimens which increases patient costs.

## Conclusions

Although there is no single endoscopic feature pathognomic for the presence of H. pylori infection but a combination of endoscopic with or without an indirect histologic finding could be diagnostic. Neutrophil activity in histology was observed only in patients with H. pylori infection. Therefore, an accurate endoscopic assessment of gastritis according to the Sydney system may show the H. pylori status confidently and may obviate the needs for biopsy in those with apparently normal endoscopy. But, we may still need to do biopsy to rule out dysplasia and probably early carcinoma especially in high risk populations.

## References

1. Russo A, Eboli M, Pizzetti P, Di Felice G, Ravagnani F, Spinelli P et al. **Determinants of Helicobacter pylori seroprevalence among Italian blood donors.** *Eur J Gastroenterol Hepatol* 1999; 11(8):867-873.
2. Malaty HM, Kim JG, El Zimaity HM, Graham DY. **High prevalence of duodenal ulcer and gastric cancer in dyspeptic patients in Korea.** *Scand J Gastroenterol* 1997; 32(8):751-754.
3. Kim JH, Kim HY, Kim NY, Kim SW, Kim JG, Kim JJ et al. **Seroepidemiological study of Helicobacter pylori infection in asymptomatic people in South Korea.** *J Gastroenterol Hepatol* 2001; 16(9):969-975.
4. Rehnberg-Laiho L, Rautelin H, Koskela P, Sarna S, Pukkala E, Aromaa A et al. **Decreasing prevalence of helicobacter antibodies in Finland, with reference to the decreasing incidence of gastric cancer.** *Epidemiol Infect* 2001; 126(1):37-42.
5. Pakodi F, Abdel-Salam OM, Debreceni A, Mozsik G. **Helicobacter pylori. One bacterium and a broad spectrum of human disease! An overview.** *J Physiol Paris* 2000; 94(2):139-152.
6. Glynn MK, Friedman CR, Gold BD, Khanna B, Hutwagner L, Iihoshi N et al. **Seroincidence of Helicobacter pylori infection in a cohort of rural Bolivian children: acquisition and analysis of possible risk factors.** *Clin Infect Dis* 2002; 35(9):1059-1065.
7. Malaty HM, El Kasabany A, Graham DY, Miller CC, Reddy SG, Srinivasan SR et al. **Age at acquisition of Helicobacter pylori infection: a follow-up study from infancy to adulthood.** *Lancet* 2002; 359(9310):931-935.
8. Veldhuyzen van Zanten SJ, Pollak PT, Best LM, Bezanson GS, Marrie T. **Increasing prevalence of Helicobacter pylori infection with age: continuous risk of infection in adults rather than cohort effect.** *J Infect Dis* 1994; 169(2):434-437.
9. Dufour C, Brisigotti M, Fabretti G, Luxardo P, Mori PG, Barabino A. **Helicobacter pylori gastric infection and sideropenic refractory anemia.** *J Pediatr Gastroenterol Nutr* 1993; 17(2):225-227.
10. Angtuaco TL, Sharma VK, Corder FA, Raufman JP, Howden CW. **Seroprevalence of H. pylori infection and symptoms of upper gastrointestinal tract disease in two groups of health-care workers.** *Dig Dis Sci* 2002; 47(2):292-297.
11. Rudi J, Toppe H, Marx N, Zuna I, Theilmann L, Stremmel W et al. **Risk of infection with Helicobacter pylori and hepatitis A virus in different groups of hospital workers.** *Am J Gastroenterol* 1997; 92(2):258-262.
12. Kamat AH, Mehta PR, Bhatia SJ, Koppikar GV. **Seroprevalence of IgG antibodies to Helicobacter pylori among gastrointestinal endoscopists, radiologists and paramedical personnel.** *J Assoc Physicians India* 1999; 47(9):866-868.

13. De Pascalis R, Del Pezzo M, Nardone G, Budillon G, Lavitola A. **Performance characteristics of an enzyme-linked immunosorbent assay for determining salivary immunoglobulin G response to *Helicobacter pylori*.** *J Clin Microbiol* 1999; 37(2):430-432.
14. Karvar S, Karch H, Frosch M, Burghardt W, Gross U. **Use of serum-specific immunoglobulins A and G for detection of *Helicobacter pylori* infection in patients with chronic gastritis by immunoblot analysis.** *J Clin Microbiol* 1997; 35(12):3058-3061.
15. Dixon MF, Genta RM, Yardley JH, Correa P. **Classification and grading of gastritis. The updated Sydney System. International Workshop on the Histopathology of Gastritis, Houston 1994.** *Am J Surg Pathol* 1996; 20(10):1161-1181.
16. Khakoo SI, Lobo AJ, Shepherd NA, Wilkinson SP. **Histological assessment of the Sydney classification of endoscopic gastritis.** *Gut* 1994; 35(9):1172-1175.
17. Sauerbruch T, Schreiber MA, Schussler P, Permanetter W. **Endoscopy in the diagnosis of gastritis. Diagnostic value of endoscopic criteria in relation to histological diagnosis.** *Endoscopy* 1984; 16(3):101-104.
18. Fung WP, Papadimitriou JM, Matz LR. **Endoscopic, histological and ultrastructural correlations in chronic gastritis.** *Am J Gastroenterol* 1979; 71(3):269-279.
19. Mihara M, Haruma K, Kamada T, Komoto K, Yoshihara M, Sumii K, Kajiyama G. **The role of endoscopic findings for the diagnosis of *Helicobacter pylori* infection: evaluation in a country with high prevalence of atrophic gastritis.** *Helicobacter* 1999; 4(1):40-8.
20. Pettrou CW, Appleman MD, Cohen H, Valenzuela JE, Chandrasoma P, Laine LA. **Prevalence of *Campylobacter pylori* and association with antral mucosal histology in subjects with and without upper gastrointestinal symptoms.** *Dig Dis Sci* 1988; 33(6):649-653.
21. Rokkas T, Pursey C, Uzoechina E, Dorrington L, Simmons NA, Filipe MI et al. ***Campylobacter pylori* and non-ulcer dyspepsia.** *Am J Gastroenterol* 1987; 82(11):1149-1152.
22. Stolte M, Batz C, Eidt S. **Giant fold gastritis--a special form of *Helicobacter pylori* associated gastritis.** *Z Gastroenterol* 1993; 31(5):289-293.
23. Laine L, Cohen H, Sloane R, Marin-Sorensen M, Weinstein WM. **Interobserver agreement and predictive value of endoscopic findings for *H. pylori* and gastritis in normal volunteers.** *Gastrointest Endosc* 1995; 42(5):420-423.
24. Yasunaga Y, Shinomura Y, Kanayama S, Yabu M, Nakanishi T, Miyazaki Y et al. **Improved fold width and increased acid secretion after eradication of the organism in *Helicobacter pylori* associated enlarged fold gastritis.** *Gut* 1994; 35(11):1571-1574.
25. Yasunaga Y, Shinomura Y, Kanayama S, Higashimoto Y, Yabu M, Miyazaki Y et al. **Increased production of interleukin 1 beta and hepatocyte growth factor may contribute to foveolar hyperplasia in enlarged fold gastritis.** *Gut* 1996; 39(9):787-794.
26. Barthel JS, Westblom TU, Havey AD, Gonzalez F, Everett ED. **Gastritis and *Campylobacter pylori* in healthy, asymptomatic volunteers.** *Arch Intern Med* 1988; 148(5):1149-1151.
27. Graham DY, Klein PD, Opekun AR, Boutton TW. **Effect of age on the frequency of active *Campylobacter pylori* infection diagnosed by the [<sup>13</sup>C]urea breath test in normal subjects and patients with peptic ulcer disease.** *J Infect Dis* 1988; 157(4):777-780.
28. Dooley CP, Cohen H. **The clinical significance of *Campylobacter pylori*.** *Ann Intern Med* 1988; 108(1):70-79.
29. Drumm B, Perez-Perez GI, Blaser MJ, Sherman PM. **Intrafamilial clustering of *Helicobacter pylori* infection.** *N Engl J Med* 1990; 322(6):359-363.
30. Marshall BJ, McGeachie DB, Rogers PA, Glancy RJ. **Pyloric *Campylobacter* infection and gastroduodenal disease.** *Med J Aust* 1985; 142(8):439-444.
31. Maarros HI. ***Helicobacter pylori* infection in Estonian population: is it a health problem?** *Ann Med* 1995; 27(5):613-616.
32. de Wit NJ, Mendive J, Seifert B, Cardin F, Rubin G. **Guidelines on the management of *H. pylori* in primary care: development of an implementation strategy.** *Fam Pract* 2000; 17 Suppl 2:S27-S32.
33. Hopkins RJ, Russell RG, O'Donnoghue JM, Wasserman SS, Lefkowitz A, Morris JG, Jr. **Seroprevalence of *Helicobacter pylori* in Seventh-Day Adventists and other groups in Maryland. Lack of association with diet.** *Arch Intern Med* 1990; 150(11):2347-2348.
34. Perez-Perez GI, Taylor DN, Bodhidatta L, Wongsrichanalai J, Baze WB, Dunn BE et al. **Seroprevalence of *Helicobacter pylori* infections in Thailand.** *J Infect Dis* 1990; 161(6):1237-1241.