

# ***H pylori* infection among 1000 southern Iranian dyspeptic patients**

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## **Abstract**

**AIM:** To describe the frequency of *H pylori* infection among 1000 southern Iranian dyspeptic patients.

**METHODS:** A prospective study was performed in a referral hospital in south of Iran from 1999 to 2005. One thousand dyspeptic patients (518 males, mean  $\pm$  SD age of  $49.12 \pm 12.82$  years) consecutively underwent upper gastrointestinal endoscopy. Multiple gastric antral biopsy samples were taken from all patients for rapid urease test and histopathologic examination (96.9% satisfactory samples). Patients were considered *H pylori*-infected if one or both tests were positive.

**RESULTS:** Six hundred and seventy-one patients (67.1%, 95% confidence interval [CI]: 64.2%-70.0%) were *H pylori*-infected. *H pylori* positivity was significantly more frequent in patients with peptic ulcer disease (PUD) than in those with non-ulcer dyspepsia ( $P < 0.001$ ). Male-to-female ratio for duodenal and gastric ulcers was 2.7:1 and 1.5:1, respectively. Moreover, the duodenal-to-gastric ulcer ratio was 1.95:1. The frequency of *H pylori* infection among those with endoscopic diagnosis of gastritis, duodenal ulcer, gastric ulcer, and normal mucosa was 70.1% (398/568), 86.2% (150/174), 71.9% (64/89), and 33.5% (54/161), respectively. *H pylori* infection, male sex, and older age were independently associated with PUD in multivariate analysis. *H pylori* positivity was associated with chronic gastritis, and chronic active gastritis with odds ratios of 34.21 (95% CI: 12.19%-96.03%) and 81.21 (95% CI: 28.85%-228.55%), respectively.

**CONCLUSION:** *H pylori* and PUD are highly frequent in dyspeptic patients from south of Iran. *H pylori* is a cardinal risk factor for chronic active or inactive gastritis.

## **INTRODUCTION**

*H pylori* is a major cause of gastritis and peptic ulcer disease (PUD), and has been implicated in the development of gastric malignancy<sup>[1-3]</sup>. The prevalence of *H pylori*, a worldwide infection, varies greatly among countries and among population groups within the same country<sup>[4]</sup>. *H pylori* is highly prevalent in the developing countries<sup>[5-11]</sup> and is common in 57%-91% of Iranian population<sup>[5,12-14]</sup>. However, studies regarding *H pylori* prevalence in different regions of Iran, a country with a miscellaneous climate, are limited<sup>[5,12-16]</sup>. Thus, we studied the frequency of *H pylori* infection among 1000 southern Iranian dyspeptic patients. Furthermore, we report *H pylori* association with different histopathologic and upper gastrointestinal endoscopy (UGIE) findings in this large number of patients.

## **MATERIALS AND METHODS**

### **Subjects**

A prospective study was performed in the Gastroenterology Division, Shahid-Mohammadi Referral Hospital, Bandarabbas, Iran from October 1999 to August 2005. One thousand consecutive patients (518 males, mean  $\pm$  SD age of  $49.12 \pm 12.82$  years, range 13-89 years) with dyspepsia underwent UGIE. Those with age over 12 years, no prior gastric surgery, no active bleeding, and no consumption of antibiotics, bismuth preparations, or proton pump inhibitors in the 4 wk prior to UGIE were eligible to enter the study. All patients enrolled gave their informed consent and the study was performed according to the Declaration of Helsinki.

### **Methods**

UGIE reported signs of gastritis, PUD, polyp, mucosal atrophy, and tumor. When PUD was present, concomitant gastritis was not mentioned in the study questionnaire. Moreover, when none of the above-mentioned pathologic

Table 1 Numbers and proportions of *H pylori* infected patients

	<i>n</i>	%	95% CI
Total	671/1000	67.1	64.2-70.0
Age (yr) <sup>a</sup>			
≤ 20	57/105	54.3	44.7-63.9
21-50	380/559	68.0	64.1-71.9
≥ 51	234/336	69.6	64.7-74.5
Sex			
Male	362/518	69.9	66.0-73.8
Female	309/482	64.1	59.8-68.4
UGIE finding <sup>b</sup>			
PUD	214/263	81.4	76.7-86.1
NUD	453/732	61.9	58.4-65.4
Tumor	4/5	80.0	40.8-100

PUD: Peptic ulcer disease; NUD: Nonulcer dyspepsia. <sup>a</sup>*P* < 0.05 between groups regarding *H pylori* infection; <sup>b</sup>*P* < 0.001 between PUD and NUD groups regarding *H pylori* infection.

features was present, the UGIE examination was considered normal. During UGIE, at least three biopsy specimens were taken from the antrum lesser curvature mucosa 3-4 cm proximal to the pylorus. One specimen was for rapid urease test (RUT). The RUT was monitored for color change up to 6 h after addition of the gastric tissue. The test was scored as positive if the color changed from yellow to red. The remaining two specimens were fixed in formaldehyde and submitted for histologic examination and HE staining. Nine hundred and sixty-nine antral mucosa biopsies (96.9%) were satisfactory for histopathological examination. One experienced pathologist, blinded to the results of RUT and UGIE, evaluated the coded samples. Thirty percent of coded samples (*n* = 291) were randomly evaluated by a second experienced pathologist. When the results were different (*n* = 11), the slides were discussed in joint sessions where a third pathologist was also present. The slides were observed under an optical microscope at several magnifications (including oil immersion). An increase in lymphocytes and plasma cells in the lamina propria characterized the gastritis as chronic. Activity in the context of chronic gastritis referred to the density of neutrophil polymorphs in the lamina propria, gastric pits, and surface epithelium. The presence of any pathology in at least one biopsy sample was considered a positive finding. The absence of abnormal findings in all specimens was regarded as normal. Detection of any *H pylori* was contemplated evidence of infection. Patients were considered *H pylori* positive if RUT and/or histology were/was positive. When the histologic sample was unsatisfactory, patient's of *H pylori* infection was determined by the RUT.

The frequency of *H pylori* was evaluated by means of cross tables regarding different age, sex, endoscopic and histopathologic diagnoses and tested by chi-square ( $\chi^2$ ) test and Fisher's exact test. Multivariate analysis was performed by entering sex, age groups, and *H pylori* status in a logistic regression model to identify the independent risk factors for endoscopic diagnoses of duodenal ulcer, gastric ulcer, and gastritis (normal endoscopy was set as a reference category). The same model was built to identify the independent risk factors for histopathologic diagnoses (normal mucosa was set as a reference category). For all

Table 2 Histological findings of satisfactory 969 antral biopsies

Histological finding	<i>n</i>	% (95% CI)
Normal mucosa	84	8.7 (6.9-10.4)
Chronic inactive gastritis	365	37.7 (34.6-40.7)
Chronic active gastritis	456	47.1 (43.9-50.2)
Atrophic changes	242	25.0 (23.6-27.7)
Intestinal metaplasia/malignancy	81	8.9 (7.1-10.7)
Glandular dysplasia	1	0.1 (-0.1-0.3)
Adenocarcinoma	4	0.4 (0.0-0.8)

point prevalences, 95% confidence intervals (CI) were calculated. Statistical significance was set at *P* < 0.05.

## RESULTS

Six hundred and seventy-one patients (67.1%, Table 1) were *H pylori*-infected. PUD was found in 263 enrolled patients (26.3%, 95% CI: 23.6%-29.0%). Those with PUD were significantly more *H pylori*-infected than those with non-ulcer dyspepsia (NUD) (*P* < 0.001, Table 1). Fisher's exact test displayed that PUD was more frequent in male patients than in female patients (68.8%, 95% CI: 63.2%-74.5%) *vs* 31.2% (95% CI: 25.5%-36.8%) (*P* < 0.001). Male-to-female ratio for duodenal and gastric ulcers was 2.7:1 (127/47) and 1.5:1 (54/35), respectively. While the duodenal-to-gastric ulcer ratio was 1.9:1 (174/89), endoscopic signs of gastritis were evident in 568 (56.8%), polyp in 7 (0.7%), mucosal atrophy in 5 (0.5%), raised/thickened area in 5 (0.5%), and accompanying duodenal and gastric ulcers in 3 (0.3%) patients. Thus, 161 patients (16.1%) had normal endoscopic results. A histologic diagnosis of chronic active gastritis was assigned to 47.1% of biopsy samples. Table 2 summarizes the histopathological findings.

While *H pylori* was frequent in 33.5% of those with normal UGIE, 86.2% of those with duodenal ulcer were *H pylori*-infected (*P* < 0.001, Table 3). Those with histologic diagnosis of chronic active gastritis were significantly more *H pylori*-infected than those with chronic inactive gastritis (*P* < 0.001, Table 3). Table 3 summarizes the frequency of *H pylori* infection regarding different endoscopic and histopathologic findings. Multivariate logistic regression analysis proved *H pylori* positivity, older age, and male gender as predictors of duodenal ulcer, gastric ulcer, and gastritis (Table 4). The second model to identify the risk factors for histopathologic findings, had a 56.1% agreement between predicted and observed results and the amount of variance accounted for 21.4% (Cox & Snell) - 25.3% (Nagelkerke). This model suggested that *H pylori* positivity was associated with chronic gastritis, and chronic active gastritis with odds ratios (OR) of 34.21 (95% CI: 12.19%-96.03%) and 81.21 (95% CI: 28.85%-228.55%), respectively.

## DISCUSSION

In the developing world, *H pylori* is a challenging health problem as 20% prevalence of *H pylori* infection among adolescents in the United States pales in comparison with infection rates exceeding 90% by five years of age in parts of the developing world<sup>[17]</sup>. One study in northwest of

**Table 3** *H pylori* infection regarding endoscopic and histologic diagnoses *n* (%)

Diagnosis	<i>H pylori</i> infection		
	Negative	Positive	Total
Endoscopic findings			
Normal	107 (66.5)	54 (33.5)	161
Gastritis	170 (29.9)	398 (70.1) <sup>b</sup>	568
Duodenal Ulcer	24 (13.8)	150 (86.2) <sup>b,d</sup>	174
Gastric Ulcer	25 (28.1)	64 (71.9) <sup>b</sup>	89
Histopathologic findings			
Normal mucosa	80 (95.2)	4 (4.8)	84
Chronic inactive gastritis	130 (35.6)	235 (64.4) <sup>f</sup>	365
Chronic active gastritis	87 (19.1)	369 (80.9) <sup>h</sup>	456
Atrophic changes	76 (31.4)	166 (68.6) <sup>f</sup>	242
Metaplasia/dysplasia/adenocarcinoma	15 (17.4)	71 (82.6) <sup>f</sup>	86

<sup>b</sup>*P* < 0.001 *vs* normal endoscopic findings; <sup>d</sup>*P* < 0.001 *vs* gastritis and gastric ulcer; <sup>f</sup>*P* < 0.001 *vs* normal histopathologic findings; <sup>h</sup>*P* < 0.001 *vs* histopathologic findings and chronic inactive gastritis (Fisher's exact test).

Iran, a region with the highest mortality rate from gastric cancer throughout the country, reported that *H pylori* infection occurs in 89.2% (883/990) of the residents<sup>[5]</sup>. Other surveys in different age groups from various regions of the country reported that *H pylori* infection occurs in 57%-91% of the study subjects<sup>[12-14]</sup>. In this prospective survey, we report *H pylori* infection in 67.1% of 1000 enrolled dyspeptic patients from south of Iran. Variation in study powers as well as ethnicity, place of birth, socioeconomic factors, diet, occupation, smoking, or alcohol consumption habits among study populations may be the reasons for erratic rates of *H pylori* infection reported from the country<sup>[6,18]</sup>. Similarly, *H pylori* seems to be a health problem in the neighboring regions of Iran. In India, *H pylori* is positive in 38 (56.7%) asymptomatic individuals and in 49 (61.3%) symptomatic individuals<sup>[6]</sup>. In Saudi-Arabia, *H pylori* is present in 54.9% of gastric biopsies from 488 dyspeptic patients<sup>[7]</sup>. In Yemen, 82.2% of 275 dyspeptic patients are *H pylori*-infected<sup>[8]</sup>. In Jordan, *H pylori* is frequent in 82% of 197 study subjects<sup>[9]</sup>. In United Arab Emirates<sup>[10]</sup> and in Kuwait<sup>[11]</sup>, 90.39% of 437 and 96.6% of 204 studied subjects are infected with *H pylori*, respectively.

About a quarter of dyspeptic patients in this study were proved to have PUD. Nevertheless, in another large cohort of residents in northwest of Iran, the frequency of PUD is just 4.9%<sup>[5]</sup>. This relatively low frequency of PUD might be due to the enrollment of unnecessarily dyspeptic subjects in the latter survey. PUD frequencies are divergent in reports from different countries. In a literature review by the American Gastroenterology Association<sup>[19]</sup>, 19 out of 41 studies report duodenal ulcer in  $\geq 10\%$  of dyspeptic patients and the overall prevalence of PUD in these groups of symptomatic patients is  $\geq 15\%$  in 21 studies. Duodenal ulcer was approximately twice as common as gastric ulcer in the present survey, which is in quite contrast to the 12:1 ratio reported from India<sup>[6]</sup>. Moreover, *H pylori* infection is significantly more frequent in PUD than in NUD patients. Regarding the significantly higher rate of *H pylori* infection in those with duodenal (86.2%) and gastric (71.9%) ulcers in comparison with the subjects with normal endoscopic findings

**Table 4** Multivariate logistic regression of selected model variables on endoscopic findings<sup>1</sup>

Variable	B	SE	Wald test	P	Odds ratio (95% CI)
Duodenal ulcer					
Sex (male)	1.91	0.26	55.14	< 0.001	6.75 (4.08-11.17)
Age (in three ascending groups)	0.59	0.19	9.211	< 0.01	1.80 (1.23-2.63)
<i>H pylori</i> (+)	2.54	0.28	79.21	< 0.001	12.66 (7.24-22.14)
Constant	-3.75	0.50			
Gastric Ulcer					
Sex (male)	1.34	0.28	22.13	< 0.001	3.83 (2.19-6.69)
Age (in three ascending groups)	0.65	0.22	8.49	< 0.01	1.91 (1.24-2.95)
<i>H pylori</i> (+)	1.63	0.29	30.74	< 0.001	5.12 (2.87-9.11)
Constant	-3.45	0.56			
Gastritis					
Sex (male)	0.91	0.20	20.15	< 0.001	2.48 (1.67-3.68)
Age (in three ascending groups)	0.65	0.15	18.35	< 0.001	1.92 (1.42-2.58)
<i>H pylori</i> (+)	1.54	0.19	61.81	< 0.001	4.65 (3.17-6.82)
Constant	-1.30	0.361			

<sup>1</sup>Normal endoscopy was set as a reference category; agreement between predicted and observed results: 57.2%; the amount of variance accounted for 17.6% (Cox & Snell)- 19.4% (Nagelkerke).

(33.5%) (Table 3), also the significant association of *H pylori* positivity with duodenal (OR: 12.66) as well as gastric ulcers (OR: 5.12) (Table 4), *H pylori* can be introduced as an aetiological agent for PUD, thus strengthening prior findings<sup>[10,20,21]</sup>. Furthermore, current evidence shows the cardinal role of *H pylori* in the pathogenesis of PUD<sup>[22-24]</sup>. In favor of the results of some studies<sup>[25-27]</sup> and against the findings of others<sup>[6,28,29]</sup>, we found significantly more *H pylori* infections in male than in female PUD subjects, but *H pylori* was not significantly more prevalent in males. Regarding these two latter findings, one may deduce that *H pylori* infection independently results in PUD in males more frequent than in females. The regression model also confirms this judgment as entering both sex and *H pylori* status in the model showed an independent significant role of both factors in prediction of different endoscopic findings (Table 4). Nevertheless, despite more than a 50% agreement between the predicted and observed results of both models in this survey, outcomes should be carefully interpreted due to the limited factors entered into these models as other factors with a possible predictive role were beyond the scope of the current study and thus were not entered into the model.

In the present study, histologic findings of chronic active and inactive gastritis were frequent in about 85% of dyspeptic subjects, which is comparable with the previous 77.8% of chronic active gastritis in northwest of Iran<sup>[5]</sup>, 80.6% and 67% of chronic gastritis in Saudi-Arabia<sup>[30]</sup> and India<sup>[6]</sup>, respectively. Similarly, *H pylori* with a significantly higher frequency in those with chronic active and inactive gastritis compared to those with normal histology, showed a strong association with chronic active gastritis (OR: 81.21) and chronic inactive (OR: 34.21) gastritis, although more frequent in those with chronic active gastritis, which is suggestive of its causative role in chronic gastritis and gastritis activity. Despite some doubts<sup>[31]</sup>, *H pylori* is globally believed to have a fundamental role in the pathogenesis of gastric cancer<sup>[3,32,33]</sup>. Chronic *H pylori* gastritis leads in more



than half of the affected subjects to a gradual loss of the glandular structures with its specialized cells and a collapse of the reticulin skeleton of the mucosa, a condition of atrophic gastritis<sup>[34]</sup>. Indeed, the most common type of gastric cancer, the intestinal type, is preceded by chronic atrophic gastritis, which is 22%-37% prevalent in asymptomatic European adult subjects<sup>[35]</sup>. In this survey, a quarter of satisfactory antral biopsies were proved to have atrophic changes in histology, about two thirds of which were associated with *H pylori* infection. Compared to our findings in south of Iran as well as those in the developed world<sup>[35]</sup>, northwest of Iran with a relatively higher frequency of atrophic changes in the antral biopsies of the sampled population (45.2%)<sup>[5]</sup> might be at a higher risk of prevalence of gastric malignancies in the near future, an alarming condition that necessitates further investigations and thoughtful interventions.

In conclusion, *H pylori* and PUD are frequent in dyspeptic patients from south of Iran. *H pylori* infection, male sex, and older age are independently associated with PUD. *H pylori* is associated with chronic gastritis and even more with chronic active gastritis.

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