



Association between Pattern of Gastritis and Gastroesophageal Reflux Disease in Patients with *Helicobacter Pylori* Infection

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ABSTRACT

BACKGROUND

Reflux disease is a common gastrointestinal problem. The association between reflux disease and gastritis pattern is controversial.

AIM: To determine the association between reflux disease and gastritis pattern in patients with *Helicobacter pylori* (*H. pylori*) infection.

METHODS

470 patients with dyspepsia and reflux disease were enrolled in this study. The inclusion criteria were willing to participate in the study, age over 40 years, and having the criteria of ROME III for at least 3 months. Patients with history of *H. pylori* eradication therapy during the 3 months before the study, a history of gastric surgery, and gastric cancer were excluded. All of the participants underwent upper endoscopy and two biopsy samples were taken from antrum, body, and fundal areas.

RESULTS

H. pylori infection rate was 367 (78.1%) with mean age of 59.8 ± 11.4 years. Of them 131 patients (35.7%) were male. Reflux disease was detected in 273 (74.4%) patients. 216 (58.9%) and 102 (27.8%) patients had non-erosive reflux disease (NERD) and gastroesophageal reflux disease (GERD), respectively. Corpus predominant and antral predominant gastritis were seen in 72 (19.6%) and 129 (35.2%) patients, respectively. Antral gastritis was significantly associated with GERD ($p < 0.01$). In regression analysis, antral predominant gastritis had a significant association with GERD (OR=1.92; 95%CI: 1.22-3.12). The same result was observed in mild to moderate antral and greater curvature gastritis (OR= 1.26; 95%CI: 0.25-6.40 and OR= 3.0; 95%CI: 0.63-14.17, respectively).

CONCLUSION

According to these findings, we could suggest that the pattern of gastritis could be associated with reflux disease and GERD.

KEYWORDS

Gastroesophageal Reflux; GERD; Gastritis; Esophagus

Please cite this paper as:

Nobakht H, Boghratian AH, Sohrabi MR, Panahian M, Rakhshani N, Nikkhah M, Ajdarkosh H, Gholami A, Hemmasi GR, Khonsari MR, Rabiei N, Zamani F. Association between Pattern of Gastritis and Gastroesophageal Reflux Disease in Patients with *Helicobacter Pylori* Infection. *Middle East J Dig Dis* 2016;8:206-211. DOI :10.15171/mejdd.2016.33

INTRODUCTION

Reflux disease is considered as a common cause of referring patients to medical care.¹ Risk factors for reflux esophagitis include the presence of hiatal hernia, transient relaxation of the lower esophageal sphincter, and impaired clearance of regurgitated gastric contents in

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Received: 12 Feb. 2016

Accepted: 10 Jun. 2016

the esophagus.² Despite these facts, the underlying mechanism of reflux disease has not been completely defined.³ It was suggested that *Helicobacter pylori* (*H. pylori*) could be a causative factor for many gastrointestinal diseases such as gastritis. Nevertheless, the relationship between *H. pylori* infection and gastroesophageal reflux disease (GERD) is still controversial.^{4,6}

During the last decades *H. pylori* treatment was commonly administered to patients with dyspepsia. In this context, studies on patients with non-ulcer dyspepsia showed that *H. pylori* eradication might not have a beneficial role for patients with reflux disease.^{5,7} Even some researchers suggested that presence of *H. pylori* infection might have a protective role against GERD.⁸ Although it is not confirmed in all studies.⁹ Thus the association between *H. pylori*, gastritis, and GERD is considered as a topic of interest in studies. Based on previous studies chronic active *H. pylori* gastritis is associated with milder forms of reflux disease and eradication of *H. pylori* increased the risk of developing GERD.^{5,9} Moreover there is little information about the pattern of gastritis in dyspeptic patients with developing GERD. The aim of this study was to determine the association between the presence of GERD and gastritis patterns in patients with *H. pylori* infection.

MATERIALS AND METHODS

Patients:

This is a cross-sectional study on patients with dyspepsia and reflux disease referring to gastrointestinal clinics of Firoozgar General Hospital between 2010 and 2013. The inclusion criteria were willing to participate in the study, age over 40 years, and having the criteria of ROME III for at least 3 months. The exclusion criteria were *H. pylori* eradication therapy during the last 3 months before the study, and a history of gastric surgery or gastric cancer.

The study's protocol was explained to all volunteers. The participants underwent physical examination by three trained general practitioners. Also a questionnaire including demographic as well as clinical findings, smoking habits, and alcohol use

was completed for each subject. In the case of any important findings they were referred to a relevant specialist. Consequently the participants were invited for upper endoscopy in the Endoscopy ward of the hospital. Reflux disease was defined as the presence of reflux symptoms (heartburn and regurgitation) at least twice weekly for at least 4 weeks or the presence of mucosal break in esophagus according to Los Angeles (LA) classification during endoscopy.¹⁰

Endoscopy:

Upper endoscopy was performed by two mentor gastroenterologists in our center where more than 3000 upper endoscopies are annually performed. The patients were advised to discontinue any proton pump inhibitor and antibiotics at least one month prior to endoscopy. After explaining the procedure to the patients, local oropharynx anesthesia with lidocaine 5% and midazolam were applied by a trained nurse. The endoscope was advanced to the second part of duodenum. The distal of esophagus as well as stomach was evaluated carefully and any erythema, erosion, and ulcer were reported. Endoscopic reflux was defined as the presence of either erosions or ulceration. GERD was classified according to LA classification. Two biopsy samples were taken from antrum (2–3 cm from the pylorus), body, and fundal areas. Two antral biopsy samples were also taken for *H. pylori* rapid urease test (CLOtest; Ballard, Draper, Utah, USA). Presence of *H. pylori* was identified when rapid urease test or histology was positive. During endoscopy all lesions including erythema, erosions (small superficial defect in mucosa with petechia), atrophies (whitish and thinning mucosa with or without submucosal vascular pattern), ulcer, and tumoral lesions were noted and biopsy samples were taken. The samples were stored in separate bottles.

Histological Evaluation:

The biopsy specimens were embedded in paraffin wax, then sectioned and stained with Hematoxylin-Eosin (H&E) and Giemsa. All the specimens were examined by an experienced gastrointestinal

Table 1: The demographic characteristics of the patients

Variables	N (%)	
Sex	Man	241 (51.2%)
	Woman	229 (48.8%)
Job	Housewives	147 (31.3%)
	Employees	122 (26.0%)
	Farmers	84 (17.9%)
	Other	117 (24.9%)
Educational level	Illiterate	30 (6.4%)
	Primary education	130 (27.7%)
	Third grade	150 (31.9%)
	Secondary High school or diploma	117 (24.9%)
Location	College education	43 (9.1%)
	Urban	335 (71.3%)
	Rural	135 (28.7%)
History of smoking	Yes	158 (33.6%)
	No	312 (66.4)
Mean duration of smoking	11.4± 18.8	
Body mass index (BMI)	26.14 ± 4.46	

pathologist. According to Sydney System the severity and depth of inflammation were graded as 0-311. Chronic inflammation was considered as the presence of inflammatory cells in lamina propria. Chronic active inflammation was considered as the presence of granulocyte in lamina propria or intraepithelial. The presence of *H. pylori* in any specimens was considered as positive *H. pylori*.

Data collection:

The clinical data as well as upper endoscopic results were recorded in each questionnaire. The histopathological data were also collected from pathology reports.

Statistical Analysis:

The results were analyzed by SPSS (version 20.0 SPSS, Chicago, Illinois USA) software for Windows. Descriptive analysis was used for reporting the prevalence of lesions, sex, and age distributions. The association between clinical and endoscopic data and pathology findings were analyzed by chi-square test.

Forward stepwise multivariate logistic regression was also applied for final estimations. P value less than 0.05 was considered as statistically significant.

Ethics:

The Ethics Committee of Gastrointestinal and Liver Disease Research Center approved the study protocol. The protocol was explained to subjects before enrollment. A written informed consent was obtained from all the participants. Patients' information was securely stored in the study database.

RESULTS:

Baseline characteristics:

Of the all patients with dyspepsia, 470 patients met the inclusion criteria and were enrolled in the study. The mean age of the participants was 58.3±11.6 years and 241 (51.2%) of them were male. (Table 1) show the basic characteristics of the patients.

Endoscopic and Histological Findings:

Regarding the endoscopic findings, 19 (4%) patients had normal upper endoscopy. Sliding hiatal hernia was seen in 195 (41.5%). Endoscopic GERD was found in 136 (28.9%) patients, of whom 90 (66.2%), 40 (29.4%), 3 (2.2%), and 3 (2.2%) patients had grade A, B, C, and D of esophagitis according to LA classification, respectively. The frequency of endoscopic finding is summarized in table 2.

H. pylori infection was detected in 367 (78.1%) subjects with mean age of 59.8± 11.4 years and of whom 131 (35.7%) patients were male. Positive *H. pylori* infection was detected in 202 (78%), 219 (77.6%) and 197 (79.7%) patients with bloating, pyrosis, and heart burn respectively. Among *H.pylori* positive patients reflux disease was seen in 273 (74.4%) subjects. In this group 216 (58.9%) and 102 (27.8%) patients had non-erosive reflux disease (NERD) and GERD respectively. *H. pylori* was also detected in 17(65.3%) out of 26 patients with columnar lined esophagus (Barrett's). Presence of *H. pylori* was revealed among 72 (75.0%) out of 96 and 129 (92.1%) out of 140 patients with corpus predominant and antral predominant gastritis, respectively. The association between the frequencies of endoscopic findings and the presence of *H. pylori* is summarized in table 2.

Table 2: The frequency of endoscopic findings in association with *H. pylori* (N=470)

		HP status		p value
Hiatal hernia	Present	152	43	0.81
	Absent	215	59	
	None	265	70	
Endoscopic GERD (Los Angeles Class)	A	67	23	0.31
	B	32	8	
	C	2	1	
	D	1	2	
Corpus predominant	Present	72	24	0.41
	Absent	295	79	
Antral predominant	Present	129	18	0.13
	Absent	238	75	
Equal gastritis	Present	196	59	0.49
	Absent	171	44	

In the next step we excluded the *H. pylori* negative patients and the rest of analysis was done on *H. pylori* infected cases. In chi-square analysis we did not find any association between the presence of *H. pylori* and reflux disease ($p = 0.52$) as well as GERD ($p = 0.25$). Patients with GERD had symptoms of reflux disease ($p < 0.001$). The antral gastritis was significantly associated with GERD ($p < 0.001$). We could not obtain the same result for corpus predominant gastritis ($p = 0.10$). In general the severity of antral gastritis was associated with reflux disease ($p = 0.04$). This associations was not shown in patients with GERD ($p = 0.07$). The severity of gastritis in other parts of stomach was not associated with reflux disease or GERD. There was not any significant association between antral, cardia, or corpus atrophy and GERD. We did not find any association between atrophy of any zones of the stomach with reflux disease.

In regression analysis, antral predominant gastritis had a significant association with GERD (OR=1.92; 95%CI: 1.22-3.12) but not NERD. Moreover grade B of GERD had a significant correlation with antral predominant gastritis (OR=3.26; 95%CI: 1.53-3.19). The same result was observed in mild to moderate antral great curvature gastritis (OR=1.26; 95%CI: 0.25-6.40 and OR=3.0; 95%CI: 0.63-14.17, respectively). We did not observe a significant association between GERD and other variables in this context. The presence of NERD was not associated with the grade of GERD.

DISCUSSION:

In the present study, we found that the prevalence of *H. pylori* among patients with reflux disease and GERD were 74.4% and 75.3%, respectively. Moreover we showed that the severity of antral gastritis was associated with reflux disease.

H. pylori could contribute to many gastrointestinal diseases including GERD. The role of *H. pylori* in developing GERD still remains a controversial issue.^{9,10} Based on previous reports, the rate of *H. pylori* infection in patients with GERD, wildly varies from 30-90% and it seems that about 40% of patients with GERD are infected by this bacterium.^{5,11} Furthermore, most trials on the correlation between *H. pylori* infection and GERD have indicated no causal relationship.^{1,9,12,13} Acid contact to esophagus mucosa is considered as the main cause of esophagitis.^{2,5,15} *H. pylori* itself produces acid inhibitory proteins, while the infection induces inhibition of acid secretion. In some patients *H. pylori* is primarily colonized in the antrum, resulting in an antral predominant gastritis, which in turn induces gastrin and acid secretion. In the rest of patients *H. pylori* infection spreads from the antrum towards other parts of the stomach.^{5,16,17} When the corpus (as the main acid-producing region) is infected, the secretion of acid is affected by inflammation process and decreases. In this view of point the eradication of *H. pylori* might increase acid secretion and consequently induce esophagitis as revealed by previous reports.

It has to be reminded that our country is considered as a high prevalence area of *H. pylori* infection, which in turn it is not easy to exclude *H. pylori* factors in evaluation of patients with reflux disease. The strength point of the present study is that it focused on *H. pylori* positive patients and evaluated the pattern of gastritis on reflux disease. Many of previous studies evaluated the correlation between carditis and GERD¹⁸⁻²⁰, but in the present study we tried to determine the association between reflux disease and gastritis in each part of the stomach. This study showed a correlation between antral predominant gastritis and GERD in bivariate and regression analysis, which is not comparable with the result of previous reports. Also in previous reports it was already indicated that corpus predominant gastritis in *H. pylori* infected patients might have negative effect on gastric acid secretion via cytokines.^{18,21} Furthermore, we did not obtain the same association between other parts of the stomach and GERD, which was similar to other studies. In this study corpus gastritis was found less frequently in patients with reflux disease.

In conclusion, this study is one of the few studies focused on the relationship between GERD and pattern of gastritis in *H. pylori* infected patients. We found that pattern of gastritis could be associated with GERD.

CONFLICT OF INTEREST

The author declares no conflict of interest related to this work.

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