Helicobacter pylori Infection in Superficial Gastritis, Erosive Gastritis and Gastric Ulcer

Jacobus Albertus, Abdul Aziz Rani**, Marcellus Simadibrata***
*Murdani Abdullah**, Ari Fahrial Syam***
*Department of Internal Medicine, Tugurejo District General Hospital, Semarang
**Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine
University of Indonesia/Dr. Cipto Mangunkusumo General National Hospital, Jakarta

ABSTRACT

Background: *Helicobacter pylori (H. pylori) infection leads to inflammation of the gastric mucosa. It damages the gastric epithelium and related to the risk of developing gastric cancer. Over time, it may develop into the development of glandular atrophy and intestinal metaplasia. This study was aimed to evaluate the histological features of gastric mucosa, including H. pylori infection in patients with endoscopically found superficial gastritis, erosive gastritis and gastric ulcer.*

Method: *Subjects with abdominal complaints who underwent consecutive upper gastrointestinal endoscopy were prospectively selected at Tugurejo Hospital between November 2004 and December 2010. Eligible subjects were those with endoscopic diagnosis of superficial gastritis, erosive gastritis or gastric ulcer. The biopsy specimens were taken from the corpus, angulus and antrum of all the patients. Giemsa and hematoxylin-eosin staining were used for the histological diagnosis H. pylori and gastric mucosa inflammation.*

Results: *The overall prevalence of H. pylori infection in superficial gastritis, erosive gastritis and gastric ulcer were 24.3%. There was significant difference between H. pylori infection rate in antrum of patients with superficial gastritis 19.4%, erosive gastritis 26.3%, and gastric ulcer 34.7%. The positivity rate of glandular atrophy and intestinal metaplasia of superficial gastritis with H. pylori-positivity was 12.5%, 14.0%; erosive gastritis 26.3%, 16.6%; and of gastric ulcer 38.9%, 29.3%; respectively. However, there was no significant difference.*

Conclusion: *Patients with gastric ulcer have H. pylori infection, atrophic gastritis and metaplasia intestinal more than superficial gastritis and erosive gastritis. Progression of the gastric ulcer to atrophic gastritis and intestinal metaplasia is related to H. pylori infection.*

Keywords*: Helicobacter pylori infection, superficial gastritis, erosion and ulcer*

ABSTRAK

Latar belakang*: Infeksi Helicobacter pylori (H. pylori) dapat menyebabkan terjadinya peradangan pada mukosa lambung. Hal tersebut dapat merusak epitel lambung dan menjadi risiko terkena kanker lambung. Seiring dengan berjalannya waktu, atropi kelenjar lambung dan metaplasia intestinal dapat berkembang menjadi kanker lambung. Penelitian ini bertujuan untuk mengevaluasi histologi dari mukosa lambung meliputi infeksi H. pylori pada pasien dengan temuan endoskopi sebagai penyebab gastritis ringan, gastritis erosif dan ulkus lambung.*

Metode: *Pengumpulan data dilakukan secara prospektif dengan rancangan penelitian potong lintang. Subjek penelitian adalah semua pasien yang menjalani prosedur esofagogastroduodenoskopi secara konsekutif di Rumah Sakit Tugurejo Semarang pada November 2004-Desember 2010 dengan keluhan pada saluran cerna bagian atas dan ditemukan sebagai gastritis ringan, gastritis erosif atau ulkus lambung. Pengambilan biopsi dilakukan pada korpus, angulus dan antrum. Pewarnaan Giemsa dan Hematoxyllin Eosin dilakukan untuk mendiagnosis infeksi H. pylori dan inflamasi pada mukosa lambung.*

Hasil: *Secara keseluruhan diketahui prevalensi infeksi H. pylori sejumlah 24,3%. Terdapat perbedaan bermakna secara statistik untuk infeksi H. pylori di antrum pada gastritis superfisial 19,4%, gastritis erosif 26,3%, dan ulkus lambung 34,7%. Infeksi H. pylori pada atropi kelenjar dan metaplasia intestinal masing-masing ditemukan pada gastritis superfisial sebesar 12,5% dan 14,0%, pada gastritis erosif 26,3% dan 16,6%; dan ulkus lambung sebesar 38,9% dan 29,3%, namun secara statistik tidak terdapat perbedaan bermakna.*

Simpulan: *Pasien dengan ulkus lambung mempunyai infeksi H. pylori, atropi dan metaplasia yang lebih banyak dibandingkan dengan gastritis superfisial dan gastritis erosif. Infeksi H. pylori dapat mempercepat perkembangan ulkus menjadi atropi dan metaplasia intestinal.*

Kata kunci: *infeksi Helicobacter pylori, gastritis superfisial, erosi dan ulkus*

INTRODUCTION

In the early 20th century, the pathogenesis of acid-peptic disease was believed to be related to stress and dietary factors. Later on, other factors such as gastric secretions, age, sex, smoking and alcohol consumption were held responsible as the cause.[1] Warren and Marshall in 1982 discovered a spiral, flagellated gram-negative organism known as *Helicobacter pylori (H. pylori)* which has been implicated in the etiology of these diseases.[2] While the prevalence of *H. pylori* is decreasing in the Western world, it still constitutes a significant medical burden in less industrialized countries, with constant higher infection rates and a more widespread distribution.[3] The challenge now is to fill in the remaining gaps in our knowledge such as transmission routes as well as genetic preconditions, as antibiotic resistance increases, develop preventative strategies including improved hygiene conditions and vaccination.[4-7]

Infection with *H. pylori* is a co-factor in the development of duodenal or gastric ulcers (reported to develop in 1 to 10% of infected patients), gastric cancer (0.1 to 3%) and gastric mucosa associated lymphoid tissue (MALT) lymphoma (< 0.01%).[8,9] Infection with *H. pylori* may lead to inflammation of the gastric mucosa with subsequent ulceration.[9] Infection is a major cause of chronic gastritis, a condition that initiates the pathogenic sequence of events leading to atrophic gastritis, intestinal metaplasia, dysplasia and subsequently cancer.[8,10-14] While the bacterium is not a direct cause of cancer, its presence and resultant reduction in acid production are necessary factors in causation.[8,15] The risk of these disease outcomes in infected patients varies widely among different populations and the great majority of patients with *H. pylori* will not have any clinically significant complications.[16-18]

Diagnosis of *H. pylori* infection is done either by rapid urease test in biopsy specimen or microscopic examination and culture of the specimen or by other non-endoscopic methods like urea breath test, *H. pylori* stool antigen assay or anti-*H. pylori* antibodies in the serum.[8,19] *H. pylori* eradication has been recommended by various consensus conferences and its eradication has led to marked reduction in peptic ulcer disease and need for further therapy.[19,20-22] *H. pylori* infection has worldwide distribution and is found to be prevalent and strongly associated with peptic ulcer disease and gastritis in Pakistani population.[23] Data of *H. pylori* infection in superficial gastritis and ulcer disease in Indonesia was limited. This study was aimed to evaluate the histological features of gastric mucosa, including *H. pylori* infection, in patients with endoscopically found superficial gastritis, erosive gastritis and gastric ulcer.

METHOD

A cross-sectional study was conducted. All patients were prospectively selected from subjects with abdominal complaints who underwent consecutive upper gastrointestinal endoscopy at Tugurejo Hospital Semarang between November 2004 and December 2010. The inclusion criteria were subjects with endoscopic diagnosis of superficial gastritis, erosive gastritis and gastric ulcer. Subjects were excluded from the study if they had history of receiving anti-ulcer agents or antibiotics during two weeks before endoscopy or had previous history of duodenal ulcers, or gastric surgery. All patients have given their informed consent prior to endoscopy.

Biopsy specimens for histological diagnosis were obtained endoscopically from the greater curvature of the lower, the upper corpus and the lesser curvature of the lower corpus of the stomach, according to the triple-site gastric biopsy method. The specimens were fixed overnight in buffered formalin, embedded in paraffin, cut into three μm thickness, and stained with hematoxylin-eosin

staining. In accordance with the Updated Sydney System, the degree of gastric mucosal inflammation (mononuclear and poly-morphonuclear cell infiltration), glandular atrophy, and intestinal metaplasia were classified into four grades as follows: 0 = none, 1 = mild, 2 = moderate and 3 = severe.[14] Histologically, *H. pylori* infection was considered negative if *H. pylori* were absent from all biopsy sites stained with hematoxylin-eosin staining. *H. pylori* infection was considered positive if at least one of the histology tests was positive.

The prevalence of *H. pylori* infection, rates of gastric mucosal inflammation, polymorphonuclear cell infiltration, glandular atrophy and intestinal metaplasia were compared using the chi-square test for 4-fold table. The difference in grades of mononuclear cell infiltration, polymorphonuclear cell infiltration, glandular atrophy and intestinal metaplasia between diseases was compared by Mann-Whitney test. If $p < 0.05$ was considered statistically significant.

RESULTS

Two hundred and sixteen patients were enrolled in this study consisted of 72 patients with superficial gastritis aged from 38 to 68 years (mean age 56.3 ± 9.9); 72 patients with erosive gastritis aged from 38 to 66 years (mean age 65.3 ± 10.4); 72 patients with gastric ulcer aged from 38 to 70 years (mean age 65.7 ± 10.8).

Predominant sites of lesions based on endoscopical diagnosis are shown in Table 1. The positivity rates for *H. pylori* infection in studied patients are shown in Table 2. There was no data of *H. pylori* at angulus sites since the pathologist had not evaluated *H. pylori* from the antrum and angulus. The prevalence of *H. pylori* infection in gastric ulcer was significantly higher than that of superficial gastritis and erosive gastritis.

Table 1. Endoscopical diagnosis and predominant sites of lesion

Endoscopical diagnosis	Predominant site of location lesion n (%)		
	Corpus	Antrum	Corpus and antrum
Superficial gastritis	3 (4.16)	37 (51.38)	30 (41.67)
Erosive gastritis	19 (26.39)	51 (70.83)	2 (2 .78)
Gastric ulcer	16 (22.22)	47 (65.28)	9 (12.5)

Table 2. *Helicobacter pylori* infection identified in antrum and associated diseases

Endoscopical diagnosis	*H. pylori* infective rate (%)	p*
Superficial gastritis	19.4	
Erosive gastritis	26.3	0.042
Gastric ulcer	34.7	

*Chi-square test

The grades of mononuclear cell and polymorphonuclear cell infiltration, mucosal glandular atrophy and intestinal metaplasia in patients are shown in Table 3 and 4. The grades of mononuclear cell infiltration and polymorphonuclear cell infiltration in gastric ulcer were higher than that in superficial gastritis patients and erosive gastritis, but it was not significantly different.

The positivity rate of mucosa glandular atrophy and intestinal metaplasia of superficial gastritis, erosive gastritis, and gastric ulcer patients with *H. pylori* positivity was significantly higher in gastric ulcer than superficial gastritis (Table 5).

Table 3. The grade of gastric mucosal inflammation in patients

Diagnosis	Mononuclear (%)				Polymorphonuclear (%)				p*
	0	1	2	3	0	1	2	3	
Superficial gastritis	44.3	30.9	10.1	14.7	72.7	3.5	4.5	19.2	
Erosive gastritis	3.8	27.0	23.0	43.4	36.7	3.8	10.1	52.1	0.091
Gastric ulcer	4.2	11.3	17.0	67.5	17.8	3.1	17.5	61.5	

0: none; 1: mild; 2: moderate; 3: severe; *Mann-Whitney test

Table 4. The grade of glandular atrophy and intestinal metaplasia in patients

Diagnosis	Atrophy				Intestinal metaplasia				p*
	0	1	2	3	0	1	2	3	
Superficial gastritis	77.6	18.7	2.2	1.5	85.3	4.2	4.9	5.6	
Erosive gastritis	62.3	13.1	10.5	14.1	81.7	8.5	3.4	6.4	0.087
Gastric ulcer	56.2	10.7	11.8	21.3	71.7	6.7	8.1	13.5	

0: none; 1: mild; 2: moderate; 3: severe; *Mann-Whitney test

Table 5. Glandular atrophy and intestinal metaplasia in patients with *Helicobacter pylori* infection and associated disease

Diagnosis	Glandular atrophy *H. pylori* + (%)	Intestinal metaplasia *H. pylori* + (%)	p*
Superficial gastritis	12.5	14.0	
Erosive gastritis	23.6	16.6	0.038
Gastric ulcer	38.9	29.3	

*Chi-square

DISCUSSION

H. pylori infections tend to be initiated at the antrum and extend proximally into the corpus along the lesser curvature. This study showed antrum-predominant gastritis. Such result is similar to the results of studies in Asian countries, including China, Vietnam, Thailand and Myanmar.[24] In Japanese patients, *H. pylori* infection and chronic active gastritis progress to the corpus with advancing age, resulting in corpus-predominant gastritis. In constant, antrum gastritis will not develop into corpus gastritis in the Nepalese like other Asian populations.[24] The difference of mucosal changes induced by *H. pylori* infection between the Japanese and other Asian populations may be correlated with the different incidences of gastric cancer in the Japanese and other Asian populations.[24] Uemura et al, reported that among *H. pylori* infected Japanese patients, those with severe atrophy accompanying intestinal metaplasia, corpus-predominant gastritis or both, are particularly high risk.[25]

Epidemiological evidence indicates that *H. pylori* infections are much more prevalent in developing countries than in developed nations such as the United States. It has been estimated that 30–40% of the United States population is infected with *H. pylori*.[9,26] *H. pylori* remains one of the most common worldwide human infections and is associated with a number of important upper gastrointestinal (GI) conditions including chronic gastritis, peptic ulcer disease, and gastric malignancy.[26]

The prevalence of *H. pylori* in this study is 24.3%, which is lower than study reports by Elseweidy et al, in Egypt (84%), Hashemi et al, in Iran (67.4%), and Khan et al, in Pakistan (85%).[23,27,28] In India, *H. pylori* is positive in 38 (56.7%) asymptomatic individuals and in 49 (61.3%) symptomatic individuals.[29] In Jordan, *H. pylori* is frequent in 82% of 197 study subjects.[30] Prevalence of *H. pylori* in Indonesia reported by Albertus et al, using polymerase chain reaction (PCR) to detect *H. pylori* is 46.7%,[31] Syam AF et al, using rapid urea test (Pronto Dry) found 10.2% of prevalence.[32] Previous studies have shown that the prevalence of *H. pylori* infections is affected by several factors, including living conditions, income, ethnicity, socio-economic status, especially infection in childhood, availability of public water supplies and sewers, the number of family support organizations, and the number of rooms in the home.[1-3] The reasons for erratic rates of *H. pylori* infection may be reported from the country.

In comparison between *H. pylori*- positive and *H. pylori*-negative patients, mononuclear cell infiltration was more severe in *H. pylori*-positive patients with superficial gastritis, erosive gastritis and gastric ulcer than *H. pylori*-negative patients. We assume that it was related with the grade of mononuclear cell infiltration, polymorphonuclear cell infiltration and the grade of *H. pylori* infection. More intense bacterial infection and more severe polymorphonuclear cell infiltration may contribute more to DNA damage and promote carcinogenesis in patients with gastric cancer. Furthermore, chronic *H. pylori* infection is also associated with increased gastric cell turnover, probably of importance in malignant transformation.[33-37]

Glandular atrophy and intestinal metaplasia were found in more than half of *H. pylori* negative patients but were remarkably low in the *H. pylori*-positive patients. However, there was no significant difference between *H. pylori*-positive and negative patients. Glandular atrophy scores and intestinal metaplasia scores of all sites in *H. pylori*-infected Japanese patients was significantly higher compared to this study.[24,38]

Zhang and Yamada reported that there was a tight link between atrophic gastritis and intestinal metaplasia in stomachs of Japanese patients with early gastric cancer.[39] Occasionally, glandular atrophy and intestinal metaplasia tissues were found in *H. pylori*-negative patients; while in the tissues without glandular atrophy or intestinal metaplasia, we may found *H. pylori* positive. These findings suggest that most patients with intestinal metaplasia and glandular atrophy have been infected with *H. pylori* at some stage. *H. pylori* infection may provide the proper environment for atrophic gastritis and intestinal metaplasia to occur. At the final stage of the disease, gastric atrophy with intestinal metaplasia is not a hospitable environment for *H. pylori.* It may also associated with a dramatic reduction or even disappearance of the organism.[40-43]

This study did not explore *H. pylori* strains and (interleukin) IL-1 polymorphisms because there is no facility for culture**.** Several *H. pylori* virulence and associated genes have been found in Western populations to be correlated to an increased risk of gastric cancer and pre-cancerous lesions.[34] Moreover, it has been confirmed that IL-1 polymorphisms contributes to the gastric acid secretory response, facilitating *H. pylori* infection and subsequently developing clinical sequelae.[43]

CONCLUSION

Patients presenting with gastric ulcer have *H. pylori* infection, atrophic gastritis and metaplasia intestinal more than superficial gastritis and erosive gastritis. Progression of the gastric ulcer to atrophic gastritis and intestinal metaplasia is related to *H. pylori* infection.

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Correspondence:
Jacobus Albertus
Department of Internal Medicine
Tugurejo District General Hospital
Jl. Raya Tugurejo Semarang 50185 Indonesia
Phone/facsimile: +62-24-7605578
E-mail: bert_smg@yahoo.co.id