

# ***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, atrofi 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 erosi 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 erosi atau ulkus lambung. Pengambilan biopsi dilakukan pada korpus, angulus dan antrum. Pewarnaan Giemsa dan Hematoxylin 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 atrofi 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*, atrofi dan metaplasia yang lebih banyak dibandingkan dengan gastritis superfisial dan gastritis erosif. Infeksi *H. pylori* dapat mempercepat perkembangan ulkus menjadi atrofi dan metaplasia intestinal.

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

## INTRODUCTION

In the early 20<sup>th</sup> 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.<sup>1</sup> 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.<sup>2</sup> 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.<sup>3</sup> 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.<sup>4-7</sup>

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%).<sup>8,9</sup> Infection with *H. pylori* may lead to inflammation of the gastric mucosa with subsequent ulceration.<sup>9</sup> 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.<sup>8,10-14</sup> While the bacterium is not a direct cause of cancer, its presence and resultant reduction in acid production are necessary factors in causation.<sup>8,15</sup> 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.<sup>16-18</sup>

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.<sup>8,19</sup> *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.<sup>19,20-22</sup> *H. pylori* infection has worldwide distribution and is found to be prevalent and strongly associated with peptic ulcer disease and gastritis in Pakistani population.<sup>23</sup> 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.<sup>14</sup> 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  $56.3 \pm 9.9$ ); 72 patients with erosive gastritis aged from 38 to 66 years (mean age  $65.3 \pm 10.4$ ); 72 patients with gastric ulcer aged from 38 to 70 years (mean age  $65.7 \pm 10.8$ ).

Predominant sites of lesions based on endoscopic 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. Endoscopic diagnosis and predominant sites of lesion**

Endoscopic 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**

Endoscopic diagnosis	<i>H. pylori</i> infective rate (%)	p*
Superficial gastritis	19.4	0.042
Erosive gastritis	26.3	
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	0.091
Erosive gastritis	3.8	27.0	23.0	43.4	36.7	3.8	10.1	52.1	
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	0.087
Erosive gastritis	62.3	13.1	10.5	14.1	81.7	8.5	3.4	6.4	
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 <i>H. pylori</i> + (%)	Intestinal metaplasia <i>H. pylori</i> + (%)	p*
Superficial gastritis	12.5	14.0	0.038
Erosive gastritis	23.6	16.6	
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.<sup>24</sup> 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.<sup>24</sup> 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.<sup>24</sup> 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.<sup>25</sup>

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*.<sup>9,26</sup> *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.<sup>26</sup>

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%).<sup>23,27,28</sup> In India, *H. pylori* is positive in 38 (56.7%) asymptomatic individuals and in 49 (61.3%) symptomatic individuals.<sup>29</sup> In Jordan, *H. pylori* is frequent in 82% of 197 study subjects.<sup>30</sup> Prevalence of *H. pylori* in Indonesia reported by Albertus et al, using polymerase chain reaction (PCR) to detect *H. pylori* is 46.7%,<sup>31</sup> Syam AF et al, using rapid urea test (Pronto Dry) found 10.2% of prevalence.<sup>32</sup> 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.<sup>1-3</sup> 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.<sup>33-37</sup>

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.<sup>24,38</sup>

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.<sup>39</sup> 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.<sup>40-43</sup>

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.<sup>34</sup> 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.<sup>43</sup>



## 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.

## REFERENCES

1. Tan V, Wong B. *Helicobacter pylori* and gastritis: untangling a complex relationship 27 years on. *J Gastroenterol Hepatol* 2011;26:42-5.
2. Suerbaum S, Michetti P. *Helicobacter pylori* infections. *N Engl J Med* 2002;347:1175-86.
3. Bauer B, Meyer TF. The human gastric pathogen *Helicobacter pylori* and its association with gastric cancer and ulcer disease. *Ulcer* 2011;2011:3-26.
4. Talley NJ. Gastric cancer consensus conference recommends *Helicobacter pylori* screening and treatment in asymptomatic persons from high-risk populations to prevent gastric cancer. *Am J Gastroenterol* 2008;103:510-21.
5. Rozen P. Cancer of the gastrointestinal tract: early detection or early prevention? *Eur J Cancer Prev* 2004;13:71-5.
6. O'Keefe J, Moran AP. Conventional, regulatory and unconventional T cells in the immunologic respon to *Helicobacter pylori*. *Helicobacter* 2008;13:1-19.
7. EL-Zimaity HM. Recent advances in the histopathology of gastritis. *Curr Diagn Pathol* 2007;13:340-8.
8. Lopes J. *Helicobacter pylori* infection: update on diagnosis and management. *J Am Acad Physic Assistants* 2010;23:20-37.
9. McColl KE. *Helicobacter pylori* infection. *N Eng J Med* 2010;362:1597-604.
10. Amiri M, Janssen F, Kunst A. The decline in stomach cancer mortality: exploration of future trends in seven European countries. *Eur J Epidemiol* 2011;26:23-8.
11. Capelle L, de Vries A, Looman C. Gastric MALT lymphoma: epidemiology and high adenocarcinoma risk in a nation-wide study. *Europ J Cancer* 2008;44:2470-6.
12. Take S, Mizuno M, Ishiki K, Yoshida T, Ohara N, Yokota K, et al. The long-term risk of gastric cancer after the successful eradication of *Helicobacter pylori*. *J Gastroenterol* 2011;46:318-24.
13. Caruso ML, Fucci L. Histological identification of *Helicobacter pylori* in early and advanced gastric cancer. *J Clin Gastroenterol* 1990;12:601-2.
14. 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;20:1161-81.
15. Luminari S, Cesaretti M, Marcheselli L. Decreasing incidence of gastric MALT lymphomas in the era of anti-*Helicobacter pylori* interventions: results from a population based study on extranodal marginal zone lymphomas. *Annals Oncol* 2009;21:855-9.
16. Cheung TK, Wong CY. Treatment of *Helicobacter pylori* and prevention of gastric cancer. *J Dig Dis* 2008;9:8-13.
17. Alsolaiman MM, Bakis G, Nazeer T, MacDermott RP, Balint JA. Five years of complete remission of gastric diffuse large B cell lymphoma after eradication of *Helicobacter pylori* infection. *Gut* 2003;52:507-9.
18. Bornschein J, Rokkas T, Selgrad M, Malfertheiner P. *Helicobacter pylori* and clinical aspects of gastric cancer. *Helicobacter* 2009;14:41-5.
19. Yeomans N. The ulcer sleuths: the search for the cause of peptic ulcers. *J Gastroenterol Hepatol* 2011;26:35-41.
20. O'Connor A, Gisbert J, McNamara D, O'Morain C. Treatment of *Helicobacter pylori* infection 2010. *Helicobacter* 2010;15:46-52.
21. Welin M, Holmgren NM, Nilsson P, Enroth H. Statistical model of the interactions between *Helicobacter pylori* infection and gastric cancer development. *Helicobacter* 2003;8:72-8.
22. Kabir S. Effect of *Helicobacter pylori* eradication on incidence of gastric cancer in human and animal models: underlying biochemical and molecular events. *Helicobacter* 2009;14:159-71.
23. Khan SS, Zulfiqar A, Danish KF. Prevalence of *H. pylori* infection in patients with gastroduodenal disease in Pakistan. *Rawal Med J* 2008;33:88-90.
24. Matsuhisa T, Miki M, Yamada N, Sharma SK, Shrestha BM. *Helicobacter pylori* infection, glandular atrophy, intestinal metaplasia and topography of chronic active gastritis in the Nepalese and Japanese population: the age, gender and endoscopic diagnosis matched study. *Kathmandu Univ Med J* 2007;5:295-301.
25. Uemura N, Okamoto S, Yamamoto S, Matsumura N, Yamaguchi S, Yamakido M, et al. *Helicobacter pylori* infection and the development of gastric cancer. *N Engl J Med* 345;2001:784-9.
26. Chey WD, Wong BC, and the Practice Parameters Committee of the American College of Gastroenterology. Guideline on the management of *Helicobacter pylori* infection. *Am J Gastroenterol* 2007;102:1808-25.
27. Elseweidy M, Taha MM, Younis NN, Khadiga S, Hamouda HA, Eldosouky MA, et al. Pattern of gastritis as manipulated by current state of *Helicobacter pylori* infection. *Intern J Biol Biomed Enginer* 2010;4:12-21.
28. Hashemi MR, Rahnnavardi M, Bikdeli B, Zahedani MD. *H. pylori* infection among 1,000 Southern Iranian dyspeptic patients. *World J Gastroenterol* 2006;12:5479-82.
29. Singh V, Trikha B, Nain CK, Singh K, Vaiphei K. Epidemiology of *Helicobacter pylori* and peptic ulcer in India. *J Gastroenterol Hepatol* 2002;17:659-665.
30. Abu-Ahmad NM, Odeh JA and Sallal AKJ. Prevalence of *Helicobacter pylori* gastritis at the North of Jordan. *Jordan J Biol Sci* 2011;4:71-6.
31. Albertus J, Rani AA, Simadibrata M, Abdullah M, Syam AF, Gani RA. Mucus thickness of the gastric mucosa and *H. pylori* infection in dyspeptic patient with or without diabetic symptom. *Indones J Gastroenterol Hepatol Digest Endosc* 2010;11:112-20.
32. Syam AF, Murdani A, Rani A, Nurdjanah H, Adi P, Jumhana A, et al. Evaluation of the use of rapid urea test: pronto dry to detect *H. pylori* in patient with dyspepsia in several cities in Indonesia. *World J Gastroenterol* 2006;2:6316-8.
33. Testoni PA, Bonassi U, Bagnolo F, Colombo E, Scelsi R. In diffuse atrophic gastritis, routine histology underestimates *Helicobacter pylori* infection. *J Clin Gastroenterol* 2002;35:234-9.
34. Welin M, Holmgren NM, Nilsson P, Enroth H. Statistical model of the interactions between *Helicobacter pylori* infection and gastric cancer development. *Helicobacter* 2003;8:72-8.

35. Kim JJ, Tao H, Carloni E, Leung WK, Graham DY, Sepulveda AR. *Helicobacter pylori* impairs DNA mismatch repair in gastric epithelial cells. *Gastroenterology* 2002;123:542-53.
36. Tahara T, Shibata T, Nakamura M, Yoshioka D, Okubo M, Arisawa T, et al. Gastric mucosal pattern by using magnifying narrow-band imaging endoscopy clearly distinguishes histological and serological severity of chronic gastritis. *Gastrointest Endosc* 2009;70:246-53.
37. Peek RM, Crabtree JE. *Helicobacter* infection and gastric neoplasia. *J Pathol* 2006;208:233-48.
38. Rugge M, Correa P, Dixon MF, Fiocca R, Hattori T, Lechago J, et al. Gastric mucosal atrophy: interobserver consistency using new criteria for classification and grading. *Aliment Pharmacol Ther* 2002;16:1249-59.
39. Zhang C, Yamada N. *Helicobacter pylori* infection, glandular atrophy and intestinal metaplasia in superficial gastritis, gastric erosion, erosive gastritis, gastric ulcer and early gastric cancer. *World J Gastroenterol* 2005;11:791-6.
40. Kapadia CR. Gastric atrophy, metaplasia, and dysplasia: a clinical perspective. *J Clin Gastroenterol* 2003;36:S29-36.
41. Kabir S. Effect of *Helicobacter pylori* eradication on incidence of gastric cancer in human and animal models: underlying biochemical and molecular events. *Helicobacter* 2009;14:159-171.
42. Lauwers GY, Srivastava A. Gastric preneoplastic lesions and epithelial dysplasia. *Gastroenterol Clin North Am* 2007;36:813-29.
43. Figueiredo C, Machado JC, Pharoah P, Seruca R, Sousa S, Carvalho R, et al. *Helicobacter pylori* and interleukin 1 genotyping: an opportunity to identify high risk individuals for gastric carcinoma. *J Natl Cancer Inst* 2002;94:1680-7.

---

*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

---