



BRIEF ARTICLE

## ***Helicobacter pylori* infection and gastropathy: A comparison between Indonesian and Japanese patients**

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### **Abstract**

**AIM:** To compare the effects of *Helicobacter pylori* (*H. pylori*) infection on gastropathy between Indonesian and Japanese patients.

**METHODS:** Biopsy specimens were obtained during upper gastrointestinal endoscopy from 167 subjects (125 Indonesians and 42 Japanese) with uninvestigated symptoms of dyspepsia. The specimens were analyzed for the presence of *H. pylori* using urease analysis, histopathology, and cell culture. The grade and activity of gastritis was assessed using the updated Sydney system.

**RESULTS:** The percentages of Indonesian and Japanese patients who were *H. pylori*-positive at the antrum or body of the stomach were similar (68% and 59.5%, respectively;  $P = 0.316$ ). Of those who were *H. pylori*-positive, more Japanese patients than Indonesian patients had high levels of polymorphonuclear cells ( $P = 0.001$ ), mononuclear cells ( $P = 0.013$ ), glandular atrophy ( $P = 0.000$ ), and intestinal metaplasia ( $P = 0.011$ ) in both the antrum and body of the stomach.

**CONCLUSION:** The grade of gastritis and prevalence of mucosal atrophy and intestinal metaplasia were higher in Japanese patients. The difference between Indonesian and Japanese patients was significant.

### **INTRODUCTION**

There is abundant evidence of an association between *Helicobacter pylori* (*H. pylori*) chronic infection and gastric cancer<sup>[1-5]</sup>. Some population-based studies show that high levels of *H. pylori* infection are not necessarily accompanied by high mortality from gastric cancer, the so-called African<sup>[6-8]</sup> and Asian enigmas<sup>[9]</sup>.

Indonesia and Japan have a similar prevalence of *H. pylori* infection, but the incidence of gastric cancer is much higher in Japan than Indonesia<sup>[10]</sup>. We conducted this cross-sectional study to compare the effects of *H. pylori* infection on gastropathy between Indonesian and Japanese patients.

We consider the old concept of a cascade of mucosal changes that develop from acute/chronic gastritis to atrophic gastritis with intestinal metaplasia, and finally to dysplasia and gastric cancer, as proposed by P. Correa before the discovery of *H. pylori* in the stomach<sup>[11]</sup>. This is relevant because a difference in the pattern of *H. pylori*-associated gastritis may explain the difference in the incidence of gastric cancer between Indonesia and Japan.

### **MATERIALS AND METHODS**

#### **Selection of patients**

Patients were eligible to participate in the study if they were aged 18 years or older and had experienced uninvestigated symptoms of dyspepsia for at least 3 mo before enrollment. We defined dyspepsia as epigastric pain or discomfort perceived to originate in

Table 1 Baseline characteristics of patients *n* (%)

Characteristic	Indonesian ( <i>n</i> = 125)	Japanese ( <i>n</i> = 42)	Total ( <i>n</i> = 167)	<i>P</i>
Age (yr)	50.30 (18-82)	57 (20-79)		0.060
Sex				
Male	58 (46.4)	25 (59.5)	83 (49.7)	0.141
Female	67 (53.6)	17 (40.5)	84 (50.3)	
<i>Helicobacter pylori</i> ( <i>H pylori</i> )-positive				
Antrum and/or body	85 (68)	25 (59.5)	110 (65.9)	0.316
Antrum	85 (68)	22 (52.4)	107 (64.1)	0.068
Body	5 (4)	20 (47.6)	25 (15)	0.000

the upper gastrointestinal tract, including heartburn, acid regurgitation, excessive belching, abdominal bloating, nausea, a perception of abnormal or slow digestion, and early satiety<sup>[12,13]</sup>. Patients who experienced only heartburn and/or regurgitation were considered to have gastroesophageal reflux disease and were excluded. We also excluded patients who underwent upper gastrointestinal endoscopy and/or barium radiography less than 6 mo before the study or underwent these procedures on more than two separate occasions within the preceding 10 years, and patients who received eradication therapy for *H pylori* less than 6 mo before the study. We excluded patients who had undergone gastric surgery and those who had a documented history of ulcer disease, esophagitis, irritable bowel syndrome, or clinically significant abnormal results on laboratory analyses. None of the patients who enrolled in the study received treatment with nonsteroidal anti-inflammatory drugs, aspirin (> 325 mg/d), antibiotics, H2-receptor antagonists, proton pump inhibitors, misoprostol, sucralfate, prokinetic agents, or a bismuth compound within 14 d of the study.

From 1998 to 1999, 42 Japanese patients at Yamanashi Medical University Hospital, Koufu and 125 Indonesian patients at Metropolitan Medical Centre Hospital, Jakarta were diagnosed as having dyspepsia and were consecutively enrolled in the study. Informed consents were obtained from all of the patients. This study was reviewed and approved by the ethics committee of Faculty of Medicine University of Indonesia, who approved the protocol.

### Intervention and measurements

All patients underwent an upper gastrointestinal endoscopy procedure to identify lesions and to obtain biopsy specimens from the antrum and body of the stomach. The grade and activity of gastritis was assessed using the updated Sydney system<sup>[14]</sup>. The presence of *H pylori* in Indonesian patients was determined using histopathology, culture, and rapid urease test (RUT)<sup>[15,16]</sup>. The presence of *H pylori* in Japanese patients was determined using urease analysis, histopathology, cell culture, and RUT.

### Statistical analysis

SPSS for Windows version 14 software (SPSS Inc., Chicago, Illinois) was used to analyze data. The prevalence of *H pylori*, polymorphonuclear cells, mononuclear cells, glandular atrophy, and intestinal metaplasia in the antrum

Table 2 Comparison of the effects of *H pylori* infection on gastropathy in Indonesian and Japanese patients who were positive for *H pylori* at the antrum and/or body of the stomach *n* (%)

Characteristic	None or mild	Moderate or severe	<i>P</i>
Polymorphonuclear cells			
Indonesian ( <i>n</i> = 85)	71 (83.53)	14 (16.47)	0.001
Japanese ( <i>n</i> = 25)	12 (48)	13 (52)	
Mononuclear cells			
Indonesian ( <i>n</i> = 85)	31 (36.47)	54 (63.53)	0.013
Japanese ( <i>n</i> = 25)	2 (8)	23 (92)	
Glandular atrophy			
Indonesian ( <i>n</i> = 85)	84 (98.82)	1 (1.18)	0.000
Japanese ( <i>n</i> = 25)	16 (64)	9 (36)	
Intestinal metaplasia			
Indonesian ( <i>n</i> = 85)	85 (100)	0 (0)	0.011
Japanese ( <i>n</i> = 25)	22 (88)	3 (12)	

and body of the stomach was analyzed using the  $\chi^2$  test or Fisher's exact test, as appropriate.

## RESULTS

### Baseline characteristics of patients

We studied 125 Indonesian patients and 42 Japanese patients (males, 49.7%; females, 50.3%), of whom 110 (65.9%) tested positive for *H pylori* at the antrum and/or body of the stomach. The percentages of Indonesian and Japanese patients who were *H pylori*-positive at the antrum or body of the stomach were similar (68% and 59.5%, respectively; *P* = 0.316). The percentage of Japanese patients (52.4%) positive for *H pylori* at the antrum of the stomach was similar to that of Indonesian patients (68%) (*P* = 0.068) but more Japanese patients were positive for *H pylori* at the body of the stomach (47.6%) than Indonesian patients (4%) (*P* < 0.000) (Table 1).

### Comparison of the effects of *H pylori* infection on gastropathy in Indonesian and Japanese patients who were positive for *H pylori* at the antrum and/or body of the stomach

Of patients who were *H pylori*-positive at the antrum and/or body of the stomach, more Japanese patients had high numbers of polymorphonuclear cells (*P* = 0.001) and mononuclear cells (*P* = 0.013), glandular atrophy (*P* = 0.000), and intestinal metaplasia (*P* = 0.011) than Indonesian patients (Table 2).

## DISCUSSION

The development of gastric cancer is a long process and caused by many factors. Although *H pylori* is an important risk factor for gastric cancer, it is not the only factor that is involved in the etiology of gastric cancer. The association between gastric cancer and *H pylori* infection should be considered from the perspective of the multi-agent compound etiological theory<sup>[17]</sup>. The *H pylori* infection rate is very high both in Indonesian and Japanese populations. The reason why Indonesians with *H pylori* infection do not develop gastric cancer to

the same extent as their Japanese counterparts remains unknown.

The limitation of this study was that samples were obtained from a hospital population. Consequently, the results may not represent the community. However, this is the first study in which the effects of *H pylori* infection on gastropathy between Indonesian and Japanese patients were compared.

This study showed that the grade and activity of gastritis was higher among Japanese *H pylori*-positive patients. The prevalence of mucosal atrophy was also greater in Japanese *H pylori*-positive patients than in Indonesians. In addition, more Japanese *H pylori*-positive patients had severe atrophic gastritis and intestinal metaplasia than Indonesians. The difference between those two groups was significant statistically.

Japanese *H pylori*-positive patients had higher grade and activity of gastritis than Indonesian *H pylori*-positive patients. This finding was consistent with the study by Kang *et al*<sup>[18]</sup> which observed differences in gastritis among Chinese, Malays, and Indians. This indicates that risk factors other than *H pylori*, such as genetic factors, are associated with the development of gastric cancer in Japanese patients. Moreover, atrophic gastritis in Japanese subjects originating from autoimmune gastritis may explain the high grade and activity of gastritis in these patients.

Another important risk factor is a dietary factor because this affects the rate of development of gastric cancer<sup>[19,20]</sup>. Japanese dietary habits such as high consumption of nitrite-rich, salty pickled vegetables and dried fish, and alcohol, are associated with atrophic gastritis and gastric cancer<sup>[21-24]</sup>. A low consumption of fresh fruit and raw vegetables may increase this risk. Such dietary habits may act in synergy with *H pylori* in causing gastric cancer<sup>[25]</sup>. Migrants to countries with low gastric cancer rates have a diminished risk of gastric cancer<sup>[26]</sup>.

In conclusion, although the prevalence of *H pylori* infection was similar in Indonesian and Japanese patients, the grade and activity of gastritis was higher in Japanese *H pylori*-positive patients. Moreover, the prevalence of mucosal atrophy and intestinal metaplasia was also higher in Japanese group. The difference between Indonesian and Japanese *H pylori*-positive patients was found to be significant. That difference may be responsible for the disparity in the incidence of gastric cancer in Indonesia and Japan. Further studies will be needed.

## COMMENTS

### Background

Although *Helicobacter pylori* (*H pylori*) has been classified as a class I (or definite) carcinogen by WHO, the controversy as to why only a minority of infected patients develop distal adenocarcinoma still remains. Moreover, in Asian countries such as Indonesia, Japan, China, and Thailand, where the *H pylori* infection rates are similar, there is a significant difference regarding the outcome of gastric cancer. In the present study, the authors evaluated the transformation of gastric mucosa that is induced by *H pylori* infection prior to gastric cancer. The authors also compared the transformation between Indonesian and Japanese patients, the two countries that represent an "Asian paradox".

### Innovations and breakthroughs

By means of this study, the authors revealed that there was a significant

difference in the grade and activity of gastritis and the prevalence of mucosal atrophy and intestinal metaplasia between Indonesian and Japanese *H pylori*-positive patients. These findings may be responsible for the difference in the incidence of gastric cancer in Indonesia and Japan.

### Applications

This study indicates that there is a difference in host response between Indonesian and Japanese patients regarding *H pylori* infection.

### Peer review

The study is a good idea. Patients were enrolled consecutively with no selection bias. There was no difference in patients' clinical features. The endoscopic features were assessed using OMED Database of Digestive Endoscopy. The histological differences were assessed using the Updated Sydney System by two observers with good interobserver degree of agreement.

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