Correlation Between the Degree of Duodenal Bulbar Deformity and the Density of *Helicobacter pylori* Infection in Patients with Active Duodenal Ulcers

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Background: Duodenal ulcer with deformity of the bulb is evidence of a chronic process of ulcer disease. This prospective study was carried out to investigate the relationship between the degree of bulbar deformity and the density of *Helicobacter pylori* infection in patients with duodenal ulcer.

Methods: Patients with endoscopically proven active duodenal ulcers and a positive diagnosis of *H. pylori* infection were enrolled. Duodenal ulcers were divided into three types according to the degree of deformity of the bulb: type I, normal bulb; type II, mildly deformed; type III, markedly deformed. In each case, we evaluated the *H. pylori* density histologically. The density was graded according to the Sydney system (normal, mild, moderate, and marked).

Results: A total of 95 duodenal ulcer patients were studied, including 25 with type I, 40 with type II, and 30 with type III duodenal ulcers. *H. pylori* density was correlated with deformity of the duodenal bulb: 16/25 (64%) patients with a type I ulcer had mild infection, 19/40 (47.5%) patients with a type II ulcer had moderate infection, and 15/30 (50%) patients with a type III ulcer had marked infection.

Conclusion: Patients with active type II or III duodenal ulcers had greater densities of *H. pylori* than did those with type I ulcers. A tendency for higher *H. pylori* density was seen as the degree of deformity of the duodenal bulb increased.

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Key words:
bulb deformity
duodenal ulcer
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infection density

Helicobacter pylori infects more than 90% of patients with duodenal ulcer (DU) [1], and its eradication may cure DU disease [2]. Recent evidence suggests that *H. pylori* plays a significant role in the development of gastritis and ulceration [3]. Increased bacterial density of *H. pylori* in the stomach may lead to increased levels of inflammation and epithelial injury. This may be a marker for duodenal damage or may itself cause increased acid output and, hence, predispose the duodenum to ulceration [4].

Alam et al showed that the prevalence of DU increased with increasing *H. pylori* density, and a greater likelihood of ulceration was noted among patients with high concentrations of *H. pylori* [5]. Sheu et al found that heavy bacterial loads of *H. pylori* infection might precipitate bleeding episodes in patients with DU, and cases with recurrent bleeding had higher bacterial density than did non-rebleeding cases [6].

DU with deformity of the bulb is evidence of a chronic process of ulcer disease and has a high incidence of recurrence [7], so *H. pylori* infection in the stomach and its bacterial density are thought to be related to this process. In this study, we aimed to assess the density of *H. pylori* infection using histology in patients with different types of DU with or without bulbar deformity, and to investigate the correlation

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between the degree of deformity of the bulb and *H. pylori* density in the stomach.

Methods

Patient recruitment

From January 2000 through June 2001, consecutive outpatients with endoscopically proven active DU (5 mm in diameter) at Cathay General Hospital were studied. All panendoscopic examinations were performed and interpreted by the same group of experienced endoscopists. We only enrolled cases with a positive diagnosis of *H. pylori* infection proven by both histology and ^{13}C-urea breath test (UBT). To avoid interference in evaluating the *H. pylori* status, the following patients were excluded: those who had ingested bismuth, antibiotics, anti-secretory medication, or a proton pump inhibitor in the past 4 weeks; those who used nonsteroidal antiinflammatory drugs (NSAIDs); those who were pregnant or immunocompromised; and those who had a history of gastric surgery or of attempted eradication of *H. pylori*. All procedures were performed after obtaining informed consent from the patient.

Based on the endoscopic morphologic patterns of the duodenal bulb, we divided DU into three types. Type I had a normal-shaped bulb, type II had a ridge across the bulb with pseudodiverticulum formation (mild degree of deformity), and type III had multiple ridges occupying the bulb (marked deformity) [7].

Histology

During endoscopy, three biopsies were taken from the gastric antrum (1 near the incisura and the other 2 on the greater and lesser curvature, 2 cm within the pyloric ring) [8]. We used an Olympus GIF-XQ 200 endoscope (Olympus Optical Co Ltd, Tokyo, Japan) and FB 25-K biopsy forceps (Olympus Optical Co Ltd). Specimens were stained with hematoxylin-eosin and with a modified Giemsa stain, and were then examined for the presence of *H. pylori* by an experienced histopathologist unaware of the patient's clinical diagnosis. The updated Sydney system visual analogue scale was used to grade the density of *H. pylori* (normal, no bacteria; mild, focally few bacteria; moderate, more bacteria in several areas; and marked, abundance of bacteria in most glands) [9]. If the density varied, the highest grade of density was used.

The UBT was performed immediately after endoscopy and before the start of H_2-blocker or proton pump inhibitor therapy. We chose 3/mL as the cut-off level for the rise in the delta value of $^{13}CO_2$ 15 minutes after the ingestion of ^{13}C-urea. A positive UBT was defined as $\Delta\delta$ above this value.

Statistical analysis

The age of the patients was considered as a continuous variable and normally distributed, so we used Student's *t*-test for analysis. The Chi-square test was applied to test the correlation between *H. pylori* density and different types of DU. The relationship between age and *H. pylori* density was assessed using the Kruskal-Wallis test. A *p* value of less than 0.05 was considered significant.

Results

In total, 95 cases were enrolled in this study, 53 males and 42 females. The mean age of all cases was 46.9 ± 12.7 years. Age differences among all types were statistically significant: type I *vs* II, $p < 0.001$; type I *vs* III, $p = 0.01$; type II *vs* III, $p = 0.049$). Patients with type III DU had the greatest mean age (Table 1).

H. pylori density distribution

Table 2 shows the *H. pylori* density in patients with the three types of DU. Most patients with type I DU had mild infection density. More patients with type II DU had moderate infection density than either mild or marked infection density. In contrast, almost all patients with type III DU had moderate or marked infection density. These findings revealed a correlation between the grade of *H. pylori* density and the degree of the deformity of the duodenal bulb. Statistical analysis by Chi-square test was significant.

Age and *H. pylori* density

Figures 1 to 3 show the results of evaluation of the relationship between age and *H. pylori* density in different types of DU. *H. pylori* infection density was not correlated with age for any type of DU ($p > 0.05$).

Table 1. Demographic data for patients with different types of duodenal ulcers

Type	n	Sex (M/F)	Age (yr)*
I	25	13/12	40.0 ± 10.0
II	40	22/18	46.6 ± 13.7
III	30	18/12	53.2 ± 13.6

*Mean ± standard deviation.

Table 2. *Helicobacter pylori* (HP) density in different types of duodenal ulcers

HP density	Type I (n = 25)	Type II (n = 40)	Type III (n = 30)	*p**
Mild	16 (64.0%)	10 (25.0%)	2 (6.7%)	0.001
Moderate	7 (28.0%)	19 (47.5%)	13 (43.3%)	
Marked	2 (8.0%)	11 (27.5%)	15 (50.0%)	

Data are presented as case number (percentage of total). *Chi-square test.

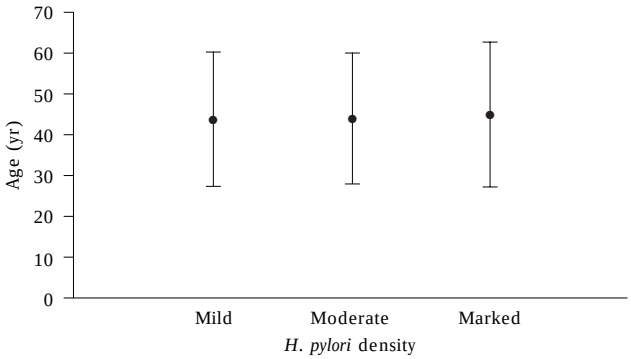

Fig. 2. *Relationship between age and* Helicobacter pylori *density in type II duodenal ulcer.* p = *0.99.*

Discussion

H. pylori infection predominantly involves the antral mucosa of the stomach. However, the ulcers most closely associated with the infection occur not in the gastric antrum but in the duodenum [10]. In this study, we found that the density of *H. pylori* in the gastric antrum increased with increments in the degree of deformity of the duodenal bulb. A tendency for increased *H. pylori* bacterial density could be demonstrated in patients with DU from type I to type III.

With more *H. pylori* inhabiting the antrum, the gastric mucosa will suffer greater damage [5, 10]. The virulent aspects of *H. pylori* include direct mucosal injury by urease, bacterial toxins, and invasive bacterial metabolites [10–12]. *H. pylori* can also induce a series of inflammatory responses triggered by chemotaxis of neutrophils and lymphocytes, or enhanced by tumor necrosis factor, prostaglandin E_2, interleukin, leukotriene B_4, and other eicosanoids [6, 13, 14]. A denser infection of *H. pylori* associated with greater antral inflammation may cause lower somatostatin expression [4], leading to higher levels of gastrin and acid production, which may, therefore, predispose the duodenum to ulceration [15, 16].

If *H. pylori* is not adequately treated and eradicated in ulcer patients, the process of ulceration will persist, and deformity of the duodenal bulb might, thus, ensue. With prolonged duration of ulcer disease, the deformity of the duodenal bulb will become more marked. The relationship between age and the degree of deformity of the duodenal bulb in ulcer patients might result from the longer duration of inadequately treated ulcer disease in older patients. After dividing the patients into three groups according to the degree of bulbar deformity, we could not find a correlation between age and *H. pylori* density in individual groups.

H. pylori infection can cause diverse host–bacterial interactions that result in various clinical diseases. Specific host and bacterial virulence factors are rel-

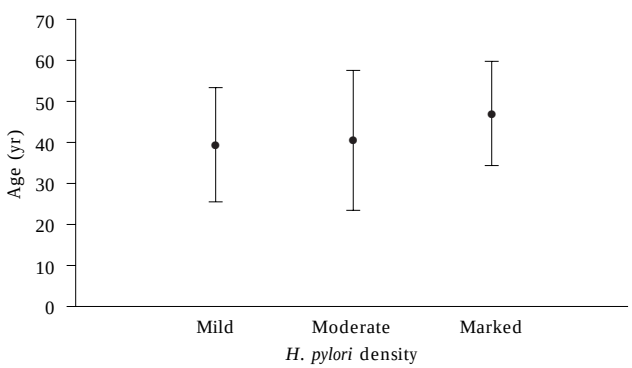

Fig. 1. *Relationship between age and* Helicobacter pylori *density in type I duodenal ulcer.* p = *0.70.*

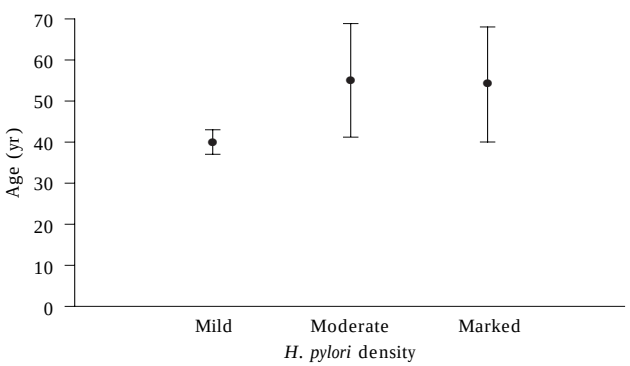

Fig. 3. *Relationship between age and* Helicobacter pylori *density in type III duodenal ulcer.* p = *0.25.*

evant to different clinical outcomes [17]. The assessment of bacterial virulence determinants and host immune responses in our patients will clarify the relationship between bacterial density in the antrum and the severity of deformity of the duodenal bulb in greater detail.

Deformity of the duodenal bulb has been reported to significantly adversely affect the healing of DU [18, 19], and ulcer recurrence rates are higher in patients with bulbar deformity [20]. Bulbar deformity is thought to be an unfavorable prognostic factor influencing the clinical course of DU, but the underlying cause is not fully understood.

With the recent progress in *H. pylori* detection, high antral *H. pylori* density has been found to increase the rate of ulcer recurrence [21]. Moreover, increased *H. pylori* density is associated with a reduction in the eradication rate after treatment with bismuth or proton pump inhibitor-based triple therapy [22–24]. The pretreatment bacterial load of *H. pylori* may serve as a contributing factor that can alter the efficacy of eradication therapy. The higher the *H. pylori* density, the less effective triple therapy will be [23].

In our study, we demonstrated the correlation of *H. pylori* density with the degree of deformity of the bulb in DU patients. Patients with a more deformed bulb have more *H. pylori* in their stomach, which may, thus, become an important factor that adversely influences the healing and recurrence of DU. If this postulation holds true, eradication of *H. pylori* will reduce the unfavorable effect caused by the deformity of the duodenal bulb. Successful eradication of *H. pylori* could result in better healing and lower recurrence of DU even in patients with a deformed bulb, which deserves further investigation.

In summary, our preliminary data showed that patients with DU of types II and III had higher histologic *H. pylori* densities than did those with type I ulcers. There is a trend toward increased *H. pylori* density from type I to type III. Although more studies concerning different aspects, such as mucosal production of cytokines, *H. pylori*-specific toxins, host–pathogen interactions, gastric metaplasia in the duodenum, etc., are necessary, we may still conclude that, as the deformity of the duodenal bulb increases, a greater density of *H. pylori* can be expected in the stomach. Eradication of *H. pylori* in such patients may improve the unfavorable effect attributed to a deformed duodenal bulb.

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