Asian Biomedicine Vol. 9 No. 1 February 2015; 87 - 93
DOI: 10.5372/1905-7415.0901.373

Brief communication (Original)

Epidemiology of upper gastrointestinal bleeding and *Helicobacter pylori* infection: review of 3,488 Thai patients

Sakolwan Suchartlikitwong[a], Kamolyut Lapumnuaypol[b], Rungsun Rerknimitr[b], Duangporn Werawatganon[a]
[a]*Department of Physiology, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand*
[b]*Department of Internal Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand*

Background: The current epidemiology of upper gastrointestinal bleeding (UGIB) in Thailand is poorly understood and the reported prevalence of *Helicobacter pylori* infection is outdated.
Objectives: To investigate the etiologies of UGIB and prevalence of *H. pylori* infection in Thailand, including its association with UGIB.
Methods: We retrieved information regarding patients attending the endoscopic unit of King Chulalongkorn Memorial Hospital from June 2007 to January 2013. A database search using keywords "upper gastrointestinal bleeding" and "iron deficiency" was used. From 4,454 diagnoses, after exclusion criteria, 3,488 patients (2,042 male (58.5%) and 1,446 female (41.5%); mean age 63.3 ± 15.94 years, range 13–103 years) were included.
Results: The three most common causes of UGIB were peptic ulcer (38.2%), nonulcer-mucosal lesions (23.4%), and esophageal-related causes (20.4%). The 5 year-incidence of *H. pylori* was 25%–30%. The overall prevalence was 27%. The prevalence of *H. pylori* infection was found to decrease with age from 43.8% at <40 years to 21.7% at >79 years old. *H. pylori* infection was significantly associated with duodenal and gastroduodenal ulcers. Cirrhosis and nonulcer-mucosal lesions were significantly unrelated to *H. pylori* infection. Patients with concurrent cirrhosis with peptic ulcer were found to be negative for *H. pylori* infection.
Conclusion: Peptic ulcer is the leading cause of UGIB in Thailand. However, its incidence is declining. Patients who presented to hospital with UGIB were older, compared with those a decade ago. *H. pylori* infection plays an important role in UGIB and its incidence was stable during the past 5 years.

Keywords: Epidemiology, *Helicobacter pylori*, Thailand, UGIB, upper gastrointestinal bleeding

Upper gastrointestinal bleeding (UGIB) is a common problem in emergency and inpatient departments. The mortality rate ranges from 0.8% to 14% [1-3]. Higher mortality is associated with increasing age, presence of severe comorbidity, and rebleeding [3].

The etiology of UGIB is classified into two major groups, nonvariceal bleeding and variceal bleeding. Peptic ulcers and gastritis are mostly found in the nonvariceal group, whereas, variceal bleeding is associated with cirrhosis or liver disease. The proportions found vary between studies. In some studies, the most frequent causes are peptic ulcer and gastric erosion [4, 5].

Correspondence to: Duangporn Werawatganon, Department of Physiology, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand. E-mail: duangporn.t@chula.ac.th

Helicobacter pylori infection and NSAIDs are believed to be major causes of peptic ulcers [6]. The prevalence of *H. pylori* infection is higher in developing than developed countries [7]. In developing countries, acute infection occurs during childhood and turns into chronic infection in adults [7, 8]. The prevalence of *H. pylori* increases with age [9, 10]. Thailand still has a high prevalence of *H. pylori* infection [8]. *H. pylori* infection is routinely identified during endoscopy by gastroenterologists.

Esophago–gastro–duodenoscopy is used globally to assess gastrointestinal bleeding. It can be performed under local anesthesia and in emergency settings. It allows not only direct visualization of the upper gastrointestinal tract, but intervention to stop bleeding and tissue biopsy. Endoscopy findings can predict the likelihood of rebleeding [11], and provide information for further management planning.

It has been 20 years or more since the epidemiology of UGIB in Thailand, and the prevalence of *H. pylori* infection have been reported [5, 7, 8]. We conducted a study to bring this information up to date.

Patients and methods

After approval from Institutional Review Board of Faculty of Medicine Chulalongkorn University, Bangkok, Thailand (IRB approval number is 359/57), data from patients who attended the endoscopy unit of the Department of Internal Medicine, King Chulalongkorn Memorial Hospital, from June 2007 to January 2013 were retrieved from the MasterScope database. King Chulalongkorn Memorial Hospital is a tertiary care university medical center, located in central Bangkok. All information including sex, age, indications, procedures, endoscopic finding, treatment, Campylobacter-like organism (CLO) test results and whether biopsy was performed was recorded in a computer-based system.

Inclusion and exclusion

The keywords "upper gastrointestinal bleeding" and "iron deficiency" in indication were used to select subjects from the database. Data from patients less than 10 years old, those with successive endoscopic studies to follow up, incomplete study, uncertain diagnosis, and normal findings were excluded. Data from patients with iron deficiency where the findings did not explain iron deficiency, or who needed lower gastro–enteroscopy, were excluded. Furthermore, data from patients with diagnoses that were outside the upper gastrointestinal tract, such as jejunal ulcer and gastrojejunal ulcer were also excluded from the study. The CLO test from tissue biopsy under endoscopy was used to diagnose *H. pylori* infection. Sensitivity was 90%–95% and specificity was 90%–95% [12]. Cutler et al. [13] also reported high positive predictive value (100%) and negative predictive value (84.1%) in their study. From 4,454 diagnoses, after exclusion criteria, 3,488 patients (2,042 male (58.5%) and 1,446 female (41.5%); mean age 63.3 ± 15.94 years, range 13–103 years) were included. The mean age of female patients (66.43 ± 15.36 years) was significantly higher than that of males (61.09 ± 15.98 years) (95%CI 4.28 to 6.39, $P < 0.001$) **(Figure 1)**.

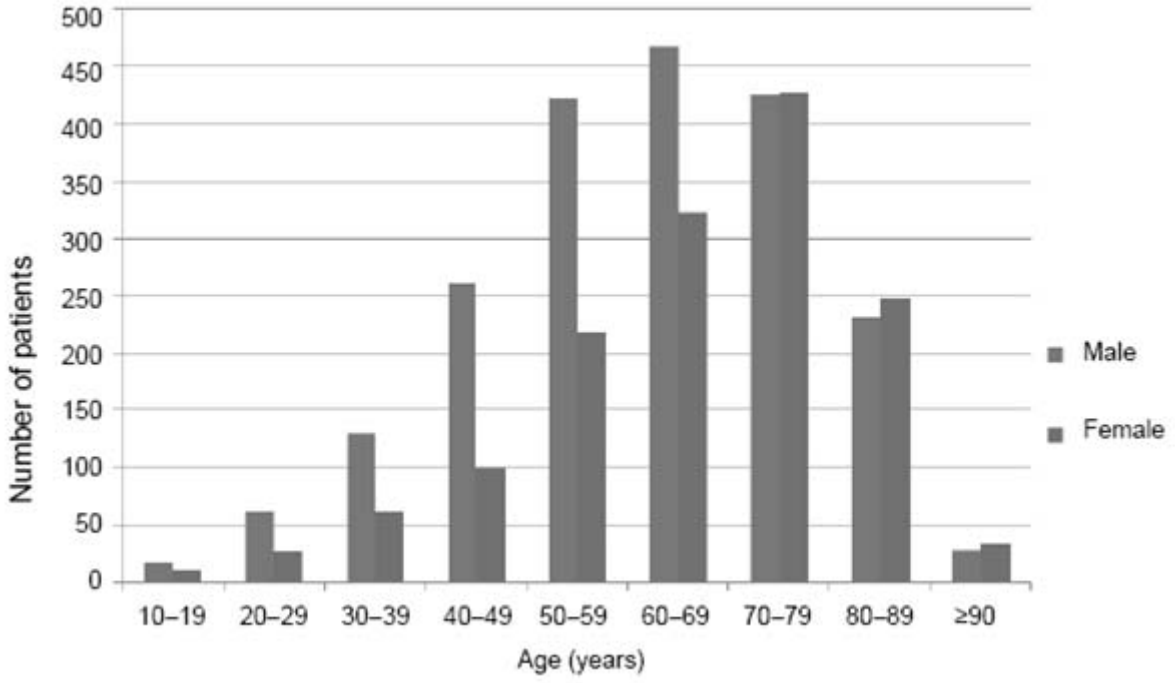

Figure 1. Age and sex distribution of patients with "upper gastrointestinal bleeding" and "iron deficiency" after exclusion of data from patients less than 10 years old, those with successive endoscopic studies to follow up, incomplete study, uncertain diagnosis, and normal findings, with iron deficiency where the findings did not explain iron deficiency, or who needed lower gastro–enteroscopy. Furthermore, data from patients with diagnoses that were outside the upper gastrointestinal tract, such as jejunal ulcer and gastrojejunal ulcer were also excluded.

Statistical analysis

The etiology of upper gastrointestinal bleeding was categorized into 10 groups. Patients were categorized into the groups, based on endoscopic findings and diagnoses. Statistical data were calculated using SPSS Statistics version 17.0 (SPSS, Chicago, IL, USA). Chi-square and Student *t* tests were used to analyze the categorical and quantitative data respectively.

Results

Etiologies were classified into 10 groups: gastric ulcer, duodenal ulcer, concurrent gastroduodenal ulcer, nonulcer-mucosal lesion, esophageal-related cause, cirrhosis, concurrent peptic ulcer disease with cirrhosis, malignancy, vascular lesion, and miscellaneous **(Table 1)**. Nonulcer-mucosal lesions included gastritis, duodenitis, gastric erosion, duodenal erosion and hemorrhagic gastritis. Esophagitis, gastroesophageal reflux disease (GERD), esophageal ulcer, hiatal hernia, hiatal ulcer (Cameron ulcer), Mallory–Weiss syndrome, esophageal candidiasis, and Barrett's esophagus were categorized into an esophageal-related cause group. The cirrhosis group included patients with varices (gastric or esophageal) and portal hypertensive gastropathy. Finally, hemangioma, Dieulafoy's lesion (bleeding abnormal submucosal artery of stomach), telangiectasia and vascular ectasia were classified into a vascular lesion group.

Patients with mucosal lesions and ulcers were categorized into the ulcer group only. For example, a patient who had gastritis and gastric ulcer, was placed into an ulcer group. Nevertheless, there was 26% of patients who had more than one endoscopic finding. The percentage of each cause was based on numbers of diagnoses because some patients had more than one potential bleeding lesion at endoscopy.

The leading cause of UGIB in this study was peptic ulcer (38.2%). There was 21% of gastric ulcers, 10.6% of duodenal ulcers, and 6.6% of concurrent gastroduodenal ulcers. The second and third leading causes were nonulcer-mucosal lesion (23.4%), and esophageal-related causes (20.4%). Cirrhosis was 9% and concurrent peptic ulcer disease with cirrhosis was 4.3%. Malignancy was 2.3%. Vascular lesion and miscellaneous groups were least prevalent at 1.6% and 0.8% respectively **(Table 1)**.

Table 1. The 4,454 endoscopic findings, association with *H. pylori* and mean age

Endoscopic finding	Number (%)	*H. pylori* positive cases/total[a] (%)	Odds ratio	*P*[b]	Mean age ± SD (years)		*P*[c]
					Lesion positive	Lesion negative	
Gastric ulcer	936 (21)	150/589 (25.5)	0.89	0.3	66.52 ± 13.9	62.12 ± 16.5	<0.001
Duodenal ulcer	472 (10.6)	99/277 (35.7)	1.62	<0.001	62.29 ± 17.7	63.46 ± 15.6	0.18
Concurrent gastroduodenal ulcer	293 (6.6)	71/194 (36.6)	1.63	0.001	67.15 ± 13.9	62.95 ± 16.1	<0.001
Non-ulcer-mucosal lesion	1,043 (23.4)	147/634 (23.2)	0.73	0.007	63.58 ± 16.1	63.18 ± 15.9	0.50
Esophageal-related cause	910 (20.4)	115/424 (27.1)	1.00	0.94	64.16 ± 17.3	63.00 ± 15.4	0.08
Cirrhosis	399 (9)	1/32 (3.1)	0.08	0.002	54.87 ± 13.5	64.39 ± 15.9	<0.001
Concurrent peptic ulcer disease with cirrhosis	192 (4.3)	9/62 (14.5)	0.45	0.024	58.71 ± 13.4	63.57 ± 16.0	<0.001
Malignancy	103 (2.3)	8/26 (30.8)	1.19	0.66	62.44 ± 14.3	63.33 ± 15.9	0.58
Vascular lesion	69 (1.6)	2/11 (18.2)	0.59	0.51	67.87 ± 13.4	63.21 ± 15.9	0.01
Miscellaneous	37 (0.8)	0/2 (0)	0.00	0.39	62.97 ± 18.9	63.30 ± 15.9	0.90

[a]"Total" means numbers of patients who had the lesion and were on Campylobacter-like organism (CLO) test. "Case" means patients who had the lesion and were positive on CLO test.
[b]Significant difference between *H. pylori* positive and negative group
[c]Significant difference between the mean age of a lesion and lesion-free on each endoscopic finding

When lesions or masses suspected of malignancy were identified at endoscopy, each patient's medical record was reviewed to confirm the diagnosis with tissue-pathology results. Malignancy was diagnosed in 103 of patients (2.3%). There were 12 types of cancer that caused UGIB. These cancers are presented in **(Table 2)**.

There were 37 patients who were classified into a miscellaneous group. They were 22 of post-procedural bleeding (i.e. sphincterotomy, gastrectomy, and balloon dilation), 5 of anastomosis bleeding, 3 of hemobilia, 3 of bleeding from duodenal diverticulum, 2 of Crohn's disease, 1 of bleeding gastric benign polyp, and 1 of pancreatic pseudo-aneurysm.

The incidence of *H. pylori* associated with UGIB was stable during the past 5 years at 25%–30%. The overall prevalence was 27%. **(Figure 2)**

Of 3,488 patients, 1,712 subjects (49.1%) had a CLO test during endoscopy. Physicians performing endoscopy decided whether the patient should have a CLO test. This depended on the characteristics of lesions found under endoscopy.

Data revealed that duodenal ulcers and concurrent gastroduodenal ulcers as endoscopic findings were significantly associated with *H. pylori* infection with an odds ratio of 1.62 and 1.63 respectively. By contrast nonulcer-mucosal lesions and cirrhosis were significantly unrelated to *H. pylori* infection, showing odds ratios of 0.73 ($P = 0.007$) and 0.08 ($P = 0.002$) successively. Nevertheless, if peptic ulcer disease was found concurrently with cirrhosis, *H. pylori* was less likely to be a coinfection (OR = 0.45, $P = 0.024$). Gastric ulcer, esophageal-related causes, malignancy, vascular lesion and miscellaneous were found not related to *H. pylori* infection **(Table 1)**.

Table 2. Type of malignancy that caused upper gastrointestinal bleeding with proved tissue-pathology

Type of cancer	Number of patients
Gastric cancer (adenocarcinoma)	36
Gastric lymphoma	15
Other cancers metastasis	15
Esophageal cancer (squamous cell carcinoma)	12
Gastrointestinal stromal tumor (GIST)	11
Ampullary cancer (adenocarcinoma)	4
Periampullary cancer	3
Pancreatic cancer	3
Duodenal cancer (adenocarcinoma)	1
Pancreatic endocrine tumor	1
Epiglottic cancer	1
Pyriform sinus cancer	1

Figure 2. Incidence of *H. pylori* infection in patients presenting with upper gastrointestinal bleeding
*Data June–December in 2007

Patients, who were infected with *H. pylori*, were younger than those who were *H. pylori* free. The mean age of *H. pylori*-positive patients was 60.47 ± 16.9 years, while those free of infection were 65.73 ± 14.8 years old (95%CI 3.5 to 7.0, $P < 0.001$). *H. pylori* infection was more prevalent in male (30.8%) than female (22.1%) patients ($P < 0.001$).

The mean age of patients with cirrhosis was 54.87 ± 13.5 years and differed significantly from noncirrhosis patients (64.39 ± 15.9 years). Patients with vascular lesions and concurrent gastroduodenal ulcer had the oldest mean age of 67 years. Malignancy was found mostly in age 62.44 ± 14.3 years and was not significantly different from the mean age of patients in the group without malignancy group **(Table 1)**.

The prevalence of *H. pylori* infection declined with older age. The highest prevalence was 43.8% in patients <40 years old and the lowest prevalence was 21.7% in patients older than 79 years. The prevalence was significantly different ($P < 0.001$) between each age group. This implies that *H. pylori* infection was frequently found in younger patients who presented with upper gastrointestinal bleeding more than the older ones **(Table 3)**.

Some endoscopic findings were significantly different between age groups. Gastric ulcer was significantly more often identified in older patients. By contrast, duodenal ulcer was significantly more frequent than in patients <40 years and >79 years. Cirrhosis was more often found in the younger patients. Malignancy prevalence was around 2% to 3% in every age group. Vascular lesions were more often found in older patients; however, there was no significant difference between age groups. The prevalence of nonulcer-mucosal lesions was not significantly different between age groups **(Table 3)**.

Discussion

UGIB is a common presentation at hospitals. The male to female patient ratio was 1.4:1 and the mean age of patients was 63.3 years, higher than a decade ago. One study conducted of the Thai population in the 1990s, found that the mean age was 5.3 years younger at 54 years [5]. The ratio of male and female patients was 3.3:1 in the early 1990s [5]. This means that there were more female patients presenting at hospital with UGIB.

In a meta-analysis conducted by Huang et al. [6], peptic ulcer was found to be more common in patients taking NSAIDs, irrespective of *H. pylori* infection. However, risk of peptic ulcer disease is increased by *H. pylori* infection in patients taking NSAIDs over the risk of taking NSAIDs alone.

Gastric ulcer was more frequently found than duodenal ulcer in this study. The ratio of gastric ulcer to duodenal ulcer did not change, compared with that found in a study in the Thai population more than a decade earlier [5]. Duodenal ulcer and concurrent gastroduodenal ulcer were associated with *H. pylori* infection, while gastric ulcer alone was not. This finding was consistent with the meta-analysis by Huang et al. [6]. They reported that duodenal ulcer had a closer relationship with *H. pylori* infection than gastric ulcer. This has practical clinical applications. When physicians find duodenal ulcer or concurrent gastroduodenal ulcer in endoscopy, they should test for *H. pylori* infection.

Table 3. Age-specific prevalence of *H. pylori* infection and causes of upper gastrointestinal bleeding

Age group (y)	H. pylori positive no. of cases (%*)	NUM no. of cases (%)	GU no. of cases (%)	DU no. of cases (%)	esophageal-related cause no. of cases (%)	Cirrhosis no. of cases (%)	Malignancy no. of cases (%)	Vascular no. of cases (%)
<40	63 (43.8)	95 (31.5)	44 (14.6)	58 (19.2)	96 (31.8)	49 (16.2)	8 (2.6)	2 (0.7)
40–59	134 (31.4)	276 (27.5)	212 (21.2)	128 (12.8)	219 (21.9)	209 (20.9)	33 (3.3)	17 (1.7)
60–79	205 (23.7)	512 (31.1)	511 (31.1)	203 (12.3)	416 (25.3)	128 (7.8)	52 (3.2)	38 (2.3)
>79	60 (21.7)	160 (29.7)	169 (31.4)	83 (15.4)	179 (26.1)	13 (2.4)	10 (1.9)	12 (2.2)
Total	**462 (27.0)**	**1043 (29.9)**	**936 (26.8)**	**472 (13.5)**	**910 (26.1)**	**399 (11.4)**	**103 (3.0)**	**69 (2.0)**
P**	**<0.001**	**0.242**	**<0.001**	**0.006**	**<0.001**	**<0.001**	**0.389**	**0.239**

NUM = nonulcer-mucosal lesion, GU = gastric ulcer, DU = duodenal ulcer

*Percentage of *H. pylori* positive or lesion positive comparing within each age groups

**age-specific groups and *H. pylori*-positive or lesion-positive cases

Nonulcer-mucosal lesions (NUM) included less severe mucosal lesions such as gastritis, duodenitis, mucosal erosion, and hemorrhagic gastritis. They were the second leading cause of UGIB in our study. The prevalence of NUM declined during the past decade. A study in the Thai population found a prevalence of 31.6% in the 1990s [5]. The study by Gilbert et al. in the United States in 1981, found a prevalence of 38.7% [4]. In our study, NUM was significantly unrelated to *H. pylori* infection.

Esophageal-related causes included GERD, esophageal ulcer, hiatal hernia, Cameron ulcer, Mallory–Weiss syndrome, esophageal candidiasis, and Barrett's esophagus. *H. pylori* infection was not associated with this group of patients. However, some studies found that *H. pylori* prevalence was significantly lower in patients with reflux esophagitis compared to age-matched asymptomatic subjects [14, 15]. A mechanism was proposed that *H. pylori* infection was associated with gastric hyposecretion. Thus, *H. pylori* was less prevalent in patients with reflux esophagitis, which is associated with hyperacidic secretion [15].

Cirrhosis and concurrent peptic ulcer disease with cirrhosis were found to be negatively associated with *H. pylori* infection. This implies that, although peptic ulcer was related to *H. pylori* infection, endoscopic finding of peptic ulcer and cirrhosis in UGIB patients is less likely to be *H. pylori* coinfection. The prevalence of cirrhosis and concurrent peptic ulcer disease with cirrhosis was 9% and 4.3% respectively, which is almost the same as it was a decade earlier [4].

Malignancy was found in 2.3% of all cases. It increased from 1.66% [5] to 2.3% during the past decade or more. The difference in prevalence might be the result of the variety of cancers diagnosed. Saowaros et al. [5] reported only three types of cancer, which were esophageal, stomach, and ampulla cancer. However, in our study, we found 12 types of cancers in patients who presented at our hospital with UGIB. The most common cancer was adenocarcinoma of stomach. Lymphoma and other cancer metastasis were the second most common. The least found cancers were duodenal adenocarcinoma (1 case), pancreatic endocrine tumor, epiglottic cancer, and pyriform sinus cancer. The last two cancers were found in patients with UGIB. Although, some studies show that *H. pylori* infection increased the risk of gastric cancer [16, 17], the association between *H. pylori* infection and malignancy was not apparent in our study. The proposed mechanism was that chronic infection of *H. pylori* induced chronic gastritis and led to degenerative changes of gastric mucosa, and then metaplasia and dysplasia of the gastric mucosa [18].

Neither vascular lesions nor a miscellaneous group were associated with *H. pylori* infection.

The mean age of patients with each diagnosis was different. Most patients were >60 years, except for those with cirrhosis or concurrent peptic ulcer with cirrhosis, who were 54.9 and 58.7 years old respectively. Patients diagnosed with concurrent gastroduodenal ulcer and vascular lesions were oldest at a mean 67 years for both groups, and were significantly older compared with patients without lesions.

Annual incidence of *H. pylori* infection was lower in developed countries (0.3%–0.7%) than in developing countries (6%–14%) [12]. The present study showed the incidence of *H. pylori* was 25%–30% during 2007 to 2012. Overall prevalence was 27%. Prevalence significantly different between each age group and was highest in patients <40 years old (43.8%) and lowest in patients >79 years old (21.7%). Whereas, Perez-Perez et al. [8] found seroprevalence of *H. pylori* infection in Thailand increased with age. The prevalence of *H. pylori* infection in Chinese was 44.2% and increased about 1% per year with age [9]. The reasons for these discrepancies might be the result of different populations studied. Our study focused only patients with UGIB, and not the general population like the other two studies. Another reason may be that older patients had more varied etiologies causing UGIB, including malignancy, cirrhosis, or vascular lesion, while the younger patients tended to have milder lesions such as peptic ulcer, which was related to *H. pylori* infection.

For each diagnosis, we also found a statistical difference in the number of patients between age-specific groups with gastric ulcer, duodenal ulcer, esophageal-related causes, and cirrhosis. Gastric ulcer was found increasingly with greater age, while, cirrhosis was found to decline with age. Cirrhosis possibly had decreased prevalence with age because cirrhotic patients have shorter life expectancy [19]. Esophageal-caused UGIB prevalence was significantly different in each age group, but this may be not be clinically important. It ranged from 20%–30% in all age group. Although the prevalence of

duodenal ulcer was bimodal, peaking at age <40 and >79 years, this may not be clinically important. Malignancy was found mostly at age 40–79 years. It was less found in age groups at either extreme, <40 years and >79 years. This may be because it is less likely that malignancy occurs in younger patients and fewer patients with cancer will live through the age of 80 years.

Conclusion

The most common cause of UGIB was peptic ulcer disease. Nonulcer-mucosal lesion and esophageal-related causes are the second and third most common etiology. *H. pylori* infection plays a role in UGIB associated with duodenal ulcer and concurrent gastroduodenal ulcer. Cirrhosis was unrelated to *H. pylori*, and peptic ulcers found concurrently with cirrhosis reduce the likelihood of *H. pylori* infection.

Acknowledgments

All members of Endoscopic unit of Gastroenterology, Department of Internal Medicine, King Chulalongkorn Memorial Hospital. The authors have no conflict of interest to report.

References

1. van Leerdam ME. Epidemiology of acute upper gastrointestinal bleeding. Best Pract Res Clin Gastroenterol. 2008; 22:209-24.
2. Rockall T, Logan R, Devlin H, Northfield T. Incidence of and mortality from acute upper gastrointestinal haemorrhage in the United Kingdom. BMJ. 1995; 311: 222-6.
3. van Leerdam M, Vreeburg E, Rauws E, Geraedts A, Tijssen J, Reitsma J, et al. Acute upper GI bleeding: did anything change? Am J Gastroenterol. 2003; 98: 1494-9.
4. Gilbert DA, Silverstein FE, Tedesco FJ, Buenger NK, Persing J. The national ASGE survey on upper gastrointestinal bleeding. III. Endoscopy in upper gastrointestinal bleeding. Gastrointest Endosc. 1981; 27:94-102.
5. Saowaros V, Udayachalerm W, Wee-Sakul B, Tienpaitoon V. Causes of upper gastrointestinal bleeding in Thai patients: review of 5,000 upper gastrointestinal endoscopy. J Med Assoc Thai. 1994; 77:561-5.
6. Huang J-Q, Sridhar S, Hunt RH. Role of *Helicobacter pylori* infection and non-steroidal anti-inflammatory drugs in peptic-ulcer disease: a meta-analysis. Lancet. 2002; 359:14-22.
7. Pounder RE, Ng D. The prevalence of *Helicobacter pylori* infection in different countries. Aliment Pharmacol Ther. 1995; 9 (Suppl 2):33-9.
8. Perez-Perez GI, Taylor DN, Bodhidatta L, Wongsrichanalai J, Baze WB, Dunn BE, et al. Seroprevalence of *Helicobacter pylori* infections in Thailand. J Infect Dis. 1990; 161:1237-41.
9. Mitchell HM, Li YY, Hu PJ, Liu Q, Chen M, Du GG, et al. Epidemiology of *Helicobacter pylori* in southern China: identification of early childhood as the critical period for acquisition. J Infect Dis. 1992; 166:149-53.
10. Malaty HM, Kim JG, Kim SD, Graham DY. Prevalence of *Helicobacter pylori* infection in Korean children: inverse relation to socioeconomic status despite a uniformly high prevalence in adults. Am J Epidemiol. 1996; 143:257-62.
11. Katschinski B, Logan R, Davies J, Faulkner G, Pearson J, Langman M. Prognostic factors in upper gastrointestinal bleeding. Dig Dis Sci. 1994; 39:706-12.
12. Logan RP, Walker MM. ABC of the upper gastrointestinal tract: epidemiology and diagnosis of *Helicobacter pylori* infection. BMJ. 2001; 323:920-2.
13. Cutler AF, Havstad S, Ma CK, Blaser MJ, Perez-Perez GI, Schubert TT. Accuracy of invasive and noninvasive tests to diagnose *Helicobacter pylori* infection. Gastroenterology. 1995; 109:136-41.
14. Varanasi RV, Fantry GT, Wilson KT. Decreased prevalence of *Helicobacter pylori* infection in gastroesophageal reflux disease. Helicobacter. 1998; 3:188-94.
15. Koike T, Ohara S, Sekine H, Iijima K, Abe Y, Kato K, et al. *Helicobacter pylori* infection prevents erosive reflux oesophagitis by decreasing gastric acid secretion. Gut. 2001; 49:330-4.
16. Forman D, Webb P, Newell D, Coleman M, Palli D, Moller H, et al. The EUROGAST Study Group. An international association between *Helicobacter pylori* infection and gastric cancer. Lancet. 1993; 341:1359-62.
17. Miwa H, Go MF, Sato N. *H. pylori* and gastric cancer: the Asian enigma. Am J Gastroenterol. 2002; 97: 1106-12.
18. Forman D. *Helicobacter pylori*: the gastric cancer problem. Gut. 1998; 43 (Suppl 1):S33-4.
19. Propst A, Propst T, Zangerl G, Öfner D, Judmaier G, Vogel W. Prognosis and life expectancy in chronic liver disease. Dig Dis Sci. 1995; 40:1805-15.