RESEARCH ARTICLE

Clinical Characteristics and *Helicobacter pylori* Status of Gastric Cancer in Thailand

Ratha-korn Vilaichone[1]*, Wirat Panarat[1], Surasak Aekpongpaisit[2], Voracha Mahachai[3]

Abstract

Background: Gastric cancer is the second leading course of cancer death worldwide and *H. pylori* infection is an important risk factor for gastric cancer development. This study was design to evaluate the clinical, pathological features, survival rate and prevalence of *H. pylori* infection in gastric cancer in Thailand. Materials and Methods: Clinical information, histological features, endoscopic findings and *H. pylori* status were collected from gastric cancer patients from Thammasat university hospital during June 1996-December 2011. *H. pylori* infection was assessed by histological evaluation, rapid urease test and serological test. Clinical information, endoscopic findings and histopathology of all patients were recorded and compared between patients with active or non-active *H. pylori* infection. Results: A total of 100 gastric cancer patients (55 men and 45 women with mean age of 55±16.8 years) were enrolled in this study. Common presenting symptoms were dyspepsia (74%), weight loss (66%), anemia (63%) and anorexia (38%). Mean duration of symptoms prior to diagnosis was 98 days. Overall prevalence of *H. pylori* infection was 83% and active *H. pylori* infection was 40%. 1-year and 5-year survival rates were 43% and 0%. There was no significant difference between active *H. pylori* infection in different locations (proximal *vs* non-proximal: 47.1% *vs* 48.5%; P-value = 0.9, OR=0.9; 95%CI =0.3-3.1) and histology of gastric cancer (diffuse type *vs* intestinal type: 47.4% *vs* 50%; P-value= 0.8, OR=0.9, 95%CI=0.3-2.7). However, *linitis plastica* was significantly more common in non-active than active *H. pylori* infection (27.9% *vs* 0%; P-value <0.0001, OR =13.3, 95%CI=3.2-64.5). Moreover, gastric cancer stage 4 was higher in non-active than active *H. pylori* infection (93% *vs* 50%, P-value<0.001). Conclusions: Prevalence of *H. pylori* infection in Thai gastric cancer patients was high but active infection was low. Most gastric cancer patients presented in advance stage and had a grave prognosis. Screening for gastric cancer in high risk individuals might be an appropriate tool for early detection and improve the treatment outcome for this particular disease in Thailand.

Keywords: Gastric cancer - *H. pylori* - clinicopathological status - Thailand

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Introduction

Gastric cancer is the fourth most common cancer worldwide, with nearly 1 million cases per year. Gastric cancer is also the second leading cause of cancer-related death annually. Approximately three quarters of gastric cancer occur in Asia, with 80% of cases originating in Japan and China. There is a definite causal link between *H. pylori* infection and gastric cancer. The prevalence of gastric cancer is highest in Asian countries, as mentioned above, but the prevalence of gastric cancer varies among different countries in Asia despite similarly high rate of infection with *H. pylori* in these countries (Vilaichone et al., 2006; Mahachai et al., 2011). The highest incidence rates currently reported in Japan, Taiwan, Costa Rica, Chile, the former Soviet Union, Central and Eastern Europe, whereas India, Africa (eg. Uganda), United States and Southeast Asia have the lowest incidence of gastric cancer. Due to the high incidence of gastric cancer, Japan developed the effective gastric cancer screening and *H. pylori* eradication program for prevention and early detection of this cancer (Asaka et al., 2014; Lin et al., 2014; Sano et al., 2014). In Thailand, gastric cancer is the sixth most common cancer in males and ninth in females. The annual incidence is 5 cases per 100,000 populations and had poor prognosis (Mahachai et al., 2011). Previous studies have suggested risk factors of gastric cancer included *H. pylori* infection, smoking, eating salty foods or fermented foods, family history of gastric cancer, gastric polyp and ethnic Japan, Chinese and Korean (Nomura et al., 1991; Parsonnet et al., 1991; Talley et al., 1991; Mahachai et al., 2011).

The pathogenesis of *H. pylori* in the development of gastric cancer has been suggested primarily from both epidemiological and basic research studies (Parsonnet et al., 1991, Uemura et al., 2001, Demirel et al., 2013,

*[1]GI Unit, Department of Medicine, Thammasat University Hospital, Pathumthani, [2]GI and Liver Center, Smithivej Hospital, [3]GI and Liver Center, Bangkok Medical Center, Bangkok, Thailand *For correspondence: vilaichone@hotmail.co.th*

Karami et al., 2013, Basiri et al., 2014). The World Health Organization and International Agency for Research on Cancer consensus group stated in 1994 based on epidemiologic and histological evidence has classified *H. pylori* as a definite class I carcinogen (IARC 1994; Abeba et al., 2014). Prevalence of *H. pylori* infection in gastric cancer varies from 19% to 94% according to study from Spain (Martin-de Argila et al., 1997). In one meta-analysis, *H. pylori* seropositivity was 82.4% for patients with gastric cancer (Haung et al., 1998).

In Thailand, there are few studies on this area and the prevalence of *H. pylori* in gastric cancer may be underestimated. We conducted this study to evaluate the prevalence of active *H. pylori* infection and to compare the clinical spectrum and histology between active and non-active *H. pylori* infection of gastric cancer patients in our country.

Materials and Methods

All patients who have been detected as gastric cancer by histological evaluation in Thammasat university hospital between June 1996-December 2011 were included in this study. Active *H. pylori* infection was defined as positive from rapid urease test or histology. Non-active *H. pylori* infection was diagnosed if positive only from *H. pylori* serologic test (Anti-*Helicobacter pylori* ELISA IgG). Clinical information, endoscopic findings and histopathology of gastric cancer patients were recorded and compared between patients with active and non-active *H. pylori* infection. The gastric cancer was classified histologically according to the Lauren system into intestinal type and diffuses type by a single pathologist. Endoscopic features of gastric cancer were described as fungating mass, ulcerative mass or linitis plastica. The location of tumor was recorded as proximal (cardia/fundus) and non-proximal area (body and antrum). Staging of gastric carcinoma was classified according to TMN system.

Statistical analysis

The statistical analysis was performed by using descriptive statistics calculated the patient characteristics. The clinical findings of the patients were compared by independent-test or Chi-square test or Fisher's exact test where appropriate. The P-value <0.05 was considered to be statistically significant. All statistic analyses were performed using SPSS for Windows Version 19.0 (IBM Corp., Armonk, NY). The study was conducted according to the good clinical practice guideline, and was approved by our local ethics committee.

Results

A total of 100 patients with gastric cancer were included in the study. The mean age of the patients was 55 ±16.8 years (range 23-86 years). There were 55 men and 45 women with a male to female ratio of 1.2:1. Common presenting symptoms were dyspepsia (74%), weight loss (66%), anemia (63%) and anorexia (38%). The mean duration of symptoms prior to diagnosis was 98 days.

Table 1. Clinical and Histological Characteristic of Gastric Cancer Patients

	Active *H. pylori* infection	Non-Active *H. Pylori* infection
	(N=40)(%)	(N=43)(%)
Age (yr)	58.8±15.7	51.7±13.4
Sex (n)		
Male	27 (67.5%)	21 (48.8%)
Female	13 (32.5%)	22 (51.2%)
Duration of symptom (days)	88	108
Endoscopic feature		
Fungating mas	8 (20%)	14 (32.6%)
Ulcerative mass	32 (80%)	17 (39.5%)
Linitis plastica	0 (0%)	12 (27.9%)*
TNM Staging		
I	0 (0%)	0 (0%)
II	4 (10%)	0 (0%)
III	16 (40%)	3 (7%)
IV	20 (50%)	40 (93%)**

*P-value<0.001; **P-value <0.0001

Table 2. Location of Gastric Cancer and Association with *H. pylori* Infection

Location (n)	Active *H. pylori* Infection (%)	Non-Active *H. pylori* Infection (%)
Proximal area (17)	8 (47.1%)	9 (52.9%)
Non-proximal area (66)	32 (48.5%)	34 (51.5%)

p value=0.9

Table 3 Histologic Type of Gastric Cancer and Association with *H. pylori* Infection

Hitological type (n)	Active *H. pylori* Infection (%)	Non-Active *H. pylori* Infection (%)
Diffuse type (38)	18 (47.4%)	20 (52.6%)
Intestinal type (28)	14 (50%)	14 (50%)

p value=0.8

Overall prevalence of *H. pylori* infection was 83% and active *H. pylori* infection was 40%. 1-year and 5-year survival rates were 43% and 0%. The mean ages of active and non-active *H. pylori* infection gastric cancer patients were 58.8 year and 51.7 year and duration of symptom prior to diagnosis in active and non-active *H. pylori* groups was 88 and 108 days (table 1). There was no significant difference between active *H. pylori* infection in different location (proximal *vs* non-proximal: 47.1% *vs* 48.5%; P-value = 0.9, OR=0.9; 95%CI =0.3-3.1) and histology of gastric cancer (diffuse type *vs* intestinal type: 47.4% *vs* 50%; P-value= 0.8, OR=0.9, 95%CI=0.3-2.7) as in table 2 and 3. However, linitis plastica was significantly more common in non-active than active *H. pylori* infection (27.9% *vs* 0%; P-value <0.0001 OR =13.3, 95%CI=3.2-64.5). Moreover, gastric cancer stage 4 was higher in non-active than active *H. pylori* infection (93% *vs* 50%, P-value<0.001).

Discussion

Gastric cancer is one of the common cancer especially in the Asian countries. Since Warren and Marshall first isolated *H. pylori* and found its association with gastritis

(Warren et al., 1983), many studies have suggested the relationship between *H. pylori* infection and gastric cancer (Parsonnet et al., 1991, Uemura et al., 2001, Demirel et al., 2013, Karami et al., 2013). In this study, the prevalence of active and non-active *H. pylori* infection in gastric cancer was 40% and 43% respectively. We demonstrated that active and non-active *H. pylori* infection were similar in the mean age, sex, gastric location and histological features of this tumor. However, linitis plastica and advanced gastric cancers (stage 4) were significantly more common in non-active than active *H. pylori* infection. The previous studies suggested that very advanced atrophic gastritis or in gastric cancer were unhealthy environment for *H. pylori* and might be not suitable for bacterial survival. Finally, *H. pylori* in those lesions was frequently disappear (Hazell et al., 1987, Robey-Cafferty et al., 1989, Haung et al., 1998, Vilaichone et al., 2003).

The prevalence of *H. pylori* infection was high among gastric cancer patients in many countries such as 91% in Singapore (Chau et al., 2002), 78% in Japan (Ono et al., 2012) and 100% in Iran (Karami et al., 2013). In this study, we demonstrated that overall *H. pylori* infection in gastric cancer was 83%. However, the prevalence of *H. pylori* in gastric cancer depended on examine test. If used only the rapid urease test or histology to detect *H. pylori* infection, prevalence of *H. pylori* infection in gastric cancer patients would be only 53%. On the other hand, if use the serologic test, prevalence of *H. pylori* could be up to 93% in same group of patients (Vilaichone et al., 2003). Serologic tests are widely used for the diagnosis of *H. pylori* infection because of simple and convenient. IgM and IgA antibody testing have not proven to be useful clinically, whereas anti-*H. pylori* IgG had more reliable track record. IgG anti-*H. pylori* antibodies generally can be expected to be present by 4 weeks after infection. However the major disadvantage of serologic test was insufficient efficacy to detect active or current *H. pylori* infection because antibody tests could be remain positive for years even after *H. pylori* eradication. For these reasons, serologic test have limited clinical use especially to confirm cure of this bacterial infection (Vilaichone et al., 2006).

H. pylori screening and treatment is recommended as gastric cancer risk reduction strategy in high risk countries such as Japan, China and Korea and is most effective if screening before developing of atrophic gastritis (Fock et al., 2008). However, *H. pylori* screening and treatment is not recommended for gastric cancer prevention in low risk countries such as Thailand due to low cost effectiveness. In our study, the mortality and survival rate of Thai gastric cancer patients was very poor. To enhance the chance of early gastric cancer detection for better treatment outcome in low risk countries, the authors suggested to perform screening in high risk individuals such as family members of gastric cancer (esp. 1st degree relationship), age more than 40 years especially with alarming symptoms, previously document precancerous lesions (eg. atrophic gastritis, intestinal metaplasia or dysplasia) and certain ethnic group (eg. Japanese, Korean or Chinese people).

In conclusion, the prevalence of *H. pylori* infection in Thai gastric cancer patients was high but active *H. pylori* infection was low due to unhealthy environment for *H. pylori* survival in cancer tissue. Most of gastric cancer patients in Thailand were presented in advance stage and had grave prognosis. Screening of gastric cancer in high risk individuals might be an appropriate tool to early detection and improve the treatment outcome of gastric cancer in Thailand.

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