CHAPTER VI

DISCUSSION

H. pylori is the major causative agent of chronic gastritis and plays a critical role in the etiology of peptic ulcer disease. Evidence suggests that *H. pylori* infection is also a risk for development of gastric carcinoma. *H. pylori* has become a world-wide infective agent ranging from 25 % in developed countries to more than 80 % in the developing world (200). Not all individuals infected with *H. pylori* developed gastric carcinoma together with this might be related to various factors such as environmental factors, host genetic factors and bacterial factor (111). The geographic distribution of distinct *H. pylori* genotypes can be divide into seven populations and subpopulations. These modern populations derive their gene from ancestral populations that arose in Africa, Central Asia, and East Asia (105). The prevalence of virulent bacterial genotypes in certain areas may have important epidemiological consequences and may be associated with the severity of *H. pylori* – related diseases in such regions (152, 201)

The prevalence of *H. pylori* infection in PUD and NUD is not significantly different in different regions of Thailand in this study (Table 8). The aim of this study was to examine the prevalence of genes *cagA vacA,* and *iceA* of *H. pylori* in patients with PUD compared with patients with NUD in Thai strains. The result of this study demonstrated that all *H. pylori* isolates from PUD and NUD patients in Thailand contained *cagA* and *vacA* genes and these genes were not associated with PUD. This is similar to previous studies that in East Asia, these genotypes are predominant and irrespective of clinical outcome (26, 34, 35, 167, 168, 189). This finding suggests that *cagA* and *vacA* genes are not useful markers to predict clinical outcome of Thai patients.

The *vacA* gene of *H. pylori* was predominantly detected in the isolates from diverse geographic areas. Different genotypes of *H. pylori* have been demonstrated in patients with PUD and NUD from different countries in Europe such as Portugal, Netherlands, UK, Germany, France, Sweden, (39, 44, 175, 176, 181, 183, 186-188) the United States (38, 43) and Asia such as China, Japan and Taiwan (35, 167, 168, 189).

In Europe and the United States the *vacA* s1 genotype was more frequently found in patients with PUD than in patients with NUD (38, 39, 43, 44, 168, 175, 176, 181, 186-188). In addition, previous studies in Portugal, Netherlands, Germany and the United States demonstrated that presence of *vacA* s1a genotype was more common in PUD than patients with NUD (38, 43, 44, 181, 186). In contrast, studies in East Asian countries such as Japan, China and Taiwan (35, 167, 168, 189) demonstrated that the *vacA* s1a genotype was dominant irrespective of clinical outcome. In this study, *vacA* s1a gene was predominantly found in patients with PUD (97.5 %) and NUD (92.5 %) and not associated with PUD.

Previous studies demonstrated that *vacA* s1, m1 genotype was more frequently found in *H. pylori* from gastric cancer than from benign gastroduodenal disease (48.) In contrast, this study demonstrated that there was no significant difference in the distribution of the *vacA* s1,m1 and s1, m2 genotype between PUD and NUD.

The present study showed that the *vacA* m2 was predominant in Thai strains. This is similar with China, Taiwan and Hong Kong (33, 167, 168, 189, 202) but different from Japan and Korea (35) which *vacA* m1genotype was predominant.

The present study demonstrated that the *iceA2* allele was also predominant in Thai strains, compatible with the situation in the United States, Columbia and Brazil (35, 171, 199). In contrast, recent reports of strains from Japan, Korea, Hong Kong and Taiwan suggested that the *iceA1* gene was found predominant in this population. (34-36, 203). Either *iceA1* or *iceA2* was not associated with clinical outcome in this study. This confirms the findings reported for *H. pylori* strains isolated from Japanese (35), Korean (35), Columbian,

Indian (184) and Brazilian (199). High prevalence of mixed *iceA* isolates (48.75%) was found in Thai patients. All of these isolates contained single *vacA* genotype which suggests the presence of mixed *iceA* genotype in one strain. Previous studies demonstrated that mixed *iceA* genotype had wide rage of prevalence 7.7% in Brazil, 15% in Netherlands, 22% in Columbia and 40% in South Africa (35, 44, 46, 199). These studies did not include the mixed *iceA* genotype for the analysis between *iceA* genotype with clinical outcome. In this study the interaction between *vacA* s1a, mixed *iceA* was significantly associated with peptic ulcer disease as analyzed by multivariate analysis (P = 0.04, OR = 2.51, 95 % CI = 1.05 – 6.04). This finding suggests the association of *vacA* s1a, mixed *iceA* genotype with peptic ulcer disease.

Determination of the presence of these putative mixed *iceA* genotype is needed to verify its association with clinical outcome. This may be done by perfoming repeat PCR for *iceA* genotype from recultured colonies from mixed *iceA* parent strains. Multiple isolated clones (5 to 25 colonies) from the recultured *H. pylori* should be amplified by PCR to detect the presence of single *iceA* allele or mixed *iceA*. In addition, subtyping of other genes such as *cagA* 3' repeat and *cag* right end (184) may be performed to find the presence of single subtype or mixed subtype.

In this study, neither *cagA*, *vacA* and *iceA* nor their combinations have a predictive value as risk markers for the development of peptic ulcer in Thai patients. However, infection by a *H. pylori* strain with the gene *vacA* s1a, mixed *iceA* genotype may increase the risk of peptic ulcer disease if the mixed *iceA* genotype really exists in nature.