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Editorial

What is responsible for the development of the distinctive pattern of gastritis induced by *Helicobacter pylori* infection?

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Topography of chronic active gastritis in *Helicobacter pylori*-positive Asian populations: age-, gender-, and endoscopic diagnosis-matched study

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Compared to Western countries, the prevalence of *Helicobacter pylori* infection in Asian countries is generally very high, ranging from 40% to 70% of the general population, and such high prevalence appears to be linked to a high incidence of gastric cancer in this region. For instance, in Japan nearly 50% of the general population is infected with *H. pylori*, and approximately 50000 gastric cancer deaths of 300000 total cancer deaths were reported in 2000.[1]

However, it should be emphasized that even within Asian countries there exists a considerable difference in the incidence of gastric cancers. Moreover, there also exists a remarkable difference in clinical outcome, such as duodenal ulcer: gastric ulcer (DU–GU) ratio, due to *H. pylori* infection in different Asian countries. Indeed, in southeast Asia, such as south China and Thailand, in spite of a similarly high prevalence of *H. pylori* infection, the incidence of gastric cancer is much lower than that of Japan and Korea.[2] Moreover, in Gangzhou, a large city in southern China, there are very few patients with not only gastric cancer but also GU, and in addition, their DU–GU ratio is between 5 and 10 (personal communication; P.J. Hu, Sun-Yat-sen University, Gangzhou). Contrasting with their data from Southern China, our DU–GU ratio in Japan is less than 1.[3] It is well accepted that patients with DU have antrum-predominant gastritis with very little mucosal atrophy, whereas patients with GU almost invariably have corpus-predominant gastritis with various degrees of mucosal atrophy, Accordingly, it is believed that DU is negatively associated with gastric cancer, and the reverse is true for GU. Supporting this hypothesis, Uemura et al.[4] recently reported that by following up 1246 Japanese subjects with *H. pylori* infection, no gastric cancer developed in patients with DU, but 3.4% of patients with GU developed gastric cancer. Taken together, it may be speculated that the different cancer risk among different regions in Asia is attributed to a distinct pattern of gastritis induced by *H. pylori* infection in each region.

In this issue of *Journal of Gastroenterology*, Matsuhisa et al.[5] reported a remarkable difference in the patterns of gastritis induced by *H. pylori* infection between Japanese patients and those in other Asian countries. By comparing age-, gender-, and endoscopic diagnosis-matched pairs, they showed that corpus-predominant gastritis, which is believed to be a precursor to the development of gastric cancer, is more common in Japanese patients with *H. pylori* infection than those in any other Asian countries, and stated that low prevalence of corpus gastritis in Thai and Vietnamese patients correlates with low incidence of gastric cancer in those countries. Thus, their data confirm the idea already described that corpus-predominant gastritis is associated with development of gastric cancer.

However, the most important and interesting question raised by their data, as well as by several previous studies, is which factors are responsible for such different outcomes due to *H. pylori* infection even within Asia. There have been numerous studies trying to explain the reasons for such divergent clinical outcomes according to differences in *H. pylori* strains. However, it is evident that both GU and DU patients are infected with CagA/CagPAI-positive *H. pylori*, the so-called virulent strain. Higashi et al.[6] reported a distinct amino acid sequence motif in proximity to the tyrosine phosphorylation site of CagA in a Japanese *H. pylori* isolate

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that has a higher affinity to src homology 2-containing protein tyrosine phosphatase (SHP-2) than that of Western isolates. Thus, it might be considered that the Japanese isolate with distinct phosphorylation sites of CagA is specifically linked to corpus gastritis or GU followed by development of gastric cancer. However, no difference has been reported so far between *H. pylori* strains from patients with DU and those with GU in Japan.

Therefore, many investigators are now focusing on host factors or environmental factors. Recent studies have highlighted IL-1β as a key host factor for the development of corpus gastritis. Indeed, El-Omar et al.[7] showed the association of IL-1β gene polymorphism and increased risk of gastric cancer by *H. pylori* infection. However, not all recent studies have found an association between IL-1β polymorphism and cancer risk.[8] Indeed, there appear to be considerable so-called negative data on the association of the IL-1β gene, which have not been published, in many institutions worldwide including ours. Moreover, we now recognize that the DU–GU ratio is increasing in Japan. This fact cannot be explained by host factors alone and may rather reflect the significance of environmental factors. In this regard, it may be noted that Matsuhisa et al.[5] have found in this study that antral gastritis is more prominent in patients from southeast Asia than in Japanese patients, and conversely corpus gastritis is less prominent in Thai and Vietnamese patients than in Japanese patients, although it is not the case for Fuzhou, a city located in the south of China. Interestingly, in Okinawa in the far south of Japan, in spite of a similarly high prevalence of *H. pylori* infection the incidence of gastric cancer is the lowest in Japan,[1] and moreover, the DU–GU ratio is much higher than that in mainland Japan. Thus, the gastric cancer risk appears to increase as we go north. Whether this phenomenon can be explained by environmental factors, such as the degree of salt intake and food, is an interesting question to be elucidated in the future.

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