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***Observational Study***

**Comparison of gastric mucosa in Mongolian and Japanese patients with reference to gastric cancer and *Helicobacter pylori* infection**

Matsuhisa T *et al*. Gastric mucosa in Mongolians and Japanese

Takeshi Matsuhisa, Yoshio Yamaoka, Tomohisa Uchida, Davaadorj Duger, Battulga Adiyasuren, Oyuntsetseg Khasag, Tserentogtokh Tegshee, Byambajav Tsogt-Ochir

**Takeshi Matsuhisa**, Department of Gastroenterology, Tama-Nagayama University Hospital, Nippon Medical School, Tokyo 206-8512, Japan

**Yoshio Yamaoka**, Department of Environmental and Preventive Medicine, Oita University of Medicine, Oita 879-5593, Japan

**Tomohisa Uchida**, Department of Molecular Pathology, Oita University of Medicine, Oita 879-5593, Japan

**Davaadorj Duger**, Vice President of Mongolian National University of Medical Sciences and President of Mongolian Society of Gastroenterology, Ulaanbaatar 14210, Mongolia

**Battulga Adiyasuren**, Department of Endoscopy, Ulaanbaatar Songdo Hospital, Ulaanbaatar 14210, Mongolia

**Oyuntsetseg Khasag**, **Byambajav Tsogt-Ochir**, Department of Gastroenterology, Mongolian National University of Medical Sciences, Ulaanbaatar 14210, Mongolia

**Tserentogtokh Tegshee**, Department of Gastroenterology, Third Central State Hospital, Ulaanbaatar 16081, Mongolia

**Author contributions:** Matsuhisa T and Yamaoka Y contributed to study conception and design, data interpretation, and writing, editing, review and approval of the article; Matsuhisa T, Yamaoka Y, Uchida T, Duger D, Adiyasuren B, Khasag O, Tegshee T and Tsogt-Ochir B contributed to data acquisition.

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**Correspondence to: Takeshi Matsuhisa, MD, Professor**, Department of Gastroenterology, Tama-Nagayama University Hospital, Nippon Medical School, Tama, Tokyo 206-8512, Japan. matuhisa@nms.ac.jp

**Telephone:** +81-42-3712111

**Fax:** +81-42-3727381

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**abstract**

**AIM:** To investigate the characteristics of gastric cancer and gastric mucosa in the Mongolian populations by comparison with the Japanese population.

**METHODS:** A total of 484 Mongolian patients with gastric cancer were enrolled to study gastric cancer characteristics in Mongolians. In addition, a total of 208 Mongolian and 3205 Japanese consecutive outpatients who underwent endoscopy, had abdominal complaints and had no history of gastric operation or*Helicobacter pylori* (*H. pylori*) eradication treatment and no use of gastric secretion inhibitors such as histamine H2-receptor antagonists and proton pump inhibitors were enrolled. This study was conducted with the approval of the ethics committees of all hospitals. The triple-site biopsy method was used for the histological diagnosis of gastritis and *H. pylori* infection in all Mongolians and Japanese cases. The infection rate of *H. pylori* and the status of gastric mucosa in *H. pylori*-infected patients were compared between Mongolian and Japanese subjects. Age (± 5 years), gender and endoscopic diagnosis were matched between the two countries.

**RESULTS:** Approximately 70% of Mongolians with gastric cancer were in their 50-s, 60-s and 70-s, and approximately half of the Mongolian cancers were located in the upper part of the stomach. Histologically, 65.7% of early cancers exhibited differentiated adenocarcinoma, whereas 73.9% of advanced cancers displayed undifferentiated adenocarcinoma. The infection rate of *H. pylori* was higher in Mongolians than Japanese (75.9% and 48.3%, respectively, *P* < 0.0001). When stratified by age group, the prevalence was highest amongyoung people and tended to decrease in people aged 50 years or older. The anti-East Asian CagA-specific antibody was negative in 99.4% of *H. pylori* positive Mongolians. Chronic inflammation, neutrophil activity, glandular atrophyand intestinal metaplasia scores were significantly lower in Mongolians than Japanese *H. pylori*-positive patients (*P* < 0.0001), with the exception of the intestinal metaplasia score of specimen #2 (greater curvature of the upper body). The type of gastritis changed from antrum-predominant gastritis to corpus-predominant gastritis with age in both populations.

**CONCLUSION:** Approximately half of the gastric cancer in Mongolian patients was located in the upper part of the stomach. Mongolians were infected with non-East Asian-type *H. pylori* strains.

**Key words:** Gastric cancer; *Helicobacter pylori*; Non-East Asian-type strain; Chronic inflammation; Neutrophile activity; Glandular atrophy; Intestinal metaplasia; Mongolians; Japanese

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**Core tip:** Characteristics of gastric cancer and gastric mucosa in Mongolian patients were observed. Approximatery half of the Mongolian cancers were located in the upper part of the stomach. The infection rate of *Helicobacter pylori* (*H. pylori*) was higher in Mongolians than Japanese (75.9% and 48.3%, respectively, *P* < 0.0001). Mongolians were infected with non-East Asian-type *H. pylori* strains. Both atrophic scoreand intestinal metaplasia score were lower in *H. pylori* infected Mongolians than in Japanese (*P* < 0.0001). The type of gastritis changed from antrum-predominant gastritis to corpus-predominant gastritis with age in both populations.

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**INTRODUCTION**

*Helicobacter pylori* (*H. pylori*) infections cause not only peptic ulcer disease (PUD), but also gastric cancer[1,2]. Among *H. pylori* strains, there is a Western-type and an East Asian-type; the East Asian-type strain greatly influences the development of atrophic gastritis and gastric cancer. Mongolia, South Korea and Japan are located in Eastern Asia and have the highest incidence of gastric cancer in the world (age-standardized incidence rates (ASR): 47.4, 62.3, and 45.8 cases per 100000 males, respectively)[3]. In spite of the high prevalence of *H. pylori* infection in Bangladeshi[4,5], Thai[6], and Indian populations, the incidence of gastric cancer in these countries is extremely low. These trends have been denoted Asian enigmas[7] or the Asian Paradox[8]. In this report, the characteristics of gastric cancer in Mongolian patients, *H. pylori* infection and gastric mucosa in Mongolians andJapanese populations were observed and compared**.**

**MATERIALS AND METHODS**

***Patients***

Between January 2011 and December 2013, 484 consecutive gastric cancer patients (aged 26 to 93 years, with a mean age of 60.5 years, male-to-female ratio of 1:0.51) in the Department of Endoscopy of Ulaanbaatar Songdo Hospital (Ulaanbaatar, Mongolia) were enrolled to study the characteristics of gastric cancer in Mongolian patients.

In addition, we performed endoscopy on 208 consecutive outpatients (aged 17 to 79 years, with a mean age of 41.6 years, male-to-female ratio of 1:1.89) in the Department of Gastroenterology, Health Sciences University of Mongolia; the Department of Endoscopy, Ulaanbaatar Songdo Hospital; and the Department of Gastroenterology, Third Central State Hospital, November 2013 in Ulaanbaatar, Mongolia. The data were compared with our independent endoscopy survey of 3205 consecutive outpatients (aged 14 to 93 years**,** with a mean age of 55.1 years, male-to-female ratio of 1:0.73) at Nippon Medical School between January 2008 and March 2014 in Tokyo, Japan. All patients in both countries had abdominal complaints, no history of gastric operation or*H. pylori* eradicationtreatment, and no use of gastric secretion inhibitors such as histamine H2-receptor antagonists and proton pump inhibitors.

This study was conducted with the approval of the ethics committees of all hospitals. Written informedconsent to participate in the study was obtained from all patients except minors, whose consent was obtained from the guardian. All endoscopy procedures in Mongolian patients were performed by Matsuhisa T. and Yamaoka Y. using the same criteria used for the Japanese patients. All endoscopy procedures in Japanese patients were performed by Matsuhisa T.

***Classification of gastric cancer***

The 3rd English edition of Japanese Classification of Gastric Carcinoma was used for histological classification and to describe the location of the gastric cancer [Upper (U), Middle (M), and Lower (L)][9]. Cancer lesions involved in more than 2 regions were excluded. Among gastric cardia cancers, cancers in the stomach less than 2 cm distal to the esophagogastric junction (EGJ) were included in the cases of the U region. Nishi’s criterion (in Japanese) was used for the definition of gastric cardia cancer (esophagogastric cancer). According to this criterion, the tumor center must be located in the stomach or esophagus within 2 cm of the EGJ irrespective of histology. This criterion is also included in the 3rd English edition of Japanese Classification of Gastric Carcinoma[9]. The location of gastric cancers was diagnosed by Mongolian doctors (Tegshee T and Adiyasuren B).

Cancer limited to mucosa or submucosa was defined as early gastric cancer, regardless of the presence or absence of lymph node metastases[9]. Advanced gastric cancer was defined as cancer that has infiltrated a deeper layer than the muscularis propria[9].

Papillary adenocarcinoma (pap), well-differentiated type (tub1), and moderately-differentiated type (tub2) were considered differentiated adenocarcinoma; poorly differentiated adenocarcinoma (por), signet-ring cell carcinoma (sig), and mucinous adenocarcinoma (muc) were considered undifferentiated adenocarcinoma[9]. Gastric cancer in Mongolian patients included endoscopically operated patients (endoscopic submucosal dissection or endoscopic mucosal resection), surgically operated patients, patients not operated on, and inoperable patients. Biopsy specimens were used for the histological diagnosis of gastric cancer. Cancers were diagnosed by a single Mongolian pathologist (Baldandorj T).

***Diagnosis of gastritis and H. pylori infection***

The triple-site biopsy method (Figure 1)[5,6,10,11] was used for the histological diagnosis of gastritis and *H. pylori* infection in all Mongolians and Japanese cases. Chronic inflammation, neutrophil activity, glandular atrophy, intestinal metaplasia and *H. pylori* were scored using a 4-point scale ranging from 0 to 3 (0: none, 1: mild, 2: moderate and 3: severe) based on the Updated Sydney system[12]. Specimen #1 was taken from the greater curvature of the lower antrum (Antrum), specimen#2 was taken from the greater curvature of the upper corpus (Corpus), and specimen#3 was takenfrom the lesser curvature of the lower corpus (Angulus). Specimen #4 and others were taken from ulcers or cancer lesions.

In Mongolian endoscopy cases, all biopsy specimens were subjected to hematoxylin-eosin staining, Giemsa staining, and anti-East Asian CagA-specific antibody (α-EAS Ab) staining in Japan[13]. α-EAS Ab is specifically immunoreactive with East Asian CagA but not Western CagA. All Japanese cases were subjected to hematoxylin-eosin staining and Giemsa staining. One pathologist (Yamada N) diagnosed all sections to minimize anybias in the histological diagnoses.

In total, 203 pairs of 406 patients from 208 Mongolian and 3205 Japanese patients matched by age (± 5 years), gender and endoscopic diagnosis were used to compare the prevalence of *H. pylori* infection between the 2 countries.

From 158 *H. pylori*-positive Mongolian and 1,736 *H. pylori*-positive Japanese patients matched by age (± 5 years), gender and endoscopic diagnosis, 137 pairs of 274 *H. pylori*-positive patients were used to compare the characteristics of gastric mucosa.

***C/A ratio***

The ratio of the Corpus activity score (C) (#2, Figure 1) to the Antrum activity score (A) (#1, Figure 1) (C/A ratio), was used to diagnose the type of gastritis in *H. pylori****-***positive patients[10,11]. The C/A ratio in every age group was calculated using the mean score of C divided by themean score of A. Patients with a C/A ratio of less than 1 were assessed as having antrum**-**predominant gastritis and those with a C/A ratio of greater than 1 were assessed as having corpus**-**predominant gastritis.

***Statistical analysis***

McNemar’s test was used to compare the prevalence of *H. pylori* infection**,** and the Mann-Whitney *U*-test was usedto compare the gastric mucosa. *P*< 0.05 was considered significant.

**RESULTS**

***Characteristics of gastric cancer in Mongolians***

In 484 consecutive cases of gastric cancer in Mongolian patients, early gastric cancer accounted for 29.5% (143/484). When stratified by age group, total gastric cancer, early gastric cancer and advanced gastric cancer were most frequent in patients in their 60-s, followed by those in their 50-s and then 70-s; in total, patients in their 50-s, 60-s and 70-s accounted for 71.9%, 72.0%, and 71.8% of these cancers, respectively (Figure 2). Moreover, 6.5%-9.8% of gastric cancer presented in young adults ages 39 and younger (Figure 2). The male-to-female ratio was 1:0.51.

The percentages of the sites most affected by total gastric cancer were 46.5% in the U region, followed by 28.1% in the L region, and 25.4% in the M region (Figure 3). Lesions occurring 2 or 3 regions (UM region: 91 cases, ML region: 16 cases, UML region: 7 cases; all were advanced gastric cancer) were excluded. The affected area of early gastric cancer and advanced gastric cancer was also largest in the U region (47.5% and 45.8%, respectively) (Figure 3). Among gastric cancer in Mongolian patients, gastric cardia cancer accounted for 3.9% (19/484) of total gastric cancer.

A greater percentage of total gastric cancer cases were undifferentiated adenocarcinoma (61.8%) than differentiated adenocarcinoma (37.2%). Similarly, in advanced gastric cancer, cases of undifferentiated adenocarcinoma (73.9%) were greater than those of differentiated adenocarcinoma (25.2%) (Figure 4). By contrast, in early gastric cancer, differentiated adenocarcinoma (65.7%) was more prevalent than undifferentiated adenocarcinoma (32.9%) (Figure 4).

***Infection rate of H. pylori***

The infection rate of *H. pylori* was 76.0% (158 out of 208 patients) in Mongolian patients. When stratified by ages, *H. pylori* infection was highest amongyoung people (younger than 19 years: 88.9%, 20 to 29 years: 76.9%, 30 to 39 years: 89.7%) and tended to decrease in people ages 50 and older (50 to 59 years: 68.4%, 60 to 69 years: 61.5%, 70 years or older: 71.4%) (Figure 5).

The infection rate of *H. pylori* was higher in Mongolian than in Japanese patients (75.9% and48.3%, respectively, *P* < 0.0001).

***α-EAS Ab positivity***

α-EAS Ab was negative in 99.4% (157 of 158 patients) of *H. pylori*-positive Mongolians.

***Gastric mucosa***

The mean scores for gastritis and *H. pylori* in the*H. pylori*-positive cases were all significantly lower in Mongolians than Japanese patients. The only exception was the intestinal metaplasia scores of specimen #2, which did not differ significantly between Mongolian and Japanese patients (all except intestinal metaplasia of #2: *P* < 0.0001; intestinal metaplasia of #2: *P* = 0.1907) (Table 1).

***C/A ratio***

TheC/A ratio in 137 matched pairs of 274 *H. pylori*infected Mongolians and Japanese patients revealed antrum-predominant gastritis in age groupsyounger than 49 and 39 years, respectively, and corpus-predominant gastritis in age groupsolder than 50 and 40 years, respectively (Figure 6). The mean C/A ratio of the Japanese patients over 60 years of age was higher than that of the Mongolian patients (1.43, 1.01, respectively, *P* <0.01).

**DISCUSSION**

The incidence and mortality of gastric cancer are high in Eastern Asia and Central and Eastern Europe. According to the age-adjusted cancer incidence in Mongolian males, the liver is the most common cancer site (ASR: 97.8 cases per 100000 males), followed by the stomach (47.4), lungs (27.7), esophagus (21.2), and colorectum (5.7) (Globocan 2012)[3]. By contrast, in Japanese males, the stomach is the most common cancer site (45.8), followed by the colorectum (42.1), lungs (38.8), prostate (30.4) and liver (14.6)[3]. In South Korean males, the stomach is also the most common cancer site (62.3)[3]. South Korea, Mongolia, and Japan have the highest incidences of gastric cancer in the world. We previously examined gastric mucosa in relation to *H. pylori* infection in South Koreans[14], Chinese[6,11], Vietnamese[6,11], Thais[6,11], Burmese (Lecture, Nay Pyi Daw, Myanmar, 2008), Bangladeshi[4,5], and Nepalese[11] patient, and reported that atrophic score and intestinal metaplasia score were very high in Japanese and South Koreans. In this study, we investigated the characteristics of gastric cancer and the gastric mucosa in the context of *H. pylori* infection in Mongolians, who belong to the East Asian population, and compared them with those of Japanese patients.

***Characteristics of gastric cancer in Mongolians***

Other than incidence and mortality, very few data relating to Mongolians with gastric cancer are available via PubMed. Therefore, we determined the ratio of early gastric cancer to total gastric cancer, age group frequency, and region and histological type in gastric cancer in Mongolian patients. Globally, gastric cancer is more common in men than women[3], and this was also true for Mongolians (male-to-female ratio 1:0.51). The percentage of early gastric cancer among total gastric cancer was 29.5% in Mongolians, lower than that in Japanese (80%)[15]; the delayed spread of gastric examination screening, endoscopy devices and early gastric cancer diagnostics in Mongolia may be a determining factors. In addition, because of *H. pylori* testing is not widespread in Mongolia, it is not clear if these cases included in this study were infected with *H. pylori*.

In countries and regions with a high incidence of gastric cancer, gastric cancer occurs more frequently in the distal portion of the stomach; in countries and regions with a low incidence, gastric cancer occurs more frequently in the proximal portion[16]. Approximately half of the Japanese with cases of gastric cancer occurred in the M region, (M region > L region > U region)[15], while approximately half of the Mongolians with gastric cancer cases occurred in the U region, indicating a large considerable difference in the location frequency. Mongolians reportedly have high meat and salt intake (15 g/d). Other common practices include consuming large amounts of hot tea, regular alcohol intake, hurried eating, and low intake of fruit and vegetables[17,18]. Although *H. pylori* infection is not a risk factor for gastric cardia cancer[19], obesity is an onset risk factor of gastric cardia cancer[20,21]. Furthermore, obesity may influences the development of early gastric cancer and differentiated adenocarcinoma in males regardless of *H. pylori* infection[22]. No data regarding the degree of obesity in gastric cancer patients have been reported; however, the percentage of obese Mongolian adults (16.4%) is high compared with Japanese adults (4.5%) according to age-standardized data[23]. In this context, patients with a body mass index (BMI) greater than or equal to 30 kg/m2 are defined as obese. Gastric cardia cancer accounted for 3.9% of total gastric cancer in Mongolians, and 3.2% of Japanese gastric cancer patients who underwent either endoscopic surgery or an open surgery in the 2000s[24]. Many cancers were located in the U region, including the cardia, in Mongolians (Figure 7a, b), but the frequency of gastric cardia cancer did not differ compared with that in Japanese patients. Because there are so many advanced cancer cases among Mongolian patients, we must consider the possibility that gastric cardia cancers enlarged in size that were classified as U region cancers. The factors (other than obesity) that contribute to the high incidence of gastric cancer in the U region remain to be determined. A detailed investigation of environmental factors and host factors is also necessary.

In Mongolian patients, the most prevalent histological types of total gastric cancer, early gastric cancer and advanced gastric cancer are undifferentiated adenocarcinoma, differentiated adenocarcinoma and undifferentiated adenocarcinoma, respectively. In Japanese patients, undifferentiated adenocarcinoma was prevalent before the 1970s and differentiated adenocarcinoma has been dominant since the 1980s due to the aging of *H. pylori*-infected patients[15]. According to a report by Yamada *et al*[15], who examined 10132 cases of patients who underwent a surgical treatment in the 2000s by histological type, differentiated adenocarcinoma accounted for 68% and undifferentiated adenocarcinoma accounted for only 32%. The trend of prevalent differentiated adenocarcinoma is weaker in advanced gastric cancer but significantly stronger in early gastric cancer[16]. In Mongolians, differentiated adenocarcinoma is common in early gastric cancer, as in Japanese; however, a different trend was observed for advanced gastric cancer and total gastric cancer. The prevalence of undifferentiated adenocarcinoma in total gastric cancer in Mongolia may be due to differences in the criteria used by pathologist in Mongolia and the lower mean age of gastric cancer in Mongolian patients (60.5 years) compared to the Japanese (64 years)[15].

Based on the results of our field study in Asian countries, the gastric ulcer which included gastroduodenal ulcer/duodenal ulcer ratio (GU/DU ratio) was different. There are big differences among Asian countries. Japanese[14] and South Korean[14] patients exhibit as GU**-**predominant (1.69 and 1.75, respectively), whereas Bangladeshi[5] and Nepalese[11] exhibit as DU-predominant (0.31 and 0.25, respectively). According to a personal communication with one Mongolian doctor who previously investigated this topic (Khasag O), Mongolia is a country of GU-predominance (1.9 in 2003 in her unpublished data from Mongolian National University of Medical Sciences). Regarding the relationship between PUD and gastric cancer, a higher GU/DU ratio in a country or region has been associated with a greater incidence of gastric cancer[25]. Furthermore, the development of gastric cancer is positively correlated with GU but negatively correlated with DU[26]. Based on these reports, gastric cancer is likely common among Japanese, South Koreans, and Mongolians.

***Infection rate of H. pylori***

Approximately half of the world’s population is infected with *H. pylori*, and the infection rate is higher in developing countries than in developed countries[27]. The infection rate of *H. pylori* is reported to be 5% or less in people younger than 20 years of age and 40% in people in their 50-s in developed countries[27]. In Japan, the infection rate is decreasing gradually, and the prevalence is 6.4% in children (0-12 years old)[28] and 5.2% in high school students (16 or 17 years old)[29]. In developing countries, the infection rate of *H. pylori* can be as high as 50% in teenagers and more than 90% in people in their 30-s[30]. Our results indicate that *H. pylori* infection rates are high (76.0%) in Mongolians and very high in Mongolians aged 17 to 19 years (88.9%), revealing a developing country-type prevalence.

***Positive rate of α–EAS Ab***

The Japanese are infected with East Asian-type *H. pylori*, but the type of *H. pylori* that infects Mongolians has not been determined. Therefore, the Mongolian biopsies were stained with α-EAS Ab, which specifically reacts to East Asian-type *H. pylori*. In *H. pylori-*positive Mongolian cases, the rate of α-EAS Ab positivity was 0.6% (1 in 158 *H. pylori* positive cases), indicating that despite the location of Mongolia in East Asia, Mongolians are not infected with East Asia-type *H. pylori* (i.e. Western-type *cagA* or *cagA*-negative strains). The *H. pylori* strains are currently being characterized by one of the authors (Yamaoka Y).

***Gastric mucosa***

The scores for gastritis and *H. pylori* were significantly lower in *H. pylori-*infected Mongolians than in Japanese at all gastri**c** sites, with the exception of the intestinal metaplasia score in specimen #2. East Asian-type *H. pylori* strains induce stronger chronic inflammation and neutrophil activity than Western-type *H. pylori* strains[31] and are involved in gastric mucosal atrophy and gastric cancer[32]. According to a report by Uemura *et al*[1], atrophic changes and intestinal metaplasia are strongly related to the risk of gastric cancer, and severe atrophic change and intestinal metaplasia**,** in particular, leads to a high risk of both intestinal-type and diffuse-type gastric cancer[9]. Because the South Asian population is infected with Western-type *H. pylori*[33,34], glandular atrophy and intestinal metaplasia scores were significantly lower in Bangladeshi[5] and Nepalese[12] in our previously reportedresults. Therefore, the incidence of gastric cancer is very low in Bangladesh and Nepal (ASR: 7.2 and 7.4 cases per 100000 males, respectively)[3]. Although glandular atrophy and intestinal metaplasia scores are low in Mongolians, the incidence of gastric cancer is high; however, it is important to note that these scores were not obtained from patients with gastric cancer. To address this paradox, the gastric mucosa of Mongolian patients with gastric cancer should be examined. We are planning a gastric mucosal survey of patients with gastric cancer in Uvs, a western province with the highest prevalence of gastric cancer in Mongolia (ASR: 114.6 cases per 100000 males).

***C/A ratio***

The prevalence of antrum**-**predominant gastritis tends to decrease in favor of corpus**-**predominant gastritis in Mongolians and Japanese with aging. The C/A ratio in patients older 60 years was higher in Japanese patients than in Mongolian patients. All age groups ofBangladeshi and Nepalesesubjects had antrum**-**predominant gastritis[5,12]**.** The risk of gastric cancer is 23.3 times higher for corpus-predominant gastritis than for antrum-predominant gastritis[1]. This report is consistent with the low incidence of gastric cancer in South Asian countries (Bangladesh and Nepal) and the high incidence in East Asian countries (Japan, South Korea and Mongolia). Therefore, a high C/A ratio, indicating corpus-predominant gastritis, is one of the causative factors of gastric cancer.

In conclusion, acomparative analysis of gastric mucosa in Mongolia and Japan, two countries with a high incidence of gastric cancer, was conducted. Gastric cancer occurred most frequently in the U region of Mongolians, and peaked among those in their 60-s. The most prevalent histological types in early gastric cancers and advanced gastric cancers are differentiated adenocarcinoma and undifferentiated adenocarcinoma, respectively. The infection rate of *H. pylori* washigh in Mongolians, particularly those 17-19 years old. The scores for gastric mucosa may have been lower in Mongolians than Japanese because the majority of Mongolians were infected with non-East Asian-type *H. pylori* strains. *H. pylori*-positive young Mongolians had antrum-predominant gastritis and developed more corpus-predominant gastritis with aging similar to the Japanese population. Further studies should clarify the reason for the high gastric cancer prevalence in Mongolians infected with non-East Asian-type *H. pylori*.

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**COMMENTS**

***Background***

*Helicobacter pylori* (*H. pylori*) infections cause not only peptic ulcer disease, but also gastric cancer. Mongolia, South Korea and Japan, which are located in Eastern Asia, have the highest incidence of gastric cancer in the world. Other than incidence and mortality, very few data relating to Mongolians with gastric cancer are available in PubMed. The characteristics of gastric cancer in Mongolian patients, *H. pylori* infection and gastric mucosa were observed and comparedbetween Mongolians andJapanese populations.

***Research frontiers***

There are Western-type and East Asian-type strain of *H. pylori*: the East Asian-type strain influences the development of atrophic gastritis and gastric cancer greatly. There are no data about the type of *H. pylori* strain that tends to infect Mongolians or the gastric mucosa and type of gastritis in Mongolians.

***Innovations and breakthroughs***

Gastric cancer occurred most frequently in the U region of Mongolians and peaked in those in their 60-s. The most prevalent histological types in early gastric cancers and advanced gastric cancers were differentiated adenocarcinoma and undifferentiated adenocarcinoma, respectively. The infection rate of *H. pylori* was high in Mongolians, particularly those 17-19 years old. The majority of Mongolians were infected with non-East Asian-type *H. pylori* strains (99.4%), which may explain the lower gastric mucosa scores of Mongolians compared to Japanese. *H. pylori*-positive young Mongolians had antrum-predominant gastritis and developed more corpus-predominant gastritis with aging similarly to the Japanese.

***Applications***

There are many differences between Mongolians and Japanese in the location of gastric cancer, *H. pylori* strain type, and gastric mucosa. Future studies should clarify the reason for the high gastric cancer prevalence in Mongolians infected with non-East Asian-type *H. pylori*.

***Terminology***

Anti-East Asian CagA-specific antibody (α-EAS Ab) is specifically immunoreactive with East Asian CagA but not Western CagA. Patients with a C/A ratio less than 1 were assessed as having antrum**-**predominant gastritis, and those with a C/A ratio of greater than 1 were assessed as having corpus**-**predominant gastritis.

***Peer-review***

In this study, the authors investigated the characteristics of gastric cancer and gastric mucosa in Mongolian patients by comparing the gastric mucosa of Mongolian and Japanese patients. Approximately 70% of older Mongolians had gastric cancer, and approximately half of the Mongolian cancers were located in the upper part of the stomach. Three fourths of advanced cancer displayed undifferentiated adenocarcinoma. Many differences in stomach characteristics were observed in Mongolians compared with Japanese. The prevalence of *H. pylori* infection was higher in Mongolians than in Japanese (75.9% and 48.3%, respectively, *P* < 0.0001). The most surprising result was that 99.4% of *H. pylori*-positive cases were infected with non-East Asian-type *H. pylori*. In general, this study is novel, interesting and scientific and, importantly, has clinical significance.

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**Figure 1 Triple-site biopsy**. Triple-site biopsy specimens were used for the histological diagnosis of chronic inflammation, neutrophil activity, glandular atrophy, intestinal metaplasia and *Helicobacter pylori* in the gastric mucosa. Specimen #1 was taken from the greater curvature of the lower antrum (Antrum), #2 from the greater curvature of the upper corpus (Corpus), and #3 from the lesser curvature of the lower corpus (Angulus). Specimen #4 and others were taken from ulcers or cancer lesions.



**Figure 2** **Analysis of gastric cancer in Mongolians.** Analysis of gastric cancer cases by age group revealed that for all cases of total gastric cancer, early gastric cancer, and advanced gastric cancer, a peak occurred among those patients in their 60-s, followed by those in their 50-s and 70-s. Patients in their 50-s, 60-s and 70-s accounted for 71.9%, 72.0% and 71.8%, respectively, of these cancers. Moreover, 6.5%-9.8% gastric cancer cases occurred in young adults younger than 39 year.



**Figure 3 Distribution of gastric cancer in Mongolians.** The most affected site in total gastric cancer cases was the U region, 46.5%, followed by the L region, 28.1%, the M region, 25.4%. Lesions involving 2 or 3 regions (UM region: 91 cases, ML region: 16 cases, UML region: 7 cases, all were advanced gastric cancer) were excluded. The most affected area of early gastric cancer and advanced gastric cancer was the U region (47.5% and 45.8%, respectively).



**Figure 4 Histological distribution of gastric cancer in Mongolians.** Analysis of the percentages of differentiated adenocarcinoma (papillary adenocarcinoma (pap), well-differentiated type (tub1) and moderately differentiated type (tub2)) and undifferentiated adenocarcinoma (poorly differentiated adenocarcinoma (por) and signet-ring cell carcinoma (sig) revealed that undifferentiated adenocarcinoma (61.8%) accounts for a higher proportion of total gastric cancer cases than differentiated adenocarcinoma (37.2%). Similarly, among advanced gastric cancer cases, undifferentiated adenocarcinoma (73.9%) accounts for a higher proportion than differentiated adenocarcinoma (25.2%). By contrast, in early gastric cancer, differentiated adenocarcinoma (65.7%) was more prevalent than undifferentiated adenocarcinoma (32.9%).



**Figure 5** **prevalence of *Helicobacter pylori* infection in Mongolian subjects according to age distribution.** The prevalence of *Helicobacter pylori* infection in Mongolian subjects was highest for ages 17-19, 20-29 and 30-39. The prevalence tended to decrease among patients ages 50 and older (68.4% at ages 50-59, 61.5% at ages 60-69 and 71.4% at ages 70 or older).



**Figure 6 C/A ratio in *Helicobacter pylori-*positive Mongolians and Japanese matched by age, gender and endoscopic diagnostics.** The ratio of the corpus gastritis score to the antrum gastritis score (C/A ratio) was compared between *Helicobacter pylori*-positive Mongolian and Japanese patients in each age group. Mongolians aged 49 years or younger had a C/A ratio indicating antrum predominant gastritis, whereas those aged 50 years or older had a C/A ratio greater than 1, indicating that older Mongolians had corpus-predominant gastritis rather than antrum-predominant gastritis. Japanese patients aged 39 years or younger exhibited antrum-predominant gastritis, whereas those aged 40 years or older displayed corpus-predominant gastritis. This trend was similar in both countries.

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**Figure 7 Gastric cancer cases in the U region.** A: Sixty-seven-year-old-woman. Cancer located near the cardia (U region), type 2; b: Eighty-eight-year-old-man. Cancer located around the cardia (U region), type 3.

**Table 1 Gastritis scores of *Helicobacter pylori*-positive Mongolians and Japanese matched by age, gender and endoscopic diagnosis**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Specimen** | **Chronic inflammation** | **Neutrophil activity** | **Glandular atrophy** | **Intestinal metaplasia** | ***Helicobacter pylori*** |
| Mongolians | #1 (Antrum) | 1.32 ± 0.59 | *P* < 0.0001 | 0.38 ± 0.54 | *P* < 0.0001 | 0.15 ± 0.36 | *P* < 0.0001 | 0.07 ± 0.40 | *P* < 0.0001 | 0.93 ± 0.79 | *P* < 0.0001 |
| Japanese | 2.30 ± 0.72 | 2.05 ± 1.01 | 0.48 ± 1.72 | 0.34 ± 0.78 | 1.91 ± 1.01 |
| Mongolians | #2 (Corpus) | 1.12 ± 0.50 | *P* < 0.0001 | 0.26 ± 0.47 | *P* < 0.0001 | 0.02 ± 0.19 | *P* < 0.0001 | 0.05 ± 0.35 |  | 1.08 ± 0.84 | *P* < 0.0001 |
| Japanese | 2.03 ± 0.74 | 1.93 ± 0.96 | 0.28 ± 0.73 | 0.10 ± 0.44 | 2.20 ± 0.79 |
| Mongolians | #3 (Angulus) | 1.50 ± 0.62 | *P* < 0.0001 | 0.55 ± 0.61 | *P* < 0.0001 | 0.16 ± 0.41 | *P* < 0.0001 | 0.17 ± 0.60 | *P* < 0.0001 | 1.15 ± 0.87 | *P* < 0.0001 |
| Japanese | 2.21 ± 0.80 | 1.93 ± 1.04 | 0.81 ± 1.02 | 0.59 ± 1.02 | 2.07 ± 0.95 |

The total number is 137, Mann-Whitney *U*-test.