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Original Article

Seroprevalences of *Helicobacter pylori* Infection and Chronic Atrophic Gastritis in the United Republic of Tanzania and the Dominican Republic

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Abstract

Objective: The aim of this survey was to compare the seroprevalences of *Helicobacter Pylori* (*H. pylori*) and chronic atrophic gastritis (CAG) in Tanzania and the Dominican Republic, both of which are tropical countries, and thereafter compare the prevalences in Tanzania and the Dominican Republic with prevalences from our previous studies done in Japan (1991) and China (1996/97).

Methods: Community-based study in which 573 inhabitants of Tanzania and 1,215 inhabitants of the Dominican Republic answered detailed questionnaires on upper digestive tract diseases, and then underwent screening for gastric cancer by serum pepsinogen and testing for antibody to *H. pylori*.

Results: After adjusting to the 'Age-Standardized Rate' (ASR) using the world population in 1995, the seroprevalences of *H. pylori* infection in male and female subjects for Tanzania (m=85.3% & f=88.2%) were very high compared to those for the Dominican Republic (m=63.5% & f=62.4%) and Japan (m=62.0% & f=46.8%), and similar to those of China (m=78.0% & f=77.3%). Also, the age-standardized prevalences of CAG in males and females for Tanzania (m=0.237 & f=0.458) were higher than those of the Dominican Republic (m=0.168 & f=0.211) and China (m=0.111 & f=0.107) and compared well with those of Japan (m=0.266 & f=0.352).

Conclusions: Although Tanzania and the Dominican Republic are both developing countries, Tanzania had a very high age-standardized prevalence of *H. pylori* and CAG compared to that of the Dominican Republic, which showed a trend similar to that of Japan.

Key words: *Helicobacter pylori*, chronic atrophic gastritis, gastric cancer, Tanzania, Dominican Republic

Introduction

Although it is known that *Helicobacter pylori* (*H. pylori*) causes chronic gastritis as well as duodenal ulcers, and there is strong evidence that it is associated with chronic atrophic gastritis (CAG) and gastric cancer, there have not been many epidemiological studies done in tropical countries (1–3). The prevalences of *H. pylori* infection differ among countries, and these differences are thought to be due to race, age, sex, and sanitary conditions, particularly those in food hygiene and drinking water (4, 5). In the United States of America the prevalence of *H. pylori* is higher among native Africans than Caucasians (6). In general, sanitary conditions in subtropical and tropical countries are worse than those in Western countries, depending on economic conditions in individual countries. For example, about 70% of the population in Tanzania live in rural areas, yet <30% of the rural inhabitants have safe water, sewage systems and good pit latrines (7, 8). In urban areas, 67% have access to safe water but many of the sewage systems are only partially functioning, and due to the poor economic conditions, the governments are unable not only to repair the sewage systems and water treatment plants but also to buy the chemicals for water treatment (7, 8).

Customs, particularly dietary habits and climate, may contribute to the differences in prevalences of *H. pylori* in different countries (9, 10). In tropical countries, especially in many African countries, the weather is hot and humid; therefore, food like meat and fish easily rot when stored at room

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Table 1 Number and age (years) of subjects in the four investigated countries: Japan, China, Tanzania, and the Dominican Republic

	Sex					
	Male		Female		Total	
Investigated country	Num. of subjects	Age (years)	Num. of subjects	Age (years)	Num. of subjects	Age (years)
Japan	323	59.4±14.59*	536	57.0±14.11	859	57.9±14.33
China	648	46.6±12.30	1,093	44.9±12.05	1,741	45.6±12.17
Tanzania	245	32.4±20.87	328	31.3±19.55	573	31.9±20.19
Dominican Republic	451	35.2±18.65	764	33.9±14.55	1,215	34.4±16.20

*: Values are expressed as mean±SD.

temperature for >24 hours. Food poisoning is common, as households cannot afford refrigerators and freezers for preservation of their extra meat and it consequently becomes infected with bacteria. The most common method of storing fish and meat in the villages is by salting, smoking and drying. Similarly, the post-harvest handling of maize, cassava, yams, potatoes and legume grains presents different problems. For these crops, the drying stage is very important, to reduce attack and damage from fungi and insects. Damaged potatoes are especially susceptible to infection by fungi and when livestock eat them they may get food poisoning (11). Several studies have shown that both the custom of eating food that has been stored by salting, and cereals infected with fungus, are associated with an increased risk for gastric cancer (12–15).

We decided to conduct this survey because, as far as we know, no study exists on the seroprevalences of *H. pylori* and CAG in the general population in the tropical and subtropical countries of the United Republic of Tanzania and the Dominican Republic. We wanted to 1) compare the seroprevalences of *H. pylori* infection and CAG in Tanzania and the Dominican Republic, 2) compare the seroprevalences of *H. pylori* infection and CAG in Tanzania and the Dominican Republic with those of Japan and China, which were previously investigated using the same protocol as that used in the tropical countries study (16, 17), and 3) determine the relationship between the age-standardized prevalances of *H. pylori* infection and CAG in Tanzania and the Dominican Republic, as compared with those in Japan and China.

Subjects and Method

This study on the prevalence of *H. pylori* and CAG took place in Tanzania and the Dominican Republic and was similar to our previous studies done in Japan in 1991 and China in 1996/97, and the same protocol was used. Tanzania is a tropical country in East Africa and the subjects came from four villages in two different districts. The first and second villages were in the Kibaha district in the suburbs of the Tanzanian capital, Dar-Es-Salaam, and the third and fourth villages were in the Moshi district at the foot of Mt. Kilimanjaro. The districts and villages were randomly chosen and all of the subjects in the four villages participated in the study except those acutely ill on that day, while those with chronic diseases such as AIDS, tuberculosis and cancer were excluded from the study. In the Dominican Republic, the project was done in communities in Santo Domingo, the capital of the Dominican Republic, and in the suburbs of Santiago and San Pedro de Macolis, which are cities. The communities of these three cities in the Dominican Republic were randomly chosen and all the subjects took part except those with illnesses, as described above for Tanzania. The subjects were assembled by local leaders and the study was explained to them. A written voluntary consent to participate in the study was obtained. A total of 573 subjects in Tanzania and 1,215 subjects in the Dominican Republic were eligible for the study, as shown in Table 1.

Screening for upper digestive tract diseases was done using a detailed questionnaire, and blood testing for serum pepsinogen (PG) I and II, as well as antibody to *H. pylori*, was performed at the same time. Fasting blood samples were used and sera were separated after suitable treatment, frozen in freezers and stored until testing was conducted. The measurements of serum PG I and II were made by immunoradiometric assay (IRMA), a radioimmunoassay (RIA) solid phase assay, and that of IgG-antibody to *H. pylori* was made by enzyme immunoassay (EIA). The diagnosis of CAG was made using both the value of serum pepsinogen I and the ratio of PG I/PG II, and the cut-off values were PG I≤70 (μg/l) and PG I/PG II≤3.

The populations studied in the four countries were largely deviated, and differed in age as well as sex; in order to compare the prevalences among them, adjustment to an age-standardized rate (ASR) was necessary, as without ASR, comparison would be difficult and inadequate. We adopted the world population in 1995 for the ASR of the prevalences of H. pylori and CAG. The world population in 1995 was chosen as a standard population because populations in individual countries and especially in the tropics have changed in recent years, and our study was done between 1991 and 2002 (18).

Statistical analysis in the international comparative study among the four countries was calculated by SPSS after the ASR adjustment to the world population in 1995 (18, 19). χ^2-test was used for comparison of the ASR of *H. pylori* and CAG between males and females.

Results

The crude and age-adjusted prevalence rates of *H. pylori* infection in the four countries are shown in Table 2. In both sexes, Tanzania had the highest prevalence of *H. pylori* infection and the prevalences in the four countries increased in this order: Japan (53.0%), the Dominican Republic (62.1%), China (77.6%), and Tanzania (86.2%). According to sex, in Japan the age-standardized prevalence of *H. pylori* in males (62.0%) was significantly higher than that of females (46.8%) ($p<0.01$),

Table 2 Prevalences (%) of *H. pylori* infection in Japan, China, Tanzania and the Dominican Republic, after adjusting for the age-standardized rate of the world population in 1995

Country	Sex						Total		
	Male			Female					
	Crude	ASR*	95% confidence interval for ASR of *H. pylori*	Crude	ASR*	95% confidence interval for ASR of *H. pylori*	Crude	ASR*	95% confidence interval for ASR of *H. pylori*
Japan	72.8	62.0	[56.6–67.1]**	63.3	46.8	[42.6–51.0]	66.9	53.0	[49.7–56.3]
China	72.5	78.0	[74.7–81.0]	73.8	77.3	[74.7–79.7]	73.4	77.6	[75.6–79.5]
Tanzania	91.3	85.3	[80.3–89.2]	91.6	88.2	[84.3–91.3]	91.5	86.2	[83.1–88.8]
Dominican Republic	62.5	63.5	[59.0–67.8]	60.2	62.4	[58.9–65.8]	61.1	62.1	[59.3–64.8]

*: Prevalence (%) of *H. pylori* infection after adjusting for the age-standardized rate of the world population in 1995.
**: The square bracket [ ] indicates 95% confidence interval for the prevalence of *H. pylori*.

Table 3 Prevalence of chronic atrophic gastritis (CAG) in Japan, China, Tanzania and the Dominican Republic, after adjusting to the age-standardized rate of the world population (1995)

Country	Sex						Total		
	Male			Female					
	Crude	ASR*	95% confidence interval for ASR of CAG	Crude	ASR*	95% confidence interval for ASR of CAG	Crude	ASR*	95% confidence interval for ASR of CAG
Japan	0.495	0.266	[0.221–0.317]**	0.491	0.352	[0.313–0.393]	0.492	0.318	[0.288–0.350]
China	0.138	0.111	[0.089–0.138]	0.103	0.107	[0.090–0.127]	0.117	0.109	[0.095–0.125]
Tanzania	0.267	0.237	[0.188–0.294]	0.358	0.458	[0.405–0.512]	0.319	0.262	[0.228–0.300]
Dominican Republic	0.189	0.168	[0.136–0.205]	0.209	0.211	[0.184–0.241]	0.202	0.205	[0.183–0.229]

* ASR implies age-standardized rate of CAG prevalence, adjusting for the world population in 1995.
**: The square bracket [ ] indicates 95% confidence interval for the prevalence of CAG.

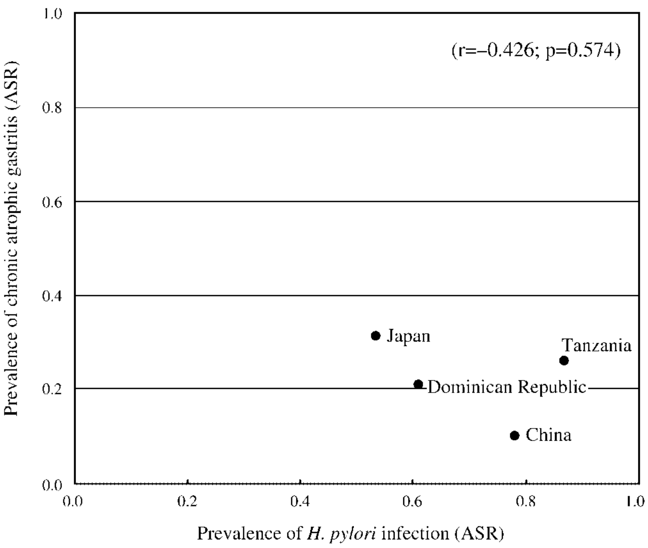

Fig. 1 Correlation between prevalences of *Helicobacter pylori* (*H. pylori*) and chronic atrophic gastritis among Japan, China, Tanzania, and the Dominican Republic. ASR: Age-standardized rate of the world population in 1995.

whereas in other countries there were no sex differences. The prevalence of *H. pylori* infection was over ~50% in each of the four countries, and there were no sex differences in the prevalence of *H. pylori* infection in any of the countries except Japan.

The crude and age-standardized prevalence rates of CAG are shown in Table 3. Although differences between males and females in the age-standardized prevalences were observed in Tanzania (m=0.237 & f=0.458) and Japan (m=0.266 & f=0.352), no differences were seen in the Dominican Republic (m=0.168 & f=0.211) and China (m=0.111 & f=0.107). According to sex in both Tanzania and Japan, the ASR of CAG for Tanzanian females (0.458) was significantly higher than that of males (0.237) ($p<0.01$), and the ASR of CAG for Japanese females (0.352) was also significantly higher than that of males (0.266) ($p<0.01$). Likewise, in the Dominican Republic, the ASR of CAG was higher in females (0.211) than in males (0.168), but the difference was not significant, whereas in China the ASR of CAG in females (0.107) was almost similar to that of males (0.111). Among the four countries studied, Tanzania had the highest age-standardized prevalence of CAG for females (0.458), and the ASR of CAG in males increased in this order: China (0.111), the Dominican Republic (0.168), Tanzania (0.237), Japan (0.266).

As shown in Fig. 1, there was no linear correlation between the prevalences of *H. pylori* and CAG ($r=-0.426$; $p=0.574$).

Discussion

Our study showed that the prevalence rates of *H. pylori* infection were largely different in Tanzania and the Dominican Republic, though both are developing countries in the tropics; the prevalence of *H. pylori* infection was very high in Tanzania (86.2%), while that in the Dominican Republic (62.1%) was low and comparable to that in Japan (53.0%). Tanzania also had the highest prevalence of *H. pylori* among the four countries while the Dominican Republic had almost the same prevalence of *H. pylori* as Japan, especially in males. To the best of our knowledge, no study on the prevalence of *H. pylori* infection in Tanzania and the Dominican Republic has been done before, as both are tropical countries, and the prevalence of *H. pylori* infection has been considered to be high in tropical countries and approximately inversely proportional to socio-economic status (GDP, GNP per capita), health indices (life span and infant mortality), educational level (adult and youth illiteracy rate) and living environment (safe water, sewage system, and necessary household accessories such as refrigerator and freezer) (20, 21). The reasons for Tanzania's high *H. pylori* prevalence rate compared to that of the Dominican Republic could be due to the poor economy and hence, income per capita, as the Dominican Republic's income per capita is 10 times that of Tanzania (8, 20, 22). The poor economy in Tanzania makes it difficult for the government to improve sanitation, access to safe water, and food hygiene. Less than 20% of Tanzania's rural population, which consists of 70% of its total population, has access to clean and safe water, compared to the Dominican Republic, where 67% of the rural population has access to clean and safe water (7, 8, 22). Furthermore, although ~67% of the cities get tap water in Tanzania compared to 74% in the Dominican Republic, in Tanzania, there are not adequate funds to continuously buy chemicals for water treatment or repair the broken treatment plants (7, 22). Also, due to lack of funds, <20% of Tanzania's 52 cities have a sewage system and <45% of the rural population have latrines; therefore, water sources are often polluted by sewage, leading to epidemics such as cholera and food poisoning, whereas in the Dominican Republic about 80% have functioning sewage systems and latrines (23, 24).

Race has also been associated with an increase in the prevalence of *H. pylori* in the United States of America, where the prevalence is higher in the native Africans than in Caucasians (6). Ninety-nine percent of Tanzanians are native Africans while the rest are Asians, Arabs and Caucasians, compared to the Dominican Republic where 11%, 16%, and 73% are native Africans, Caucasians, and mixed, respectively (25, 26).

There has also been no report on the prevalence of CAG in the general population in Tanzania and the Dominican Republic. The ASR prevalence of CAG in Tanzania was high for both sexes (m=0.237 & f=0.458) and comparable with that of Japan (m=0.266 & f=0.352), while those in the Dominican Republic and China were lower (m=0.168 & f=0.211, and m=0.111 & f=0.107, respectively).

The correlation between *H. pylori* infection and CAG has been shown by several previous papers (13, 27–29). We failed to demonstrate a correlation between the prevalence of *H. pylori* and that of CAG. We consider that one of the reasons is because our sample sizes were small and from only four countries. However, in studies done in some Southeast Asian countries, it was found that despite a high prevalence of *H. pylori*, no correlation was observed with the mortality and/or incidence of gastric cancer. Some researchers have called this phenomenon the 'African enigma' and 'Asian paradox' as the mortality and the incidence of gastric cancer were extremely low despite the high prevalence of *H. pylori* (2, 30–32). The age-standardized mortality and incidence rates [the latter in brackets] of gastric cancer in Tanzania are 2.21 and 4.78 [2.56 and 5.57] for males and females, respectively, and both indices are higher in females than in males (33). It is interesting that the prevalences of *H. pylori* and CAG in our study were also higher in females than in males, hence preserving the sex ratio indices, as for the mortality and incidence rates of gastric cancer above.

The age-standardized mortality and incidence rates for gastric cancer in males and females in the Dominican Republic, China, and Japan increased in this order: 7.94 & 5.04 [10.02 &6.43], 27.04 & 13.02 [36.13 &17.47], and 31.24 & 13.83 [69.20 & 28.64], respectively, and the mortality rate for Japanese males was almost the same as that for Chinese males. The ASR of mortality and incidence of gastric cancer in Japan and China were about four times higher than those in the Dominican Republic, the rates of which were about four times higher than those in Tanzania. However, the ASR prevalence of *H. pylori* in males in the Dominican Republic was almost same as that in Japan (33). This phenomenon may be called the 'Caribbean wonder', because despite the similarities in prevalence (ASR) of *H. pylori* between the Dominican Republic and Japan, the mortality and incidence rates of gastric cancer were completely different, namely, low in the Dominican Republic and very high in Japan.

Furthermore, the progression from *H. pylori* infection to CAG and finally to gastric cancer is complex and has been associated with age, sex, racial difference, socio-economic status, health indices, educational level and living environment (13, 27, 34). This complexity in the progression from *H. pylori* infection to CAG to cancer is clearly demonstrated in that although Japan has the highest mortality from gastric cancer in the world, the prevalence of *H. pylori* infection in Japan was the lowest. Simultaneously, the prevalence of CAG, which shows a stronger correlation with gastric cancer than *H. pylori*, was the highest. However, it is well known that the progression of CAG is due not only to *H. pylori* infection but also to many factors such as 1) diet, including dietary intake high in salt, excessive intake of the scorched part of foods, and low intake of fresh vegetables, fruit, and milk (35–37), 2) lifestyle, including customs and culture (38, 39), 3) living environment, including a clean drinking water supply, a sewage system, and sanitary facilities (40, 41), and 4) education on hygiene, including hand-washing, clean and safe water, and food hygiene (34, 42). Tanzania has poor sanitation, water and food hygiene, and a high intake of salt in villages, because in the villages fish and meat are preserved by salting and drying (7), and yet there is a low incidence and mortality from gastric cancer; this phenomenon, called "the African enigma", may be partially due to the low average life span in Tanzania, compared to that in Japan, China and the Dominican Republic. Tanzania at present has an average life span of 51 years for males and 53 years for females, as opposed to that of Japan (m=78 years and f=85 years), China (m=69 years & f=73 years) and the Dominican Republic (m=67 years & f=71 years); therefore, due to the recent improvement of the Tanzanian economy and standard of living, the life span may increase in the future, and simultaneously the incidence and mortality of gastric cancer may also increase (43, 44).

In addition to the phenomena of the 'African enigma' in Tanzania and the 'Caribbean wonder' in the Dominican Republic, it is possible that the *H. pylori* positivity in Japan differed from those in the African countries and Caribbean countries according to the commercial EIA measurement kit for *H. pylori*. We are now investigating whether the genotypes in Tanzania and the Dominican Republic are the same as those in Japan and China, as described in previous studies (45, 46). In conclusion, Tanzania had very high prevalances of *H. pylori* and CAG compared to those in the Dominican Republic, Japan and China, but the incidence and mortality rates for gastric cancer were low in both Tanzania and the Dominican Republic compared to those in Japan and China. Further studies are required to clarify this "African enigma" and "Caribbean wonder".

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