Special Section

Trends in *Helicobacter pylori* Infection and Gastric Cancer in Mexico

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Infection by *Helicobacter pylori* affects about 50% of the human population. Of those infected, 10% to 15% will develop peptic ulcer and up to 3% will present with gastric cancer. These estimates suggest that around 7% of the world's population will eventually develop *H. pylori*–associated gastroduodenal disease. In fact, gastric cancer remains the second cause of cancer mortality worldwide (1). Fortunately, evidence suggests that the prevalence of *H. pylori* infection is decreasing in developed countries; accordingly, a decrease in peptic ulcer and cancer is also being observed (2). It remains uncertain whether the infection is also decreasing in developing countries. The aim of this review is to present the trend of both *H. pylori* infection and gastric cancer in Mexico, a country where sanitary and public health conditions have been improving during the last decades.

Trends in Gastric Cancer

A recent report addresses the issue of gastric cancer trends in Mexico (3). The rate of gastric cancer mortality was ~4.5 per 100,000 in 1980 and has increased to 6.5 per 100,000 in 10 years (Fig. 1). The increase was more evident in males, where the rate increased from below 4.0 per 100,000 in 1980 to over 6.5 per 100,000 in 1998. Although a fraction of the increase in cases might be due to improvements in reporting of gastric cancer to the cancer registry, the increase is still important and of concern for health authorities. Thus, in contrast to reports from other countries, in Mexico, gastric cancer rates are not decreasing; on the contrary, trends show it is on the rise.

As expected, the mortality rates associated with gastric cancer increase with increasing age (3); thus, it is <1.0 per 100,000 in individuals below the age of 30 years, between 1 and 10 per 100,000 in the 30- to 50-year-old group; around 10 per 100,000 in the 50th to 60th decade and close to 100 per 100,000 in individuals over age 70. The same study (3) documents an increase in mortality rates mainly in the 20- to 40-year-old age group, suggesting that the increase in mortality in the younger age groups is of greatest concern.

Trends in *H. pylori* Infection

In 1998 we reported on a national seroprevalence survey that tested over 11,000 serum samples collected in Mexico from 1987 to 1988 for *H. pylori* infection (4). Samples represented all ages and all regions of the country and included all socioeconomic levels. The study documented a seropositivity of 20% in children as young as 1-year-old, and by the age of 10 years almost 50% of the children were infected (Fig. 2). In adolescents, prevalence of infection increased steadily, and by the age of 20 years, 70% of the populations was infected. These seroprevalence values are similar to reports from other developing countries (5) and further document that the acquisition of *H. pylori* is more common during childhood. In fact, the calculated increment in seropositivity per year was >6% for children <5 years old; this rate decreased to below 3% in children 10 to 14 years and to <0.5% in individuals 30 to 69 years of age. In individuals older than 70 years, the annual change in seropositivity became negative.

Overcrowding, low educational level, and low socioeconomic level were risk factors for infection, as previously reported. Geography had little influence on *H. pylori* infection; regions with different levels of development had similar rates of infection, and no difference in infection between urban and rural communities was found. Females were slightly but significantly more likely to be infected than were males.

We recently reported a study where over 5,000 adolescents from the central part of Mexico were tested for *H. pylori* infection (6). Samples were collected during 1999 to 2000 and included individuals from 11 to 24 years of age. The *H. pylori* seroprevalence was directly related to age in multivariate analyses. The likelihood of infection increased with each year of increase in age (odds ratio, 1.10; 95% confidence interval, 1.08-1.13). Availability of sewerage and availability of home appliances at the time of the subject's birth were also inversely associated with *H. pylori* seroprevalence. The associations of infection with region, flooring material, overcrowding, sexual intercourse, and history of use of illicit drugs, alcohol, and tobacco were not significant after adjusting for other potential confounders.

Seroprevalence found in this study was compared with that of the national seroprevalence survey conducted during 1987 to 1988 (Fig. 3). It should be noted that the trend of increasing prevalence with age was similar in both studies, although the seroprevalence was in general lower in the Morelos study. A difference of almost 15% was observed in children 11 to 14 years of age and 10% in adolescents; the gap decreased to <10% in young adults. The same ELISA in the same laboratory was used in both studies; thus, the observed differences are not likely to be due to the assay methodology. A possible explanation is that in the sample used in this study (1999-2000), the rate of infection had decreased as compared with the 1987 to 1988 sample of the National Survey. The greatest decrease would correspond to the preadolescent group (see Fig. 3), suggesting that socioeconomic status and development have improved in the last few years in our country.

Distribution of Gastric Cancer Mortality Rates and *H. pylori* Seroprevalence in the Country

We analyzed the distribution of *H. pylori* seroprevalence found in the 1987 to 1988 national survey and the mortality

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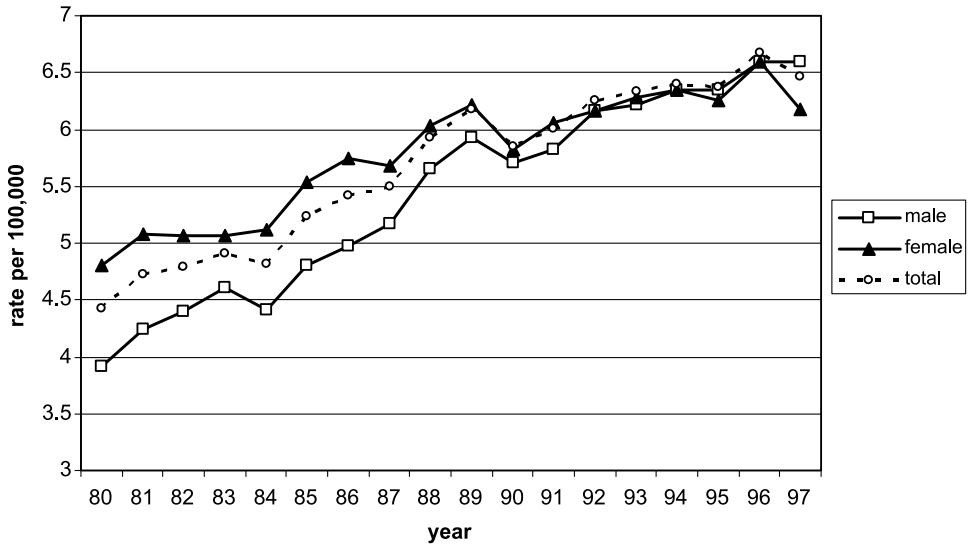

Figure 1. Trends in rates of stomach cancer mortality, according to sex in Mexico during the period 1980 to 1997, adjusted by age (3).

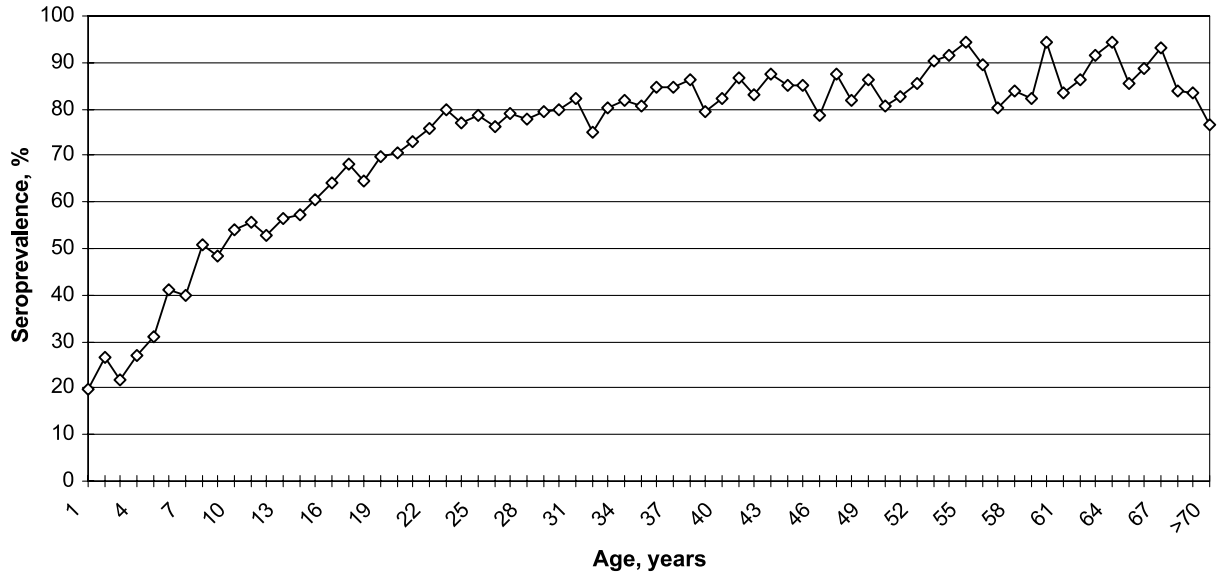

Figure 2. Community-based national seroprevalence survey of *H. pylori* infection in Mexico during 1987 to 1988. Figure modified from ref. 4.

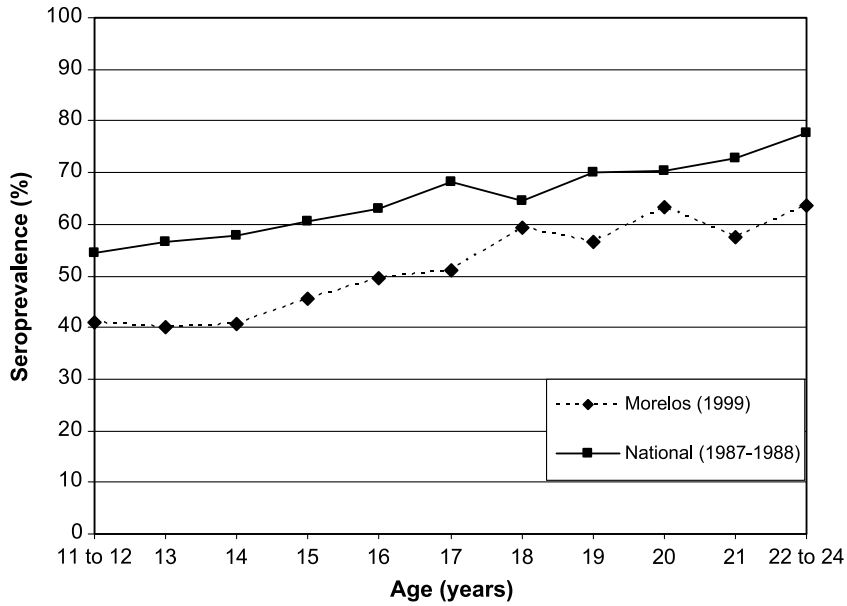

Figure 3. Community-based seroprevalence studies of *H. pylori* infection among adolescents in the state of Morelos, Mexico (1999) and in a National Survey (1987-1988). Taken from Constanza et al. (6), with permission from Blackwell Publishing.

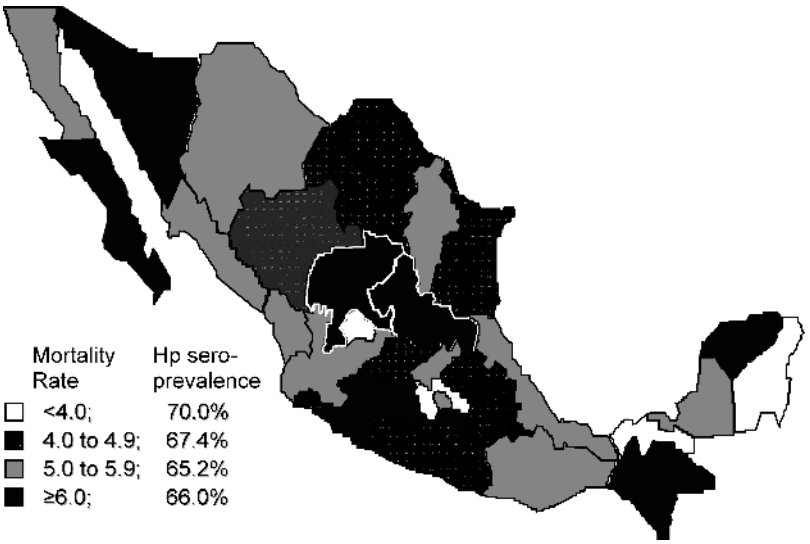

Figure 4. Analyses of the distribution of gastric cancer mortality rates and *H. pylori* seroprevalence in the 32 states of Mexico. Gastric cancer mortality rates are those reported by the National Institute of Geography and Statistics, Mexico (1991), whereas seroprevalence values are from the national 1987 to 1988 survey. Seroprevalence from each region is the mean of the prevalence values of each individual state.

rates of gastric cancer in Mexico (National Institute for Geography and Statistics, 1991); Fig. 4 describes this analyses. For the analyses, the 32 states of the country were divided according to their gastric cancer mortality rates into four groups and the mean of the *H. pylori* seroprevalence for the region was calculated from the seroprevalence values of each state. The four states with the lowest gastric cancer mortality rate (<4.0) are located in the center and south of the country and had the highest *H. pylori* seroprevalence (70%). On the other hand, the eight states with the highest gastric cancer mortality rates (≥6.0) are located in the north, center, and south of the country and had a seroprevalence of 66%. Thus, there is no clear regionalization of gastric cancer mortality rates or *H. pylori* prevalence in the country. In general, the states of the north of the country have the highest, whereas those in the south have the lowest socioeconomic development; still, the highest mortality rates of gastric cancer are observed in both north and south of the country.

Seropositivity to CagA and Gastric Cancer

A series of studies have analyzed the association of infection with *CagA*-positive *H. pylori* and gastric cancer in Mexico. A community-based study (7) documented that seropositivity to CagA was higher in individuals from states with higher rates of gastric cancer (Table 1). In a hospital-based, case-control study (8), we compared seroprevalence in histologically confirmed cases of gastric cancer and in age- and sex-matched controls (attended for other diseases). The adjusted risk for gastric cancer was significantly higher among CagA-positive subjects compared with CagA-negative subjects (odds ratio, 2.04; 95% confidence interval, 1.37-3.02), with a significant dose-response relationship ($P < 0.001$; Table 2). In the same study, nitrite and ascorbic acid intake were also analyzed. No significant effects due to nitrite and ascorbic acid consumption nor interactions of these nutrients with CagA seropositivity were detected.

Taken together, these studies suggest the following in Mexico: (a) Gastric cancer mortality rates are not decreasing. (b) In contrast, the rate of infection had decreased in the last decade, suggesting that socioeconomic status and development have improved in our country. (c) Infection with *CagA*-positive strains is more prevalent in populations with higher rates of gastric cancer. (d) There is no clear regionalization of neither prevalence of *H. pylori* infection nor gastric cancer mortality rates in the country.

Table 1. Prevalence of *H. pylori* infection with CagA-positive strains is higher in Mexican states with higher mortality rates of gastric cancer

Seroprevalence		% Positive rate of gastric cancer (state studied)			P_{trend}
H. pylori	CagA	Low, 2.5 (Estado de México)	Medium, 4.5 (Distrito Federal)	High, 6.4 (Chiapas)	
+	+	47.6	55.6	63.4	<0.01
+	−	18.6	15.2	9.6	<0.01
−	+	4.8	8.9	8.3	<0.01
−	−	29	20.3	18.7	<0.01

NOTE: Modified from ref. 7.

Table 2. Seroprevalence to CagA and the intensity of IgG antibody response is associated with gastric cancer risk in Mexican patients

	Cases	Controls	Odds ratio (95% confidence interval)*	Odds ratio (95% confidence interval)†
CagA, seroprevalence				
Negative	45	155	1.0	1.0
Positive	166	299	2.00 (1.35-2.96)	2.04 (1.37-3.02)
CagA, intensity of antibody response				
0.506-1.20	28	113	1.0	1.0
1.21-2.34	49	114	1.84 (1.07-3.19)	1.87 (1.08-3.23)
2.35-6.26	65	114	2.45 (1.44-4.15)	2.50 (1.47-4.25)
6.26-37.76	69	113	2.49 (1.47-4.22)	2.53 (1.49-4.30)
P_{trend}			0.001	0.0001

*Adjusted by age, gender, residence, energy, change in socioeconomic level and years of education.
†Adjusted by age, gender, residence, energy, change in socioeconomic level, years of education, and nitrite and ascorbic acid consumption. Taken from Lopez-Carrillo et al. (8), with permission from Elsevier.

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