

## Decrease in prevalence of peptic ulcer and gastric adenocarcinoma at the Policlínico Peruano Japonés, Lima, Peru, between the years 1985 and 2002. Analysis of 31,446 patients

Alberto Ramírez-Ramos,<sup>1</sup> José Watanabe-Yamamoto,<sup>2</sup> Juan Takano-Morón,<sup>2</sup> Robert H. Gilman,<sup>1</sup> Sixto Recavarren Arce,<sup>1</sup> Javier Arias-Stella,<sup>1,3</sup> Elena Yoshiwara-Wakabayashi,<sup>2</sup> Carlos Rodríguez-Ulloa,<sup>2</sup> Juan Miyagui-Maeda,<sup>2</sup> Erick Chinga-Alayo,<sup>4</sup> Daniel Mendoza-Requena,<sup>1</sup> Julio Leey-Casella,<sup>1</sup> Angel Rosas-Aguirre,<sup>1</sup> Billie Velapatiño-Cochachi,<sup>1</sup> Daniel Guerra Valencia<sup>1</sup>

*Acta Gastroenterol Latinoam* 2006;36:139-146

### Summary

**Aim:** To determine the prevalence of peptic ulcer and gastric adenocarcinoma in a population of middle and high socio-economic status in Lima, Peru, between 1985 and 2002. **Materials and methods:** The prevalence of gastroduodenal ulcer and gastric adenocarcinoma was determined after studying by esophagogastroduodenoscopy 31,446 patients at the Policlínico Peruano Japonés (PPJ) between 1985 and 2002. All patients had chronic upper gastrointestinal symptoms and had endoscopically proven diagnosis of active peptic ulcer or histological diagnosis of gastric adenocarcinoma. **Results:** Analysis of PPJ population identified a decrease in the prevalence of gastric ulcer and duodenal ulcer from 3.15% and 5.05% respectively in 1985, to 1.62% and 2.00% respectively in 2002. Gastric adenocarcinoma prevalence also decreased from 3.19% in 1988 to 0.92% in 2002. The prevalences of gastric ulcer (OR=1.49, 95% IC 1.26-1.77,  $p<0.001$ ), duodenal ulcer (OR=1.32, 95% IC 1.15-1.51,  $p<0.001$ ) and gastric adenocarcinoma

(OR=1.53, 95% IC 1.25-1.86,  $p<0.001$ ), decreased in the last eight years. **Conclusions:** Over the study period, there was a significant decrease in the prevalence of peptic ulcer and gastric adenocarcinoma at the Policlínico Peruano Japonés, where patients from middle and high socio economic status are attended.

**Index (Key words):** Gastro duodenal ulcer, gastric adenocarcinoma, prevalence - decrease

### Resumen

**Disminución de la prevalencia de la úlcera péptica y el adenocarcinoma gástrico en el policlínico Peruano-Japonés, Lima, Perú**

**Objetivo:** Determinar la prevalencia de la úlcera péptica y el adenocarcinoma gástrico, en una población de nivel socioeconómico medio y alto en Lima, Perú, entre los años 1985 y 2002. **Material y métodos:** Se determinó la prevalencia de la úlcera gastroduodenal y el adenocarcinoma gástrico, después de evaluar por esofagogastroduodenoscopia 31,446 pacientes en el Policlínico Peruano Japonés (PPJ) entre 1985 y 2002. Todos los pacientes presentaron síntomas crónicos del tracto gastrointestinal superior, y en ellos se realizó el diagnóstico endoscópico de úlcera péptica activa e histológico de adenocarcinoma gástrico. **Resultados:** Luego del análisis de la población estudiada se identificó una disminución de la prevalencia de úlcera gástrica y úlcera duodenal de 3,15% y 5,05% respectivamente en 1985, a 1,62% y 2,00% respectivamente en el año 2002. La prevalencia de adenocarcinoma gástrico tam-

<sup>1</sup> Universidad Peruana Cayetano Heredia. Lima, Perú.

<sup>2</sup> Policlínico Peruano-Japonés. Lima, Perú.

<sup>3</sup> Instituto de Patología y Biología Molecular Arias Stella, Lima, Perú.

<sup>4</sup> John H. Stroger Jr. Hospital of Cook County. Department of Medicine. Chicago, IL.

**Correspondence:** Alberto Ramírez Ramos  
Manuel Villavicencio 1331 - Lima 14 - Perú  
Phone +511 440-4069/ Fax +511 446-2684  
E-mail: ramirezramoscaza@yahoo.com

bién disminuyó de 3,19% en 1992 a 0,92% en el año 2002. Las prevalencias de úlcera gástrica (OR =1.49, 95% IC 1.26-1.77,  $p<0.001$ ), úlcera duodenal (OR =1.32, 95% IC 1.15-1.51,  $p<0.001$ ) y adenocarcinoma gástrico (OR =1.53, 95% IC 1.25-1.86,  $p<0.001$ ), disminuyeron en los últimos 8 años cuando comparamos con los primeros años. **Conclusiones:** Durante este período de estudio se observó una significativa disminución de la prevalencia de la úlcera péptica y el adenocarcinoma gástrico en pacientes peruanos de nivel socio económico medio y alto que son atendidos en este nosocomio.

*Helicobacter pylori* (*H. pylori*), a gram-negative microorganism which infects the human stomach, is considered the causal agent of chronic active gastritis and a contributory factor in the multifactorial pathogenesis of peptic ulcer disease, gastric adenocarcinoma and MALT lymphoma.<sup>1,2</sup>

The prevalence of *H. pylori* infection varies worldwide, from 10 to 50% reported in developed countries, to 80 to 90% rates in developing countries.<sup>3-7</sup>

Industrialized countries have reported a decrease in the prevalence of infection by *H. pylori* and its associated illnesses, chronic active gastritis, peptic ulcer disease and gastric adenocarcinoma.<sup>8,9</sup> Proposed explanations for this decrease in industrialized countries include improved chlorination of potable water, more strict hygienic measures in food preparation, a decrease in household overcrowding and improved education.<sup>5,10</sup>

The high prevalence of *H. pylori* in developing countries has been associated with the higher proportion of low socio-economic strata in inhabitants,<sup>11</sup> poor sanitary conditions,<sup>4</sup> and contaminated drinking water.<sup>12,13</sup> Reports of fecal-oral transmission of *H. pylori* support the association between poor sanitary conditions and infection by *H. pylori*.

In addition, isolation of this bacteria from water sources destined both for irrigation<sup>14</sup> and consumption<sup>12,15</sup> supports the association between contaminated water and the propagation of infection by *H. pylori*.

Our group has studied the epidemiology of *H. pylori* for the past two decades.<sup>6,16-20</sup> Although prior studies have reported a decrease in the prevalence of *H. pylori* in developed countries, no similar observations were noted in developing countries.

After evaluating 1,815 patients from middle and high socio economic status in a private clinic in Li-

ma during seventeen years (1985 to 2002), we reported a significant decrease in the prevalence of *H. pylori* gastric infection in patients with chronic dyspeptic symptoms with histological diagnosis of chronic active gastritis, and endoscopic diagnosis of active gastric and duodenal ulcer.<sup>19</sup>

The purpose of this study was to determine the prevalence of peptic ulcer and gastric adenocarcinoma in a population of middle and high socio-economic status attending a hospital in Lima-Peru, between 1985 and 2002.

## Materials and methods

### Setting

This study was performed in a medical setting in Lima, Peru, a non profit-making institution, the Policlínico Peruano Japonés (PPJ). All of the patients were of middle or high socio-economic status, and resided in adequate housing with access to municipal water sources, light and sewage. All of the patients sought medical care due to chronic dyspeptic symptoms between 1985 and 2002.

This study was approved by the ethics committee of the Cayetano Heredia Peruvian University and Policlínico Peruano Japonés Lima, Peru.

### Patients

There was a total of 31,446 patients from PPJ that were evaluated in order to determine the variation in prevalence of peptic ulcer disease and gastric adenocarcinoma. Patients were divided into three groups: those with endoscopic diagnosis of active duodenal ulcer, those with endoscopic diagnosis of active gastric ulcer and those with histologic diagnosis of gastric adenocarcinoma. From all patients who consulted for acute or chronic digestive symptoms, 31,446 with chronic upper gastrointestinal symptoms were scheduled for esophagogastroduodenoscopy.

### Determination of socio economic status

For the determination of socio economic level we prepared a special questionnaire asking for the following information: place of residence in the city, educational level, occupation, type of house, characteristics of the house, number of persons who live there, material of the house, characteristics of water supply and drainage, number of meals a day, income per year or per month.

### Procedure

After informed consent was obtained, all patients

underwent esophago-gastroduodenoscopy (EGD) according to our previously described methodology.<sup>16</sup> All equipment was adequately sterilized according to the manufacturer's recommendations using glutaraldehyde antimicrobial solution, sterile water and acid alcohol.

All PPJ patients underwent EGD but only a subset had routine surveillance antral biopsies for detection of *H. pylori*. Patients with an endoscopic diagnosis of gastric ulcers had directed biopsies for histological confirmation of benign lesions, and patients with suspicious malignant lesions also had biopsies for histological confirmation of malignancy. Patients with peptic ulcer disease diagnosis had completed files since 1985 whereas patients with adenocarcinoma diagnosis had completed files since 1988.

The prevalence of duodenal ulcer, gastric ulcer, and gastric adenocarcinoma was determined by calculating the ratio of the number of patients with endoscopic diagnosis of the above pathologies to the total number of endoscopic procedures performed during the same period of time.

Patients with endoscopic evidence of ulcerative scar (gastric or duodenal) were excluded given the great degree of inter-observer variability (subjectivity in the observation) when reporting these findings. This subjectivity does not happen when an expert endoscopist finds an ulcerative cycle in active phase.

#### Analysis

Chi Square analysis was used to compare all study groups. Prevalence tendencies were determined using Chi Square, linear tendency or linear regression

analysis. A p value of <0.05 was considered statistically significant. Processing and analysis of all raw data was performed using the STATA 7 software.

#### Results

There was a total of 31,446 patients from PPJ who were evaluated in order to determine the variation in prevalence of gastro duodenal ulcer and gastric adenocarcinoma between 1985 and 2002. The number of cases, sex distribution and mean age by pathology are presented in table 1, and the number of cases by year is presented in table 2. A decreasing trend in the prevalence of gastric ulcer ( $r=0.79$ ;  $p<0.0001$ ), duodenal ulcer ( $r=0.21$ ;  $p=0.04$ ) and gastric adenocarcinoma ( $r=0.86$ ;  $p<0.0001$ ) was observed during study period (figures 1 and 2). The prevalence rates of gastric ulcer and duodenal ulcer decreased from 3.15% and 5.05% respectively in 1985, to 1.62% and 2.00% respectively in 2002. The prevalence rates of gastric adenocarcinoma also decreased from 3.19% in 1988 to 0.92% in 2002.

We observed a significant decrease in the prevalence of gastric ulcer (OR=1.49, 95% IC 1.26-1.77,  $p<0.001$ ) and duodenal ulcer (OR=1.32, 95% IC 1.15-1.51,  $p<0.001$ ), when we compared the prevalence of the first ten years (1985-1994 period) to the prevalence of the last years (1995-2002 period). Also, there was a significant decrease in the prevalence of gastric adenocarcinoma (OR=1.53, 95% IC 1.25-1.86,  $p<0.001$ ), when we compared the prevalence of the first seven years (1988-1994 period) to the prevalence of the last years.

**Table 1.** Number of cases, sex distribution and mean age by pathology at PPJ, Lima, Peru. 1985-2002

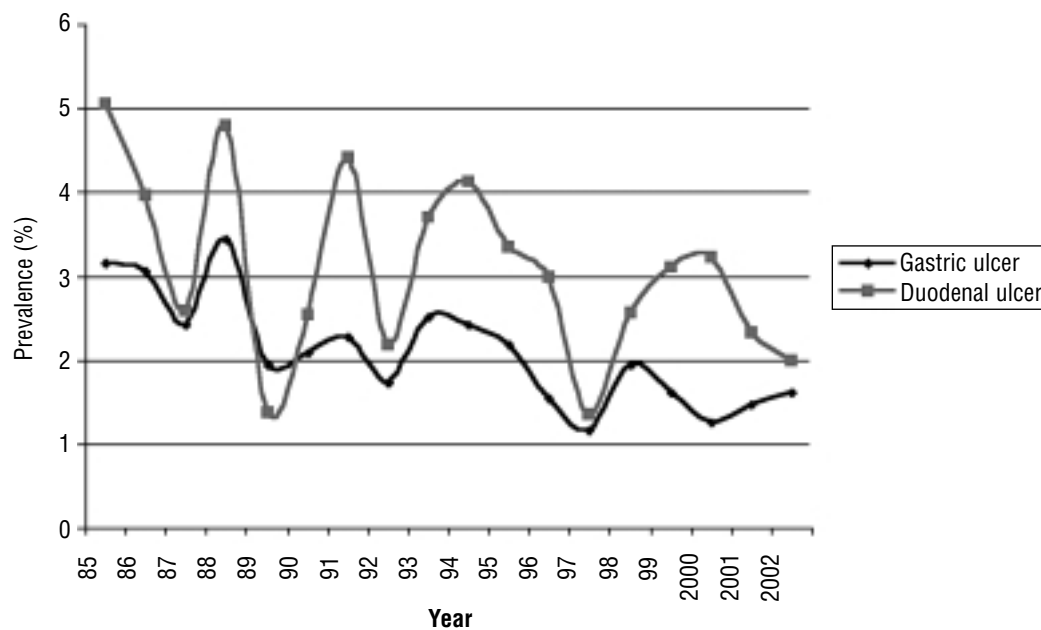
	Gastric ulcer	Duodenal ulcer	Adenocarcinoma
Number of cases	583	911	409
Female	279 (47.9%)	340 (37.3%)	185 (46.5%)
Male	304 (52.1%)	571 (62.7%)	224 (53.5%)
Mean Age	Age 52.7 ± 14.7 years	48.4 ± 24.5 years	63.7 ± 13.9 years
Range	15 – 97 years	17 – 90 years	20 – 94 years

\*There were included Adeno carcinoma diagnoses between 1988 and 2002.

**Table 2.** Number of cases by year by pathology at PPJ, Lima, Peru. 1985 -2002

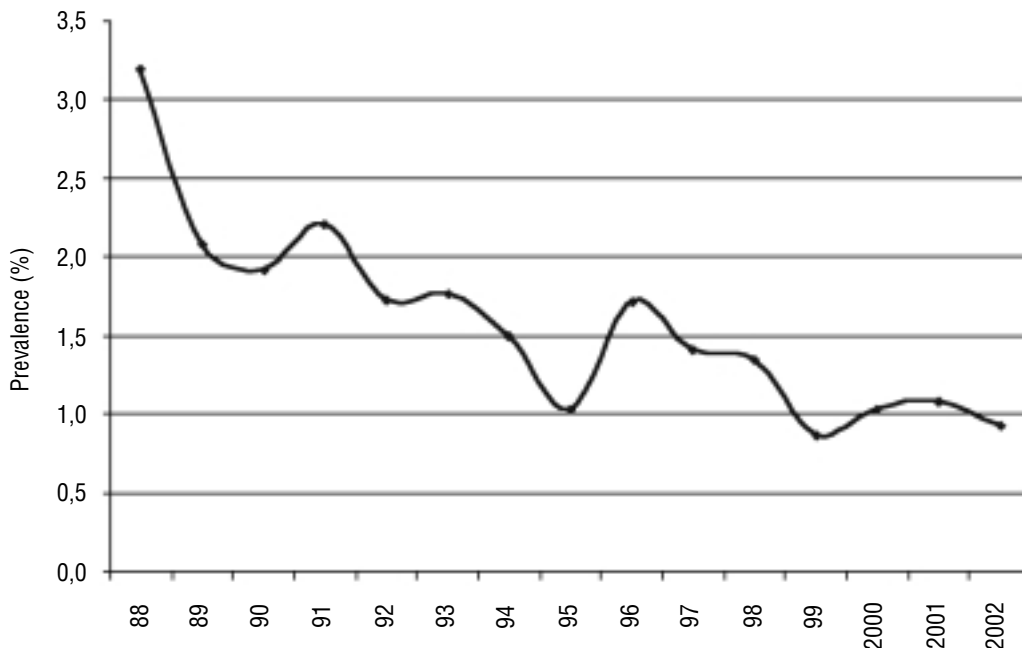
Year	Gastric ulcer	Duodenal ulcer	Adenocarcinoma	Number of evaluated patients
1985	10	16	-	317
1986	10	13	-	328
1987	13	14	-	540
1988	28	39	26	814
1989	14	10	15	723
1990	23	28	21	1100
1991	32	62	31	1406
1992	30	38	30	1736
1993	47	69	33	1866
1994	47	80	29	1940
1995	49	75	23	2240
1996	29	56	32	1870
1997	23	27	28	1989
1998	46	61	32	2371
1999	47	90	25	2906
2000	38	97	31	3012
2001	46	73	34	3140
2002	51	63	29	3148

**Figure 1.** Prevalence of duodenal and gastric ulcer at PPJ, Lima, Peru. 1985-2002



\* Gastric ulcer:  $r=0.79$ ,  $p<0.0001$   
 Duodenal ulcer:  $r=0.21$ ,  $p=0.045$

**Figure 2.** Prevalence of gastric adenocarcinoma at PPJ, Lima, Peru. 1988-2002

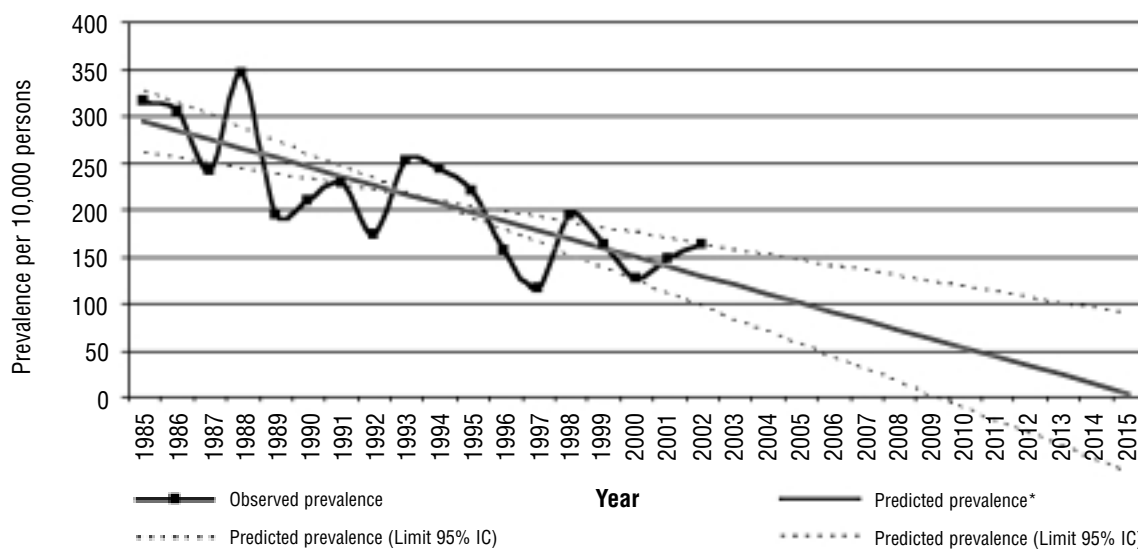


\* Adenocarcinoma:  $r=0.86, p<0.001$

Estimates of the slope of the decrease using a simple linear equation declines over the next ten to 20 years for gastric ulcers and adenocarcinoma in

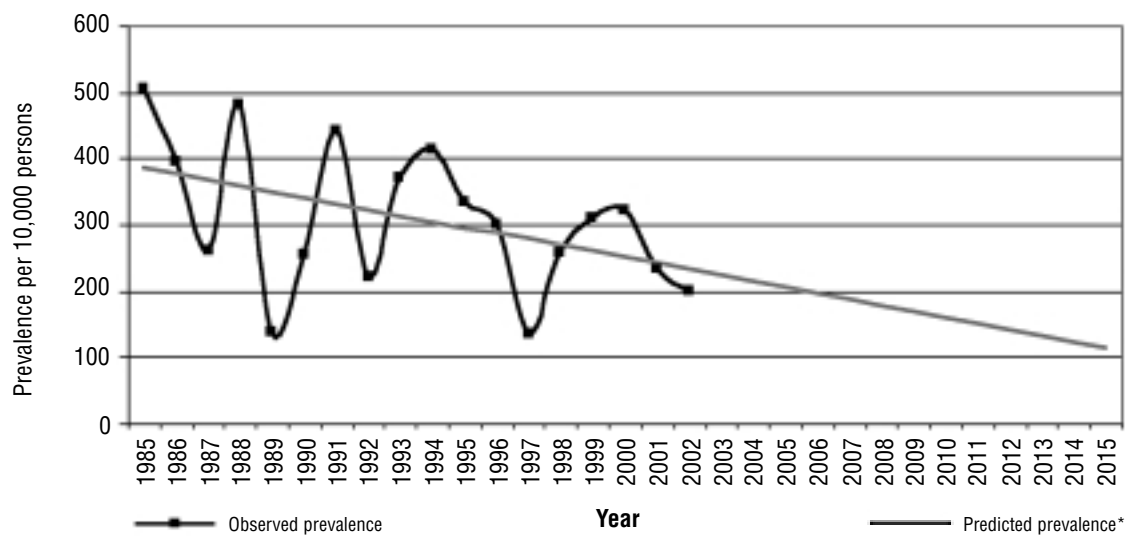
this middle and high socioeconomic population. Duodenal ulcer also decline but with a slower rate. (figures 3, 4, 5).

**Figure 3.** Prevalence of gastric ulcer at PPJ, Lima, Peru. 1985 - 2002 (31,746 evaluated patients).



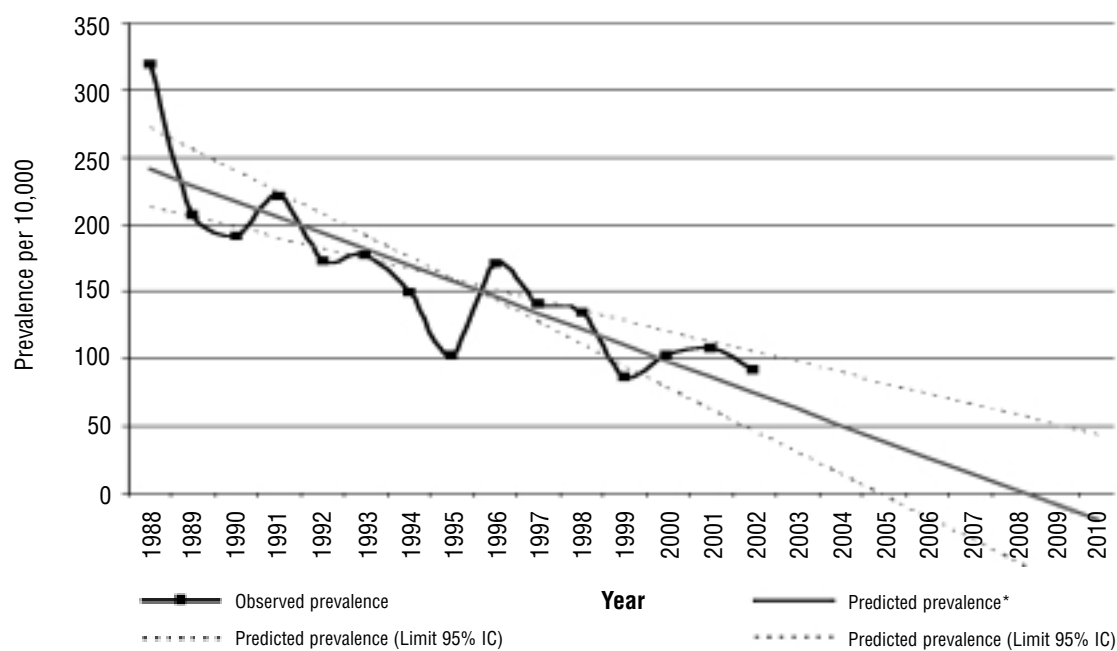
\* Predicted prevalence through the equation: Predicted prevalence =  $9.66(\text{Year}) + 19474.02$ . ( $r=0.79; p<0.0001$ ).

**Figure 4.** Prevalence of duodenal ulcer at PPJ, Lima, Peru. 1985 - 2002 (31,746 evaluated patients).



\* Predicted prevalence through the equation: Predicted prevalence = 9.04 (Year) + 18334.06. (r=0.21;p=0.045).

**Figure 5.** Prevalence of gastric adenocarcinoma at PPJ, Lima, Peru. 1988-2002 (30,261 evaluated patients).



\* Predicted prevalence through the equation: Predicted prevalence = 11.89 (Year) + 23870.12. (r=0.86;p<0.001).

We have previously reported that the prevalence of *H. pylori* infection is decreasing among patients of middle and high socio-economic status with chronic active gastritis and peptic ulcer disease.<sup>19</sup> In addition, in the same study we also reported that the prevalence of two major *H. pylori* associated pathologies, peptic ulcer disease and gastric adenocarcinoma, parallels the decline in the overall rates of *H. pylori* infection.<sup>19</sup>

## Discussion

To our knowledge this report demonstrates for the first time that in a developing country, in a population of middle and high socio-economic strata, there is a decrease in the prevalence of peptic ulcer and gastric adenocarcinoma in a period of seventeen years. This declining trend is mirrored by similar trends in developed countries,<sup>21-23</sup> and some publications point out that this decline might be attributed to the decreasing prevalence of *H. pylori* infection.<sup>24,25</sup>

The decrease in prevalence of peptic ulcer and gastric adenocarcinoma observed in the PPJ populations parallels the overall decrease in infection rates of *H. pylori* reported in our previous study performed in a private clinic in the same city, during the same period of time and in patients from the same socio economic status<sup>19</sup> similar to those described in industrialized countries.<sup>8,9</sup>

In that study we observed a consistent decrease in the prevalence of *H. pylori* infection in patients with chronic active gastritis (from 83.3% in 1985 to 58.7% in 2002) as well as in those with gastric ulcer (from 89.5% in the 1985-1990 period to 71.9% in the 1991-2002 period) and duodenal ulcer (from 84.8% in the 1985-1990 period to 77.3% in the 1991-2002 period).<sup>19</sup> Similar observations can be made regarding other subpopulations our study group has previously evaluated. For example, the prevalence of *H. pylori* infection has significantly decreased among Japanese immigrants living in Peru from 67.6% in 1985<sup>26</sup> to 45.5% in 2002 (unpublished observations).

In comparison to industrialized countries, over the past decade Peru has maintained similar population characteristics and birth rates.<sup>27</sup> However, improvement in sanitation, nutrition and health practice, may be related to the decrease in *H. pylori* prevalence in middle and high socioeconomic groups.<sup>28</sup>

If there is a direct connection between the prevalence of *H. pylori* infection and the prevalence of peptic ulcer and gastric adenocarcinoma, and these gastrointestinal diseases keep these trends, peptic ulcer and gastric cancer will become uncommon conditions in some groups of middle and high socio-economic status in Peru. In contrast, we expect no such decrease in the majority of Peruvians who are poor since rates of *H. pylori* have not decreased in the last however, seventeen years.<sup>20</sup> Longitudinal studies in this group of poor Peruvians for peptic ulcer disease and adenocarcinoma have not been reported yet to confirm this hypothesis.

Although we should recognize that other factors that we did not collect with accuracy could have contributed to the decrease of peptic ulcer disease (use of acid suppressants and NSAIDs), the implications of our observations are important since prevention and/or treatment of *H. pylori* infection could help decrease not only the prevalence of such common disease processes as gastritis and peptic ulcer disease, but most importantly, it could reduce the prevalence of gastric cancer. In Peru, gastric cancer is the first cause of death from malignancies in males and the third in women after breast and uterine cervix cancer.

## Acknowledgements

*The invaluable help of Aurora Cataldo, RN and Carmen Tamamoto, RN as well as the Gastroenterology Department of the PPJ is appreciated. Special thanks as well to Mrs. Yenyffer Barreto de Guzmán for her secretarial support.*

## Sources of financial support

*Global Research Training grant II – Fogarty - NIH.*

## References

1. Taylor DN, Blaser MJ. The epidemiology of Helicobacter pylori infection. *Epidemiol Rev* 1991;13:42-58.
2. Eurogast Study Group. An international association between Helicobacter pylori infection and gastric cancer. *Lancet* 1993;341:1359-1362.
3. Torres J, Leal-Herrera Y, Perez-Perez G, et al. A community-based seroepidemiologic study of Helicobacter pylori infection in Mexico. *J Infect Dis* 1998;178:1089-1094.
4. Pajares-García JM, Correa P, Pérez-Pérez GI. Helicobacter pylori infection in gastro duodenal lesions, the second decade, 1st ed. Barcelona: Prous Science, 2000.

5. Rothenbacher D, Brenner H. Burden of *Helicobacter pylori* and *H. pylori* related diseases in developed countries: recent developments and future implications. *Microbes Infect* 2003;5:693-703.
6. The Gastrointestinal Physiology Working Group: Ecology of *Helicobacter pylori* in Peru: Infection rates in coastal, high altitude and jungle communities. *Gut* 1992;33:604-605.
7. Everhart J, Kruszon-Moran D, Perez-Perez G, et al. Seroprevalence and Ethnic Differences in *Helicobacter pylori* Infection among Adults in the United States. *JID* 2000; 81:1359-1363.
8. Blaser MJ. Hipotesis: The Changing Relationships of *Helicobacter pylori* and Humans: implications for health and disease. *JID* 1999;179:1523-1530.
9. Marshall BJ. Epidemiology of *H. pylori* in Western countries. In: Hunt RH, Tytgat NJ eds. *Helicobacter pylori* basic mechanism to clinical cure. London: Kluwer Academic 1994:75-84.
10. Thomas JE, Gibson GR, Darboe MK, et al. Isolation of *Helicobacter pylori* from human feces. *Lancet* 1992; 340:1194-1195.
11. Gastrointestinal Physiology Working Group. *Helicobacter pylori* and gastritis in Peruvian patients: Relationship to socioeconomic level, age and sex. *Am J Gastroenterol* 1990;85:819-823.
12. Horiuchi T, Ohkusa T, Watanabe M, et al. *Helicobacter pylori* in Drinking Water in Japan. *Microbiol Immunol* 2001;45:515-519.
13. Klein PD, Gastrointestinal Physiology Working Group, Graham DY, et al. Water source as risk factor for *Helicobacter pylori* infection in Peruvian children. *Lancet* 1991;337:1503-1506.
14. Sutton LD, Wilke WW, Lynch NA, et al. *Helicobacter pylori*-containing sewage detected by an automated polymerase chain reaction amplification procedure, abstr. C-395, p. 69. In Abstracts of the 95th General Meeting of the American Society for Microbiology 1995. American Society for Microbiology, Washington, D.C.
15. Hopkins RJ, Vial PA, Ferreccio C, et al. Seroprevalence of *Helicobacter pylori* in Chile: vegetables may serve as one route of transmission. *J. Infect Dis* 1993;168:222-226.
16. Gilman RH, León-Barúa R, Cok J, et al. Rapid identification of *Campylobacter pylori* in Peruvians with gastritis. *Dis Dis Sci* 1986;31:1089-1094.
17. Ramírez-Ramos A, Recavarren S, León-Barúa R, et al. *Campylobacter pylori*, gastritis crónica, duodenitis crónica, úlcera gástrica y úlcera duodenal. *Arq Gastroenterol. Sao Paulo* 1987;24:10-15.
18. Recavarren-Arce S, León-Barúa R, Cok J, et al. The Gastrointestinal Physiology Working Group. *Helicobacter pylori* and progressive gastric pathology that predisposes to gastric cancer. *Scand J Gastroenterol* 1991;26:S181,51-57.
19. Ramírez-Ramos A, Gilman RH, Watanabe J, et al. Variación de la prevalencia del *Helicobacter pylori* en el Perú. Período 1985-2002, en una población de nivel socioeconómico medio y alto. *Rev Gastroenterol Peru* 2003;23:92-98.
20. Soto G, Bautista C, Roth D, et al. *Helicobacter pylori* reinfection is common in Peruvian adults following antibiotic eradication therapy. *J Infect Dis.* 2003;188:1263-1275.
21. Sonnenberg A, El-Serag HB. Opposing time trends of peptic ulcer and reflux disease. *Gut* 1998;43:327-333.
22. Roder DM. The epidemiology of gastric cancer. *Gastric Cancer* 2002;5 (suppl 1):5-11.
23. Kang JY, Tinto A, Higham J, Majeed A. Peptic ulceration in general practice in England and Wales 1994-1998; period prevalence and drug management. *Aliment Pharmacol Ther* 2002;16:10067-10074.
24. Xia HH, Phung N, Altiparmak E, Berry A, Matheson M, Talley NJ. Reduction of peptic ulcer disease and *Helicobacter pylori* infection but increase of reflux esofagitis in Western Sydney between 1990 and 1998. *Dig Dis Sci* 2001; 46:2716-2723.
25. Changing trend in peptic ulcer prevalence in a tertiary care setting in the Philippines: A seven- year study. *Journal of Gastroenterology and Hepatology* 2005;20:628-632.
26. Ramírez-Ramos A, Gilman RH, Watanabe J, et al. *Helicobacter pylori* infection in long-term and short-term Japanese visitors to Peru. *Lancet* 1994;344:1017.
27. Instituto Nacional de Estadística e Informática. Encuesta Nacional a Hogares. Lima-Peru, 1996.
28. Klein D, Gilman RH, León-Barúa R, et al. The epidemiology of *Helicobacter pylori* in Peruvian children between 6 and 30 months of age. *Am J Gastroenterol* 1994;89:2196-2200.