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Gastrointestinal Tract

Decreasing prevalence of *Helicobacter pylori* according to birth cohorts in urban China

Xinjuan Yu[1], Xuan Yang[2], Tingting Yang[3], Quanjiang Dong[1], Lili Wang[1], Lei Feng[1]

[1]Central Laboratories, Qingdao Municipal Hospital, Qingdao, China
[2]Department of Cardiology, Qingdao Municipal Hospital, Qingdao, China
[3]Laboratories, the Affiliated Hospital of Qingdao University, Qingdao, China

ABSTRACT

Background/Aims: The *Helicobacter pylori (H. pylori)* prevalence has been decreasing in many parts of the world. This study aimed to investigate the current epidemiological status of *H. pylori* infection in urban China.

Materials and Methods: The study included 51,299 subjects aged ≥18 years who underwent health checkups between April 2013 and June 2016 in a city of China. *H. pylori* infection was determined by detecting *H. pylori* urease-IgG antibodies. Statistical analyses included chi-square tests for trends and curve fitting.

Results: The overall *H. pylori* prevalence was found to be 31.9%, with the highest prevalence in the 1950-1959 birth cohort. It was lower in the subsequent birth cohorts (trends, $p<0.001$). The decrease in *H. pylori* prevalence was correlated with the increase in per capita gross domestic product (GDP) and real per capita GDP; the power model was best fitted ($R^2=0.914$ and 0.997 and $p=0.011$ and 0.000, respectively).

Conclusion: There has been a striking decrease in the *H. pylori* prevalence in urban China. The birth cohort effect and economic growth are the most likely causes of this phenomenon.

Keywords: *Helicobacter pylori*, prevalence, birth cohort, economic status

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INTRODUCTION

Helicobacter pylori (H. pylori) is a gram-negative pathogenic bacillus that colonizes the stomach mucosa and causes gastrointestinal tract diseases, such as peptic ulcer, chronic gastritis, gastric cancer, and gastric mucosa-associated lymphoid tissue lymphoma (1). It is also associated with many extra-gastrointestinal conditions, including diabetes mellitus, cardiovascular disease, and autoimmune disease (2). Its prevalence has been found to considerably vary with respect to age, ethnicity, geography, and socioeconomic factors and tends to be low in developed countries and high in developing countries. However, recently, there has been a decreasing trend in the *H. pylori* prevalence in many areas of the world (3).

The birth cohort effect and economic growth may account for this phenomenon. The acquisition of *H. pylori* is considered to exclusively occur during childhood (4), persisting during the individual's lifetime without eradication (5). Reduced acquisition rates in successive birth cohorts are believed to be a vital contributor to the decreasing *H. pylori* prevalence over time (6,7). Many studies have shown low socioeconomic status to be significantly associated with a high risk for *H. pylori* infection (8,9). Improvements in dwelling environment and hygiene conditions are crucial factors in decreasing the *H. pylori* prevalence.

The *H. pylori* prevalence has been reported to be high in China, a developing country, ranging from 41.4% to 80.4% (10). This study aimed to assess the current epidemiological status of *H. pylori* infections in urban China and estimate the trends in *H. pylori* infections with respect to the birth year and economic status.

MATERIALS AND METHODS

Subjects

The study included individuals aged ≥18 years who underwent health checkups in a city of China between April 2013 and June 2016. Each participant's identification

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number, sex, birth date, inspection date, and *H. pylori* infection status were retrieved from the electronic database. To minimize the influence of possible eradication treatment, only the results of the first test were considered if an individual underwent more than one diagnostic test for *H. pylori*.

H. pylori Detection

H. pylori urease-IgG antibodies were serologically detected using a specific ELISA kit, the *Hp* Urease Immunogold Testing Kit (Beijing Kangmeitianhong Biotechnology Co., Ltd., Beijing, China). The ELISA kit had a sensitivity of 98.91% and specificity of 98.29% for detecting *H. pylori* in the populations tested (11).

Economic Data Search

Per capita gross domestic product (GDP) is usually used to evaluate the economic status of a country or district. However, real per capita GDP can estimate the economic status more accurately because it discounts the impact of inflation. Data concerning per capita GDP and real per capita GDP (1952 year=100 ¥) for the entire China were collected from the National Bureau of Statistics of China (http://www.stats.gov.cn/tjsj/). The median per capita GDP of every 10-year period was used to represent the average per capita GDP for those 10 years.

Statistical Analysis

Statistical Package for the Social Sciences 18.0 (SPSS Inc.; Chicago, IL, USA) was used to perform statistical analyses. The univariate log- binomial regression model was used to compare the *H. pylori* prevalence between sexes. The risk ratio (RR) and 95% confidence intervals (CIs) represented the comparison of males and females. The chi-square test was used to estimate the trends in *H. pylori* infection in different birth cohorts. Curve fitting was used to identify the "best fit" curve for the association of per capita GDP and real per capita GDP with the *H. pylori* prevalence. The F-test was used to select the best fitting curve to test the hypothesis. R^2 values of >0.80 were considered significant (12). P values of <0.05 (two-tailed) were considered statistically significant.

RESULTS

Data regarding 64,986 individuals were retrieved from the electronic database. We excluded 13,508 repeatedly detected subjects, 13 subjects whose age was not listed, and 166 subjects aged <18 years. A total of 51,299 individuals (27,061 males and 24,238 females) with a mean birth year of 1969 (1918-1998) were included in the final analysis. These 16,382 individuals had a positive *H. pylori* status, resulting in an *H. pylori* prevalence of 31.9% for the overall cohort. Table 1 presents the characteristics of the study population.

The *H. pylori* prevalence was 33.9% in the male participants and 29.8% in the female participants. Infection was more common in males than in females (RR, 1.14; 95% CI, 1.11-1.17; p=0.000). Sex ratios ranged from 1.08 to 1.15 and showed no significant difference among each 10-year birth cohort group (p=0.138). There was a difference in the *H. pylori* prevalence between males and females in each 10-year birth cohort group, except in subjects born after 1990 (p=0.070), although the positive rate of males (22.5%) was higher than that of females (19.5%).

Table 1. Characteristics of the study subjects

Characteristics	Category	*H. pylori* positive [n (%)] (n=16,382)	*H. pylori* negative [n (%)] (n=34,917)	Total [n (%)] (n=51,299)
Sex	Male	9,170 (33.9)	17,891 (66.1)	27,061 (52.8)
	Female	7,212 (29.8)	17,026 (70.2)	24,238 (47.2)
Birth year	Mean (SD)	1968 (14)	1971 (14)	1969 (14)
Birth cohort	-1949	1,579 (36.0)	2,810 (64.0)	4,389 (8.6)
	1950-1959	3,279 (37.5)	5,465 (62.5)	8,744 (17.0)
	1960-1969	3,894 (35.8)	6,986 (64.2)	10,880 (21.2)
	1970-1979	3,687 (31.3)	8,111 (68.7)	11,798 (23.0)
	1980-1989	3,417 (26.3)	9,574 (73.7)	12,991 (25.3)
	1990-	526 (21.1)	1,971 (78.9)	2,497 (4.9)

SD: standard deviation

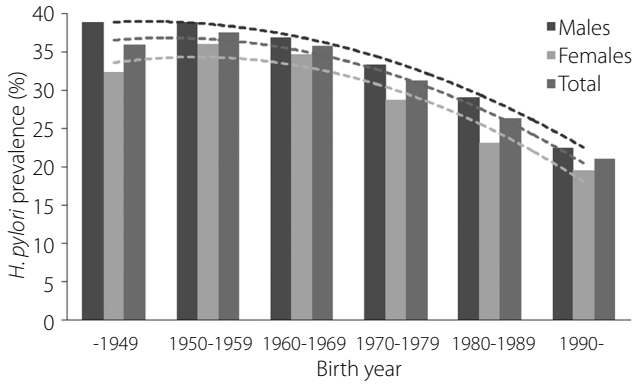

Figure 1. Birth year and the *H. pylori* prevalence. Males: χ^2=222.232, p value for trends=0.000; females: χ^2=266.960, p value for trends=0.000; total: χ^2=482.885, p value for trends=0.000

The *H. pylori* prevalence was highest in the 1950-1959 birth cohort and was lower in the subsequent birth cohorts in both male and female participants. The p values for trends were all 0.000 (Figure 1). The decrease in the *H. pylori* prevalence was correlated with an increasing per capita GDP and real per capita GDP; the power model was best fitted (R^2=0.914 and 0.997 and p=0.011 and 0.000, respectively) (Figure 2, 3).

DISCUSSION

The overall *H. pylori* prevalence in urban China was found to be 31.9%. The *H. pylori* prevalence previously reported in some parts of China was 46.8%-66.4% (13-15), reaching a maximum of 80.4% (16). In this study, the *H. pylori* prevalence in China was found to be significantly lower than that reported in previous studies (13-16). This prevalence was consistent with those reported in some Western developed countries, and even it was surprisingly lower than those reported in some developed countries (17-20). The

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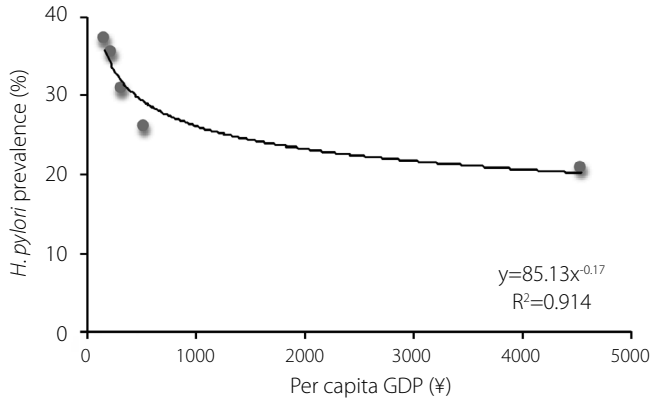

Figure 2. Association between per capita GDP and the *H. pylori* prevalence. $y=85.13x^{-0.17}$, $R^2=0.914$, F=31.705, p=0.011

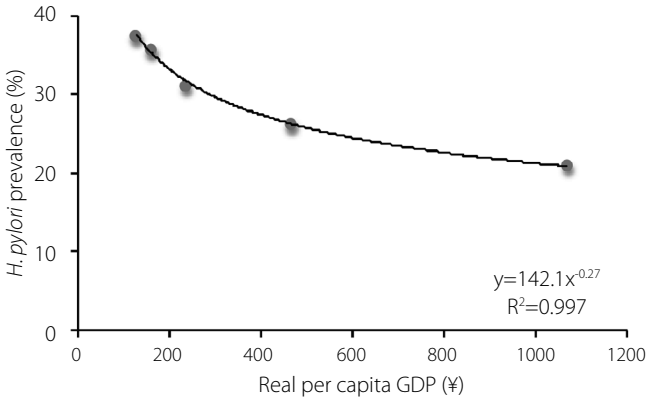

Figure 3. Association between real per capita GDP and the *H. pylori* prevalence. $y=142.1x^{-0.27}$, $R^2=0.997$, F=1167.056, p=0.000

prevalence was 32.7% in the United States (17), 31.7% in the Netherlands (18), 44.3% in Japan (19), and 54.4% in Korea (20). This low prevalence was partially because of the urban population recruited in our study. Urban populations have much lower rates of *H. pylori* infection than rural populations (21). Poor household crowding and a lack of running water and other basic services might be, in part, associated with a high prevalence of *H. pylori*.

In recent years, the *H. pylori* prevalence has been decreasing in many areas of the world (22,23). The birth cohort effect may partially account for this phenomenon (24). *H. pylori* acquisition is considered to almost exclusively occur during childhood and adolescence. Unless eradicated, it generally persists colonizing in the stomach as a chronic infection into adulthood (25,26). The acquisition rate of infection in the younger birth cohort was significantly lower than that reported in the previous generation as the living standards have improved in recent decades. This study demonstrated that the *H. pylori* prevalence was subject to a prominent birth cohort effect in urban China. There has been a striking decrease in the prevalence of this infection in younger populations. The progressively decreasing *H. pylori* prevalence appears to be linked with the decrease in related upper gastrointestinal diseases. A study conducted in southeastern China demonstrated a downward trend of *H. pylori* infection, which was parallel with the decrease in the peptic ulcer incidence from 2003 to 2012. The *H. pylori* prevalence decreased from 42.40% to 23.82%. Meanwhile, the prevalence of duodenal and gastric ulcer rapidly decreased from 12.65% to 6.57% and from 7.51% to 3.78%, respectively (27). Therefore, chronic gastric diseases appear to be decreasing with the decreasing *H. pylori* prevalence.

The socioeconomic status is closely related to the *H. pylori* prevalence (28). The economic base determines the socioeconomic status. One study showed that low income was a potential risk factor for *H. pylori* infection (29). The economic conditions in China have significantly improved in recent decades. The per capita GDP increased from ¥119 in 1952 to ¥7199 in 1999. The *H. pylori* prevalence decreased with increasing per capita GDP, indicating that the *H. pylori* prevalence would decrease with improved sanitation and living standards.

The current study found that males were on an average 14% more likely to be infected with *H. pylori* than females; this was consistent with that found in a meta-analysis, which confirmed the male predominance of *H. pylori* infection in adults (30). This could explain the reason for males being more prone to contract *H. pylori* related diseases. Relative immunodeficiency in males has been postulated as an explanation for the male predominance in the incidence of infectious diseases (31). Females have higher plasma IgM levels than males; estrogen stimulates immune responses, whereas testosterone is immunosuppressive (32). Smoking is an independent risk factor for *H. pylori* infection (33,34). In China, the smoking rate is obviously higher in males than in females (35), which may be a factor accounting for the male predominance of *H. pylori* infection. Our study found that the differences in the *H. pylori* prevalence between males and females in each birth cohort group were constant, despite the increase in GDP. This indicated that the economic status had no effect on the differences in the *H. pylori* prevalence between sexes.

Our study has several limitations. First, only subjects who underwent health checkups were included, possibly limiting the validity of the findings for the whole population. Second, we used the per capita GDP and real per capita GDP for the entire China as socioeconomic markers. These GDP data could only represent a trend of the socioeconomic status. It would be more reasonable to use the familial income of each birth cohort group or GDP of the urban area that participates in the study.

In summary, there has been a striking decrease in the *H. pylori* prevalence in urban China. The birth cohort effect and economic growth are the most likely causes of this phenomenon. This study has important public health implications for the prevention of *H. pylori* infection.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Qingdao Municipal Hospital.

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