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Original Article

Helicobacter pylori infection status among health check-up populations in China: a 3-year follow-up study

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Abstract: *Background*: Currently, most health care centers in China perform detection of *Helicobacter pylori (H. pylori)* infection, but changes in *H. pylori* infection among these populations are rarely reported. Here, a 3-year follow-up study of *H. pylori* infection status was performed using ^{13}C-urea breath tests (UBTs) performed in the health care center of our hospital from 2013 to 2015 to study changes in the *H. pylori* infection status among health check-up populations in China. *Methods:* A total of 5,779 subjects examined at our institution between January 2013 and December 2013 were enrolled in this study. These participants were tested for *H. pylori* infection and followed up for 3 years. The current infection rate, annual incidence, annual reinfection rate and spontaneous clearance rate were determined. Further univariate and multivariate logistic regression analyses were performed to determine the causes of eradication failure. *Results:* Among the entire cohort (3,806 (65.86%) male; 1,973 (34.14%) female; average age 54.28 years), the *H. pylori* current infection rate was 40.27%, with males presenting a significantly higher rate than females ($p<0.001$). A total of 2,587 *H. pylori*-positive subjects were diagnosed before 2015, and 1,370 underwent eradication therapy. The eradication rate of *H. pylori* among these 1,370 cases was 85.04% (1,165/1,370). The annual incidence, annual reinfection and spontaneous clearance rates of *H. pylori* infection were approximately 7.69%, 2.66% and 3.18%, respectively. Multivariate logistic regression analysis suggested that the following factors were related to eradication failure: male sex, smoking history, a low education level, no gastroscopy and poor treatment compliance. *Conclusions:* Efforts should be directed towards treating *H. pylori*-infected patients after screening, including implementation of standard initial treatments to improve the eradication rate and reduce the resistance rate.

Keywords: Eradication rate, follow-up study, *Helicobacter pylori*, current infection rate, reinfection rate, spontaneous clearance rate

Introduction

Helicobacter pylori (*H. pylori*), a gram-negative bacterium that specifically colonizes the gastric epithelium, infects more than 50% of human beings, with an even higher rate in developing countries [1]. *H. pylori* is associated with many gastrointestinal diseases, such as chronic gastritis, peptic ulcers, and gastric mucosa-associated lymphoid tissue (MALT) lymphoma. It is also considered a class I carcinogen that can induce gastric cancer [2, 3].

The Kyoto Global Consensus Meeting and the most recent Maastricht V/Florence Consensus Report proposed that *H. pylori* gastritis should be defined as an infectious disease. *H. pylori*-infected individuals should be offered eradication therapy, unless competing considerations are present [4, 5]. Nagy et al. [6] conducted a systematic literature analysis of 25 studies performed in China through January 19, 2015. The weighted mean prevalence of *H. pylori* infection across all years was 55% (range: 28-82% [1983-2013]).

Currently, most health care centers in China perform the detection of *H. pylori* infection, but the changes in *H. pylori* infection in these patient populations are rarely reported. A 3-year follow-up study of *H. pylori* infection status was conducted using ^{13}C-urea breath tests (UBTs) performed in the health care center of our hospital from 2013 to 2015 in order to ana-

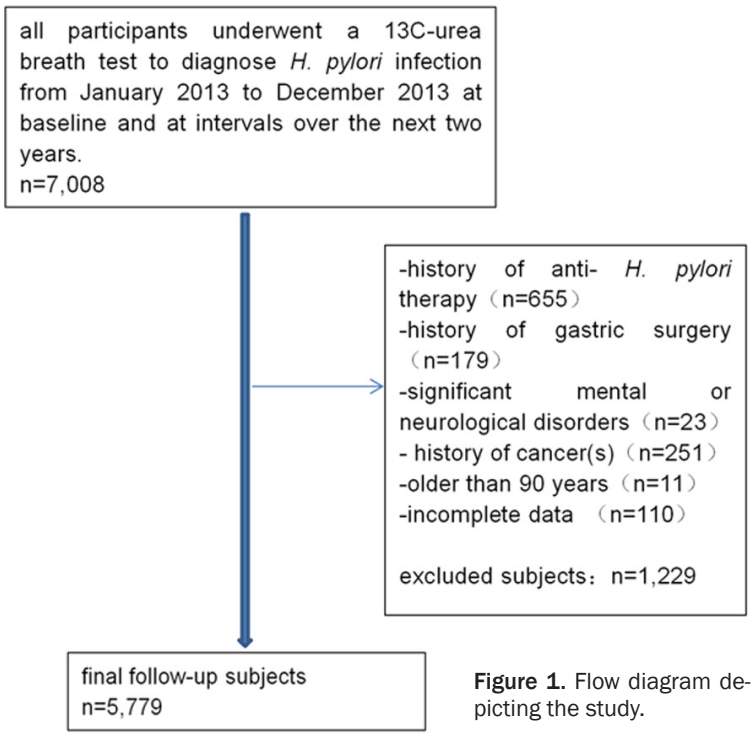

Figure 1. Flow diagram depicting the study.

lyze the current infection rate of *H. pylori*, annual incidence rate of *H. pylori*, eradication rate after *H. pylori* infection and reinfection rate after treatment.

Materials and methods

Study participants

The health check-up participants were recruited from our health care center between January and December 2013. Physical examinations included a UBT to detect *H. pylori* infection. The inclusive criteria were: 1) health check-up participants in our care center; 2) aged 18 to 89 years; 3) using ^{13}C-UBT to diagnose *H. pylori* infection. The exclusion criteria were: 1) a history of anti-*H. pylori* therapy; 2) a history of gastric surgery; 3) use of antacids, such as H_2 blockers or proton pump inhibitors (PPIs), or antibiotics within the previous month; 4) significant disorders; 5) a history of cancer(s); and 6) an age greater than 90 years. All participants provided written informed consent before the examination. The present study was reviewed and approved by the Ethics Committee of the 2nd Affiliated Hospital, School of Medicine, Zhejiang University (2012-218).

Questionnaires

A questionnaire was administered before the UBT to collect information on each participant's history of illness, surgery, drug use, cancer(s), smoking, drinking, *H. pylori* infection status, living conditions, and education level. The questionnaire was designed to be simple and concise to ensure that the participants responded carefully and truthfully to each question.

Diagnosis of H. pylori infection

Prior to the ^{13}C-UBT, the health check-up participants were required to stop using drugs that may affect the test results for at least 4 weeks. Breath samples were collected twice, including before (T0) and 30 minutes after ^{13}C-urea administration (T30). A delta over baseline (DOB) value ≥4.0 can diagnose *H. pylori* infection.

Statistical analysis

STATA 14.0 software (StataCorp, College Station, Texas, USA) was used for statistical analysis. A t-test was used to evaluate normally distributed data, and a Chi-square test was used for qualitative data. Further univariate and multivariate logistic regression analyses on the causes of eradication failure were performed. Age, sex, BMI, smoking, drinking, living environment, education, stomach diseases and treatment compliance were included as covariates in the logistic regression analysis. Odds ratios (ORs) and 95% confidence intervals (CIs) were then calculated. All *p* values were based on a two-sided test of statistical significance. Significance was accepted at the level of $p<0.05$.

Results

Clinical and demographic characteristics

Ultimately, 5,779 subjects were recruited for the analysis. A flow diagram depicting this study is shown in **Figure 1**. Of the 5,779 partici-

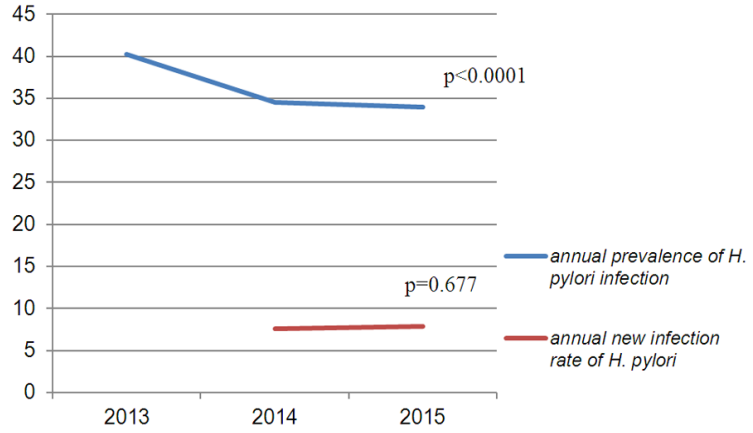

Figure 2. Analysis of the annual prevalence of *H. pylori* infection and the annual rate of new *H. pylori* infection cases.

pants, 3,806 (65.86%) were male, and 1,973 (34.14%) were female; the average age was 54.28 years. The UBT for *H. pylori* was positive in 40.27% (2,327/5,779) of the subjects, among whom the *H. pylori* infection rate was 42.54% (1,619/3,806) in males and 35.88% (708/1,973) in females. The current infection rate of *H. pylori* was significantly higher in males than in females (p<0.001). No significant difference in the total infection rate was found among the age groups (p=0.262).

Analysis of the annual prevalence and annual incidence rate of H. pylori infection

Annual rates of *H. pylori* infection in 2013, 2014 and 2015 were 40.27% (2,327/5,779), 34.50% (1,994/5,779) and 33.93% (1,961/5,779), respectively, reflecting significant decreases each year (p<0.0001). Annual incidence rates of *H. pylori* infection were 7.55% (261/3458) in 2014 and 7.82% (250/3197) in 2015, which were not significantly different (p=0.677). The results are shown in **Figure 2**.

Changes in the H. pylori infection status over 3 years

For *H. pylori*-positive patients, a quadruple regimen was recommended for 14 days, which included esomeprazole 20 mg bid + pectin capsule 200 mg bid + amoxicillin capsule 1000 mg bid (allergic patients received clarithromycin 500 mg bid) + furazolidone 100 mg bid orally. A total of 2,587 *H. pylori*-positive subjects were diagnosed before 2015, and 2,118 of these patients remembered their treatment history accurately. Of the 2,118 patients, 1,370 underwent treatment. The intervention rate was 64.68% (1,370/2118), and the final eradication rate of *H. pylori* was 85.04% (1,165/1,370). The annual reinfection rate was 2.66%, and the spontaneous clearance rate of *H. pylori* infection was 3.18% (184/5,779). The results are shown in **Table 1**.

Univariate and multivariate logistic regression analyses of the causes of eradication failure

Univariate and multivariate regression analyses revealed that the following factors were related to eradication failure: sex (male) (OR 1.269, 95% CI 1.121-1.684, p=0.002), smoking history (OR 3.385, 95% CI 1.351-1.983, p=0.004), education level (below undergraduate) (OR 2.621, 95% CI 1.025-4.832, p<0.001), concurrent stomach disease (no gastroscopy) (OR 2.793, 95% CI 1.445-5.454, p<0.001), and treatment compliance (OR 3.118, 95% CI 1.112-8.260, p<0.001). Details are shown in **Tables 2** and **3**.

Discussion

Our study showed that the current infection rate of *H. pylori* was 33.93-40.27%. Sun et al. [7] analyzed 22,103 patients in Shanghai who underwent routine physical examinations and found that the total *H. pylori* infection rate as assessed by the ^{13}C UBT was 44.5%, which is close to our result. The authors also found that the number of men infected with *H. pylori* tended to be higher than the number of women (45.9% vs. 42.8%; p<0.01). The highest positive rate was found in the age group of 30-39 years (46.8%), and the lowest rate was found in the age group younger than 30 years (40.5%). Previously, Shi et al. [8] performed a study of 1,371 Chinese individuals, and the *H. pylori* infection rate, as assessed by ^{13}C UBT and serum IgG antibodies, was 62%. The peak age of infection was between 30 and 40 years (67%), with no difference between the sexes. Porras et al. [9] analyzed the prevalence of *H. pylori* infection in a total of 1,852 patients from

Table 1. Changes in *H. pylori* infection over 3 years

Index	Percentage	Index	Percentage
H. pylori infection rate	40.27%	Annual infection rate	7.55%
Intervention rate	64.68%	Reinfection rate	2.66%
Eradication rate	85.04%	Spontaneous clearance rate	3.18%

seven major centers in six countries in Latin America. No differences in sex (females: 78.4%, males: 80.9%; p=0.20) or age (p=0.08) were found. In this study, 5,779 patients were recruited, including 3,806 (65.86%) males and 1,973 (34.14%) females, and the average age was 54.28 years. The infection rate was higher in males than in females (p<0.001), and no significant differences were found in the total infection rate among the age groups (p=0.262). *H. pylori* infection usually occurs during childhood, which could explain why no differences were found between the age groups. These sex difference results are in accordance with the findings of Sun et al. [7].

This study further analyzed the annual incidence rate of *H. pylori* infection, which showed no significant difference between the studied years (p=0.677). The two-year average rate was 7.69%. The literature on the annual incidence rate of *H. pylori* infection is limited. Weck and Brenner [10] reviewed 32 studies and found that the annual incidence rate was less than 1.0%. However, most of the studies were conducted in developed countries. Duque et al. [11] examined 718 schoolchildren in developing countries and found that the incidence rate of *H. pylori* was 6.36% per year, which is consistent with our findings.

According to the follow-up results, 2,587 patients had *H. pylori*-positive infections that occurred before 2015, 2,118 of whom could remember their treatment history accurately. The eradication indication was based on the individual request for treatment according to the Fourth Chinese National Consensus Report on the management of *H. pylori* infection at that time [12]. Ultimately, 1,370 patients underwent treatment, and the eradication rate was higher than the latest domestic report of 72.9% in China using a 10-day quadruple anti-*H. pylori* treatment [13]. The univariate and multivariate regression analyses revealed that the following factors were related to eradication failure: sex (male), smoking history, education level (below undergraduate), concurrent stomach disease (no gastroscopy) and treatment compliance.

Gisbert [14] published a review showing that the global prevalence of *H. pylori* reinfection varies widely. The average annual reinfection rate was 3.4% (95% CI, 3.1-3.7%) in developed countries and 8.7% (95% CI, 8.8-9.6%) in developing countries. Niv and Hazazi [15] examined 10 studies from developed countries (3,014 patients, 24 to 60 months of follow-up) and 7 studies conducted in developing countries (2,071 patients, 12 to 60 months of follow-up) and found that the average annual rate of reinfection of *H. pylori* in developed countries was 2.67% compared to 13% in developing countries. In China, Yan et al. [16] reviewed 1,226 cases of *H. pylori*, and the recurrence rate was 2.82±1.16% per patient-year. Recently, Zhou et al. [17] also evaluated 743 patients and found that the annual reinfection rate of *H. pylori* was 1.75% (95% CI, 0.81-2.69%). Multivariate analysis revealed that peptic ulcer disease, contact with other individuals with *H. pylori* infection and hospitalization were independent risk factors for *H. pylori* reinfection. This study estimated that the *H. pylori* reinfection rate in the general population was 2.66% per year, which is consistent with the values reported in the literature.

Here, the spontaneous clearance rate was estimated to be 3.18% (184/5,779). The literature on the spontaneous clearance rate of *H. pylori* infection is also limited. Duque et al. [11] reported that the spontaneous clearance rate of *H. pylori* infection was 4.74% per year, which is similar to our results. However, these data have limitations. First, this study evaluated a population who underwent regular physical examinations, which does not fully reflect the conditions of infection in the overall population and may represent selection bias. However, the majority of the population in our country receives a health check-up every year, and our subjects included a variety of occupational groups. Second, recall bias may have been present in the follow-up in the study, which may have affected the final statistical results. Third, the sensitivity and specificity of the UBT in our study were approximately 0.96 (95% CI, 0.95-0.97) and 0.93 (95% CI, 0.91-0.94), respectively [18]. Overall, the results are based on the accuracy of the UBT, and deficits in the accura-

Table 2. Univariate logistic regression analysis of the causes of eradication failure

Index	Total (n=844)	Eradicated group (n=599)	Uneradicated group (n=245)	*P*-value
Sex (%)				<0.001
Male	530 (62.80)	345 (57.60)	185 (75.51)	
Female	314 (37.20)	254 (42.40)	60 (24.49)	
Age (years)	56.25±9.17	57.02±10.25	53.14±8.95	0.458
BMI (kg/m^2)	24.56±3.17	23.16±3.65	24.01±3.44	0.342
Smoking (%)				0.015
Yes	270 (31.99)	165 (27.55)	105 (42.86)	
No	574 (68.01)	434 (72.45)	140 (57.14)	
Drinking (%)				0.605
Yes	324 (38.39)	227 (37.90)	97 (39.59)	
No	520 (61.61)	372 (62.10)	148 (60.41)	
Living condition (%)				0.877
Urban	647 (76.66)	458 (76.46)	189 (77.14)	
Country	197 (23.34)	141 (23.54)	56 (22.86)	
Education level (%)				<0.001
College graduate	477 (56.52)	371 (61.94)	106 (43.27)	
Below undergraduate	367 (43.48)	228 (38.06)	139 (56.73)	
Concurrent stomach disease (%)				<0.001
Yes	171 (20.26)	160 (26.71)	11 (0.04)	
No	194 (22.99)	125 (20.87)	69 (28.16)	
No gastroscopy	479 (56.75)	314 (52.42)	165 (67.34)	
Treatment compliance (%)				<0.001
Good	746 (88.39)	599 (100.00)	147 (60.00)	
Bad	98 (11.61)	0 (0)	98 (40.00)	

Table 3. Multivariate logistic regression analysis of the causes of eradication failure

Variable	OR (95% CI)	*P*-value
Sex	1.269 (1.121, 1.684)	0.002
Smoking	1.351 (1.131, 1.983)	0.004
Education level	2.621 (1.025, 4.832)	<0.001
Concurrent stomach disease	2.793 (1.445, 5.454)	<0.001
Treatment compliance	3.188 (1.112, 8.260)	<0.001

cy may have affected the final statistical results. In the future, further follow up this group of patients will performed in the form of a cohort study the related influencing factors will be analyzed.

Conclusions

This study found that the *H. pylori* infection rate was still high and that the eradication rate was not ideal. The annual incidence rate and reinfection rate were also high. According to the Fifth Chinese National Consensus Report on the management of *Helicobacter pylori* infection [19], *H. pylori* infection confirmation is included in the eradication indications. Therefore, intervention in *H. pylori* infection screening management is an important task of health management centers. Close attention should be paid to the treatment of *H. pylori*-infected individuals after screening, and standard initial treatments should be administered to improve the eradication rate and reduce the resistance rate. Additionally, health education should be strengthened to reduce the reinfection rate.

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Disclosure of conflict of interest

None.

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