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Prevalence and risk factors for *Helicobacter pylori* infection in southwest China: a study of health examination participants based on 13C-urea breath test

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Background/aim: *Helicobacter pylori* (*H. pylori*) has a high prevalence in developing countries. We aimed to investigate the current prevalence of *H. pylori*, as well as its potential serum risk factors, in a population from southwest China.

Materials and methods: This cross-sectional study included 10,912 subjects who received medical examinations at the First Affiliated Hospital of Chongqing Medical University in 2014. Data regarding physical examinations and biochemical measurements were collected, and *H. pylori* infection was diagnosed with a ^{13}C-urea breath test. Logistic regression was conducted to identify the risk factors for *H. pylori* infection.

Results: The infection rate of *H. pylori* was 34.4% (3750/10,912). Older age, lower albumin levels, and higher total cholesterol, LDL-cholesterol, and fasting blood sugar were significantly associated with increased incidence of *H. pylori* infection. Moreover, logistic regression analysis showed that older age, low albumin, and hyperglycemia were independent risk factors for *H. pylori* infection after adjusting for other covariables.

Conclusion: The results from our study showed that *H. pylori* was prevalent in southwest China. Older age, low albumin levels, and hyperglycemia were significant risk factors associated with *H. pylori* infection.

Key words: *Helicobacter pylori*, prevalence, risk factors, southwestern China

1. Introduction

It has been well established that peptic ulcer disease, chronic gastritis, and gastric malignancies are strongly related to *Helicobacter pylori* (*H. pylori*) infection. *H. pylori* has been identified by the WHO as a dangerous carcinogen (1). In addition, *H. pylori* plays a leading role in gastritis, which can result in gastric cancer (2,3). The incidence of gastric cancer was significantly reduced when *H. pylori* was eradicated in infected Asian individuals who were asymptomatic and healthy (4). Researchers have also found that infection with *H. pylori* can result in cardiovascular, hematological, hepatobiliary, and metabolic diseases (5–9). Currently, many epidemiological surveys have been performed to identify risk factors for *H. pylori* infection; age, obesity, and type 2 diabetes mellitus have been identified as risk factors (10–13). In terms of diagnosis, stool antigen testing, gastric biopsies, CLO-test, and urea breath test are used. However, ^{13}C-urea breath test is the best known and most widely used test for detecting the presence of *H. pylori* infection and showed excellent accuracy compared to histology (14,15).

According to previously published studies on the prevalence of *H. pylori* infection in China, the rates ranged from 41.35% to 72.3% and varied among different populations and different geographic areas (16). However, similar studies that focused on southwest China, such as in Chongqing, have rarely been performed. We studied a cohort from Chongqing, China. We used a ^{13}C-urea breath test to analyze the prevalence of *H. pylori* infection and explore the potential risk factors for *H. pylori* infection in this population. It is our hope that our study may contribute to the current knowledge on the prevention and management of *H. pylori* infection.

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2. Materials and methods

The study was carried out at the medical examination center in the First Affiliated Hospital of Chongqing Medical University, China in 2014. The study was approved by the Research Ethics Committee of the First Affiliated Hospital of Chongqing Medical University, and informed consent was obtained from each participant.

2.1. Study subjects and medical examination

The data in this study were collected from January to December 2014. Participants enrolled in this study were healthy subjects aged 18 years or older who received annual medical examinations. Participants with malignant tumors, severe cardiovascular diseases, acute infection, endocrine diseases, or incomplete data were excluded, accounting for 239 subjects. The final sampling size was 10,912. All participants received physical examinations and laboratory tests. The heights and weights of subjects were measured in a fasting state; the systolic and diastolic blood pressures (SBP and DBP) were measured twice with a standard apparatus during the medical examinations. Venous blood samples were collected following an overnight fast. Fasting blood sugar (FBS), serum total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), fasting serum triglycerides (TGs), albumin, high-density lipoprotein cholesterol (HDL-C), γ-glutamine transferase (γ-GT), alanine transaminase (ALT), and aspartate aminotransferase (AST) were measured using an automatic biochemical analyzer (AU5400, Olympus, Tokyo, Japan).

2.2. Case definition

H. pylori status was measured via ^{13}C-urea breath test. As previously described, the ^{13}C- urea breath test was performed using standard procedures (17). In brief, a baseline breath sample was collected, and then the subject drank a test solution containing 75 mg ^{13}C-urea. The $^{13}CO_2$ in the breath was measured after 30 min. The breath samples were analyzed with an infrared heterodyne radiometer. If the two values showed a difference greater than 0.4%, then he/she was confirmed as being infected with *H. pylori*. Otherwise, he/she would be declared free of infection.

Hyperglycemia was defined as fasting blood sugar ≥6.1 mmol/L. Body mass index (BMI) was defined as weight divided by height squared (kg/m^2). According to the Chinese guidelines for the prevention and control of obesity, BMI <24 kg/m^2 was considered normal BMI, BMI ≥24 kg/m^2 was considered overweight, and BMI ≥28 kg/m^2 was considered obese. Waist circumference was measured at the midway point between the costal margins. The waist-to-height ratio (WHtR) was calculated by waist circumference/height; WHtR ≥ 0.5 was considered central obesity. Subjects were also divided into groups based on serum albumin (g/L) quartiles (Qs): Q1 <45, Q2 45–47, Q3 47–48, and Q4 ≥48. Low albumin was defined as the lowest quartile of albumin (≤45 g/L). According to the joint committee for developing Chinese guidelines on the prevention and treatment of dyslipidemia in adults formulated in 2007, serum TGs ≥2.26 mmol/L were defined as high TGs, and HDL-C <1.04 mmol/L was considered low HDL-C. Serum TGs ≥6.22 mmol/L or LDL-C ≥4.14 mmol/L were defined as hypercholesterolemia.

2.3. Statistical analysis

All statistical analyses were performed with SPSS v.20.0 (SPSS Inc, Chicago, IL, USA). Variables distributed normally are presented as mean ± SD, while variables with a skewed distribution are presented as medians (interquartile range). The significance of differences between two groups was determined with a Student's t-test for continuous data following a normal distribution. A Wilcoxon rank sum test was used for skewed distribution data and a chi-square test was used for dichotomous data. Logistic regression was performed to identify risk factors for *H. pylori* infection. Statistical differences were defined by P values (2-tailed) less than 0.05.

3. Results

3.1. General information on subjects

The baseline characteristics of all subjects are shown in Table 1. The prevalence of *H. pylori* was 34.4% (3750/10,912); 33.8% and 35.1% in males and females, respectively. Of the 10,912 participants, 5774 (47.1%) were male and 5138 (52.9%) were female. The mean age was 44.1 ± 10.8. The mean age of the *H. pylori*-infected subjects was older than *H. pylori*-negative subjects. In the *H. pylori*-infected group, TC, LDL-C, and FBS were higher while albumin was lower, with each of these differentials reaching statistical significance (P < 0.05). However, BMI, WHtR, SBP, DBP, γ-GT, ALT, AST, TGs, and HDL-C did not differ significantly.

3.2. Logistic regression for *H. pylori* with its risk factors and prevalence of *H. pylori* infection among the risk factors

We further analyzed the risk factors for *H. pylori* infection. As shown in Table 2, for univariate logistic regression analysis, *H. pylori* infection was significantly associated with older age, low albumin, high total cholesterol, high LDL-cholesterol, and hyperglycemia. After adjusting for other confounding factors, results showed older age (35–45: 1.343, 95% confidence interval 1.021–1.765; ≥45: 1.610, 95% confidence interval 1.228–2.111), low albumin (1.136, 95% confidence interval 1.031–1.251), and hyperglycemia (1.258, 95% confidence interval 1.103–1.434) remained as statistically significantly associated with risk factors for *H. pylori* infection (Table 3).

Table 1. Characteristics of study participants and comparison for *H. pylori*-positive and *H. pylori*-negative subjects**.

Characteristics	Total (n = 10,912)	*H. pylori* (+) (n = 3750)	*H. pylori* (–) (n = 7162)	P *value
Age (years)	44.1 ± 10.8	45.2 ± 10.6	43.5 ± 10.9	<0.001
Male (%)	5774 (52.9)	1949 (52.0)	3825 (53.4)	0.154
BMI (kg/m^2)	23.7 ± 3.3	23.7 ± 3.2	23.6 ± 3.3	0.086
WHtR	0.49 ± 0.05	0.50 ± 0.06	0.49 ± 0.05	0.245
SBP (mmHg)	120.6 ± 17.9	121.0 ± 18.3	120.4 ± 17.7	0.135
DBP (mmHg)	75.7 ± 12.1	75.8 ± 12.1	75.7 ± 12.1	0.526
Albumin (g/L)	46.5 ± 2.7	46.2 ± 2.6	46.6 ± 2.7	<0.001
γ-GT (U/L)	21.00 (14.00–36.00)	29.00 (20.00–51.00)	15.00 (11.00–21.00)	0.138
ALT (U/L)	19.00 (14.00–29.00)	25.00 (18.00–37.00)	15.00 (12.00–21.00)	0.645
AST (U/L)	21.00 (18.00–25.00)	23.00 (19.00–27.00)	20.00 (17.00–23.00)	0.434
TG (mmol/L)	1.27 (0.89–1.91)	1.53 (1.05–2.31)	1.05 (0.78–1.47)	0.157
TC (mmol/L)	5.0 ± 1.0	5.1 ± 0.9	5.0 ± 1.0	0.026
HDL-C (mmol/L)	1.4 ± 0.4	1.4 ± 0.4	1.4 ± 0.4	0.070
LDL-C (mmol/L)	3.0 ± 0.9	3.1 ± 0.8	3.0 ± 0.9	0.003
FBS (mmol/L)	5.4 ± 1.3	5.5 ± 1.4	5.4 ± 1.2	0.001

*P values were calculated by Student's t-test for continuous variables, Wilcoxon rank sum test for skewed distribution data, and chi-square test for dichotomous data.
**Data are presented as mean ± standard deviation, median (interquantile range), or number.
BMI, body mass index; *WC*, waist circumference; *WHtR*, waist-to-height ratio; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure; γ-GT, γ-glutamyl transpeptidase; *ALT*, alanine aminotransferase; *AST*, aspartate aminotransferase; *TG*, triglycerides; *TC*, total cholesterol; *HDL-C*, high-density lipoprotein cholesterol; *LDL-C*, low-density lipoprotein cholesterol; *FBS*, fasting blood sugar.

Meanwhile, we analyzed prevalence of *H. pylori* infection among each risk factor. As shown in Table 4, the prevalence of *H. pylori* infection increased with increasing age; 26.0% of infected subjects were <25 years old, 29.7% were 35–44 years old, and 32.8% were ≥45 years old. Subjects with hyperglycemia had a higher rate of infection without considering sex differences. Low albumin was associated with a higher incidence for *H. pylori* infection.

4. Discussion

The rates of *H. pylori* infection have significantly decreased in developed Western countries, but the situation is less well-defined in developing countries like China. In this study, we aimed to investigate the prevalence of *H. pylori* infection and explore the potential risk factors for *H. pylori* infection. Our results showed that the prevalence of *H. pylori* infection was 34.4% in Chongqing. The results of this study also showed that older age, hyperglycemia, and low albumin are independent risk factors for *H. pylori* infection in the population from southwest China.

Age plays an important role in infection among the elderly. However, previous studies have shown ambiguous associations between *H. pylori* infection and age. Tarkhashvili et al. showed that *H. pylori* infection was associated with older age, and they attributed the higher infection rate to lower socioeconomic conditions (18). A study that aimed to explore associations between *H. pylori* infection and metabolic syndrome also showed a higher prevalence in older age groups (19). Another study, however, showed that the elderly had a relatively lower infection rate (10). In our study, the prevalence of *H. pylori* infection increased along with increasing age, and age was an independent risk factor for *H. pylori* infection. On one hand, adults who had relatively poor childhood living conditions experienced higher rates of *H. pylori* infection; the infection persisted throughout life unless specific measures were taken (20,21). On the other hand, although *H. pylori* infection was highly prevalent, only 10%–20% of infected people became symptomatic, which leads to lack of accurate measures for eradication (22). Both factors may

Table 2. Univariate logistic regression analysis for risk factors associated with *H. pylori* infection.

Age (years)	P-value	*OR*	95% *CI* of *OR*
25–34	0.202	1.200	0.907–1.587
35–44	0.020	1.383	1.053–1.817
≥45	0.000	1.715	1.310–2.244
Sex	0.154	0.944	0.872–1.022
BMI			
Overweight	0.138	1.067	0.979–1.161
Obese	0.729	1.025	0.890–1.181
WHtR > 0.5	0.346	1.039	0.960–1.124
SBP	0.131	1.002	0.999–1.004
DBP	0.526	1.001	0.998–1.004
Low albumin	0.000	1.205	1.097–1.325
γ-GT	0.456	1.000	0.999–1.001
ALT	0.478	0.999	0.998–1.001
AST	0.245	0.998	0.994–1.001
High TC	0.608	1.034	0.909–1.177
High TG	0.091	1.092	0.986–1.210
Low HDL-C	0.087	0.900	0.797–1.015
High LDL-C	0.188	1.096	0.956–1.255
Hyperglycemia	0.000	1.353	1.190–1.539

BMI, body mass index; *WC*, waist circumference; *WHtR*, waist-to-height ratio; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure; γ-GT, γ-glutamyl transpeptidase; *ALT*, alanine aminotransferase; *AST*, aspartate aminotransferase; *TG*, triglycerides; *TC*, total cholesterol; *HDL-C*, high-density lipoprotein cholesterol; *LDL-C*, low-density lipoprotein cholesterol; *OR*, odds ratio; *CI*, confidence interval.

Table 3. Multivariable logistic regression analysis for risk factors associated with *H. pylori* infection.

Age (years)	P	*OR*	95% *CI*
35–44	0.035	1.343	1.021–1.765
≥45	0.001	1.610	1.228–2.111
Low albumin (g/L)	0.010	1.136	1.031–1.251
Hyperglycemia (mmol/L)	0.001	1.258	1.103–1.434

OR, odds ratio; *CI*, confidence interval.

Table 4. Prevalence of *H. pylori* infection among the risk factors.

Age (years)	Total	(%)	Men	(%)	Women	(%)
<25	75/288	26.0	41/149	27.5	34/139	24.5
25–34	605/2037	29.7	352/1179	29.9	253/858	29.5
35–44	1089/3325	32.8	574/1839	31.2	99/289	34.3
≥45	1981/5262	37.6	982/2607	37.7	999/2655	37.6
FBS (mmol/L)						
Normoglycemia	3311/9834	33.7	1652/5036	32.8	1659/4798	34.6
Hyperglycemia	439/1078	40.7	297/738	40.2	142/340	41.8
Albumin (g/L)						
<P25	896/2376	37.7	336/882	38.1	560/1494	37.5
P25–P50	1150/3074	37.4	566/1451	39.0	584/1623	36.0
P50–P75	568/1640	34.6	295/889	33.2	273/751	36.4
≥P75	1136/3822	29.7	752/2552	29.5	384/1270	30.2

BMI, body mass index; *FBS*, fasting blood sugar.

have resulted in a cumulative effect in the older group and thus a higher prevalence in the elderly. However, further studies are needed to understand the associations between age and *H. pylori* infection.

The main physiological function of serum albumin is to maintain the colloid osmotic pressure and as a marker for liver synthetic function. In our study, we found a significant association between low serum albumin and *H. pylori* infection. Our data showed that the group with serum albumin ≥48 g/L had the lowest rate of infection, while the group with serum albumin <45 g/L had the highest rate of infection. However, there is ambiguity in the current published literature about the pathophysiologic relationship between serum albumin and *H. pylori* infection. The mechanisms might involve declining physiologic functions in the elderly and compromised liver synthetic function, which resulted in low serum albumin; low serum albumin was shown to be linked to infection and longer duration of hospitalization (23,24). Furthermore, previous studies have shown that albumin has important immunomodulation and anti-inflammatory activities (25). Infusion of albumin had positive effects in patients suffering from infection (26,27). Those results indicate that the subjects with low albumin are more likely to be infected with *H. pylori*.

As demonstrated previously, some reports have shown that there is a significantly higher infection rate and lower eradication rate among subjects with diabetes mellitus (11,28,29). In the present study, hyperglycemia has been shown to be a significant risk factor for *H. pylori* infection. Although the pathological mechanism is unclear, available findings can partially explain the potential mechanisms through which hyperglycemia can lead to higher rates of *H. pylori* infection. Hyperglycemia has been shown to increase endothelial permeability and alter basement membrane composition and structure (30,31), making it easier for *H. pylori* infection to occur. Meanwhile, a study from Shew-Meei Sheu's group also showed that hyperglycemia played a positive role in maintaining *H. pylori* growth and viability and enhancing bacterial adhesion (32).

Some results of the present study appear to be discordant with expected patterns. The prevalence of *H. pylori* infection was 34.4% in Chongqing at the time of this study, similar to our previous study (33). However, it was much lower than previously published studies (16). Several reasons may contribute to the differences. First, a previous study showed that *H. pylori* infection was significantly and inversely associated with socioeconomic status (34). The subjects in this study who had a health check-up in third-level Grade A hospitals had a relatively better income, which might have resulted in the lower rates of *H. pylori* infection in this study. Secondly, identification of the presence of *H. pylori* infection was obtained via different methods, and some of the tests for *H. pylori* may have resulted in a higher false-positive rate than the urea breath test. Previous studies have shown that *H. pylori* infection was associated with high BMI, lower HDL-

cholesterol, sex differences, higher levels of blood pressure, and total cholesterol (35,36). However, we did not find an association between the above-mentioned factors and *H. pylori* infection in this study. The reasons may be that the populations enrolled in different studies may have had different characteristics and genetic backgrounds, different inclusion criteria, different cultural traditions or eating patterns, or were from different geographic regions. Those factors need to be investigated further.

We must acknowledge that there were limitations in this study. First, we did not collect information on the use of drugs for *H. pylori* infection treatment before the ^{13}C-urea breath test examination and excluded the subjects with a history of antibiotic use for *H. pylori* infection, which might have led to underestimation of the prevalence of *H. pylori* infection. Second, although we had a large population, the analysis was based on data from only one center and there was limited information on the subjects. A multicenter study and additional information such as education status, smoking, number of people in household, alcohol intake, socioeconomic status, and quality of water supply should be collected to reduce bias and validate the results in this study. Finally, because this was a cross-sectional design, the association between the potential risk factors and infection with *H. pylori* could not be proven conclusively. Longitudinal studies should be carried out to confirm the results before extrapolating them to other areas.

In conclusion, our study showed that the current infection rate of *H. pylori* was 34.4% in Chongqing. We also showed that older age, low albumin, and hyperglycemia were independent risk factors for *H. pylori* infection. However, further studies are needed to further identify the risk factors that will be helpful in developing strategies for the prevention of *H. pylori* infection.

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