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ORIGINAL RESEARCH

Sex-Specific Risk Factors Associated with *Helicobacter pylori* Infection Among Individuals Undergoing Health Examinations in China

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Purpose: *Helicobacter pylori* is one of the most common causes of peptic ulcers, gastritis, and gastric cancers. This study investigated sex-specific differences in the prevalence of *H. pylori* infection and its associated factors among individuals undergoing hospital-based health examinations in southern China.

Methods: This study enrolled consecutive healthy individuals who underwent regular health examinations at a hospital physical examination center between September 2020 and September 2021. Anthropometric characteristics and biochemical profiles were measured. All individuals underwent carbon-13 urea breath tests. Univariate and multivariate analyses were used to evaluate the factors associated with *H. pylori* infection.

Results: A total of 5035 individuals (men, 59.1%; women, 40.9%) were included in the analyses. The total rate of *H. pylori* infection was 35.0% (men, 35.5%; women, 34.3%). In the multivariate analysis, the risk factors identified for *H. pylori* infections were high fasting blood glucose levels and blood pressure ≥160 mmHg in men and older age, high body mass index, and low albumin levels in women.

Conclusion: These findings suggest that physicians must be aware of the metabolic factors associated with *H. pylori* infections in the Chinese population. Early detection of these factors and timely intervention are expected to reduce *H. pylori* infections and provide a theoretical basis for the primary prevention of several gastrointestinal diseases.

Keywords: *Helicobacter pylori* infection, gastrointestinal disease, sex differences, prevalence, metabolic factors

Introduction

Helicobacter pylori is a spiral-shaped Gram-negative bacterium, which plays a role in the development of gastritis, peptic ulcers, and gastric cancers in humans. In recent years, *H. pylori* infections have been reported to be closely related to cardiovascular disease and its risk factors.[1] Moreover, *H. pylori* has recently been listed as a human carcinogen by the National Toxicology Program of the US Department of Health and Human Services.[2]

H. pylori infections are estimated to exist in more than half of the global population,[3] especially in developing countries where the incidence may reach 80–90%.[4] China is a high-incidence area of *H. pylori* infection.[5] In addition, the prevalence of *H. pylori* infections varies based on geographical locations, environmental factors, sociodemographic characteristics, and socioeconomic status.[6] With the rapid economic growth and development observed in recent decades, an evaluation of the prevalence of *H. pylori* infections observed during routine checkups in a small segment of the population is expected to reflect the prevalence of these infections in the general population.

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The factors associated with *H. pylori* infections have not been firmly established. Socioeconomic status is an important determinant that is negatively correlated with *H. pylori* infection.[7] Additionally, *H. pylori* infections appears to be more prevalent among men than among women. Recently, metabolic factors have gained increasing attention owing to their possible association with *H. pylori* infection. Individuals who are overweight or obese tend to have a higher prevalence of *H. pylori* infections.[8] Moreover, potential associations between metabolic syndrome, insulin resistance, and *H. pylori* infection have been observed in several studies.[9] However, few data are available regarding sex-specific differences associated with *H. pylori* infections, especially in urban, developed areas in China.

In this study, we evaluated the prevalence of *H. pylori* infection in healthy individuals undergoing routine health examinations in one region of China to identify sex-specific metabolic factors associated with *H. pylori* infection.

Methods

Participant Selection and Study Design

This retrospective study enrolled adults aged ≥18 years undergoing the regular health examination at the Third People's Hospital of Shenzhen between September 2020 and September 2021. The analyses were limited to participants with complete anthropometric and biochemical data and those who had *H. pylori* test results.

The study was approved by the Ethics Committee of the Third People's Hospital of Shenzhen and conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent. In this study, personal identification information was anonymized and replaced with a coding system.

Information Collection

Information on sex, age, and clinical examinations was collected from the medical records. Each participant's clinical examination included anthropometric and laboratory measurements. Age was categorized into five groups: <30 years, 30–39 years, 40–49 years, 50–59 years, and ≥60 years.

Anthropometry

Anthropometric indicators included height, weight, and blood pressure. All measurements were performed by trained doctors or nurses using standard methods. Height and weight were measured with the participant wearing light clothing and no shoes. Blood pressures, both diastolic (DBP) and systolic (SBP), were recorded using an automated sphygmomanometer. Diagnoses of hypertension and diabetes were based on participant self-reports or medical records. Body mass index (BMI) was calculated using the following formula: weight [kilogram (kg)] divided by the square of the height [meter (m)]. Participants with a BMI <24.0 kg/m^2, 24.0~27.9 kg/m^2 and ≥28.0 kg/m^2 were defined as the normal weight, overweight, and obesity groups, respectively.

Laboratory Measurements

Fasting blood samples were obtained for biochemical examinations following an overnight fast of at least 12 hours. Laboratory measurements included fasting blood glucose (FBG), total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), serum albumin, and uric acid.

H. pylori Test

H. pylori infections were diagnosed based on the results of a fasting carbon-13 urea breath test (^{13}C-UBT). A ^{13}C-UBT is one of the most reliable, widely applied, and noninvasive methods used to test for *H. pylori* infection.[10,11]

The ^{13}C-UBT was carried out according to standard procedures.[12] Briefly, participants were required to fast for at least 2 hours; discontinue various antibiotics within 1 month of the test; and discontinue use of any proton pump inhibitors, bismuth, or H2-receptor inhibitors within 2 weeks of the test. A baseline breathing sample was collected by asking each person to blow through a straw into a 10-mL plastic container. Then, the individual was required to take a tablet containing 75 mg of ^{13}C-urea with 100 mL of water. A second breath sample was collected 30 minutes later. The breath samples were analyzed using an infrared heterodyne radiometer. If the 30-minute sample demonstrated a value that was >4% different from the baseline value, the participant was considered to have tested positive for an *H. pylori* infection.

Statistical Analysis

Continuous variables (including age, BMI, SBP, DBP, FBG, TC, TG, HDL-C, LDL-C, uric acid, and albumin) were presented as means and standard deviations, while categorical variables (including sex, age group, BMI group, hypertension, diabetes, and nutrition risk) were presented as frequencies and percentages. Student's *t*-tests and Pearson's chi-squared tests were used to analyze differences in the means and proportions between patients with and without *H. pylori* infections and between the sexes. Factors associated with *H. pylori* infection were assessed separately for men and women using univariate and multivariable regression analyses. Significant variables ($P<0.1$) in the two-tailed univariate analyses were selected for multivariable logistic regression analyses. Age and BMI were analyzed as continuous variables in the multivariable logistic regression analyses. The results of the multivariate analysis are presented as odds ratios (ORs) and 95% confidence intervals (CIs), after adjusting for covariates. A two-tailed *P*-value of <0.05 was considered significant. All statistical analyses were performed using SPSS software (Version 19.0; SPSS; Chicago, IL, USA).

Results

Study Participant Characteristics by Sex

Of the 5035 participants enrolled in this study, 59.1% were men and 40.9% were women (Table 1). The overall average age of the participants was 39.18 years, with <5% of the participants being >60 years old. In the overall study population,

Table 1 Characteristics of All Participants by Gender

Category	Total	Men	Women	*P*-value
Total	5035 (100)	2974 (59.1)	2061 (40.9)	
Age, means (SD), years	39.18 (10.71)	39.14 (10.17)	39.24 (11.45)	0.729
Age group, n (%)				<0.001
<30 years	947 (18.8)	489 (12.4)	458 (22.2)	
30–39 years	1942 (38.6)	1223 (41.4)	719 (34.9)	
40–49 years	1200 (23.8)	758 (25.5)	442 (21.4)	
50–59 years	756 (15.0)	411 (13.8)	345 (16.7)	
≥60 years	190 (3.8)	93 (3.1)	97 (4.7)	
BMI, means (SD), Kg/m^2	23.93 (3.62)	24.88 (3.51)	22.55 (3.30)	<0.001
BMI group, n (%)				<0.001
Normal	2634 (52.6)	1200 (40.5)	1434 (70.0)	
Overweight	1744 (34.8)	1264 (42.7)	480 (23.4)	
Obesity	632 (12.6)	496 (16.8)	136 (6.6)	
Hypertension, n (%)	631 (12.6)	435 (14.7)	196 (9.6)	<0.001
Diabetes mellitus, n (%)	368 (7.3)	279 (9.4)	89 (4.3)	<0.001
H. pylori positive, n (%)	1761 (35.0)	1055 (35.5)	706 (34.3)	0.373
SBP, means (SD), mmHg	120.45 (15.60)	123.36 (14.08)	116.26 (16.69)	<0.001
DBP, means (SD), mmHg	75.54 (10.57)	77.88 (10.51)	72.15(9.70)	<0.001
FBG, means (SD), mmol/L	5.33 (1.44)	5.46 (1.66)	5.15 (1.01)	<0.001
TC, means (SD), mmol/L	4.85 (0.95)	4.94 (0.96)	4.71 (0.92)	<0.001
TG, means (SD), mmol/L	1.62 (1.32)	1.93 (1.48)	1.18 (0.87)	<0.001
HDL-C, means (SD), mmol/L	1.30 (0.35)	1.17 (0.28)	1.50 (0.34)	<0.001
LDL-C, means (SD), mmol/L	3.09 (0.86)	3.22 (0.86)	2.90 (0.82)	<0.001
Uric acid, means (SD), umol/L	362.27 (98.97)	410.25 (87.34)	292.82 (69.11)	<0.001
Albumin, means (SD), g/L	46.64 (2.63)	47.28 (2.58)	45.75 (2.43)	<0.001

Abbreviations: SD, standard deviation; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; FBG, fasting blood glucose; TC, total cholesterol; TG, triglycerides; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol.

the prevalence of hypertension and diabetes was 12.6% and 7.3%, respectively. The overall average BMI (23.93 kg/m^2), SBP (120.45 mmHg), DBP (75.54 mmHg), FBG (5.33 mmol/L), TC (4.85 mmol/L), TG (1.62 mmol/L), HDL (1.30 mmol/L), LDL (3.09 mmol/L), uric acid (362.27 μmol/L), and albumin (46.64 g/L) levels were determined.

H. pylori Infection Prevalence

H. pylori infections were diagnosed in 1761 (35.0%) participants, with a prevalence of 35.5% and 34.3% among men and women, respectively. The difference between the prevalence rates was not significant (*P*=0.373; Table 1).

Risk Factors of *H. pylori* Infection in Men

We analyzed the risk factors for *H. pylori* infection by sex. Table 2 shows the univariate analysis, demonstrating that the primary risk factor for *H. pylori* infection in men was the FBG level (*P*=0.002).

After adjusting for age, blood pressure, and FBG levels (all *P*<0.1 in the univariate analysis), a high FBG level (OR=1.089; 95% CI, 1.024–1.157; *P*=0.007) and blood pressure ≥160 mmHg (OR=2.202; 95% CI, 1.173–4.138; *P*=0.014) remained significantly associated with a high risk of *H. pylori* infection in the multivariate analysis (Table 3). The nomogram shows that 42 points for blood pressure ≥160 mmHg, 100 points for FBP (Supplemental Figure 1).

Risk Factors of *H. pylori* Infection in Women

For women, the univariate analysis showed that age, BMI, SBP, FBG, TC, HDL-C, LDL-C, and albumin levels were associated with *H. pylori* infection (all *P*<0.05; Table 2).

After adjusting for all variables with *P*<0.1 in the univariate analysis (age, BMI, SBP, FBG, HDL-C, LDL-C, and albumin), only age (OR=1.203; 95% CI, 1.031–1.405;*P*=0.019), BMI (OR=1.169; 95% CI, 1.012–1.352; *P*=0.034), and

Table 2 Associated Factors of *Helicobacter Pylori* Infection by Gender in Univariate Analysis

Risk Factors	Men			Women		
	HP+ Group	HP-Group	*P*-value	HP+ Group	HP-Group	*P*-value
Age, means (SD), years	36.92 (10.24)	39.87 (10.07)	0.052	40.95 (11.90)	38.35 (11.11)	<0.001
Age group, n (%)			0.406			<0.001
<30 years	172 (35.2)	317 (64.8)		128 (27.9)	330 (72.1)	
30–39 years	414 (33.9)	809 (66.1)		236 (32.8)	483 (67.2)	
40–49 years	279 (36.8)	479 (63.2)		165 (37.3)	277 (62.7)	
50–59 years	151 (36.7)	260 (63.3)		125 (36.2)	220 (63.8)	
≥60 years	39 (41.9)	54 (58.1)		52 (53.6)	45 (46.4)	
BMI, means (SD), kg/m^2	24.93 (3.54)	24.95 (3.50)	0.560	23.02 (3.34)	22.31 (3.27)	<0.001
BMI group, n (%)			0.423			0.001
Normal	419 (34.9)	781 (65.1)		455 (31.7)	979 (68.3)	
Overweight	444 (35.1)	820 (64.9)		188 (39.2)	292 (60.8)	
Obesity	189 (38.1)	307 (61.9)		58 (42.6)	78 (75.4)	
Hypertension, n (%)	171 (39.3)	264 (60.7)	0.069	75 (38.3)	121 (61.7)	0.205
Diabetes mellitus, n (%)	114 (40.9)	165 (59.1)	0.044	38 (42.7)	51 (57.3)	0.084
SBP, means (SD), mmHg	123.97 (14.60)	123.02 (13.77)	0.078	118.27 (17.03)	115.22 (16.42)	<0.001
DBP, means (SD), mmHg	78.11 (10.70)	77.76 (10.42)	0.390	72.51 (9.54)	71.97 (9.79)	0.227
FBG, means (SD), mmol/L	5.61 (2.04)	5.38 (1.41)	0.002	5.21 (1.06)	5.12 (0.98)	0.036
TC, means (SD), mmol/L	4.95 (0.95)	4.93 (0.96)	0.609	4.79 (0.96)	4.67 (0.90)	0.007
TG, means (SD), mmol/L	1.96 (1.61)	1.91 (1.40)	0.427	1.20 (0.76)	1.16 (0.92)	0.372
HDL-C, means (SD), mmol/L	1.16 (0.29)	1.17 (0.28)	0.457	1.48 (0.34)	1.51 (0.35)	0.037
LDL-C, means (SD), mmol/L	3.22 (0.85)	3.22 (0.87)	0.976	3.00 (0.85)	2.86 (0.80)	<0.001
Uric acid, means (SD), umol/L	412.21 (86.86)	409.16 (87.61)	0.363	295.29 (69.18)	291.54 (69.06)	0.245
Albumin, means (SD), g/L	47.13 (2.61)	47.37 (2.56)	0.603	45.46 (2.30)	45.91 (2.49)	0.001

Abbreviations: SD, standard deviation; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; FBG, fasting blood glucose; TC, total cholesterol; TG, triglycerides; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol.

Table 3 Multivariable Analysis for Risk Factors Associated with *Helicobacter Pylori* Infection in Men and in Women

Categories	References	OR (95% CI)	*P-value*
Men:			
SBP group	<140 mmHg		—
140 mmHg ~		1.177 (0.914, 1.516)	0.207
≥160 mmHg		2.202 (1.173, 4.138)	0.014
Diabetes	No	0.896 (0.630, 1.276)	0.543
FBG	-	1.089 (1.024, 1.157)	0.007
Women:			
Age	-	1.203 (1.031, 1.405)	0.019
BMI	-	1.169 (1.012, 1.352)	0.034
SBP	-	0.985 (0.860, 1.128)	0.826
FBG	-	0.976 (0.875, 1.089)	0.662
HDL-C	-	0.987 (0.870, 1.119)	0.835
LDL-C	-	1.106 (0.981, 1.247)	0.099
Albumin	-	0.868 (0.770, 0.980)	0.022

Abbreviations: OR, odd ratio; SBP, systolic blood pressure; FBG, fasting blood glucose; BMI, body mass index; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol.

albumin level (OR=0.868; 95% CI, 0.770–0.980; *P*=0.002) were significantly associated with *H. pylori* infection (Table 3). The nomogram shows that 92.5 points for age, 93 points for BMI, and 85 points for albumin (Supplemental Figure 2).

Discussion

H. pylori infections are becoming an important health and social issue, especially in China, because of their increasing prevalence. In this study, we investigated the sex-specific differences of *H. pylori* infection based on health examination data from hospitals in first-tier cities in China. In our study, 35.0% of our cohort was positive for *H. pylori* infection (35.5% men and 34.3% women). Some metabolic factors were associated with *H. pylori* infection, including high FBG levels and blood pressure ≥160 mmHg in men and older age, high BMI, and low serum albumin levels in women.

Globally, *H. pylori* infection is the most common chronic infection, resulting in a serious disease burden. In addition to being an important pathogen associated with chronic gastritis and stomach cancers, *H. pylori* is also closely associated with the occurrence of non-gastrointestinal diseases. Interestingly, the prevalence of *H. pylori* infection varies by country and race. In developed countries, the prevalence of infection is declining,[13–15] however, *H. pylori* infections remains high in developing countries. A study from the gastroenterology department of an internal medicine facility in Beijing, China showed that the *H. pylori*-positive rate was as high as 50% among Chinese adults.[16] A recent study reported that the total prevalence of *H. pylori* infection among asymptomatic individuals was 55.2% in Wenzhou, China.[17] In our study, the prevalence of *H. pylori* infection was 35.0%, which is lower than the previously reported rate of 60% in the rural areas of China.[18,19] Considering that China is one of the most rapidly developing countries and that the socioeconomic status of residents has been improving significantly over recent decades, especially in the Shenzhen area where socioeconomic status and income levels are high, a declining trend in the prevalence of *H. pylori* infection may be occurring. Additionally, a study conducted in Taiwan showed a similar trend to our study in the prevalence of *H. pylori* infections in men and women.[20]

There is accumulating evidence that *H. pylori* infection are associated with a higher risk of diabetes and cardiovascular disease.[21–23] A study of 8820 participants in China revealed that *H. pylori*-positive participants had significantly higher BMIs, waist circumferences, SBPs, and serum levels of TC and LDL-C as well as lower serum HDL-C levels compared to *H. pylori*-negative participants.[24] Some studies have reported that *H. pylori* infections tend to be more prevalent in obese individuals.[8,9] A cross-sectional study of Taiwanese adults reported that *H. pylori* infection was positively associated with metabolic syndrome, especially in women.[20] In the present study, we found an association between *H. pylori* infection and elevated FBG levels and increased blood pressure in men but not in women. However, a positive correlation was found between *H. pylori* infection and BMI in women. These results support the hypothesis that sex-specific metabolic factors are associated with *H. pylori* infections. Larger sample sizes and additional studies are needed to further identify sex-specific risk factors of *H. pylori* infection.

Epidemiologic studies have shown that the prevalence of *H. pylori* infection varies considerably with age.[20] A cross-sectional study conducted in a university hospital in mainland China suggested that the rate of *H. pylori* infection increased with age in individuals <36 years old, but no significant correlation was detected between age and prevalence in individuals >36 years old.[25] An observational study from an outpatient clinic in Turkey reported that *H. pylori* seropositivity was associated with increasing age, representing the combined effect of a lower childhood exposure rate (correlated with improved living standards) and a greater chance of acquiring an infection associated with duration of life.[26] A nationwide, multicenter study conducted over a 13-year period in Korea reported that the clinical risk factors associated with *H. pylori* infection were male sex and older age.[27] As expected from the results of previous studies, our results also showed that *H. pylori* infection was more prevalent in older women; however, this trend was not observed in men. This inconsistency may arise from differences in the study population, sample size, and *H. pylori* infection testing methodologies.

Serum albumin, the most abundant plasma protein, is the main determinant of plasma osmotic pressure and the main modulator of fluid distribution between body compartments.[28] Furthermore, previous studies have shown that albumin plays an important part in immunomodulation.[29] The results of our study showed that low albumin levels are associated with a higher prevalence of *H. pylori* infection in women, consistent with the findings of a previous study conducted in southwest China.[30] The study demonstrated that low albumin levels were an independent risk factor for *H. pylori* infection, with individuals with serum albumin levels ≥48 g/L having the lowest rate of infection and individuals with serum albumin levels <45 g/L having the highest rate.[30] Low serum albumin levels have been associated with increased infection susceptibility and hospitalization duration;[31] moreover, albumin infusions have been shown to have positive effects on patients with infections.[32]

This study has several limitations. First, the retrospective design of our study prevents the determination of causal relationships. Second, the participants attending the hospital-based health examination may not have been representative of the general Chinese population. For example, the socioeconomic status of the individuals who underwent health checkups may have been higher than the national average, limiting our ability to extend these findings to other regions. Third, some information was not recorded, including antibiotic use, history of gastrointestinal disease, smoking, drinking, and residence information, which can impact the relationship between metabolic factors and *H. pylori* infection. Thus, further investigation is needed to understand the underlying mechanisms of the association between metabolic factors and infection risk.

Conclusions

This study identified sex-specific differences in the association of metabolic factors with *H. pylori* infection in a population from southern China, providing data relevant to China's first-tier urban areas. However, the overall prevalence of *H. pylori* infection was 35.0%, with no significant difference between the sexes. High FBG levels and blood pressure ≥160 mmHg were positively associated with *H. pylori* infection in men, whereas older age, high BMI, and low albumin levels were risk factors in women. These findings support the importance of early detection of sex-specific metabolic factors related to *H. pylori* infections. Monitoring of these metabolic factors and appropriate intervention are needed to reduce the prevalence and burden of *H. pylori* infection in China.

Disclosure

The authors report no conflicts of interest in this work.

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