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The prevalence of Helicobacter pylori infection and the possible risk factors in Qingdao: a population based cross-sectional study

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Abstract: **Helicobacter pylori (H. pylori), a gram-negative, spiral-shaped pathogenic bacterium, causes many gastrointestinal and extra-gastric diseases. The prevalence of Helicobacter pylori varies in different countries of the world. The purpose of this study was to investigate the prevalence and risk factors of H. pylori infection in Qingdao. A population based cross-sectional study was carried out at the physical examination center of the Affiliated Hospital of Qingdao University from April to August 2018. 1690 cases were given H. pylori urease-IgG antibodies detection in serum for the diagnosis of H. pylori infection. The rate of H. pylori infection was 27.6%. The univariate logistic regression analysis indicated that the neutrophil count, the rate of age⩾45, male, overweight/obesity, smoking, alcohol using, high total cholesterol (TC), high white blood cell (WBC), hypertension, diabetes and nonalcoholic fatty liver disease (NAFLD) in H. pylori-positive subjects were significantly higher than the indicators of H. pylori-negative subjects (P<0.05). The multivariate logistic regression analysis indicated that age⩾45 (OR=1.30, 95%CI: 1.01-1.66), overweight/obesity (OR=1.36, 95%CI: 1.05-1.75), high WBC (OR=2.09, 95%CI: 1.16-3.77), diabetes (OR=1.78, 95%CI: 1.14-2.76) and NAFLD (OR=1.63, 95%CI: 1.21-2.19) were associated with the increased rate of H. pylori infection. Armed with these data, medical doctors will be able to better identify high-risk groups of H. pylori and provide patients with education about management and prevention/eradication strategies.**

Keywords: Helicobacter pylori; Body mass index; White blood cell; Diabetes; Nonalcoholic fatty liver disease

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1. Introduction

Helicobacter pylori (H. pylori), a gram-negative, spiral-shaped pathogenic bacterium, specifically colonizes the gastric epithelium and causes many gastrointestinal diseases[1], including peptic ulcers, chronic gastritis, gastric mucosa-associated lymphoid tissue lymphoma, and even gastric cancer[2, 3]. This latter condition is particularly important in China because gastric cancer is the second leading cause of cancer death[4]. One study showed that H. pylori-positive Asians had at least twice the risk of developing gastric cancer compared to H. pylori-negative Asians[5]. It is also associated with many diseases outside the stomach, including cardiovascular disease and autoimmune disease[6].

A meta-analysis shows that about 50% of the world population are infected with H. pylori, and the number of infected people was 4.4 billion in 2017[7], and the prevalence tends to be low in developed countries and high in developing countries[8]. It was reported that the infection rate of H. pylori in China, a developing country, was high in 2015, ranging from 41.4% to 80.4%[9]. Recently, however, the prevalence of H. pylori has declined in many parts of the world, especially in developed areas[10, 11].

Although the exact pathogeny of H. pylori infection is unknown, some authors have emphasized the role of factors such as age, sex, body mass index (BMI), smoking, alcohol consumption, hypertension, diabetes and nonalcoholic fatty liver disease (NAFLD) in the acquisition and transmission of H. pylori[12-17]. So far, there has been no large-scale research on countrywide H. pylori infection in China. Regional studies on the prevalence or possible risk factors of H. pylori infection have been reported in only some parts of China[9, 10, 12, 17, 18]. Qingdao, one of the more modernized cities in China, has not yet been reported on the risk factors of H. pylori infection. Therefore, a study has been initiated by us in the Affiliated Hospital of Qingdao University to elucidate this question.

2. Materials and methods

2.1. Study participants

Participants who volunteered for general health screening from April to August 2018 were recruited from the physical examination center of the Affiliated Hospital of Qingdao University.

Participants with any of the following characteristics were excluded from the study:

1) a history of gastric surgery;

2) the use of bismuth, antibiotics, proton pump inhibitors or H2 blockers in the prior 4 weeks;

3) severe infection;

4) a significant mental or neurological illness; and

5) a history of cancer;

6) a history of anti-H. pylori therapy

All subjects underwent a detailed physical examination, including serum tests for H. pylori urease-IgG antibodies. All participants provided informed consent before the inspection.

2.2. Data collection

The medical history of each subject was obtained through a questionnaire, including the history of the current illness, history of gastric surgery, history of major mental or neurological illness, history of cancer(s), use of bismuth, antibiotics, H2 blockers or proton pump inhibitors or in the past 4 weeks, alcohol consumption, and cigarette smoking. Smoking is defined as having smoked 400 or more cigarettes in the past and is currently smoking. Drinking is defined as drinking at least once a week for a month at the time of the survey.

BMI was defined as weight divided by height squared (kg/m^2). Fasting plasma high white blood cell (WBC), neutrophil, lymphocyte, fasting blood glucose (FBG), total cholesterol (TC), and triglyceride (TG) levels were measured after overnight fasting for 8 hours. Blood pressure measurements were obtained after taking a rest for at least 10 minutes.

According to the standards specified in the guidelines for the prevention and control of overweight and Obesity in Chinese Adults, BMI$<$ 18.5 kg/m^2 is underweight, 18.5$\leqslant$BMI$<$24.0 kg/m^2 is normal weight, 24.0 $\leqslant$ BMI $<$ 28.0 kg/m^2 is overweight, and BMI $\geqslant$ 28.0 kg/m^2 is obesity. According to the standards set by the World Health Organization, patients with FBG$\geqslant$7mmol/L or those who have been clearly diagnosed with diabetes and are taking hypoglycemic drugs are diagnosed with diabetes.

NAFLD was defined according to the guidelines issued by the American Association for the Study of Liver Diseases (AASLD), the American College of Gastroenterology (ACG), and the American Gastroenterological Association (AGA) in 2012[19]. In this study, the diagnostic requirements of NAFLD were as follows:

(1) hepatic steatosis detected by ultrasonography;

(2) no obvious alcohol using (in order to strictly eliminate the influence of alcohol, we chose individuals with alcohol consumption of less than 3 drink units per week);

(3) no co-existing causes of chronic liver disease, such as hepatitis C, parenteral nutrition, medications, Wilson's disease or severe malnutrition.

2.3. Statistical analysis

The fundamental information and results were described and compared. Mean± SD was used to describe normally distributed data and a t-test was used to compare the difference between the two groups. Data with a skewed distribution were described by the medians (interquartile range), and the difference of groups was compared with Wilcoxon rank-sum test. Frequency (percentage) is used to describe qualitative data, also the chi-square test was used to compare the difference between the two groups.

The univariate logistic regression was used to assess the association between some characters and Helicobacter pylori. Furthermore, we used a multivariate logistic regression model to build the risk factor models of Helicobacter pylori. The following factors were considered covariates: age, sex, overweight/obesity, smoking, alcohol using, high TG, high TC, high WBC, neutrophil count, lymphocyte count, hypertension, diabetes, and NAFLD, which were included when P-value$\leqslant$0.05. All P values were determined using a bilateral hypothesis test and the 95%CI was calculated. All statistical analyses were conducted using SPSS (version17.0).

3. Results

3.1. Demographic characteristics

Table1 showed demographic information. In general, 1690 individuals (1,222 men and 468 women) were enrolled in this study (Figure1). The medians (interquartile range) of age were 39(22) years in Helicobacter pylori positive group (HP+ group) and 35(20) years in Helicobacter pylori negative group (HP- group). What's more, the Wilcoxon rank sum test results showed that there was a difference between Helicobacter pylori positive group and negative group about ages($P<0.001$), and the percentage of people older than 45 in Helicobacter pylori positive group was higher than in Helicobacter pylori negative group. The rate of H. pylori infection was 27.6% (467 in 1690) in the physical examination population. In addition, just as the chi-square test showed, individuals who were smoking and/or alcohol use in HP+ group were higher than in HP- group ($P=0.019$, $P=0.007$ respectively). In addition, the BMI in HP+ group (Mean± SD) (25.73±5.47) was higher than in HP- group (24.26±4.84), and the T-test showed that the BMI was different between the two groups ($P<0.001$). The table1 also showed that from the demographic distribution of BMI groups the percentage of overweight and normal weight people in the HP+ group was the highest as well as in the HP- group.

3.2. Clinical characters

The median (interquartile range) of Triglyceride (TG) and total cholesterol (TC) were 1.15(0.86) mmol/L and 5.03 (1.24) mmol/L respectively in HP+ group, which were higher than in HP- group (the medians (interquartile range) of TG and TC were 1.04 (0.87) mmol/L and 4.80 (1.26) mmol/L) (both P<0.001). Moreover, the individuals who suffered high TC in the HP+ group were less than in HP- group (64 vs 117, P=0.014). We also reached that the blood WBC count in the HP+ group was (10^9/L, Mean± SD) 6.68±1.75, which was higher than in the HP- group 6.39±1.59 (P<0.001). The difference between the two groups in the results of the Neutrophil count was like the WBC count (3.88±1.35 vs 3.66±1.33) (P<0.001). The individuals who suffered from NAFLD, hypertension or diabetes in HP+ group were less than in HP- group (all P<0.001) (See table 2 for details).

3.3. Univariate logistic regression analysis

A univariate logistic regression analysis was applied to evaluate the risk of the infection of H. pylori. The results were shown in Table 3. It indicated that the neutrophil count, the rate of age≥45, male, overweight/obesity, smoking, alcohol use, High TC, High WBC, hypertension, diabetes, and NAFLD in HP+ subjects were significantly higher than the indicators of HP- subjects (All P<0.05), which indicated that these factors are risks for increased the infection of H. pylori.

3.4. Multivariate logistic regression analysis

We further built a multivariate logistic regression model to analyze the risk factors of H. pylori infection by considering the combination of age≥45, male, overweight/obesity, smoking, alcohol use, high TC, high WBC, hypertension, diabetes, and NAFLD. After adjusting male, smoking, alcohol use, high TC, and hypertension, the results indicated that age≥45 (OR=1.30, 95%CI: 1.01-1.66), overweight/obesity (OR=1.36, 95%CI: 1.05-1.75), High WBC (OR=2.09, 95%CI: 1.16-3.77), diabetes (OR=1.78, 95%CI: 1.14-2.76) and NAFLD (OR=1.63, 95%CI: 1.21-2.19) were associated with the increased rate of H. pylori infection.

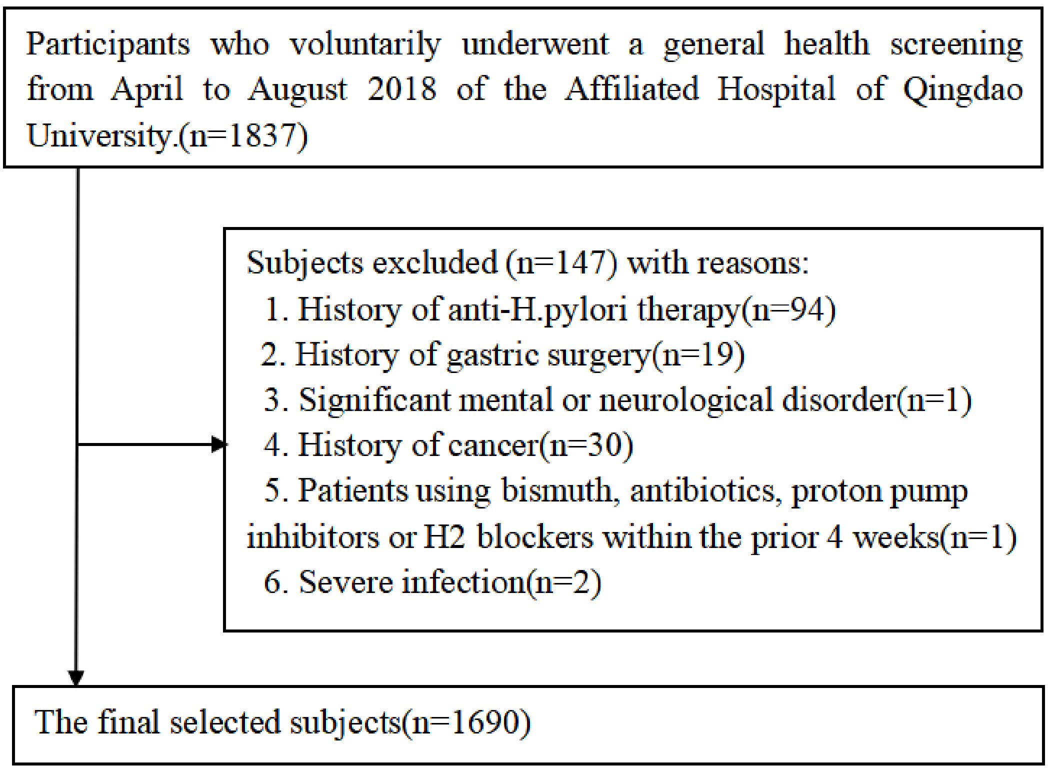

Figure 1. Flow diagram.

Table 1.Characteristics of the physical examination population

Variable	Total	HP+	HP-	*P*
N of subjects, %	1690	467(27.6)	1223(72.4)	-
Age (year, M, Q)	36,20	39,22	35,20	<0.001[a]
Age groups (year, n, %)	-	-	-	<0.001[b]
15~44	1091(64.6)	264(56.5)	827(67.6)	-
45~86	599(35.4)	203(43.5)	396(32.4)	-
Male (n, %)	1222(72.3)	354(75.8)	868(71.0)	0.047[b]
Smoking (n, %)	413(24.6)	133(28.5)	280(23.0)	0.019[b]
Alcohol using (n, %)	377(22.4)	125(26.8)	252(20.7)	0.007[b]
Height(cm, Mean±SD)	169.63±8.31	169.67±8.35	169.62±8.29	0.904[c]
Weight(kg, Mean±SD)	72.13±14.44	75.85±15.94	70.71±13.57	<0.001[c]
BMI(kg/m^2, Mean±SD)	24.65±5.02	25.73±5.47	24.26±4.84	<0.001[c]
BMI groups (kg/m^2, n, %)	1686	467(27.7)	1219(72.3)	<0.001[b]
Underweight	50(3.0)	6(1.3)	44(3.6)	-
Normal weight	658(39.0)	143(30.6)	515(42.2)	-
Overweight	643(38.1)	181(38.8)	462(37.9)	-
Obesity	335(19.9)	137(29.3)	198(16.2)	-

Note: BMI: body mass index, HP: Helicobacter pylori; M, Q: median, interquartile range.
a: Wilcoxon rank sum test.
b: Chi-square test.
c: t test.

Table 2. Biochemical indicators and disease characteristics of physical examination population

Variable	Total	HP+	HP-	*P*
N of subjects	1690	467	1223	-
TG (mmol/L, M, Q)	1.07,0.89	1.15,0.86	1.04,0.87	<0.001[a]
TC (mmol/L, M, Q)	4.85,1.26	5.03,1.24	4.80,1.26	<0.001[a]
High TG (n, %)	207(12.3)	63(13.5)	144(11.9)	0.352[b]
High TC (n, %)	181(10.8)	64(13.8)	117(9.6)	0.014[b]
WBC count(10^9/L, Mean±SD)	6.47±1.65	6.68±1.75	6.39±1.59	<0.001[c]
High WBC (n, %)	52 (3.1)	23 (4.9)	29 (2.4)	0.006[b]
Neutrophil count (10^9/L, Mean±SD)	3.72±1.34	3.88±1.35	3.66±1.33	<0.001[c]
Lymphocyte count (10^9/L, Mean±SD)	2.21±0.60	2.23±0.62	2.20±0.59	0.298[c]
Hypertension (n, %)	364(21.6)	135(28.9)	229(18.6)	<0.001[b]
Diabetes (n, %)	100(5.9)	48(10.3)	52(4.3)	<0.001[b]
NAFLD (n, %)	359(21.5)	133(28.9)	226(18.7)	<0.001[b]

Note: TG: Triglyceride; TC: Total cholesterol; High TG: TG⩾2.27mmol/L; High TC： TC⩾6.19 mmol/L; WBC: white blood cell; High WBC: WBC⩾10×10^9/L; NAFLD: non-alcoholic fatty liver disease. M, Q: median, interquartile range.
a: Wilcoxon rank sum test.
b: Chi-square test.
c: t test.

Table 3. Univariate Logistic regression analysis of Risk of Helicobacter pylori infection in physical examination population

Variable	OR	95%CI	*P*
Age≥45(year)	1.61	1.29-2.00	<0.001
Male	1.28	1.01-1.64	0.048
Overweight/Obesity	1.81	1.44-2.26	<0.001
Smoking	1.33	1.05-1.70	0.019
Alcohol using	1.40	1.09-1.79	0.008
High TG	1.16	0.85-1.60	0.352
High TC	1.50	1.08-2.07	0.015
High WBC	2.14	1.23-3.74	0.007
Neutrophil count	1.13	1.04-1.22	0.002
Lymphocyte count	1.10	0.92-1.31	0.298
Hypertension	1.75	1.37-2.24	<0.001
Diabetes	2.58	1.72-3.88	<0.001
NAFLD	1.77	1.38-2.27	<0.001

Note: TG: Triglyceride; TC: Total cholesterol; High TG: TG⩾2.27mmol/L; High TC: TC⩾6.19 mmol/L; WBC: white blood cell; High WBC: WBC ⩾10×10^9/L; NAFLD: non-alcoholic fatty liver disease

4. Discussion

In our study, the rate of H. pylori infection was 27.6%. This is somewhat surprising as China is considered a developing country, suggesting that the prevalence of current H. pylori infection is lower than in other developing countries and even some developed countries. The prevalence was 32.7% in the United States[20], 31.7% in the Netherlands[21], 44.3% in Japan[22], and 54.4% in Korea[23]. This low prevalence was partially because of the urban population recruited in our study. In the city of Guangzhou, Chen et al. studied the rates of H. pylori infection in 1993 and 2003. The H. pylori infection rate was reported as 63.2% in 1993, and it declined to 49.3% in 2003, which suggests that the seroprevalence of H. pylori infection significantly decreased in Guangzhou during that 10-year period. This change may be attributable to the improvement in the socioeconomic conditions in this city[24]. This result has also been verified by other studies. The H. pylori infection rate among rural laborers in Dongguan is 57.9%, while in Beijing and Dalian, the prevalence seems to be substantially lower[12, 25]. A 2017 study shows that the prevalence in a Chinese city is 31.9%, which is very close to the results of our study. This study clearly pointed out that the prevalence rate of H. pylori infection was related to gross domestic product (GDP)[10].

This study also indicated that age ⩾ 45, overweight/obesity, High WBC, diabetes and NAFLD were associated with the increased rate of H. pylori infection.

Table 4. Multivariate logistic regression analysis of Risk of Helicobacter pylori infection in physical examination population

Variate	OR	95%CI	*P*
Age≥45(year)	1.30	1.01-1.66	0.038
Male	1.00	0.74-1.33	0.970
Overweight/Obesity	1.36	1.05-1.75	0.020
Smoking	1.09	0.80-1.46	0.595
Alcohol using	1.32	0.95-1.85	0.103
High TC	1.16	0.82-1.64	0.405
High WBC	2.09	1.16-3.77	0.014
Hypertension	1.25	0.94-1.64	0.121
Diabetes	1.78	1.14-2.76	0.011
NAFLD	1.63	1.21-2.19	0.001

Note: TC: Total cholesterol; High TC: TC⩾6.19 mmol/L; WBC: white blood cell; High WBC: WBC ⩾ 10×10^9/L; NAFLD: non-alcoholic fatty liver disease.

The birth cohort effect may explain this phenomenon. The acquisition of H. pylori occurs almost entirely in children and adolescence. Unless it is eradicated, it usually persists in the stomach as a chronic infection into adulthood[26]. With the improvement of living standards in recent decades, the infection acquisition rate in the young birth cohort was significantly lower than that of the previous generation.

Obesity can change innate and adaptive immunity and immunity deterioration is related to the degree of obesity. Morbidly obese patients have lower maturation of monocytes into macrophages and reduced polymorphonuclear (PMN) bactericidal ability. The activity of NK cells in severely obese patients is significantly lower than that in comparison to normal individuals matched for age and gender. The immune response of obese people is also suggested to be impaired, indicating that the immune environment of obese people is more beneficial to the survival of H. pylori[13].

H. pylori infection may interact with obesity. Several potential factors may be involved. (1) Ghrelin and leptin, gastrointestinal hormones, are involved in metabolic control and energy balance. Ghrelin is produced in the stomach and stimulates food intake. The effect of leptin is just the opposite.

Studies reported lower levels of serum leptin and Ghrelin in H. pylori-positive patients[27]. Leptin can inhibit eating, and its reduction may be related to excessive eating and obesity. While the decrease in plasma Ghrelin concentration represented a physiological adaptation to the positive energy balance associated with obesity[28]. (2) Insulin resistance is an important risk factor for many common metabolic disorders. Insulin resistance is an important risk factor for many common metabolic disorders. A Japanese study found that H. pylori infection has a potential role in promoting insulin resistance[29]. As a result, people infected with H. pylori may be more likely to be obese.

Although there is no concrete evidence demonstrating that diabetes plays a role in H. pylori infection, there are several pieces of evidence that diabetic patients are more susceptible to infection. (1) Impaired cellular and humoral immunity caused by diabetes may increase individual sensitivity to H. pylori infection[30]. (2) Diabetes-induced decrease of gastrointestinal motility and gastric acid secretion may promote colonization and infection rate of pathogenin in the gut[31]. (3) Individuals with diabetes are exposed to pathogens more frequently than their healthy counterparts because they regularly go to the hospital[32].

NAFLD was associated with an increased rate of H. pylori infection, but the possibility for a causal relationship is an intriguing issue worthy of discussion. Polyzos et al[33] demonstrated that patients with NAFLD had significantly higher anti-H. pylori IgG, homeostasis model assessment of insulin resistance (HOMA-IR), and tumor necrosis factor (TNF)-a levels than those in the control group. They further studied the eradication of H. pylori and the results showed that the NAFLD fibrosis score tended to improve[34]. Histological evaluation showed that H. pylori infection was related to hepatocyte ballooning. Ying-ying Yu et al found that chronic H. pylori infection can cause higher inflammatory response as indicated by the WBC level, which was consistent with our study. H. pylori infection was more frequently observed in NAFLD patients than in the control group. H. pylori infection with high WBC levels may be related to the pathogenesis of NAFLD[17].

This study had some limitations. (1) The subjects were recruited from the physical examination center and do not represent the general population. (2) The H. pylori infection status was only based on serum IgG results from a rapid urease test, without pathological examination or bacteria culture. Serological results cannot distinguish between current and past infections. (3) This is a cross-sectional study, which can only draw conclusions about the association between H. pylori infection and the factors, but not the cause-effect relationship.

5. Conclusion

In conclusion, this study has important public health significance. Armed with these data, medical doctors will be able to better identify high-risk groups of H. pylori and provide patients with education about management and prevention/eradication strategies. Future studies should include prospective studies to show the cause-effect relationship between H. pylori and other diseases.

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Conflicts of Interest

The authors declare no conflict of interest.

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