JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Original Article

Association between *Helicobacter pylori* infection and overweight or obesity in a Chinese population

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Abstract

Introduction: Recent studies found that *Helicobacter pylori* (*H. pylori*) infection plays a role in cardiometabolic disorders. The objective of this study was to assess the association between *H. pylori* infection and overweight or obesity in a Chinese population.

Methodology: A cross-sectional analysis using data from the subjects who underwent a health examination between January 2010 and June 2012 in the department of comprehensive medicine was performed. Diagnosis of *H. pylori* infection was achieved using the carbon urea breath test (^{14}C-UBT). The participants were divided into *H. pylori* infection-positive group and *H. pylori* infection-negative group by ^{14}C-UBT.

Results: A total of 2,050 subjects were enrolled in the study. The *H. pylori* infection-positive group had significantly higher body mass index (BMI) levels than did the *H. pylori* infection-negative group (25.32 *vs* 24.95, p = 0.008). There was a positive association between *H. pylori* infection and BMI levels ($\beta = 0.30 \pm 0.12$, p = 0.015). After additional adjustment for white blood cell count (WBCC), the statistical significance disappeared ($\beta = 0.24 \pm 0.12$, p = 0.053). Furthermore, a positive association between *H. pylori* infection and overweight/obesity according to different BMI criteria (BMI ≥ 24, BMI ≥ 23) was found. However, the association between *H. pylori* infection and obesity was consistently significant only based on the Asian criteria (BMI ≥ 27.5), but not significant based on the Chinese criteria (BMI ≥ 28).

Conclusion: *H. pylori* infection was significantly and positively associated with overweight/obesity in a Chinese population.

Key words: *Helicobacter pylori* infection; body mass index; overweight; obesity.

J Infect Dev Ctries 2015; 9(9):945-953. doi:10.3855/jidc.6035.

(Received 08 October 2014 – Accepted 01 April 2015)

Introduction

Obesity has become a severe public health problem worldwide. Health conditions caused or exacerbated by obesity include diabetes mellitus, hypertension, sleep apnea, coronary heart disease, hyperlipidemia, tumors, and other severe chronic diseases [1,2]. The World Health Organization (WHO) defines obesity as a global epidemic. The prevalence of overweight or obesity in China increased rapidly in recent years [3,4]. Obesity is traditionally considered a non-communicable disease, but studies from several laboratories over the past 30 years suggest that some microbe infections might be linked to obesity in animals and humans, a condition termed "infectobesity". On the other hand, obese subjects show an altered response to infection [5,6].

Helicobacter pylori (*H. pylori*) are Gram-negative bacteria that colonize gastric mucosal epithelium of humans and some primates [7,8]. In recent years, studies have shown that *H. pylori* infection not only leads to various gastro-duodenal diseases such as chronic gastritis, peptic ulcer, mucosa-associated lymphoid tissue lymphoma (MALT), and gastric cancer [9,10], but also plays a role in cardiometabolic disorders[11]. While conclusive evidence for a causative role of *H. pylori* infection in human obesity is lacking, the relationship between *H. pylori* and obesity is still controversial[12-14]. Reports from different areas and countries were not consistent with each other. The aim of this study was to determine the association between *H. pylori* infection and overweight or obesity in a Chinese population.

Methodology

Study population

In total, 2,588 Chinese subjects who underwent a health examination between January 2010 and June 2012 in the department of comprehensive medicine in

Tongji Hospital (Wuhan, China) were enrolled in the present study. If the subjects received repeated health examinations, only the first health examination results were observed. These subjects were all employed in administrative units of Wuhan and thus had a similar socioeconomic status, judged by work type and level of instruction. In all, 538 subjects were excluded from the study: 274 who had a history of taking, within a week, proton pump inhibitor (PPI), antibiotics, or bismuth subcitrate, or a history of taking eradication therapy of *H. pylori* infection within six months; 23 with chronic liver and renal failure; 6 with malignancy; 15 with acute infection; 4 with connective tissue disorders; and 216 with missing data. Finally, 2,050 subjects (588 female, 1,462 male) were enrolled in the study. The subjects' ages ranged from 26 to 95 years (52.21 ± 11.31 years, mean ± standard deviation [SD]). The study was conducted after obtaining written informed consent from all subjects and was approved by the ethics committee of Tongji Medical College, Huazhong University of Science and Technology.

Anthropometry and biochemical measurements

A medical interview provided information about age, sex, cigarette smoking habits, alcohol consumption, and histories of current and previous illnesses. Height and weight were measured in the morning, in the fasting state. Body mass index (BMI) was calculated by dividing the body weight (kg) with squared height (m^2). Blood pressure was measured twice in a quiet state at five-minute intervals on the right arm using a sphygmomanometer. The mean of the two readings was used in data analyses. On the morning of the survey, overnight fasting venous blood samples were collected from each participant, and all blood samples were processed within 30 minutes of collection. White blood cell count (WBCC) was measured using a hematology analyzer. Plasma level of glucose was determined by the glucose oxidase method. Glucosylated hemoglobin (HbA1c) was measured by ion-exchange high-performance liquid chromatography (HPLC). Serum level of high-density lipoprotein cholesterol (HDL-c) was measured by the chemical precipitation method, and serum levels of total cholesterol (TC) and triglyceride (TG) were measured by enzymatic methods. Low-density lipoprotein cholesterol (LDL-c) was estimated using the Friedewald formula [15].

Diagnosis of H. pylori infection

Diagnosis of *H. pylori* infection was achieved using the carbon urea breath test (^{14}C-UBT). For the ^{14}C-UBT, patients first fasted for two hours, washed their mouths before dosing, and were in a sitting position. Breath samples were collected at 20-minute intervals. The breath samples were analyzed using a gas chromatography mass spectrometer. *H. pylori* infection was considered positive if the estimated value was ≥ 100 dpm/mmol CO_2 and was considered negative if the estimated value was < 100 dpm/mmol CO_2.

Definitions

According to the criteria recommended by the Working Group on Obesity in China [16], overweight was defined as BMI equal to or greater than 24 kg/m^2 and less than 28 kg/m^2, and obesity was defined as BMI equal to or greater than 28 kg/m^2. According to the WHO Expert Consultation for Asians, overweight was defined as BMI equal to or greater than 23 kg/m^2 and less than 27.5 kg/m^2, and obesity was defined as BMI equal to or greater than 27.5 kg/m^2 [17]. Type 2 diabetes mellitus (T2DM) was diagnosed according to the 1999 WHO criteria: fast plasma glucose (FPG) equal to or greater than 126 mg/dL, or self-reported physician diagnosis or insulin use. According to the Seventh Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure guidelines [18], hypertension was defined as systolic blood pressure equal to or more than 140 mmHg , diastolic blood pressure equal to or more than 90 mmHg, and/or self-reported treatment of hypertension. Dyslipidemia was defined according to Adult Treatment Panel (ATP) III.

Statistical analyses

Categorical variables were presented as numbers and percentages. The Chi-square test was performed to assess differences in proportions across groups. Continuous variables were presented as mean ± SD for variables distributed normally, or as medians (25th to 75th percentiles) for skewed distributions. Differences between two groups were examined using Student's unpaired *t* test or by the Mann-Whitney U test as appropriate. One-way analysis of variance (ANOVA) or Kruskal-Wallis analysis of median test was applied to compare differences in means across groups. The Bonferroni correction was applied to adjust p values for multiple comparisons. Forced-entry multiple linear regression models were conducted to evaluate the relationship between *H. pylori* status and BMI levels.

Potential confounders were controlled for the following three models. Model 1 was adjusted for age and gender. Model 2 was adjusted for all the variables in model 1 plus smoking status, drinking status, hypertension, coronary heart disease, type 2 diabetes, and dyslipidemia. Model 3 was adjusted for all the variables in model 2 plus WBCC. These variables were chosen because of their potential role as confounders from the clinical point of view. To evaluate the association between *H. pylori* status and overweight or obesity according to different BMI categories, odds ratios (ORs) and 95% confidence intervals (95% CIs) for overweight or obesity in relation to *H. pylori* were estimated using unconditional logistic regression, controlling for the same three models. A two-tailed p value of < 0.05 was considered statistically significant. All analyses were conducted using SPSS software version 13.0.

Results

In total, there were 2,050 subjects (588 female, 1462 male) enrolled in this study whose ages ranged from 26 to 95 years (mean ± SD, 52.21 ± 11.31 years). They were divided into *H. pylori* infection-positive group and *H. pylori* infection-negative group by ^{14}C-UBT. The *H. pylori* infection-positive group had 839 subjects, accounting for 40.93% of the total participants, and the *H. pylori* infection-negative group had 1,211 subjects, accounting for 59.07% of the total participants. As shown in Table 1, a summary of demographics, metabolic, anthropometric and *H. pylori* status of participants, no differences were found between the two groups with regard to gender, systolic blood pressure, diastolic blood pressure, fasting blood glucose, glucosylated hemoglobin, lipid profiles and the morbidity of hypertension, coronary heart disease, and dyslipidemia. However, the *H. pylori* infection-positive group had significantly higher BMI levels than did the *H. pylori* infection-negative group (25.32 *vs* 24.95, p = 0.008). There were more subjects (127/839, 15.14%) in the *H. pylori* infection-positive group who had type 2 diabetes than there were in the *H. pylori* infection-negative group (146/1,211, 12.06%; p = 0.044). In addition, subjects in the *H. pylori* infection-positive group were younger than those in the *H. pylori* infection-negative group (51.57 *vs* 52.65, p = 0.034).

Figure 1 illustrates the prevalence of *H. pylori* infection in normal, overweight, and obese subjects according to different BMI criteria. Figure 1A shows that the prevalence of *H. pylori* infection in normal (BMI < 24), overweight (24 ≤ BMI < 28), and obese (BMI ≥ 28) subjects was 37.36%, 41.88%, and 45.77%, respectively (p for trend = 0.006). Figure 1B shows that the prevalence of *H. pylori* infection in normal (BMI < 23), overweight (23 ≤ BMI < 27.5), and obese (BMI ≥ 27.5) subjects was 38.67%, 39.41%, and 47.20%, respectively (p for trend = 0.009).

Figure 1. Prevalence of *H. pylori* infection in normal, overweight, and obese subjects according to different body mass index (BMI) criteria; p for trend = 0.006 (A), p for trend = 0.009 (B).

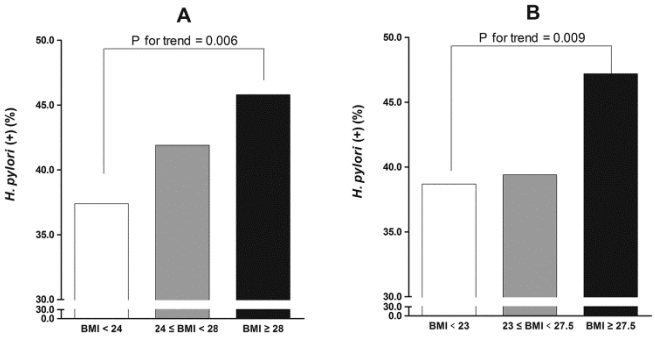
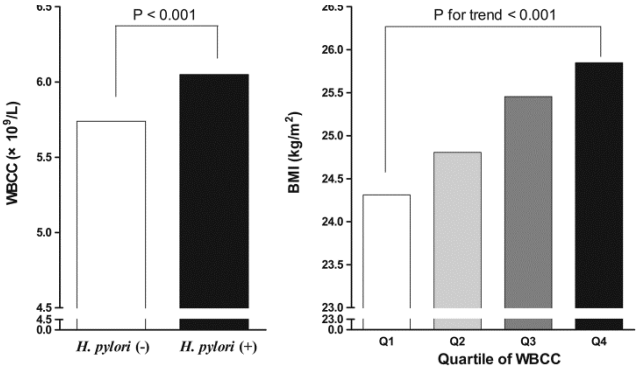


Figure 2. The mean white blood cell count (WBCC) levels in *H. pylori*-positive and *H. pylori*-negative group; p < 0.001 (A).



Quartiles of WBCC with body mass index (BMI) levels, p for trend < 0.001 (B). Quartile cut-off values for WBCC were 4.83×10^9/L, 5.65×10^9/L, and 6.68×10^9/L. Medians and ranges for quartile 1 were 4.37 (2.70–4.83)$\times10^9$/L; for quartile 2 were 5.24 (4.84–5.65)$\times10^9$/L; for quartile 3 were 6.08 (5.66–6.68)$\times10^9$/L; and for quartile 4 were 7.61 (6.69–11.60)$\times10^9$/L(B).

As shown in Figure 2A, the mean levels of WBCC were significantly higher in the *H. pylori*-positive group than in the negative group (p < 0.001). Quartile cut-off values for WBCC were 4.83×10^9/L, 5.65×10^9/L, and 6.68×10^9/L. Medians and ranges for quartile 1 were 4.37 (2.70–4.83)$\times10^9$/L; for quartile 2 were 5.24 (4.84–5.65)$\times10^9$/L; for quartile 3 were 6.08 (5.66–6.68)$\times10^9$/L; and for quartile 4 were 7.61 (6.69–11.60)$\times10^9$/L.

Table 1. Demographics, metabolic and anthropometric characteristics and *H. pylori* status of participants

Characteristics	Overall (n = 2,050)	*H. pylori* (-) (n = 1,211)	*H. pylori* (+) (n = 839)	P value
Age (years)	52.21 ± 11.31	52.65 ± 11.30	51.57 ± 11.31	0.034
Female [n (%)]	588 (28.68)	341 (28.15)	247 (29.44)	0.528
Current smokers [n (%)]	364 (17.75)	210 (17.34)	154 (18.36)	0.555
Current drinkers [n (%)]	381 (18.59)	211 (17.42)	170 (20.26)	0.106
SBP (mmHg)	124.00 (116.00–134.00)	123.00 (116.00–134.00)	124.00 (116.00–134.00)	0.935
DBP (mmHg)	77.00 (70.00–85.00)	78.00 (70.00–85.00)	77.00 (70.00–84.00)	0.636
BMI (kg/m^2)	25.10 ± 3.14	24.95 ± 3.04	25.32 ± 3.26	0.008
Hypertension [n (%)]	741 (36.15)	432 (35.67)	309 (36.83)	0.592
Type 2 diabetes [n (%)]	273 (13.31)	146 (12.06)	127 (15.14)	0.044
CHD [n (%)]	103 (5.02)	65 (5.37)	38 (4.53)	0.393
Dyslipidemia [n (%)]	1,199 (58.48)	698 (57.64)	501 (59.71)	0.348
WBCC (×10^9/L)	5.87 ± 1.47	5.74 ± 1.44	6.05 ± 1.49	< 0.001
FPG (mg/dL)	97.85 ± 20.36	97.20 ± 19.08	98.64 ± 21.78	0.094
HbA1c (%)	5.79 ± 0.70	5.78 ± 0.67	5.79 ± 0.74	0.783
TC (mg/dL)	184.07 ± 34.80	183.30 ± 35.19	185.23 ± 34.03	0.211
TG (mg/dL)	122.27 (83.28–184.29)	121.38 (81.51–178.09)	124.93 (85.06–189.60)	0.065
LDL-c (mg/dL)	109.44 ± 30.55	108.28 ± 29.39	110.60 ± 32.10	0.075
HDL-c (mg/dL)	46.02 ± 11.60	46.40 ± 11.21	45.63 ± 11.60	0.197

Data are presented as the mean ± standard deviation (SD) for normal variables, as the median (interquartile range) for skewed variables, or column (percentage). P values were obtained by comparing *H. pylori*-negative and *H. pylori*-positive groups.; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; CHD: coronary heart disease; FPG: fasting blood glucose; HbA1c: glucosylated hemoglobin; TC: total cholesterol; TG: triglyceride; LDL-c: low density lipoprotein cholesterol; HDL-c: high-density lipoprotein cholesterol; WBCC: white blood cell count

Table 2. Multiple linear regression models for body mass index (BMI) levels with *H. pylori* and other potential confounders

	Variable	β	Standard error	Beta	T	P value
Model 1						
	H. pylori	0.42	0.13	0.07	3.18	0.002
	Age	0.02	0.01	0.09	4.08	< 0.001
	Gender	2.22	0.15	0.31	14.65	< 0.001
Model 2						
	H. pylori	0.30	0.12	0.05	2.43	0.015
	Age	0.01	0.01	0.01	0.61	0.541
	Gender	1.13	0.15	0.16	7.59	< 0.001
	Current smoking	-0.22	0.19	-0.03	-1.17	0.243
	Current drinking	0.74	0.18	0.09	4.06	< 0.001
	Hypertension	1.43	0.14	0.22	10.20	< 0.001
	Type 2 diabetes	0.64	0.19	0.07	3.42	0.001
	CHD	-0.13	0.29	-0.01	-0.45	0.651
	Dyslipidemia	1.60	0.13	0.25	12.21	< 0.001
Model 3						
	H. pylori	0.24	0.12	0.04	1.93	0.053
	Age	0.01	0.01	0.03	1.38	0.168
	Gender	1.04	0.15	0.15	6.99	< 0.001
	Current smoking	-0.34	0.19	-0.04	-0.18	0.069
	Current drinking	0.76	0.18	0.09	4.23	< 0.001
	Hypertension	1.38	0.14	0.21	9.96	< 0.001
	Type 2 diabetes	0.53	0.19	0.06	2.82	0.005
	CHD	-0.09	0.29	-0.01	-0.33	0.742
	Dyslipidemia	1.56	0.13	0.25	11.94	< 0.001
	WBCC	0.25	0.04	0.12	5.89	< 0.001

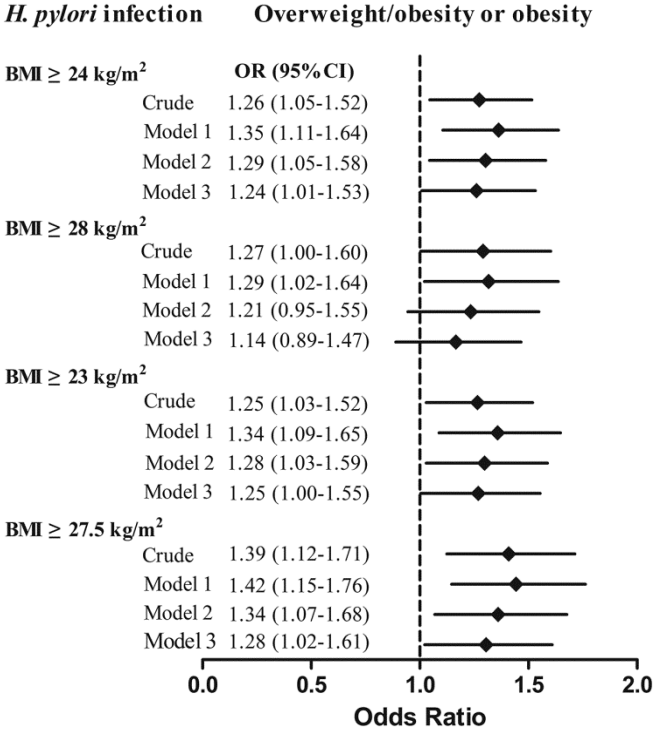
CHD: coronary heart disease; WBCC: white blood cell count; Model 1 was adjusted for age and gender; Model 2 was adjusted for all the variables in model 1 plus smoking status, drinking status, hypertension, coronary heart disease, diabetes, and dyslipidemia; Model 3 was adjusted for all the variables in model 2 plus WBCC.

Figure 1B illustrates that the mean levels of BMI increased progressively with increasing quartiles of WBCC (p for trend < 0.001).

In exploring factors associated with BMI levels, multiple linear regression models were used, with *H. pylori* status, gender, age, smoking status, drinking status, hypertension, coronary heart disease, type 2 diabetes, dyslipidemia, and WBCC as independent variables and BMI level as the dependent variable (Table 2). After adjustment for gender and age (model 1), the *H. pylori*-positive group showed positive association with BMI levels ($\beta = 0.42 \pm 0.13$, $p = 0.002$). The association remained statistically significant ($\beta = 0.30 \pm 0.12$, $p = 0.015$) after additional adjustment for potential intermediate variables, including smoking status, drinking status, hypertension, coronary heart disease, type 2 diabetes, and dyslipidemia (model 2). Finally, after adjustment for all the variables in model 2 plus WBCC (model 3), although BMI levels still showed positive association with *H. pylori*-positive status, the statistical significance disappeared ($\beta = 0.24 \pm 0.12$, $p = 0.053$). In model 3, BMI levels showed positive association with gender ($\beta = 1.04 \pm 0.15$, $p < 0.001$), current drinking ($\beta = 0.76 \pm 0.18$, $p < 0.001$), hypertension ($\beta = 1.38 \pm 0.14$, $p < 0.001$), type 2 diabetes ($\beta = 0.53 \pm 0.19$, $p = 0.005$), dyslipidemia ($\beta = 1.56 \pm 0.13$, $p < 0.001$), and WBCC ($\beta = 0.25 \pm 0.04$, $p < 0.001$).

Figure 3 illustrates multiple logistic regression analysis of *H. pylori* infection and overweight/obesity or obesity according to different BMI criteria. Data are expressed as odds ratios and 95% confidence intervals. For BMI ≥ 24 kg/m^2 as the dependent variable, the crude OR (95% CI) of *H. pylori* infection was 1.26 (1.05–1.52), and the age- and gender-adjusted OR (95% CI) of *H. pylori* infection (model 1) was 1.35 (1.11–1.64). The association remained statistically significant after additional adjustment for smoking status, drinking status, hypertension, coronary heart disease, diabetes, and dyslipidemia (model 2), and slightly attenuated after adjustment for all the variables in model 2 plus WBCC (model 3). For BMI ≥ 28 kg/m^2 as the dependent variable, the crude OR (95% CI) of *H. pylori* infection was 1.27 (1.00–1.60); the other corresponding figures of adjusted OR (95% CI) were 1.29 (1.02–1.64), 1.21 (0.95–1.55), and 1.14 (0.89–1.47), respectively. Though there were positive associations between *H. pylori* infection and obesity (BMI ≥ 28), the statistical significance disappeared in model 2 and model 3. For BMI ≥ 23 kg/m^2 as the dependent variable, the crude OR (95% CI) was 1.25 (1.03–1.52); the other corresponding figures were

Figure 3. Multiple logistic regression analysis of *H. pylori* infection and overweight/obesity or obesity according to different BMI criteria. Data are expressed as odds ratio and 95% confidence interval.



Model 1 was adjusted for age and gender. Model 2 was adjusted for all the variables in model 1 plus smoking status, drinking status, hypertension, coronary heart disease, diabetes, and dyslipidemia. Model 3 was adjusted for all the variables in model 2 plus WBCC.

1.34(1.09–1.65), 1.28 (1.03–1.59), and 1.25 (1.00–1.55), respectively. For BMI ≥ 27.5 kg/m^2 as the dependent variable, the crude OR (95% CI) was 1.39 (1.12–1.71); the other corresponding figures were 1.42 (1.15–1.76), 1.34 (1.07–1.68), and 1.28 (1.02–1.61), respectively. There were statistically significant associations between *H. pylori* infection and overweight/obesity (BMI ≥ 23 kg/m^2) and obesity (BMI ≥ 27.5 kg/m^2). Based on BMI categories, the associations were all attenuated after additional adjustment for WBCC.

Discussion

In this cross-sectional study, the increased prevalence of *H. pylori* infection was found in patients with higher BMI levels. On the other hand, a positive association between *H. pylori* infection and BMI levels was found without adjustment for WBCC in Chinese subjects. In addition, the association was consistent between *H. pylori* infection and overweight/obesity.

The incidence of overweight or obesity in China has increased year by year. In the present study, the prevalence of overweight was 64.49% (BMI ≥ 24) or 75.02% (BMI ≥ 23), and the prevalence of obesity was 16.73% (BMI ≥ 28) or 21.80% (BMI ≥ 27.5) in the subjects who were employed in the local administrative units of Wuhan. Increasing evidence indicates in various ways that obesity in animals and humans may be linked to several microbes, including animal and human viruses, bacteria, and parasites [5,6]. In 1982, it was first reported that canine distemper virus could induce obesity in mice infected with the virus [19]. Since then, pneumonia chlamydia, *Selenomonas noxia*, herpes simplex virus 1 or 2, gut microflora, and *H. pylori* have been reported to be associated with obesity [20-23].

H. pylori are prevalent bacteria worldwide. In our present study, about half of the population was infected with *H. pylori*. The infection rate was related to geographical location, race, age, and socioeconomic status. From January 2002 to June 2004, the team of collaboration of *H. pylori* research in China conducted an investigation of *H. pylori* infection among 26,341 people in 19 provinces, municipalities, and autonomous regions in China. The results indicated that the mean *H. pylori* total infection rate was 56.22%. The *H. pylori* infection rate in Guangdong province was the lowest, approximately 42%, and the rate in Tibetan monks was the highest, approximately 84% [24]. But there were no data about the *H. pylori* infection rate in Wuhan city. In this study, the *H. pylori* infection rate in Wuhan city was 40.9%, and there was no difference between genders. The possible reasons that the *H. pylori* infection rate in our study was lower than that in the other regions were (i) the subjects in our study were employed in local administrative units of Wuhan, had higher education, and were in the middle-high socioeconomic class, which might be relevant to the low prevalence of *H. pylori* infection; (ii) diagnosis of *H. pylori* infection in our study was achieved by using ^{14}C-UBT, which could reflect current *H. pylori* infection status of the whole stomach. The vast majority of testing methodology of *H. pylori* infection that the team of collaboration of *H. pylori* research in China used was the *H. pylori* IgG enzyme-linked immunosorbent assay (ELISA), which indicates not only current *H. pylori* infection but also previous *H. pylori* infection. This method might be prone to false positives, which could result in the higher rate of *H. pylori* infection that was found.

The relationship between *H. pylori* and obesity remains controversial. These interactions could be classified as (i) the effect of obesity on *H. pylori* infection; (ii) the effect of *H. pylori* infection on obesity.

The effect of obesity on H. pylori infection

Obese individuals show an increased susceptibility to infections with different pathogens [25]. Erol *et al*. found that the *H. pylori* infection rate in the obese group was 57.2% (59/103), and the *H. pylori* infection rate in the control group was 27.0% (30/111). There was a significant association between the obesity and serum antibody positive for *H. pylori* (OR, 2.11; 95% CI, 1.49–3.00) [22]. Another study in Greece indicated that the incidence of *H. pylori* infection was not increased among overweight/obese young individuals (median age, 22.84 years) [11]. In our study, we found that the prevalence of *H. pylori* infection in normal, overweight, and obese subjects was 37.36%, 41.88%, and 45.77%, respectively, based on the criteria recommended by the Working Group on Obesity in China (p for trend = 0.006). The mean age of our subjects was 52.21 years, much older than the subjects in previous studies. As natural elimination of *H. pylori* infection is difficult, it is commonly believed that *H. pylori* infection perpetuates in those who never receive eradication therapy. Consequently, the older *H. pylori*-positive subjects were believed to have longer-term *H. pylori* infection, which might induce age-related influence or a life-course perspective of *H. pylori* infection in the body. Yang *et al*. found that obesity was positively associated with increased risk of gastric *H. pylori* infection in 324 elderly Chinese subjects [26].

Obesity is usually associated with impaired immune function, and immune deterioration is also related to the grade of obesity [27]. The maturation of monocytes into macrophages was found to be lower, and the capacity of polymorphonuclear (PMN) to be bactericidal was found to be reduced in obese individuals [28,29]. Severely obese individuals also have a significant decrease in NK cell activity compared with control individuals after adjustment for age and gender [30]. People with diabetes mellitus are also easily affected by chronic infections. A significant association was also observed between *H. pylori* infection and type 2 diabetes mellitus in our study (p =0.044).

The effect of H. pylori infection on obesity

Kopacova *et al*. studied 2,436 people (between 4 and 100 years of age) and found that there were positive associations between *H. pylori* infection and the levels of BMI both in overweight/obese and obese subjects over 15 years of age [31]. But in that study, the risk factors (drinking status, diabetes, dyslipidemia, etc.) of overweight or obese subjects were not adjusted. In our study, the *H. pylori*-positive group had significantly higher BMI levels than did the *H. pylori*-negative group (25.32 *vs* 24.95, p = 0.008). In multiple linear regression models with BMI levels as the dependent variable, the association between *H. pylori* positivity and BMI levels was statistically significant (β = 0.30 ± 0.12, p = 0.015) after adjustment for *H. pylori* status, gender, age, smoking status, drinking status, hypertension, coronary heart disease, diabetes, and dyslipidemia. Furthermore, we found a positive association between *H. pylori* infection and overweight/obesity according to different BMI criteria. However, the association between *H. pylori* infection and obesity was consistently significant only according to the Asian criteria (BMI ≥ 27.5), but not significant according to the more restrictive Chinese criteria (BMI ≥ 28). Obesity is multifactorial disorder that involves environmental, lifestyle, genetic, and social factors. In this study, we found that gender, current drinking, hypertension, diabetes, and dyslipidemia had more impact on BMI levels than did *H. pylori* infection. Hence, we deduced that *H. pylori* infection might improve BMI levels, but the effect of *H. pylori* infection that could be attributable to obesity is limited. The main reason of the increased prevalence of obesity in China is the change of dietary structure and decreased physical activity, which resulted from the economic transformation in recent decades. Therefore, though the *H. pylori* infection rates have been in a decreasing trend in China, the incidence of overweight or obesity in China has increased year by year.

The mechanism underlying the adipogenic action of microbial infection is unclear. One study showed that *H. pylori*-infected subjects have lower serum leptin levels[32]. As leptin exerts anorexigenic effects, *H. pylori* infection may stimulate overfeeding and be involved in the mechanisms of obesity[33,34]. Furthermore, *H. pylori* could promote gastric mucosa to produce a variety of vasoactive substances and inflammatory cytokines, such as tumor necrosis factor alpha (TNF-α), interleukin-1 (IL-1), interleukin-6 (IL-6), and other cytokines. These mediators may be transported through the bloodstream and may cause a chronic low-grade inflammatory response in extra digestive sites [35]. As a result, these inflammatory mediators may lead to insulin resistance and induce overweight or obesity [36-38]. As chronic infections could improve WBCC levels and lead to a series of inflammatory reactions, WBCC is a universally available marker of chronic low-grade inflammation. In our study, WBCC levels were significantly higher in the *H. pylori*-positive group than in the negative group (p < 0.001). Furthermore, the levels of BMI increased progressively with increasing quartiles of WBCC (p for trend < 0.001). There was a positive association between *H. pylori* infection and BMI levels in our study (β = 0.30 ± 0.12, p = 0.015). However, after additional adjustment for WBCC, the statistical significance disappeared (β = 0.24 ± 0.12, p = 0.053). In multiple logistic regression analysis of different BMI categories, we also found that the OR values between *H. pylori* infection and overweight/obesity were weakened after additional adjustment for WBCC. This indicated that *H. pylori* infection might improve of BMI levels through chronic inflammatory reaction mediated by WBCC.

There are some limitations in current study that require consideration in interpretation of our findings. First, because our present research was a cross-sectional study, the cause-effect relation between *H. pylori* infection and overweight or obesity could not be proved conclusively. Second, the subjects in our study had a similar socioeconomic status and were in the middle-high socioeconomic class. Hence, we need to conduct further longitudinal and larger scale epidemiological investigation in general population to elucidate the relationship between *H. pylori* infection and overweight or obesity.

Conclusions

In summary, our study indicated that *H. pylori* infection was significantly and positively associated with the risk of overweight/obesity in a Chinese population.

Acknowledgements

The authors thank all study participants for their cooperation.

References

1. Pi-Sunyer FX (2002) The medical risks of obesity. Obes Surg 12 Suppl 1:6S-11S.
2. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath CW Jr (1999) Body-mass index and mortality in a prospective cohort of U.S. adults. N Engl J Med 341:1097-1105.

3. Reynolds K, Gu D, Whelton PK, Wu X, Duan X, Mo J, He J; InterASIA Collaborative Group (2007) Prevalence and risk factors of overweight and obesity in China. Obesity (Silver Spring) 15: 10-18.
4. Du T, Sun X, Yin P, Huo R, Ni C, Yu X (2013) Increasing trends in central obesity among Chinese adults with normal body mass index, 1993-2009. BMC Public Health 13: 327.
5. Hegde V, Dhurandhar NV (2013) Microbes and obesity--interrelationship between infection, adipose tissue and the immune system. Clin Microbiol Infect 19: 314-320.
6. Pasarica M, Dhurandhar NV (2007) Infectobesity: obesity of infectious origin. Adv Food Nutr Res 52: 61-102.
7. [No authors listed] (1983) Unidentified curved bacilli on gastric epithelium in active chronic gastritis. Lancet 1: 1273-1275.
8. Wolle K, Leodolter A, Malfertheiner P (2002) [Epidemiology and pathogenesis of Helicobacter pylori infection]. Wien Med Wochenschr 152: 117-122.
9. Wotherspoon AC, Ortiz-Hidalgo C, Falzon MR, Isaacson PG (1991) Helicobacter pylori-associated gastritis and primary B-cell gastric lymphoma. Lancet 338: 1175-1176.
10. Nomura A, Stemmermann GN (1993) Helicobacter pylori and gastric cancer. J Gastroenterol Hepatol 8: 294-303.
11. Banic M, Franceschi F, Babic Z, Gasbarrini A (2012) Extragastric manifestations of Helicobacter pylori infection. Helicobacter 17 Suppl 1: 49-55.
12. Kyriazanos ID, Sfiniadakis I, Gizaris V, Hountis P, Hatziveis K, Dafnopoulou A, Datsakis K (2002) The incidence of Helicobacter pylori infection is not increased among obese young individuals in Greece. J Clin Gastroenterol 34: 541-546.
13. Wu MS, Lee WJ, Wang HH, Huang SP, Lin JT (2005) A case-control study of association of Helicobacter pylori infection with morbid obesity in Taiwan. Arch Intern Med 165: 1552-1555.
14. Thjodleifsson B, Asbjornsdottir H, Sigurjonsdottir RB, Gislason D, Olafsson I, Cook E, Gislason T, Jogi R, Janson C (2007) Seroprevalence of Helicobacter pylori and cagA antibodies in Iceland, Estonia and Sweden. Scand J Infect Dis 39: 683-689.
15. Friedewald WT, Levy RI, Fredrickson DS (1972) Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 18: 499-502.
16. Zhou BF, Cooperative Meta-Analysis Group of the Working Group on Obesity in C (2002) Predictive values of body mass index and waist circumference for risk factors of certain related diseases in Chinese adults--study on optimal cut-off points of body mass index and waist circumference in Chinese adults. Biomed Environ Sci 15: 83-96.
17. WHO Expert Consultation (2004) Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet 363: 157-163.
18. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ; National Heart Lung, and Blood Institute Joint National Committee on Prevention Detection, Evaluation, and Treatment of High Blood Pressure; National High Blood Pressure Education Program Coordinating Committee (2003) The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA 289: 2560-2572.
19. Lyons MJ, Faust IM, Hemmes RB, Buskirk DR, Hirsch J, Zabriskie JB (1982) A virally induced obesity syndrome in mice. Science 216: 82-85.
20. Dart AM, Martin JL, Kay S (2002) Association between past infection with Chlamydia pneumoniae and body mass index, low-density lipoprotein particle size and fasting insulin. Int J Obes Relat Metab Disord 26: 464-468.
21. Goodson JM, Groppo D, Halem S, Carpino E (2009) Is obesity an oral bacterial disease? J Dent Res 88: 519-523.
22. Arslan E, Atilgan H, Yavasoglu I (2009) The prevalence of Helicobacter pylori in obese subjects. Eur J Intern Med 20: 695-697.
23. Ley RE, Turnbaugh PJ, Klein S, Gordon JI (2006) Microbial ecology: human gut microbes associated with obesity. Nature 444: 1022-1023.
24. Zhang W, Hu F, Xiao S, Xv Z (2010)[Prevalence of Helicobacter pylori infection in China]. Mod DigestIntervent 15: 265-270.
25. Falagas ME, Kompoti M (2006) Obesity and infection. Lancet Infect Dis 6: 438-446.
26. Yang GH, Wu JS, Yang YC, Huang YH, Lu FH, Chang CJ (2014) Obesity associated with increased risk of gastric Helicobacter pylori infection in an elderly Chinese population. J Am Geriatrics Society 62: 190-192.
27. Marti A, Marcos A, Martinez JA (2001) Obesity and immune function relationships. Obes Rev 2: 131-140.
28. Krishnan EC, Trost L, Aarons S, Jewell WR (1982) Study of function and maturation of monocytes in morbidly obese individuals. J Surg Res 33: 89-97.
29. Palmblad J, Hallberg D, Engstedt L (1980) Polymorphonuclear (PMN) function after small intestinal shunt operation for morbid obesity. Br J Haematol 44: 101-108.
30. Moulin CM, Marguti I, Peron JP, Rizzo LV, Halpern A (2009) Impact of adiposity on immunological parameters. Arq Bras Endocrinol Metabol 53: 183-189.
31. Kopacova M, Bures J, Koupil I, Rejchrt S, Vorisek V, Seifert B, Pozler O, Zivny P, Douda T, Palicka V, Holcik J; European Society for Primary Care Gastroenterology (2007) Body indices and basic vital signs in Helicobacter pylori positive and negative persons. Eur J Epidemiol 22:67-75.
32. Roper J, Francois F, Shue PL, Mourad MS, Pei Z, Olivares de Perez AZ, Perez-Perez GI, Tseng CH, Blaser MJ (2008) Leptin and ghrelin in relation to Helicobacter pylori status in adult males. J Clin Endocrinol Metab 93: 2350-2357.
33. Schwartz MW, Seeley RJ, Campfield LA, Burn P, Baskin DG (1996) Identification of targets of leptin action in rat hypothalamus. J Clin Invest 98:1101-1106.
34. Shintani M, Ogawa Y, Ebihara K, Aizawa-Abe M, Miyanaga F, Takaya K, Hayashi T, Inoue G, Hosoda K, Kojima M, Kangawa K, Nakao K (2001) Ghrelin, an endogenous growth hormone secretagogue, is a novel orexigenic peptide that antagonizes leptin action through the activation of hypothalamic neuropeptide Y/Y1 receptor pathway. Diabetes 50: 227-232.
35. Peek RM Jr (2005) Pathogenesis of Helicobacter pylori infection. Springer Semin Immunopathol 27: 197-215.
36. Longo-Mbenza B, Nkondi Nsenga J, Vangu Ngoma D (2007) Prevention of the metabolic syndrome insulin resistance and the atherosclerotic diseases in Africans infected by Helicobacter pylori infection and treated by antibiotics. Int JCardiol 121: 229-238.

37. Eshraghian A, Eshraghian H, Ranjbar Omrani G (2011) Insulin resistance and metabolic syndrome: is Helicobacter pylori criminal? Minerva Gastroenterol Dietol 57: 379-385.
38. Eshraghian A, Hashemi SA, Hamidian Jahromi A, Eshraghian H, Masoompour SM, Davarpanah MA, Eshraghian K, Taghavi SA (2009) Helicobacter pylori infection as a risk factor for insulin resistance. Dig Dis Sci 54: 1966-1970.

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Conflict of interests: No conflict of interests is declared.

Erratum in

J Infect Dev Ctries 2015; 9(1):001-007. doi:10.3855/jidc.5065. Grant number in article text.

Acknowledgements
This work was funded by the EWABO Co., Germany, and the Deanship of Scientific Research (DSR), King Abdulaziz University, Jeddah, under grant no. MG/34/25. The authors thankfully acknowledge the technical and financial support from DSR.

PMID: 25596565 [PubMed - in process]