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Helicobacter pylori infection and the prevalence of hypertension in Chinese adults: The Dongfeng-Tongji cohort

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Abstract

Although many studies explored the association between *helicobacter pylori* (*H pylori*) infection and hypertension, there is no consensus. This study is to investigate the association between *H pylori* infection and the prevalence of hypertension among a middle- and old-age Chinese population. A cross-sectional study including 17,100 participants from the Dongfeng-Tongji cohort study was performed. All participants underwent a ^{14}C-urea breath test and a routine health check-up. Logistics and linear regression with multivariable adjustment were used to quest the association between *H pylori* infection and hypertension. The individuals with *H pylori* infection had a higher prevalence of hypertension (57.5% vs 55.1%, $P = .002$), and infection rate of *H pylori* in patients with hypertension is higher than that in non-hypertensive individuals (48.8% vs 46.4%, $P = .002$). After adjustment for potential confounders, *H pylori* infection increased the prevalence of hypertension (odds ratio, 1.117, 95% confidence interval (CI), 1.029-1.213, $P = .008$). Moreover, compared with participants without *H pylori* infection, individuals infected had an increase of 0.905 mm Hg (95% CI, 0.025-1.785, $P = .044$) for diastolic blood pressure. However, there was no interaction between *H pylori* infection and traditional risk factors on hypertension. These findings suggested that *H pylori* infection was positively associated with the prevalence of hypertension.

1 | INTRODUCTION

Hypertension is a most important risk factor for cardiovascular and cerebrovascular diseases and can cause complications such as stroke, myocardial infarction, heart failure, and chronic kidney disease. Hypertension is considered to be a complex disease caused by the interaction of genetic and environmental factors.[1] Moreover, increasing studies show that inflammation plays a very important role in the pathophysiology of hypertension, and some researchers even believe that hypertension involves mild inflammation that occurs in the cardiovascular system.[2,3]

Pathogen infection may be one of the inflammatory stimulating factors that is related to the occurrence and development of hypertension. *Helicobacter pylori* (*H pylori*) is one of the most common chronic bacterial infections. This bacterium enters the stomach through the mouth and settles on the gastric mucus layer and the surface of the gastric epithelial cells.[4] Humans can develop *H pylori* infection in childhood. Without treatment, the infection can last a lifetime.[5] Epidemiological studies have shown that *H pylori* infection is associated with the development of obesity, metabolic syndrome, and cardiovascular disease.[6-8] As the correlation between *H pylori* infection and parenteral diseases is becoming increasingly confirmed, more studies related to hypertension are being conducted. Some studies have shown that *H. p*ylori is positively correlated with the risk of hypertension.[9] However, Tang et al[10] showed that after adjusting for confounding factors, *H pylori* infection was not associated

with hypertension. Liu et al[11] had similar findings in the Mongolian population. These indicated that infection may not be a risk factor for hypertension.

Therefore, exploring the correlation between *H pylori* infection and hypertension is of great importance in determining the pathogenesis of the disease, prevention, and evaluation of drug intervention. We conducted this study to assess the relationship between *H pylori* infection and hypertension as well as the traditional risk factors.

2 | SUBJECTS AND METHODS

2.1 | Study participants

A cross-sectional study was conducted in the Dongfeng-Tongji cohort, which was launched among retirees of Dongfeng Motor Corporation (DMC) in 2008. DMC is one of the three largest auto manufactures in China. After the first follow-up in 2013, we recruited a total of 38,295 retirees, and 34,708 retirees underwent physical examination and responded to a questionnaire. After excluding those with missing information and users of antibiotics, 17,100 individuals were included in this study. The study was approved by the Medical Ethics Committee of the School of Public Health, Tongji Medical College, and Dongfeng General Hospital. Written informed consent was obtained from all participants.

2.2 | Assessment of *H pylori* infection

In the health check-up, the status of *H pylori* infection was measured using the ^{14}C-urea breath test, which is considered to be the "gold standard" technique for the detection of *H pylori* infection.[12] All participants fasted overnight before taking capsules containing ^{14}C-urea. No food or drink was allowed until a breath sample was collected after 25 minutes. Results were expressed as disintegrations per minute (dpm). Subjects with dpm ≥ 100 were considered to be infected with *H pylori*.

2.3 | Definition of hypertension

Each subject's blood pressure (BP) values were measured using a manual sphygmomanometer in accordance with the World Health Organization guidelines. The criteria for a diagnosis of hypertension were as follows: (a) systolic blood pressure (SBP) ≥140 mm Hg and/or diastolic blood pressure (DBP) ≥90 mm Hg; (b) self-reported physician diagnosis of hypertension; and (c) self-reported current use of antihypertensive medication. The mean arterial pressure (MAP) was calculated as [SBP + (2 × DBP)]/3. The pulse pressure (PP) was calculated by subtracting DBP from SBP.

2.4 | Assessment of covariates

A semi-structured questionnaire was administered by trained interviewers during face-to-face meetings with participants to collect information on sociodemographic factors, health status, and lifestyle. The height and weight of each participant were measured with the participant dressed in light clothing and with bare feet. Body mass index (BMI) was calculated as body weight (kg) divided by height (m^2). Blood samples were collected at Dongfeng General Hospital by an experienced nurse. Venous blood was drawn with each subject in the sitting position after fasting overnight. Blood routine examination (white blood cell [WBC], neutrophil) were measured in the hospital laboratory using an automatic hematology analyzer (Sysmex, UKB). Blood lipids (total cholesterol [TC], triglyceride [TG], high-density lipoprotein cholesterol [HDL-C], and low-density lipoprotein cholesterol [LDL-C]), hepatic function (alanine aminotransferase [ALT], aspartate aminotransferase [AST]), renal function (blood urea nitrogen [BUN], creatinine, and uric acid), and homocysteine (Hcy) were measured using the ARCHITECT ci8200 automatic analyzer (Abbott Core Laboratory). Measurement of fasting plasma glucose (FPG) was performed using an Aeroset automatic analyzer (Abbott Core Laboratory).

According to the self-reported smoking status of the respondents, the participants were divided into former smokers, current smokers, and non-smokers. Current smoking was defined as having smoked at least one cigarette per day for more than half a year. Those who had smoked but stopped smoking for more than one month during the survey were defined as former smoking. The same categories were used for drinking status: current alcohol consumption referred to those who were drinking at least one time per week for more than half a year, and former drinker referred to those who had previously consumed alcohol but stopped drinking for more than 6 months. Because the proportion of former smokers (11.8%) and former drinkers (5.6%) were too small, we divided them into non-smokers and non-drinkers.

2.5 | Data analysis

All statistical analyses were performed using SPSS Statistics version 22.0 (IBM Corp.). The chi-square test was used for categorical variables, which are expressed as percentages. The t test was used to compare continuous variables, which are expressed as the means ± standard deviation. The odds ratio (OR) and 95% confidence interval (CI) were used to examine the relationship between *H pylori* infection and the prevalence of hypertension in multivariable logistic regression models. In multivariate model 1, we adjusted for age, sex, family history of hypertension plus smoking status, and alcohol consumption status. In multivariate model 2, we adjusted for the same set of variables as model 1 plus BMI. Model 3 adjusted for covariates in model 2 plus TC, TG, LDL-C, HDL-C, BUN, creatinine, uric acid, AST, ALT, FPG, and Hcy. We conducted

subgroup analyses to explore the association between *H pylori* infection and hypertension according to age (< 66 or ≥66 years, the median age for participants), sex (male or female), and BMI (< 24 or ≥24 kg/m^2, the cutoff value for overweight status for Chinese), smoking (yes/no), alcohol consumption (yes/no), and family history of hypertension (yes/no).

Multivariate linear regression models were used to assess the association of SBP, DBP, and MAP with *H pylori* infection. Subjects taking antihypertensive drugs were excluded from the multiple linear regression analysis because they were likely to have normal SBP, DBP, and MAP. A two-side $P < .05$ was considered to be statistically significant.

3 | RESULTS

3.1 | Characteristics of the participants

A total of 17,100 participants were included in the current study. The prevalence of *H pylori* infection was 47.75%. Table 1 shows the characteristics of the study population according to the status of *H pylori* infection. Compared with participants who were not infected with *H pylori*, individuals infected with *H pylori* had higher TC, ALT, AST, BUN, creatinine, FPG, Hcy, WBC, neutrophil, SBP, DBP, and PP levels, and lower HDL-C level. Additionally, those infected with *H pylori* were more likely to have a higher prevalence of hypertension and diabetes mellitus. Prevalence of hypertension was significantly different between *H pylori*-negative and *H pylori*-positive individuals.

We summarized the characteristics of the participants according to hypertension (Table 2). Hypertensive subjects were older, female, had higher level of BMI, BUN, creatinine, uric acid, FPG, Hcy, WBC, neutrophil, MAP, PP, and SBP levels, lower HDL-C, LDL-C and TC, TG, levels, and a higher prevalence of *H pylori* infection and diabetes mellitus. Those with hypertension also had higher proportion of cigarette consumers and drinkers.

TABLE 1 Characteristics between subjects according to *Helicobacter pylori* infection status

Variable	*H pylori* negative (n = 8934)	*H pylori* positive (n = 8166)	*P* value
Age (y)	66.14 ± 7.78	66.02 ± 8.07	.317
female, n (%)	4581 (51.3%)	4241 (51.9%)	.391
BMI (kg/m^2)	24.63 ± 3.44	24.63 ± 3.39	.982
smoking, n (%)	1214 (17.4%)	1069 (16.9%)	.475
Alcohol consumption, n (%)	1501 (21.4%)	1403 (22.0%)	.367
Hypertension, n (%)	4923 (55.1%)	4695 (57.5%)	.002
Diabetes, n (%)	2271 (25.4%)	2211 (27.1%)	.014
TC (mmol/L)	4.72 ± 1.11	4.79 ± 1.10	<.001
TG (mmol/L)	1.54 ± 1.05	1.55 ± 1.12	.510
LDL-C (mmol/L)	2.71 ± 0.87	2.72 ± 0.90	.460
HDL-C (mmol/L)	1.50 ± 0.46	1.48 ± 0.45	.001
ALT (U/L)	20.15 ± 15.82	21.50 ± 16.64	<.001
AST (U/L)	22.87 ± 12.42	23.64 ± 16.36	.001
BUN (mmol/L)	5.41 ± 1.74	5.47 ± 1.67	.029
Creatinine (μmol/L)	78.13 ± 39.66	80.69 ± 38.03	<.001
Uric acid (μmol/L)	324.62 ± 95.95	321.98 ± 93.53	.069
FPG (mmol/L)	6.06 ± 1.78	6.21 ± 4.03	.001
Hcy (μmol/L)	14.75 ± 9.24	16.46 ± 9.35	<.001
SBP (mm Hg)	146.06 ± 22.55	147.50 ± 22.82	<.001
DBP (mm Hg)	81.97 ± 12.89	82.75 ± 13.11	<.001
MAP (mm Hg)	101.03 ± 14.21	100.68 ± 14.44	.108
PP (mm Hg)	60.19 ± 17.29	60.75 ± 18.01	.038
WBC (×10^9/L)	6.02 ± 1.36	6.35 ± 1.27	<.001
Neutrophil (×10^9/L)	3.51 ± 1.26	3.86 ± 1.14	<.001

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, Body mass index; BUN, blood urea nitrogen; DBP, diastolic blood pressure; FPG, fasting plasma glucose; Hcy, homocysteine; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MAP, mean arterial pressure; PP, pulse pressure; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; WBC, white blood cell.

3.2 | Association between *H pylori* infection and BP

Multiple linear regression analyses were performed to assess the relationship between *H pylori* infection and BP. Table 3 shows that *H pylori* infection was positively associated with DBP. There was no evidence of significant associations between *H pylori* infection and SBP, PP, and MAP in all models. After adjustment for age, sex, family history of hypertension, smoking status, alcohol consumption status, BMI, blood lipids, hepatic function, renal function, FPG, and Hcy, the association between *H pylori* infection and DBP was slightly attenuated. In model 3, compared with those without *H pylori* infection, DBP increased by 0.905 mm Hg (95% CI, 0.025-1.785) in those who were infected with *H pylori*.

3.3 | Association between *H pylori* infection and hypertension

We calculated the ORs and 95% CIs for hypertension according to the status of *H pylori* infection (Table 4). The unadjusted analysis indicated that *H pylori* infection was positively associated with the prevalence of hypertension (OR, 1.102, 95% CI, 1.037-1.170). After adjustment for age, sex, family history of hypertension plus smoking status, and alcohol consumption status (model 1), the OR was 1.15 (95% CI, 1.063-1.243) for those with *H pylori* infection. Model 2 showed that the association between *H pylori* infection and hypertension was not materially changed (OR, 1.162, 95% CI, 1.073-1.259).

TABLE 2 Characteristics between subjects with and without hypertension

Variable	no Hypertension (n = 7462)	Hypertension (n = 9638)	*P* value
Age (y)	63.54 ± 8.12	68.05 ± 7.16	<.001
female, n (%)	3646 (48.90%)	5176 (53.70%)	<.001
BMI (kg/m^2)	24.00 ± 3.41	24.15 ± 3.36	.004
smoking, n (%)	704 (9.43%)	1579 (16.38%)	<.001
Alcohol consumption, n (%)	845 (11.32%)	2059 (21.36%)	<.001
H pylori (+), n (%)	3463 (46.40%)	4703 (48.80%)	.002
Diabetes, n (%)	1406 (18.80%)	3076 (31.90%)	<.001
TC (mmol/L)	4.81 ± 1.09	4.71 ± 1.12	<.001
TG (mmol/L)	1.59 ± 1.10	1.49 ± 1.06	<.001
HDL-C (mmol/L)	1.48 ± 0.46	1.50 ± 0.45	.004
LDL-C (mmol/L)	2.78 ± 0.87	2.67 ± 0.90	<.001
ALT (U/L)	20.82 ± 15.72	20.78 ± 16.61	.873
AST (U/L)	23.16 ± 12.41	23.30 ± 15.83	.529
BUN (mmol/L)	5.27 ± 1.55	5.57 ± 1.81	<.001
Creatinine (μmol/L)	76.74 ± 34.11	81.58 ± 42.02	<.001
Uric acid (μmol/L)	314.74 ± 90.74	330.03 ± 97.32	<.001
FPG (mmol/L)	5.94 ± 1.64	6.28 ± 3.82	<.001
Hcy (μmol/L)	15.36 ± 9.23	15.86 ± 9.42	<.001
SBP (mm Hg)	117.4 ± 11.3	148.80 ± 21.70	<.001
DBP (mm Hg)	71.4 ± 7.6	82.26 ± 12.44	<.001
MAP (mm Hg)	100.81 ± 14.42	101.49 ± 14.41	.002
PP (mm Hg)	56.4 ± 16.97	64.78 ± 17.3	<.001
Neutrophil (×10^9/L)	2.13 ± 0.65	2.32 ± 0.62	<.001
WBC (×10^9/L)	5.64 ± 1.10	6.63 ± 2.03	<.001

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, Body mass index; BUN, blood urea nitrogen; DBP, diastolic blood pressure; FPG, fasting plasma glucose; *H pylori*, *helicobacter pylori*; Hcy, homocysteine; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MAP, mean arterial pressure; PP, pulse pressure; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; WBC, white blood cell.

Similar results were obtained with additional adjustments for blood lipids, hepatic function, renal function, FPG, and Hcy (OR, 1.117, 95% CI, 1.029-1.213). All *P*<.05.

3.4 | Subgroup analysis

We further conducted subgroup analysis stratified by some traditional risk factors including age (< 66 and ≥66 years), sex (male and female), BMI (<24 and ≥24 kg/m^2), smoking (yes/no), alcohol consumption (yes/no), and family history of hypertension (yes/no). After full adjustments were made in model 3, a positive association between *H pylori* infection and hypertension was observed among women (OR, 1.157, 95% CI, 1.038-1.289, *P* = .008). When the participants were stratified on the basis of BMI, a positive association was found among those with BMI < 24 kg/m^2 (OR, 1.140, 95% CI, 1.017-1.278, *P* = .024). Similar results were observed among individuals who did not smoke (OR, 1.104, 95% CI, 1.008-1.209, *P* = .033), did not consume alcohol (OR, 1.122, 95% CI, 1.022-1.232, *P* = .016), and those without family history of hypertension (OR, 1.122, 95% CI, 1.027-1.225, *P* = .011). There was no evidence of significant interaction between *H pylori* and any of the mentioned traditional risk factors on the prevalence of hypertension (Table S1).

3.5 | Interaction between *H pylori* infection and hypertension risk factors among those who did not have hypertension

To clarify the associations between *H pylori* infection and hypertension, we further assessed the association between *H pylori* infection and several traditional risk factors among individuals with normal BP. As Table S2 indicates, individuals who were infected with *H pylori* had higher levels of TC (*P* = .009), LDL-C (*P* = .048), Hcy (*P* < .001), and FPG (*P* = .001) than non-infected individuals. Additionally, individuals with *H pylori* infection had a higher prevalence of diabetes mellitus. Meantime, SBP (*P* = .020), DBP (*P* = .013), and MAP

TABLE 3 Regression coefficients and 95% CIs of blood pressure according of *Helicobacter pylori* infection status

	SBP		DBP		MAP		PP	
	Coefficient	*P* value	Coefficient	*P* value	Coefficient	*P* value	Coefficient	*P* value
unadjusted	1.339 (−0.371, 3.049)	.125	1.025 (0.119, 1.930)	.027	−0.529 (−1.568, 0.510)	.318	0.315 (−0.955, 1.584)	.627
Model 1	1.450 (−0.199, 3.098)	.085	1.033 (0.138, 1.929)	.024	−0.467 (−1.509, 0.576)	.38	0.416 (−0.782, 1.615)	.496
Model 2	1.384 (−0.230, 2.997)	.093	1.00 (0.121, 1.880)	.026	−0.465 (−1.507, 0.578)	.382	0.384 (−0.803, 1.570)	.526
Model 3	1.088 (−0.512, 2.688)	.183	0.905 (0.025, 1.785)	.044	−0.528 (−1.583, 0.526)	.326	0.183 (−0.997, 1.362)	.761

Note: Model 1: adjusted for age, sex, family history of hypertension, smoking status, and alcohol consumption status. Model 2: adjusted for the same set of variables as model 1 plus BMI. Model 3: adjusted for covariates in model 2 plus TC, TG, LDL-C, HDL-C, BUN, creatinine, uric acid, ALT, AST, FPG, and Hcy.

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; DBP, diastolic blood pressure; FPG, fasting plasma glucose; Hcy, homocysteine; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MAP, mean arterial pressure; PP, pulse pressure. BMI, Body mass index; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride.

TABLE 4 Adjusted ORs and 95% CIs of hypertension according to *H pylori* infection status

	H pylori negative	*H pylori* positive	*P* value
Case/participants	4923/8934	4695/8166	
Unadjusted	1.00 (reference)	1.102 (1.037, 1.17)	.002
Model 1	1.00 (reference)	1.15 (1.063, 1.243)	.000
Model 2	1.00 (reference)	1.162 (1.073, 1.259)	.000
Model 3	1.00 (reference)	1.117 (1.029, 1.213)	.008

Note: Model 1: adjusted for age, sex, family history of hypertension, smoking status, and alcohol consumption status. Model 2: adjusted for the same set of variables as model 1 plus BMI. Model 3: adjusted for covariates in model 2 plus TC, TG, LDL-C, HDL-C, BUN, creatinine, uric acid, ALT, AST, FPG, and Hcy.

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, Body mass index; BUN, blood urea nitrogen; FPG, fasting plasma glucose; Hcy, homocysteine; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride.

($P = .009$), of *H pylori* infectors were slightly higher, but the difference in PP ($P = .214$) was not statistically significant.

4 | DISCUSSION

In this large cross-sectional study, we found a positive association between *H pylori* infection and prevalence of hypertension independent of other traditional risk factors. The *H pylori* infection was independently associated with higher DBP but not SBP, PP, and MAP. The *H pylori* infection was positive with TC, LDL-C, FPG, and Hcy levels, and negatively with HDL-C level. There was no interaction between *H pylori* infection and traditional risk factors of hypertension.

In our study, BP was significantly higher in *H pylori*-positive adults than in those who tested negative for *H pylori*. However, we found that *H pylori* infection was related to a higher DBP but not SBP, PP, and MAP. A cross-sectional study indicated that *H pylori* infection was positively associated with DBP but not SBP.[9] Meanwhile, Migneco et al[13] demonstrated a significant decrease in DBP after *H pylori* eradication in hypertensive patients. Kopacova et al[14] found that there was a negative effect of *H pylori* positivity on systolic and diastolic blood pressure in subjects below 25 and a relatively strong positive effect on blood pressure in subjects older 65 years. However, some studies have also shown that *H pylori* infection did not influence SBP nor DBP.[6,15,16]

Controversial data have been published in the literature regarding the positive and negative effects of *H pylori* infection on hypertension. A large-scale, community-based study in an Iranian population indicated that *H pylori* infection showed a significant association with hypertension by testing for immunoglobulin G (IgG) antibodies.[17] The results of a cross-sectional study performed by Wan et al[9] were consistent with our findings. In contrast with the results of our study, Hartog et al[18] tested for *H pylori* using antibodies among 440 Dutch, 320 Turkish, and 272 Moroccan participants and found that *H pylori* infection was weakly associated with hypertension but was not statistically significant. A cross-sectional study of 488 hypertensive and 942 normotensive Chinese Mongolian subjects also demonstrated that *H. p*ylori had no association with hypertension.[10] These inconsistent findings may be due to the different methods of measurement for *H pylori*, the selected population, sample size, and adjustment for different potential factors.

Although there is no consensus on the relationship between *H pylori* infection and hypertension, the mechanism remains to be investigated and may involve several aspects such as inflammation,

metabolism, and hormones. The antibody of *H pylori's* virulence factor CagA can directly cross-react with the surface antigen of the blood vessel wall,[19] stimulate lymphocyte proliferation, and promote the body to release a series of pro-inflammatory factors such as interleukin-1 (IL-1), tumor necrosis factor-α (TNF-α), C-reactive protein (CRP), and fibrinogen.[20,21] These factors enhance the local inflammatory response by recruiting inflammatory cells. This study found that the WBC count in the *H pylori*-positive group was higher than the negative group, which also indicated that chronic infection caused by *H pylori* caused changes in the body's inflammatory response. The subsequent low-intensity inflammatory response in the body leads to a significant increase in the total number of white blood cells and CRP concentrations in the blood, causing local inflammation of the arterial wall, eventually leading to vascular endothelial cell damage and dysfunction, smooth muscle cell proliferation, and atherosclerosis.[22] Meanwhile, these factors are inflammatory cytokines related to insulin resistance and the pathogenesis of diabetes.[23] It has been confirmed that insulin resistance is an important cause of hypertension.

Moreover, studies have found that chronic *H pylori* infection can cause abnormal metabolism of the body's LDL-C, HDL-C, and TC.[24,25] Majka et al[26] found that the TC and LDL-C levels in patients with *H pylori* infection significantly decreased after receiving anti-*H pylori* treatment. Moreover, some studies have found that after eradication of *H pylori*, the levels of HDL-C in patients increased significantly, while the levels of TG, CRP, fibrinogen, and LDL-C decreased significantly.[27] Actively eradicating *H pylori* infection is beneficial to reduce the occurrence of dyslipidemia, thereby preventing the occurrence of cardiovascular disease. It may be that these inflammatory factors caused by *H pylori* infection affect lipids: (a) TNF-α can inhibit the activity of lipoprotein lipase, and transfer lipids from the tissue, so that the level of TG in the blood increased and the level of HDL-C decreased.[28] (b) IL-6 and TNF-α can increase liver cholesterol synthesis by affecting the expression of 3-hydroxy-3-methyl glutaryl coenzyme A (HMG-CoA) reductase gene, and inhibit cholesterol hydroxylase to reduce liver cholesterol catabolism.[29] However, the levels of LDL-C and TC were lower in the hypertension group, which was likely due to lifestyle revision and the intervention of antihypertensive agents after diagnosis of hypertension.

H pylori infection often leads to chronic gastritis and peptic ulcers in patients. These diseases often affect the digestive and absorption functions of the stomach and cause gastric dysfunction by damage to gastric parietal cells. As a result, *H pylori* infection is likely to result in the deficiency of vitamin B_6, vitamin $B_{12,}$ and folic acid, which are indispensable and important coenzymes in the process of methionine metabolism.[30] Deficiency of these substances can lead to methionine metabolic disorders and methylation failure, causing elevated serum Hcy levels in patients with *H pylori* infection. This is in accordance with our finding that with or without hypertension, individuals with *H pylori* infection had higher levels of Hcy. However, Hcy inhibits the secretion of nitric oxide (NO) by endothelial cells, causing platelet aggregation and vasoconstriction. It leads to endothelial cell damage and weakening of the protective effect of endothelial cell-derived relaxation factors.[31] Hcy can also promote the binding of lipoproteins to fibrinogen and promote the occurrence of arteriosclerosis and hypertension.[32]

DBP largely depends on peripheral resistance, while SBP mainly depends on cardiac output. *H pylori*-infected subjects had significantly higher levels of fibrinogen, a marker of vascular inflammation that inhibits the reduction of NO, leading to vasoconstriction and an increase in peripheral blood vessel tension.[33] As mentioned above, Hcy can inhibit the release of NO and promote the binding of lipoproteins to fibrinogen. This may explain why *H pylori* infection was associated with DBP but not SBP. This was also consistent with the characteristics that the participants infected with *H pylori* had a higher level of PP.

The main advantages of our study include a large sample size and sufficient result certainty. In addition, the available information on various covariates, including medical history, medication history, and family history, allowed us to adapt to the underlying risk factors for hypertension and increased the reliability of the results.

There are some limitations in our study. First, the cross-sectional design did not allow us to demonstrate a causal relationship between *H pylori* infection and hypertension prevalence. Second, participants were middle-aged and older adults, and their findings might not be generalized to populations of all ages, different health conditions, or other ethnicities. Third, although we adjusted for many confounding factors, the possibility of residual confounding could not be ruled out, for example, for such factors as diet and CRP. Fourth, the association between *H pylori* infection and hypertension was significant statistically. Although it was unlikely to be clinically important, our results add to the evidence supporting the notion for that *H pylori* has a role in promoting hypertension.

In conclusion, we observed significant associations between *H pylori* and the prevalence of hypertension in a Chinese population. Our findings require confirmation but may have important implications for public health both in China and worldwide.

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CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

AUTHOR CONTRIBUTIONS

Study design: Handong Yang and Tangchun Wu. Data collection: Xuelian Xiong, Chen Jun, Meian He, and Tangchun Wu. Data analysis and interpretation of the results: Xuelian Xiong and Meian He. Manuscript drafting: Xuelian Xiong and Chen Jun. Manuscript edition: Xuelian Xiong and Hangdong Yang. Study supervision: Handong Yang and Tangchun Wu.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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