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Effect of *Helicobacter pylori* infection on body fat percentage in middle-aged and elderly populations

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ABSTRACT

Background: Obesity, which is associated with excessive accumulation of body fat, is emerging as a new public health problem. Bioelectrical impedance analysis (BIA) is a non-invasive and straightforward method to analyze body composition, providing a more accurate estimate of obesity than the commonly used body mass index. The primary objective of this study was to examine the potential impact of *Helicobacter pylori (H. pylori)* infection on body fat percentage in a population using cross-sectional and cohort studies. Methods: A population of people who underwent physical examinations at Taizhou Hospital between 2017 and 2022 was included. The participants underwent various tests, including urea breath test, hematological examination, and anthropometric measurement, in addition, their body fat percentage was determined through the use of BIA. Univariate and multifactorial regression analyses were conducted to identify factors associated with excess body fat. Results: There was a difference in body fat percentage between *H. pylori* positive and negative populations. The population was divided into young and middle-aged and elderly according to age, and *H. pylori* infection was found to differ only in the middle-aged and elderly population. Multifactorial logistic regression showed that *H. pylori* infection remained associated with excess body fat in the middle-aged and elderly population. A subsequent cohort study confirmed the association of persistent *H. pylori* infection with excess body fat in the population. Conclusion: *H. pylori* was negatively associated with excess body fat in middle-aged and elderly populations, and long-term *H. pylori* infection has a negative effect on body fat in people.

1. Introduction

Helicobacter pylori (H. pylori), is a Gram-negative bacterium that predominantly colonizes human gastric epithelial cells, infecting approximately more than 50 % people worldwide (Hooi et al., 2017). *H. pylori*, which has various virulence factors, induces local and systemic immune responses and triggers multiple adaptive mechanisms during its adherence and colonization (Sharndama and Mba, 2022). The evidence overwhelmingly suggests that *H. pylori* infection has a significant impact on the development of a variety of digestive tract disorders, including but not limited to gastric ulcers, gastritis, gastric mucosal lymphoma, and gastric cancer (Jonaitis et al., 2018). Moreover, numerous studies have found a strong association between *H. pylori* infection and extragastric conditions, including diabetes, atherosclerosis, dyslipidemia, and metabolic syndrome (Tsay and Hsu, 2018; Shi et al., 2022; Hashim et al., 2022).

Obesity is emerging as a new public health problem, increasing the risk of many metabolic and cardiovascular diseases, leading to a decrease in quality of life as well as life expectancy, and creating social and economic burden (Blüher, 2019). Body mass index (BMI), as a common anthropometric parameter, was used to determine obesity (Apovian, 2016). However, obesity is distinguished by the accumulation of excessive body fat, which is widely considered to be a major indicator of poor health (Blundell et al., 2014). While BMI correlates with body fat percentage, it is not an accurate reflection of the actual level of body fat in an individual, and therefore, serves as an indirect means of assessing obesity[9]. Bioelectrical impedance analysis (BIA) has become increasingly popular for measuring body fat in large-scale studies due to its non-invasive and simple nature as a method of body composition analysis (Böhm and Heitmann, 2013; Wang et al., 2022). BIA provides a more

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accurate estimate of body composition than BMI, making it a more reliable method for assessing obesity (Anwer et al., 2023).

New findings suggest that *H. pylori* infection has a broader impact beyond the stomach, as it not only disturbs the balance of commensal bacteria in the stomach but also induces changes in the microbiota of the human gut (Lopetuso et al., 2018; Martin-Nuñez et al., 2021). Gut microbes are involved in host immunity as well as metabolic homeostasis, and their imbalance may lead to inflammatory bowel disease, malnutrition, obesity, and diabetes (DeGruttola et al., 2016). Obesity has been shown to be associated with certain infectious diseases (Honce and Schultz-Cherry, 2019; Marjani et al., 2022; Hasan et al., 2021). However, the correlation between *H. pylori* and obesity remains inconclusive.

The aim of this study is to explore the potential correlation between *H. pylori* infection and body fat percentage in the human population by means of conducting cross-sectional and cohort studies on a large sample. Providing new insights into future approaches to reducing obesity through the link between *H. pylori* and obesity.

2. Materials and methods

2.1. Research participants

The participants in this study were those who underwent health examinations at Taizhou Hospital between 2017 and 2022. Inclusion criteria were as follows: 18 years of age or older, complete personal information, blood biochemical results, completion of urea breath test and BIA. Blood biochemical results included low-density lipoprotein (LDL), high-density lipoprotein (HDL), total cholesterol (TC), triglyceride (TG), fasting blood glucose (FBG) and glycated hemoglobin A1c (HbA1c). People with missing clinical information, history of gastrointestinal surgery, severe cardiovascular disease, suffering from malignancy, and diabetes were excluded. In this study, we defined patients with diabetes as individuals who had previously been diagnosed with the condition and were receiving treatment with hypoglycemic agents, or those who displayed a FBG level of $\geq$ 7.0 mmol/L or HbA1c level of $\geq$ 6.5 % at the time of physical examination. The study included a total of 14,711 individuals. Moreover, the study included 571 middle-aged and elderly individuals who underwent at least two medical examinations, with a time interval of more than 1 year between the initial and final check-ups.

2.2. Detection of H. pylori

In health screening, *H. pylori* status was detected using the ^{13}C or ^{14}C urea breath test. ^{13}C breath test: In fasting state, participants gargled and completed normal exhalation and collected breath samples, then participants took ^{13}C urea capsules orally, sat for 30 min and collected breath samples again, and the two samples were tested and analyzed on the instrument. ^{14}C breath test: Participants took ^{14}C urea capsules orally, sat for 15 min and exhaled through the exhalation port into the breath collection card, and then the breath collection card was tested.

2.3. Human parameters and blood biochemical results

Participants' age, gender, past medical history, systolic blood pressure (SBP), and diastolic blood pressure (DBP) were recorded and measured by a trained nurse. Additionally, the blood samples were obtained from each participant after an overnight fast to measure levels of FBG, HbA1c, TC, TG, HDL, and LDL.

2.4. Detection of body fat percentage

For all participants, we measured the body fat percentage of them using BIA. In the fasted state, the metal accessories were removed from the subject's body before the measurement, and the subject was dressed in light clothing, standing barefoot on the pedal, holding the electrodes with both hands and aligning the heels with the electrodes at the rear end of the foot, keeping the arms straight and the thighs untouched by each other. Men with a body fat percentage of more than 25 % and women with 30 % were considered to have excess body fat (Okorodudu et al., 2010; Kim et al., 2013).

2.5. Statistical analysis

Continuous variables were presented as mean ± standard deviation using t-tests, while categorical variables were presented as counts and percentages using the chi-square test. After adjusting for confounders, the relationship between *H. pylori* infection and excess body fat was scrutinized through multivariable logistic regression, and odds ratios (OR) and 95 % confidence intervals (CI) were computed. All statistical analyses were performed using R (4.1.3) software, whereby, a p-value of $<$ 0.05 was considered statistically significant.

3. Result

3.1. Clinical characteristics of the population

The study included a total of 14,711 individuals, and Table 1 presents the demographic and laboratory characteristics of the entire population. People who were positive for *H. pylori* were more often male, older, have higher SBP and DBP, but lower TC, LDL, HDL, and body fat percentage.

3.2. Risk factors for excess body fat in different populations

Considering that young people are more likely to control their body fat percentage through fitness, diet and exercise, we conducted a stratified analysis of young people (less than 45 years old) and middle-aged and elderly people (45 years old and above) (Zhao et al., 2014). In young adults, there were differences in gender, TC, TG, LDL, HDL, DBP, SBP, FBG, HbA1c, but age (p = 0.117) and *H. pylori* infection (p = 0.825) had no effect on excess body fat, as shown in Table 2. In contrast, individuals with excess body fat in the middle-aged and elderly population were found to have lower rates of *H. pylori* infection as compared to those with normal body fat (36.0 % vs. 39.0 %, p = 0.012), as illustrated in Table 3.

Table 1
Baseline characteristics of all physical examination populations of Taizhou Hospital, China, 2017 to 2022.

Variables	*H. pylori*-negative (n = 9410)	*H. pylori*-positive (n = 5301)	p-value
Gender (n, %)			0.004
Female	3397 (36.1)	1790 (33.8)	
Male	6013 (63.9)	3511 (66.2)	
Age (year)	46.04 ± 10.67	46.56 ± 10.55	0.004
Triglycerides (mmol/L)	1.97 ± 1.62	2.00 ± 1.66	0.270
Total cholesterol (mmol/L)	5.16 ± 0.97	5.12 ± 0.96	0.024
High density lipoprotein (mmol/L)	1.37 ± 0.31	1.35 ± 0.30	<0.001
Low density lipoprotein (mmol/L)	2.87 ± 0.74	2.83 ± 0.72	0.002
Diastolic blood pressure (mmHg)	76.19 ± 11.67	77.00 ± 12.05	<0.001
Systolic blood pressure (mmHg)	125.82 ± 16.59	126.87 ± 17.45	<0.001
Fasting blood glucose (mmol/L)	5.12 ± 0.54	5.12 ± 0.54	0.415
Glycated hemoglobin A1c (%)	5.63 ± 0.35	5.64 ± 0.34	0.204
Body fat percentage (%)	29.86 ± 5.49	29.61 ± 5.51	0.008

Table 2
Baseline characteristics of normal and excess body fat in young people of Taizhou Hospital, China, 2017 to 2022.

Variables	Normal (n = 1790)	Excess (n = 4283)	p-value
Gender (n, %)			<0.001
Female	411 (23.0)	1593 (37.2)	
Male	1379 (77.0)	2690 (62.8)	
Age (year)	35.8 ± 6.06	36.07 ± 5.81	0.117
Triglycerides (mmol/L)	1.85 ± 1.76	2.10 ± 1.78	<0.001
Total cholesterol (mmol/L)	4.92 ± 0.90	5.04 ± 0.93	<0.001
High density lipoprotein (mmol/L)	1.37 ± 0.30	1.30 ± 0.30	<0.001
Low density lipoprotein (mmol/L)	2.69 ± 0.69	2.80 ± 0.72	<0.001
Diastolic blood pressure (mmHg)	72.69 ± 10.61	74.41 ± 11.49	<0.001
Systolic blood pressure (mmHg)	120.00 ± 13.93	121.87 ± 14.65	<0.001
Fasting blood glucose (mmol/L)	4.94 ± 0.48	5.05 ± 0.52	<0.001
Glycated hemoglobin A1c (%)	5.47 ± 0.31	5.51 ± 0.33	<0.001
H. pylori			0.825
negative	1168 (65.3)	2782 (65.0)	
positive	622 (34.7)	1501 (35.0)	

Table 3
Baseline characteristics of normal and excess body fat in middle-aged and elderly people of Taizhou Hospital, China, 2017 to 2022.

Variables	Normal (n = 2249)	Excess (n = 6389)	p-value
Gender (n, %)			<0.001
Female	347 (15.4)	2836 (44.4)	
Male	1902 (84.6)	3553 (55.6)	
Age (year)	52.96 ± 6.17	53.59 ± 6.64	<0.001
Triglycerides (mmol/L)	1.81 ± 1.47	2.00 ± 1.54	<0.001
Total cholesterol (mmol/L)	5.12 ± 0.95	5.30 ± 1.00	<0.001
High density lipoprotein (mmol/L)	1.41 ± 0.31	1.39 ± 0.31	0.023
Low density lipoprotein (mmol/L)	2.82 ± 0.71	2.95 ± 0.75	<0.001
Diastolic blood pressure (mmHg)	77.40 ± 11.53	78.61 ± 11.95	<0.001
Systolic blood pressure (mmHg)	127.03 ± 16.70	130.54 ± 17.89	<0.001
Fasting blood glucose (mmol/L)	5.11 ± 0.53	5.22 ± 0.55	<0.001
Glycated hemoglobin A1c (%)	5.68 ± 0.32	5.73 ± 0.33	<0.001
H. pylori			0.012
negative	1372 (61.0)	4088 (64.0)	
positive	877 (39.0)	1501 (36.0)	

3.3. Effect of H. pylori infection on excess body fat

Results from the univariate analysis demonstrated that age, blood pressure, glucose, and lipids were potential risk factors for excess body fat. However, being male (OR = 0.229, 95 % CI = 0.202–0.259, $p < 0.05$) and *H. pylori* infection (OR = 0.881, 95 % CI = 0.798–0.972, p = 0.012) became negative associations with excess body fat, as demonstrated in Fig. 1. After controlling confounding factors such as age, gender, blood lipid, blood pressure and glucose, *H. pylori* infection was still negatively associated with excess body fat ($p < 0.05$) by using multifactorial logistic regression analysis, as shown in Table 4.

3.4. Longitudinal association between H. pylori infection status and excess body fat

Out of the total number of participants, 571 middle-aged and elderly individuals underwent at least two physical examinations. The population was divided into four categories: persistent negative, new infection, persistent infection, and eradicated infection based on *H. pylori* infection status during the first and last physical examinations, as shown in Fig. 2A. We found a substantial reduction in the proportion of excess body fat within the persistent infection group (Fig. 2B) as well as in the new infection group (Fig. 2C) compared to the persistent negative group ($p < 0.05$). However, the discrepancy was not statistically significant between the eradication group and the persistent infection group (p = 0.786, Fig. 2D).

4. Discussion

In previous studies, there are still inconsistent results regarding the correlation between *H. pylori* infection and obesity. For example, an investigation involving a sample of 235,107 individuals showed an increase in BMI with *H. pylori* infection (Suki et al., 2018). However, a retrospective study conducted in China reported no connection between *H. pylori* infection and obesity (Xu et al., 2017). Conversely, in another study, a significant negative correlation was found between the prevalence of *H. pylori* and the local prevalence of obesity (Lender et al., 2014). Additionally, there have been studies demonstrating a negative correlation between *H. pylori* seropositivity and obesity (Wu et al., 2005). Similarly, some studies have confirmed an increase in BMI after *H. pylori* eradication (Lane et al., 2011; Park et al., 2023). However, in these studies, no additional analysis was performed on age, an important confounding factor, which may have led to different findings.

Previous partial studies, confirming the negative association of *H. pylori* with obesity in children, may lead to malnutrition (Moran-Lev et al., 2017; Szaflarska-Popławska and Soroczyńska-Wrzyszcz, 2021). However, no studies have been conducted on the relationship between *H. pylori* and body fat percentage in the middle-aged and elderly population. In our study, we observed that the *H. pylori* positive population exhibited a lower body fat percentage compared to the negative population. Nonetheless, upon conducting age stratification, we discovered no association between *H. pylori* infection and excess body fat in young adults. This may be due to the fact that young people pay more attention to keeping fit and reduce their body fat percentage through sports, diet control, fitness and other ways. In contrast, the prevalence of excess body fat was found to be lower in the middle-aged and elderly population with *H. pylori* infection. Moreover, this protective effect was sustained even after adjusting for multiple confounders. Considering that *H. pylori* may cause diabetes, which is more likely to cause obesity, fatty liver, and hypertension, the diabetic population was not included in this study (Zhou et al., 2022; Tanase et al., 2020; Ruze et al., 2023; Sun et al., 2019). In addition, subsequent cohort studies have demonstrated that continuing *H. pylori* infection is associated with a notable reduction in the prevalence of excess body fat among middle-aged and elderly individuals. However, the mechanisms involved remained unclear. *H. pylori* infection is thought to affect the brain-gut axis, which may, in turn, alter appetite by influencing the host's neurological, endocrine, and immune responses (Budzyński and Kłopocka, 2014). It has been suggested that *H. pylori* infection may affect leptin and ghrelin expression, reduce energy intake, and lead to malnutrition in the elderly (Salles et al., 2006). Following the complete removal of *H. pylori*, the secretion of ghrelin increases, leading to an augmented appetite and subsequent weight gain (Francois et al., 2011). However, some studies have shown that although ghrelin levels were restored after *H. pylori* eradication, weight did not increase significantly (Jang et al., 2008). In addition, prolonged *H. pylori* infection may lead to impaired absorption of nutrients and vitamins, which may further affect body fat (Franceschi et al., 2014; Aimasso et al., 2019). It is well known that diet and gut microbiota are closely related to obesity. However, it is unclear whether other gut microbes have a potential effect on body fat changes after *H. pylori* infection. Based on the negative correlation between *H. pylori* and obesity in this study, it provides some insights for future studies exploring the mechanisms of *H. pylori* and obesity.

Our study, which involved a large sample of individuals, confirmed

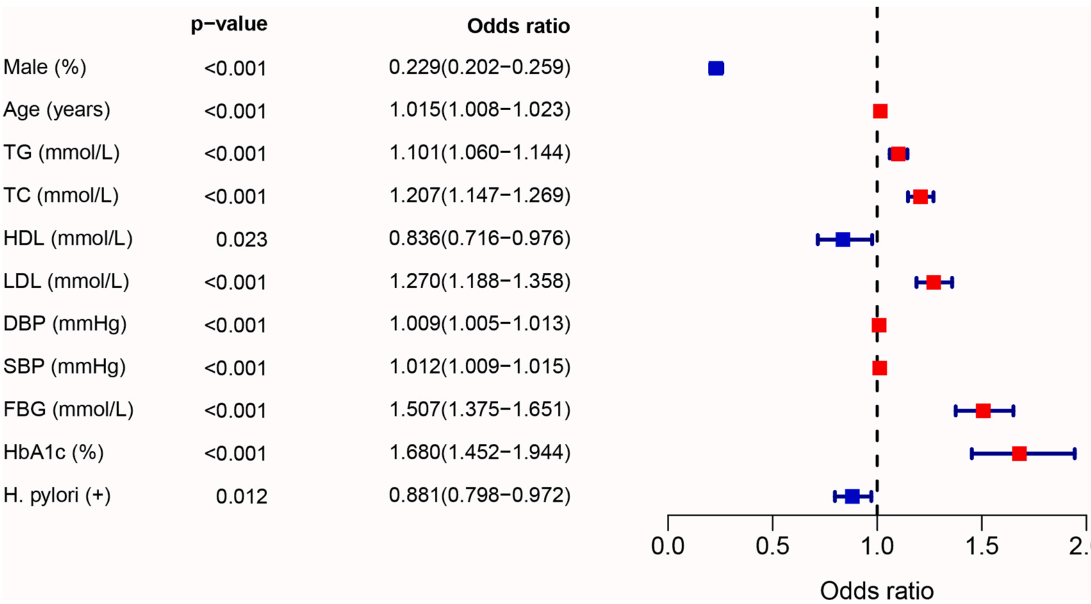

Fig. 1. Univariate analysis of risk factors for excess body fat in middle-aged and elderly people of Taizhou Hospital, China, 2017 to 2022.

Table 4
Multivariable regression analysis of *H. pylori* and excess body fat in middle-aged and elderly people of Taizhou Hospital, China, 2017–2022.

	OR (95 % CI)	p-value
Model 1	0.90 (0.81–1.00)	0.049
Model 2	0.89 (0.80–0.99)	0.034
Model 3	0.88 (0.79–0.98)	0.020
Model 4	0.89 (0.80–0.99)	0.027

Model 1 is adjusted for age, sex.
Model 2 is adjusted for age, sex, TG, TC, HDL, LDL.
Model 3 is adjusted for age, sex, TG, TC, HDL, LDL, DBP, SBP.
Model 4 is adjusted for age, sex, TG, TC, HDL, LDL, DBP, SBP, FBG, HbA1c.

the inverse association between *H. pylori* infection and excess body fat. Nevertheless, our study is not without limitations. The study lacked information on socioeconomic status and diet, which are also important factors in obesity. Secondly, during the infection process, *H. pylori* releases various virulence factors, such as cytotoxin-associated gene A and Vacuolating cytotoxin A, and it is still unclear which specific virulence factor is associated with obesity (Bridge and Merrell, 2013). Third; the assessment of body fat percentage in this study was performed using the method of BIA rather than the more accurate dual-energy X-ray absorptiometry. Additionally, the mechanism through which *H. pylori* influences obesity is unknown and requires further investigation via biological experiments.

5. Conclusion

Our study, which involved a large sample of middle-aged and elderly individuals, confirmed the negative association between *H. pylori* infection and excess body fat, highlighting that long-term *H. pylori* infection has a negative effect on body fat in people.

CRediT authorship contribution statement

Yi Chen: Writing – original draft, Visualization, Formal analysis, Data curation, Conceptualization. **Dan Yan:** Writing – original draft, Data curation, Conceptualization. **Ningning You:** Visualization, Formal analysis. **Binbin Gu:** Writing – original draft. **Qinya Wang:** Writing – original draft. **Jinshun Zhang:** Writing – review & editing, Supervision, Methodology, Formal analysis, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence

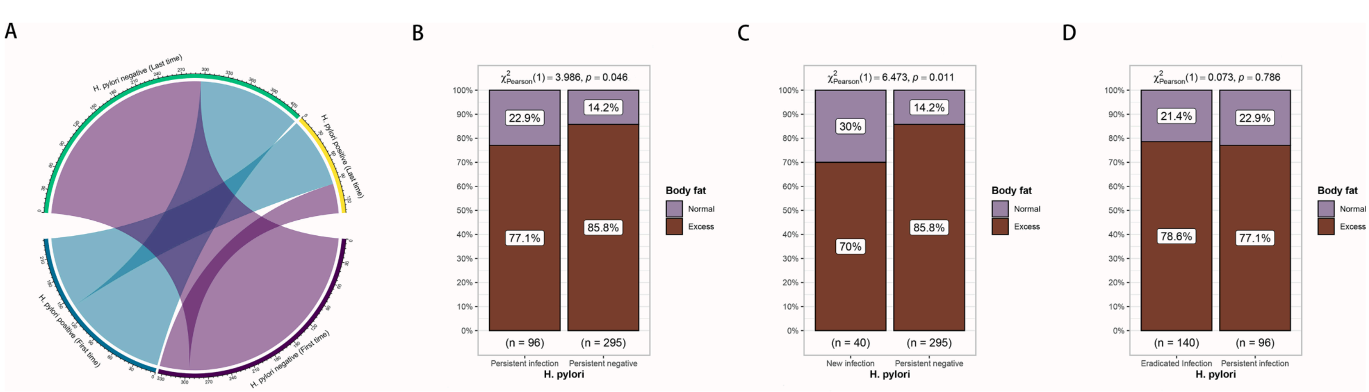

Fig. 2. Differences in excess body fat among middle-aged and elderly people with different *H. pylori* infection status of Taizhou Hospital, China, 2017 to 2022. (A) Changes in the status of first and last *H. pylori* infections. (B) Difference in excess body fat between persistent infection and persistent negative. (C) Difference in excess body fat between new infection and persistent negative. (D) Difference in excess body fat between eradication infection and persistent infection.

the work reported in this paper.

Data availability

Data will be made available on request.

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Availability of data and materials

The dataset in the current study is available from the corresponding author by reasonable request.

Ethics approval and consent to participate

This research has been approved by the Ethics Committee of Taizhou Hospital (K20220790). This study was a retrospective analysis of clinical data obtained during the course of the study, and the written informed consent requirement was waived by the ethics committee of Taizhou Hospital. We confirm that all methods are performed in accordance with the relevant guidelines and regulations.

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