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Comparative Analysis of *Helicobacter pylori* Infection Status in High Altitude and Plain Areas of China

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Abstract

Background: China has a high prevalence of *HP* infection, and the rate of *HP* infection in highland populations is higher than the average rate of *HP* infection in natural populations. However, there is a lack of comparative studies on the current status of *HP* infection in high- and low-altitude. Therefore, this study aims to investigate the current status and differences in *HP* infection between the health check-up populations in the highland region and the plain area. **Methods:** This is a multicenter cross-sectional study, using convenience sampling method, which included the health check-up population of Ruoergai County People's Hospital and the health check-up population of Deyang City People's Hospital from January 2023 to December 2023, to carry out the questionnaire survey of *HP*-related factors, and to detect *HP* infection by a ^{13}C-urea breath test. **Results:** The number of positives was 144 out of 260 health checkups in the plateau region, with a detection rate of 55.4%, which was significantly higher than that of 29.8% in the plains ($P < 0.05$). In the *H. pylori* infection-positive population, the health checkups in the plateau group had a lower education level, a higher proportion of overweight and obesity, a higher proportion of frequent smokers, a higher frequency of frequent eating out, and a lower proportion of abnormalities of uric acid, total cholesterol, LDL cholesterol, alanine aminotransferase, aspartate aminotransferase, and direct bilirubin but a higher proportion of abnormalities of total bilirubin. There was no statistically significant difference between the two groups in terms of age, gender, history of alcohol consumption, family history, urea, creatinine, and blood glucose. **Conclusion:** Preliminary results indicate that the rate of *HP* infection in the plateau population is significantly higher than that in the plains, and *HP*-related health education should be strengthened in the plateau region.

Keywords

Helicobacter pylori, Epidemiology, Cross-Sectional Study, Health Check-Up Population, Plateau, Plain

1. Background

Helicobacter pylori (*HP*) infection is a major cause of chronic gastritis, peptic ulcer, gastric mucosa-associated lymphoid tissue lymphoma, and gastric cancer, as well as being closely associated with a variety of extra gastrointestinal diseases [1] [2]. It has been reported that approximately half of the global population is infected with *HP* [3]. Although the *HP* infection rate in China has continued to decline over the past decades (overall infection rate of 58.3% during 1983-1994 and 40.0% during 2015-2019) [4] [5], the disease burden associated with *HP* is still significant due to the large population base. Therefore, the investigation and prevention of *HP* infection has become a public health issue of particular concern to the medical field in China.

HP infection has a global distribution, and the prevalence of *HP* infection in different populations varies greatly depending on age, family history of gastric cancer, geographic location, regional economic development, and sanitary conditions [3] [6]. An epidemiologic survey in 2021 that included a total of 10,735 households (31,098 individuals) in 29 provinces in mainland China, excluding Guangxi and Tibet, showed that the prevalence of individual *HP* infection in the 29 provinces ranged from 25.33% to 59.61% [7]. A recent meta-analysis of the temporal and spatial distribution of *HP* infections in mainland China also showed that the plateau is a high-prevalence area for *HP* infections [8]. Eradication of *HP* can effectively control the disease progression associated with *HP* infection and is the most controllable measure to reduce the risk of gastric cancer [9]. There have been some investigations and analyses focusing on the current status of *HP* infection in different regions of China, but there is a lack of comparative studies on the current status and differences between *HP* infection in highland areas and plains. In this study, we used a multicenter cross-sectional study to explore and compare the current status and differences of *HP* infection in the highland and plains areas, to provide data for the prevention and control of HP infection in the highland and plains areas, and guide how to formulate public health policies and preventive and control strategies targeting. *HP* infection by local conditions, to prevent *HP* infection-related diseases and to improve the level of health.

The global prevalence of *HP* in adults between 2011 and 2022 is 43.1%, with similar rates for men and women. However, there is regional variability in the infection rate, with the Middle East having the highest rate of 56.1%, followed by Asia with 53.3%. The overall *HP* infection rate in our population is higher than the global rate, 46.7%, and is higher in rural than in urban areas, with the highest rate (>50%) in people aged 30 - 60 years. The results of the urea breath test showed

that the prevalence of *HP* infection in the medical checkup population in different regions ranged from 25.8% to 38.82%, indicating that it is necessary to actively carry out *HP* screening in the medical checkup population and strengthen the post-test intervention and management, which can help to reduce the risk of gastric cancer in this opportunistic population, and it is one of the most important strategies for gastric cancer prevention and control.

2. Methods

2.1. Study Population

The study was a multi-center cross-sectional study and the survey was conducted using a convenience sampling method. Health check-ups who completed ^{13}C-UBT examination at the Health Management Center of Deyang People's Hospital and the Health Management Center of Ruoergai County People's Hospital from January 2023 to December 2023 were selected as the study subjects and completed basic information collection, physical examination, blood routine, biochemical indexes, and lipid indexes examination. Ethical approval for the study was granted by the Ethics Committee of the People's Hospital of Deyang City (Ethical Review Approval No. 2023-04-024-K01).

2.2. Inclusion and Exclusion Criteria

Inclusion criteria: 1) No related medications such as proton pump inhibitors, antimicrobials, or nonsteroidal anti-inflammatory drugs have been taken in the last 4 weeks; 2) Have not been diagnosed with a digestive system-related disease or undergone surgery on the gastrointestinal area within the last 1 year; 3) Obtaining informed consent and signing an informed consent form from the medical examiner himself/herself and his/her family.

Exclusion Criteria: 1) Those who have had previous *HP* infections; 2) Received *HP* eradication therapy in the previous 3 months; 3) Those who cannot perform the 13-C urea breath test; 4) Familial hypercholesterolemia and hypertriglyceridemia.

2.3. *Helicobacter pylori* Seropositivity

The subjects were fasted for at least 2 h before the examination, and 0 min of expiratory breath was collected before taking a urea capsule (containing 75 mg of 13C-urea) with room-temperature drinking water, and the expiratory breath was collected for 30 min after the drug was taken. Connect the 2 breath sample bags to the HY-IREXB plus 13C breathalyzer (Beijing Huagan Anbang Science and Technology Co., Ltd.) and perform the 13C-urea breath test. Results Judgement: DOB values ≥4.0 were defined as positive for *HP* infection and <4.0 as negative for *HP* infection.

2.4. Data Collection and Measurement

1) Basic information collection

Basic information was collected using a uniform, self-administered questionnaire for health check-up populations in the Plateau and Plains, including gender, age, education level, smoking history, alcohol consumption history, dining patterns, and family history.

Body Mass Index (BMI) = weight (kg)/height (m^2).

2) Collection of blood indicators

Biochemical indicators: Including triglycerides（TG）, total cholesterol（TC）low density lipoprotein (LDL) low density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), alanine transferase (ALT), aspartate amino transferase (AST), total bilirubin (TB), fasting plasma glucose (FPG), uric acid (UA), urea nitrogen (UREA), creatinine (CREA). All tests were performed using a Beckman 5800 fully automated biochemical analyzer (Beckman Coulter Co., Ltd., USA) and Sysmex XE-2100 analyzer (Sysmex Corporation, Japan).

2.5. Decision Criteria

1) Body mass index: According to the relevant guidelines [10] [11], 4 groups of body mass were categorized as lean, normal, overweight and obese according to BMI <18.5, 18.5~, 24.0~ and ≥28.0 kg/m^2.

2) Blood biochemistry and lipid levels: The normal ranges for alanine aminotransferase, total bilirubin, direct bilirubin, albumin, aspartate aminotransferase, total cholesterol, triglycerides, low-density lipoprotein cholesterol, uric acid, creatinine, fasting blood glucose, and urea nitrogen were 7 - 40 U/L, 0 - 21 umol/L, 0 - 5.1 umol/L, 40 - 55 g/L, 13 - 35 U/L, 0 - 5.18 mmol/L, 0 - 1.7 mmol/L, 0 - 3.3 mmol/L, 155 - 357 umol/L, 41 - 81 umol/L, 3.9 - 6.1 mmol/L, 3.1 - 8.8 mmol/L。Classification of normal/abnormal based on the range of normal values.

2.6. Quality Control

To ensure the accuracy and reliability of the results, strict quality control measures were implemented during the data collection and analysis process. 13CUBT operations are performed by professionally trained technicians to ensure standardization of testing. All biochemical tests are performed in a certified laboratory using standard operating procedures and calibrated equipment. Data cleaning and validation were performed before data entry and statistical analysis to ensure the accuracy of the analysis.

2.7. Statistical Analysis

Data analysis was performed using SPSS 26.0 software. Before performing statistical tests on the data, the normality of the data was first tested using the Kolmogorov-Smirnov test. For measures that conformed to a normal distribution, independent samples t-tests were used for between-group comparisons. Non-parametric tests (e.g., Mann-Whitney U test) were used for measures that did not fit a normal distribution. Count data were compared using the χ^2 test. All statistical tests for

normally distributed information are described using mean ± standard deviation, and non-normally distributed measures are expressed as median and quartiles [M (P25, P75)]. $P < 0.05$ was considered a statistically significant difference.

3. Results

3.1. Participants' Baseline Characterization

This study included 260 cases of health checkups in the highland area and 10,972 cases of health checkups in the plains area. There were no statistically significant differences between the plateau and the plains in terms of family history, urea, creatinine, and albumin levels (all $P > 0.05$). The average age of the highland residents was (39.33 ± 12.69) years, which was lower than the (44.05 ± 12.38) years of the plains residents ($P < 0.05$). The proportion of highly educated highland residents was significantly lower than that of Han Chinese residents, and the proportion of smokers, non-drinkers, non-exercisers, eating out, was significantly higher than that of plains residents, and the differences were all statistically significant ($P < 0.05$), as shown in Table 1.

Table 1. Comparison of general information between the highland group and the plains group.

Variable	Plains group (n = 10,972)	Plateau group (n = 260)	P value
Sex, n (%)			<0.001
Male	6211 (56.6%)	130 (50.0%)	
Female	4761 (43.4%)	130 (50.0%)	
Age, mean ± SD	44.05 ±12.38	39.33±12.69	<0.001
Educational levels, n (%)			<0.001
Junior high school or below	17 (0.2%)	4 (1.5%)	
High school	2588 (23.6%)	68 (26.2%)	
College or above	8367 (76.3%)	188 (72.3%)	
BMI[a]			<0.001
Undernutrition (<18)	2163 (20.0%)	14 (5.4%)	
Normal (18.5 - 23.9)	4289 (39.7%)	125 (48.4%)	
Overweight (25 - 30)	3246 (30.0%)	91 (35.3%)	
Obese (30+)	1112 (10.3%)	28 (10.9%)	
Smoking, n (%)			0.006
Never	8393 (76.5%)	144 (55.4%)	
Occasional smoking	696 (6.3%)	53 (20.4%)	
Smoker	1883 (17.2%)	63 (24.2%)	

Continued

Drinking, n (%)			<0.001
Never	5960 (54.3%)	174 (66.9%)	
Occasional alcohol consumption	3514 (32.0%)	51 (19.6%)	
Drinker	1498 (13.7%)	35 (13.5%)	
Physical activity, n (%)			0.021
<150 min/week	9259 (97.5%)	233 (89.6%)	
≥150 min/week	1713 (15.6%)	27 (10.4%)	
Dine way, n (%)			<0.001
Eat at home	4390 (40.0%)	148 (756.9%)	
Eat at cafeteria	4729 (43.1%)	46 (17.7%)	
Eat at restaurant	1853 (16.9%)	66 (25.4%)	
Family history, n (%)			0.080
No	7392 (67.4%)	158 (60.8%)	
Yes	3580 (32.6%)	102 (39.2%)	
Urea nitrogen, M (P25, P75)	5.25 (4.43, 6.22)	5.19 (4.49, 6.09)	0.909
Creatinine, M (P25, P75)	70.90 (61.10, 78.50)	69.80 (60.03, 81.78)	0.665
Uric acid, M (P25, P75)	356. 80 (293.5, 425.7)	317.75 (271.45, 386.25)	<0.001
Fasting blood glucose, M (P25, P75)	4.96 (4.62, 5.39)	5.05 (4.78, 5.42)	0.003
Total cholesterol, M (P25, P75)	5.30 (4.56, 6.98)	5.03 (4.34, 5.60)	<0.001
Triglycerides, M (P25, P75)	1.70 (1.05, 5.29)	1.30 (0.97, 1.90)	<0.001
Low-density lipoprotein cholesterol, M (P25, P75)	3.19 (2.52, 4.55)	2.90 (2.37, 3.43)	<0.001
High-density lipoprotein cholesterol, M (P25, P75)	1.47 (1.17, 2.18)	1.34 (1.11, 1.60)	<0.001
Albumin, M (P25, P75)	44.40 (27.00, 47.00)	43.60 (42.63, 45.20)	0.409
Alanine aminotransferase, M (P25, P75)	17.00 (9.00, 27.00)	21.00 (15.00, 33.00)	<0.001
Glutathione aminotransferase, M (P25, P75)	20.00 (14.00, 25.00)	21.00 (17.00, 25.00)	<0.001
Total bilirubin, M (P25, P75)	12.40 (7.30, 16.70)	21.07 (16.53, 26.96)	<0.001
Direct bilirubin, M (P25, P75)	3.70 (2.90, 4.90)	2.14 (1.38, 3.10)	<0.001
HP infection, n (%)	3253 (29.8%)	144 (55.4%)	<0.001

3.2. *HP* Infection

The number of positives was 144 out of 260 health checkups in the highlands, a detection rate of 55.4%. The number of positive cases was 3253 out of 10,972

cases of health checkups in the plains, with a detection rate of 29.8%, a statistically significant difference (P < 0.05). Among the *HP*-infected subjects, the differences between the highland and plains populations were statistically significant in terms of education, BMI, smoking history, dining patterns, uric acid, TC, TG, LDL-C, ALT, AST, total bilirubin, and direct bilirubin. The proportion of those with low education, overweight and obesity ratio, smoking history, eating out, and total bilirubin abnormality was higher than that of those who had health checkups in the plain area, and the proportion of those with abnormality in TC, TG, LDL-C, ALT, AST, and direct bilirubin was lower than that of those who had health checkups in the plain area, and the difference was statistically significant (P < 0.05). There was no statistically significant difference between the two groups in the percentage of gender, age, history of alcohol consumption, family history, urea, creatinine, and fasting blood glucose abnormalities (P > 0.05), see Table 2.

Table 2. Comparative analysis of clinical data of *HP*-infected patients in highland group and plains group.

Variable	Plains group (n = 3253)	Plateau group (n = 144)	P value
Sex, n (%)			0.053
Male	2001 (61.5%)	77 (53.5%)	
Female	1252 (38.5%)	67 (46.5%)	
Age (mean ± SD)			0.093
<60 years	2863 (88.0%)	120 (83.3%)	
≥60 years	390 (12.0%)	24 (16.7%)	
Educational levels			<0.001
Junior high school or below	3 (0.1%)	3 (2.1%)	
High school	742 (22.8%)	37 (25.7%)	
College or above	2508 (77.1%)	104 (72.2%)	
BMI			0.001
Undernutrition (<18)	662 20.6%)	11 (7.7%)	
Normal (18.5 - 23.9)	1126 (35.1%)	58 (40.8%)	
Overweight (25 - 30)	1047 (32.6%)	60 (42.3%)	
Obese (30+)	372 (11.6%)	13 (9.2%)	
Smoking, n (%)			<0.001
Never	2362 (72.6%)	82 (56.9%)	
Occasional smoking	227 (7.0%)	25 (17.4%)	
Smoker	664 (20.4%)	37 (25.7%)	

Continued

Drinking, n (%)			0.060
Never	1760 (54.0%)	94 (65.3%)	
Occasional alcohol consumption	1007 (31.0%)	33 (22.9%)	
Drinker	486 (15.0%)	17 (11.8%)	
Dine way, n (%)			<0.001
Eat at home	1323 (40.7%)	67 (46.5%)	
Eat at cafeteria	1405 (43.2%)	26 (18.1%)	
Eat at restaurant	525 (16.1%)	51 (35.4%)	
Family history, n (%)			0.092
No	1641 (50.4%)	86 (59.7%)	
Yes	1612 (49.6%)	58 (40.3%)	
Urea nitrogen (mmol/L, n %)			0.636
Normal	3120 (96.6%)	138 (95.8%)	
Abnormal	110 (3.4%)	6 (4.2%)	
Creatinine (umol /L, n %)			0.193
Normal	2569 (80.5%)	107 (75.9%)	
Abnormal	621 (19.5%)	34 (24.1%)	
Uric acid (umol/L, n %)			<0.001
Normal	1569 (48.4%)	92 (63.9%)	
Abnormal	1670 (51.6%)	52 (36.1%)	
Fasting blood glucose (mmol/L, n %)			0.889
Normal	2865 (89.4%)	128 (90.1%)	
Abnormal	340 (10.6%)	14 (9.9%)	
Total cholesterol (mmol/L)			0.013
Normal	1482 (45.6%)	81 (56.3%)	
Abnormal	1771 (54.4%)	63 (43.8%)	
Triglycerides (mmol/L, n %)			<0.001
Normal	1606 (50.6%)	101 (73.2%)	
Abnormal	1567 (49.4%)	37 (26.8%)	
Low-density lipoprotein cholesterol (mmol/L, n %)			<0.001
Normal	1732 (54.8%)	97 (70.8%)	
Abnormal	1427 (45.2%)	40 (29.2%)	

Continued

Alanine aminotransferase (U/L, n %)			0.005
Normal	2149 (67.1%)	113 (78.5%)	
Abnormal	1052 (32.9%)	31 (21.5%)	
Glutathione aminotransferase (U/L, n %)			<0.001
Normal	2244 (69.0%)	129 (89.6%)	
Abnormal	1009 (31.0%)	15 (10.4%)	
Total bilirubin (umol/L, n %)			<0.001
Normal	2888 (90.4%)	77 (55.00%)	
Abnormal	305 (9.6%)	63 (45.00%)	
Direct bilirubin (umol/L, n %)			<0.001
Normal	2547 (78.3%)	135 (95.1%)	
Abnormal	705 (21.7%)	7 (4.9%)	

4. Discussion

This study is the first to compare the current status and differential characteristics of *HP* infection in a healthy physical examination population in highland and plains areas. The survey included 260 cases of health checkups in the highlands and 10,972 cases in the plains, and the results showed that the prevalence of *HP* infection was significantly higher in the highlands than in the plains. *HP* infection is influenced by many factors such as environment, cultural level, and living habits. People who live at high altitudes, have low levels of education, and eat out more frequently are usually more susceptible to *HP* infection than the rest of the population [7] [12]. The results of this study showed that the *HP* infection rate in the health checkup population in the plateau region was 55.4%, which was lower than the national average infection level, which may be related to the improved hygiene and health awareness of the local population as well as the small sample size of this survey in the plateau region. Cui Ying *et al.* [13] showed that the *HP* prevalence rate in the health checkup population in the plateau region was 62.47%, which was slightly higher than the average of this study and China, which may be related to the higher proportion of patients included in the study who frequently used pickled or barbecued foods and had a history of chronic gastric disease.

In addition, some researchers have pointed out that the high rates of *HP* infection and gastric cancer among plateau residents are not only due to the backwardness of health and economy, but may also be related to the environmental characteristics of the plateau [14]. Plateau populations living in alpine and hypoxic environments may undergo a series of adaptive changes in their respiratory system, cardiovascular system, and metabolic characteristics [15]. A survey comparing the prevalence of *HP* infection among residents at different altitudes showed that the

prevalence of *HP* infection among residents living at high altitudes was 68.67%, which was significantly higher than that of 57.33% among residents who moved to low altitudes [16]. This is consistent with the results of this study. A study investigating patients with digestive symptoms in high-altitude regions of India found a higher prevalence of *HP* infection through histopathology and endoscopy [17]. In addition, a recent study indicated that high-altitude hypoxia exacerbates gastric mucosal inflammation and injury by enhancing oxidative stress and inflammatory response induced by *HP* infection [18]. However, a previous study showed that high altitude and the colder climate do not influence on the prevalence of *HP* in Saudi nationals sharing similar genetic and cultural habits, which is possibly related to sample size, and differences between study areas [19]. The causal relationship between altitude and HP infection needs to be further investigated.

In the *HP*-infected population, the percentage of overweight or obese group was higher in the plateau region than in the plains, which may be related to the dietary habits and lifestyle in the plateau region. It is also associated with the role of the intestinal immune system in prompting the body to secrete inflammatory factors and increase insulin resistance after *HP* infection. The recent meta-analysis results showed that there was a positive correlation between the risk of *HP* infection and the prevalence of obesity development [20]. *HP* infection triggers the release of the orexigenic hormone, ghrelin, which regulates the appetite [21]. Obese/overweight individuals have been shown to exhibit reduced circulating levels of ghrelin, indicating a potential association between ghrelin and obesity [22]. In addition, *HP*-positive individuals have been shown to exhibit reduced serum levels of leptin [23] [24]. Reduced leptin levels induce appetite, which leads to overfeeding, resulting in overweight and obesity [25]. However, in a meta-analysis, previous studies were found to be geographically diverse, with more retrospective studies and fewer observational studies, and many uncontrollable confounding factors may be involved in the process of obesity development and *HP* infection [26], and there is still a need for large cohort studies and large-sample randomized controlled trials to study the relationship between obesity and *HP*.

Results are inconsistent between studies regarding the possible relationship between *HP* infection and smoking. No relationship between *HP* infection and smoking was found in the majority of cases. In this study, the smoking rate of *HP*-infected patients was higher in the plateau than in the plains, which was consistent with previous studies [27]. Features of high-altitude environments allow hypoxia, energy depletion, and tissue acidosis in localized tissues, which may damage intestinal epithelial cells and disrupt tight junction protein complexes, leading to intestinal barrier dysfunction [28]. In this environment accompanied by tobacco and alcohol addiction, gastric acid, and duodenal bicarbonate secretion increased, damage to the gastric mucosal barrier. Furthermore, Nicotine appears to enhance gastric invasive factors (e.g., gastric acid and pepsin secretion, duodenal gastric reflux, and free radical production) and weaken mucosal defenses (e.g., prosta-

glandin synthesis, mucus production, and epidermal growth factor secretion), which may enhance colonization following *H. pylori* exposure [29]. Although the available data were insufficient to examine the causal relationships between smoking and the risk of *HP* infection, smoking cessation should be advocated to reduce *HP* infection; in the meantime, it is necessary to make individualized health management and intervention programs for people who smoke and are infected with *HP* to reduce the infection and prevalence, which in turn effectively reduces the incidence of secondary diseases, such as gastric ulcers, and gastric cancer.

In this study, it has been shown [30] that alcohol consumption destroys the barrier effect of gastric mucosa and triggers gastrointestinal diseases, and that *HP* infection and long-term alcohol consumption lead to the inhibition of IL10-induced CD8+ cell dysfunction and the inhibition of NKX6.3 expression-induced gastric carcinogenesis. However, the study did not find any difference between *HP* infection individuals from the plateau and the plains, which may be related to the small number of alcohol drinkers included in the study.

This study showed that the serum total bilirubin was significantly higher in the plateau than in the plains, but direct bilirubin lower than in the plains, and this study is similar to the findings of Zeng *et al.* [31], which showed that the percentage of total bilirubin abnormalities in plateau officers and soldiers at altitudes >3000 m was higher than that in the population at altitudes <1000 m. The increase of bilirubin is mainly due to the hypoxia-induced increase in secretion of erythropoietin after the organism enters the plateau, driving the compensatory mass production of red blood cells and hemoglobin, and the corresponding increase in senescence and destruction of red blood cells, and a large amount of hemoglobin is converted into indirect bilirubin, which is more than the processing capacity of the liver, and it can't be completely converted into direct bilirubin, so the level of serum total bilirubin is elevated [32]. In addition, TBIL and DBIL in the Han population were significantly higher than those in the Tibetan population for 3 consecutive years. Even the average level of TBIL in the Han nationality has exceeded the upper limit of the normal reference value for three consecutive years, which shows that the metabolic burden of the liver is heavier in the Han population at extremely high altitudes [33]. Studies have shown that *HP* infection may be associated with decreased bilirubin concentrations within the reference range [34]. The possible mechanism is that *HP* itself acts as an immunogen, and its virulence factor induces the recruitment of immune cells, releasing a large number of cytokines that can function far from the gastric mucosa, such as IL-6, IL-8, and tumor necrosis factor-alpha, which inhibit the activity of heme hydroxylase and reduce bilirubin production [35]. Furthermore, *HP* infection has been shown to result in chronic inflammation and influence bile reflux [36], which may at least in part explain the bilirubin changes, but further research relating to possible mechanisms is required.

In this study, the two groups of *HP*-infected patients also differed in TC, TG, LDL-C, ALT, and AST, which is related to the fact that chronic *HP* infection may

affect lipid metabolism, stimulate the body to initiate systemic immune responses and inflammatory reactions and promote atherosclerosis [37] [38]. The results of several studies at home and abroad have shown that TC, TG, and LDL-C levels are elevated in *HP*-infected patients, which is consistent with the results of this study [39]-[41].

This study is the first to compare and analyze the *HP* infection status of health check-up populations in the plateau and plains based on multicenter real-world big data, providing strong data on ethnic and regional differences in *HP* infection in the plateau region. The shortcomings of the study are mainly in the following three areas. First, the sample size of the highland areas included in the survey was small and from a concentrated source, and a large-scale, multiregional sampling survey has yet to be organized to provide more convincing evidence. Second, the study population did not undergo gastroscopy, so it was not possible to assess the differences in the pathologic changes in the gastric mucosa of the *HP* infection population in the highlands and plains. Future studies could incorporate gastroscopy and histological examination to confirm *HP* infection and assess the severity of gastritis and other gastric lesions to provide a more complete picture of the disease burden. Thirdly, the populations sampled (health check-up attendees) might not accurately represent wider community *HP* infection rates. Therefore, large-scale, multiregional sampling surveys need to be organized to better explore the current status of *HP* infection. In summary, the rate of *HP* infection is higher in the population of health checkups in the plateau region, and the population in the plateau region mostly has lifestyle-related factors such as low educational level, high percentage of smoking, a large percentage of overweight or obesity, and high percentage of eating out. The prevention and control of *HP*-related infection factors should be strengthened in highland areas.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Sugano, K., Tack, J., Kuipers, E.J., Graham, D.Y., El-Omar, E.M., Miura, S., *et al.* (2015) Kyoto Global Consensus report on *Helicobacter pylori* Gastritis. *Gut*, **64**, 1353-1367. https://doi.org/10.1136/gutjnl-2015-309252

[2] Malfertheiner, P., Megraud, F., Rokkas, T., *et al.* (2022) Management of *Helicobacter pylori* Infection: The Maastricht VI/Florence Consensus Report. *Gut*, **71**, 1724-1762.

[3] Hooi, J.K.Y., Lai, W.Y., Ng, W.K., Suen, M.M.Y., Underwood, F.E., Tanyingoh, D., *et al.* (2017) Global Prevalence of *Helicobacter pylori* Infection: Systematic Review and Meta-Analysis. *Gastroenterology*, **153**, 420-429. https://doi.org/10.1053/j.gastro.2017.04.022

[4] Li, M., Sun, Y., Yang, J., de Martel, C., Charvat, H., Clifford, G.M., *et al.* (2020) Time Trends and Other Sources of Variation in *Helicobacter pylori* Infection in Mainland China: A Systematic Review and Met-Analysis. *Helicobacter*, **25**, e12729. https://doi.org/10.1111/hel.12729

[5] Ren, S., Cai, P., Liu, Y., Wang, T., Zhang, Y., Li, Q., *et al*. (2021) Prevalence of *Helicobacter pylori* Infection in China: A Systematic Review and Meta-Analysis. *Journal of Gastroenterology and Hepatology*, **37**, 464-470. https://doi.org/10.1111/jgh.15751

[6] Malfertheiner, P., Camargo, M.C., El-Omar, E., Liou, J., Peek, R., Schulz, C., *et al*. (2023) *Helicobacter pylori* Infection. *Nature Reviews Disease Primers*, **9**, Article No. 19. https://doi.org/10.1038/s41572-023-00431-8

[7] Zhou, X., Lyu, N., Zhu, H., Cai, Q., Kong, X., Xie, P., *et al*. (2023) Large-Scale, National, Family-Based Epidemiological Study on *Helicobacter pylori* Infection in China: The Time to Change Practice for Related Disease Prevention. *Gut*, **72**, 855-869. https://doi.org/10.1136/gutjnl-2022-328965

[8] Lu, T., Zhang, J., Li, S. and Chen, C. (2022) Spatial-temporal Distribution and Influencing Factors of *Helicobacter pylori* Infection in Chinese Mainland, 2001-2020. *Journal of Clinical Gastroenterology*, **56**, e273-e282. https://doi.org/10.1097/mcg.0000000000001691

[9] Liu, W.Z., Xie, Y., Lu, H., Cheng, H., Zeng, Z.R., Zhou, L.Y., *et al*. (2018) Fifth Chinese National Consensus Report on the Management of *Helicobacter pylori* Infection. *Helicobacter*, **23**, e12475. https://doi.org/10.1111/hel.12475

[10] The People's Republic of China (2013) WS/T 428-2013 Criteria of Weight for Adults。China Standard Press.

[11] Bao, Y., Lu, J., Wang, C., Yang, M., Li, H., Zhang, X., *et al*. (2008) Optimal Waist Circumference Cutoffs for Abdominal Obesity in Chinese. *Atherosclerosis*, **201**, 378-384. https://doi.org/10.1016/j.atherosclerosis.2008.03.001

[12] Li, Y., Choi, H., Leung, K., Jiang, F., Graham, D.Y. and Leung, W.K. (2023) Global Prevalence of *Helicobacter pylori* Infection between 1980 and 2022: A Systematic Review and Meta-analysis. *The Lancet Gastroenterology & Hepatology*, **8**, 553-564. https://doi.org/10.1016/s2468-1253(23)00070-5

[13] Cui, Y., Jin, Y., Liu, X.L., *et al*. (2024) HP Infection Rate, Antibody Typing and Logistic Regression Analysis of 1111 Cases of HP Infection in Health Check-Up Population in Highland Area. *Public Health and Preventive Medicine*, **35**, 53-56.

[14] Zhang, T., Luo, C., Hu, Z.Q., *et al*. (2022) Research Progress of Gastric Cancer in Highland Areas. *China Cancer Clinic*, **49**, 95-98.

[15] Storz, J.F. and Cheviron, Z.A. (2021) Physiological Genomics of Adaptation to High-Altitude Hypoxia. *Annual Review of Animal Biosciences*, **9**, 149-171. https://doi.org/10.1146/annurev-animal-072820-102736

[16] Bai, W.C., Xiang, R., Zhao, F.C., *et al*. (2020) Analysis of the Results of Carbon 14 Breath Test for *Helicobacter pylori* in Tibetan and Chinese Residents at Different Altitudes. *Chinese Practical Medicine*, **15**, 160-162.

[17] Sharma, P.K. (2014) Atrophic Gastritis with High Prevalence of *Helicobacter pylori* Is a Predominant Feature in Patients with Dyspepsia in a High Altitude Area. *Tropical Gastroenterology*, **35**, 246-251. https://doi.org/10.7869/tg.224

[18] Li, C., Wang, X. and Cui, S. (2024) Impact of High-Altitude Hypoxia on *Helicobacter pylori*-Induced Gastritis Pathological Manifestations and Inflammatory Responses. *Journal of Physiological Anthropology*, **43**, Article No. 17. https://doi.org/10.1186/s40101-024-00364-5

[19] Ahmed, M.E.B.K., Al-Knawy, B., Al-Wabel, A. and Foli, A. (1997) Duodenal Ulcer and *Helicobacter pylori* Infection at High Altitude: Experience from Southern Saudi Arabia. *Canadian Journal of Gastroenterology and Hepatology*, **11**, 313-316. https://doi.org/10.1155/1997/589701

[20] Baradaran, A., Dehghanbanadaki, H., Naderpour, S., Pirkashani, L.M., Rajabi, A., Rashti, R., *et al*. (2021) The Association between *Helicobacter pylori* and Obesity: A Systematic Review and Meta-Analysis of Case-Control Studies. *Clinical Diabetes and Endocrinology*, **7**, Article No. 15. https://doi.org/10.1186/s40842-021-00131-w

[21] Cummings, D.E. (2006) Ghrelin and the Short- and Long-Term Regulation of Appetite and Body Weight. *Physiology & Behavior*, **89**, 71-84. https://doi.org/10.1016/j.physbeh.2006.05.022

[22] Nwokolo, C.U. (2003) Plasma Ghrelin Following Cure of *Helicobacter pylori*. *Gut*, **52**, 637-640. https://doi.org/10.1136/gut.52.5.637

[23] Farbstein, D. and Levy, A.P. (2012) HDL Dysfunction in Diabetes: Causes and Possible Treatments. *Expert Review of Cardiovascular Therapy*, **10**, 353-361. https://doi.org/10.1586/erc.11.182

[24] Gunji, T., Matsuhashi, N., Sato, H., Fujibayashi, K., Okumura, M., Sasabe, N., *et al*. (2009) *Helicobacter pylori* Infection Significantly Increases Insulin Resistance in the Asymptomatic Japanese Population. *Helicobacter*, **14**, 496-502. https://doi.org/10.1111/j.1523-5378.2009.00705.x

[25] Choi, H.R., Lim, H., Lee, J.H., Park, H. and Kim, H.P. (2021) Interruption of *Helicobacter pylori*-Induced NLRP3 Inflammasome Activation by Chalcone Derivatives. *Biomolecules & Therapeutics*, **29**, 410-418. https://doi.org/10.4062/biomolther.2020.192

[26] Chen, J., Ma, J., Liu, X., Duan, S., Liang, N. and Yao, S. (2020) The Association between *Helicobacter pylori* Infection with Overweight/Obesity: A Protocol for a Systematic Review and Meta Analysis of Observational Studies. *Medicine*, **99**, e18703. https://doi.org/10.1097/md.0000000000018703

[27] Hussein, R.A., Al-Ouqaili, M.T.S. and Majeed, Y.H. (2022) Association between Alcohol Consumption, Cigarette Smoking, and *Helicobacter pylori* Infection in Iraqi Patients Submitted to Gastrointestinal Endoscopy. *Journal of Emergency Medicine, Trauma and Acute Care*, **2022**, Article 12. https://doi.org/10.5339/jemtac.2022.aimco.12

[28] McKenna, Z.J., Gorini Pereira, F., Gillum, T.L., Amorim, F.T., Deyhle, M.R. and Mermier, C.M. (2022) High-Altitude Exposures and Intestinal Barrier Dysfunction. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, **322**, R192-R203. https://doi.org/10.1152/ajpregu.00270.2021

[29] Endoh, K. and Leung, F.W. (1994) Effects of Smoking and Nicotine on the Gastric Mucosa: A Review of Clinical and Experimental Evidence. *Gastroenterology*, **107**, 864-878. https://doi.org/10.1016/0016-5085(94)90138-4

[30] Aziz, F., Chakraborty, A., Liu, K., Zhang, T., Li, X., Du, R., *et al*. (2021) Gastric Tumorigenesis Induced by Combining *Helicobacter pylori* Infection and Chronic Alcohol through IL-10 Inhibition. *Carcinogenesis*, **43**, 126-139. https://doi.org/10.1093/carcin/bgab114

[31] Zeng, R.P., Wang, D.L. and Qian, P. (2023) Liver Function Impairment and Its Correlation with Altitude in Highland Training Officers and Soldiers. *Armed Police Medicine*, **34**, 291-294.

[32] Zeng, R.P., Wang, D.L. and Qian, P. (2023) Liver Function Impairment of Officers and Soldiers Stationed on Plateau and Its Correlation with Altitude. *Armed Police Medicine*, **34**, 291-294.

[33] Yuan, Z., Zou, Y., Liu, X., Wang, L. and Chen, C. (2023) Longitudinal Study on Blood and Biochemical Indexes of Tibetan and Han in High Altitude Area. *Frontiers in Public Health*, **11**, Article 1282051. https://doi.org/10.3389/fpubh.2023.1282051

[34] Zhao, M., Krebs, J., Cao, X., Cui, J., Chen, D., Li, Y., *et al*. (2019) *Helicobacter pylori* Infection as a Risk Factor for Serum Bilirubin Change and Less Favourable Lipid Profiles: A Hospital-Based Health Examination Survey. *BMC Infectious Diseases*, **19**, Article No. 157. https://doi.org/10.1186/s12879-019-3787-8

[35] Jiao, L.L., Zhang, L., Li, Y.Z., *et al*. (2022) Analysis of *Helicobacter pylori* Infection and Its Correlation with Serum Bilirubin in Railway Drivers. *Chinese Occupational Medicine*, **49**, 577-581.

[36] Elizalde, J.I., Piqué, J.M., Moreno, V., Morillas, J.D., Elizalde, I., Bujanda, L., *et al*. (2002) Influence of *helicobacter Pylori* Infection and Eradication on Blood Lipids and Fibrinogen. *Alimentary Pharmacology & Therapeutics*, **16**, 577-586. https://doi.org/10.1046/j.1365-2036.2002.01202.x

[37] Shi, H., Li, Y., Dong, C., Si, G., Xu, Y., Peng, M., *et al*. (2021) *Helicobacter pylori* Infection and the Progression of Atherosclerosis: A Systematic Review and Meta-Analysis. *Helicobacter*, **27**, e12865. https://doi.org/10.1111/hel.12865

[38] Shuai, X.J., Chen, G. and Ma, Q. (2021) The Correlation between Carotid Plaque and *Helicobacter pylori* Infection. *Chinese Journal of Health Management*, **15**, 390-394.

[39] Zhang, L., Zhang, Y., Zhang, X., *et al*. (2020) Relationship between *Helicobacter pylori* Infection and Blood Glucose and Lipid Metabolism in Health Check-Up Population. *Chinese Journal of Gastroenterology*, **40**, 126-128.

[40] Dore, M.P., Saba, P.S., Tomassini, G., Niolu, C., Monaco, M. and Pes, G.M. (2022) Increased Risk to Develop Hypertension and Carotid Plaques in Patients with Long-Lasting *Helicobacter pylori* Gastritis. *Journal of Clinical Medicine*, **11**, Article 2282. https://doi.org/10.3390/jcm11092282

[41] Wang, L., Cao, Z., Zhang, L., Dai, X., Liu, Z., Zeng, Y., *et al*. (2022) *Helicobacter pylori* and Autoimmune Diseases: Involving Multiple Systems. *Frontiers in Immunology*, **13**, Article 833424. https://doi.org/10.3389/fimmu.2022.833424