

Analysis of influencing factors associated with Hp infection in H-type hypertension

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Abstract: Objective to investigate the influencing factors of *Helicobacter pylori* (Hp) infection in patients with H type hypertension. Methods A total of 1089 patients with h-type hypertension who underwent physical examination in Lanzhou Petrochemical Company of petrochina in Lanzhou city, Gansu Province from May 2021 to September 2021 were selected as the research objects. All the patients were tested by 14C urea breath test and divided into Hp infected group (278 cases) and Hp non-infected group (811 cases) according to the test results. For collected age, sex and other general demographic indicators and determined systolic blood pressure (SBP) diastolic blood pressure (DBP) albumin (ALB) globulin (GLB) total protein (TP) albumin/globulin (ALB/GLB) uric acid (UA) triglyceride (TG) Total cholesterol (TC) High-density lipoprotein (HDL) Low density lipoprotein (LDL) fasting blood glucose (GLU) and other biochemical indicators were analyzed by univariate analysis and multivariate unconditiona Logistic regression analysis. Results Univariate analysis showed that albumin (ALB) in h-type hypertension patients in infection group was lower than that in lung infection group, and the difference was statistically significant ($T = 3.383, P < 0.05$). Systolic blood pressure (SBP), globulin (GLB), triglyceride (TG) and fasting blood glucose (GLU) were higher than those in the non-infected group, but the differences were not statistically significant (ALL $P > 0.05$). Diastolic blood pressure (DBP), total protein (TP), uric acid (UA), total cholesterol (TC) and low density lipoprotein (LDL) were higher than those in the non-infected group. There were no significant differences (all $P > 0.05$); Multivariate non-conditional Logistic regression showed that high density lipoprotein (DHL) was an independent protective factor for Hp infection in h-type hypertension patients ($OR = 0.49, P < 0.05$). Conclusions Hp infection is associated with lipid metabolism disorder, and high density lipoprotein is a protective factor of *HELICobacter pylori* infection in patients with H type hypertension.

Keywords: Homocysteine; Type H hypertension; *Helicobacter pylori*; Industrial estate

Type H hypertension is primary hypertension with hyperhomocysteinemia, referred to as hyperhomocysteinemia. Hp infection is currently considered a chronic infectious disease, with a global infection rate close to 50% and developing China up to 70%-90%^[1], and among Chinese adults with hypertension, type H hypertension accounts for 75%, including 91% of men and 60% of women^[2]. Recent related studies have found a correlation between the occurrence of H hypertension and *Helicobacter pylori* (Hp) infection, which affects the absorption of B6 and B12 in the digestive tract, decreases folic acid intake and synthesis, leads to impaired methionine metabolism and methylation failure thereby increasing homocysteine levels, and ultimately induces H hypertension^[3,4]. Workers in industrial areas are characterized by irregular lifestyle and high work intensity, and with the reform and innovation of industrial areas, their work pressure is enhanced, which also has an impact on their mental health, and related studies have shown that Hp infection is associated with poor lifestyle habits^[5] (e.g., smoking, drinking, use of public chopsticks), special dietary characteristics (e.g., high salt and spicy pickled foods, take-out, eating out), sleep time and sleep quality^[6] (overtime work, shift work, insomnia), and neuropsychological disorders^[7,8] (e.g., depression, anxiety) are closely related to each other. The manufacturing industry is the mainstay of the national economy and is the foundation of the country, the instrument of prosperity, and the basis of a strong country, so it is important to ensure the health of workers. Therefore, this study aimed to analyze the risk factors associated with Hp infection in patients with H hypertension and provide a theoretical basis for the development of health strategies for workers in industrial areas.

1. Object and method

1.1 General information

A total of 1,089 cases of H-type hypertension were collected from May 1, 2021 to September 30, 2021 from the physical examination population of China Petroleum Lanzhou Petrochemical Corporation, Lanzhou, Gansu Province. Diagnostic criteria (Data sets generated and/or analyzed during the current study period are available from corresponding authors upon reasonable request) : (1) systolic blood pressure > 140 mmHg or diastolic blood pressure > 90 mmHg; (2) blood Hcy ≥ 10 /L. Inclusion criteria: those who met the above diagnostic criteria and were confirmed by three consecutive blood pressure; all could be tested for Hp infection and blood pressure level; patients or family members who signed informed consent. Exclusion criteria: women during pregnancy or lactation; history of H. pylori eradication; those with a history of malignancy, myocardial infarction and stroke; those with genetic factors and patients with abnormal folate metabolism genes.

1.2 Methods

1.2.1 General information collection methods

Weight and height were measured using a corrected scale and height measuring device; systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured using a mercury sphygmomanometer; 3 ml of venous fasting blood was collected, and uric acid (UA), triglycerides (TG), total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), and fasting blood glucose (GLU) were measured using a fully automated biochemical analyzer; 3 ml of venous fasting blood was collected in an anticoagulated vacuum tube containing EDTA. GLU); 3 ml of venous fasting blood was collected in an anticoagulated vacuum tube containing EDTA, and routine albumin (ALB), globulin (GLB), and total protein (TP) measurements were performed with a hematocrit analyzer.

1.2.2 ^{14}C -urea breath test

^{14}C -urea capsules were produced by Shenzhen Haidewei Biotechnology Co., Ltd. with the strength of 27.75 kPa per capsule and CO_2 absorber (2 ml/bottle) scintillation solution prepared according to the instructions. Operation method: The subject is tested in the morning after fasting or eating for 2 h. Rinse the mouth before the test, take 1 capsule of ^{14}C -urea, sit still for 20 min, open 1 bottle of CO_2 absorber (2 ml in the liquid flash bottle), blow into the liquid flash bottle with CO_2 absorber through a gas catheter with anti-backflow device, the lower end of the catheter should be invaded into the absorbing liquid, with moderate strength to avoid spilling the liquid, and reverse suction is strictly prohibited, when CO_2 absorber saturation, from red to colorless stop blowing (about 1 ~ 3 min), such as more than 5 min, still not completely faded, also stop blowing, to the sample bottle to add diluted scintillation solution 4.5 ml, sealed with a lid, dissolve and shake well, in the liquid flash instrument for the sample ^{14}C radioactivity (dpm) measurement 2 min, when ^{14}C -UBT>100 dpm, can be judged Hp positive.

1.3 Observation indexes

The observation indexes of the study subjects were general demographic data, physical examination and biochemical indexes. The general demographic indexes included gender and age; physical examination SBP and DBP; biochemical indexes included ALB, GLB, TP, ALB/GLB, UA, TG, TC, HDL, LDL, and GLU.

1.4 Statistical methods

The data were statistically analyzed using SPSS 23.0. The measurement data were tested for normality to obey normal distribution to describe, grouped according to the presence or absence of Hp infection, and the two-sample independent samples t-test was used to compare the differences between groups; the count data were expressed as the number of cases (composition ratio), grouped according to demographic characteristics, and the test was used to compare between groups. The relationship between different biochemical indices and Hp infection in H hypertension was analyzed by multifactorial logistic regression. The test level was $\alpha=0.05$.

2. Results

2.1 General Information

Of the 1,098 cases in the physical examination population, 278 cases were Hp infected and 811 cases were non-infected, with an overall infection rate of 25.32%. There were 243 (87.41%, 243/278) male and 35 (12.59%, 35/278) female cases in the infected group, and 689 (84.96%, 689/811) male and 122 (15.04%, 122/811) female cases in the non-infected group, with no statistically significant difference between the male Hp infection rate compared to the female Hp infection rate ($= 1.010$, $P > 0.05$). the mean age of the Hp infected group was 47.97 years and the mean age of the Hp non-infected group was 47.92 years, the difference was not statistically significant ($t = 0.094$, $P > 0.05$).

2.2 Hp infection in patients with H-type hypertension with different individual characteristics and biochemical indices

The results of univariate analysis showed that albumin (ALB), albumin to globulin ratio (ALB/GLB), and high-density lipoprotein (HDL) levels were higher in the infected group than in the non-infected group, and all differences were statistically significant (all $P < 0.05$). See Table 1.

Table 1 Hp infection in patients with H-type hypertension in an industrial area of Lanzhou City ($n = 1089$, $\bar{x} \pm s$)

Variables	Infection groups($n=278$)	Non-infected groups($n=811$)	χ^2/t	P
Gender				
Male	243(87.41)	689(84.96)	1.010	0.325
Female	35(12.59)	122(15.04)		
Ages	47.97 \pm 7.61	47.92 \pm 7.45	0.094	0.925
DBP	72.55 \pm 4.19	72.77 \pm 4.22	0.145	0.885
SBP	1.68 \pm 0.32	1.72 \pm 0.31	-1.147	0.252
ALB	380.64 \pm 86.82	381.88 \pm 85.64	3.383	0.001
GLB	2.48 \pm 2.09	2.39 \pm 2.09	-1.454	0.146
TP	4.51 \pm 0.79	4.53 \pm 0.88	0.766	0.444
ALB/GLB	1.09 \pm 0.24	1.13 \pm 0.25	1.983	0.048
UA	2.95 \pm 0.84	2.97 \pm 0.90	0.209	0.835
TG	6.10 \pm 2.26	5.93 \pm 2.14	-0.629	0.530
CGOL/TC	19.91 \pm 15.70	18.03 \pm 12.36	0.369	0.712
HDL	1.09 \pm 0.24	1.13 \pm 0.25	2.337	0.020
LDL	2.95 \pm 0.84	2.97 \pm 0.90	0.234	0.815
GLU	6.10 \pm 2.26	5.93 \pm 2.14	-1.089	0.276

Note: Figures in parentheses are composition ratios(%)

2.3 Multi-factor unconditional logistic regression analysis

The presence or absence of Hp infection in patients with H hypertension was used as the dependent variable, and the observed indicators in the univariate that were consistent with multifactorial unconditional logistic regression analysis were used as independent variables, with biochemical indicators as continuous variables and gender as a reference for women. The results showed that the effect of HDL on Hp infection in patients with H-type hypertension was statistically significant (OR=0.49, 95% CI: 0.258-0.929, $P < 0.05$), as shown in Table 2.

Table 2 Multifactorial unconditional logistic regression analysis of Hp infection in patients with hypertension type H

Variables	β	$S_{\bar{x}}$	Wald χ^2	P -value	OR	95% CI
Gender	0.127	0.226	0.316	0.57	1.136	0.729~1.770
SBP	0.009	0.006	1.837	0.18	1.009	0.996~1.022
TP	-0.012	0.017	0.511	0.48	0.988	0.955~1.022
UA	-0.001	0.001	0.365	0.55	0.999	0.998~1.001
TG	0.004	0.038	0.011	0.92	1.004	0.931~1.083
HDL	-0.714	0.327	4.776	0.03	0.490	0.258~0.929
LDL	0.036	0.086	0.172	0.68	1.036	0.876~1.226
GLU	0.024	0.032	0.545	0.46	1.024	0.962~1.090

3. Discussions

Hp is an infectious gram-negative pathogenic bacterium that can be transmitted through fecal-oral, oral-oral, and gastric-oral routes, and the incidence of *H. pylori* infection varies from region to region and from lifestyle to lifestyle^[9]. The inflammatory substances, lipase proteins and toxic substances secreted by Hp can damage the gastric barrier leading to chronic gastritis, peptic ulcer, gastric cancer and extra-gastrointestinal diseases^[10]. In recent years, it was reported that the prevalence of Hp infection was positively correlated with the prevalence of hypertension in Chinese adults^[11,12], which is a risk factor for cardiovascular and ocular diseases, while *H. pylori* infection can increase homocysteine levels^[4,13,14], which in turn is an important risk factor for cardiovascular and cerebrovascular pathogenesis, as well as an independent risk factor for osteoporosis. In addition, the poor living conditions, irregular living habits, and stressful life of workers make them more likely to be infected with Hp and highly susceptible to related diseases, therefore, workers should be considered as a key concern, so it is urgent to study the risk factors of *H. pylori* infection and H hypertension.

The results of univariate analysis showed that the infection rate of *H. pylori* was 25.32%, which was lower than the overall infection rate in China^[15], the reasons for this result may be that the sample size of this experiment was too small, and also related to the dietary habits of this population in the region, and differences in economic conditions. The albumin in the *H. pylori*-infected group was less than that in the non-infected group, which is consistent with the findings of Li Xiaobing^[16], Wang Yongye^[17], and Zhao Yunman^[18], and may be related to the nutritional status of the organism and the inflammatory response of the organism. Endotoxin released by Hp infection causes an inflammatory response that can lead to serum tumor necrosis factor-(TNF (TNF-6), interleukin-6 (IL-6) and other inflammatory factors^[19-21], which can not only inhibit albumin synthesis, but also accelerate the rate of protein degradation in the body, as well as inhibit gastric acid secretion and slow down gastrointestinal motility, stimulate hormone synthesis, and ultimately affect nutritional status of the organism^[22-24], which decreases the immunity of the organism and increases the chance of Hp infection in workers with Hp hypertension. In addition, Hp infection can also cause a series of gastrointestinal complications, which can seriously affect the nutritional status of the body, and the most direct indicator of the nutritional status of the body is ALB^[25].

The results of multifactorial unconditional logistic regression showed that the level of HDL in the Hp-infected group was lower than that in the Hp-uninfected group. The higher the level of HDL, the lower the risk of Hp infection in patients with H-type hypertension, which is consistent with the statement that HDL cholesterol is the "good cholesterol"^[26], and with the findings of Huang Zhen^[27] et al. The results of IWAI^[28] et al. also showed that Hp infection was closely associated with lipid profile. HDL is a heterogeneous lipoprotein complex composed of multiple proteins and lipids, and the possible reasons for this phenomenon are as follows: (1) The reduced risk of Hp infection is closely related to the antioxidant effect of HDL. By modulating various antioxidant enzymes contained in HDL particles, such as elevated levels of lecithin-cholesterol acyltransferase (LCAT), cholesteryl ester transfer protein, hepatic lipase, and reduced levels of endothelial lipase, all lead to increased levels of high-density lipoprotein cholesterol (HDL-C)^[29,30], in addition to glutathione peroxidase in HDL, platelet-activating factor-acetyl hydrolase (PAF-AH) and paraoxonase (PON) in HDL are also closely associated with anti-inflammatory properties to resist *H. pylori* invasion^[31]; (2) the reduced risk of Hp infection is closely associated with HDL-regulated immune response. When *H. pylori* infection occurs, HDL not only inhibits the activity of endotoxins such as LPS/LTA, but also enhances the innate immune response. For example, in the immune response, penetratin 3 (pentraxin 3, PTX3) is regulated by HDL, which is able to promote PTX3 expression by activating the P13K/Akt pathway, and PTX3 has a pentraxin structural domain at the carboxy terminus, which is able to bind to the amino terminus of other proteins to perform immune functions, thus reducing *H. pylori* infection^[32]; (3) Hp infection HDL can inhibit the expression and release of inflammatory factors such as tumor necrosis factor- α (TNF- α), interleukin-1 β (IL-1 β), and intercellular adhesion factor, and inhibit the activation of complement, thus exerting an anti-inflammatory effect and suppressing the inflammatory response caused by *H. pylori* infection^[33], in addition to the findings^[34] that high doses of HDL promote the interaction of lipopolysaccharide (LPS) with LPS-binding protein (LBP), which contributes to the clearance of LPS; high concentrations of LBP inhibit the leukocyte response to LPS, while HDL inhibits the inhibitory activity of high concentrations of LBP and maintains the sensitivity of leukocytes to LPS, thereby inducing a response to *H. pylori* and other Gram-negative bacteria in early inflammatory responses.

In summary, the development of good dietary habits should not be neglected, such as reducing the frequency of eating out, changing the bad habit of mixing utensils, eating less pickled and barbecued

foods, drinking more yogurt, reducing the inflammatory response induced by the stimulation of the mucosa of the gastrointestinal tract, strengthening the immunity of the body, increasing the resistance to *H. pylori* infection, in addition to improving the level of education of workers, the correct and appropriate publicity and popularization of disease knowledge, establish the correct health concept, let workers know Hp, understand Hp, and be familiar with the fact that the treatment of Hp does not only rely on costly drug therapy, but also through lifestyle changes, attaching importance to prevention over treatment, and combining prevention and treatment measures to achieve the purpose of precise prevention and control of anti-Hp; finally, studies have shown ^[35] that sleep duration and sleep quality are also associated with Hp infection, so that maintaining adequate sleep and high quality sleep are especially important for workers working overtime and shift work, while maintaining a good mood and avoiding psychological disorders, such as anxiety and depression, can also strengthen the resistance to Hp infection.

There are some limitations in this study. Since this study is a cross-sectional study, the strength of the causality argument is relatively weak, so whether there is a clear causal relationship between Hp infection and HDL remains to be verified by further prospective experiments.

Conflict of interest

The authors declare that they have no competing interests.

Authors' contributions

LIU YB, QI SS carried out clinical studies; LI SS and WU JJ carried out data collection and data analysis; LI SS were in charge of manuscript writing.

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All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from the participants for publication of this clinical trial details.

Abbreviations

SBP systolic blood pressure
DBP diastolic blood pressure
ALB albumin
GLB globulin
TP total protein
ALB/GLB albumin/globulin
UA uric acid
TG triglyceride
TC Total cholesterol
HDL High-density lipoprotein
LDL Low density lipoprotein
GLU fasting blood glucose

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