

Effect of Helicobacter Pylori Infection on Glucose Metabolism, Lipid Metabolism and Inflammatory Cytokines in Nonalcoholic Fatty Liver Disease Patients

Qing-Yu Xiao¹, Ren-Ling Wang², Hai-Jun Wu¹, Wen-Bin Kuang³, Wei-Wei Meng⁴, Zhen Cheng⁵

¹Department of Blood Transfusion, Shenzhen Baoan Shiyuan People's Hospital, Shenzhen, 518108, China; ²Department of Oncology, Kaiping Central Hospital, Jiangmen City, Guangdong Province, 529399, People's Republic of China; ³Department of Laboratory, Longhua District Central Hospital, Shenzhen, 518110, People's Republic of China; ⁴Department of Laboratory, Shenzhen Baoan Shiyuan People's Hospital, Shenzhen, 518108, China; ⁵Guantian Community Healthcare Center, Shenzhen Baoan Shiyuan People's Hospital, Shenzhen, Guangdong province, 518100, People's Republic of China

Correspondence: Zhen Cheng, Guantian Community Healthcare Center, Shenzhen Baoan Shiyuan People's Hospital, About 50 Meters South of hkc Huike Industrial Park, Dezheng Road, Baoan District, Shenzhen, Guangdong province, 518100, People's Republic of China, Tel +86 13632854050, Email cheng_3003_zhen@163.com

Objective: To probe into the influence of Helicobacter pylori (Hp) infection on glucose metabolism, lipid metabolism, and inflammatory cytokines in patients with nonalcoholic fatty liver disease (MASLD).

Methods: A total of 140 MASLD patients admitted to our Hospital between June 2020 and May 2021 were selected as the research objects. Based on the presence or absence of Hp infection, they were divided into the study group (73 cases with infection) and control group (67 cases without infection). Glucose metabolism indicators [fasting blood glucose (FBG), 2-hour postprandial glucose (2hPG), fasting insulin (FINS), glycated hemoglobin (HbA1c)], lipid metabolism indicators [total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C)], and inflammatory indicators [interleukin-37 (IL-37), interleukin-18 (IL-18)] were measured and compared between the two groups.

Results: In terms of glucose metabolism indicators, the study group exhibited higher levels of FBG (5.84 ± 0.49 vs 5.40 ± 0.51 , $t=2.535$, $P=0.012$), 2hPG (7.26 ± 1.30 vs 6.50 ± 1.53 , $t=3.321$, $P<0.001$), and FINS (11.13 ± 4.13 vs 9.12 ± 3.72 , $t=3.224$, $P<0.001$), and Insulin resistance index (HOMA-IR) (2.97 ± 0.35 vs 2.13 ± 0.54 , $t=3.761$, $P<0.001$) and a lower level of HbA1c (5.25 ± 0.56 vs 6.12 ± 0.57 , $t=5.473$, $P<0.001$) compared to the control group. Regarding lipid metabolism indicators, the study group exhibited higher levels of TC (5.64 ± 1.49 vs 5.01 ± 1.32 , $t=3.332$, $P<0.001$), TG (1.89 ± 0.34 vs 1.32 ± 0.43 , $t=3.411$, $P<0.001$), and LDL-C (3.31 ± 0.43 vs 2.12 ± 0.29 , $t=4.142$, $P<0.001$), and a lower level of HDL-C (1.45 ± 0.21 vs 1.78 ± 0.42 , $t=4.347$, $P<0.001$) compared to the control group. As for the inflammatory indicators, the study group exhibited higher levels of IL-37 (45.56 ± 6.02 vs 34.02 ± 3.28 , $t=9.332$, $P<0.001$) and IL-18 (73.57 ± 5.82 vs 60.34 ± 4.84 , $t=10.141$, $P<0.001$) compared to the control group.

Conclusion: It is crucial to place appropriate emphasis on the impact of Hp infection on the glucose metabolism, lipid metabolism, and inflammatory response in MASLD patients, warranting careful consideration during the treatment of these patients.

Keywords: Helicobacter pylori, infection, nonalcoholic fatty liver disease, glucose metabolism, lipid metabolism, inflammatory indicators

Introduction

Nonalcoholic fatty liver disease (MASLD) refers to hepatic disorders with a lipid content alteration of over 5%, is now recognized as a global public health problem. MASLD affects 20% to 45% of the general population, and prevalence is increasing globally.¹ This condition is mainly caused by obesity, diabetes, hyperlipidemia and other metabolic syndrome or malnutrition, total parenteral nutrition, sharp weight loss after weight loss surgery, drugs / environment and so on.²

Failure to implement timely preventive and therapeutic measures can result in the progression of MASLD to more severe conditions, including advanced liver fibrosis, cirrhosis, and even the development of malignancies. Nonalcoholic steatohepatitis (NASH) has emerged as the primary cause of chronic liver inflammation.^{3–5} MASLD can give rise to a spectrum of clinical pathological syndromes.^{6–8} The etiology of MASLD involves insulin resistance (IR) and genetic defects, which profoundly impact the normal physiological functioning of the body and may have negative effects on the patients' quality of life.

In recent years, extensive research has identified the etiology of MASLD, which includes obesity, visceral adiposity, dyslipidemia, type 2 diabetes, and hypertension. Consequently, MASLD is regarded as an integral component of metabolic syndrome within the liver.⁹ Currently, MASLD has proven a significant hepatic disorder with global health implications. Additionally, MASLD has the third highest incidence in the United States, behind only hepatitis C and alcoholic liver disease (ALD). Therefore, prioritizing effective strategies for the prevention and treatment of MASLD is paramount. Based on pertinent studies, it is anticipated that NASH will soon surpass other causes and become the primary determinant of mortality in liver transplantation.^{10,11} However, the underlying mechanisms involved in the pathogenesis of MASLD remain enigmatic. Current evidence suggests that its onset may stem from multifaceted factors, including dysfunctional adipose tissue, insulin resistance, and genetic mutations.^{12,13} Nonetheless, the implementation of effective measures for MASLD prevention and control remains of utmost urgency.

Helicobacter pylori (Hp), a helical-shaped microaerobic Gram-negative bacterium, is capable of transmission via the fecal-oral or oral-oral route.^{14,15} It invades the gastric mucosa, thereby causing a range of gastrointestinal disorders,¹⁶ including gastritis, duodenal ulcers, gastric cancer, and lymphoid tissue lymphoma.^{17,18} Recent research suggests that Hp infection not only contributes to gastrointestinal diseases but also gives rise to extraintestinal manifestations. Moreover, persistent Hp infection can elicit immune and inflammatory responses in the host organism.^{19–21} One study found that 39.4% of 505 MASLD patients were infected with HP.²² Conversely, Hp infection has also been implicated in the development of MASLD. If preventive and therapeutic measures are not implemented in time, MASLD may progress to more serious conditions, including advanced liver fibrosis, cirrhosis, and even malignant tumors. A previous study established a close link between MASLD and bladder cancer, which is one of the most serious malignant tumors in the elderly, as evidenced by the association between MASLD and insulin resistance and non-metastatic bladder cancer patients: a cross-sectional retrospective study.²³ Individuals with this condition commonly exhibit disturbances in both glucose and lipid metabolism.²⁴ The relationship between Hp infection and MASLD has attracted extensive attention from scholars at home and abroad. A meta-analysis involving 15 studies showed that Hp infection was positively correlated with MASLD.²⁵ The study results of Tang et al²⁶ showed that Hp infection was an independent risk factor for MASLD progression. Polyzos et al²⁷ also reached a similar conclusion. However, no significant difference was found in Hp infection rate between patients with nonalcoholic simple fatty liver and MASLD during intra-group analysis, suggesting that Hp infection was not a factor promoting the progression of nonalcoholic simple fatty liver to nonalcoholic steatohepatitis. Therefore, exploring the mechanism of Hp infection in MAFLD is of great significance to guide the prevention or treatment of MAFLD. The purpose of this study is to investigate the influence of Hp infection on glucose metabolism, lipid metabolism, and inflammatory cytokines in patients with MASLD.

Objects and Methods

Research Objects

Convenient sampling was employed to select 140 patients with MASLD who were admitted to our Hospital between June 2020 and May 2021. Based on the presence or absence of Hp infection, they were divided into the study group (73 cases with infection) and control group (67 cases without infection). Inclusion criteria: (1) clinical diagnosis meeting the diagnostic criteria of the "Prevention and Treatment Guidelines for Nonalcoholic Fatty Liver Disease"²⁸ (2) MASLD activity score (NAS) >4 scores; (3) no history of excessive alcohol consumption, with a weekly ethanol intake of <140 g for males and <70 g for females; (4) No severe anemia or acute infection / inflammation. Exclusion criteria: (1) severe cardiovascular, liver, or lung diseases; (2) patients with other severe malignant tumors, drug-induced hepatitis, cirrhosis, acute or chronic viral hepatitis, or endocrine disorders; (3) recent use of antibiotics; (4) those unwilling to adhere to

medical advice or cooperate closely. This study was approved by the Ethics Committee of our Hospital. All study participants were fully informed and provided written consent.

Data Collection

Demographic characteristic and serological data were collected from the patients. The demographic characteristics included age, gender, disease duration, smoking history, height, BMI, hypertension, and diabetes. The collection and detection of all indicators were carried out before the hospital treatment.

Serological indicators included: (1) glucose metabolism indicators [fasting blood glucose (FBG), 2-hour postprandial glucose (2hPG), fasting insulin (FINS), glycated hemoglobin (HbA1c), Insulin resistance index (HOMA-IR)]; (2) lipid metabolism indicators [total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C)]; (3) inflammatory indicators [interleukin-37 (IL-37), interleukin-18 (IL-18)].

Hp detection was conducted using the ^{14}C -urea breath test. The test kit was provided by Shenzhen Zhonghe Headway Bio-Sci & Tech Co., Ltd., with the Chinese Medical Approval Number H20068129. The detection process was as follows: (1) All patients took one ^{14}C -urea pill (Chinese Medical Approval Number H20000020, Shenzhen Zhonghe Headway Bio-Sci & Tech Co., Ltd., drug specification: 278 KBq (0.75 μCi)) on an empty stomach in the morning and remained seated for 30 minutes; (2) A disposable breath tube was inserted into the bottom of a carbon dioxide (CO_2) reagent tube, and the patient breathed normally until the CO_2 reagent discoloration stopped; (3) Take the liquid in 5mL scintillation bottle and use LKB1217 type liquid scintillation counter to measure the decay number per minute to detect the value $\geq 100\text{dpm}$ is positive.

MASLD testing and diagnosis: Diagnosis of MASLD is made when liver imaging findings are consistent with diffuse fatty liver and no other explanations are present; or when patients with components of metabolic syndrome have unexplained persistent elevation of serum ALT or AST, GGT for more than six months. Confirmation of MASLD diagnosis can be made when abnormal liver enzymes and imaging findings improve or return to normal after weight loss and improvement of IR.²⁸

Process of serological indicator testing: All patients had 3 mL of venous blood drawn in the morning. The blood samples were centrifuged at 1000 r/min to separate the upper clear liquid, which was then stored at -60°C for further testing. (1) Glucose metabolism indicators: FINS levels were measured using radioimmunoassay, with the test kit provided by Beijing Furui Runze Biotechnology Co., Ltd. FBG and 2hBG levels were measured using the glucose oxidase method, with the test kit provided by Shanghai Enzyme Linked Biotechnology Co., Ltd. HOMA-IR is calculated by the following formula: $\text{HOMA-IR} = \text{FPG} \times \text{FINS} / 22.5$. HbA1c levels were measured using high-performance liquid chromatography, with the test kit provided by Hepeng (Shanghai) Biotechnology Co., Ltd. (2) Lipid metabolism indicators: Detection was performed using the BK-400 fully automated biochemical analyzer (Biobase Biodustry (Shandong) Co., Ltd.), with the test kit provided by Shanghai Enzyme Linked Biotechnology Co., Ltd. (3) Inflammatory indicators: Detection was performed using the BK-2008R ELISA Reader (Shanghai Huanxi Medical Co., Ltd.), with the test kit provided by Shanghai Jingkang Bioengineering Co., Ltd.

Statistical Analysis

Statistical software IBM SPSS Statistics version 21.0 (IBM SPSS Inc., Chicago, USA) was employed for data analysis. Quantitative data were tested for normality using the K-S method. If the quantitative data conformed to a normal distribution, it was represented as mean \pm standard deviation ($\bar{x} \pm s$), with inter-group comparisons being performed using *t*-tests. If the quantitative data did not conform the normal distribution, it was expressed by the median (quartile range). Count data were presented as frequency (n) or percentage (%), and inter-group comparisons were conducted using χ^2 tests. A difference was considered statistically significant at $P < 0.05$.

Results

Demographic Characteristics

The study group included 73 cases (^{14}C -urea detection value $\geq 100\text{dpm}$, mean detection value of 424.05 ± 51.38), while the control group included 67 cases (^{14}C -urea detection value $< 100\text{dpm}$, mean detection value of 74.36 ± 19.63). In the study

group, there were 37 males and 36 females, with an age range of 27 to 62 years and a mean age of 51.21 ± 9.76 years. The disease duration ranged from 2.5 to 13.5 years, with a mean duration of (9.51 ± 2.53) years. In the control group, there were 32 males and 35 females, with an age range of 28 to 62 years and a mean age of 53.0 ± 12.0 years. The disease duration ranged from 2 to 14 years, with a mean duration of (9.75 ± 2.56) years. There were no statistically significant differences between the two groups in terms of age, gender, disease duration, smoking history, height, body mass index (BMI), percentage of hypertension, percentage of diabetes, ALT and AST ($P > 0.05$), as shown in Table 1.

Comparison of Glucose Metabolism Indicators Between Two Groups

The results showed statistically significant differences ($P < 0.05$) in FBG, 2hPG, FINS, and HbA1c levels between the two groups. The study group exhibited higher levels of FBG (5.84 ± 0.49 VS 5.40 ± 0.51 , $t = 2.535$, $P = 0.012$), 2hPG (7.26 ± 1.30 VS 6.50 ± 1.53 , $t = 3.321$, $P < 0.001$), and FINS (11.13 ± 4.13 VS 9.12 ± 3.72 , $t = 3.224$, $P < 0.001$), HOMA-IR (2.97 ± 0.35 VS 2.13 ± 0.54 , $t = 3.761$, $P < 0.001$) and a lower level of HbA1c (5.25 ± 0.56 VS 6.12 ± 0.57 , $t = 5.473$, $P < 0.001$) compared to the control group, as suggested in Table 2.

Comparison of Lipid Metabolism Indicators Between Two Groups

The results demonstrated statistically significant differences ($P < 0.05$) in TC, TG, LDL-C, and HDL-C levels between the two groups. The study group exhibited higher levels of TC (5.64 ± 1.49 VS 5.01 ± 1.32 , $t = 3.332$, $P < 0.001$), TG (1.89 ± 0.34 VS 1.32 ± 0.43 , $t = 3.411$, $P < 0.001$), and LDL-C (3.31 ± 0.43 VS 2.12 ± 0.29 , $t = 4.142$, $P < 0.001$), and a lower level of HDL-C (1.45 ± 0.21 VS 1.78 ± 0.42 , $t = 4.347$, $P < 0.001$) compared to the control group, as indicated in Table 3.

Comparison of Inflammatory Indicators Between Two Groups

The results revealed that the study group exhibited higher levels of IL-37 (45.56 ± 6.02 VS 34.02 ± 3.28 , $t = 9.332$, $P < 0.001$) and IL-18 (73.57 ± 5.82 VS 60.34 ± 4.84 , $t = 10.141$, $P < 0.001$) compared to the control group, as presented in Table 4.

Table 1 Comparison of Baseline Data Between Two Groups

Clinical Data	Study Group (n=73)	Control Group (n=67)	χ^2/t	95% CI	P
Gender (Male/Female)	37/36	32/35	0.119	0.579–2.183	0.730
Age (years, $x \pm s$)	51.21 ± 9.76	53.0 ± 12.0	1.371	–5.433–1.853	0.252
Height (cm, $x \pm s$)	158.45 ± 9.73	159.66 ± 10.37	1.122	–4.549–2.129	0.275
BMI (kg/m^2 , $x \pm s$)	19.52 ± 7.63	20.32 ± 8.75	0.798	–3.530–1.930	0.440
Disease duration (years, $x \pm s$)	9.51 ± 2.53	9.75 ± 2.56	1.735	–1.084–0.604	0.145
Smoking history (cases)	31	29	0.010	0.495–1.890	0.922
History of hypertension (cases)	28	30	0.593	0.391–1.506	0.441
History of diabetes (cases)	14	17	0.778	0.313–1.555	0.378
ALT ($\mu\text{ mol}/\text{L}$)	53.13 ± 9.36	53.99 ± 9.97	0.132	–4.071–2.351	0.600
AST ($\mu\text{ mol}/\text{L}$)	52.08 ± 10.12	51.39 ± 10.26	0.576	–2.690–4.070	0.690

Abbreviations: CI, Confidence interval; BMI, Body mass index; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase.

Table 2 Comparison of Glucose Metabolism Indicators Between Two Groups ($x \pm s$)

Glucose Metabolism Indicator	Study Group (n=73)	Control Group (n=67)	t value	95% CI	P value
FBG (mmol/L)	5.84 ± 0.49	5.40 ± 0.51	2.535	0.274–0.606	0.012
2hPG (mmol/L)	7.26 ± 1.30	6.50 ± 1.53	3.321	0.288–1.233	<0.001
FINS (mIU/L)	11.13 ± 4.13	9.12 ± 3.72	3.224	0.710–3.310	<0.001
HOMA-IR	2.97 ± 0.35	2.13 ± 0.54	3.761	0.688–0.992	<0.001
HbA1c (%)	5.25 ± 0.56	6.12 ± 0.57	5.473	–1.057–0.683	<0.001

Abbreviations: CI, Confidence interval; FBG, Fasting blood glucose; 2hPG, 2-hour postprandial glucose; FINS, Fasting insulin; HbA1c, Glycated hemoglobin; HOMA-IR, Insulin resistance index.

Table 3 Comparison of Lipid Metabolism Indicators Between Two Groups ($\bar{x}\pm s$)

Lipid Metabolism Indicator	Study Group (n=73)	Control Group (n=67)	t value	95% CI	P value
TC (mmol/L)	5.64±1.49	5.01±1.32	3.332	0.165–1.096	<0.001
TG (mmol/L)	1.89±0.34	1.32±0.43	3.411	0.441–0.699	<0.001
LDL-C (mmol/L)	3.31±0.43	2.12±0.29	4.142	1.069–1.311	<0.001
HDL-C (mmol/L)	1.45±0.21	1.78±0.42	4.347	–0.442–0.219	<0.001

Abbreviations: CI, Confidence interval; TC, Total cholesterol; TG, Triglycerides; LDL-C, Low-density lipoprotein cholesterol; HDL-C, High-density lipoprotein cholesterol.

Table 4 Comparison of Inflammatory Indicators Between Two Groups ($\bar{x}\pm s$)

Inflammatory Indicator	Study Group (n=73)	Control Group (n=67)	t value	95% CI	P value
IL-37 (pg/mL)	45.56±6.02	34.02±3.28	9.332	9.951–13.129	<0.001
IL-18 (pg/mL)	73.57±5.82	60.34±4.84	10.141	11.462–14.998	<0.001

Abbreviations: CI, Confidence interval; IL-37, Interleukin-37; IL-18, Interleukin-18.

Discussion

The results of this study revealed statistically significant differences ($P<0.05$) in the glucose metabolism indicators and lipid metabolism indicators namely FBG, 2hPG, FINS, HOMA-IR, HbA1c, TC, TG, LDL-C, and HDL-C between the two groups of patients. The study group exhibited higher levels of FBG, 2hPG, FINS, HOMA-IR, TC, TG and LDL-C and a lower level of HbA1c and HDL-C compared to the control group.

In recent years, scientific research has revealed a significant association between Hp and MASLD. The presence of Hp has been found to impact the occurrence and progression of MASLD. A prospective cohort multicenter pilot study with 2 years of follow-up in 369 adults without MASLD at baseline indicated that HP infection was positively associated with MASLD development. This was shown by increased markers of insulin resistance, inflammatory mediators such as interleukin-6 and C-reactive protein, and lipid metabolism such as the leptin/adiponectin ratio, and decreased lipid metabolism marker, HDL. Furthermore, these MASLD risk factors can be recovered after eradication of HP infection.²⁹ Besides, the lipid metabolism markers of TC, triglyceride, HDL-C and LDL-C showed no significant difference between HP-positive and HP-negative MASLD patients in a study. Notably, a significant difference occurred after removal of the confounding factor of MASLD status.³⁰ Obesity is an important cause of MASLD, and central obesity is significantly associated with infection of Hp, so infection with Hp may indirectly lead to the disease of MASLD,³¹ searchers postulate that IR may serve as a bridge between Hp and MASLD.³² In the pathogenesis of MASLD, IR plays a pivotal role.³³ Over the years, clinical trials have confirmed the substantive contribution of chronic inflammation to IR. Hp is capable of enhancing the expression of tumor necrosis factor, C-reactive protein, interleukin, and other insulin resistance indicators, consequently increasing IR.^{34,35} Fetuin-A, as an integral pro-inflammatory mediator, exerts a significant influence on inflammation and other immunological disorders.³² Recent research has revealed a substantial elevation in levels of fetuin-A in populations affected by Hp infection, suggesting its potential to facilitate IR,^{36,37} which possesses considerable implications in the treatment of diabetes. Additionally, the reciprocal interaction between IR and the immune system fosters metabolic inflammation, while Hp infection influences immune cells such as mast cells, dendritic cells, and eosinophils, thereby contributing to IR.³⁸ Hp can also invade the liver via the hepatobiliary duct in a retrograde manner, triggering chronic liver inflammation and causing severe damage and apoptosis of liver cells.^{39,40} IR can result in disturbances in glucose and lipid metabolism within the organism, which can impede the activity of microsomal lipid peroxidase and subsequently lead to lipid accumulation in patients.⁴¹ Furthermore, Hp infection has been observed to induce significant alterations in blood lipid levels, thus establishing abnormal blood lipid profiles as prevalent phenomena among MASLD patients.⁴²

The presence of Hp may induce the generation of inflammatory cytokines in gastric epithelial cells, thereby initiating a chronic inflammatory response. Additionally, these inflammatory cytokines may also inhibit the activity of lipoprotein lipase, affecting lipid levels in the bloodstream. Moreover, certain inflammation cytokines can potentially influence the

activity of hepatic lipase, resulting in alterations of TC, TG, LDL-C, and HDL-C levels. Furthermore, these inflammation cytokines affect the expression of glucose transporters on cell membranes, significantly impacting insulin sensitivity in patients, leading to abnormal glucose metabolism and consequent hyperglycemia.^{43,44}

As an important member of the IL-1 family, IL-37 can be expressed in various cell types, including monocytes, macrophages, lymphocytes, and neutrophils, exerting anti-inflammatory effects. According to recent research,⁴⁵ the levels of IL-37 in the bloodstream of MASLD patients are significantly elevated. This alteration provides valuable insight into the extent of liver cell damage and aids in the assessment of severity of the disease. IL-18 plays a crucial role in the therapeutic process of MASLD. It is not solely sourced from monocytes and macrophages but also possesses diverse additional functions. According to the latest research,⁴⁶ there is a remarkable increase in the levels of IL-18 within the bodies of MASLD patients, which might be a key factor in the pathogenesis of MASLD. The activation of IL-18 triggers the production of numerous inflammatory mediators, thereby exacerbating the inflammatory response in hepatocytes.⁴⁷ Our study results demonstrate that the levels of IL-37 (45.56 ± 6.02 VS 34.02 ± 3.28 , $t=9.332$, $P<0.001$) and IL-18 (73.57 ± 5.82 VS 60.34 ± 4.84 , $t=10.141$, $P<0.001$) in the study group were significantly higher compared to the control group, aligning with the aforementioned research findings. Previous studies have shown that there is an increase in interleukin-37 in patients with peptic ulcer infected with *Helicobacter pylori*, which is significant in the circulating concentration of interleukin-37 in patients with peptic ulcer infected with *Helicobacter pylori*.⁴⁸ It can be hypothesized that the presence of Hp may induce an inflammatory response by stimulating the large release of IL-6, IL-8, IL-37, IL-18, and NF- κ B, which are potent vascular active substances, thereby contributing to the development of inflammation.⁴⁹ In addition, *Helicobacter pylori* activates NLRP3 inflammatory bodies through ROS signaling pathway and induces human monocytes to produce IL-1 β and IL-18.⁵⁰ To sum up, alleviating Hp infection will contribute to the treatment of MASLD to some extent, such as some natural products, which will play an important role in alleviating Hp infection and MASLD.^{51,52}

It was shown that fasting insulin, HOMA-IR, CRP and C-LDL levels decreased in HP positive patients 6 weeks after successful eradication with a sequential regimen, suggesting a beneficial effect on atherogenic metabolic abnormalities and CLGI.⁵³ An argument favouring the role of low-grade inflammation in the lipid profile alterations is that successful eradication of HP infection induced an increase of HDL-C, apo A, while TC and LDL remained unchanged.^{54,55} These results were not reproduced in large Spanish and Chinese trials and the minor changes of blood lipids were attributed rather to lifestyle modifications.^{56–58} Based on these data, some experts suggested to perform large interventional trials aimed at evaluating the benefit of HP eradication on the prevention of metabolic syndrome and type 2-diabetes mellitus.⁵⁹ In the most recent study of 308 Lebanese subjects, no association of HP with insulin resistance and metabolic syndrome was found and the authors concluded, that eradication of the infection to prevent these conditions is not warranted. Metabolic syndrome, however, is a multifactorial condition in which HP infection seems to play only a minor, if any role. The prevalence of the infection is decreasing spontaneously in the developed countries, while that of metabolic syndrome is constantly increasing: parallel epidemiologic studies of these 2 conditions have not been performed and it would be intriguing to see whether spontaneous and/or eradication-induced decrease of HP burden of the general population will result any change in the development and natural course of metabolic syndrome. It must be proven by future controlled long-term trials, whether eradicating the infection will result prevention of these conditions.

To sum up, the novelty of this study is to explore the relationship between *Helicobacter pylori* infection and non-alcoholic fatty liver, and to study its effects on glucose metabolism, lipid metabolism and the level of inflammatory cytokines. It provides a new perspective for understanding the pathogenesis of nonalcoholic fatty liver. Despite achieving some notable results, this study exhibits several limitations. Firstly, the small sample size may introduce selection bias and hinder the generalizability of the findings, thereby imposing certain restrictions on the accuracy of the conclusions. Secondly, the limited sample size and potential interactions between IL-37, IL-18, and Hp infection among MASLD patients may complicate the elucidation of certain mechanisms, necessitating the exclusion of these interactive effects for subsequent analysis. In addition, the diagnostic methods of *Helicobacter pylori* infection used in the study may have some limitations. Different detection methods may lead to missed diagnosis or misdiagnosis of *Helicobacter pylori* infection, thus affecting the accuracy of the results. In addition to *Helicobacter pylori* infection, there are many other factors that may affect the development and metabolic disorders of non-alcoholic fatty liver, such as genetic factors, lifestyle, eating habits and so on. The existence of these factors may interfere with the association between *Helicobacter*

pylori infection and non-alcoholic fatty liver disease. Future research endeavors should employ large-scale and multi-center randomized controlled trials to objectively and effectively assess the influence of Hp infection on the glucose metabolism, lipid metabolism, and inflammatory cytokines, in MASLD patients.

In sum, it is crucial to place appropriate emphasis on the impact of Hp infection on the glucose metabolism, lipid metabolism, and inflammatory response in MASLD patients, warranting careful consideration during the treatment of these patients.

Data Sharing Statement

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the Research Ethics Committee of Shiyuan People's Hospital (No. EC-20230118-1004), and informed consent was obtained from all participants. All methods were carried out in accordance with relevant guidelines and regulations.

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Disclosure

The authors report no conflicts of interest in this work.

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