Research Article

Association between *Helicobacter pylori* Infection and Nonalcoholic Fatty Liver Disease: A Single-Center Clinical Study

Ou Cai,¹ Zhenpeng Huang,² Ming Li,¹ Chaoqun Zhang,¹ Fengbo Xi,³ and Shiyun Tan¹

¹Department of Gastroenterology, Renmin Hospital of Wuhan University, Wuhan, Hubei, China
²Teaching and Research Section of Internal Medicine, College of Clinical Medicine, Xi’an Medical University, Xi’an, Shaanxi, China
³Enshi Prefecture Center for Disease Control and Prevention, Enshi, China

Correspondence should be addressed to Shiyun Tan; tanshiyun@medmail.com.cn

Received 2 September 2017; Revised 11 November 2017; Accepted 23 November 2017; Published 21 January 2018

Academic Editor: Francesco Selvaggi

Copyright © 2018 Ou Cai et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

**Objective.** To investigate the association between *Helicobacter pylori* (*H. pylori*) infection and nonalcoholic fatty liver disease (NAFLD). **Methods.** Data from 2051 participants who underwent ¹³C urea breath test and abdominal ultrasound examinations was collected. Participants were allocated to NAFLD risk group and NAFLD nonrisk group based on definite risk factors for NAFLD. The relationship between *H. pylori* infection and NAFLD was analyzed. **Results.** No significant difference was found between rates of *H. pylori* infection and NAFLD using the chi-square test (*P* = 0.30) or regression analysis (*P* = 0.70). There was no significant difference between rates of *H. pylori* infection with and without NAFLD (*P* = 0.47) in the NAFLD risk group or in the NAFLD nonrisk group (*P* = 0.59). There was no significant difference between rates of *H. pylori* infection in men (*P* = 0.69) and in women (*P* = 0.27) or in participants aged 18–40 years (*P* = 0.43), 41–65 years (*P* = 0.14), and ≥66 years (*P* = 0.66) with and without NAFLD in the NAFLD risk group or between the same sex or age groups (*P* = 0.82, *P* = 0.66, *P* = 0.24, *P* = 0.53, and *P* = 1.00, resp.) in the NAFLD nonrisk group. **Conclusions.** *H. pylori* infection does not appear to increase the NAFLD prevalence rate or to be associated with, or a risk factor for, NAFLD.

1. **Introduction**

Nonalcoholic fatty liver disease (NAFLD) is a type of liver injury induced by metabolic stress and is related to insulin resistance (IR) and hereditary susceptibility [1]. It is generally deemed to be the hepatic manifestation of metabolic syndrome [2]. NAFLD comprises simple nonalcoholic fatty liver (NAFL), nonalcoholic steatohepatitis (NASH) and NASH-associated liver cirrhosis, and hepatocellular carcinoma [1]. The incidence of and morbidity from NAFLD have increased rapidly worldwide, with corresponding increases in clinical and economic burden [3]. Apart from known and common risk factors, such as obesity, type 2 diabetes, hypertension, and dyslipidemia, it has recently been postulated that *Helicobacter pylori* infection is involved in the pathogenesis of insulin resistance (IR) [1, 4] and may be associated with NAFLD.

*H. pylori* is a Gram-negative bacterium which selectively colonizes the gastric mucosa [5] and is considered to be the main pathogenic bacteria involved in peptic ulcers, chronic active gastritis, mucosa-associated lymphoid tissue lymphoma, and gastric cancer [6–8]. Recently, *H. pylori* infection has been implicated in various nongastrointestinal diseases including idiopathic thrombocytopenic purpura, cardiovascular disease, type II diabetes, and iron deficiency anemia [9–11]. However, the findings of recent studies focusing on the relationship between *H. pylori* infection and NAFLD
are inconsistent [12–15]. Our study used data from volunteers who underwent physical examinations in the Renmin Hospital of Wuhan University from June 2016 to December 2016 in order to analyze the association between H. pylori infection and NAFLD prevalence rates, to elucidate this relationship, and to provide a new strategy for treatment of NAFLD.

### 2. Materials and Methods

#### 2.1. Study Subjects

It was a cross-sectional study of Chinese asymptomatic adults who underwent physical examination in the Renmin Hospital of Wuhan University from June 2016 to December 2016 and entered into our study voluntarily (Figure 1). This study gained approval by the ethics committees of the Renmin Hospital of Wuhan University. We included participants who underwent 13C urea breath test and abdominal ultrasound (n = 2985). We excluded 934 subjects due to the following reasons: younger than 18 years old (n = 3); positive for HBs antigen or HCV antibody (n = 65); history of gastrectomy (n = 21); drug taking history, such as antihypertension drugs, antidiabetic drugs, anticholesterol drugs, corticosteroids, proton pump inhibitors (n = 313); and alcohol consumption more than 140 g/week for male and 70 g/week for female (n = 532, male = 436 and female = 96). 2051 participants older than 18 years with available H. pylori status and abdominal ultrasound were finally analyzed. All participants were divided into NAFLD risk group and NAFLD nonrisk group according to definite NAFLD risk factors, including dyslipidemia (TG ≥ 1.70 mmol/L, TC ≥ 5.20 mmol/L, HDL-C < 1.00 mmol/L, LDL-C ≥ 3.10 mmol/L), high blood glucose (FPG ≥ 6.10 mmol/L), high blood pressure (SBP ≥ 140 mmHg and DBP ≥ 90 mmHg), and alcohol consumption more than 140 g/week for male and 70 g/week for female (n = 532, male = 436 and female = 96). 2051 participants older than 18 years with available H. pylori status and abdominal ultrasound were finally analyzed.

#### Table 1: Definition of H. pylori infection, NAFLD, and NAFLD risk group.

<table>
<thead>
<tr>
<th>Item</th>
<th>Value</th>
<th>Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>H. pylori infection</td>
<td>13C urea breath test &lt;delta&gt;% (30 minutes) minus &lt;delta&gt;% (0 minutes)</td>
<td>Positive: ≥4, Negative: &lt;4</td>
</tr>
</tbody>
</table>
| NAFLD Abdominal ultrasound | (i) The near-field echo of the liver is diffusely increased and more than the kidney.  
(ii) The intrahepatic duct structure is not clear.  
(iii) The far-field echo of the liver is decreased gradually. | Positive: any two of the three satisfied, Negative: none or only one satisfied |
| Blood lipid                 | TG ≥ 1.70 mmol/L, TC ≥ 5.20 mmol/L, HDL-C < 1.00 mmol/L, LDL-C ≥ 3.10 mmol/L | Risk group: one or more of the eight satisfied, Nonrisk group: none of the eight satisfied |
| Fast plasma glucose         | FPG ≥ 6.10 mmol/L, SBP ≥ 140 mmHg                                    | Risk group: one or more of the eight satisfied, Nonrisk group: none of the eight satisfied |
| Blood pressure              | DBP ≥ 90 mmHg                                                        | Risk group: one or more of the eight satisfied, Nonrisk group: none of the eight satisfied |
| Body mass index             | BMI ≥ 24.90 kg/m²                                                     | Risk group: one or more of the eight satisfied, Nonrisk group: none of the eight satisfied |

NAFLD: nonalcoholic fatty liver disease; TG: triglyceride; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; FPG: fast plasma glucose; SBP: systolic blood pressure; DBP: diastolic blood pressure; BMI: body mass index.
the urea (13C) capsule with 80 to 100 milliliter water for the 0 minute sample; (iii) collect the air again after taking by the participant in quiet condition in one collection bag as in the two prepared collection bags; (ii) collect the air exhaled get the corresponding value; (iv) detect the sample minus the result and detection value equals participant was in current infection.

\[
\text{Fourth Chinese National Consensus Report on the management of } \text{Helicobacter pylori} \text{ infection} \] [16] (Table 1), the management of nonalcoholic fatty liver disease: update 2010 [1], participants who possessed two of the following three characteristics could be diagnosed as fatty liver: (i) the near-field echo of the liver is decreased gradually and more than the kidney; (ii) the intrahepatic duct structure is not clear; (iii) the far-field echo of the liver is decreased gradually (Table 1). Three professional ultrasound doctors were uniformly trained for the diagnosis of fatty liver, and each participant was measured by two of them. The diagnosis could not be made until at least two of the doctors made an agreement.

2.5. Ultrasonic Measurement. Philips iE Elite and iE 33 (Philips China Investment Co., Beijing, China) were used for abdominal ultrasound by professional ultrasound doctors. According to the guidelines for the diagnosis and management of nonalcoholic fatty liver disease: update 2010 [1], participants who possessed two of the following three characteristics could be diagnosed as fatty liver: (i) the near-field echo of the liver is diffusely increased and more than the kidney; (ii) the intrahepatic duct structure is not clear; (iii) the far-field echo of the liver is decreased gradually (Table 1). Three professional ultrasound doctors were uniformly trained for the diagnosis of fatty liver, and each participant was measured by two of them. The diagnosis could not be made until at least two of the doctors made an agreement.

2.6. Statistical Analysis. Software SPSS version 18.0 was used for statistical analysis. Continuous data accorded with normal distribution were presented as average ± standard deviation, and categorical data were presented as number (percentage). Continuous variables were compared by t-test, and categorical variables were compared by chi-square test. Regression analysis was used to identify independent risk factors. \( P < 0.05 \) was regarded as indicating statistical significance.

3. Results

3.1. Baseline Characteristics. Baseline characteristics of the participants are shown in Table 2. The mean age was 38.11 ± 10.49 years, and the prevalence of NAFLD was 21.11% (433/2051). Compared to participants without NAFLD, those with NAFLD were more likely to be older and male, with higher BMI, SBP, and DBP, higher levels of TG, TC, LDL-C, and FPG, and lower levels of HDL-C (\( P = 0.00 \)). However, there was no association between Helicobacter pylori infection and NAFLD (\( P = 0.30 \)) (Table 2).

| Table 2: Baseline characteristics of study participants. |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Age (y)         | 38.11 ± 10.49   | 37.25 ± 10.38   | 41.31 ± 10.30   | \( t = -7.24 \)  | \( P = 0.00 \)  |
| Sex (male/female) | 714/1337        | 446/1172        | 268/165         | \( \chi^2 = 177.39 \) | \( P = 0.00 \)  |
| BMI (kg/m²)     | 23.45 ± 3.05    | 22.63 ± 2.55    | 26.52 ± 2.77    | \( t = -27.66 \) | \( P = 0.00 \)  |
| SBP (mmHg)      | 118.30 ± 14.52  | 116.37 ± 13.71  | 125.53 ± 15.18  | \( t = -12.07 \) | \( P = 0.00 \)  |
| DBP (mmHg)      | 71.11 ± 10.07   | 69.77 ± 9.62    | 76.11 ± 10.18   | \( t = -12.03 \) | \( P = 0.00 \)  |
| TG (mmol/L)     | 1.29 ± 1.15     | 1.06 ± 0.66     | 2.18 ± 1.91     | \( t = -12.01 \) | \( P = 0.00 \)  |
| TC (mmol/L)     | 4.43 ± 0.80     | 4.35 ± 0.77     | 4.73 ± 0.85     | \( t = -8.46 \)  | \( P = 0.00 \)  |
| HDL-C (mmol/L)  | 3.40 ± 0.36     | 1.40 ± 0.36     | 1.11 ± 0.24     | \( t = 19.29 \)   | \( P = 0.00 \)  |
| LDL-C (mmol/L)  | 2.44 ± 0.67     | 2.37 ± 0.64     | 2.73 ± 0.70     | \( t = -10.14 \) | \( P = 0.00 \)  |
| FPG (mmol/L)    | 5.19 ± 0.98     | 5.07 ± 0.56     | 5.66 ± 1.76     | \( t = -6.96 \)  | \( P = 0.00 \)  |
| H. pylori infection (−/+ | 1406/645        | 1118/500        | 288/145         | \( \chi^2 = 1.06 \) | \( P = 0.30 \)  |

Values are expressed as means ± standard deviation. NAFLD: nonalcoholic fatty liver disease; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; TG: triglyceride; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; FPG: fast plasma glucose.
3.2. Risk Factors for NAFLD by Regression Analysis. Regression analysis was used to analyze the independent risk factors for NAFLD, and all the factors which were significant according to t-tests or chi-square tests were included, plus H. pylori infection. Analysis showed that sex ($P = 0.01$) and BMI and levels of TG, HDL-C, and FPG were independent risk factors for NAFLD ($P = 0.00$) but H. pylori infection was not ($P = 0.70$) (Table 3).

3.3. Association between H. pylori Infection and NAFLD. In the NAFLD risk group, the H. pylori infection rate among participants with NAFLD (34.16%) was slightly higher than that among participants without NAFLD (32.04%), although the difference was not significant ($P = 0.47$). There was also no significant difference between the rates of H. pylori infection and NAFLD in men ($P = 0.69$) and women ($P = 0.27$). Moreover, after age stratification, no significant difference was found between the rates of H. pylori infection and NAFLD in younger (18–40 years) ($P = 0.43$), middle-aged (41–65 years) ($P = 0.14$), and older ($\geq 66$ years) participants ($P = 0.66$). In the NAFLD nonrisk group, the H. pylori infection rate among participants with NAFLD (25.00%) was lower than that among participants without NAFLD (30.10%), although the results were not significant ($P = 0.59$). Similar results were also obtained for men ($P = 0.82$), women ($P = 0.60$), younger ($P = 0.24$), middle-aged ($P = 0.53$), and older participants ($P = 1.000$) (Table 4).

4. Discussion

NAFLD is a common metabolic disorder that affects approximately 13.48%–31.79% of the general population [3], although its mechanism remains unclear. Genetic, environmental, and metabolic factors may be involved in the pathogenesis of NAFLD, and some recent research provides insights into the link between H. pylori infection...
and NAFLD. In 2008, Cindoruk et al. [17] found *H. pylori* 16S rDNA in a biopsy taken from a 44-year-old woman with NASH and, in 2009, Pirouz et al. [18] found 5 *H. pylori* 16S rRNA-positive patients among 11 biopsy-proven NAFLD and NASH. In 2009, Pirouz et al. [18] found 5 *H. pylori* 16S rDNA in a biopsy taken from a 44-year-old woman with *H. pylori* and NAFLD. In 2008, Cindoruk et al. [17] found 5 *H. pylori* 16S rDNA in a biopsy taken from a 44-year-old woman with *H. pylori* and NAFLD. In 2009, Sumida et al. [15] found that the prevalence of NASH and the grade of hepatocyte ballooning were higher in *H. pylori*-seropositive patients, indicating that *H. pylori* infection may act as a contributing factor in the progression of NAFL to NASH but not in early-stage NAFLD. In spite of its limitations, our study has some advantages. To our knowledge, ours is the first study to group data by definite risk factors for NAFLD into an NAFLD risk group and NAFLD nonrisk group. We also excluded the effect of age and sex by analyzing and stratifying the data and found a similar trend of no association between the stratified data; this strengthens our conclusions.

To conclude, although, to date, the association between *H. pylori* infection and NAFLD has been controversial and our research found no association despite limitations in the design of our study. Our large cross-sectional study focused on the relationship between *H. pylori* infection and NAFLD. We found that *H. pylori* infection did not associate with NAFLD, even when the data were stratified according to sex and age. Our findings therefore indicate that *H. pylori* infection has no association with NAFLD. Further large-scale multicenter prospective studies are urgently needed to investigate whether there is any association between *H. pylori* infection and NAFLD and to clarify the intrinsic mechanisms involved.

**Conflicts of Interest**

The authors declare that they have no conflicts of interest.

**References**


K. Okushin, Y. Takahashi, N. Yamamichi et al., "Helicobacter pylori infection is not associated with fatty liver disease including non-alcoholic fatty liver disease: a large-scale cross-sectional study in Japan," *BMC Gastroenterology*, vol. 15, no. 1, p. 25, 2015.


Y. Sumida, K. Kanemasa, S. Imai et al., "Helicobacter pylori infection might have a potential role in hepatocyte ballooning in nonalcoholic fatty liver disease," *Journal of Gastroenterology*, vol. 50, no. 9, pp. 996–1004, 2015.


