

Recurrence of *Helicobacter pylori* infection: incidence and influential factors

Yan Xue, Li-Ya Zhou, Hao-Ping Lu, Jin-Zhe Liu

Department of Gastroenterology, Peking University Third Hospital, Beijing 100191, China.

Abstract

Background: *Helicobacter pylori* (*H. pylori*) eradication has been widely used. The recurrence rate of *H. pylori* after eradication and its related factors are gaining more and more attention. Our study aimed to determine the recurrence rate of *H. pylori* infection after successful eradication, and analyze its influential factors.

Methods: We prospectively studied 1050 patients with upper gastrointestinal symptoms who were diagnosed as *H. pylori* infection by gastroscopy and underwent eradication therapies from April 2013 to January 2014. The ¹³C-urea breath test (UBT) or Warthin-Starry (WS) staining was done at 8 to 12 weeks after the therapy. Patients with successful eradication were followed by repeated UBT or gastroscopy at one year and 3 years after therapy, as well as, questionnaire surveys. Recurrence was considered if the UBTs or WS staining of biopsy were positive. One-year and 3-year recurrence rates were calculated, and analyzed the differences between recurred patients and others in basic data, sociological characteristics, lifestyle.

Results: A total of 743 patients finished the 1-year follow-up, and the 1-year recurrence rate was 1.75%. Of the 607 patients who finished the 3-year follow-up, 28 patients recurred, and the 3-year recurrence rate was 4.61%. Analysis of variance showed that low-income, poor hygiene condition of dining out place, and receiving invasive diagnoses or treatments were significant risk factors for *H. pylori* infection recurrence. Logistic regression analysis demonstrated that the combination of invasive diagnoses or treatments, the level of income, and the hygiene standard of dining out place were significant and independent influential factors of the recurrence of *H. pylori*.

Conclusions: The 1-year and 3-year recurrence rates of *H. pylori* infection after eradication therapy are 1.75% and 4.61%. Low-income, poor hygiene condition of dining out place, and a combination of invasive diagnoses or treatments are independent risk factors of *H. pylori* recurrence.

Keywords: Affecting factors; Follow-up study; *Helicobacter pylori*; Recurrence

Introduction

Helicobacter pylori (*H. pylori*) infection is associated with many upper gastrointestinal tract diseases like chronic gastritis, peptic ulcer, and gastric mucosa associated lymphoid tissue (MALT) lymphoma.^[1] Eradication therapy has been proved to be beneficial in alleviating active gastritis, cure peptic ulcer and MALT lymphoma, and even prevent gastric mucosa cancerization. However, the recurrence of *H. pylori* may erase these benefits of eradication, and lead to the recurrence of ulcer or lymphoma.^[2,3] Owing to the wide application of eradication therapy, the recurrence of *H. pylori* infection and its affecting factors are gaining more and more attention. The recurrence rate varies among different countries, and has negative correlation with the socioeconomic level.^[4] Some previous studies found that the recurrence rate was related to factors such as prevalence of *H. pylori* infection, hygiene

conditions, and population susceptibility, while few other studies gave contrary conclusions. Till now, there are no large-scale studies on *H. pylori* recurrence, or studies focusing on the factors affecting the recurrence in our country. Therefore, we aimed to determine the recurrence rate of *H. pylori* infection after successful eradication in Chinese population, and analyze its affecting factors.

Methods

Ethical approval

The study was approved by the Ethics Committee of Peking University Third Hospital. All the participants have signed the informed consent form.

Patients and study design

Patients who have received *H. pylori* eradication therapy successfully for the first time from April 2013 to January

Access this article online

Quick Response Code:



Website:
www.cmj.org

DOI:
10.1097/CM9.000000000000146

Correspondence to: Prof. Li-Ya Zhou, Department of Gastroenterology, Peking University Third Hospital, Beijing 100191, China
E-Mail: zhoullyabysy@163.com

Copyright © 2019 The Chinese Medical Association, produced by Wolters Kluwer, Inc. under the CC-BY-NC-ND license. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Chinese Medical Journal 2019;132(7)

Received: 02-11-2018 Edited by: Li-Shao Guo

2014 in a previous study^[5] from Peking University Third Hospital, Qilu Hospital of Shandong University, and Peking Union Medical College Hospital were enrolled in our study. All patients were informed in detail about the aim, process, benefits, and possible risks of the study before participation.

The inclusion criteria of the previous study were patients aged 18 to 70 years, having upper digestive tract symptoms, and in agreement with endoscope examination.

The exclusion criteria were as follows: Patients receiving eradication therapy in the past; taking proton pump inhibitors, H₂-receptor antagonists, bismuth, antibiotics or other medications that interfere with the result of the examination in the recent 4 weeks; history of digestive cancer; operation history of stomach or esophagus; Zollinger-Ellison syndrome; with severe diseases of liver, kidney, cardiovascular system, respiratory system, blood system, nervous and mental system, or endocrine system; allergic to medications used for treatment; women in gestation or lactation period; alcohol abuse or any other clinical situation which may increase the risk of therapeutic side-effects.

The diagnosis of *H. pylori* infection in the previous study was confirmed when both the rapid urease test and WS staining were positive.

A total of 1050 *H. pylori* infected patients received who received eradication therapy were randomly divided into three groups with 10-day therapeutic schemes: tailored therapy, quadruple therapy (esomeprazole 20 mg bid, amoxicillin 0.5 g bid, clarithromycin 0.5 g bid, Bismuth potassium citrate capsules 220 mg bid), and concomitant therapy (esomeprazole 20 mg bid, amoxicillin 0.5 g bid, clarithromycin 0.5 g bid, tinidazole 0.5 g bid). The ¹³C urea breath test (¹³C-UBT) or gastroscopy was applied 8 to 12 weeks after the therapy, and eradication was considered successful if the result of ¹³C-UBT or gastroscopy was negative.

A total of 827 patients succeeded eradication, and were enrolled in the following study. Patients were followed-up at 1 and 3 years after the eradication of *H. pylori* infection using ¹³C-UBT or gastroscopy [Figure 1].

We calculated 1-year and 3-year eradication rates, and compared the differences between recurred patients and

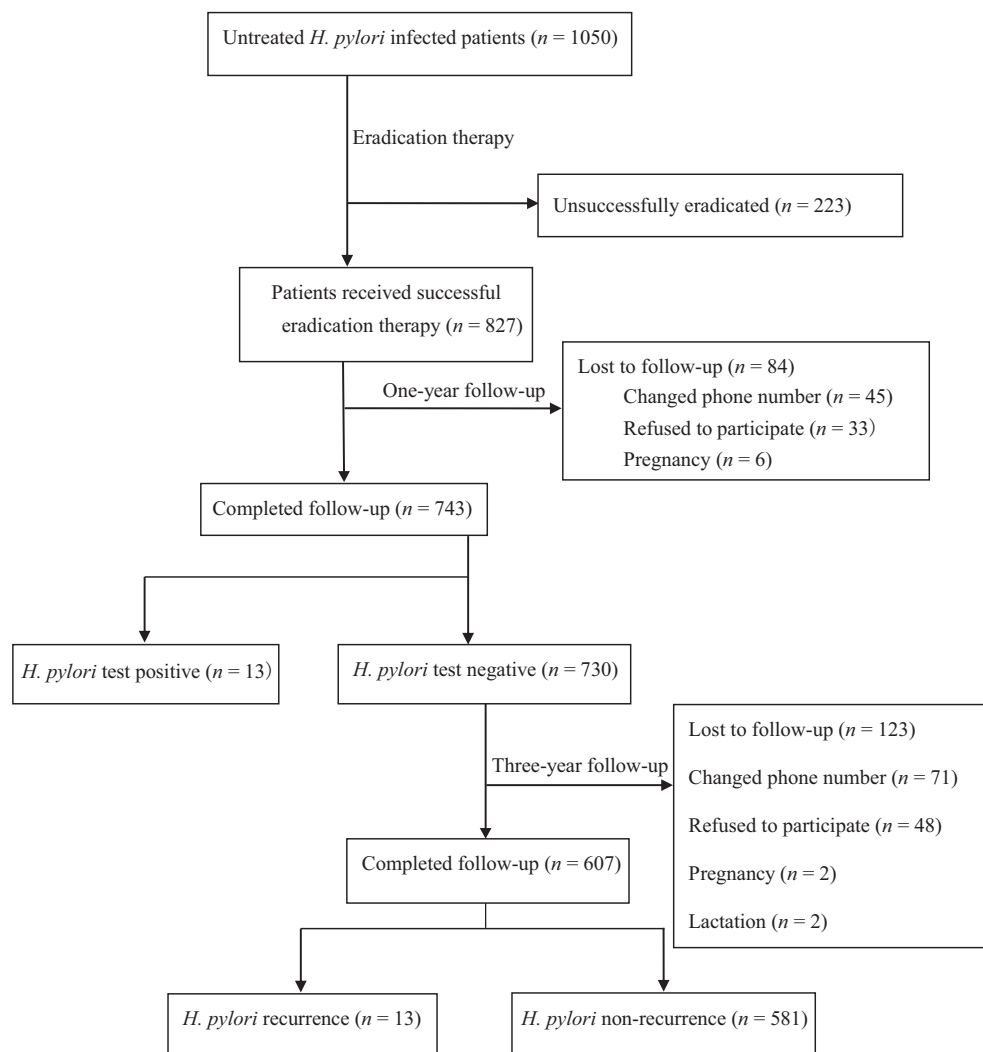


Figure 1: The flow chart of this study.

others using their basic data, sociological characteristics, lifestyle, and disease history.

¹³C-UBT

Patients prior to undergoing ¹³C-UBT were required to stop taking antibiotics, bismuth, proton pump inhibitors, H₂-receptor antagonists, or other medicines that might interfere with the result of examination for at least 4 weeks.

Operation process

(1) The patient should be kept on an empty stomach before the test. (2) The patient's name, age and gender were filled on three labeled gas containers. (3) Breath sample was collected at 0 min: patient's exhalation was collected through a disposable plastic straw connected to the bottom of the first container for 4 to 5 s, then the straw was pulled out, and the cap of the container was closed. (4) The patient was given a capsule containing 75 mg of ¹³C-labeled urea, and sat still. (5) Breath sample was collected at 30 min as described above. (6) These two samples were analyzed and compared by ¹³C-exhalation mass spectrometer (type ZHP-2001), and the results were expressed as difference per thousand (‰). $\delta\text{‰} = (\text{isotopic abundance of } ^{13}\text{C working sample} - \text{isotopic abundance of } ^{13}\text{C reference sample}) / \text{isotopic abundance of } ^{13}\text{C reference sample} \times 1000$. (7) The judgment of *H. pylori* infection: the test value was expressed as the difference value of breath sample in 30 min and in 0 min, namely, test value = $\delta\text{‰}_{(30\text{ min})} - \delta\text{‰}_{(0\text{ min})}$. Infection state of *H. pylori* was considered positive if the test value exceeded 4.0‰, and otherwise, negative.

Questionnaires

We determined the potential factors that affect the recurrence of *H. pylori* infection by literature review and formulated questionnaires accordingly. The contents of the questionnaires included basic data (such as occupation, ethnicity, height, mess, the native place of father, the native place of mother, permanent residence, educational level, and income), lifestyle (living space, family members, source of drinking water, cooking habits, and frequency, and way of dining), and disease history (any history of hospitalization in the past 1 year, receiving invasive diagnoses or treatment, contact with other *H. pylori* infected patients, and combination of underlying diseases). The procedure of survey was conducted by researchers in person, or under the guidance of strict training investigators.

Statistical analysis

EpiData 3.1 was used for data entry and management, and the data entry quality was checked by double data entry verification method. Statistical analyses were performed using SPSS for Windows 22.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were subjected to normality test using one-sample Kolmogorov-Smirnov test. Normally distributed variables were expressed as mean \pm standard deviation, while abnormally distributed variables were expressed as medians and quartiles, and categorical variables were described as frequencies and percentages. Normally distributed variables were compared using independent sample *t* test, while abnormally distributed variables were compared using non-parametric test. Categorical variables were compared using the Chi-squared test. Multivariate analyses were performed using binary non-conditional logistic regression to detect the affecting factors of recurrence of *H. pylori* infection. Odd's ratio (OR) and 95% confidence interval (95% CI) were applied to measure the degree of its association. All the tests involved were two-tailed, and $P < 0.05$ was considered statistically significant.

Results

Characteristics of patients

A total of 734 patients completed the follow-up tests 1 year after eradication therapy, and 607 patients completed the tests 3 years after eradication therapy, and included 321 males and 274 females, with a mean age of 48.5 ± 12.9 years. The average body mass index (BMI) was 23.6 ± 3.1 kg/m², and the average living space was 32.7 ± 21.9 m². One hundred ninety patients were diagnosed with peptic ulcers, while the remaining 417 patients had non-ulcer dyspepsia [Table 1].

Recurrence of *H. pylori* infection

The recurrence of *H. pylori* infection 1 year after eradication was positive in 13 patients, and the 1-year recurrence rate was 1.75%. Likewise, a total of 28 patients had recurrence at 3 years after eradication, and the cumulative 3-year recurrence rate of *H. pylori* infection was 4.61%.

Factors affecting the recurrence of *H. pylori* infection

Of the 607 patients who completed the follow-up tests, 595 valid questionnaires were returned, with a response rate of 98.02%, including 26 in the recurrence group and 569 in the non-recurrence group.

Table 1: The general factors of the recurrence and non-recurrence patients with *H. pylori* infection.

General information	Total patients (n=595)	<i>H. pylori</i> recurrence group (n=26)	<i>H. pylori</i> non-recurrence group (n=569)	<i>t</i>	<i>P</i>
Body mass index (kg/m ²)	23.6 \pm 3.1	23.6 \pm 2.9	23.6 \pm 3.1	0.049	0.961
Living space (m ²)	32.7 \pm 21.9	30.1 \pm 12.7	32.9 \pm 22.2	0.884	0.391
Age (years)	48.5 \pm 12.9	47.2 \pm 13.7	48.6 \pm 12.8	1.060	0.297

Data are expressed as mean \pm standard deviation.

Single factor analysis of variance showed that low-income, poor hygiene condition of dining out place, and receiving invasive diagnoses or treatments were considered as risk factors of recurrence of *H. pylori* infection [Table 2].

The recurrence rates of patients with a monthly income less than and more than 5000 RMB Yuan were 0.8% and 6.8%, respectively ($\chi^2 = 12.255$, $P = 0.000$).

Five hundred forty-one patients had a habit of dining out. Among them, the recurrence rate was as high as 27.27% with poor hygiene condition of dining out place, while the rate was 3.96% with good hygiene condition ($\chi^2 = 13.812$, $P = 0.001$).

Patients who received invasive diagnoses or treatments, such as oral treatment and gastrointestinal endoscopy examinations, showed a recurrence rate of 9.04%, while the remaining had a recurrence rate of 2.56% ($\chi^2 = 11.997$, $P = 0.001$). The recurrence rate was 18.64% in patients who received gastrointestinal endoscopy examinations, and was higher than the patients who received oral treatment, which was 4.40% ($\chi^2 = 10.600$, $P = 0.009$).

Logistic regression analysis was performed by these three factors, as well as combination of peptic ulcer and hospitalization. Results revealed that the combination of invasive diagnoses or treatments, the level of income, and the hygiene standard of dining out place were independent influential factors of *H. pylori* recurrence ($P = 0.001$, 0.004, 0.008, 95% CI 1.828–10.585, 0.026–0.499, 1.672–33.086) [Table 3].

Relationship between $^{13}\text{C-UBT}$ value and recurrence of *H. pylori*

Among all 575 patients who had successful eradication of *H. pylori* with $^{13}\text{C-UBT}$, the values of $^{13}\text{C-UBTs}$ in 522 patients were < 2 , and had a recurrence rate of 4.02%. The values of $^{13}\text{C-UBTs} \geq 2$ in 53 patients had a recurrence rate of 7.55%. There were no significant differences between these two groups ($F = 1.204$, $P = 0.601$).

Discussion

Eradication therapy of *H. pylori* play an important role in curing peptic ulcer, prevent the recurrence of ulcer recurrence, and treatment of MALT lymphoma, and even prevents gastric mucosa cancerization. Because of the wide application of eradication therapy in the treatment of *H. pylori* infection, the recurrence of *H. pylori* after eradication has been attracting more and more attention.

The recurrence of *H. pylori* is defined as urea breath test or histological examinations showing negative value of *H. pylori* infected patient who has finished eradication therapy for at least 4 weeks, and turns positive during the follow-up period.

The recurrence of *H. pylori* infection was divided into two clinical situations, namely recrudescence and reinfection.^[6,7] The recrudescence of *H. pylori* refers to a

situation where the *H. pylori* stain was suppressed by medicines, thus failing to detect its colonization for the first time with follow-up infection test in 4 weeks or more after eradication, but latter tests become positive with the reproduction of original *H. pylori* bacterial stain. Reinfection of *H. pylori* is defined as successful elimination of *H. pylori* bacterial stain, and when the patient is infected with a new strain or a homogeneous strain of the former one, resulting in positive in latter follow-up infection tests. Many molecular fingerprint techniques could identify the strains of *H. pylori*. Since the procedures of these techniques are very complicated and the demands on staff and facilities are high, there is still a long way to go for the use of applications. Thus, most former studies classified the recurrence of infection of *H. pylori* after eradication in less than 1 year as recrudescence, while reinfection if it was more than 1 year. Recurrence in our study patients at 1 year after eradication may be caused by recrudescence or reinfection, and the main cause of recurrence at 3 years after eradication was reinfection.

The recurrence rate varied in different studies, ranging between 0% and 23.4%.^[8-14] However, it was deduced that the recurrence rates of developed countries are lower than that of the developing countries. A region with higher prevalence rate of *H. pylori* has higher recurrence rate correspondingly. Annualized recurrence rates in developed countries like Japan, United Kingdom, and Spain are lower than 1%, while the rates are more than 10% in developing countries such as Latin American countries, Bolivia, and Vietnam.

According to eight research studies conducted 10 years ago in China, with sample sizes were below 300, and subjects with peptic ulcers showed a recurrence rate of *H. pylori* infection between 1.08% and 17%.^[15,16] The factors affecting the recurrence of *H. pylori* infection was rarely investigated and analyzed. With the wide application of eradication therapy for *H. pylori* infection, the prevalence of *H. pylori* was declined in the recent years. Moreover, the recurrence may reveal some new changes and characteristics with the promotion of socioeconomic developing status and improvement of hygiene condition. Hence, we conducted this prospective study to detect the recurrence rate of *H. pylori* infection in China. In our study, the recurrence rate one year after eradication therapy was 1.75%, and the cumulative recurrence rate in 3 years was 4.61%. Thus, the recurrence rates in the second and third year after eradication therapy are lower than that in the first year, illustrating reinfection, and the reason for the recurrence of *H. pylori* 1 year after eradication might be due to recrudescence.

A meta-analysis by Yan *et al* on the recurrence of *H. pylori* infection covering 77 researches,^[14] and 1226 patients (in total 43,525 patient-years) showed a world-wide annual average recurrence rate of *H. pylori* infection of $2.82 \pm 1.16\%$. In this article, the nation's socioeconomic level was evaluated by human development index (HDI), which is an integrated and objective consideration index based on lifespan, quality of life, education level and so on. The article demonstrated a negative linear correlation between recurrence rate and the nations HDI ($r = -0.633$), and that

Table 2: Univariate analysis of the factors affecting the recurrence of *H. pylori* infection.

Variables	Sample-size, <i>n</i> (%)	Recurrence group, <i>n</i> (%)	Non-recurrence group, <i>n</i> (%)	<i>P</i>
Gender	595 (100.0)	26 (100.0)	569 (100.0)	0.414
Male	321 (53.9)	13 (50)	308 (54.1)	
Female	274 (46.1)	13 (50)	261 (45.9)	
Occupation	595 (100.0)	26 (100.0)	569 (100.0)	0.597
Medical worker	9 (2.2)	0	9 (1.6)	
Farmer	11 (13.1)	1 (3.8)	10 (1.8)	
Others	575 (84.7)	25 (96.2)	550 (96.7)	
Ethnicity	595 (100.0)	26 (100.0)	569 (100.0)	0.476
Han	559 (93.9)	24 (92.3)	535 (94.0)	
Minority	36 (6.1)	2 (7.7)	34 (6.0)	
Education level	595 (100.0)	26 (100.0)	569 (100.0)	0.370
Master or above	113 (19.0)	6 (23.1)	107 (18.8)	
Bachelor or below	482 (81.0)	20 (76.9)	462 (81.2)	
Combination of PU	595 (100.0)	26 (100.0)	569 (100.0)	0.087
Yes	190 (31.9)	12 (46.2)	178 (31.3)	
No	405 (68.1)	14 (53.8)	391 (68.7)	
Native place of father	595 (100.0)	26 (100.0)	569 (100.0)	0.299
Beijing	147 (24.7)	8 (30.8)	139 (24.4)	
Others	448 (75.3)	18 (69.2)	430 (75.6)	
Native place of mother	595 (100.0)	26 (100.0)	569 (100.0)	0.249
Beijing	161 (27.1)	9 (34.6)	152 (26.7)	
Others	434 (72.9)	17 (65.4)	417 (73.3)	
Permanent residence	595 (100.0)	26 (100.0)	569 (100.0)	0.469
Beijing	581 (97.4)	25 (96.2)	556 (97.7)	
Others	14 (2.6)	1 (3.8)	13 (2.3)	
Income per month	595 (100.0)	26 (100.0)	569 (100.0)	0.000
<5000 RMB Yuan	353 (59.3)	24 (92.3)	329 (57.8)	
≥5000 RMB Yuan	242 (40.7)	2 (7.7)	240 (42.2)	
Residential area	592 (100.0)	26 (100.0)	566 (100.0)	0.648
Suburban	28 (4.7)	1 (3.8)	27 (4.8)	
Urban	594 (95.3)	25 (96.2)	539 (95.2)	
Main source of drinking water	594 (100.0)	26 (100.0)	568 (100.0)	0.764
Clean	588 (99.0)	26 (100.0)	562 (98.9)	
Probable polluted	6 (1.0)	0	6 (1.1)	
Cooking habit	595 (100.0)	26 (100.0)	569 (100.0)	0.609
Cooked food	584 (98.2)	26 (100)	558 (98.1)	
Not cooked food	11 (1.8)	0	11 (1.9)	
Dining out frequency	595 (100.0)	26 (100.0)	569 (100.0)	0.320
Frequent	290 (48.7)	11 (42.3)	279 (49.0)	
Occasional	305 (51.3)	15 (57.7)	290 (51.0)	
Hygiene of dining out place	541 (100.0)	24 (100.0)	517 (100.0)	0.010
Good	530 (54.5)	21 (87.5)	509 (98.5)	
Poor	11 (45.5)	3 (12.5)	8 (1.5)	
Way of dining	592 (100.0)	26 (100.0)	566 (100.0)	1.000
Dining alone	118 (19.9)	5 (23.1)	113 (20.0)	
Group dining	474 (80.1)	21 (76.9)	453 (80.0)	
Hospitalization after eradication	593 (100.0)	25 (100.0)	568 (100.0)	0.568
Yes	13 (2.2)	0	13 (2.3)	
No	580 (97.8)	25 (100)	555 (97.7)	
Invasive diagnosis or treatment	595 (100.0)	26 (100.0)	569 (100.0)	0.001
Yes	166 (27.9)	15 (57.1)	151 (26.5)	
No	429 (72.1)	11 (42.3)	418 (73.5)	
Type of invasive operation	166 (100.0)	15 (100.0)	151 (100.0)	0.009
Oral treatment	91 (54.8)	4 (12.5)	87 (57.6)	
Endoscope	59 (35.5)	11 (75.0)	48 (31.8)	
Both	16 (9.6)	0 (12.5)	16 (10.6)	
Combination of underlying disease	595 (100.0)	26 (100.0)	569 (100.0)	0.752

(continued)

Table 2
(continued).

Variables	Sample-size, <i>n</i> (%)	Recurrence group, <i>n</i> (%)	Non-recurrence group, <i>n</i> (%)	<i>P</i>
None	477 (80.2)	22 (84.6)	455 (80.0)	
Diabetes mellitus	33 (5.5)	2 (7.7)	31 (5.4)	
Anemia	11 (1.8)	0	11 (1.9)	
Others	474 (12.4)	2 (7.7)	72 (12.7)	

Table 3: Multivariate analysis of factors affecting the recurrence of *H. pylori* infection.

Variables	<i>P</i>	OR	95%CI	
			The lower limit	The upper limit
Invasive diagnosis or treatment				
Yes		1		
No	0.001	4.399	1.828	10.585
Income per month				
<5000 RMB Yuan		1		
≥5000 RMB Yuan	0.004	0.114	0.026	0.499
Hygiene of dinning out place				
Good		1		
Poor	0.008	7.438	1.672	33.086

the recurrence rate in very-high HDI nations were significantly different compared with nations with high, medium, and low HDI. In the developing countries, the poor populations have a higher recurrence rate of *H. pylori*, while this rate in the rich populations was similar to the Western countries. Hence, it was considered that the recurrence rate of *H. pylori* infection was closely related to local economic level. Moreover, hygiene condition, prevalence of *H. pylori*, and close contact in family members may be associated with recurrence.

We also discovered that the recurrence rate in low-income patients was significantly higher than high-income patients. Besides, hygiene condition of dining out place has been proved to be an influential factor for the recurrence of *H. pylori* infection as well, with a higher recurrence rate in patients with poor hygiene condition of dining out place. From these views of sociology and public health, it is of great importance to raise the income and health consciousness in people for the prevention of recurrence of *H. pylori* infection.

Research studies showed that 40% to 50% dental plaques were *H. pylori* positive. Dental plaque is a bacterial membrane, which can protect microorganisms from antibacterial medicines.^[17-19] Thus, the systemic antibiotic therapeutic regimens lose their efficiency due to it. Dental plaques could be regarded as reserve pool, leading to the recurrence of *H. pylori* infection in the stomach. Meanwhile, inadequate washing and sterilization of endoscope may also spread *H. pylori* bacteria, thus finally causing the recurrence of *H. pylori*. In our study, we also observed high recurrence rates in patients receiving oral treatment and gastrointestinal endoscopy examinations. A

meta-analysis conducted by Bouziane *et al* in 2012,^[20] which enrolled 298 patients from three studies, demonstrated a significant reduction of recurrence rate in the experimental group (RR=0.37, 95% CI 0.21–0.64) patients receiving eradication therapy of *H. pylori* infection compared to control group receiving only eradication therapy. These results suggested that the combination of periodontal scaling can reduce the recurrence of *H. pylori* infection. On the other side, the procedure of washing and sterilization of endoscopes should be monitored and executed strictly to prevent the spreading of *H. pylori* infection when performing endoscopy examinations.

The ¹³C-UBT value after eradication therapy may influence the judgment of recurrence. Patients whose ¹³C-UBT values are between 2 and 4 have the possibility of false negative, and when ¹³C-UBT values are found positive in further follow-up tests, these eradication-failed patients may be classified into recurrence group.^[21] In our study, we compared the recurrence rate of patients whose values of ¹³C-UBT were lower than 2 for the first time after eradication therapy and patients whose values of ¹³C-UBT were between 2 and 4, which eventually showed no statistical difference.

In a word, we have found in our study that the recurrence rate of *H. pylori* in urban population of China was similar to that of the developed countries. Low-income, poor hygiene condition of dining out place, and combination of invasive diagnoses or treatments are considered as independent risk factors of the recurrence of *H. pylori* infection. A regular surveillance on infectious state in high-risk population is necessary.

Conflicts of interest

None.

References

- Malfertheiner P, Megraud F, O'Morain CA, Gisbert JP, Kuipers EJ, Axon AT, *et al.* European Helicobacter and Microbiota Study Group and Consensus panel. Management of *Helicobacter pylori* infection—the Maastricht V/Florence Consensus Report. *Gut* 2017;66:6–30. doi: 10.1136/gutjnl-2016-312288.
- Lai KC, Hui WM, Wong WM, Wong BC, Hu WH, Ching CK, *et al.* Treatment of *Helicobacter pylori* in patients with duodenal ulcer hemorrhage—a long-term randomized, controlled study. *Am J Gastroenterol* 2000;95:2225–2232. doi: 10.1111/j.1572-0241.2000.02249.x.
- Papa A, Cammarota G, Tursi A, Gasbarrini A, Gasbarrini G. *Helicobacter pylori* eradication and remission of low-grade gastric mucosa-associated lymphoid tissue lymphoma: a long-term follow-up study. *J Clin Gastroenterol* 2000;31:169–171. doi: 10.1097/00004836-200009000-00018.
- Hu Y, Wan JH, Li XY, Zhu Y, Graham DY, Lu NH. Systematic review with meta-analysis: the global recurrence rate of *Helicobacter pylori*. *Aliment Pharmacol Ther* 2017;46:773–779. doi: 10.1111/apt.14319.
- Liya Zhou, Jianzhong Zhang, Zhiqiang Song, He L, Li Y, Qian J, *et al.* Tailored versus triple plus bismuth or concomitant therapy as initial *Helicobacter pylori* treatment: a randomized trial. *Helicobacter* 2016;21:91–99. doi: 10.1111/hel.12242.
- Kim SY, Hyun JJ, Jung SW, Koo JS, Yim HJ, Lee SW. *Helicobacter pylori* recurrence after first- and second-line eradication therapy in Korea: the problem of recrudescence or reinfection. *Helicobacter* 2014;19:202–206. doi: 10.1111/hel.12117.
- Bell GD, Powell KU, Burrige SM, Harrison G, Rameh B, Weil G, *et al.* Reinfection or recrudescence after apparently successful eradication of *Helicobacter pylori* infection: implications for treatment of patients with duodenal ulcer disease. *Q J Med* 1993;86:375–382.
- Hildebrand P, Bardhan P, Rossi L, Parvin S, Rahman A, Arefin MS, *et al.* Recrudescence and reinfection with *Helicobacter pylori* after eradication therapy in Bangladeshi adults. *Gastroenterology* 2001;121:792–798. doi: 10.1053/gast.2001.28018.
- Adachi M, Mizuno M, Yokota K, Miyoshi M, Nagahara Y, Maga T, *et al.* Reinfection rate following effective therapy against *Helicobacter pylori* infection in Japan. *J Gastroenterol Hepatol* 2002;17:27–31. doi: 10.1046/j.1440-1746.2002.02666.x.
- Wheeldon TU, Hoang TT, Phung DC, Björkman A, Granström M, Sörberg M. Long-term follow-up of *Helicobacter pylori* eradication therapy in Vietnam: reinfection and clinical outcome. *Aliment Pharmacol Ther* 2005;21:1047–1053. doi: 10.1111/j.1365-2036.2005.02408.x.
- Ramirez-Ramos A, Gilman RH, Leon-Barua R, Recavarren-Arce S, Watanabe J, Salazar G, *et al.* Rapid recurrence of *Helicobacter pylori* infection in Peruvian patients after successful eradication. Gastrointestinal Physiology Working Group of the Universidad Peruana Cayetano Heredia and The Johns Hopkins University. *Clin Infect Dis* 1997;25:1027–1031.
- Seo M, Okada M, Shirohani T, Nishimura H, Maeda K, Aoyagi K, *et al.* Recurrence of *Helicobacter pylori* infection and the long-term outcome of peptic ulcer after successful eradication in Japan. *J Clin Gastroenterol* 2002;34:129–134. doi: 10.1097/00004836-200202000-00005.
- Carta M, Dore MP, Idda M, Casu M, Realdi G. Effect of cure rate on reinfection with *H. pylori*: a three-year follow-up study. *Am J Gastroenterol* 2000;95:3324–3325. doi: 10.1111/j.1572-0241.2000.03323.x.
- Yan TL, Hu QD, Zhang Q, Casu M, Realdi G. National rates of *Helicobacter pylori* recurrence are significantly and inversely correlated with human development index. *Aliment Pharmacol Ther* 2013;37:963–968. doi: 10.1111/j.1572-0241.2000.03323.x.
- Mitchell HM, Hu P, Chi Y, Chen MH, Li YY, Hazell SL. A low rate of reinfection following effective therapy against *Helicobacter pylori* in a developing nation (China). *Gastroenterology* 1998;114:256–261.
- Chen TS, Tsay SH, Chang FY, Lee SD. Triple therapy for the eradication of *Helicobacter pylori* and reduction of duodenal ulcer relapse: comparison of 1 week and 2 week regimens and recrudescence rates over 12 months. *J Gastroenterol Hepatol* 1995;10:300–305.
- Anand PS, Kamath KP, Anil S. Role of dental plaque, saliva and periodontal disease in *Helicobacter pylori* infection. *World J Gastroenterol* 2014;20:5639–5653. doi: 10.3748/wjg.v20.i19.5639.
- Agarwal S, Jithendra KD. Presence of *Helicobacter pylori* in subgingival plaque of periodontitis patients with and without dyspepsia, detected by polymerase chain reaction and culture. *J Indian Soc Periodontol* 2012;16:398–403. doi: 10.4103/0972-124X.100919.
- Liu Y, Yue H, Li A, Wang J, Jiang B, Zhang Y, *et al.* An epidemiologic study on the correlation between oral *Helicobacter pylori* and gastric *H. pylori*. *Curr Microbiol* 2009;58:449–453. doi: 10.1007/s00284-008-9341-3.
- Bouziane A, Ahid S, Abouqal R, Ennibi O. Effect of periodontal therapy on prevention of gastric *Helicobacter pylori* recurrence: a systematic review and meta-analysis. *J Clin Periodontol* 2012;39:1166–1173. doi: 10.1111/jcpe.12015.
- Gisbert JP, Pajares JM. Review article: 13C-urea breath test in the diagnosis of *Helicobacter pylori* infection – a critical review. *Aliment Pharmacol Ther* 2004;20:1001–1017. doi: 10.1111/j.1365-2036.2004.02203.x.

How to cite this article: Xue Y, Zhou LY, Lu HP, Liu JZ. Recurrence of *Helicobacter pylori* infection: incidence and influential factors. *Chin Med J* 2019;132:765–771. doi: 10.1097/CM9.0000000000000146