

## Prospective Study

## Primary antibiotic resistance of *Helicobacter pylori* strains isolated from patients with dyspeptic symptoms in Beijing: A prospective serial study

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### Abstract

**AIM:** To determine the resistance patterns of *Helicobacter pylori* (*H. pylori*) strains isolated from patients in Beijing and monitor the change of antibiotic resistance over time.

**METHODS:** In this prospective, serial and cross-sectional study, *H. pylori* cultures were successfully obtained from 371 and 950 patients (never receiving eradication) during 2009-2010 and 2013-2014, respectively. Resistance to amoxicillin, clarithromycin, metronidazole, levofloxacin, tetracycline, and rifampicin was determined by Epsilon meter test.

**RESULTS:** The resistance rates of isolates obtained during 2009-2010 were 66.8%, 39.9%, 34.5%, 15.4%, 6.7%, and 4.9% to metronidazole, clarithromycin, levofloxacin, rifampicin, amoxicillin and tetracycline, respectively; and the corresponding rates for isolates during 2013-2014 were 63.4%, 52.6%, 54.8%, 18.2%, 4.4% and 7.3%, respectively. The resistance rates to clarithromycin and levofloxacin were significantly increased after four years. In 2009-2010, 14.6% of *H. pylori* isolates were susceptible to all tested antibiotics, with mono (33.7%), double (28.3%), triple (16.7%), quadruple (6.2%), quintuple (0.3%) and sextuple resistance (0.3%) also being detected. In 2013-2014, 9.4% were susceptible to all tested antibiotics, and mono (27.6%), double (28.4%), triple (24.9%), quadruple (7.3%), quintuple (2.3%) and sextuple resistance (0.1%) was also observed. More multiple resistant *H. pylori* isolates were found during 2013-2014. Gender (to levofloxacin and metronidazole), age (to levofloxacin) and endoscopic findings (to clarithromycin) were independent factors influencing antibiotic resistance.

**CONCLUSION:** *H. pylori* resistance to commonly used antibiotics in Beijing is high with increased multiple antibiotic resistance.

**Key words:** *Helicobacter pylori*; Antibiotic resistance; Beijing; Dyspeptic symptoms

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**Core tip:** Because the antimicrobial susceptibility of *Helicobacter pylori* (*H. pylori*) strains continues to change over time, it is very important to obtain updated information on antibiotic resistance by dynamic monitoring and serial detection, which is critical to the selection of the most optimal therapeutic regimens for eradication of *H. pylori* infection. This study provided us the comprehensive and up-to-date data about antibiotic resistance of *H. pylori*. It was showed that *H. pylori* resistance to commonly used antibiotics in China is high with increased multiple antibiotic resistances. Therefore, the eradication of *H. pylori* infection remains a challenge in China.

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## INTRODUCTION

Although studies on *Helicobacter pylori* (*H. pylori*) have been carried out since thirty years ago, eradication of *H. pylori* infection remains a challenge, mainly because of the significantly increasing prevalence of its resistance to antibiotics<sup>[1,2]</sup>. A suitable therapeutic regimen for *H. pylori* infection should be based on the specific conditions of patients, especially the antibiotic resistance, in order to achieve better long-term efficacy. In China, there is a high prevalence of *H. pylori* infection and gastric cancer<sup>[3,4]</sup>.

Because the antimicrobial susceptibility of *H. pylori* strains continues to change over time, it is very important to obtain updated information on antibiotic resistance by dynamic monitoring and serial detection, which is critical to the selection of the most optimal therapeutic regimens for eradication of *H. pylori* infection. However, the recent information on such studies conducted in Chinese patients is lacking and most studies have investigated only a few types of antibiotics<sup>[5]</sup>. Therefore, further studies with large sample sizes and serial observations are urgently needed to provide comprehensive and up-to-date information on the antibiotic resistance of *H. pylori*.

The aim of this study was to determine the resistance rates and patterns of *H. pylori* strains isolated from patients with dyspepsia and to monitor the change of antibiotic resistance over time.

## MATERIALS AND METHODS

This is a prospective, single-centre, serial, cross-sectional observational study.

### Study population

From August 2009 to February 2010 and from April 2013 to March 2014, patients undergoing upper endoscopy due to dyspeptic symptoms in a tertiary hospital in Beijing, China were enrolled in the study. Patients were included by clinical gastroenterologists if they were of 18 to 70 years old and had not received treatment for eradication of *H. pylori* infection prior to study entry.

Exclusion criteria were: (1) patients who had received proton pump inhibitors, H<sub>2</sub> receptor antagonists, bismuth salts or antibiotics during the four weeks prior to study entry; (2) patients with malignant tumors of the digestive system; (3) patients who had undergone gastrointestinal tract surgery; (4) patients whose conditions were complicated by severe heart, lung, blood, liver or kidney dysfunction; and (5) patients who would not comply to the study.

### Ethical consideration

The study was approved by the independent Ethics Committee of Peking University Health Science Center (IRB00001052-0709) and was carried out in accordance with the ethical guidelines of the Declaration of Helsinki and Good Clinical Practices. Written informed consent was obtained from each patient prior to study enrollment.

### Study methods

After obtaining general information, a gastric mucosal biopsy specimen from the antrum was collected from each patient during upper endoscopy to check the presence of *H. pylori* by rapid urease test (HPUT-H102, San Qiang Biological and Chemical Co., Fujian, China). If a patient tested positive, two mucosal biopsy specimens (one from the antrum and the other from the corpus) were put into the same vial for the culture of *H. pylori*. Two additional specimens (one from the antrum and the other from the corpus) were obtained for histological haematoxylin and eosin staining, and gastritis was evaluated using the updated Sydney system<sup>[6]</sup>.

### Isolation and identification of *H. pylori*

Briefly, gastric mucosal biopsy specimens were stored in brain heart infusion broth (Oxoid, Basingstoke, United Kingdom) with 5% glycerin at -80 °C and were transported with dry ice to the laboratory at the

**Table 1 Characteristics of the patients with *Helicobacter pylori* positive culture**

| Characteristic                  | 2009-2010<br>( <i>n</i> = 371) | 2013-2014<br>( <i>n</i> = 950) | <i>P</i> value |
|---------------------------------|--------------------------------|--------------------------------|----------------|
| Gender (male/female), <i>n</i>  | 185/186                        | 485/465                        | 0.698          |
| Age (yr), mean ± SD             | 41.9 ± 13.4                    | 42.9 ± 13.2                    | 0.215          |
| Endoscopic findings, <i>n</i>   |                                |                                |                |
| Peptic ulcer                    | 60                             | 184                            | 0.320          |
| Gastric erosions                | 75                             | 200                            |                |
| No macroscopic abnormality      | 236                            | 566                            |                |
| Histological findings, <i>n</i> |                                |                                |                |
| Non-atrophic gastritis          | 245                            | 664                            | 0.174          |
| Atrophic gastritis              | 126                            | 286                            |                |

National Institute for Communicable Disease Control and Prevention, Beijing, China. Frozen samples were thawed at room temperature for 30 min, ground and cultivated on a Columbia agar (Oxoid, Basingstoke, United Kingdom) plate supplemented with 5% defibrinated sheep blood, 3 µg/mL trimethoprim, 2.5 µg/mL vancomycin, 2 µg/mL amphotericin B and 2 µg/mL polymyxin B. The cultured plates were incubated in a microaerobic atmosphere (5% oxygen, 10% carbon dioxide and 85% nitrogen). After culture, translucent colonies of about 0.5-2 mm from selective agar plates were Gram-stained and tested for urease, catalase and oxidase activities. The organisms were identified as *H. pylori* if the isolates demonstrated curved Gram-negative rods, which were similar to *Helicobacter*, along with positive urease, catalase and oxidase reactions.

#### Antibiotic susceptibility testing

The antibiotic resistance of *H. pylori* isolates was determined by the Epsilometer test (E-test)<sup>[7]</sup>. According to the clinical breakpoints for *H. pylori* proposed by the European Committee on Antimicrobial Susceptibility Testing (EUCAST)<sup>[8]</sup>, the resistance breakpoints for amoxicillin, clarithromycin, metronidazole, levofloxacin, tetracycline and rifampicin were defined as > 0.12, > 0.5, > 8, > 1, > 1 and > 1 mg/L, respectively. After storing *H. pylori* isolates at -80 °C for two weeks, susceptibility testing for amoxicillin was performed again. All the cultures and tests were conducted at the National Institute for Communicable Disease Control and Prevention of Chinese Center for Disease Control and Prevention.

#### Statistical analysis

All statistical analyses were performed using the statistical software SPSS (version 18.0; SPSS Inc., Chicago, IL, United States). Frequencies and percentages were used to describe the antimicrobial resistance of *H. pylori* isolates. Between-group differences were evaluated using Student's *t* test for continuous variables and Pearson's  $\chi^2$  or Fisher's exact test for categorical variables. Univariate analyses were performed for the determination of factors

that could influence the antibiotic resistance of *H. pylori* isolates, such as gender (male vs female), age groups (18-35 vs 36-50 vs 51-75 years of age) and endoscopic findings (peptic ulcer disease vs non-ulcer disease). Patients with duodenal or/and gastric ulcer were considered as having peptic ulcer disease; those without ulcers were considered as patients with non-ulcer dyspepsia. Thereafter, binary logistic regression was used to analyze the relationships between independent variables (gender, age groups and endoscopic findings) and dependent variables (antibiotic susceptibility or resistance) with backward likelihood ratio analysis, which determined independent influencing factors for the antibiotic resistance of *H. pylori*. The odds ratio (OR) and 95% confidence interval (CI) of different variables related to antibiotic resistance were calculated. Differences with *P*-values less than 0.05 from a 2-tailed test were considered statistically significant.

## RESULTS

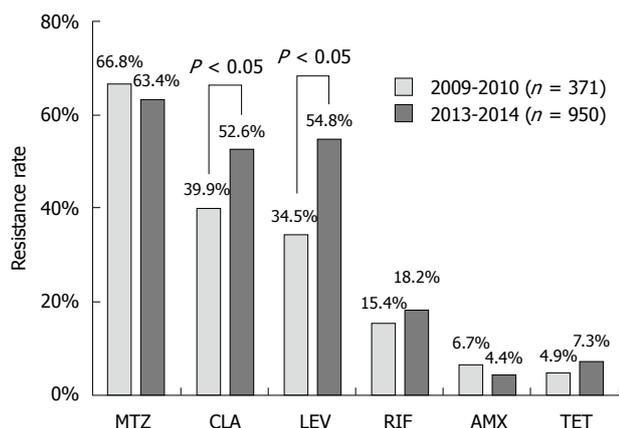
In 2009-2010, 450 patients were *H. pylori* positive as determined by the rapid urease test and bacterial cultures were successfully obtained for 371 (82.4%) patients. In 2013-2014, 1105 patients were *H. pylori* positive and bacterial cultures were successfully obtained for 950 (86.0%) patients. No significant differences were observed in the rates of positive culture, general characteristics and endoscopic and histological findings of the study population between the two groups (Table 1).

#### Overall antibiotic resistance

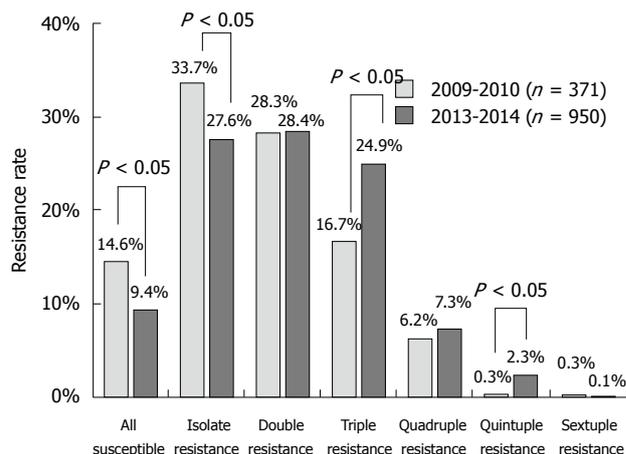
In 2009-2010, the resistance rate of 371 *H. pylori* isolates to metronidazole (66.8%) was highest, followed by clarithromycin (39.9%), levofloxacin (34.5%), rifampicin (15.4%), amoxicillin (6.7%) and tetracycline (4.9%). In 2013-2014, the resistance rate of 950 *H. pylori* isolates was also highest to metronidazole (63.4%), followed by levofloxacin (54.8%), clarithromycin (52.6%), rifampicin (18.2%), tetracycline (7.3%) and amoxicillin (4.4%). The resistance rates to clarithromycin and levofloxacin in 2013-2014 were significantly higher than those in 2009-2010, while no significant difference was found in the resistance rates to other four antibiotics (Figure 1).

#### Multiple antibiotic resistances

In 2009-2010, 14.6% of *H. pylori* isolates were susceptible to all tested antibiotics. Monoresistance (33.7%), double resistance (28.3%), triple resistance (16.7%), quadruple resistance (6.2%), quintuple resistance (0.3%) and sextuple resistance (0.3%) were also observed. In 2013-2014, 9.4% of *H. pylori* isolates were susceptible to all tested antibiotics, and mono resistance (27.6%), double resistance (28.4%), triple resistance (24.9%), quadruple resistance (7.3%),



**Figure 1** Comparisons of overall antibiotic resistance rates between the two groups. AMX: Amoxicillin; CLA: clarithromycin; LEV: Levofloxacin; MTZ: Metronidazole; RIF: Rifampicin; TET: Tetracycline.



**Figure 2** Comparisons of multiple antibiotic resistance rates between the two groups.

**Table 2** Multiple resistance patterns in the *Helicobacter pylori* isolates n (%)

| Multiple resistance pattern | 2009-2010 (n = 371) | 2013-2014 (n = 950) |
|-----------------------------|---------------------|---------------------|
| <b>Double resistance</b>    |                     |                     |
| CLA + MTZ                   | 36 (9.7)            | 79 (8.3)            |
| MTZ + LEV                   | 29 (7.8)            | 94 (9.9)            |
| MTZ + RIF                   | 15 (4.0)            | 14 (1.5)            |
| CLA + LEV                   | 13 (3.5)            | 40 (4.2)            |
| AMX + MTZ                   | 3 (0.8)             | 3 (0.3)             |
| MTZ + TET                   | 3 (0.8)             | 2 (0.2)             |
| CLA + RIF                   | 2 (0.5)             | 11 (1.2)            |
| AMX + CLA                   | 2 (0.5)             | 4 (0.4)             |
| CLA + TET                   | 1 (0.3)             | 5 (0.5)             |
| AMX + RIF                   | 1 (0.3)             | 2 (0.2)             |
| LEV + RIF                   | 0                   | 8 (0.8)             |
| LEV + TET                   | 0                   | 5 (0.5)             |
| AMX + LEV                   | 0                   | 1 (0.1)             |
| <b>Triple resistance</b>    |                     |                     |
| CLA + MTZ + LEV             | 34 (9.2)            | 171 (18.0)          |
| CLA + MTZ + RIF             | 7 (1.9)             | 16 (1.7)            |
| AMX + CLA + MTZ             | 6 (1.6)             | 4 (0.4)             |
| MTZ + LEV + RIF             | 4 (1.1)             | 18 (1.9)            |
| CLA + MTZ + TET             | 4 (1.1)             | 1 (0.1)             |
| CLA + LEV + RIF             | 2 (0.5)             | 11 (1.2)            |
| AMX + MTZ + LEV             | 2 (0.5)             | 2 (0.2)             |
| AMX + MTZ + RIF             | 1 (0.3)             | 0                   |
| AMX + CLA + LEV             | 1 (0.3)             | 0                   |
| CLA + LEV + TET             | 1 (0.3)             | 3 (0.3)             |
| MTZ + LEV + TET             | 0                   | 10 (1.1)            |
| AMX + CLA + RIF             | 0                   | 1 (0.1)             |
| CLA + TET + RIF             | 0                   | 1 (0.1)             |
| MTZ + TET + RIF             | 0                   | 1 (0.1)             |
| <b>Quadruple resistance</b> |                     |                     |
| CLA + MTZ + LEV + RIF       | 12 (3.2)            | 38 (4.0)            |
| AMX + CLA + MTZ + LEV       | 4 (1.1)             | 9 (0.9)             |
| CLA + MTZ + LEV + TET       | 4 (1.1)             | 8 (0.8)             |
| MTZ + LEV + TET + RIF       | 1 (0.3)             | 8 (0.8)             |
| AMX + MTZ + LEV + TET       | 1 (0.3)             | 0                   |
| AMX + MTZ + LEV + RIF       | 1 (0.3)             | 0                   |
| AMX + CLA + MTZ + RIF       | 0                   | 3 (0.3)             |
| CLA + MTZ + TET + RIF       | 0                   | 2 (0.2)             |
| CLA + LEV + TET + RIF       | 0                   | 1 (0.1)             |
| <b>Quintuple resistance</b> |                     |                     |
| CLA + MTZ + LEV + TET + RIF | 1 (0.3)             | 17 (1.8)            |
| AMX + CLA + MTZ + LEV + RIF | 0                   | 3 (0.3)             |

|                             |         |         |
|-----------------------------|---------|---------|
| AMX + CLA + MTZ + LEV + TET | 0       | 2 (0.2) |
| Sextuple resistance         | 1 (0.3) | 1 (0.1) |

AMX: Amoxicillin; CLA: Clarithromycin; LEV: Levofloxacin; MTZ: Metronidazole; RIF: Rifampicin; TET: Tetracycline.

quintuple resistance (2.3%) and sextuple resistance (0.1%) were also observed. Markedly, more multiple resistant *H. pylori* isolates were found in 2013-2014 (Figure 2). In the clarithromycin-resistant isolates in 2013-2014, 70.8% and 60.8% of isolates were also resistant to metronidazole and levofloxacin, respectively. In the metronidazole-resistant isolates, levofloxacin-resistant isolates were detected in 63.3% of isolates. The multiple resistance patterns are shown in Table 2.

### Factors influencing antibiotic resistance

Univariate analysis showed that there was a significant difference in the resistance rate to clarithromycin between the patients with peptic ulcer disease and non-ulcer dyspepsia. There were significant differences in the resistance rates to metronidazole and levofloxacin between men and women. Moreover, the significant difference in levofloxacin resistance rate was observed among different age groups. Multivariate analysis demonstrated that the above-mentioned factors were independent factors influencing the antibiotic resistance of *H. pylori* (Table 3).

## DISCUSSION

The results from the present study revealed that the treatment of *H. pylori* infection remains a challenge in China due to the high rates of *H. pylori* resistance to commonly used antibiotics. Furthermore, multiple antibiotic resistance patterns were also commonly observed in the *H. pylori* isolates investigated. The rates of clarithromycin and levofloxacin resistance were

**Table 3** Influencing factors of antibiotic resistance of *Helicobacter pylori* isolates

| Resistance rate (%) | Gender<br>Male ( <i>n</i> = 670),<br>female ( <i>n</i> = 651) | Age (yr)<br>18-35 ( <i>n</i> = 496),<br>36-50 ( <i>n</i> = 378),<br>51-75 ( <i>n</i> = 447) | Endoscopic findings<br>PUD ( <i>n</i> = 244),<br>NUD ( <i>n</i> = 1077) |
|---------------------|---|---|---|
| Amoxicillin         | 5.1, 5.1  | 4.2, 5.3, 5.8   | 2.9, 5.6  |
| Clarithromycin      | 46.6, 51.6  | 50.8, 48.7, 47.4  | 36.5, 51.9 <sup>a</sup> (OR = 1.822; 95%CI: 1.364-2.433)                |
| Metronidazole       | 59.4, 69.4 <sup>a</sup> (OR =1.504; 95%CI: 1.195-1.891)       | 63.3, 62.2, 67.3  | 58.6, 65.6  |
| Levofloxacin        | 43.6, 54.8 <sup>a</sup> (OR =1.518; 95%CI: 1.219-1.891)       | 42.9, 53.4, 52.3 <sup>a</sup> (OR =1.199; 95%CI: 1.053-1.365)                               | 45.1, 50.0  |
| Tetracycline        | 7.2, 6.0  | 6.7, 4.5, 8.3   | 6.1, 6.7  |
| Rifampicin          | 19.0, 15.8  | 16.7, 16.9, 18.6  | 20.9, 16.6  |

<sup>a</sup>*P* < 0.05, the significant difference in levofloxacin resistance rate was observed among different age groups. PUD: Peptic ulcer disease; NUD: Non-ulcer disease; OR: Odds ratio; CI: Confidence interval.

further significantly increased in the last four years and multi-resistant strains became more common.

In the present study, resistance to clarithromycin in 2013-2014 was identified in 52.6% of *H. pylori* isolates. According to the Maastricht IV/Florence consensus report<sup>[2]</sup>, the clarithromycin-based standard triple therapy is unsuitable for eradication of *H. pylori* in China, only if susceptibility testing for *H. pylori* is performed before treatment to confirm the lack of resistance to this specific antibiotic. Some studies have found that sequential and concomitant therapies are effective treatment options for patients who show clarithromycin resistance. Thus, these therapies can be recommended for patients from regions with high clarithromycin-resistance rates<sup>[2,9-12]</sup>. Unfortunately, meta-analyses also showed that dual resistance to clarithromycin and metronidazole could reduce the abilities of sequential and concomitant therapies to eradicate *H. pylori*<sup>[13,14]</sup>, which indicated that these therapies could only be used in regions with high rates of isolated clarithromycin resistance. Our recent findings also confirmed this<sup>[15]</sup>. The data in this study showed a high rate of resistance to metronidazole (70.8%) in clarithromycin-resistant isolates. Based on these results, it is reasonable to speculate that sequential and concomitant therapies are not suitable for the management of *H. pylori* infection in China.

In recent years, because of the high resistance to clarithromycin and metronidazole, levofloxacin has been extensively studied in patients with *H. pylori* infection. Moreover, levofloxacin has been proven to be effective in eradicating *H. pylori* in some trials<sup>[16-18]</sup>. Nevertheless, these studies were mainly conducted in regions where the levofloxacin resistance was lower. In this study, the resistance rate of *H. pylori* isolates to levofloxacin was found to be as high as 54.8% with a highly combined resistance to clarithromycin and metronidazole, indicating that levofloxacin-containing therapy might not be a good choice for the initial empiric treatment of *H. pylori* in China.

In the current study, the *H. pylori* isolates were found to be relatively susceptible to tetracycline with an overall resistance rate of 4.9%-7.3%, which suggested that tetracycline could be used in the initial treatment of *H. pylori* infection in China. It is generally

thought that the increase in dosage and dosing frequency of metronidazole can reduce high-level resistance to metronidazole<sup>[1,19]</sup>. Nowadays, bismuth salts have widely been used in clinical practice because they are easily obtained in China. Therefore, the classic quadruple therapy consisting of metronidazole, tetracycline, bismuth and proton pump inhibitors can be suggested as the best empirical first-line regimen for *H. pylori* eradication in China, which is consistent with the recommendations of the Maastricht IV/Florence consensus report<sup>[2]</sup>. Unfortunately, tetracycline is not generally available in China, which has affected its clinical application. Although semisynthetic tetracycline derivatives including minocycline are easily obtainable in the clinic, it is still uncertain whether these derivatives can be used as alternatives to tetracycline for the treatment of *H. pylori* infection.

In this study, the rate of resistance to amoxicillin was relatively low, suggesting that amoxicillin should be fully utilized in the eradication of *H. pylori* infection. With the general increase in the rate of resistance to commonly used antibiotics, dual therapy (proton pump inhibitor plus amoxicillin) drew attention again, but the study results were not consistent and conclusive<sup>[20,21]</sup>. Shirai *et al.*<sup>[20]</sup> have shown a very good eradication efficacy in their study, but rabeprazole and amoxicillin should be administered four times a day. Up to now, no related research has been reported in China.

Rifampicin is rarely used for the treatment of *H. pylori* infection in China. In the present study, the high rate of resistance (18.2%) to this drug in the *H. pylori* isolates studied may be due to its frequent use in the treatment of tuberculosis in China, where a high prevalence of tuberculosis infection is observed.

The study results revealed that the clarithromycin resistance rate of *H. pylori* isolates was significantly higher in the patients with non-ulcer disease than with peptic ulcer disease, which was consistent with the results of previous studies<sup>[22,23]</sup>. Additionally, resistance to levofloxacin and metronidazole was more frequent in women and in middle-aged and elderly patients. Such a phenomenon may be related to the more frequent use of levofloxacin and metronidazole in these patients, especially in women with gynecological diseases. Antimicrobial resistance is closely dependent

on antimicrobial use. In Western countries, the commercialization of quinolones as levofloxacin is more recent than that of clarithromycin, and levofloxacin is strictly limited to use as an antibiotic. Therefore, the resistance rate to levofloxacin of *H. pylori* is relatively low<sup>[2]</sup>. However, in China over the past 30 years, quinolones are widely used as the non-prescription drugs even in animal husbandry and aquaculture, which results in such a high resistance rate. Recently, restrictions in the use of levofloxacin were just demanded.

The antimicrobial susceptibility of the *H. pylori* isolates was determined by the E-test in the current study, primarily because this method was easily performed, especially in a clinical study with large sample size. Although some previous studies have suggested that the rate of metronidazole resistance may be overestimated by E-test<sup>[24,25]</sup>, the results were not consistent or conclusive. A high resistance rate to metronidazole was also found in a recent study conducted in the southeast coastal region of China by the reference agar dilution method<sup>[26]</sup>.

In this study, two gastric mucosal biopsy specimens (one from the antrum and the other from the corpus) were put into the same vial for the culture of *H. pylori*. Due to the restrictions of research funding and study conditions, the cultures of *H. pylori* from the mucosal specimens of the antrum and corpus were not obtained and tested. Hence, the difference in the antimicrobial resistance profile of *H. pylori* isolates obtained according to the location could not be analyzed. This might have underestimated the antimicrobial resistance rates, which was the potential limitation of this study.

The comprehensive and up-to-date information on *H. pylori* resistance obtained in this study will be very helpful to select the most optimal eradication regimens in both China and other regions with a high prevalence of antibiotic resistance. With the current rates of resistance, the priority would be to get new drugs and/or improved methods of detection of resistance. The use of a more accessible and comfortable method to obtain *H. pylori* was already suggested<sup>[27]</sup>, and progress in molecular detection of resistance from faecal samples<sup>[28]</sup> is a very promising line of research.

In conclusion, a prospective serial study was carried out with a large sample size to determine the resistance patterns of *H. pylori* isolates from Chinese patients and to monitor the changes in antibiotic resistance over time. It was showed that *H. pylori* resistance rates to commonly used antibiotics in China are high with increased multiple antibiotic resistance.

## COMMENTS

### Background

The eradication of *Helicobacter pylori* (*H. pylori*) infection remains a challenge, mainly because of the significantly increasing prevalence of its resistance to antibiotics.

### Research frontiers

Because the antimicrobial susceptibility of *H. pylori* strains continues to change over time, it is very important to obtain updated information on antibiotic resistance by dynamic monitoring and serial detection, which is critical to the selection of the most optimal therapeutic regimens for eradication of *H. pylori* infection.

### Innovations and breakthroughs

This study provided us the comprehensive and up-to-date data about antibiotic resistance of *H. pylori*. It was showed that *H. pylori* resistance rates to commonly used antibiotics in China are high with increased antibiotic multiple resistances.

### Applications

This comprehensive and up-to-date information on *H. pylori* resistance will be very helpful to select the most optimal eradication regimens in clinical settings.

### Terminology

Multiple antibiotic resistance is defined as *H. pylori* being resistant to two or more kinds of antibiotics simultaneously.

### Peer-review

Antibiotic resistance is a main factor with therapeutic effects on patients with *H. pylori* infection. In this manuscript, the authors reported the resistance pattern of *H. pylori* to six antibiotics in different periods. It is very helpful to select the most optimal eradication regimens.

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