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Retrospective Study

Ninety-four thousand-case retrospective study on antibacterial drug resistance of *Helicobacter pylori*

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Abstract

BACKGROUND

The resistance rate to antibacterial drugs is the key inhibitor of *Helicobacter pylori* (*H. pylori*) eradication treatment.

AIM

To evaluate the prevalence and drug resistance of *H. pylori* based on big data.

METHODS

Gastric mucosal specimens were collected from naive patients undergoing upper gastrointestinal endoscopy for *H. pylori* culture and antimicrobial susceptibility testing (AST), including clarithromycin, levofloxacin, metronidazole and amoxicillin. Every 10 years of age was grouped as an age group. The *H. pylori* infection and resistance were explored based on the age group and gender.

RESULTS

The number of *H. pylori*-positive specimen was 94509 in 283823 gastric mucosal specimens, with an infection rate of 33.30%. The infection rate increased with age, and males had a higher infection rate than females. The average resistance rate of *H. pylori* to amoxicillin and metronidazole was 0.21% and 93.72%, which remained stable. The average resistance rate to clarithromycin was 23.99% with an increasing trend from 14.43% to 38.24%. The average resistance rate to levofloxacin was 30.29%, which increased from 17.07% to 39.42% and mostly stabilized after 2017. The resistance rate of *H. pylori* increased with age, except amoxicillin. *H. pylori* in females are at higher risk of resistance to metronidazole,

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but not to amoxicillin, regardless of the age group. Meanwhile, *H. pylori* in females are at higher risk of resistance to levofloxacin and clarithromycin in the 21-50 age group. The single, dual, triple and quadruple-drug resistance rate was 54.59%, 29.03%, 11.71% and 0.11%, respectively.

CONCLUSION

The resistance of *H. pylori* in Taizhou city is serious. Guided by the consensus report, individualized treatment based on AST is recommended.

Key Words: *Helicobacter pylori*; Infection; Resistance; Age group; Gender

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Core Tip: We shared a 10-year data in prevalence and resistance of *Helicobacter pylori* (*H. pylori*) in Taizhou city, Zhejiang province, China. We found that the infection rate increased with age, and males had a higher infection rate than females. The resistance rate of *H. pylori* to metronidazole, clarithromycin and levofloxacin was increased with age. *H. pylori* in females are at higher risk of resistance to metronidazole, but not to amoxicillin, regardless of the age group. Meanwhile, *H. pylori* in females are at higher risk of resistance to levofloxacin and clarithromycin in the 21-50 age group.

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INTRODUCTION

According to the estimates by GLOBOCAN, 1033701 individuals developed gastric cancer, and an estimated 782685 related deaths occurred in 2018[1]. In China, gastric cancer is ranked second for incidence rate and third for mortality rates among all cancers, while in Western Europe, the incidence rate ranks 9th and the mortality rate ranks 6th. In North America, the incidence rate and mortality rates of gastric cancer rank 13th and 9th respectively[2]. *Helicobacter pylori* (*H. pylori*) is the most important pathogenic factor of gastric cancer which accounted for 44.2% of new gastric cancer cases globally[2]. *H. pylori* was estimated to be responsible for more than 78.00% of new gastric cancer cases in 2018, and the total number of *H. pylori*-related cases is not expected to decrease for decades due to global population growth and aging[3]. Moreover, *H. pylori* causes substantial morbidity from various peptic ulcer diseases, gastritis and even gastric lymphoma. *H. pylori* is classified as carcinogenic (Group 1) to humans by the Monographs program of the International Agency for Research on Cancer[4].

Several recent publications have demonstrated the global prevalence of *H. pylori* infection to be approximately 50%[5,6]. Large differences were observed between areas within large countries, such as China, which is one of the countries with the highest prevalence of *H. pylori* infection[7]. Wuwei city has a much higher *H. pylori* prevalence (72.28%) than all other areas in China, followed by Fengkai city (55.90%). Dali city has the lowest *H. pylori* prevalence of 11.36%[8]. Effective treatment for *H. pylori* infection with a combination of antibacterial drugs, proton pump inhibitors and bismuth all contribute to a decline in peptic ulcer disease incidence and the gastric cancer mortality rate. The resistance rate to antibacterial drugs is the key inhibitor of *H. pylori* eradication treatment. Some data that describe the resistance rates of *H. pylori* indicate a correlation with age[9]. Populations of different ages with various antibiotic usage habits may have different resistances to antibacterial drugs used for *H. pylori* treatment, and this result will be more apparent when examined by big data analysis.

Thus, big data-based *H. pylori* prevalence and drug resistance statistical programs are critical. In this study, we shared a 10-year data analysis on the prevalence and resistance of *H. pylori* in Taizhou city, Zhejiang Province, China.

MATERIALS AND METHODS

Research object

This multicenter retrospective study was conducted from January 2011 to December 2020 in Taizhou city, Zhejiang Province, China. Gastric mucosal specimens were collected from patients undergoing upper gastrointestinal endoscopy for *H. pylori* culture and *in vitro* antimicrobial susceptibility testing (AST). Patients in this study followed the enrollment criteria: (1) With gastrointestinal symptoms such as abdominal pain, bloating, acid reflux and nausea, *etc.*; (2) Gastroscopic diagnosed as gastric, duodenal peptic ulcer and chronic gastritis with erosion, *etc.*; (3) No severe damage to heart, liver, and kidney function, and no allergies to antibacterial drugs used in AST; (4) Non-pregnant or breastfeeding women, no gastrointestinal bleeding, perforation, pyloric obstruction, or cancer complications; (5) Have not taken any antibacterial drugs, bismuth, H₂ receptor antagonist or proton-pump inhibitors within half a month; and (6) Agree to conduct gastric mucosal tissue sampling, *H. pylori* culture and *in vitro* AST, and signed their informed consent. The study had been approved by the ethics committee of Taizhou Hospital of Zhejiang Province.

Sample collection

A gastric mucosal specimen was collected from lesser curvature of the gastric antrum, greater curvature of the gastric body, or the tissue adjacent to the lesion. After biopsy, the specimen was immersed in *H. pylori* preservation tube containing brain heart infusion. All specimens were transported on dry ice throughout the entire process to Zhiyuan Medical Inspection Institute Co., Ltd. for *H. pylori* culture, isolation, identification and AST.

H. pylori isolation, culture and identification

Thawed the gastric mucosal specimen at room temperature and fully ground it into homogenate with 600 μ L of brain heart infusion in a glass grinder. Spread the tissue homogenate on a Columbia blood plate (OXOID, England) containing 5% sheep blood by streaking. Cultivated the *H. pylori* in a 37 °C mixed gas incubator (5% O₂, 10% CO₂ and 85% N₂) for 2-3 d. Extended the culture time to 7 d if there was no growth. Picked out and subcultured the monoclonal colonies with typical colony morphology. Then smeared microscopy with the suspected *H. pylori* strain and carried out the biochemical experiments with urease (Haibo Biotechnology Co., Ltd., China), oxidase (Beijing Luqiao Technology Co., Ltd., China) and catalase (Haibo Biotechnology Co., Ltd., China). Suspected strains with biological morphology and biochemical reactions were identified as *H. pylori*, and the patient was diagnosed as positive for *H. pylori* infection. Extended the culture time to 7 d, and if there was still no *H. pylori* strain growth on the medium, the patient was diagnosed as negative for *H. pylori* infection.

AST

The plate incorporation assay was used to test the antimicrobial susceptibility of *H. pylori* strains[10]. The critical points of antibacterial resistance referred to the value of *H. pylori* clinical susceptibility test in China[11,12]: 1 μ g/mL for clarithromycin (National Institute for Food and Drug Control, China), 2 μ g/mL for levofloxacin (National Institute for Food and Drug Control, China), 8 μ g/mL for metronidazole (National Institute for Food and Drug Control, China), and 2 μ g/mL for amoxicillin (Dr. Ehrenstorfer GmbH, Germany).

We diluted and added these 4 kinds of antibacterial drugs to sterile Columbia culture medium containing 5% sheep blood respectively and ensured the concentration of antibacterial drugs to the critical point. After mixing well, poured into the plate to prepare 4 kinds of blood plates containing the antibacterial drugs.

Collected *H. pylori* strains with good growth status, and diluted the strains with 0.9% normal saline to a concentration of 0.5 McFarland, about 1.5×10^8 /mL[10]. Drew 2 μ L of the diluted bacterial solution and inoculated on the conventional Columbia blood plate and the Columbia blood plate containing antibacterial drug, respectively. Cultivated the *H. pylori* in a 37 °C mixed gas incubator (5% O₂, 10% CO₂ and 85% N₂) for 2 d.

Firstly, we observed the growth of *H. pylori* strains on the conventional blood plate. The *H. pylori* strains with good growth status proved that its antimicrobial susceptibility results are credible. The *H. pylori* strains with poor growth status or not growing needed to undergo a new AST. Secondly, we observed the growth of *H. pylori* strains on the blood plate containing antibacterial drug. An inhibited growth of the *H. pylori* strain on the blood plate containing antibacterial drug was judged to be sensitive to

the antibacterial drug, and the uninhibited growth of the *H. pylori* strain was judged to be resistant to the antibacterial drug. The NCTC11637 standard strain was selected as the quality control bacteria.

Statistical analysis

SPSS 19.0 software were used. Using chi-square test to perform statistical analysis on count data. Odds ratio (OR) was used to evaluate risk factors. The Mantel-Haenszel chi-square test was used to evaluate a linear relationship. Breslow-Day method was used for the test of Homogeneity of OR. $P < 0.05$ indicated that the difference was statistically significant.

RESULTS

H. pylori infection

Basic information: From 2011 to 2020, a total of 283823 gastric mucosal specimens were cultured from patients with peptic ulcer disease. The ratio of males to females was 1.01:1.00. The ages of the participants ranged from 3 to 97, and the average age was 48.52 ± 14.04 . The number of *H. pylori*-positive specimens was 94509; thus, the overall positive rate of *H. pylori* infection reached 33.30%. The ratio of male to female patients who were positive for *H. pylori* was 1.08:1.00. The ages of these patients ranged from 4 to 96, and the average age was 50.79 ± 12.76 . Every 10 years of age was grouped as an age group, resulting in division into 8 age groups: ≤ 20 years, 21-30, 31-40, 41-50, 51-60, 61-70, 71-80 and ≥ 81 years; this division was close to a normal distribution ($P = 0.383$) (Table 1).

Gender and risk of *H. pylori* infection: A total of 142851 males and 140972 females were tested for *H. pylori* infection; of these, 49139 males and 45370 females tested positive for *H. pylori* infection. Compared with females, males had a higher rate of *H. pylori* infection (OR = 1.105, 95% confidence interval (CI): 1.088-1.122).

Relationship between age and *H. pylori* infection: The results of the Mantel-Haenszel chi-square test showed that there was a linear relationship between age and the rate of *H. pylori* infection ($\chi^2 = 2577.812$, $P < 0.001$). The Pearson-related results showed that $r = 0.095$, $P < 0.001$, indicating that the *H. pylori* infection rate increased with age.

Multivariable analysis of *H. pylori* infection: The homogeneity of OR test showed $P = 0.003$, suggesting that the OR values between age groups were heterogeneous, and it was not appropriate to combine the OR values. Therefore, after stratifying according to age group, male gender was determined to be a risk factor for *H. pylori* infection, except for the population aged ≥ 81 -years-old (OR = 1.044, 95%CI: 0.844-1.292, $P = 0.690$). For the ≤ 20 -years-old age group, the risk of *H. pylori* infection was 1.240 times higher in males than in females (OR = 1.240, 95%CI: 1.082-1.421, $P = 0.002$). For different age groups between 21-years-old and 80-years-old, the risk of *H. pylori* infection was 1.073, 1.103, 1.117, 1.165, 1.050, and 1.123 times higher in males than in females, respectively (Table 1).

Antibacterial resistance of *H. pylori*

The overall resistance rate of *H. pylori*: The average resistance rate of *H. pylori* to amoxicillin was 0.21% and slightly increased in 2017 and 2018 to 1.15% and 0.87%, respectively. The average resistance rate of *H. pylori* to metronidazole was 93.72%, remained at a high level and fluctuated in the range of 92.71% to 96.92%, except for when the rate fell to 86.64% in 2016. Different from the trends of these two antibacterial drugs, the average resistance rate of *H. pylori* to clarithromycin was 23.99% and had an increasing trend (from 14.43% in 2013 to 38.24% in 2020) (Figure 1). The average resistance rate of *H. pylori* to levofloxacin was 30.29%, which increased over time (from 17.07% in 2013 to 39.42% in 2017) and mostly stabilized after 2017. The results of the Mantel-Haenszel chi-square test and Pearson-related results showed a linear increase for resistance to clarithromycin ($\chi^2 = 2389.117$, $r = 0.159$, $P < 0.001$) and for resistance to levofloxacin ($\chi^2 = 1901.809$, $r = 0.142$, $P < 0.001$).

Gender and risk of *H. pylori* resistance rates: The number of males infected with *H. pylori* who were resistant to levofloxacin was 14051, and the resistance rate was 28.59%, while the number of females infected with *H. pylori* who were resistant was 14578, with a resistance rate of 32.13%. Compared with that of males, the *H. pylori* resistance rate was higher in females (OR = 1.182, 95%CI: 1.159-1.216). The resistance

Table 1 Basic information of specimen tested for *H. pylori* infection (n)

Age group	Infection rate (%)	Tested specimen			<i>H. pylori</i> -positive specimen			Multivariable analysis		
		Total	Male	Female	Total	Male	Female	OR	95%CI ^a	P value
Total	33.30	283823	142851	140972	94509	49139	45370	-	-	-
≤ 20	22.49	4825	2576	2249	1085	624	461	1.240	1.082-1.421	0.002
21-30	26.78	21681	11655	10026	5807	3196	2611	1.073	1.010-1.140	0.022
31-40	27.24	46803	23720	23083	12750	6688	6062	1.103	1.059-1.148	0.000
41-50	29.76	80907	39271	41636	24078	12156	11922	1.117	1.084-1.152	0.000
51-60	38.86	72229	35077	37152	28066	14284	13782	1.165	1.131-1.200	0.000
61-70	43.33	40951	21065	19886	17744	9250	8494	1.050	1.010-1.092	0.014
71-80	32.39	13939	7866	6073	4515	2635	1880	1.123	1.046-1.207	0.001
≥ 81	18.65	2488	1621	867	464	306	158	1.044	0.844-1.292	0.690

^a95%confidence interval (lower bound, upper bound).
 CI: Confidence interval; *H. pylori*: *Helicobacter pylori*.

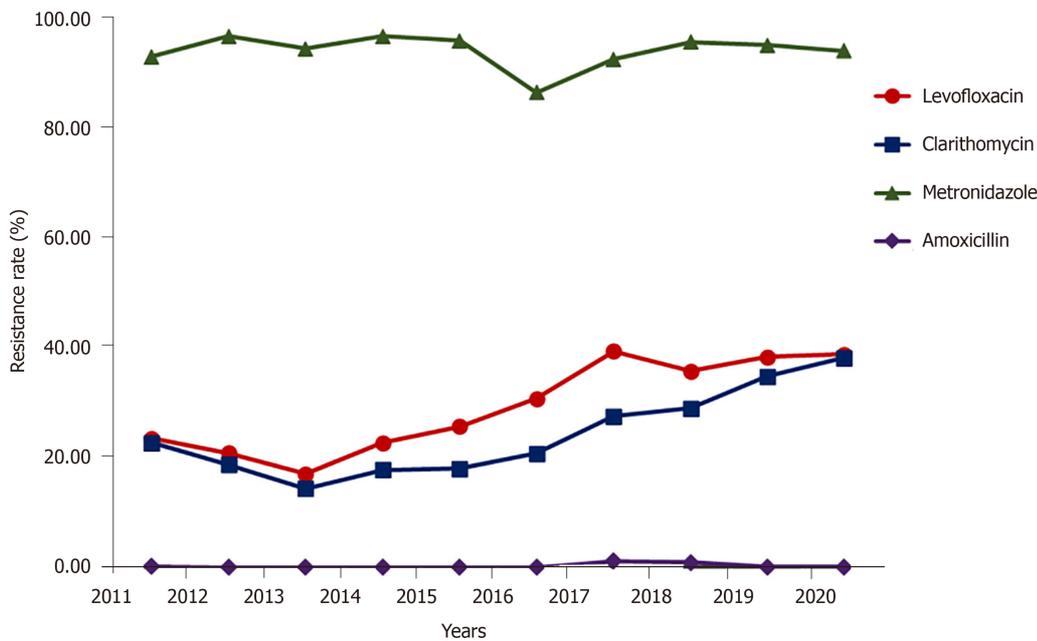


Figure 1 Trends of *Helicobacter pylori* resistance to four antibacterial drugs with years.

rates to clarithromycin in males and females were 22.93% and 25.14%, respectively, and the *H. pylori* resistance rate to clarithromycin in females was higher than that in males (OR = 1.129, 95% CI: 1.095-1.163). Similarly, the *H. pylori* resistance rate to metronidazole in females (94.44%) was higher than that in males (93.05%) (OR = 1.267, 95% CI: 1.202-1.337). There was no significant difference in the resistance rate of *H. pylori* to amoxicillin between different genders (OR = 0.880, 95% CI: 0.663-1.169).

Relationship between age and *H. pylori* resistance rates: Overall, the resistance rate to amoxicillin was low (< 0.35%). The resistance rate to metronidazole mostly stabilized after increasing from 75.39% to 96.49% in the population < 60-years-old, and the resistance rate of the population ≥ 61-years-old remained at approximately 98%. The resistance rate to clarithromycin increased rapidly in the population ≥ 61 years of age, changing from 21.02% to 39.01%. The resistance rate to levofloxacin continuously increased from 10.32% to 48.71% with increasing age. The results from the Mantel-Haenszel chi-square test and the Pearson relationship showed that there was a linear and positive relationship between age and resistance rate of *H. pylori* to the three kinds

of antibacterial drugs, except for a negative relationship to amoxicillin resistance ($\chi^2 = 1356.563$, $r = 0.120$, $P < 0.001$ for levofloxacin; $\chi^2 = 153.312$, $r = 0.040$, $P < 0.001$ for clarithromycin; $\chi^2 = 3685.476$, $r = 0.197$, $P < 0.001$ for metronidazole; and $\chi^2 = 24.710$, $r = -0.016$, $P < 0.001$ for amoxicillin) (Figure 2).

Multivariable analysis of resistance rates: Furthermore, we conducted an analysis on the correlation of age and gender with the *H. pylori* resistance rates to levofloxacin, clarithromycin and metronidazole (Figure 3).

Resistance rate to levofloxacin: The homogeneity of OR test showed $P < 0.001$, suggesting that the OR values between age groups are heterogeneous, and it is not appropriate to combine OR values. Therefore, after stratifying according to age group, there was no significant difference in the resistance rate of *H. pylori* to levofloxacin between female and male, aged ≤ 20 -years-old and aged ≥ 51 -years-old ($P > 0.05$). However, for the 21-50 age group, *H. pylori* in female was at a higher risk of resistance to levofloxacin than in male. For the 21-30 age group, the risk of *H. pylori* developing resistance to levofloxacin was 1.525 times higher in females than in males (OR = 1.525, 95%CI: 1.330-1.748, $P < 0.001$). For the 31-40 age group, the risk of *H. pylori* developing resistance to levofloxacin was 1.604 times higher in females than in males (OR = 1.604, 95%CI: 1.483-1.735, $P < 0.001$), and for the 41-50 age group, the risk was 1.325 times higher in females than in males (OR = 1.325, 95%CI: 1.253-1.400, $P < 0.001$).

Resistance rate to clarithromycin: The homogeneity of OR test showed $P < 0.001$. After stratifying according to age group, there was no significant difference in the resistance rate of *H. pylori* to clarithromycin between females and males, aged ≤ 20 -years-old and aged ≥ 51 -years-old ($P > 0.05$). For the 21-50 age groups, *H. pylori* in females was at a higher risk of resistance to clarithromycin than in males. For the 21-30 age group, the risk of *H. pylori* developing resistance to clarithromycin was 1.356 times higher in females than in males (OR = 1.356, 95%CI: 1.192-1.544, $P < 0.001$). For the 31-40 age group, the risk of *H. pylori* developing resistance to clarithromycin 1.495 times higher in females than in males (OR = 1.495, 95%CI: 1.379-1.622, $P < 0.001$). For the 41-50 age group, the risk of *H. pylori* developing resistance to clarithromycin was 1.175 times higher in females than in males (OR = 1.175, 95%CI: 1.107-1.246, $P < 0.001$).

Resistance rate to metronidazole: The homogeneity of OR test showed $P = 0.056$, suggesting that the OR values between the age groups are homogeneous. Therefore, after controlling the age groups, *H. pylori* in females was at a higher risk of the resistance to metronidazole (OR = 1.257, 95%CI: 0.190-1.327, $P < 0.001$). Thus, regardless of the age group, the *H. pylori* resistance rate to metronidazole was approximately 1.257 times in females than that in males.

Multidrug resistance of *H. pylori*

Multidrug resistance of *H. pylori* to the four antibacterial drugs is shown in Table 2. Among the 94509 positive specimens, the overall resistance rate to the four antibacterial drugs reached 95.44%, of which the single-drug resistance rate was 54.59%, the dual-drug resistance rate was 29.03%, the triple-drug resistance rate was 11.71%, and the quadruple-drug resistance rate was 0.11%. According to the comparison of gender, the single-drug resistance rate in males was significantly higher than that of females ($\chi^2 = 44.337$, $P < 0.001$), while the multidrug resistance rate in females was higher than that in males, especially the triple-drug resistance rate ($\chi^2 = 188.305$, $P < 0.001$).

DISCUSSION

The infection rate of *H. pylori* in China is approximately 55% [13], while the detection rate of *H. pylori* culture is only approximately 30%. A variety of reasons may affect the positivity rate of *H. pylori* culture, including the colonization of *H. pylori* at the biopsy site [14], the influence of PPIs and antibacterial drugs on microbial cultures [15], and even contamination in the process of microbial culture. However, the drug susceptibility test based on *H. pylori* culture can provide doctors with guidance for prescribing clinical medication and is the key to individualized treatment. With an annually increasing rate of antibacterial resistance, individualized treatment based on drug susceptibility results is recommended in China. Therefore, the cultivation of *H. pylori* is still important and is the gold standard for detecting *H. pylori* infection.

In this study, we shared a 10-year data analysis on the infection and resistance of *H. pylori* in Taizhou city, Zhejiang Province, China. A total of 283823 gastric mucosal specimens were examined, and the *H. pylori* infection rate was 33.30%. Age was determined to be related with the *H. pylori* infection. The population aged ≤ 20 -years-

Table 2 The multiple-drug resistance of *H. pylori* to the four antibacterial drugs, *n*

Antibacterial drugs	Total	Male	Female
Sensitive ^a	4314	2485	1829
LEV	626	362	264
CLA	557	332	225
MTR	50413	26642	23771
AMX	0	0	0
LEV + CLA	444	234	210
LEV + MTR	16419	8343	8076
LEV + AMX	1	1	0
CLA + MTR	10551	5599	4952
CLA + AMX	0	0	0
MTR + AMX	17	14	3
LEV + CLA + MTR	10990	5035	5955
LEV + CLA + AMX	0	0	0
LEV + MTR + AMX	48	25	23
CLA + MTR + AMX	28	16	12
LEV + CLA + MTR + AMX	101	51	50

^aSensitive to all four antibacterial drugs.

CLA: Clarithromycin; LEV: Levofloxacin; MTR: Metronidazole; AMX: Amoxicillin.

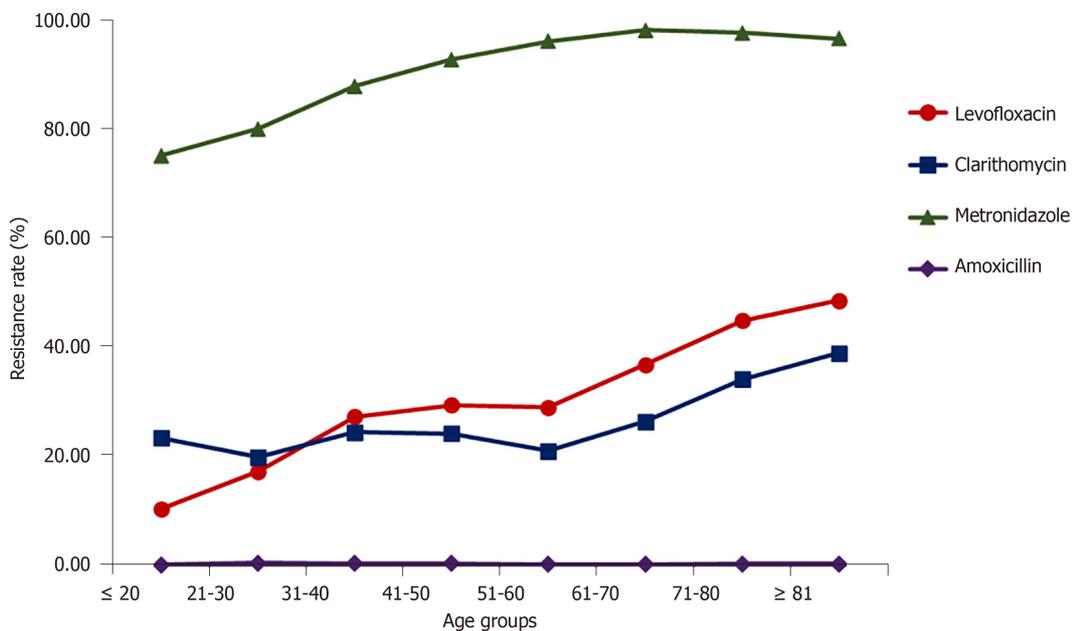


Figure 2 Trends of *Helicobacter pylori* resistance to four antibacterial drugs with age groups.

old had the lowest infection rate of 22.49%, and the population aged 61-70 years had the highest infection rate of 43.33%. The infection rate increased with age; however, the prevalence of *H. pylori* infection in children and adolescents is worthy of attention. The reported rates of *H. pylori* infection among children and adolescents in different areas of China range from 18.62% to 72.28% [16,17]. The "Kyoto global consensus report on *H. pylori* gastritis" proposes that *H. pylori* infection is an infectious disease [18], and it can be transmitted through mouth-to-mouth, stomach-to-mouth, feces-to-mouth and other routes. Thus, in addition to the limited awareness of hygiene and health, the

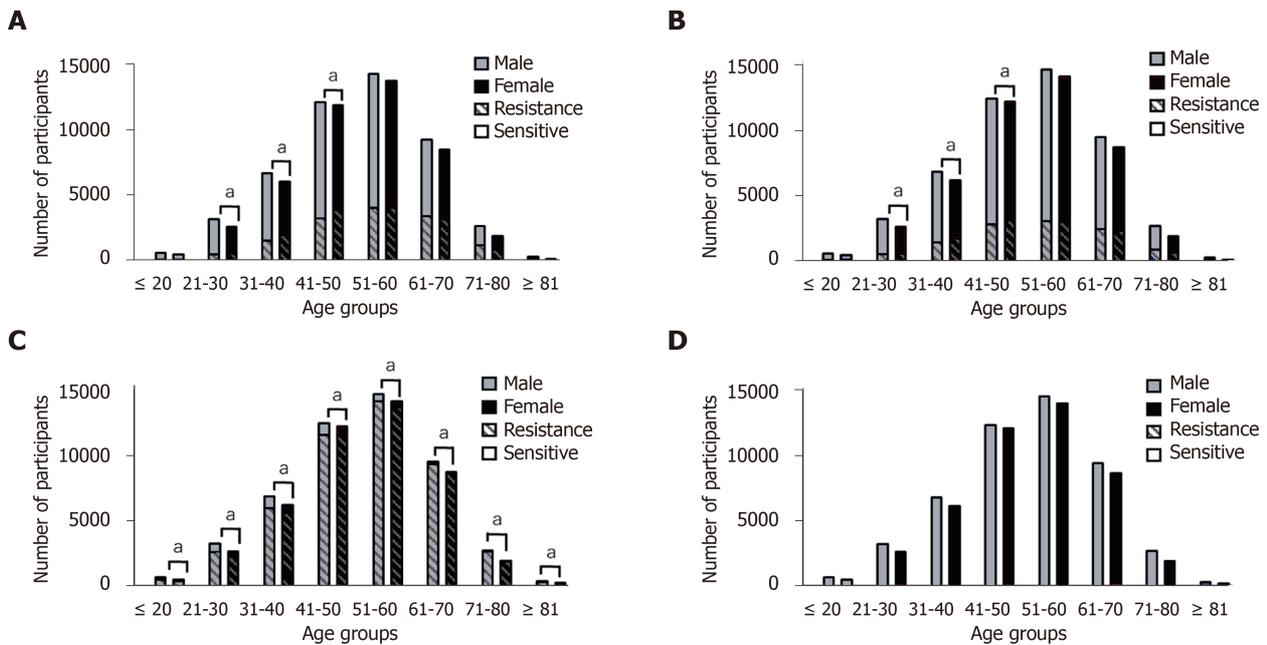


Figure 3 *Helicobacter pylori* resistance rate to four antibacterial drugs. A: The resistance to levofloxacin; B: The resistance to clarithromycin; C: The resistance to metronidazole; D: The resistance to amoxicillin. ^a $P < 0.05$. There were significant differences of the resistance between males and females.

traditional eating style (sharing food from the same plates) observed in China may play a role in the transmission of *H. pylori*. The diagnosis and treatment of *H. pylori* infection in children and adolescents requires special attention. In the absence of effective treatment, an *H. pylori* infection may be lifelong.

On the other hand, males were found to have a higher risk of *H. pylori* infection than that for females, and Dutta *et al*[19] reported the same results. Some habits, such as smoking, may be indirectly related to this result[20]. In Taizhou city, 48.00% of males smoke, while only 1.19% of females smoke[21]. The habit of smoking may lead to an increase in the secretion of gastric acid and pepsin, thereby destroying the health of the gastric mucosa and promoting the colonization of *H. pylori*.

H. pylori has high resistance rates to antibacterial drugs in Taizhou city, and these rates have gradually increased over time. The resistance of *H. pylori* to amoxicillin remains low (0.21%), while that to metronidazole is high (93.72%) throughout China [22,23]. In the 10 years examined in this study, the resistance rates to clarithromycin and levofloxacin significantly increased by 23.81% and 22.35%, respectively. The resistance rate of *H. pylori* increases with age[9]. In this study, the resistance rate to clarithromycin and metronidazole for the population aged ≥ 81 -years-old was 15.60% and 21.59% higher, respectively, than those for the population aged ≤ 20 -years-old, and the difference in levofloxacin resistance reached 38.38%. The application of antibacterial drugs in the population is one of the external factors contributing to the development of *H. pylori* resistance, and the resistance of *H. pylori* detected for the population aged ≤ 20 -years-old, who seldom use antibacterial drugs, may be related to the resistance of the *H. pylori* itself.

After controlling for age group, females showed a higher incidence of *H. pylori* resistance to metronidazole[24], which was approximately 1.257 times higher than that of males. This result is in agreement with data presented by Mirzaei *et al*[25]. Metronidazole is used in a wide variety of applications and is typically used in the treatment of anaerobic infections in the female reproductive system or for treating *Trichomonas vaginalis* infections[26]. In this study, *H. pylori* in females was at a higher risk of resistance to clarithromycin and levofloxacin for the population aged 21-50 years; this finding is different from the data presented by Shu *et al*[27]. A study by Shao *et al*[24] reported results in agreement with ours. In addition, the incidence of multidrug resistance in females was higher than that in males. These phenomena may be related to hormones, genetic differences, and the frequency of antibiotic use. For levofloxacin and clarithromycin, the younger population, aged ≤ 20 -years-old, had a similar medication background. For the population aged ≥ 51 -years-old, the physical fitness and immunity of individuals decreases with age, and medications increase and vary. Due to the accumulation of medication over the years, the difference between female and male decreases, while the difference between age group increases. For the

population in the middle-aged 21-50 group, their physical fitness is relatively healthy, and their immunity is strong. Therefore, the use of antibacterial agents will affect the resistance rates in *H. pylori*. Some research indicates that for some less serious infections, such as colds, females are relatively more willing to receive antibiotic treatment, while males are often accustomed to relying on their own immunity. Therefore, female medication habits may be one of the reasons why the resistance rate in females is higher than that in males[28].

Resistance to antibacterial drugs poses a huge challenge to *H. pylori* eradication therapy. Experts from all over the world have jointly issued some consensus reports, and a number of consensus reports have been published based on the resistance rates of *H. pylori* in China. The "Fifth Chinese National Consensus Report on the management of *H. pylori* infection" ("Fifth Chinese National Consensus Report") indicated that quadruple therapy containing clarithromycin and metronidazole was not recommended in empirical therapy when the dual-drug resistance rate is over 15.00% [29]. In Taizhou city, the dual-drug resistance rate to clarithromycin and metronidazole is 11.16%, although resistance rates to each drug individually are high. Furthermore, the "Fifth Chinese National Consensus Report", published in December 2016, proposed that treatment therapy containing levofloxacin was not recommended for initial *H. pylori* eradication because of its high resistance rate[28]. Following the consensus recommendations, the resistance rate to levofloxacin decreased slightly and remained stable after 2017 in Taizhou, which was an obvious result.

Limits of study

The purpose of this study is to study the prevalence and drug resistance of *H. pylori*. The detection methods for *H. pylori* infection include microbial culture, pathological testing, ¹³C urease breath test, nucleic acid testing, *etc.*, and the combined detection of multiple methods can improve the detection rate of *H. pylori*. However, some of these methods were not widely and continuously used in the early stages of this study. In this paper, we mainly analyzed the data obtained through microbial culture, which can reflect the changes of *H. pylori* prevalence to a certain extent.

CONCLUSION

The prevalence and resistance of *H. pylori* in Taizhou city are serious. The prevalence of *H. pylori* increased with age, and the male was at a higher risk of *H. pylori* prevalence. The resistance rate increased with age, and *H. pylori* in females, age 21-years-old to 50-years-old, was at a higher risk of resistance to levofloxacin and clarithromycin. Guided by the consensus report, individualized treatment based on an AST is recommended.

ARTICLE HIGHLIGHTS

Research background

The trend of *Helicobacter pylori* (*H. pylori*) prevalence and antibacterial drug resistance is getting more serious.

Research motivation

To provide guidance on the use of antimicrobial drugs for *H. pylori* eradication treatment based on the trend of antimicrobial resistance.

Research objectives

Big data-based research of *H. pylori* prevalence and antimicrobial resistance trends in Taizhou, Zhejiang Province were performed.

Research methods

Carried out the statistical analysis of the results of gastric mucosal tissue sample culture and drug susceptibility tests in Taizhou in the past 10 years, and explored the differences between different age groups and gender of the *H. pylori* prevalence and antibacterial drug resistance rates.

Research results

The prevalence of *H. pylori* increased with age, and males were at a higher risk of *H. pylori* prevalence. The resistance rate increased with age, and *H. pylori* in females, age 21-years-old to 50-years-old, were at a higher risk of resistance to levofloxacin and clarithromycin.

Research conclusions

The prevalence and resistance of *H. pylori* in Taizhou city are serious.

Research perspectives

Guided by the consensus report, individualized treatment based on an AST is recommended.

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