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Antibiotic Resistance of *Helicobacter pylori* Among Male United States Veterans

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Abstract

BACKGROUND & AIMS: The most recent information published on resistance of *Helicobacter pylori* to antibiotics in a large population in the United States is more than 10 years old. We assessed the susceptibility of *H pylori* to antibiotics among patients in a large metropolitan hospital, as well as demographic, clinical, and lifestyle factors associated with antimicrobial resistance.

METHODS: We performed a cross-sectional study of a random sample of 656 patients (90.2% men) from a cohort of 1559 undergoing esophagogastroduodenoscopy with collection of gastric biopsies from 2009 through 2013 at the Houston Veterans Affairs Medical Center. We performed culture analyses of gastric tissues to detect *H pylori*. The minimum inhibitory concentrations of amoxicillin, clarithromycin, metronidazole, levofloxacin, and tetracycline were determined by the Epsilometer test. Logistic regression analysis was performed to estimate the association between risk factors and antimicrobial resistance.

RESULTS: Biopsies from 135 subjects (20.6%) tested positive for *H pylori*; 128 of these were from men (94.8%). Only 65 strains were susceptible to all 5 antibiotics. The prevalence of resistance to levofloxacin was 31.3% (95% confidence interval [CI], 23.1%–39.4%), to metronidazole it was 20.3% (95% CI, 13.2%–27.4%), to clarithromycin it was 16.4% (95% CI, 9.9%–22.9%), and to tetracycline it was 0.8% (95% CI, 0.0%–2.3%). No isolate was resistant to amoxicillin. Clarithromycin resistance increased from 9.1% in 2009–2010 to 24.2% in 2011–2013. In multivariate analysis, prior treatment of *H pylori* infection and use of fluoroquinolones were significantly associated with clarithromycin and levofloxacin resistance, respectively.

CONCLUSIONS: *H pylori* resistance to clarithromycin increased between 2009 and 2013; resistance to metronidazole remains high in infected men in the United States. The high frequency of resistance to levofloxacin is a new and concerning finding.

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Conflicts of interest

The authors disclose no conflicts.

Keywords

Gastritis; Bacterial Resistance; Drug; Eradication Therapy

Eradication of *Helicobacter pylori* infection results in healing of gastritis, improved healing of peptic ulcers, and prevention of ulcer recurrence and reduces the risk of developing gastric cancer.[1–4] Until recently, the most widely recommended anti-*H pylori* antimicrobial regimens worldwide have been 3 drug regimens that use a proton pump inhibitor (PPI) and 2 antimicrobial agents, such as amoxicillin, clarithromycin, or metronidazole,[4–6] or a 4-drug combination of a PPI, a bismuth compound, tetracycline, and metronidazole, known as bismuth quadruple therapy.[7] As with other infectious diseases, treatment success is primarily predicated on the presence of susceptible organisms and patient adherence (ie, taking the medications as prescribed). The widespread use of clarithromycin and other macrolides worldwide for upper respiratory infections has resulted in widespread development of clarithromycin resistance in *H pylori* as a bystander effect, such that by 2000 the success rate with clarithromycin-containing triple therapy had generally fallen to 80% or less.[4,8,9]

The Surveillance of *H pylori* Antimicrobial Resistance Partnership study compiled data that included 3624 strains from the clinical studies done in the United States during 1993 to 1999.[10–12] It reported that resistance to clarithromycin was 10.1% (95% confidence interval [CI], 9.1%–11.1%) and 36.9% (95% CI, 35.1%–38.7%) to metronidazole. The subsequent *H pylori* Antimicrobial Resistance Monitoring Project (HARP) study included 347 strains isolated from 11 hospitals in 4 regions during 1998 to 2002[13] and reported resistance rates for clarithromycin and metronidazole of 13% and 25%, respectively. The last multicenter study was from a clinical trial in the United States reported in 2003,[14] showing resistance rates of 10.2% to clarithromycin and 29.1% to metronidazole in 796 strains. Unfortunately, information as to antibiotic resistance of *H pylori* in the United States has been lacking since 2003.[15]

Obtaining contemporary data about *H pylori* antibiotic resistance is important, because the prevalence of *H pylori* infection continues to be high among the elderly, recent immigrants from endemic areas, and lower socioeconomic groups. Pretreatment antimicrobial susceptibility testing is generally unavailable; and *H pylori* eradication regimens are typically chosen empirically, thus foregoing the opportunity to maximize the likelihood of a successful result. The rate of successful *H pylori* eradication has declined in the United States. For example, the successful eradication rate with 10-day clarithromycin-containing triple therapy (clarithromycin, amoxicillin, and omeprazole) for patients with non-ulcer dyspepsia in 2004 was 72% in an intent-to-treat analysis[16] vs 90% success reported in 1996.[17]

Updated information regarding antimicrobial susceptibility patterns is important to determine the best primary treatment regimens. In general, the antibiotic resistance rate parallels the antibiotic consumption rate in the population.[18–20] This was recently confirmed by a recent European Helicobacter Study Group study showing a significant relationship between the use of long-acting macrolides and clarithromycin resistance.[21] In the United States the prescription rates of macrolides, especially azithromycin, have increased during

the 1990s and 2000s,[22,23] which implies increasing clarithromycin resistance of *H pylori* in the United States.

Here we determined antibiotic susceptibility to commonly used drugs for which resistance has been shown to affect outcome (ie, amoxicillin, clarithromycin, metronidazole, levofloxacin, and tetracycline) among *H pylori* strains isolated in a major hospital in the United States. We also examined the demographic, clinical, and lifestyle factors that were associated with antibiotic-resistant *H pylori* strains.

Methods

Study Population

Gastric *H pylori* strains were obtained from a cross-sectional study at the Michael E. DeBakey Veterans Affairs Medical Center in Houston, Texas from June 1, 2009 to August 31, 2013, as previously described.[24,25] This medical center serves as the primary healthcare provider for almost 130,000 veterans in southeast Texas. We invited all consecutive eligible patients who were scheduled for an elective esophagogastroduodenoscopy (EGD) to participate. We also invited a group of randomly selected eligible patients who were scheduled for a primary care clinic visit at the same hospital to undergo an EGD at the same time as their screening colonoscopy. Informed consent was obtained from all participants, and this study was approved by the Institutional Review Board at Baylor College of Medicine and by Research and Development at the Michael E. DeBakey Veterans Affairs Medical Center, both in Houston, Texas.

Inclusion and Exclusion Criteria

The electronic medical records of all veterans with a scheduled EGD were screened to determine study eligibility on the basis of the previously described criteria,[24] including age between 40 and 80 years and complete EGD examination with gastric mapping biopsies. Subjects were excluded if they had any of the following exclusion criteria: (1) previous surgical resection of the esophagus or stomach; (2) previous cancer of the esophagus, lung, liver, colon, breast, or stomach; (3) current use of anticoagulants; (4) significant liver disease, indicated by platelet count below 70,000, ascites, or known gastroesophageal varices; and (5) history of major stroke or mental condition that would limit ability to answer questions.

Endoscopy and Biopsy

Endoscopic findings including gastric or duodenal ulcers were systematically recorded. Gastric mapping was performed by taking 7 mucosal biopsy samples from the antrum (from the greater curvature and from the lesser curvature), the corpus (from the distal greater curvature, distal lesser curvature, proximal greater curvature, proximal lesser curvature), and the cardia, as previously described.[24,25] Features of gastritis, gastric atrophy, and intestinal metaplasia were identified and graded according to the standardized Updated Sydney System.[26] Chronic gastritis was defined by inflammation in which mononuclear leukocytes, including lymphocytes, plasma cells, and macrophages (monocytes), predominate. Chronic active gastritis was defined by the presence of neutrophil polymorphs in a background of

chronic inflammation.[26] In addition, 1 gastric biopsy was collected from the lesser curvature of the antrum from all study subjects and placed in sterile vials containing cysteine medium with 20% glycerol and stored at −80°C until cultured for *H pylori*.

Helicobacter pylori Culture

For *H pylori* culture, frozen specimens were thawed, and the tissues were homogenized and inoculated onto 2 types of selective media, brain-heart infusion and *H pylori* Special Peptone Agar plates with 7% horse blood. The plates were incubated for up to 14 days at 37°C under microaerophilic conditions (5% O_2, 10% CO_2, and 85% N_2) in an Anoxomat (Mart Microbiology B.V., JP Drachten, Netherlands) jar. Positive growth was transferred to a fresh, nonselective brain-heart infusion blood agar plate and incubated for 48–72 hours. *H pylori* was identified definitively when the oxidase, catalase, and urease reactions were positive with a compatible Gram stain. We selected and subcultured several small round colonies from each patient's plate 1 or 2 times to obtain a pure culture. The isolated strains were stored at −80°C in cysteine storage medium containing 20% glycerol.

Antibiotic Susceptibility Testing

We used the Epsilometer test (E-test) (AB Biodisk, Solna, Sweden) to determine the minimum inhibitory concentrations (MICs) of amoxicillin, clarithromycin, metronidazole, levofloxacin, and tetracycline. Mueller–Hinton II Agar medium (Becton Dickinson, Franklin Lakes, NJ) supplemented with 5% defibrinated sheep blood was used as culture medium. The culture suspension with turbidity adjusted to be equivalent to a McFarland opacity standard of 2.0 was used to inoculate onto the plates. The E-test strip of the corresponding antibiotic was placed on the plate and incubated for 72 hours at 37°C under microaerophilic conditions. MIC was defined as the point of intersection of the elliptical inhibition zone with the E-test strip. Strains were considered resistant when the MIC was >0.12 μg/mL for amoxicillin, >0.5 μg/mL for clarithromycin, >1 μg/mL for levofloxacin, >8 μg/mL for metronidazole, and >1 μg/mL for tetracycline, according to the EUCAST *H pylori* breakpoints.[21]

Survey Questionnaire

All study participants completed a computer-assisted survey before the EGD that included questions on demographic features (age, gender, race, birthplace, education, and household income); clinical features (heartburn, acid regurgitation, stomach pain), previous treatment for *H pylori*; and lifestyle factors, including tobacco-smoking status and alcohol drinking, as previously described.[24] Prior use of macrolides (azithromycin, clarithromycin, erythromycin, and telithromycin) and fluoroquinolones (ciprofloxacin, gatifloxacin, gemifloxacin, levofloxacin, moxifloxacin, norfloxacin, and ofloxacin) was also examined in the Veterans Affairs pharmacy electric medical record.

Statistical Analysis

Our hypothesis was that antimicrobial resistance to clarithromycin would have increased from 6% in our previous study[11] to approximately 20% in the present study. We estimated the prevalence of *H pylori* infection would be 20% in the present study on the basis of recent

studies of *H pylori* prevalence in the United States.[27,28] We estimated that 90 *H pylori*–positive subjects were required to have 80% power for a 2-sided test with a significance level of .05 to detect a difference between 2 groups. Therefore, a minimum of 450 samples needed to be cultured.

We calculated the proportions and accompanying 95% CIs of patients with antibiotic-resistant and antibiotic-sensitive *H pylori* strains; we performed these calculations for each of the tested 4 antibiotics. Under conditions with rare events, the 95% CI was calculated by using the Clopper–Pearson exact method. Potential predictors of resistance (demographic, clinical, and lifestyle factors, history of prior treatment of *H pylori* and use of antibiotics) were examined in univariate analyses by using the Fisher exact test and χ^2 test for categorical variables. We also conducted an adjusted analysis by using multivariable logistic regression to examine the possible predictors of antibiotic resistance. Two patients with race category “others” were excluded in the model because the number was too small to obtain a reliable estimate. Four important biological and social factors, age group, race, isolated year, and prior *H pylori* treatment, were included in the model, regardless of the statistical significance. For other variables, those who passed the univariate screening with *P* value <.25 were considered as candidates for selection. A backward variable selection procedure was used to identify the primary main-effect models. For each variable, the odds ratio (OR) and 95% CI were calculated. A 2-tailed *P* value <.05 was considered statistically significant. All statistical analyses were performed by using SPSS version 19 (SPSS Inc, Chicago, IL), STATA software version 13.1 (Stata Corp, College Station, TX), and SAS software version 9.3 (SAS Institute, Cary, NC).

Results

During the study period, 4996 patients were scheduled for EGD. Among them, 2478 fulfilled the study inclusion criteria, and 1595 agreed to participate in the study. A total of 1559 patients underwent study EGD with biopsy samples; 656 patients were selected by computer-based random code to have their gastric biopsies cultured, and 135 were *H pylori* positive (20.6%). The 135 *H pylori* strains were isolated from 135 patients (128 men and 7 women; age range, 40–79 years; mean age, 60.0 ± 8 years) and were examined for antibiotic resistance. One hundred seventeen strains (86.7%) were isolated from previously untreated patients; 7 strains were isolated from previously treated patients. In 11 subjects prior treatment status was unknown. The racial/ethnic distribution of patients was 39 white (28.9%), 70 black (51.9%), 24 white Hispanic (17.8%), and 2 (1.5%) of other ethnic backgrounds or unknown. A total of 31 strains were isolated in 2009, 37 strains were isolated in 2010, 25 strains were isolated in 2011, 24 strains were isolated in 2012, and 18 strains were isolated in 2013. The gastric diagnoses among the *H pylori*–positive subjects were chronic active gastritis in 124 (91.9%), chronic gastritis only in 5 (3.7%), and gastric ulcer in 4 (3.0%). In addition, 10 subjects also had erosive esophagitis; and 2 patients had esophageal adenocarcinoma. Information as to location of birth was obtained from 122 of the 135 subjects; 119 were born in North America, and 3 were born in Central/South America or in the Caribbean. Of the 1559 subjects, 26.7% (416) were *H pylori* positive by pathologic examination by using the hematoxylin-eosin stain.

Helicobacter pylori Resistance Patterns

Overall, antibiotic resistance was highest for levofloxacin (31.9%; 95% CI, 24.0%–39.7%), followed by metronidazole 21.5% (95% CI, 14.6%–28.4%) and clarithromycin 17.8% (95% CI, 11.3%–24.2%), and least for tetracycline (n = 1) 0.7% (95% CI, 0.0%–4.1%). No isolate was resistant to amoxicillin.

Among the 128 strains isolated from men, 65 (50.8%) were susceptible to all 5 antibiotics tested. The pattern of resistance was the same as for the entire group (ie, highest prevalence with levofloxacin (31.3%; 95% CI, 23.1%–39.4%), followed by metronidazole 20.3% (95% CI, 13.2%–27.4%), clarithromycin 16.4% (95% CI, 9.9%–22.9%), and finally, tetracycline (n = 1) 0.8% (95% CI, 0.0%–4.3%). Among the 110 previously untreated patients, 54.5% were susceptible to all tested antibiotics; 29.1% (95% CI, 20.5%–37.7%) were resistant to levofloxacin, 17.3% (95% CI, 10.1%–24.4%) were resistant to metronidazole, 14.5% (95% CI, 7.9%–21.2%) were resistant to clarithromycin, and 0.9% (95% CI, 0.0%–5.0%) were resistant to tetracycline. The 7 strains isolated from subjects with prior *H pylori* treatment were more likely to be resistant to clarithromycin and levofloxacin than strains from untreated patients (71.4% vs 14.5%, $P = .002$; and 71.4% vs 29.1%, $P = .03$, respectively). However, no strains isolated from previously treated patients were susceptible to all 5 antibiotics. Regarding the type of patient, there were no differences in antibiotic resistance rates between the 69 patients scheduled for an elective EGD compared with the 41 scheduled as a result of a primary care clinic visit for screening colonoscopy (15.9% vs 12.2% for clarithromycin, 17.4% vs 17.1% for metronidazole, and 27.5% vs 31.7% for levofloxacin, respectively; all $P > .05$).

The pattern of drug resistance in male patients is shown in Table 1. In the 110 patients previously untreated, 34 strains (30.9%) were resistant to only 1 antibiotic. Resistance to more than 2 antibiotics was present in 14.5% (16 of 110). Triple resistance to clarithromycin, metronidazole, and levofloxacin was observed in only 2 strains (1.8%).

Among 7 strains isolated from women, resistance rates to clarithromycin, metronidazole, and levofloxacin were 42.9%, 42.9%, and 42.9%, respectively. None was resistant to amoxicillin or tetracycline.

The distribution of MIC values for each antibiotic is shown in Figure 1. Most strains susceptible to clarithromycin had MIC <0.016. On the other hand, 16 of 24 resistant strains (66.7%) had high-level resistance (>256 μg/mL). The MIC values to metronidazole ranged widely. Among the 39 levofloxacin-resistant strains, 31 (72%) had high-level resistance (≥32 μg/mL). The single-strain resistance to tetracycline had MIC of 24 μg/mL.

Factors Associated With Antibiotic Resistance

Results of univariate analysis of factors associated with antibiotic resistance are summarized in Table 2. Strains isolated in 2011–2013 showed a significantly higher prevalence of clarithromycin resistance than those isolated in 2009–2010. Prior treatment of *H pylori* and prior use of macrolides were both significantly associated with clarithromycin resistance. Metronidazole resistance was significantly more common among patients who stated they never drank alcohol compared with former drinkers and current drinkers. Smoking was also

significantly associated with metronidazole resistance. Levofloxacin resistance rate was significantly higher in the strains isolated from the patients with higher household incomes. Prior treatment of *H pylori* and prior use of fluoroquinolones were significantly associated with levofloxacin resistance. Factors significantly associated with resistance to any antibiotic included prior treatment of *H pylori*, education (some-college), higher household income, nonsmoking, the presence of heartburn or acid regurgitation, and prior use of fluoroquinolones.

Multiple logistic analysis revealed that those with prior *H pylori* treatment had a significantly higher likelihood of clarithromycin resistance than previously untreated patients, and this persisted after adjustment by age, race, isolated year, education, smoking status, the presence of heartburn or acid regurgitation, prior use of macrolides, and prior use of fluoroquinolones (Table 3). With regard to metronidazole, former drinkers were significantly less likely to have resistance than never drinkers. For levofloxacin, higher household income was significantly associated with levofloxacin resistance in the multivariate analysis. Prior use of fluoroquinolones was also significantly associated with levofloxacin resistance. The year of *H pylori* isolation (2011–2013 vs 2009–2010), higher household income, and prior use of macrolides were significantly associated with resistance to any antibiotics; prior treatment of *H pylori* was not included in the model because all 7 patients with prior *H pylori* treatment showed resistance to any antibiotics.

Discussion

Successful *H pylori* eradication therapy depends in part on whether antimicrobial resistance is present to 1 or more of the drugs used.[29] *H pylori* strains isolated from veteran patients in Houston were often resistant to commonly prescribed antibiotics, including levofloxacin, clarithromycin, and metronidazole; 32.0% showed resistance to 1 antibiotic, but only 50.8% were susceptible to all 5 antibiotics tested.

Antibiotic resistance patterns differ geographically and can change dramatically in relation to an increase in use of an antibiotic. A systematic review of articles published during 2006 to 2009 worldwide reported antibiotic resistance rates of 17.2% to clarithromycin, 26.7% to metronidazole, 16.2% to levofloxacin, 5.9% to tetracycline, and 11.2% to amoxicillin.[30] A recent study from Europe showed overall resistance rates of 17.5% to clarithromycin, 34.9% to metronidazole, 14.1% to levofloxacin, 0.9% to tetracycline, and 0.7% to amoxicillin, but with marked regional differences.[21] We previously examined antibiotic resistance rates between 1988 and 1997 in the Veterans Affairs hospital in which the current study was conducted.[11] Among 179 strains examined, resistance to clarithromycin was present in 6.1% (95% CI, 2.6%–9.7%), and 37.4% (95% CI, 30.3%–44.6%) were resistant to metronidazole. Although a higher cutoff value MIC (>2 μg/mL) of clarithromycin was used in the previous study, when we used that cutoff for the current study, the clarithromycin resistance rate was 17% (95% CI, 10.6%–23.5%). Furthermore, clarithromycin resistance significantly increased between 2009 to 2010 and 2011 to 2013 in this study, likely related to increased use of macrolides for respiratory and otorhinolaryngology reasons.[31,32] Although the metronidazole resistance rate had not increased compared with the previous study, it remains high. Dual resistance to clarithromycin and metronidazole was present in 5% in the HARP

study and in 2.8% in our previous study in the Michael E. DeBakey Veteran Affairs Medical Center in Houston.[11,13] Importantly, in our current study dual resistance to clarithromycin and metronidazole was present in only 1.8%, which makes concomitant therapy (PPI, clarithromycin, metronidazole, and amoxicillin) an excellent choice as an empiric therapy.[29]

This study reports an *H pylori* resistance rate of levofloxacin in the United States outside Alaska.[33] Levofloxacin has been recommended as a rescue drug to eradicate *H pylori* in patients who fail first-line therapy.[4,34,35] Locally, it would seem to be a poor choice on the basis of the high resistance rate (31.9%), which is higher than the 10% limit suggested as a cutoff for use of fluoroquinolone-containing triple therapy for *H pylori*.[29] Tetracycline resistance was rare in our study, and no strain exhibited amoxicillin resistance, which is consistent with previous studies.[10,13]

MIC values for clarithromycin showed a bimodal pattern; 16 strains (66.7% of resistant strains) showed high MIC (>256 μg/mL), a finding suggesting the presence of limited target sites for antimicrobial activity such as the well-known point mutations in the 23S rRNA gene of *H pylori*.[36] On the other hand, MIC values to metronidazole were widely distributed, which suggests several resistance mechanisms such as modulation in the enzymatic reductive activities.[37] With regard to levofloxacin, 31 strains (72% of resistant strains) showed high MIC (≥32 μg/mL), consistent with other reports.[33]

It is clinically useful to be able to predict which populations are at risk for resistant strains. Prior treatment of *H pylori* was significantly associated with clarithromycin, consistent with the suggestion that clarithromycin-containing triple therapy should not be used for patients with a history of prior clarithromycin use. In the HARP study, black race was a risk factor significantly associated with infection with resistant *H pylori* strains[13]; however, this study did not confirm that observation. Although it did not reach statistical significance, we found that antibiotic resistances in 3 antibiotics tended to be higher in Hispanic patients. It was previously reported that inappropriate use of antibiotics, including inadequate knowledge about health, healthcare, and the role of antibiotics, can contribute to a higher antimicrobial resistance rate among Hispanic patients.[38] Multivariate analysis showed that less alcohol drinking was associated with metronidazole resistance. Antibiotic resistance of *H pylori* has also been reported to be higher in patients with lower alcohol use in Italy.[39] It is possible that physicians do not prescribe metronidazole to patients who drink alcohol because of a disulfiram-like reaction, which might contribute to a low metronidazole resistance rate among drinkers.[40] Levofloxacin resistance was significantly associated with prior use of fluoroquinolones. The increasing use of fluoroquinolones in the United States[22] is consistent with the increasing prevalence of levofloxacin resistance among those with *H pylori*. Last, high household income was previously associated with antibiotic resistance, especially to levofloxacin,[41] a finding that may relate to increased access to healthcare. The antibiotic resistance rate of *Streptococcus pneumoniae* was also shown to be higher among patients with high household income in the United States.[42] Further studies are necessary to elucidate these associations.

Our study has several limitations. First, our findings were based on veteran patients in 1 hospital. Most patients were men between 40 and 79 years of age. Therefore, this study

population may not be adequately reflective of the general population. In addition, we cannot exclude the possibility of selection bias, in that patients in whom *H pylori* was previously detected and successfully treated were more likely to be referred for endoscopy for persistent symptoms. Although our data were based on a sample of 135 cultured *H pylori* strains randomly selected from 656 gastric biopsies from among 1559 EGDs, the proportion of *H pylori* isolated was similar to the proportion with histologically documented *H pylori* in the entire population. Although prior antibiotic use was significantly associated with antimicrobial resistance, the VA electronic medical records cover only antibiotic use since 1997. Finally, we used the E-test to examine the antibiotic resistance, which may have exaggerated the rate of metronidazole resistance, because the E-test showed significantly higher MIC values than that of agar dilution.[12]

In conclusion, clarithromycin, metronidazole, and levofloxacin resistances were all high among untreated patients, suggesting that they all should be avoided as components of empiric triple therapy (eg, PPI, amoxicillin, plus a third antibiotic). The 4-drug concomitant therapy and bismuth quadruple therapy, or antibiotic susceptibility-guided therapy, are likely be the best strategies locally and are recommended for previously untreated patients with *H pylori* infection.

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Abbreviations used in this paper:

CI	confidence interval
EGD	esophagogastroduodenoscopy
E-test	Epsilometer test
HARP study	*H pylori* Antimicrobial Resistance Monitoring Project study
MIC	minimum inhibitory concentration
OR	odds ratio
PPI	proton pump inhibitor

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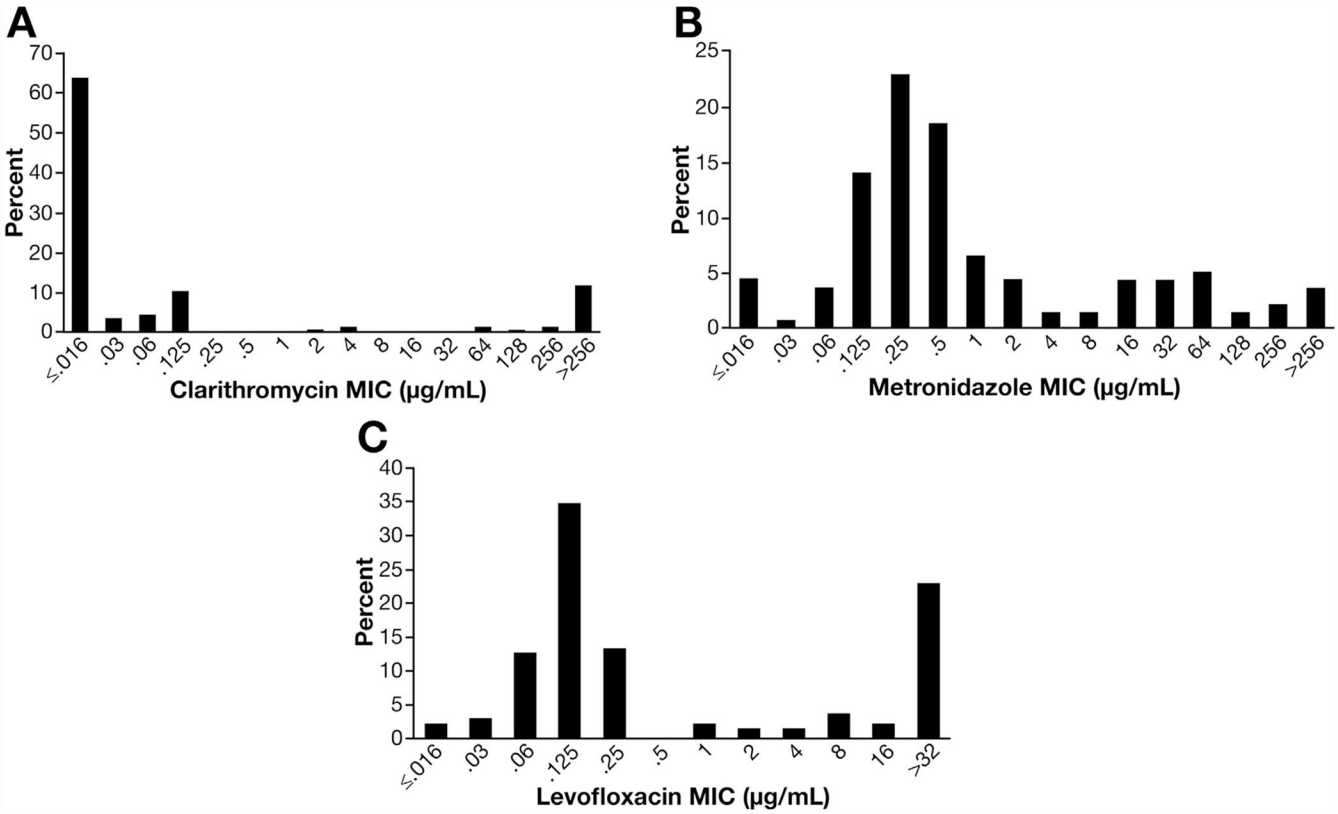

Figure 1.

Distribution of MIC for each antibiotic: (*A*) clarithromycin, (*B*) metronidazole, and (*C*) levofloxacin.

Table 1.

Resistance Pattern in *H pylori* Strains Isolated in Male Patients During 2009 to 2013

Total	All N = 128	Untreated patients N = 110
All susceptible	65 (50.8%)	60 (54.5%)
Mono resistance	41 (32.0%)	34 (30.9%)
Clarithromycin resistance only	6 (4.7%)	6 (5.5%)
Metronidazole resistance only	13 (10.2%)	9 (8.2%)
Levofloxacin resistance only	21 (16.4%)	18 (16.4%)
Tetracycline resistance only	1 (0.8%)	1 (0.9%)
Multiple resistance	22 (17.2%)	16 (14.5%)
Clarithromycin + metronidazole	3 (2.3%)	2 (1.8%)
Clarithromycin + levofloxacin	9 (7.0%)	6 (5.5%)
Metronidazole + levofloxacin	7 (5.5%)	6 (5.5%)
Clarithromycin + metronidazole + levofloxacin	3 (2.3%)	2 (1.8%)

Table 2.

Factors Associated With *H pylori* Resistance to Clarithromycin, Metronidazole, and Levofloxacin in Male Patients

	N	Clarithromycin resistance	*P* value	Metronidazole resistance	*P* value	Levofloxacin resistance	*P* value	Any resistance	*P* value
Age (*y*)									
<60	51	6 (11.8%)	.25	11 (21.6%)	.77	12 (23.5%)	.13	26 (51.0%)	.75
≥60	77	15 (19.5%)		15 (19.5%)		28 (36.4%)		37 (48.1%)	
Race/ethnic									
White	39	7 (17.9%)	.43	8 (20.5%)	1.00	11 (28.2%)	.49	18 (46.2%)	.65
Black	64	8 (12.5%)		13 (20.3%)		19 (29.7%)		33 (51.6%)	
Hispanic	23	6 (26.1%)		5 (21.7%)		10 (43.5%)		12 (52.2%)	
Other	2	0 (0.0%)		0 (0.0%)		0 (0.0%)		0 (0.0%)	
Isolated year									
2009–2010	66	6 (9.1%)	.02	14 (21.2%)	.79	17 (25.8%)	.17	27 (40.9%)	.05
2011–2013	62	15 (24.2%)		12 (19.4%)		23 (37.1%)		36 (58.1%)	
Prior treatment of *H pylori*									
Yes	7	5 (71.4%)	.002	3 (42.9%)	.12	5 (71.4%)	.03	7 (100.0%)	.01
No	110	16 (14.5%)		19 (17.3%)		32 (29.1%)		50 (45.5%)	
Missing	11	0 (0.0%)		4 (36.4%)		3 (27.3%)		6 (54.5%)	
Education									
No college	67	9 (13.4%)	.11	10 (14.9%)	.11	18 (26.9%)	.23	28 (41.8%)	.049
Some college	48	12 (25.0%)		13 (27.1%)		18 (37.5%)		29 (60.4%)	
Missing	13	0 (0.0%)		3 (23.1%)		4 (30.8%)		6 (46.2%)	
Household income ($)									
≤25,000	61	9 (14.8%)	.30	9 (14.8%)	.20	13 (21.3%)	.01	24 (39.3%)	.02
>25,000	54	12 (22.2%)		13 (24.1%)		24 (44.4%)		33 (61.1%)	
Missing	13	0 (0.0%)		4 (30.8%)		3 (23.1%)		6 (46.2%)	
Smoking status									
Nonsmoker	32	9 (28.1%)	.19	11 (34.4%)	.02	10 (31.3%)	.33	22 (68.8%)	.03
Former smoker	51	7 (13.7%)		5 (9.8%)		19 (37.3%)		20 (39.2%)	
Current smoker	36	5 (13.9%)		7 (19.4%)		8 (22.2%)		16 (44.4%)	
Missing	9	0 (0.0%)		3 (33.3%)		3 (33.3%)		5 (55.6%)	

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	N	Clarithromycin resistance	*P* value	Metronidazole resistance	*P* value	Levofloxacin resistance	*P* value	Any resistance	*P* value
Drinking status									
Never drank	11	2 (18.2%)	.81	6 (54.5%)	.01	1 (9.1%)	.24	8 (72.7%)	.24
Former drinker	47	7 (14.9%)		6 (12.8%)		15 (31.9%)		21 (44.7%)	
Current drinker	61	12 (19.7%)		11 (18.0%)		21 (34.4%)		29 (47.5%)	
Missing	9	0 (0.0%)		3 (33.3%)		3 (33.3%)		5 (55.6%)	
Heartburn or acid regurgitation									
Yes	73	16 (21.9%)	.12	16 (21.9%)	.37	26 (35.6%)	.18	41 (56.2%)	.04
No	46	5 (10.9%)		7 (15.2%)		11 (23.9%)		17 (37.0%)	
Missing	9	0 (0.0%)		3 (33.3%)		3 (33.3%)		5 (55.6%)	
Stomach pain									
Yes	37	6 (16.2%)	.78	10 (27.0%)	.15	11 (29.7%)	.83	20 (54.1%)	.44
No	82	15 (18.3%)		13 (15.9%)		26 (31.7%)		38 (46.3%)	
Missing	9	0 (0.0%)		3 (33.3%)		3 (33.3%)		5 (55.6%)	
Prior use of macrolides									
Yes	30	9 (30.0%)	.02	8 (26.7%)	.32	11 (36.7%)	.46	18 (60.0%)	.18
No	98	12 (12.2%)		18 (18.4%)		29 (29.6%)		45 (45.9%)	
Prior use of fluoroquinolones									
Yes	39	9 (23.1%)	.18	12 (30.8%)	.05	17 (43.6%)	.046	25 (64.1%)	.03
No	89	12 (13.5%)		14 (15.7%)		23 (25.8%)		38 (42.7%)	

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Table 3.

Factors Associated With *H pylori* Resistance to Clarithromycin, Metronidazole, and Levofloxacin in Male Patients in Multivariate Analysis

	Clarithromycin resistance	Metronidazole resistance	Levofloxacin resistance	Any resistance
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age (y)				
≥60 (vs <60)	2.16 (0.67–6.99)	0.74 (0.26–2.10)	2.34 (0.87–6.28)	1.04 (0.44–2.48)
Race/ethnic				
Black (vs white)	1.10 (0.32–3.83)	0.89 (0.27–2.95)	1.80 (0.62–5.27)	2.18 (0.81–5.83)
Hispanic (vs white)	1.47 (0.35–6.11)	1.87 (0.46–7.66)	2.48 (0.65–9.52)	1.78 (0.52–6.07)
Isolated year				
2011–2013 (vs 2009–2013)	2.57 (0.83–8.00)	0.69 (0.23–2.03)	1.89 (0.72–4.93)	2.52 (1.06–5.97)
Prior treatment of *H pylori*				
Yes (vs no)	11.37 (1.79–72.21)	4.64 (0.86–24.92)	3.83 (0.60–24.36)	—
Household income ($)				
>25,000 (vs ≤25,000)	—	—	3.15 (1.21–8.25)	2.61 (1.10–6.18)
Drinking status				
Former drinker (vs never drank)	—	0.12 (0.02–0.65)	—	—
Current drinker (vs never drank)	—	0.19 (0.04–0.94)	—	—
Prior use of macrolides				
Yes (vs no)	—	—	—	3.92 (1.39–11.07)
Prior use of fluoroquinolones				
Yes (vs no)	—	—	3.49 (1.30–9.36)	—