The prevalence of clarithromycin-resistant *Helicobacter pylori* isolates: a systematic review and meta-analysis

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Background: Knowledge of global clarithromycin (CLA)-resistant rates of *Helicobacter pylori* (*H. pylori*) is crucial for decision of the most appropriate eradication therapies with good clinical outcomes. Therefore, this review and meta-analysis aimed to evaluate the global prevalence of the CLA resistance in *H. pylori* to provide some guidance for selecting the first-line antibiotics. **Method**: A comprehensive search was performed for relevant literature until April 2021 in PubMed, Embase, and Web of Science databases. Freeman-Tukey double arcsine transformation was performed to estimate the weighted pooled prevalence of resistance. **Results**: The meta-analysis included 248 articles. The prevalence of CLA-resistant *H. pylori* was 27.53% (95% CI; 25.41, 29.69). The heterogeneity between reports was significant (I^2=97.80%, $P < 0.01$). The resistance rate increased from 24.28% in 2010-2017 to 32.14% in 2018-2021 ($P < 0.01$). Iran, with 38 articles, has the most report. Nevertheless, Switzerland, Portugal, and Israel had the highest resistance rates (67.16%, 48.11%, and 46.12%, respectively). The heterogeneity between the continents and the antimicrobial susceptibility methods also interpreted standard guidelines and breakpoints was insignificant ($P > 0.05$). **Conclusion**: Overall CLA resistance rate was 27.53%, worldwide. The difference in CLA resistance rate among the included studies can be due to several reasons such as differences in antibiotic prescription rates in various geographic areas, use of different breakpoints or inaccurate criteria in performed studies, and the emergence of multidrug-resistant (MDR) strains.

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Abstract

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Keywords: Antibiotic resistant; Clarithromycin; *Helicobacter pylori*; Meta analysis

Introduction

Helicobacter pylori is one of the most successful human pathogens that affects approximately 50% of the population worldwide. In developing countries 70% to 90% of the population are infected by this bacterium (1, 2). *H. pylori* infection is related to many gastric diseases, such as peptic ulcers, chronic gastritis, uninvestigated and functional dyspepsia and mucosa-associated lymphoid tissue lymphoma, and even increases the risk of gastric cancer (3). As for the high prevalence of the bacterium and its related diseases, proper treatment is very important. Today, standard treatment is a three-stage drug that consists of an acid neutralizer and two antibiotics, clarithromycin (CLA), and amoxicillin or metronidazole for 14 days (4).

However, treatment is difficult because the bacterium quickly develops resistance to the few antibiotics known to be effective (5). So that the World Health Organization (WHO) has classified it among the 12 most resistant bacteria in the world (6). The increasing failure rate of eradication treatment due to the appearance of resistant *H. pylori* strains contributes to the worldwide prevalence of this infection and subsequent inflammatory and neoplastic disorders. Unfortunately, nowadays, the success of this treatment is less than 80% worldwide (2, 7).

CLA has been emerged as the basis for *H. pylori* treatment in combined therapy because of small effect on gastric acidity, its low minimal inhibitory concentration, and relatively good mucosal diffusion (8, 9). Due to extensive usage of CLA in some geographical regions, global prevalence rate of CLA resistance is increasing. (10). In developing countries, CLA resistance and frequency of re-infection are factors that contribute to high worldwide prevalence of *H. pylori* infection and

subsequent inflammatory and neoplastic disorders (11). In most European countries, as well as the rest of the world, the prevalence of CLA resistance has reached 20%. With rare exceptions, it is no longer recommended to include CLA in empirical treatment in regions where primary resistance to this antibiotic is 20% (11, 12).

Knowledge of global CLA-resistant rates of *H. pylori* is crucial for decision of the most appropriate eradication therapies with good clinical outcomes. Therefore, the aim of current review and meta-analysis is to evaluation of the global prevalence of the CLA resistance in *H. pylori*.

Method

Search strategy

A comprehensive search was conducted by two researchers in the online databases PubMed, Embase, and Web of Science until April 2021, using relevant keywords such as clarithromycin, antibiotic resistance, and H. pylori, as well as related MeSH terms (see supplementary file 1 for the search syntax).

.The search syntax is available in Table 1.**Study selection**

All records obtained from online databases were imported into EndNote (Version 20), and duplicates were eliminated. M-H and S-K independently assessed the titles and abstracts; V-H-K resolved discrepancies. Studies were considered to be appropriate for the analysis if they presented data concerning the prevalence of H. pylori resistant to CLA. An English language restriction was imposed, while abstracts, conferences, case reports, case series, reviews, studies with unclear results, and duplicate articles were excluded from the analysis.CLA

Data Extraction

Our study included studies based on pre-defined criteria and evaluated as full-text articles. Two reviewers conducted the data extraction process independently (M-H, S-K). Any discrepancies were discussed and resolved by consensus of the two reviewers. The primary outcome of focus was the prevalence of clarithromycin-resistant Helicobacter pylori. Information extracted from each study included the first author's name, year of publication, geographical location, antimicrobial susceptibility testing method, breakpoints for interpretation of the test results, sample size, and the number of clarithromycin-resistant H. pylori. All extracted data are available in an accompanying supplementary file.CLACLA

Quality Assessment

Two reviewers (S-K and M-H) evaluated the quality of the studies using the Newcastle Ottawa Scale (NOS). In cases of disagreement, a third author (M-SH) was consulted to determine a consensus. The assessment of the studies was based on three criteria: selection, comparability, and exposure/outcome assessments.

Statistical analysis

For the present study, the sample size of isolates for antimicrobial susceptibility testing (AST) and the number of resistances to each antibiotic were used to calculate a weighted pooled resistance and their 95% confidence intervals. In order to prevent the exclusion of studies from the meta-analysis due to 0 or 100 resistance prevalence, the Inverse of Freeman-Tukey double arcsine transformation was conducted using Metaprop command in STATA software (version .17.1). A random-effects model was implemented to estimate pool proportions (13, 14). The I^2 with a $P \leq$ 05 was used to identify significant heterogeneity. The presence of a small-study effect or publication bias was assessed using Egger's linear regression test and Begg's test (15). Subgroup analyses were conducted to determine the impact of the country, continent, publication year (2010-

2017, 2018-2021), (AST) (Disc diffusion, Gradient methods), and breakpoints for interpretation of AST results on the variation.

Results

Descriptive statistics

In this research, 19169 records were acquired in EndNote version 20, a reference manager software. 8689 duplicated articles were then removed, leaving a total of 247 eligible studies that were included in the systematic review and meta-analysis. The screening and selection presage were summarized in the PRISMA flow chart (Figure 1). Overly 20936 *H. pylori* isolates have been investigated in included articles. More than half of the isolates were investigated in Asia (55.10% Isolated). Although most pieces were from Iran (38 articles), the highest number of isolates among the countries was that investigated from China (32,130 Isolates, 36.52% of total isolates). Description data are summarized in Table 2.

Publication bias

The publication bias was significant by the regression-based Egger test for small-study effects (P=0.04), but Begg's test for small-study effects was insignificant (P=0.09). The Nonparametric trim-and-fill analysis of publication bias also did not change the effect size. The funnel plot also did not have significant evidence of publication bias (Figure 2A). The sensitivity analysis or one leave-out method also had no significant bias.

Meta-analysis

In 248 included studies, 20936 isolates have been investigated, and 8736 isolates have been reported as resistant. The pooled prevalence of CLA-resistance H. pylori was 27.53 (95% CI,

25.41-29.6). Heterogeneity between reports was significant (I2 =97.80, p<0.01). The heterogeneity between countries was substantial (p<0.001). Switzerland, Portugal, and Israel had the highest resistance rates (67.16%, 48.11%, and 46.12%, respectively), and Senegal, Lithuania, and the Dominican Republic had the lowest resistance prevalence, 0.930.93%, 2.532.53%, and 3.13%, respectively) (Table 2). The heterogeneity between the continent subgroups was insignificant (P>0.05) (Figure 2B). The heterogeneity between the AST methods subgroup was insignificant (Figure 2C). The breakpoints for the interpretation AST subgroup were insignificant (*P*>0.05) (Figure 2D). The CLA-resistant *H. pylori* prevalence increased from 24.28% in 2010-2017 to 32.14% in the 2018-2021 years period (*P*<0.01) (Figure 2E). All statistics are summarized in Table 2. The regression meta-analysis for resistance rate over the publication year had a significant correlation of 0.013 (95% CI; 0.01, 0.02) (*P* < 0.001) (Figure 2F).

Discussion

Over the past years, the treatment of *H. pylori* infections has been performed using the standard triple therapy regimen, including CLA, a proton pump inhibitor, with either metronidazole or amoxicillin(16). However, in recent years, it is revealed that some *H. pylori* isolates have developed resistance to CLA(17). Therefore, the efficacy of the standard triple therapy regimen is in decline. In 2017, WHO listed the CLA-resistant *H. pylori* among antibiotic-resistant priority pathogens that need research and development of new antibiotics(18). Globally, surveillance and being aware of the frequency of resistance to antibiotics among pathogens is critical, and obtained results can be helpful in different sections such as the design of screening or follow-up programs, and the development of antimicrobial stewardship programs (19, 20).

In the present systematic review and meta-analysis study, we surveyed and analyzed the worldwide prevalence of CLA resistance among *H. pylori* isolates from 2010 to 2021. The

awareness of CLA resistance among different countries of the world and effective treatment of *H. pylori* infections are the main goal of the current study. The present systematic review and meta-analysis study included 247 eligible studies from 54 different countries. Our analyses revealed that the overall prevalence of clarithromycin-resistance *H. pylori* was 27.53%, worldwide.

Resistance to CLA among *H. pylori* is occur in two different levels including 1) a high level of resistance (MIC more than 64 mg l^{-1}) and 2) a low level of resistance ($0.5 \leq MIC \leq 1$ mg l^{-1}) (21). Point mutations, multidrug efflux pump systems, and synergistic effect of mutations in genes *rpl22 (*ribosomal protein L22) and *infB* (translation initiation factor IF-2) with 23S rRNA point mutations are the main CLA resistance mechanisms among *H. pylori* isolates (22, 23). Moreover, it is presumed that some outer-membrane proteins have a role in CLA resistance in *H. pylori* isolates (22). In the western world and among developed countries, more than 90% of CLA resistance is related to point mutations in the peptidyl transferase region of the V domain of 23S rRNA gene (24). The main point mutations related to CLA resistance are A2142G, A2143G (adenine-to-guanine transition at either position 2142 or 2143), A2142C (adenine-to-cytosine transversion at position 2142), A2115G, A2144T, G2141A, G2144T, T2289C, T2717C, and C2694A (16, 22, 23). Moreover, *hp1181* and *hp1184* mutations are associated with CLA resistance(23). Mutation in the 2142 and 2143 positions leads to restricted resistance and different levels of resistance, respectively (25).

In the present research, more than half of the included studies were performed in Asia. These results demonstrated that CLA resistance is a main public health issue in most Asian countries. Among studies surveyed CLA resistance rates in 54 different countries, Switzerland (67.16%) and Senegal (0.93%) had the highest and lowest resistance rates, respectively. The high level of CLA

resistance can be due to the following reasons: 1) inappropriate prescription and unregulated or widespread use of CLA, and 2) the use of CLA in other infections such as respiratory tract infections or intestinal parasites infections(26). Time trend analyses revealed that the CLA-resistant rates among *H. pylori* isolate increased from 24.28% in 2010-2017 to 32.14% in the 2018-2021 years' period. An increase in CLA resistance rates is an alarming finding. In areas where CLA-resistance is more than 15%, it is recommended to perform susceptibility testing before prescribing the standard triple therapy regimen (17, 27). Combination therapy with other drugs such as tinidazole can be helpful in the treatment of *H. pylori* infections. It is revealed that CLA combined with tinidazole can reduce the CLA resistance rate, decrease inflammatory reactions, and can effectively eliminate *H. pylori* infections (21). One of the limitations of this study was that we evaluated the CLA resistance rate only and the other antibiotics were not considered.

Conclusion

Our analysis revealed that CLA resistance rates varied among studies performed in different 54 countries. Altogether, results showed that the overall CLA resistance rate is 27.53%, worldwide. The difference in CLA resistance rate among the included studies can be due to several reasons such as differences in antibiotic prescription rates in various geographic areas, use of different MIC breakpoints or inaccurate criteria in performed studies, and the emergence of multidrug-resistant (MDR) strains. We performed a time trend analysis and the results revealed that the clarithromycin-resistance rates in increasing in recent years. Based on our findings, systematic surveillance, and proper monitoring of CLA resistance rates, as well as monitoring the use of CLA in patients, and performing the CLA susceptibility test before prescription may be critical actions for the inhibition and control of *H. pylori* infections.

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Reference

1. Arenas A, Serrano C, Quiñones L, Harris P, Sandoval M, Lavanderos M, Sepúlveda R, Maquilón S, Echeverría A, Ríos CJSR. High prevalence of clarithromycin resistance and effect on Helicobacter pylori eradication in a population from Santiago, Chile: cohort study and meta-analysis. 2019;9(1):1-9.
2. Kocsmár É, Buzás GM, Szirtes I, Kocsmár I, Kramer Z, Szijártó A, Fadgyas-Freyler P, Szénás K, Rugge M, Fassan MJNc. Primary and secondary clarithromycin resistance in Helicobacter pylori and mathematical modeling of the role of macrolides. 2021;12(1):1-12.
3. Savoldi A, Carrara E, Graham DY, Conti M, Tacconelli EJG. Prevalence of antibiotic resistance in Helicobacter pylori: a systematic review and meta-analysis in World Health Organization regions. 2018;155(5):1372-82. e17.
4. Hosseini RS, Rahimian G, Shafigh MH, Validi M, Khaledi M, Gholipour AJAE. Correlation between clarithromycin resistance, virulence factors and clinical characteristics of the disease in Helicobacter pylori infected patients in Shahrekord, Southwest Iran. 2021;11(1):1-9.
5. Park JY, Dunbar KB, Mitui M, Arnold CA, Lam-Himlin DM, Valasek MA, Thung I, Okwara C, Coss E, Cryer BJDd, sciences. Helicobacter pylori clarithromycin resistance and treatment failure are common in the USA. 2016;61(8):2373-80.
6. Essaidi I, Bounder G, Jouimyi RM, Boura H, Elyounsi I, Kheir F-Z, Benomar H, Badre W, Zerouali K, Maachi FJAPJoCP. Comparative Study of Helicobacter Pylori Resistance to Clarithromycin and Metronidazole and Its Association with Epidemiological Factors in A Moroccan Population. 2022;23(8):2755-61.
7. Hussein RA, Al-Ouqaili MT, Majeed YHJSJoBS. Detection of clarithromycin resistance and 23SrRNA point mutations in clinical isolates of Helicobacter pylori isolates: Phenotypic and molecular methods. 2022;29(1):513-20.
8. Marques AT, Vítor JM, Santos A, Oleastro M, Vale FFJMG. Trends in Helicobacter pylori resistance to clarithromycin: from phenotypic to genomic approaches. 2020;6(3).
9. Nishizawa T, Suzuki HJFimb. Mechanisms of Helicobacter pylori antibiotic resistance and molecular testing. 2014;1:19.
10. Zou Y, Qian X, Liu X, Song Y, Song C, Wu S, An Y, Yuan R, Wang Y, Xie YJH. The effect of antibiotic resistance on Helicobacter pylori eradication efficacy: A systematic review and meta-analysis. 2020;25(4):e12714.
11. Chilpancingo G. Clarithromycin resistance and prevalence of Helicobacter pylori virulent genotypes in patients from Southern Mexico with Chronic Gastritis. 2016.
12. Morilla AM, Álvarez-Argüelles ME, Duque JM, Armesto E, Villar H, Melón SJGyH. Primary antimicrobial resistance rates and prevalence of Helicobacter pylori infection in the north of Spain. A 13-year retrospective study. 2019;42(8):476-85.
13. Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. Bmj. 1997;315(7109):629-34.
14. Harbord R, Harris RJ, Sterne JA, Steichen T. METABIAS: Stata module to test for small-study effects in meta-analysis. 2010.
15. Harbord RM, Harris RJ, Sterne JA. Updated tests for small-study effects in meta-analyses. The Stata Journal. 2009;9(2):197-210.

16. Gong EJ, Ahn JY, Kim JM, Lee SM, Na HK, Lee JH, Jung KW, Choi KD, Kim DH, Song HJ. Genotypic and phenotypic resistance to clarithromycin in Helicobacter pylori strains. Journal of clinical medicine. 2020;9(6):1930.
17. Sanches BS, Martins GM, Lima K, Cota B, Moretzsohn LD, Ribeiro LT, Breyer HP, Maguilnik I, Maia AB, Rezende-Filho J. Detection of Helicobacter pylori resistance to clarithromycin and fluoroquinolones in Brazil: a national survey. World journal of gastroenterology. 2016;22(33):7587.
18. Khani S, Abadi ATB, Mobarez AM. Clarithromycin-susceptible but virulent Helicobacter pylori strains infecting Iranian patients' stomachs. Infection and Drug Resistance. 2019;12:3415.
19. Azimi T, Maham S, Fallah F, Azimi L, Gholinejad Z. Evaluating the antimicrobial resistance patterns among major bacterial pathogens isolated from clinical specimens taken from patients in Mofid Children's Hospital, Tehran, Iran: 2013–2018. Infection and drug resistance. 2019;12:2089.
20. Pormohammad A, Nasiri MJ, Azimi T. Prevalence of antibiotic resistance in Escherichia coli strains simultaneously isolated from humans, animals, food, and the environment: a systematic review and meta-analysis. Infection and drug resistance. 2019;12:1181.
21. He C, Kong F, Zhu X, Kong F, Zhao W, Liu Y, Wang K. Clinical Effect of Clarithromycin Combined with Tinidazole on Helicobacter pylori-Related Gastritis and Its Influence on COX-2 Expression. BioMed Research International. 2021;2021.
22. Marques AT, Vítor JM, Santos A, Oleastro M, Vale FF. Trends in Helicobacter pylori resistance to clarithromycin: from phenotypic to genomic approaches. Microbial Genomics. 2020;6(3).
23. Li X-H, Huang Y-Y, Lu L-M, Zhao L-J, Luo X-K, Li R-J, Dai Y-Y, Qin C, Huang Y-Q, Chen H. Early genetic diagnosis of clarithromycin resistance in Helicobacter pylori. World Journal of Gastroenterology. 2021;27(24):3595.
24. Mégraud F. H pylori antibiotic resistance: prevalence, importance, and advances in testing. Gut. 2004;53(9):1374-84.
25. Kim YM, Lee KH, Kim J-H, Park SY, Song YG, Jeon SY, Park H. Is only clarithromycin susceptibility important for the successful eradication of Helicobacter pylori? Antibiotics. 2020;9(9):589.
26. Chen D, Cunningham SA, Cole NC, Kohner PC, Mandrekar JN, Patel R. Phenotypic and molecular antimicrobial susceptibility of Helicobacter pylori. Antimicrobial agents and chemotherapy. 2017;61(4):e02530-16.
27. Abadi ATB. Resistance to clarithromycin and gastroenterologist's persistence roles in nomination for Helicobacter pylori as high priority pathogen by World Health Organization. World journal of gastroenterology. 2017;23(35):6379.
28. Horie R, Handa O, Ando T, Ose T, Murakami T, Suzuki N, Sendo R, Imamoto E, Itoh Y. Helicobacter pylori eradication therapy outcome according to clarithromycin susceptibility testing in Japan. Helicobacter. 2020;25(4):e12698.
29. Haddadi MH, Negahdari B, Asadolahi R, Bazargani A. Helicobacter pylori antibiotic resistance and correlation with cagA motifs and homB gene. Postgrad Med. 2020;132(6):512-20.
30. Eisig JN, Silva FM, Barbuti RC, Navarro-Rodriguez T, Moraes-Filho JPP, Pedrazzoli Jr J. Helicobacter pylori antibiotic resistance in Brazil: clarithromycin is still a good option. Arquivos de Gastroenterologia. 2011;48:261-4.
31. Aftab H, Miftahussurur M, Subsomwong P, Ahmed F, Khan AK, Yamaoka Y. Helicobacter pylori antibiotic susceptibility patterns in Bangladesh: Emerging levofloxacin resistance. J Infect Dev Ctries. 2016;10(3):245-53.
32. Ortiz V, Estevez-Ordonez D, Montalvan-Sanchez E, Urrutia-Argueta S, Israel D, Krishna US, Romero-Gallo J, Wilson KT, Peek RM, Dominguez R, Morgan DR. Helicobacter pylori antimicrobial resistance and antibiotic consumption in the low-resource Central America setting. Helicobacter. 2019;24(4):e12595.

300 33. Silva GM, Silva HM, Nascimento J, Goncalves JP, Pereira F, Lima R. Helicobacter pylori
301 antimicrobial resistance in a pediatric population. Helicobacter. 2018;23(5):e12528.
302 34. Almeida N, Romaozinho JM, Donato MM, Luxo C, Cardoso O, Cipriano MA, Marinho C,
303 Fernandes A, Calhau C, Sofia C. Helicobacter pylori antimicrobial resistance rates in the central region of
304 Portugal. Clin Microbiol Infect. 2014;20(11):1127-33.
305 35. Ilie M, Popa M, Chifiriuc MC, Baltac A, Constantinescu G, Tãnãsescu C. Helicobacter pylori
306 cultivation from gastric biopsies and susceptibility to antibiotics used in empirical therapy. Roum Arch
307 Microbiol Immunol. 2011;70(2):60-4.
308 36. Vécsei A, Innerhofer A, Graf U, Binder C, Giczi H, Hammer K, Bruckdorfer A, Hirschl AM,
309 Makristathis A. Helicobacter pylori eradication rates in children upon susceptibility testing based on
310 noninvasive stool polymerase chain reaction versus gastric tissue culture. Journal of pediatric
311 gastroenterology and nutrition. 2011;53(1):65-70.
312 37. Ranjbar R, Chehelgerdi M. Genotyping and antibiotic resistance properties of Helicobacter pylori
313 strains isolated from human and animal gastric biopsies. Infect Drug Resist. 2018;11:2545-54.
314 38. Hamza D, Elhelw R, Elhariri M, Ragab E. Genotyping and antimicrobial resistance patterns of
315 Helicobacter pylori in human and dogs associated with A2142G and A2143G point mutations in
316 clarithromycin resistance. Microb Pathog. 2018;123:330-8.
317 39. Gong EJ, Ahn JY, Kim JM, Lee SM, Na HK, Lee JH, Jung KW, Choi KD, Kim DH, Song HJ, Lee GH,
318 Kim SW, Jung HY. Genotypic and Phenotypic Resistance to Clarithromycin in Helicobacter pylori Strains. J
319 Clin Med. 2020;9(6):1930.
320 40. Wang YH, Wang FF, Gong XL, Yan LL, Zhao QY, Song YP, Zhao RL, He YJ, Zhou L, Liu DS, Xie Y.
321 Genotype profiles of Helicobacter pylori from gastric biopsies and strains with antimicrobial-induced
322 resistance. Therap Adv Gastroenterol. 2020;13:1756284820952596.
323 41. Su D-J, Chang M-H, Yang J-C, Ni Y-H, Hsu H-Y, Wu J-F. Fourteen-day sequential therapy is
324 superior to 7-day triple therapy as first-line regimen for Helicobacter pylori infected children. Journal of
325 the Formosan Medical Association. 2022;121(1):202-9.
326 42. Sugimoto M, Sahara S, Ichikawa H, Kagami T, Ban H, Otsuka T, Andoh A, Furuta T.
327 Four-times-daily dosing of rabeprazole with sitafloxacin, high-dose amoxicillin, or both for
328 metronidazole-resistant infection with Helicobacter pylori in Japan. Helicobacter. 2017;22(1):e12319.
329 43. Abadi AT, Taghvaei T, Mobarez AM, Carpenter BM, Merrell DS. Frequency of antibiotic
330 resistance in Helicobacter pylori strains isolated from the northern population of Iran. J Microbiol.
331 2011;49(6):987-93.
332 44. Teh X, Khosravi Y, Lee WC, Leow AH, Loke MF, Vadivelu J, Goh KL. Functional and molecular
333 surveillance of Helicobacter pylori antibiotic resistance in Kuala Lumpur. PLoS One. 2014;9(7):e101481.
334 45. Peng X, Song Z, He L, Lin S, Gong Y, Sun L, Zhao F, Gu Y, You Y, Zhou L, Zhang J. Gastric Juice-
335 Based Real-Time PCR for Tailored Helicobacter Pylori Treatment: A Practical Approach. Int J Med Sci.
336 2017;14(6):595-601.
337 46. Hashemi SJ, Sheikh AF, Goodarzi H, Yadyad MJ, Seyedian SS, Aslani S, Assarzadegan MA. Genetic
338 basis for metronidazole and clarithromycin resistance in Helicobacter pylori strains isolated from
339 patients with gastroduodenal disorders. Infect Drug Resist. 2019;12:535-43.
340 47. Lauener FN, Imkamp F, Lehours P, Buissonniere A, Benejat L, Zbinden R, Keller PM, Wagner K.
341 Genetic Determinants and Prediction of Antibiotic Resistance Phenotypes in Helicobacter pylori. J Clin
342 Med. 2019;8(1):53.
343 48. Domanovich-Asor T, Motro Y, Khalfin B, Craddock HA, Peretz A, Moran-Gilad J. Genomic Analysis
344 of Antimicrobial Resistance Genotype-to-Phenotype Agreement in Helicobacter pylori. Microorganisms.
345 2020;9(1):2.

49. Wu IT, Chuah SK, Lee CH, Liang CM, Lu LS, Kuo YH, Yen YH, Hu ML, Chou YP, Yang SC, Kuo CM, Kuo CH, Chien CC, Chiang YS, Chiou SS, Hu TH, Tai WC. Five-year sequential changes in secondary antibiotic resistance of Helicobacter pylori in Taiwan. World J Gastroenterol. 2015;21(37):10669-74.
50. Vala MH, Eyvazi S, Goudarzi H, Sarie HR, Gholami M. Evaluation of clarithromycin resistance among Iranian Helicobacter pylori isolates by E-test and real-time polymerase chain reaction methods. Jundishapur journal of microbiology. 2016;9(5).
51. Omar M, Crowe A, Tay CY, Hughes J. Expressions of P-glycoprotein in treatment–Resistant Helicobacter pylori patients. Journal of Applied Biomedicine. 2014;12(4):263-9.
52. Vilaichone RK, Ratanachu-Ek T, Gamnarai P, Chaithongrat S, Uchida T, Yamaoka Y, Mahachai V. Extremely High Prevalence of Metronidazole-Resistant Helicobacter pylori Strains in Mountain People (Karen and Hmong) in Thailand. Am J Trop Med Hyg. 2016;94(4):717-20.
53. Lee JY, Kim N, Kim MS, Choi YJ, Lee JW, Yoon H, Shin CM, Park YS, Lee DH, Jung HC. Factors affecting first-line triple therapy of Helicobacter pylori including CYP2C19 genotype and antibiotic resistance. Dig Dis Sci. 2014;59(6):1235-43.
54. Lee JW, Kim N, Nam RH, Lee SM, Kwon YH, Sohn SD, Kim JM, Lee DH, Jung HC. Favorable outcomes of culture-based Helicobacter pylori eradication therapy in a region with high antimicrobial resistance. Helicobacter. 2019;24(2):e12561.
55. Goudarzi M, Heidary M, Azad M, Fazeli M, Goudarzi H. Evaluation of antimicrobial susceptibility and integron carriage in Helicobacter pylori isolates from patients. Gastroenterol Hepatol Bed Bench. 2016;9(Suppl1):S47-S52.
56. Karpinski TM, Andrzejewska E, Eder P, Linke K, Szkaradkiewicz A. Evaluation of antimicrobial resistance of Helicobacter pylori in the last 15 years in West Poland. Acta Microbiol Immunol Hung. 2015;62(3):287-93.
57. Miyata E, Kudo T, Ikuse T, Tokita K, Arai N, Oka I, Kyodo R, Sato M, Hosoi K, Jimbo K, Aoyagi Y, Ohtsuka Y, Shimizu T. Eradication therapy for Helicobacter pylori infection based on the antimicrobial susceptibility test in children: A single-center study over 12 years. Helicobacter. 2021;26(1):e12764.
58. Palmitessa V, Monno R, Panarese A, Cuppone R, Burattini O, Marangi S, Curlo M, Fumarola L, Petrosillo A, Parisi A, Capozzi L, Bianco A, Lippolis A. Evaluation of Antibiotic Resistance of Helicobacter pylori Strains Isolated in Bari, Southern Italy, in 2017-2018 by Phenotypic and Genotyping Methods. Microb Drug Resist. 2020;26(8):909-17.
59. Hung KT, Yang SC, Wu CK, Wang HM, Yao CC, Liang CM, Tai WC, Wu KL, Kuo YH, Lee CH, Chuah SK. Eradication Rates for Esomeprazole and Lansoprazole-Based 7-Day Non-Bismuth Concomitant Quadruple Therapy for First-Line Anti-Helicobacter pylori Treatment in Real World Clinical Practice. Infect Drug Resist. 2021;14:1239-46.
60. Miftahussurur M, Shrestha PK, Subsomwong P, Sharma RP, Yamaoka Y. Emerging Helicobacter pylori levofloxacin resistance and novel genetic mutation in Nepal. BMC Microbiol. 2016;16(1):256.
61. Siddiqui TR, Ahmed W, Arif A, Bibi S, Khan A. Emerging trends of antimicrobial resistance in Helicobacter pylori isolates obtained from Pakistani patients: The need for consideration of amoxicillin and clarithromycin. J Pak Med Assoc. 2016;66(6):710-6.
62. Sugimoto M, Uotani T, Sahara S, Ichikawa H, Yamade M, Sugimoto K, Furuta T. Efficacy of tailored Helicobacter pylori eradication treatment based on clarithromycin susceptibility and maintenance of acid secretion. Helicobacter. 2014;19(4):312-8.
63. Jolaiya TF, Fowora MA, Onyekwere C, Ugiagbe R, Agbo II, Lesi O, Ndububa DA, Adekanle O, Njom HA, Idowu A. Efflux pump mediated antibiotic resistance in clinical isolates of Helicobacter pylori from South West Nigeria. Journal of Gastroenterology and Hepatology Research. 2020;9(4):3283-9.
64. Pandya HB, Agravat HH, Patel JS, Sodagar NR. Emerging antimicrobial resistance pattern of Helicobacter pylori in central Gujarat. Indian J Med Microbiol. 2014;32(4):408-13.

65. Lehours P, Siffré E, Mégraud F. DPO multiplex PCR as an alternative to culture and susceptibility testing to detect Helicobacter pylori and its resistance to clarithromycin. BMC gastroenterology. 2011;11(1):1-5.
66. Sun L, Talarico S, Yao L, He L, Self S, You Y, Zhang H, Zhang Y, Guo Y, Liu G, Salama NR, Zhang J. Droplet Digital PCR-Based Detection of Clarithromycin Resistance in Helicobacter pylori Isolates Reveals Frequent Heteroresistance. J Clin Microbiol. 2018;56(9):e00019-18.
67. Dekhnich N, Ivanchik N, Kozlov R, Alimov A, Steshits A, Kirsov P, Pandav K. Dynamics of antimicrobial resistance of Helicobacter pylori isolates in the Smolensk region of Russian Federation. Helicobacter. 2018;23(6):e12545.
68. Sugimoto M, Hira D, Murata M, Kawai T, Terada T. Effect of Antibiotic Susceptibility and CYP3A4/5 and CYP2C19 Genotype on the Outcome of Vonoprazan-Containing Helicobacter pylori Eradication Therapy. Antibiotics (Basel). 2020;9(10):645.
69. Siavoshi F, Saniee P, Malekzadeh R. Effective antimicrobial activity of rifabutin against multidrug-resistant Helicobacter pylori. Helicobacter. 2018;23(6):e12531.
70. Szadkowski A, Zemlak M, Muszynski J. Effectiveness of Helicobacter pylori eradication established on the basis of examination of antibiotic resistance of the bacteria. Prz Gastroenterol. 2018;13(2):93-8.
71. Costa S, Soares JB, Goncalves R. Efficacy and tolerability of culture-guided treatment for Helicobacter pylori infection. Eur J Gastroenterol Hepatol. 2017;29(11):1258-63.
72. Aguilera-Correa JJ, Urruzuno P, Barrio J, Martinez MJ, Agudo S, Somodevilla A, Llorca L, Alarcón T. Detection of Helicobacter pylori and the genotypes of resistance to clarithromycin and the heterogeneous genotype to this antibiotic in biopsies obtained from symptomatic children. Diagnostic Microbiology and Infectious Disease. 2017;87(2):150-3.
73. Akar M, Aydin F, Kayman T, Abay S, Karakaya E. Detection of Helicobacter pylori by invasive tests in adult dyspeptic patientsand antibacterial resistance to six antibiotics, including rifampicin in Turkey. Isclarithromycin resistance rate decreasing? Turkish Journal of Medical Sciences. 2021;51(3):1455-64.
74. Yula E, Nagiyev T, Kaya ÖA, İnci M, Çelik MM, Köksal F. Detection of primary clarithromycin resistance of Helicobacter pylori and association between cagA+ status and clinical outcome. Folia microbiologica. 2013;58(2):141-6.
75. Zhang XY, Shen WX, Chen CF, Sheng HH, Cheng H, Li J, Hu F, Lu DR, Gao HJ. Detection of the clarithromycin resistance of Helicobacter pylori in gastric mucosa by the amplification refractory mutation system combined with quantitative real-time PCR. Cancer Med. 2019;8(4):1633-40.
76. Macin S, Demir H, Ozen H, Yuce A, Akyon Y. Determination of Helicobacter pylori antibiotic resistance patterns in pediatric gastroenterology patients: the Hacettepe experience. Turk J Pediatr. 2015;57(3):254-7.
77. Auttajaroon J, Chotivitayatarakorn P, Yamaoka Y, Vilaichone RK. CYP2C19 Genotype, CagA Genotype and Antibiotic Resistant Strain of Helicobacter pylori Infection. Asian Pac J Cancer Prev. 2019;20(4):1243-7.
78. Eghbali Z, Mojtahedi A, Moien Ansar M, Fakhrieh Asl S, Aminian K. Detection of 23SrRNA Mutations Strongly Related to Clarithromycin Resistance in Helicobacter pylori Strains Isolated From Patients in the North of Iran. Jundishapur J Microbiol. 2016;9(2):e29694.
79. Wu JY, Wang SS, Lee YC, Yamaoka Y, Graham DY, Jan CM, Wang WM, Wu DC. Detection of genotypic clarithromycin-resistant Helicobacter pylori by string tests. World J Gastroenterol. 2014;20(12):3343-9.
80. Kocazeybek B, Sakli MK, Yuksel P, Demirci M, Caliskan R, Sarp TZ, Saribas S, Demiryas S, Kalayci F, Cakan H. Comparison of new and classical point mutations associated with clarithromycin resistance in Helicobacter pylori strains isolated from dyspeptic patients and their effects on phenotypic clarithromycin resistance. Journal of Medical Microbiology. 2019;68(4):566-73.

441 81. Egli K, Wagner K, Keller PM, Risch L, Risch M, Bodmer T. Comparison of the Diagnostic
442 Performance of qPCR, Sanger Sequencing, and Whole-Genome Sequencing in Determining
443 Clarithromycin and Levofloxacin Resistance in Helicobacter pylori. Front Cell Infect Microbiol.
444 2020;10:596371.
445 82. Khani S, Talebi Bezmin Abadi A, Mohabati Mobarez A. Clarithromycin-Susceptible But Virulent
446 Helicobacter pylori Strains Infecting Iranian Patients' Stomachs. Infect Drug Resist. 2019;12:3415-20.
447 83. Morimoto N, Takeuchi H, Nishida Y, Morisawa M, Yoshikawa T, Morita T, Morimoto M, Sugimoto
448 C, Matsumura Y, Sugiura T. Clinical Application of the DiversiLab Microbial Typing System Using
449 Repetitive Sequence-Based PCR for Characterization of Helicobacter pylori in Japan. Journal of clinical
450 laboratory analysis. 2015;29(3):250-3.
451 84. Alarcón-Millán J, Fernández-Tilapa G, Cortés-Malagón EM, Castañón-Sánchez CA, De Sampedro-
452 Reyes J, Cruz-del Carmen I, Betancourt-Linares R, Román-Román A. Clarithromycin resistance and
453 prevalence of Helicobacter pylori virulent genotypes in patients from Southern México with chronic
454 gastritis. Infection, Genetics and Evolution. 2016;44:190-8.
455 85. Tamayo E, Montes M, Fernandez-Reyes M, Lizasoain J, Ibarra B, Mendarte U, Zapata E, Mendiola
456 J, Perez-Trallero E. Clarithromycin resistance in Helicobacter pylori and its molecular determinants in
457 Northern Spain, 2013-2015. J Glob Antimicrob Resist. 2017;9:43-6.
458 86. Yoon K-H, Park SW, Lee SW, Kim BJ, Kim JG. Clarithromycin-based standard triple therapy can
459 still be effective for Helicobacter pylori eradication in some parts of the Korea. Journal of Korean
460 medical science. 2014;29(9):1240-6.
461 87. Miftahussurur M, Cruz M, Subsomwong P, Abreu JAJ, Hosking C, Nagashima H, Akada J,
462 Yamaoka Y. Clarithromycin-based triple therapy is still useful as an initial treatment for Helicobacter
463 pylori infection in the Dominican Republic. The American journal of tropical medicine and hygiene.
464 2017;96(5):1050.
465 88. Mohammad K, Maryam B, Abbas D, Sadegh G-D. Clarithromycin resistance and 23S rRNA
466 mutations in Helicobacter pylori isolates in Iran. African Journal of Microbiology Research.
467 2011;5(8):853-6.
468 89. Ha TMT, Le PTQ, Phan TN, Tran TNH. Characterisation of point mutations in domain V of the 23S
469 rRNA gene of clinical Helicobacter pylori strains and clarithromycin-resistant phenotype in central
470 Vietnam. Journal of global antimicrobial resistance. 2019;16:87-91.
471 90. Tanih NF, Ndip LM, Ndip RN. Characterisation of the genes encoding resistance to metronidazole
472 (rdxA and frxA) and clarithromycin (the 23S-rRNA genes) in South African isolates of Helicobacter pylori.
473 Ann Trop Med Parasitol. 2011;105(3):251-9.
474 91. Yeganeh M, Paritsky M, On A, Azrad M, Roshrosh H, Moalem R, Peretz A. Characteristics of
475 Antibiotic Resistance of Helicobacter pylori Among Adult Arab and Jewish Populations in Northern Israel.
476 Microbial Drug Resistance. 2019;25(1):103-7.
477 92. Liu DS, Wang YH, Zhu ZH, Zhang SH, Zhu X, Wan JH, Lu NH, Xie Y. Characteristics of Helicobacter
478 pylori antibiotic resistance: data from four different populations. Antimicrob Resist Infect Control.
479 2019;8(1):192.
480 93. Zhu Z, Huang D, Xie Y, Liu L, Lu N. Characterization of 23S rRNA gene mutation in primary and
481 secondary clarithromycin-resistant Helicobacter pylori strains from East China. Turk J Gastroenterol.
482 2013;24(1):5-9.
483 94. Farzi N, Behzad C, Hasani Z, Alebouyeh M, Zojaji H, Zali MR. Characterization of clarithromycin
484 heteroresistance among Helicobacter pylori strains isolated from the antrum and corpus of the stomach.
485 Folia microbiologica. 2019;64(2):143-51.
486 95. Abdollahi H, Hashemzadeh M, Khoshnood S, Savari M. Characterization of helicobacter pylori
487 genotypes from Iranian patients with gastric clinical diseases: predominance of vacA s1a and cagA
488 EPIYA-ABC genotypes. Gene Reports. 2019;16:100458.

96. Lee KH, Park SY, Jeong SJ, Kim J-H, Jeong SH, Kang I-M, Song YG. Can aminoglycosides be used as a new treatment for Helicobacter pylori? In vitro activity of recently isolated Helicobacter pylori. Infection & Chemotherapy. 2019;51(1):10-20.
97. De Francesco V, Zullo A, Giorgio F, Saracino I, Zaccaro C, Hassan C, Ierardi E, Di Leo A, Fiorini G, Castelli V, Lo Re G, Vaira D. Change of point mutations in Helicobacter pylori rRNA associated with clarithromycin resistance in Italy. J Med Microbiol. 2014;63(Pt 3):453-7.
98. Seo JH, Jun JS, Yeom JS, Park JS, Youn HS, Ko GH, Baik SC, Lee WK, Cho MJ, Rhee KH. Changing pattern of antibiotic resistance of H elicobacter pylori in children during 20 years in J inju, S outh K orea. Pediatrics International. 2013;55(3):332-6.
99. Kouitcheu Mabeku LB, Eyoum Bille B, Tepap Zemnou C, Tali Nguefack LD, Leundji H. Broad spectrum resistance in Helicobacter pylori isolated from gastric biopsies of patients with dyspepsia in Cameroon and efflux-mediated multiresistance detection in MDR isolates. BMC Infect Dis. 2019;19(1):880.
100. Yin G, Bie S, Gu H, Shu X, Zheng W, Peng K, Zhao H, Li F, Chen B, Botchway BOA, Fang M, Jiang M. Application of gene chip technology in the diagnostic and drug resistance detection of Helicobacter pylori in children. J Gastroenterol Hepatol. 2020;35(8):1331-9.
101. Chen J, Ye L, Jin L, Xu X, Xu P, Wang X, Li H. Application of next-generation sequencing to characterize novel mutations in clarithromycin-susceptible Helicobacter pylori strains with A2143G of 23S rRNA gene. Ann Clin Microbiol Antimicrob. 2018;17(1):10.
102. Kakiuchi T, Hashiguchi K, Imamura I, Nakayama A, Takamori A, Okuda M, Matsuo M. Assessment of a novel method to detect clarithromycin-resistant Helicobacter pylori using a stool antigen test reagent. BMC gastroenterology. 2020;20(1):1-6.
103. Cuadrado-Lavín A, Salcines-Caviedes JR, Carrascosa MF, Mellado P, Monteagudo I, Llorca J, Cobo M, Campos MR, Ayestarán B, Fernández-Pousa A. Antimicrobial susceptibility of Helicobacter pylori to six antibiotics currently used in Spain. Journal of antimicrobial chemotherapy. 2012;67(1):170-3.
104. Gehlot V, Mahant S, Mukhopadhyay AK, Das K, De R, Kar P, Das R. Antimicrobial susceptibility profiles of Helicobacter pylori isolated from patients in North India. J Glob Antimicrob Resist. 2016;5:51-6.
105. Ogata SK, Gales AC, Kawakami E. Antimicrobial susceptibility testing for Helicobacter pylori isolates from Brazilian children and adolescents: comparing agar dilution, E-test, and disk diffusion. Braz J Microbiol. 2014;45(4):1439-48.
106. Eng NF, Ybazeta G, Chapman K, Fraleigh NL, Letto R, Altman E, Diaz-Mitoma F. Antimicrobial susceptibility of Canadian isolates of Helicobacter pylori in Northeastern Ontario. Can J Infect Dis Med Microbiol. 2015;26(3):137-44.
107. Alarcón T, Urruzuno P, Martínez MJ, Domingo D, Llorca L, Correa A, López-Brea M. Antimicrobial susceptibility of 6 antimicrobial agents in Helicobacter pylori clinical isolates by using EUCAST breakpoints compared with previously used breakpoints. Enfermedades infecciosas y microbiologia clinica (English ed). 2017;35(5):278-82.
108. Akhtereeva A, Morozova L, Faizullina R, Ivanovskaya K, Pozdeev O, Valeeva IK, Abdulkhakov S. Antibiotic susceptibility assessment of Helicobacter pylori isolates by disk-diffusion method. BioNanoScience. 2018;8(3):930-4.
109. Selgrad M, Meissle J, Bornschein J, Kandulski A, Langner C, Varbanova M, Wex T, Tammer I, Schluter D, Malfertheiner P. Antibiotic susceptibility of Helicobacter pylori in central Germany and its relationship with the number of eradication therapies. Eur J Gastroenterol Hepatol. 2013;25(11):1257-60.
110. Gunnarsdottir AI, Gudjonsson H, Hardardottir H, Jonsdottir KD, Bjornsson ES. Antibiotic susceptibility of Helicobacter pylori in Iceland. Infect Dis (Lond). 2017;49(9):647-54.

111. Mahmoudi S, Mamishi S, Banar M, Keshavarz Valian S, Bahador A, Najafi M, Farahmand F, Pourakbari B. Antibiotic susceptibility of Helicobacter pylori strains isolated from Iranian children: High frequency of A2143G point mutation associated with clarithromycin resistance. J Glob Antimicrob Resist. 2017;10:131-5.
112. Shokrzadeh L, Jafari F, Dabiri H, Baghaei K, Zojaji H, Alizadeh AH, Aslani MM, Zali MR. Antibiotic susceptibility profile of Helicobacter pylori isolated from the dyspepsia patients in Tehran, Iran. Saudi J Gastroenterol. 2011;17(4):261-4.
113. Savari M, Abdolahi H, Zahedi M, Darvishmoghadam S, Hayat Bakhshe Abasi M. Antibiotic-resistance Patterns of Helicobacter pylori isolates Obtained from Patients in Kerman-2009. Journal of Kerman University of Medical Sciences. 2010;17(1):73-82.
114. Shu X, Yin G, Liu M, Peng K, Zhao H, Jiang M. Antibiotics resistance of Helicobacter pylori in children with upper gastrointestinal symptoms in Hangzhou, China. Helicobacter. 2018;23(3):e12481.
115. Mosites E, Bruden D, Morris J, Reasonover A, Rudolph K, Hurlburt D, Hennessy T, McMahon B, Bruce M. Antimicrobial resistance among Helicobacter pylori isolates in Alaska, 2000–2016. Journal of global antimicrobial resistance. 2018;15:148-53.
116. Parra-Sepúlveda C, Merino JS, Sáez-Carrillo K, González C, García-Cancino A. Antibiotic resistance surveillance of Helicobacter pylori at the Biobío region (Chile) in a decade. Arquivos de Gastroenterologia. 2019;56:361-6.
117. Fiorini G, Zullo A, Saracino IM, Pavoni M, Vaira D. Antibiotic resistance pattern of Helicobacter pylori strains isolated in Italy during 2010-2016. Scand J Gastroenterol. 2018;53(6):661-4.
118. Shao Y, Lu R, Yang Y, Xu Q, Wang B, Ye G. Antibiotic resistance of Helicobacter pylori to 16 antibiotics in clinical patients. J Clin Lab Anal. 2018;32(4):e22339.
119. Li J, Deng J, Wang Z, Li H, Wan C. Antibiotic Resistance of Helicobacter pylori Strains Isolated From Pediatric Patients in Southwest China. Front Microbiol. 2020;11:621791.
120. Su P, Li Y, Li H, Zhang J, Lin L, Wang Q, Guo F, Ji Z, Mao J, Tang W, Shi Z, Shao W, Mao J, Zhu X, Zhang X, Tong Y, Tu H, Jiang M, Wang Z, Jin F, Yang N, Zhang J. Antibiotic resistance of Helicobacter pylori isolated in the Southeast Coastal Region of China. Helicobacter. 2013;18(4):274-9.
121. Hojsak I, Kos T, Dumancic J, Misak Z, Jadresin O, Jaklin Kekez A, Lukic Grlic A, Kolacek S. Antibiotic resistance of Helicobacter pylori in pediatric patients -- 10 years' experience. Eur J Pediatr. 2012;171(9):1325-30.
122. Hamidi S, Badmasti F, Sadeghpour Heravi F, Safapoor MH, Mohammad Ali Tabrizi A, Ghorbani M, Azizi O. Antibiotic resistance and clonal relatedness of Helicobacter pylori strains isolated from stomach biopsy specimens in northeast of Iran. Helicobacter. 2020;25(2):e12684.
123. An B, Moon BS, Kim H, Lim HC, Lee YC, Lee G, Kim SH, Park M, Kim JB. Antibiotic resistance in Helicobacter pylori strains and its effect on H. pylori eradication rates in a single center in Korea. Ann Lab Med. 2013;33(6):415-9.
124. Shiota S, Reddy R, Alsarraj A, El-Serag HB, Graham DY. Antibiotic resistance of Helicobacter pylori among male United States veterans. Clinical Gastroenterology and Hepatology. 2015;13(9):1616-24.
125. Li L, Ke Y, Yu C, Li G, Yang N, Zhang J, Li Y. Antibiotic resistance of Helicobacter pylori in Chinese children: A multicenter retrospective study over 7 years. Helicobacter. 2017;22(3):e12373.
126. Bolor-Erdene M, Namdag B, Yamaoka Y, Jav S. Antibiotic resistance of Helicobacter pylori in Mongolia. J Infect Dev Ctries. 2017;11(11):887-94.
127. Boehnke KF, Valdivieso M, Bussalleu A, Sexton R, Thompson KC, Osorio S, Reyes IN, Crowley JJ, Baker LH, Xi C. Antibiotic resistance among Helicobacter pylori clinical isolates in Lima, Peru. Infection and drug resistance. 2017;10:85.
128. Ahmad N, Zakaria WR, Mohamed R. Analysis of antibiotic susceptibility patterns of Helicobacter pylori isolates from Malaysia. Helicobacter. 2011;16(1):47-51.

129. Rasheed F, Campbell BJ, Alfizah H, Varro A, Zahra R, Yamaoka Y, Pritchard DM. Analysis of clinical isolates of Helicobacter pylori in Pakistan reveals high degrees of pathogenicity and high frequencies of antibiotic resistance. Helicobacter. 2014;19(5):387-99.
130. Guo C, Liu F, Zhu L, Wu F, Cui G, Xiong Y, Wang Q, Yin L, Wang C, Wang H, Wu X, Zhang Z, Chen Z. Analysis of culturable microbiota present in the stomach of children with gastric symptoms. Braz J Microbiol. 2019;50(1):107-15.
131. Jiang ZD, He BS, Zhang ZY, Wang SK, Ran D, Wang ZB. Analysis of the Primary and Post-Treatment Antibiotic Resistance of Helicobacter pylori in the Nanjing Area. Curr Pharm Biotechnol. 2021;22(5):682-5.
132. Butenko T, Jeverica S, Orel R, Homan M. Antibacterial resistance and the success of tailored triple therapy in Helicobacter pylori strains isolated from Slovenian children. Helicobacter. 2017;22(5):e12400.
133. Tveit AH, Bruce MG, Bruden DL, Morris J, Reasonover A, Hurlburt DA, Hennessy TW, McMahon B. Alaska sentinel surveillance study of Helicobacter pylori isolates from Alaska Native persons from 2000 to 2008. J Clin Microbiol. 2011;49(10):3638-43.
134. Tuan VP, Narith D, Tshibangu-Kabamba E, Dung HDQ, Viet PT, Sokomoth S, Binh TT, Sokhem S, Tri TD, Ngov S, Tung PH, Thuan NPM, Truc TC, Phuc BH, Matsumoto T, Fauzia KA, Akada J, Trang TTH, Yamaoka Y. A Next-Generation Sequencing-Based Approach to Identify Genetic Determinants of Antibiotic Resistance in Cambodian Helicobacter pylori Clinical Isolates. J Clin Med. 2019;8(6):858.
135. Маев ИВ, Андреев ДН, Говорун ВМ, Ильина ЕН, Кучерявый ЮА, Оганесян ТС, Мельникова ЕВ, Зайратьянц ОВ, Парфенова ТВ, Джеджеиа ЛВ. Антибиотикорезистентность Helicobacter pylori в Европейской части Российской Федерации: первые результаты. Терапевтический архив. 2020;92(8):24-8.
136. Figueroa M, Cortés A, Pazos Á, Bravo LE. Sensibilidad in vitro a amoxicilina y claritromicina de Helicobacter pylori obtenido de biopsias gástricas de pacientes en zona de bajo riesgo para cáncer gástrico. Biomédica. 2012;32(1):32-42.
137. Kim JY, Kim NY, Kim SJ, Baik GH, Kim GH, Kim JM, Nam RH, Kim HB, Lee DH, Jung HC, Song IS. [Regional difference of antibiotic resistance of helicobacter pylori strains in Korea]. Korean J Gastroenterol. 2011;57(4):221-9.
138. Adeniyi BA, Lawal TO, Otegbayo JA, Oluwasola OA, Odaibo GN, Ola SO, Okolo CA, Akere A, Kehinde AO. Cultural characteristics and antibiotic susceptibility pattern of Helicobacter pylori isolated from dyspepsia patients. Gastroenterology Insights. 2012;4(2):e21.
139. Yao C-C, Kuo C-M, Hsu C-N, Yang S-C, Wu C-K, Tai W-C, Liang C-M, Wu K-L, Huang C-F, Bi K-W. First-line Helicobacter pylori eradication rates are significantly lower in patients with than those without type 2 diabetes mellitus. Infection and drug resistance. 2019;12:1425.
140. Honma H, Nakayama Y, Kato S, Hidaka N, Kusakari M, Sado T, Suda A, Lin Y. Clinical features of Helicobacter pylori antibody-positive junior high school students in Nagano Prefecture, Japan. Helicobacter. 2019;24(2):e12559.
141. Bayati S, Amirmozafari N, Alebouyeh M, Farzi N, Daryani NE, Zali MR. Antibiotic resistance among Helicobacter pylori strains isolated from patients with histopathological changes of the gastric tissue towards metronidazole, clarithromycin, and ciprofloxacin. Archives of Clinical Infectious Diseases. 2019;14(1).
142. Pichon M, Tran CT, Motillon G, Debiais C, Gautier S, Aballea M, Cremniter J, Vasseur P, Tougeron D, Garcia M. Where to biopsy to detect Helicobacter pylori and how many biopsies are needed to detect antibiotic resistance in a human stomach. Journal of Clinical Medicine. 2020;9(9):2812.
143. Tanabe H, Yoshino K, Ando K, Nomura Y, Ohta K, Satoh K, Ichiishi E, Ishizuka A, Otake T, Kohgo Y. Vonoprazan-based triple therapy is non-inferior to susceptibility-guided proton pump inhibitor-based

631 triple therapy for Helicobacter pylori eradication. Annals of Clinical Microbiology and Antimicrobials.
632 2018;17(1):1-7.
633 144. Karabiber H, Selimoglu MA, Otlu B, Yildirim O, Ozer A. Virulence factors and antibiotic resistance
634 in children with Helicobacter pylori gastritis. Journal of pediatric gastroenterology and nutrition.
635 2014;58(5):608-12.
636 145. Saracino IM, Fiorini G, Zullo A, Pavoni M, Saccomanno L, Vaira D. Trends in primary antibiotic
637 resistance in H. pylori strains isolated in Italy between 2009 and 2019. Antibiotics. 2020;9(1):26.
638 146. Liang C-M, Tai W-C, Hsu P-I, Wu D-C, Kuo C-H, Tsay F-W, Lee C-L, Chen K-Y, Chuah S-K. Trend of
639 changes in antibiotic resistance in Helicobacter pylori from 2013 to 2019: a multicentre report from
640 Taiwan. Therapeutic advances in gastroenterology. 2020;13:1756284820976990.
641 147. Khademi F, Faghri J, Moghim S, Esfahani BN, Fazeli H, Poursina F, Adibi P, Madhi M, Safaei HG.
642 The study of mutation in 23S rRNA resistance gene of Helicobacter pylori to clarithromycin in patients
643 with gastrointestinal disorders in Isfahan—Iran. Advanced Biomedical Research. 2014;3.
644 148. Milani M, Ghotaslou R, Somi MH, Rafeey M, Akhi MT, Nahaei MR, Hasani A, Sharifi Y. The status
645 of antimicrobial resistance of Helicobacter pylori in Eastern Azerbaijan, Iran: comparative study
646 according to demographics. Journal of Infection and Chemotherapy. 2012;18(6):848-52.
647 149. Famouri F, Emadoleslami MS, Riahi R, Saneian H, Nasri P. The sensitivity of H. pylori in gastric
648 tissue samples of children and adolescents to various antibiotics in center of Iran. International Journal
649 of Pediatrics. 2018;6(12):8685-96.
650 150. Bruce MG, Bruden D, Newbrough D, Hurlburt DA, Hennessy TW, Morris JM, Reasonover AL,
651 Sacco F, McMahon BJ. The relationship between previous antimicrobial use, antimicrobial resistance and
652 treatment outcome among Alaskans treated for Helicobacter pylori infection. GastroHep. 2019;1(4):172-
653 9.
654 151. Park JY, Shin T-S, Kim JH, Yoon HJ, Kim BJ, Kim JG. The prevalence of multidrug resistance of
655 helicobacter pylori and its impact on eradication in Korea from 2017 to 2019: A single-center study.
656 Antibiotics. 2020;9(10):646.
657 152. Binh TT, Shiota S, Nguyen LT, Ho DD, Hoang HH, Ta L, Trinh DT, Fujioka T, Yamaoka Y. The
658 incidence of primary antibiotic resistance of Helicobacter pylori in Vietnam. Journal of clinical
659 gastroenterology. 2013;47(3):233.
660 153. Keshavarz Azizi Raftar S, Moniri R, Saffari M, Razavi Zadeh M, Arj A, Mousavi SGA, Mirzaei Ghazi
661 Kalayeh H, Dastehgoli K. The Helicobacter pylori resistance rate to clarithromycin in Iran. Microbial Drug
662 Resistance. 2015;21(1):69-73.
663 154. Ang TL, Fock KM, Ang D, Kwek ABE, Teo EK, Dhamodaran S. The changing profile of Helicobacter
664 pylori antibiotic resistance in Singapore: a 15-year study. Helicobacter. 2016;21(4):261-5.
665 155. GOŚCINIAK G, Biernat M, Grabińska J, Bińkowska A, PONIEWIERKA E, Iwańczak B. The
666 antimicrobial susceptibility of Helicobacter pylori strains isolated from children and adults with primary
667 infection in the Lower Silesia Region, Poland. Polish Journal of Microbiology. 2014;63(1):57.
668 156. Wang D, Guo Q, Yuan Y, Gong Y. The antibiotic resistance of Helicobacter pylori to five
669 antibiotics and influencing factors in an area of China with a high risk of gastric cancer. BMC
670 microbiology. 2019;19(1):1-10.
671 157. Bai P, Zhou LY, Xiao XM, Luo Y, Ding Y. Susceptibility of H elicobacter pylori to antibiotics in C
672 hinese patients. Journal of Digestive Diseases. 2015;16(8):464-70.
673 158. Mégraud F, Alix C, Charron P, Bénéjat L, Ducournau A, Bessède E, Lehours P. Survey of the
674 antimicrobial resistance of Helicobacter pylori in France in 2018 and evolution during the previous 5
675 years. Helicobacter. 2021;26(1):e12767.
676 159. Sadeghifard N, Seidnazari T, Ghafourian S, Soleimani M, Maleki A, Qomi MA, Sekawi Z. Survey in
677 Iran of clarithromycin resistance in Helicobacter pylori isolates by PCR-RFLP. Southeast Asian Journal of
678 Tropical Medicine & Public Health. 2013;44(1):89-95.

679 160. Bedoya-Gómez IJ, Alvarez-Aldana A, Moncayo-Ortiz JI, Guaca-González YM, Santacruz-Ibarra JJ,
680 Arturo-Arias BL, Castañeda-Chávez LJ, Rodriguez DAL, Beltrán-Angarita L. Surveillance of the
681 Antimicrobial Resistance Rates of Helicobacter pylori Ten Years Later in the Western Central Region,
682 Colombia. Digestive Diseases. 2020;38(3):196-203.
683 161. Miftahussurur M, Syam AF, Nusi IA, Makmun D, Waskito LA, Zein LH, Akil F, Uwan WB,
684 Simanjuntak D, Wibawa IDN. Surveillance of Helicobacter pylori antibiotic susceptibility in Indonesia:
685 different resistance types among regions and with novel genetic mutations. PloS one.
686 2016;11(12):e0166199.
687 162. Erkut M, Uzun DY, Kaklıkkaya N, Fidan S, Yoğun Y, Coşar AM, Akyıldız E, Topbaş M, Özgür O,
688 Arslan M. Sociodemographic characteristics and clinical risk factors of Helicobacter pylori infection and
689 antibiotic resistance in the Eastern Black Sea region of Turkey. The Turkish Journal of Gastroenterology.
690 2020;31(3):221.
691 163. Zhang J, Zhong J, Ding J, Shi J, Tang T, Liu Q, Huang H, Dai L, Yang N. Simultaneous detection of
692 human CYP2C19 polymorphisms and antibiotic resistance of Helicobacter pylori using a personalised
693 diagnosis kit. Journal of Global Antimicrobial Resistance. 2018;13:174-9.
694 164. Tsay FW, Tseng HH, Hsu PI, Wang KM, Lee CC, Chang SN, Wang HM, Yu HC, Chen WC, Peng NJ.
695 Sequential therapy achieves a higher eradication rate than standard triple therapy in Taiwan. Journal of
696 Gastroenterology and Hepatology. 2012;27(3):498-503.
697 165. Mascellino MT, Oliva A, De Angelis M, Pontone S, Porowska B. Helicobacter pylori infection:
698 antibiotic resistance and eradication rate in patients with gastritis showing previous treatment failures.
699 New Microbiol. 2018;41(4):306-9.
700 166. Khoury J, Geffen Y, Shaul R, Sholy H, Chowers Y, Saadi T. Secondary antibiotic resistance of
701 Helicobacter pylori isolates in Israeli children and adults. Journal of global antimicrobial resistance.
702 2017;10:182-5.
703 167. Saracino IM, Pavoni M, Zullo A, Fiorini G, Saccomanno L, Lazzarotto T, Antonelli G, Cavallo R,
704 Borghi C, Vaira D. Rifabutin-based triple therapy or bismuth-based quadruple regimen as rescue
705 therapies for Helicobacter pylori infection. European Journal of Internal Medicine. 2020;81:50-3.
706 168. Lin T-F, Wu D-C, Tsay F-W, Tsai K-W, Tsai T-J, Peng N-J, Kao S-S, Chen W-C, Chen Y-H, Hsu P-I.
707 Reverse hybrid therapy achieves a similar eradication rate as standard hybrid therapy for Helicobacter
708 pylori infection. Journal of the Chinese Medical Association. 2020;83(3):233-7.
709 169. Alfizah H, Norazah A, Hamizah R, Ramelah M. Resistotype of Helicobacter pylori isolates: the
710 impact on eradication outcome. Journal of medical microbiology. 2014;63(5):703-9.
711 170. Fasciana T, Calà C, Bonura C, Di Carlo E, Matranga D, Scarpulla G, Manganaro M, Camilleri S,
712 Giammanco A. Resistance to clarithromycin and genotypes in Helicobacter pylori strains isolated in
713 Sicily. Journal of Medical Microbiology. 2015;64(11):1408-14.
714 171. Ayala G, Galván-Portillo M, Chihu L, Fierros G, Sánchez A, Carrillo B, Román A, López-Carrillo L,
715 Silva-Sánchez, Study Group J. Resistance to antibiotics and characterization of Helicobacter pylori strains
716 isolated from antrum and body from adults in Mexico. Microbial Drug Resistance. 2011;17(2):149-55.
717 172. Picoli SU, Mazzoleni LE, Fernández H, De Bona LR, Neuhauss E, Longo L, Prolla JC. Resistance to
718 amoxicillin, clarithromycin and ciprofloxacin of Helicobacter pylori isolated from Southern Brazil
719 patients. Revista do Instituto de Medicina Tropical de São Paulo. 2014;56:197-200.
720 173. Larsen AL, Ragnhildstveit E, Moayeri B, Eliassen L, Melby KK. Resistance rates of metronidazole
721 and other antibacterials in H elicobacter pylori from previously untreated patients in N orway. Apmis.
722 2013;121(4):353-8.
723 174. Kumar S, Sangitha R, Nachamkin I, Metz DC. Resistance patterns of refractory Helicobacter pylori
724 infection in a referral centre in the Delaware Valley. GastroHep. 2020;2(1):6-12.
725 175. Khademi F, Faghri J, Poursina F, Esfahani BN, Moghim S, Fazeli H, Adibi P, Mirzaei N, Akbari M,
726 Safaei HG. Resistance pattern of Helicobacter pylori strains to clarithromycin, metronidazole, and

amoxicillin in Isfahan, Iran. Journal of Research in Medical Sciences: the official journal of Isfahan University of Medical Sciences. 2013;18(12):1056.
176. Peretz A, Paritsky M, Nasser O, Brodsky D, Glyatman T, Segal S, On A. Resistance of Helicobacter pylori to tetracycline, amoxicillin, clarithromycin and metronidazole in Israeli children and adults. The Journal of Antibiotics. 2014;67(8):555-7.
177. Chung JW, Lee GH, Jeong JY, Lee SM, Jung JH, Choi KD, Song HJ, Jung HY, Kim JH. Resistance of Helicobacter pylori strains to antibiotics in Korea with a focus on fluoroquinolone resistance. Journal of Gastroenterology and Hepatology. 2012;27(3):493-7.
178. Ghotaslou R, Milani M, Akhi MT, Hejazi MS, Nahaei MR, Hasani A, Sharifi Y. Relationship between drug resistance and cagA Gene in Helicobacter pylori. Jundishapur Journal of Microbiology. 2013;6(10).
179. Kostamo P, Veijola L, Oksanen A, Sarna S, Rautelin H. Recent trends in primary antimicrobial resistance of Helicobacter pylori in Finland. International Journal of Antimicrobial Agents. 2011;37(1):22-5.
180. Demiray-Gürbüz E, Yılmaz Ö, Olivares AZ, Gönen C, Sarıoğlu S, Soytürk M, Tümer S, Altungöz O, Şimşek İ, Perez Perez GI. Rapid identification of H elicobacter pylori and assessment of clarithromycin susceptibility from clinical specimens using FISH. The Journal of Pathology: Clinical Research. 2017;3(1):29-37.
181. Agudo S, Pérez-Pérez G, Alarcón T, López-Brea M. Rapid detection of clarithromycin resistant Helicobacter pylori strains in Spanish patients by polymerase chain reaction-restriction fragment length polymorphism. Revista espanola de quimioterapia: publicacion oficial de la Sociedad Espanola de Quimioterapia. 2011;24(1):32.
182. Matta AJ, Zambrano DC, Pazos AJ. Punctual mutations in 23S rRNA gene of clarithromycin-resistant Helicobacter pylori in Colombian populations. World Journal of Gastroenterology. 2018;24(14):1531.
183. Song Z, Zhang J, He L, Chen M, Hou X, Li Z, Zhou L. Prospective multi-region study on primary antibiotic resistance of Helicobacter pylori strains isolated from Chinese patients. Digestive and Liver Disease. 2014;46(12):1077-81.
184. Wüppenhorst N, Draeger S, Stüger HP, Hobmaier B, Vorreiter J, Kist M, Glocker E-O, Group RS. Prospective multicentre study on antimicrobial resistance of Helicobacter pylori in Germany. Journal of Antimicrobial Chemotherapy. 2014;69(11):3127-33.
185. Shi J, Jiang Y, Zhao Y. Promising in vitro and in vivo inhibition of multidrug-resistant Helicobacter pylori by linezolid and novel oxazolidinone analogues. Journal of Global Antimicrobial Resistance. 2016;7:106-9.
186. Talebi Bezmin Abadi A, Ghasemzadeh A, Taghvaei T, Mobarez AM. Primary resistance of Helicobacter pylori to levofloxacin and moxifloxacine in Iran. Internal and Emergency Medicine. 2012;7(5):447-52.
187. Boyanova L, Gergova G, Markovska R, Kandilarov N, Davidkov L, Spassova Z, Mitov I. Primary Helicobacter pylori resistance in elderly patients over 20 years: A Bulgarian study. Diagnostic microbiology and infectious disease. 2017;88(3):264-7.
188. Manfredi M, Gismondi P, Maffini V, Bizzarri B, Fornaroli F, Madia C, Salerno A, Cangelosi AM, de'Angelis GL. Primary antimicrobial susceptibility changes in children with Helicobacter pylori infection over 13 years in Northern Italy. Gastroenterology Research and Practice. 2015;2015.
189. Morilla AM, Álvarez-Argüelles ME, Duque JM, Armesto E, Villar H, Melón S. Primary antimicrobial resistance rates and prevalence of Helicobacter pylori infection in the north of Spain. A 13-year retrospective study. Gastroenterología y Hepatología (English Edition). 2019;42(8):476-85.
190. Vekens K, Vandebosch S, De Bel A, Urbain D, Mana F. Primary antimicrobial resistance of Helicobacter pylori in Belgium. Acta Clinica Belgica. 2013;68(3):183-7.

775 191. Maleknejad S, Mojtahedi A, Safaei-Asl A, Taghavi Z, Kazemnejad E. Primary antibiotic resistance
776 to Helicobacter pylori strains isolated from children in Northern Iran: a single center study. Iranian
777 journal of pediatrics. 2015;25(6).
778 192. Oleastro M, Cabral J, Ramalho PM, Lemos PS, Paixão E, Benoliel J, Santos A, Lopes AI. Primary
779 antibiotic resistance of Helicobacter pylori strains isolated from Portuguese children: a prospective
780 multicentre study over a 10 year period. Journal of antimicrobial chemotherapy. 2011;66(10):2308-11.
781 193. Zhang Y-X, Zhou L-Y, Song Z-Q, Zhang J-Z, He L-H, Ding Y. Primary antibiotic resistance of
782 Helicobacter pylori strains isolated from patients with dyspeptic symptoms in Beijing: a prospective
783 serial study. World journal of gastroenterology: WJG. 2015;21(9):2786.
784 194. Dargiene G, Kupcinskas J, Jonaitis L, Vezbavicius M, Kadusevicius E, Kupcinskiene E, Frandsen TH,
785 Kucinskiene R, Kupcinskas L, Andersen LP. Primary antibiotic resistance of Helicobacter pylori strains
786 among adults and children in a tertiary referral centre in Lithuania. Apmis. 2018;126(1):21-8.
787 195. Liu G, Xu X, He L, Ding Z, Gu Y, Zhang J, Zhou L. Primary antibiotic resistance of Helicobacter
788 pylori isolated from Beijing children. Helicobacter. 2011;16(5):356-62.
789 196. Liu D-S, Wang Y-H, Zeng Z-R, Zhang Z-Y, Lu H, Xu J-M, Du Y-Q, Li Y, Wang J-B, Xu S-P. Primary
790 antibiotic resistance of Helicobacter pylori in Chinese patients: a multiregion prospective 7-year study.
791 Clinical microbiology and infection. 2018;24(7):780. e5-. e8.
792 197. Tang X, Chen X, Shen Y, Yang T, Hu R, Debowski AW, Stubbs KA, Benghezal M, Marshall BJ, Li H.
793 Primary antibiotic resistance of Helicobacter pylori among a Chinese Tibetan population. Future
794 Microbiology. 2020;15(14):1353-61.
795 198. Bachir M, Allem R, Tifrit A, Medjekane M, Drici AE-M, Diaf M, Douidi KT. Primary antibiotic
796 resistance and its relationship with cagA and vacA genes in Helicobacter pylori isolates from Algerian
797 patients. brazilian journal of microbiology. 2018;49:544-51.
798 199. Seck A, Burucoa C, Dia D, Mbengue M, Onambele M, Raymond J, Breurec S. Primary antibiotic
799 resistance and associated mechanisms in Helicobacter pylori isolates from Senegalese patients. Annals
800 of clinical microbiology and antimicrobials. 2013;12(1):1-5.
801 200. Karczewska E, Wojtas-Bonior I, Sito E, Zwolińska-Wcisło M, Budak A. Primary and secondary
802 clarithromycin, metronidazole, amoxicillin and levofloxacin resistance to Helicobacter pylori in southern
803 Poland. Pharmacological Reports. 2011;63(3):799-807.
804 201. Lee JY, Kim N, Nam RH, In Choi S, Lee JW, Lee DH. Primary and secondary antibiotic resistance of
805 Helicobacter pylori in Korea from 2003 to 2018. Helicobacter. 2019;24(6):e12660.
806 202. Raaf N, Amhis W, Saoula H, Abid A, Nakmouche M, Balamane A, Ali Arous N, Ouar-Korichi M,
807 Vale FF, Bénéjat L. Prevalence, antibiotic resistance, and MLST typing of Helicobacter pylori in Algiers,
808 Algeria. Helicobacter. 2017;22(6):e12446.
809 203. Hansomburana P, Anantapanpong S, Sirinthornpunya S, Chuengyong K, Rojborwonwittaya J.
810 Prevalence of single nucleotide mutation in clarithromycin resistant gene of Helicobacter pylori: a 32-
811 months prospective study by using hybridization real time polymerase chain reaction. J Med Assoc Thai.
812 2012;95(3):S28-S35.
813 204. Mirzaei N, Poursina F, Faghri J, Talebi M, Khataminezhad MR, Hasanzadeh A, Safaei HG.
814 Prevalence of resistance of Helicobacter pylori strains to selected antibiotics in Isfahan, Iran.
815 Jundishapur Journal of Microbiology. 2013;6(5).
816 205. Lee JW, Kim N, Kim JM, Nam RH, Chang H, Kim JY, Shin CM, Park YS, Lee DH, Jung HC. Prevalence
817 of Primary and Secondary Antimicrobial Resistance of H elicobacter pylori in K orea from 2003 through
818 2012. Helicobacter. 2013;18(3):206-14.
819 206. Shokrzadeh L, Alebouyeh M, Mirzaei T, Farzi N, Zali MR. Prevalence of multiple drug-resistant
820 Helicobacter pylori strains among patients with different gastric disorders in Iran. Microbial Drug
821 Resistance. 2015;21(1):105-10.

207. Oporto M, Pavez M, Troncoso C, Cerda A, Hofmann E, Sierralta A, Rios E, Coppelli L, Barrientos L. Prevalence of infection and antibiotic susceptibility of Helicobacter pylori: an evaluation in public and private health systems of Southern Chile. Pathogens. 2019;8(4):226.
208. Aumpan N, Vilaichone R-K, Gumnarai P, Sanglutong L, Ratanachu-Ek T, Mahachai V, Yamaoka Y. Prevalence and antibiotic resistance patterns of Helicobacter pylori infection in Koh Kong, Cambodia. Asian Pacific Journal of Cancer Prevention: APJCP. 2020;21(5):1409.
209. Vilaichone R-k, Aumpan N, Ratanachu-Ek T, Uchida T, Tshering L, Mahachai V, Yamaoka Y. Population-based study of Helicobacter pylori infection and antibiotic resistance in Bhutan. International Journal of Infectious Diseases. 2020;97:102-7.
210. Cerqueira L, Fernandes RM, Ferreira RM, Carneiro F, Dinis-Ribeiro M, Figueiredo C, Keevil CW, Azevedo NF, Vieira MJ. PNA-FISH as a new diagnostic method for the determination of clarithromycin resistance of Helicobacter pylori. BMC microbiology. 2011;11(1):1-7.
211. Binyamin D, Pastukh N, On A, Paritsky M, Peretz A. Phenotypic and genotypic correlation as expressed in Helicobacter pylori resistance to clarithromycin and fluoroquinolones. Gut Pathogens. 2017;9(1):1-8.
212. Camorlinga-Ponce M, Gómez-Delgado A, Aguilar-Zamora E, Torres RC, Giono-Cerezo S, Escobar-Ogaz A, Torres J. Phenotypic and genotypic antibiotic resistance patterns in Helicobacter pylori strains from ethnically diverse population in Mexico. Frontiers in Cellular and Infection Microbiology. 2021;10:539115.
213. Biernat MM, Bińkowska A, Łaczmański Ł, Biernat P, Krzyżek P, Gościniak G. Phenotypic and genotypic analysis of resistant Helicobacter pylori strains isolated from children with gastrointestinal diseases. Diagnostics. 2020;10(10):759.
214. Trespalacios AA, Otero W, Caminos JE, Mercado MM, Ávila J, Rosero LE, Arévalo A, Poutou-Piñales RA, Graham DY. Phenotypic and genotypic analysis of clarithromycin-resistant Helicobacter pylori from Bogotá DC, Colombia. Journal of Microbiology. 2013;51(4):448-52.
215. Lok C-H, Zhu D, Wang J, Ren Y-T, Jiang X, Li S-J, Zhao X-Y. Phenotype and Molecular Detection of Clarithromycin and Levofloxacin Resistance in Helicobacter pylori Clinical Isolates in Beijing. Infection and Drug Resistance. 2020;13:2145.
216. Bahmaninejad P, Ghafourian S, Mahmoudi M, Maleki A, Sadeghifard N, Badakhsh B. Persister cells as a possible cause of antibiotic therapy failure in Helicobacter pylori. Jgh Open. 2021;5(4):493-7.
217. Draeger S, Wüppenhorst N, Kist M, Glocker E-O. Outcome of second-and third-line Helicobacter pylori eradication therapies based on antimicrobial susceptibility testing. Journal of Antimicrobial Chemotherapy. 2015;70(11):3141-5.
218. Zerbetto De Palma G, Mendiondo N, Wonaga A, Viola L, Ibarra D, Campitelli E, Salim N, Corti R, Goldman C, Catalano M. Occurrence of mutations in the antimicrobial target genes related to levofloxacin, clarithromycin, and amoxicillin resistance in Helicobacter pylori isolates from Buenos Aires City. Microbial Drug Resistance. 2017;23(3):351-8.
219. Boyanova L, Ilieva J, Gergova G, Davidkov L, Spassova Z, Kamburov V, Katsarov N, Mitov I. Numerous risk factors for Helicobacter pylori antibiotic resistance revealed by extended anamnesis: a Bulgarian study. Journal of medical microbiology. 2012;61(1):85-93.
220. Tshibangu-Kabamba E, Ngoma-Kisoko PdJ, Tuan VP, Matsumoto T, Akada J, Kido Y, Tshimpi-Wola A, Tshiamala-Kashala P, Ahuka-Mundeke S, Mumba Ngoy D. Next-generation sequencing of the whole bacterial genome for tracking molecular insight into the broad-spectrum antimicrobial resistance of Helicobacter pylori clinical isolates from the Democratic Republic of Congo. Microorganisms. 2020;8(6):887.
221. Okuda M, Kikuchi S, Mabe K, Osaki T, Kamiya S, Fukuda Y, Kato M. Nationwide survey of Helicobacter pylori treatment for children and adolescents in Japan. Pediatrics International. 2017;59(1):57-61.

870 222. Vilaichone R-k, Gumnarai P, Ratanachu-Ek T, Mahachai V. Nationwide survey of Helicobacter
871 pylori antibiotic resistance in Thailand. Diagnostic Microbiology and Infectious Disease. 2013;77(4):346-
872 9.
873 223. Zhang S, Wang X, Wise MJ, He Y, Chen H, Liu A, Huang H, Young S, Tay CY, Marshall BJ.
874 Mutations of Helicobacter pylori RdxA are mainly related to the phylogenetic origin of the strain and not
875 to metronidazole resistance. Journal of Antimicrobial Chemotherapy. 2020;75(11):3152-5.
876 224. Zhang Y, Wen Y, Xiao Q, Zheng W, Long G, Chen B, Shu X, Jiang M. Mutations in the antibiotic
877 target genes related to clarithromycin, metronidazole and levofloxacin resistance in Helicobacter pylori
878 strains from children in China. Infection and drug resistance. 2020;13:311.
879 225. Mansour KB, Fendri C, Battikh H, Garnier M, Zribi M, Jlizi A, Burucoa C. Multiple and mixed
880 Helicobacter pylori infections: comparison of two epidemiological situations in Tunisia and France.
881 Infection, Genetics and Evolution. 2016;37:43-8.
882 226. Kuo C-J, Lee C-H, Chang M-L, Lin C-Y, Lin W-R, Su M-Y, Chiu C-H, Tseng C-N, Wu Y-S, Chiu C-T.
883 Multidrug resistance: the clinical dilemma of refractory Helicobacter pylori infection. Journal of
884 Microbiology, Immunology and Infection. 2021;54(6):1184-7.
885 227. Miendje Deyi VY, Bontems P, Vanderpas J, De Koster E, Ntounda R, Van den Borre C, Cadranel S,
886 Burette A. Multicenter survey of routine determinations of resistance of Helicobacter pylori to
887 antimicrobials over the last 20 years (1990 to 2009) in Belgium. Journal of clinical microbiology.
888 2011;49(6):2200-9.
889 228. Han R, Lu H, Jiang M-W, Tan K-W, Peng Z, Hu J-L, Fang D-C, Lan C-H, Wu X-L. Multicenter study of
890 antibiotic resistance profile of H. pylori and distribution of CYP2C19 gene polymorphism in rural
891 population of Chongqing, China. Gastroenterology research and practice. 2016;2016.
892 229. Bińkowska A, Biernat MM, Łaczmański Ł, Gościniak G. Molecular patterns of resistance among
893 Helicobacter pylori strains in south-western Poland. Frontiers in microbiology. 2018;9:3154.
894 230. Bachir M, Allem R, Benejat L, Tifrit A, Medjekane M, Drici AE-M, Megraud F, Douidi KT.
895 Molecular detection of mutations involved in Helicobacter pylori antibiotic resistance in Algeria. Journal
896 of Antimicrobial Chemotherapy. 2018;73(8):2034-8.
897 231. Hanafiah A, Binmaeil H, Ali RAR, Rose IM, Lopes BS. Molecular characterization and prevalence
898 of antibiotic resistance in Helicobacter pylori isolates in Kuala Lumpur, Malaysia. Infection and drug
899 resistance. 2019;12:3051.
900 232. Vazirzadeh J, Falahi J, Moghim S, Narimani T, Rafiei R, Karbasizadeh V. Molecular assessment of
901 resistance to clarithromycin in Helicobacter pylori strains isolated from patients with dyspepsia by
902 fluorescent in situ hybridization in the center of Iran. BioMed Research International. 2020;2020.
903 233. Rezaei S, Abadi ATB, Mobarez AM. Metronidazole-resistant Helicobacter pylori isolates without
904 rdxA mutations obtained from Iranian dyspeptic patients. New Microbes and New Infections.
905 2020;34:100636.
906 234. Yakoob J, Abid S, Jafri W, Abbas Z, Mumtaz K, Hamid S, Ahmed R. Low rate of recurrence of
907 Helicobacter Pylori infection in spite of high clarithromycin resistance in Pakistan. BMC
908 gastroenterology. 2013;13(1):1-7.
909 235. Gehlot V, Mahant S, Mukhopadhyay AK, Das K, Alam J, Ghosh P, Das R. Low prevalence of
910 clarithromycin-resistant Helicobacter pylori isolates with A2143G point mutation in the 23S rRNA gene
911 in North India. Journal of Global Antimicrobial Resistance. 2016;6:39-43.
912 236. Boyanova L, Ilieva J, Gergova G, Evstatiev I, Nikolov R, Mitov I. Living in Sofia is associated with a
913 risk for antibiotic resistance in Helicobacter pylori: a Bulgarian study. Folia microbiologica.
914 2013;58(6):587-91.
915 237. Boyanova L, Evstatiev I, Gergova G, Yaneva P, Mitov I. Linezolid susceptibility in Helicobacter
916 pylori, including strains with multidrug resistance. International journal of antimicrobial agents.
917 2015;46(6):703-6.

238. Otth L, Wilson M, Fernández H, Otth C, Toledo C, Cárcamo V, Rivera P, Ruiz L. Isolation of Helicobacter pylori in gastric mucosa and susceptibility to five antimicrobial drugs in Southern Chile. Brazilian Journal of Microbiology. 2011;42:442-7.
239. McNulty C, Lasseter G, Shaw I, Nichols T, D'Arcy S, Lawson A, Glocker E. Is H elicobacter pylori antibiotic resistance surveillance needed and how can it be delivered? Alimentary pharmacology & therapeutics. 2012;35(10):1221-30.
240. Wang B, Zhao Q, Yin W, Yuan Y, Wang X, Wang Y-h, Wang H, Ye W, Chen S, Guo H-l. In-vitro characterisation of a novel antimicrobial agent, TNP-2092, against Helicobacter pylori clinical isolates. Swiss Medical Weekly. 2018;148(2930).
241. Alavifard H, Mirzaei N, Yadegar A, Baghaei K, Smith SM, Sadeghi A, Zali MR. Investigation of Clarithromycin Resistance-Associated Mutations and Virulence Genotypes of Helicobacter pylori Isolated from Iranian Population: A Cross-Sectional Study. Current Microbiology. 2021;78(1):244-54.
242. Regnath T, Raecke O, Enninger A, Ignatius R. Increasing metronidazole and rifampicin resistance of Helicobacter pylori isolates obtained from children and adolescents between 2002 and 2015 in southwest Germany. Helicobacter. 2017;22(1):e12327.
243. Lu HH, Lai FP, Lo HY, Sheu BS, Yang YJ. Increasing antimicrobial resistance to clarithromycin and metronidazole in pediatric Helicobacter pylori infection in southern Taiwan: a comparison between two decades. Helicobacter. 2019;24(5):e12633.
244. Di Giulio M, Di Campli E, Di Bartolomeo S, Cataldi V, Marzio L, Grossi L, Ciccaglione AF, Nostro A, Cellini L. In vitro antimicrobial susceptibility of Helicobacter pylori to nine antibiotics currently used in Central Italy. Scandinavian journal of gastroenterology. 2016;51(3):263-9.
245. Enany S, Abdalla S. In vitro antagonistic activity of Lactobacillus casei against Helicobacter pylori. Brazilian Journal of Microbiology. 2015;46:1201-6.
246. Trespalacios AA, Rimbara E, Otero W, Reddy R, Graham DY. Improved allele-specific PCR assays for detection of clarithromycin and fluoroquinolone resistant of Helicobacter pylori in gastric biopsies: identification of N87I mutation in GyrA. Diagnostic microbiology and infectious disease. 2015;81(4):251-5.
247. Gatta L, Scarpignato C, Fiorini G, Belsey J, Saracino I, Ricci C, Vaira D. Impact of primary antibiotic resistance on the effectiveness of sequential therapy for Helicobacter pylori infection: lessons from a 5-year study on a large number of strains. Alimentary Pharmacology & Therapeutics. 2018;47(9):1261-9.
248. Goudarzi M, Seyedjavadi SS, Fazeli M, Roshani M, Azad M, Heidary M, Navidinia M, Goudarzi H. Identification of a novel cassette array in integronbearing Helicobacter Pylori strains isolated from Iranian patients. Asian Pacific Journal of Cancer Prevention. 2016;17(7):3309-15.
249. Bayati S, Alebouyeh M, Amirmozafari N, Ebrahimi Daryani N, Talebi M, Zali MR. Histological changes in refractory Helicobacter pylori infection and its relationship with increased levels of resistance to antibiotics and therapeutic regimens: one-year follow-up. Apmis. 2020;128(1):25-34.
250. Dang NQH, Ha TMT, Nguyen S-T, Le NDK, Nguyen TMT, Nguyen TH, Pham TTH. High rates of clarithromycin and levofloxacin resistance of Helicobacter pylori in patients with chronic gastritis in the south east area of Vietnam. Journal of Global Antimicrobial Resistance. 2020;22:620-4.
251. Phan TN, Santona A, Tran TNH, Cappuccinelli P, Rubino S, Paglietti B. High rate of levofloxacin resistance in a background of clarithromycin-and metronidazole-resistant Helicobacter pylori in Vietnam. International journal of antimicrobial agents. 2015;45(3):244-8.
252. Khashei R, Dara M, Bazargani A, Bagheri Lankarani K, Taghavi A, Moeini M, Dehghani B, Sohrabi M. High rate of A2142G point mutation associated with clarithromycin resistance among Iranian Helicobacter pylori clinical isolates. Apmis. 2016;124(9):787-93.
253. Shetty V, Lamichhane B, Tay CY, Pai GC, Lingadakai R, Balaraju G, Shetty S, Ballal M, Chua EG. High primary resistance to metronidazole and levofloxacin, and a moderate resistance to clarithromycin in Helicobacter pylori isolated from Karnataka patients. Gut pathogens. 2019;11(1):1-8.

966 254. Macías-García F, Llovo-Taboada J, Díaz-López M, Bastón-Rey I, Domínguez-Muñoz JE. High
967 primary antibiotic resistance of Helicobacter pylori strains isolated from dyspeptic patients: a prevalence
968 cross-sectional study in Spain. Helicobacter. 2017;22(6):e12440.
969 255. Farzi N, Yadegar A, Sadeghi A, Asadzadeh Aghdaei H, Marian Smith S, Raymond J, Suzuki H, Zali
970 MR. High prevalence of antibiotic resistance in Iranian Helicobacter pylori isolates: importance of
971 functional and mutational analysis of resistance genes and virulence genotyping. Journal of clinical
972 medicine. 2019;8(11):2004.
973 256. Lyu T, Cheung KS, Ni L, Guo J, Mu P, Li Y, Yang Q, Yu X, Lyu Z, Wu J. High prevalence and risk
974 factors of multiple antibiotic resistance in patients who fail first-line Helicobacter pylori therapy in
975 southern China: a municipality-wide, multicentre, prospective cohort study. Journal of Antimicrobial
976 Chemotherapy. 2020;75(11):3391-4.
977 257. Shmuely H, Topaz S, Berdinstein R, Yahav J, Melzer E. High Metronidazole and Clarithromycin
978 Resistance of Helicobacter Pylori Isolated from Previously Treated and Naïve Patients. The Israel Medical
979 Association Journal: IMAJ. 2020;22(10):562-6.
980 258. Ogata SK, Godoy APO, da Silva Patricio FR, Kawakami E. High Helicobacter pylori resistance to
981 metronidazole and clarithromycin in Brazilian children and adolescents. Journal of pediatric
982 gastroenterology and nutrition. 2013;56(6):645-8.
983 259. Abadi AT, Taghvaei T, Ghasemzadeh A, Mobarez AM. High frequency of A2143G mutation in
984 clarithromycin-resistant Helicobacter pylori isolates recovered from dyspeptic patients in Iran. Saudi
985 journal of gastroenterology: official journal of the Saudi Gastroenterology Association. 2011;17(6):396.
986 260. korn Vilaichone R, Gamnarai P, Subsomwong P, Uchida T, Yamaoka Y, Mahachai V. High
987 fluoroquinolone resistant strains of Helicobacter pylori in the Golden triangle. Asian Pacific Journal of
988 Cancer Prevention: APJCP. 2017;18(2):455.
989 261. Ferenc S, Gnus J, Kościelna M, Kinda M, Yarka A, Stewart L, Witkiewicz W. High antibiotic
990 resistance of Helicobacter pylori and its effect on tailored and empiric eradication of the organism in
991 Lower Silesia, Poland. Helicobacter. 2017;22(2):e12365.
992 262. Azzaya D, Gantuya B, Oyuntsetseg K, Davaadorj D, Matsumoto T, Akada J, Yamaoka Y. High
993 antibiotic resistance of Helicobacter pylori and its associated novel gene mutations among the
994 Mongolian population. Microorganisms. 2020;8(7):1062.
995 263. Mi M, Wu F, Zhu J, Liu F, Cui G, Wen X, Hu Y, Deng Z, Wu X, Zhang Z. Heterogeneity of
996 Helicobacter pylori strains isolated from patients with gastric disorders in Guiyang, China. Infection and
997 Drug Resistance. 2021;14:535.
998 264. Boyanova L, Davidkov L, Gergova G, Kandilarov N, Evstatiev I, Panteleeva E, Mitov I. Helicobacter
999 pylori susceptibility to fosfomycin, rifampin, and 5 usual antibiotics for H. pylori eradication. Diagnostic
1000 microbiology and infectious disease. 2014;79(3):358-61.
1001 265. Boyanova L, Gergova G, Evstatiev I, Spassova Z, Kandilarov N, Yaneva P, Markovska R, Mitov I.
1002 Helicobacter pylori resistance to six antibiotics by two breakpoint systems and resistance evolution in
1003 Bulgaria. Infectious Diseases. 2016;48(1):56-62.
1004 266. Megraud F, Bruyndonckx R, Coenen S, Wittkop L, Huang T-D, Hoebeke M, Bénéjat L, Lehours P,
1005 Goossens H, Glupczynski Y. Helicobacter pylori resistance to antibiotics in Europe in 2018 and its
1006 relationship to antibiotic consumption in the community. Gut. 2021;70(10):1815-22.
1007 267. Megraud F, Coenen S, Versporten A, Kist M, Lopez-Brea M, Hirschl AM, Andersen LP, Goossens
1008 H, Glupczynski Y. Helicobacter pylori resistance to antibiotics in Europe and its relationship to antibiotic
1009 consumption. Gut. 2013;62(1):34-42.
1010 268. Ducournau A, Bénéjat L, Sifré E, Bessède E, Lehours P, Mégraud F. Helicobacter pylori resistance
1011 to antibiotics in 2014 in France detected by phenotypic and genotypic methods. Clinical Microbiology
1012 and Infection. 2016;22(8):715-8.

269. Bouihat N, Burucoa C, Benkirane A, Seddik H, Sentissi S, Al Bouzidi A, Elouennas M, Benouda A. Helicobacter pylori primary antibiotic resistance in 2015 in Morocco: a phenotypic and genotypic prospective and multicenter study. Microbial Drug Resistance. 2017;23(6):727-32.
270. Fernández-Reyes M, Tamayo E, Rojas-Rengifo D, Fischer W, Carrasco-García E, Alonso M, Lizasoain J, Bujanda L, Cosme Á, Montes M. Helicobacter pylori pathogenicity and primary antimicrobial resistance in Northern Spain. European Journal of Clinical Investigation. 2019;49(8):e13150.
271. Saniee P, HosseinI F, Kadkhodaei S, Siavoshi F, Khalili-Saman S. Helicobacter pylori multidrug resistance due to misuse of antibiotics in Iran. Archives of Iranian Medicine. 2018;21(7):283-8.
272. MOKHTAR NA, Muttaqillah NAS, Hussin S, Soh TST. Helicobacter pylori Infection: Prevalence, Demographic Characteristics, Clarithromycin Resistance and Evaluation of the In-House Rapid Urease Test in Sungai Buloh Hospital, Malaysia. Sains Malaysiana. 2019;48(12):2675-82.
273. Montes M, Villalon FN, Eizaguirre FJ, Delgado M, Muñoz-Seca IM, Fernández-Reyes M, Pérez-Trallero E. Helicobacter pylori infection in children. Antimicrobial resistance and treatment response. Helicobacter. 2015;20(3):169-75.
274. Deyi VYM, Burette A, Ntounda R, Elkilic O, Cadranel S, Bontems P, Hallin M. Update of primary Helicobacter pylori resistance to antimicrobials in Brussels, Belgium. Diagnostic Microbiology and Infectious Disease. 2019;95(4):114875.
275. Tang X, Shen Y, Hu R, Yang T, Benghezal M, Li H, Tang H. Re-assessment of the disk diffusion technique for routine antimicrobial susceptibility testing for Helicobacter pylori. Helicobacter. 2020;25(4):e12703.

Table 1(on next page)

A systematic search including PubMed, Embase, and Web of Science with relevant keywords such as clarithromycin, antibiotic resistance, and *Helicobacter pylori*.

First author (Reference)	Country	Enrollment time	Published Year	Type of study	N. patients	Mean age	N. HP	N. Clarithromycin-resistant	AST method	Breakpoint
Horie et al. (28)	Japan	2005-2018	2020	RET	5249	58.3	1300	426	MIC	1
Haddadi et al.(29)	Iran		2020	CS	280	46	128	3	DD	CLSI 2015 21
Eisig et al.(30)	Brazil		2011	PCS	54	46.6	39	3	MIC	1
Aftab et al.(31)	Bangladesh	2014-2014	2015	CS	133	35.2	56	22	MIC	0.25
Ortiz et al.(32)	Honduras	2013-2013	2019	CS	189	54	116	13	MIC	0.5
Silva et al.(33)	Portugal	2013-2017	2018	PCS	74	14	58	7	MIC	1
Almeid et al.(34)	Portugal	2009-2013	2014	PCS	180	43.4	180	90	MIC	1
Ilie et al.(35)	Romania		2011	CS	100	Range: 19–80	70	22	DD	>20 CLSI 2010
Ve´Csei et al.(36)	Austria	2007-2009	2011	RET	96	10.8	96	16	MIC	1
Ranjbar et al.(37)	Iran	2016-2017	2018	CS	700	Range: 3–72	526	335	DD	21
Hamza et al.(38)	Egypt		2018	CS	150		20	12	DD	21
Gong et al.(39)	South Korea	2017-2018	2020	RET	13		46	38	MIC	0.5
Wang et al.(40)	China	2018-2019	2020	CS	124		124	44	MIC	0.5
Su et al.(41)	Taiwan	2009-2019	2021	RET	87	13.5	65	15	MIC	1
Sugimo-et al.(42)	Japan	2011-2015	2016	RET	111	55.2	111	90	MIC	1
Abadi et al.(43)	Iran	2009-2009	2011	CS	210	40.7	197	89	DD	30
Teh et al.(44)	Malaysia		2014	CS	110		102	7	MIC	1
Peng et al.(45)	China	2013-2014	2017	CS	178	41.6	78	38	MIC	1
Hashemi et al.(46)	Iran	2015-2016	2019	CS	150		157	38	MIC	1
Lauener et al.(47)	Switzerland	2013-2017	2019	CS	140		140	96	MIC	1
Domanovich et al.(48)	Israel	2015–2019	2020	CS	48		48	26	MIC	1
Wu et al.(49)	Taiwan	2010-2014	2015	RET	137		137	95	MIC	1
Hakemi Vala et al.(50)	Iran	2011-2012	2016	CS	80		20	4	MIC	0.5
Omar et al.(51)	Australia		2014	CS	11	46.8	11	8	MIC	1
Vilaichone et al.(52)	Thailand	2013-2013	2016	CS	291	46.6	124	7	MIC	0.5
Lee et al.(53)	South Korea	2003-2013	2014	PCS	2202	52.9	475	147	MIC	1
Lee et al.(54)	South Korea	2014-2018	2018	PCS	85	55.2	74	24	MIC	1
Goudarzi et al.(55)	Iran	2014-2014	2016	CS	65	42	65	28	MIC	1
Karpinski et al.(56)	Poland	1998-1999 2013-2014	2015	CS	108		108	9	MIC	1
Miyata et al.(57)	Japan	2007-2018	2020	CS	119	12	45	26	MIC	1
Palmitessa et al.(58)	Italy	2017-2018	2020	CS	224	48.6	92	49	MIC	0.5
Hung et al.(59)	Taiwan	2016-2019	2021	RET	197	54.8	62	9	MIC	1
Miftahussurur et al.(60)	Japan	2012-2012	2016	CS	146	42.2	42	9	MIC	0.25
Siddiqui et al.(61)	Pakistan	2008-2013	2016	CS	889	35.6	92	5	MIC	0.5
Sugimo-et al.(62)	Japan	2009-2013	2014	CS	153		153	64	MIC	1

Jolaiya et al.(63)	Nigeria		2020	CS	492		104	41	MIC	0.5
Pandya et al.(64)	India	2008-2011	2014	CS	125		80	47	DD	30
Lehours et al.(65)	France	2009-2009	2011	CS	127		43	26	MIC	0.5
Sun et al.(66)	China		2018	CS	49	range: 27-76	43	9	MIC	0.75
Dekhnich et al.(67)	Russia	2009-2017	2018	CS	783	51.8	276	16	MIC	0.5
Sugimo-et al.(68)	Japan	2015-2019	2020	RET	307	62.3	307	102	MIC	1
Siavoshi et al.(69)	Iran		2018	CS	450	44.1	104	37	MIC	2
Szadkowski et al.(70)	Poland	2005-2015	2018	CS	154		55	15	DD	21
Costa et al.(71)	Portugal	2012-2016	2017	RET	42	48.9	42	36	DD	17
Correa et al.(72)	Spain		2016	CS	136		84	48	MIC	0.5
Akar et al.(73)	Turkey	2018-2019	2021	CS	422	50	133	25	MIC	0.5
Yula et al.(74)	Turkey	2010-2011	2012	CS	110	41.4	79	7	MIC	1
Zhang et al.(75)	China	2015-2016	2018	CS	150		149	104	MIC	1
Maçin et al. (76)	Turkey	2006-2012	2015	CS	311	Range: 5-19	93	28	MIC	1
Auttajaroon et al.(77)	Thailand	2017-2017	2019	CS	93	54.5	70	9	MIC	0.5
Eghbali et al.(78)	Iran	2012-2013	2016	CS	89	53.6	89	5	MIC	1
Wu et al.(79)	Taiwan		2014	CS	231		43	5	MIC	1
Kocazeybek et al.(80)	Turkey	2014-2017	2019	CS	63	47.08	63	24	MIC	1
Egli et al.(81)	Switzerland	2013-2017	2020	CS	76		76	49	MIC	1
Khani et al.(82)	Iran	2017-2018	2019	CS	81	56.8	61	13	MIC	0.5
Morimo-et al.(83)	Japan		2014	RET	135	62.3	135	35	MIC	1
Millan et al.(84)	Mexico		2016	CS	144	48.3	45	8	DD	18
Tamayo et al.(85)	Spain	2013-2015	2017	CS	6228		1986	349	MIC	1
Yoon et al.(86)	South Korea	2005-2010	2014	RET	204	52.5	212	18	MIC	1
Miftahussurur et al.(87)	Dominican		2017	CS	158	47.1	64	2	MIC	8
Kargar et al.(88)	Iran	2007-2007	2011	CS	263		84	19	MIC	1
Tran et al. (89)	Vietnam	2012-2017	2018	CS	185	42.3	104	56	MIC	1
Tanih et al.(90)	South Africa		2011	CS	254	44.5	200	40	MIC	1
Yeganeh et al.(91)	Israel	2016-2016	2019	PCS	218	42	218	96	MIC	1
Liu et al.(92)	China	2010-2017	2019	RET	1463		1463	296	MIC	0.5
Zhu et al.(93)	China	2002-2006	2012	CS	365		365	42	MIC	1
Farzi et al.(94)	Iran	2014-2015	2018	CS	97	Ranging 10-70	40	14	MIC	0.25
Abdollahi et al.(95)	Iran	2017-2018	2019	CS	191	38.2	63	20	DD	21
Lee et al.(96)	South Korea	2015-2018	2018	CS	1422		140	43	MIC	0.5
De Francesco et al.(97)	Italy	2011-2012	2014	CS	82		82	42	MIC	0.5
Seo et al.(98)	South Korea	1990–1994 2005–2009	2013	CS	91	11.8	91	10	MIC	1
Mabeku et al.(99)	Cameroon	2013-2015	2019	CS	140		140	19	DD	21
Yin et al.(100)	China	2016-2016	2016	CS	267	9.4	169	57	MIC	1
Chen et al.(101)	China		2018	CS	12		12	6	MIC	1
Kakiuchi et al.(102)	Japan	2018-2018	2020	CS	71	14.7 years	23	7	MIC	0.5
Lavi´N et al.(103)	Spain	2010-2010	2011	CS	76		68	10	MIC	2

Gehlot et al.(104)	India	2011-2014	2015	CS	68	Range: 18-86	68	8	MIC	0.5
Ogata et al.(105)	Brazil	2008-2009	2014	CS	77	11.1	77	16	MIC	1
Eng et al.(106)	Canada	2012-2013	2015	CS	301		20	8	MIC	0.5
AlarcoN et al.(107)	Spain	2007-2014	2017	CS	824	26	824	422	MIC	0.5
Akhtereeva et al.(108)	Russia	2011-2013	2018	CS	76	13.6	30	9	DD	30
Selgrad et al.(109)	Germany	2005-2012	2013	RET	436	51.7	159	12	MIC	1
Gunnarsdottir et al.(110)	Iceland	2012-2013	2017	PRO	613	57	105	9	MIC	1
Mahmoudi et al.(111)	Iran	2014-2015	2017	CS	90	9.4	32	7	MIC	1
Shokrzadeh et al.(112)	Iran	2007-2008	2010	CS	92	45±18 M 38±14 F	42	6	MIC	1
Savari et al.(113)	Iran	2009-2009	2010	CS	191	Range: 14-84	63	19	DD	21
Shu et al.(114)	China	2012-2014	2018	CS	1390	9.5	545	112	MIC	8
Mosites et al.(115)	Usa	2000-2016	2018	CS	763	52	800	238	MIC	1
Parra-Sepulveda et al.(116)	Chile	2005-2007 2015-2017	2019	CS	1655	48.8	405	96	DD	21
Fiorini et al.(117)	Italy	2010-2016	2018	CS	1730	51.1	1424	114	MIC	0.5
Shao et al.(118)	China	2013-2016	2017	CS	2283		2283	519	MIC	1
Li et al.(119)	China	2019-2019	2021	CS	157	10.9	87	48	MIC	0.5
Su et al.(120)	China	2010-2012	2013	CS	51891		17731	3810	MIC	1
Hojsak et al.(121)	Croatia	2001-2010	2012	RET	2313	12.9	168	20	MIC	1
Hamidi et al.(122)	Iran	2017-2018	2020	CS	80	50.2	50	11	MIC	0.5
An et al.(123)	Korea	2009-2012	2013	RET	165		165	20	MIC	1
Shiota et al.(124)	Usa	2009-2013	2015	CS	656		128	6	MIC	1
Li et al.(125)	China	2009-2015	2017	RET	5610	14	1746	286	MIC	1
Erdene et al.(126)	Mongolia	2011-2014	2017	CS	320	43.7	152	54	MIC	1
Boehnke et al.(127)	Peru	2011-2013	2017	CS	109		76	27	MIC	0.5
Ahmad et al.(128)	Malaysia	2004-2007	2011	CS	777		187	4	MIC	1
Rasheed et al.(129)	Usa	2011-2012	2014	CS	93	47.4	46	22	MIC	1
Guo et al.(130)	China	2016-2017	2018	CS	346	Range: 1-15	22	8	MIC	1
Jiang et al.(131)	China	2017-2019	2021	CS	1533		1533	721	MIC	0.5
Butenko et al.(132)	Slovenia	2011-2014	2017	RET	107	12	104	25	MIC	8
Tveit et al.(133)	Alaska	2000-2008	2011	CS	1181	51	531	159	MIC	1
Tuan et al.(134)	Vietnam		2019	CS	206	45.3	55	14	MIC	8
Maev et al.(135)	Russia	2015-2018	2020	CS	27		27	3	MIC	0.5
Figueroa et al.(136)	Colombia		2012	CS	203	40	146	29	MIC	1
Kim et al.(137)	Korea	2008-2008	2011	CS	99	54.6	99	26	MIC	1
Adeniyi et al.(138)	Nigeria		2012	CS	52	Range: 10-90	43	3	DD	30
Yao et al.(139)	Taiwan	2013-2014	2019	RET	719	61.2	41	14	MIC	1
Honma et al.(140)	Japan	2012-2015	2018	CS	1298	14	13	5	MIC	1
Bayati et al.(141)	Iran	2014-2015	2019	CS	170	Range: 30-75	55	27	MIC	0.5
Pichon et al.(142)	France	2012–2014	2020	CS	3	33.3	189	1	MIC	0.5
Tanabe et al.(143)	Japan	2013-2016	2018	RET	1355		212	50	MIC	1
Karabiber et al.(144)	Turkey.		2014	CS	159		98	23	DD	30

Saracino et al.(145)	Italy	2009-2019	2020	NA	3178	52.3	1646	553	MIC	0.5
Liang et al.(146)	Taiwan	2013-2019	2020	RET	1369	54.0±11.9	1369	226	MIC	1
Khademi et al.(147)	Iran	2011-2012	2014	CS	130		30	4	MIC	1
Milani et al.(148)	Iran	2010-2011	2012	CS	395	35 ± 19	112	16	MIC	1
Famouri et al.(149)	Iran	2015-2018	2018	CS	102	8.65± 3.88	48	17	MIC	2
Bruce et al.(150)	Alaska	1998-2006	2019	PRO	362		260	74	MIC	1
Park et al.(151)	Korea	2017-2019	2020	PRO	174		70	20	MIC	0.5
Binh et al.(152)	Vietnam	2008-2008	2013	CS	103	44.8	103	34	MIC	1
Azizi Raftar et al.(153)	Iran		2013	CS	246	45.78 ±16.23	95	32	MIC	1
Ang et al.(154)	Singapore	2000-2014	2016	RET	708		708	97	MIC	1
Gościniak et al.(155)	Poland	2008-2011	2014	CS	165		165	50	MIC	1
Wang et al.(156)	China	1998-2017	2019	CS	454	50.74 ± 10.942	100	31	MIC	1
Bai et al.(157)	China	2013-2013	2015	CS	181	44.9	181	56	MIC	0.5
Mégraud et al.(158)	France	2014-2018	2020	CS	951	52.4 ± 15.7	741	157	MIC	0.5
Sadeghifard et al.(159)	Iran	2009-2010	2013	CS	50		50	16	DD	20
Bedoya-Gómez et al.(160)	Colombia		2019	PRO	115	41.8	61	5	MIC	0.5
Miftahussurur et al.(161)	Japan	2012-2015	2016	PRO	849	49.25	77	7	MIC	0.25
Erkut et al.(162)	Turkey	2010-2011	2020	PRO	344	39.3	104	29	MIC	1
Zhang et al.(163)	China	2013	2018	CS	394		136	10	MIC	1
Tsay et al.(164)	Taiwan	2005-2009	2011	RET	233	55.7	32	2	MIC	1
Mascellino et al.(165)	Italy	2017	2020	RET	80	59	80	28	MIC	0.5
Khoury et al.(166)	Israel	2012-2015	2017	RET	107		64	26	MIC	0.5
Saracino et al.(167)	Italy	2016-2019	2020	RET	270	51.4	221	202	MIC	0.5
Lin et al.(168)	Taiwan	2008-2017	2019	RET	490	54.5	228	33	MIC	1
Alfizah et al.(169)	Malaysia	2004-2007	2014	CS	99		161	2	MIC	1
Fasciana et al.(170)	Italy		2015	CS	100		100	25	MIC	0.5
Ayala et al.(171)	Mexico	2002-2004	2011	CS /PRO	460		90	9	MIC	2
Picoli et al.(172)	Brazil	2011-2012	2014	CS	342		54	6	MIC	1
L. Larsen et al.(173)	Norway	2008-2009	2012	CS	NA		102	6	MIC	0.5
Kumar et al.(174)	Usa	2009-2019	2019	RET	109		65	39	MIC	0.5
Khademi et al.(175)	Iran	2011-2012	2013	CS	260	45.8 ± 17.8	78	12	MIC	1
Peretz et al.(176)	Israel	2011– 2012	2014	CS	176		85	20	MIC	1
Chung et al.(177)	Korea	2004-2007	2011	CS	185	50.7 ± 14.4	185	20	MIC	1
Ghotaslou et al.(178)	Iran		2013	CS	123	35 ± 18	123	21	DD	30
Kostamo et al.(179)	Finland	2000–2008	2010	RET	3045	62	1037	83	MIC	1
Gürbüz et al.(180)	Turkey	2006-2011	2016	CS	234	43.8±14.0	114	32	MIC	1
Agudo et al.(181)	Usa	2008	2011	CS	118		118	42	MIC	1
Matta et al.(182)	Colombia		2018	CS	409		74	34	MIC	1
Song et al.(183)	China	2008-2012	2014	PRO/C S	600	42.5±13.2	600	225	MIC	0.5
Wu¨Ppenhorst et al.(184)	Germany	2001-2012	2014	PRO	1651		1523	475	MIC	1
Shi et al.(185)	China		2016	CS	328		328	78	MIC	1

Talebi et al.(186)	Iran	2009-2010	2011	CS	170	38.6	150	51	MIC	1
Boyanova et al.(187)	Bulgaria	2011-2016	2017	CS	233	59.1	233	60	MIC	0.5
Manfredi et al.(188)	Italy	2011-2012	2015	CS	66	9.8	46	12	MIC	4
Morilla et al.(189)	Spain	2004-2016	2019	RET	3426	55.7 ± 16.9	1439	278	MIC	0.5
Vekens et al.(190)	Belgium	2009-2010	2013	PRO	507	48.8	180	24	MIC	1
Maleknejad et al.(191)	Iran	2012-2014	2015	CS	169	7.30 ± 3.12	21	1	DD	30
Oleastro et al.(192)	Portugal	2000-2009	2011	PRO	1115	10.17 ± 4.03	1115	387	MIC	1
Zhang et al.(193)	China	2009-2010 2013-2014	2015	PRO/CS	1555	42.4	1321	648	MIC	0.5
Dargiene et al.(194)	Lithuania	2013–2015	2017	CS	297	32.85	79	2	MIC	0.5
Liu et al.(195)	China	2009-2010	2011	CS	120	10.0 ± 5.8	73	62	MIC	1
Liu et al.(196)	China	2010-2016	2017	PRO	1117		960	247	MIC	1
Tang et al.(197)	China	2017-2019	2020	CS	400	44.7	117	52	MIC	0.5
Bachir et al.(198)	Algeria	2012-2015	2017	CS	200		151	38	MIC	0.5
Seck et al.(199)	Senegal	2007-2009	2013	CS	108	45.3	108	1	MIC	1
Karczewska et al.(200)	Poland	2006-2008	2011	CS	115		115	39	MIC	1
Lee et al.(201)	South Korea	2003-2018	2019	PRO	740	56.3	740	280	MIC	1
Raaf et al.(202)	Algeria	2015-2016	2017	PRO	147		43	16	DD	17
Hansomburana et al.(203)	Thailand	2006-2008	2012	PRO	200	52.8	82	11	MIC	1
Mirzaei et al.(204)	Iran	2011-2011	2013	CS	110	34	48	7	MIC	1
Lee et al.(205)	Korea	2003–2012	2013	PRO	433	55.53	433	127	MIC	1
Shokrzadeh et al.(206)	Iran	2010-2011	2014	CS	197	46	111	29	MIC	1
Oporto et al.(207)	Chile	2018	2019	CS	229	50.68	44	18	MIC	0.5
Aumpan et al.(208)	Thailand	2019	2020	CS	58	43.8	14	4	MIC	0.5
Vilaichone et al.(209)	Thailand	2010-2015	2020	CS	1178	41.5	357	7	MIC	0.5
Cerqueira et al.(210)	Portugal		2011	CS	NA		33	21	MIC	1
Binyamin et al.(211)	Israel	2015-2016	2017	CS	85		54	34	MIC	1
Camorlinga-Ponce et al.(212)	Chile	1997-2017	2021	CS	167	50.72	167	15	MIC	0.5
Maria Biernat et al.(213)	Poland	2016-2019	2020	RET	108	12.5	91	28	MIC	0.5
Trespalacios et al.(214)	Colombia	2009-2011	2013	CS	256		276	42	MIC	1
Lok et al.(215)	China	2018-2019	2020	CS	176	48.4.	65	34	MIC	0.5
Bahmaninejad et al.(216)	Iran	2020-2020	2021	CS	100		50	33	MIC	1
Draeger et al.(217)	Germany	2004-2013	2015	RET	481		481	409	MIC	1
De Palma et al.(218)	Argentina	2011-2013	2015	CS	52		52	14	MIC	0.5
Boyanova et al.(219)	Bulgaria	2004–2010	2012	CS	519	52.16	519	93	MIC	1
Kabamba et al.(220)	Congo	2017-2018	2020	CS	220	45.3 ± 15.3	102	24	MIC	0.5
Okuda et al.(221)	Japan	1997-2013	2016	RET	332	11.6 ± 3.4	76	33	MIC	1
Vilaichone et al.(222)	Thailand	2004-2012	2013	CS	3964	53.3	400	15	MIC	0.5
Zhang et al.(223)	China	2017-2019	2020	CS	238		238	84	MIC	0.5
Zhang et al.(224)	China	2012-2014	2020	CS	79	9.7± 2.8	79	29	MIC	1
Ben Mansour et al.(225)	France	2009-2009	2015	PRO	149	53.65	42	12	MIC	1
Kuo et al.(226)	Taiwan	2017-2020	2021	CS	64	53.8	41	38	MIC	0.5

Deyi et al.(227)	Belgium	1990-2009	2011	CS	9430	29.3	9430	524	MIC	1
Han et al.(228)	China	2015-2015	2016	CS	325	47.2	325	65	MIC	1
Bincowska et al.(229)	Italy	2008-2016	2018	CS	170		170	29	MIC	1
Bachir et al.(230)	Algeria	2014-2016	2018	PRO	270		212	53	MIC	0.5
Hanafiah et al.(231)	Malaysia	2014-2015	2019	CS	288	52.41±16.44	59	21	MIC	1
Vazirzadeh et al.(232)	Iran	2018-2018	2020	CS	165	50:3 ± 15:5	83	21	MIC	0.5
Rezaei et al.(233)	Iran	2015–2018	2019	CS	200	54	73	17	MIC	0.5
Yakoob et al.(234)	Pakistan	2008– 2010	2013	CS	120	41 ± 13	47	17	MIC	1
Gehlot et al.(235)	India	2011–2013	2016	CS	483	43	68	8	MIC	0.5
Boyanova et al.(236)	Bulgaria	2007– 2012	2013	RET	588		588	118	MIC	1
Boyanova et al.(237)	Bulgaria	2012–2014	2015	CS	53	50.7	53	9	MIC	0.5
Otth et al.(238)	Chile		2010	CS	240	54.5 ± 15.7	88	8	MIC	2
Mcnulty et al.(239)	Uk	2009-2010	2012	CS	2063		241	86	MIC	1
Ben et al.(240)	China	2013-2014	2018	CS	NA		100	13	MIC	0.5
Alavifard et al.(241)	Iran	2017-2019	2020	CS	82	49.7 ± 3.33	82	36	MIC	0.5
Regnath et al.(242)	Germany	2002-2015	2016	RET	582	12 years	608	75	MIC	0.5
Han Lu et al.(243)	Taiwan	1998-2018	2019	RET	70	13.2 ± 3.2	70	16	MIC	1
Di Giulio et al.(244)	Italy	2010-2014	2015	CS	115		181	131	MIC	0.5
Enany et al.(245)	Egypt		2015	CS	150		107	6	DD	40
Trespalacios et al.(246)	Colombia		2014	CS	127		107	42	MIC	1
Gatta et al.(247)	Italy	2010-2015	2018	RET	1682		1325	478	MIC	0.5
Goudarzi et al.(248)	Iran	2015-2015	2016	CS	154		110	28	MIC	1
Bayati et al.(249)	Iran		2019	CS	170	30 ±75.	55	27	MIC	0.5
Dang et al.(250)	Vietnam	2014-2016	2020	CS	153	38.3+_10.7	153	111	MIC	1
Phan et al.(251)	Vietnam	2012-2014	2014	CS	92	44.1 ± 13.4	92	39	MIC	1
Khashei et al.(252)	Iran	2014-2014	2016	CS	318	41.5	100	20	MIC	1
Shetty et al.(253)	Australia	2014-2017	2019	CS	180	46.2±14	113	23	MIC	0.5
García et al.(254)	Spain	2014-2016	2017	PROCS	217	64	76	17	MIC	1
Farzi et al.(255)	Iran	2016-2017	2019	CS	160	46.5 ± 8.3	68	23	MIC	1
Lyu et al.(256)	China	2016-2018	2020	PRO	1113	43	791	271	MIC	0.5
Shmuely et al.(257)	Israel	2013-2017	2020	RET/CS	128	45	128	70	MIC	256
Ogata et al.(258)	Brazil	2008-2009	2013	CS	77	11.1 ±3.9	77	15	MIC	2
Abadi et al.(259)	Iran	2008-2010	2011	CS	147	34.5	147	32	MIC	1
Vilaichone et al.(260)	Thailand	2016-2016	2017	CS	148	56.3±13.3	50	1	MIC	0.5
Ferenc et al.(261)	Poland	2011 and 2013	2016	CS	185	49 ± 16.8	67	37	MIC	1
Azzaya et al.(262)	Mongolia	2014-2016	2020	CS	361	44.3 ± 13.4	361	108	MIC	0.5
Mi et al.(263)	China	2018-2018	2021	CS	48		65	21	MIC	0.5
Boyanova et al.(264)	Bulgaria	2012–2013	2014	CS	50	50.5	50	11	MIC	0.5
Boyanova et al.(265)	Bulgaria	2010–2015	2015	CS	299	47.3	299	84	MIC	0.5
Megraud et al.(266)	France	2018-2019	2021	PRO	1211	51.2	1211	259	MIC	0.5
Megraud et al.(267)	France	2008-2009	2013	PRO	2204		2204	431	MIC	1

Ducournau et al.(268)	France	2014-2015	2016	CS	984	51.5 ± 15.9	266	59	MIC	1
Bouihat et al.(269)	France	2015-2016	2016	PRO	255	47.5	177	45	MIC	0.5
Reyes et al.(270)	Spain	2014-2017	2019	PRO	112		99	12	MIC	0.5
Saniee et al.(271)	Iran	2010-2017	2018	CS	985		218	75	DD	2
Mokhtar et al.(272)	Malaysia	2015-2016	2019	CS	352	52	13	4	MIC	0.5
Montes et al.(273)	Spain	2008-2012	2014	RET	143		74	25	MIC	1
Miendje Deyi et al.(274)	Belgium	2015-2016	2019	CS	846		846	141	MIC	0.5
Tang et al.(275)	China	2016-2019	2020	CS	NA		301	201	MIC	0.5

1

Table 2(on next page)

Clarithromycin-resistant *Helicobacter pylori* prevalence. 95% Confidence Intervals (CI) were used. $P \leq 0.05$ was considered statistically significant.

High confidence interval (HCI), low confidence interval (LCI), I-squared (I^2), Degrees of freedom (DF).

	No of Article	Clar-resistant, Total isolates	Proportion (LCI, HCI)	Weight	I^2 (*P*)
Overall	248	8736, 87991	27.53 (25.41, 29.69)	100.00	97.80% (P=0.00)
2010-2017	143	12891, 60452	24.28 (21.7, 26.96)	57.68	97.91% (P=0.00)
2018-2021	105	8045, 27476	32.14 (28.69, 35.69)	42.32	97.24% (P=0.00)
Iran	38	1193, 3628	27.24 (21.68, 33.18)	14.91	93.14% (P=0.00)
Finland	1	83, 1037	8.00 (6.43, 9.83)	0.43	NA
Chile	4	137, 704	18.56 (8.47, 31.34)	1.62	91.76% (P=0.00)
Brazil	4	40, 247	15.29 (9.79, 21.7)	1.55	38.94% (P=0.18)
Romania	1	22, 70	31.43 (20.85, 43.63)	0.40	NA
Austria	1	16, 96	16.67 (9.84, 25.65)	0.41	NA
France	8	990, 4873	21.13 (15.26, 27.66)	3.31	95.23% (P=0.00)
Eastern Cape	1	40, 200	20 (14.69, 26.22)	0.42	NA
Spain	8	1161, 4650	27.41 (17.03, 39.18)	3.30	98.22% (P=0.00)
Malaysia	5	38, 522	10.2 (1.59, 23.94)	1.91	93.33% (P=0.00)
Alaska	2	233, 791	29.45 (26.31, 32.68)	0.86	NA
Korea	5	213, 952	20.59 (12.26, 30.37)	2.07	90.69% (P=0.00)
Taiwan	10	453, 2088	29.16 (15.9, 44.45)	3.92	96.85% (P=0.00)
Mexico	2	17, 135	12.3 (7.14, 18.53)	0.78	NA
USA	5	347, 1157	32.98 (17.21, 50.95)	2.03	95.84% (P=0.00)
Portugal	5	541, 1428	48.11 (30.07, 66.41)	1.97	95.52% (P=0.00)
China	32	8227, 32130	34.05 (29.33, 38.92)	13.14	98.16% (P=0.00)
Poland	6	178, 601	29.77 (18.41, 42.52)	2.42	90.49% (P=0.00)
Belgium	3	689, 10456	11.28 (3.95, 21.67)	1.29	NA
Turkey	7	170, 684	25.78 (19.44, 32.67)	3.22	76.74% (P=0.00)
Croatia	1	20, 168	11.9 (7.43, 17.79)	0.42	#VALUE!
Colombia	5	152, 664	24.26 (12.96, 37.68)	2.04	92.33% (P=0.00)
Nigeria	2	44, 147	28.22 (21.13, 35.86)	0.78	NA
Norway	1	6, 102	5.88 (2.19, 12.36)	0.41	NA
Thailand	7	54, 1097	6.24 (2.73, 10.86)	2.73	81.45% (P=0.00)
Bulgaria	6	375, 1742	21.89 (18.2, 25.81)	2.48	66.49% (P=0.01)
UK	1	86, 241	35.68 (29.64, 42.09)	0.42	NA
South Korea	7	560, 1778	31.4 (19.68, 44.43)	2.88	96.35% (P=0.00)
Germany	4	971, 2771	32.08 (6.55, 65.66)	1.71	99.64% (P=0.00)
Vietnam	5	254, 507	45.72 (28.85, 63.11)	2.02	93.56% (P=0.00)
Senegal	1	1, 108	0.93 (0.02, 5.05)	0.41	NA
Pakistan	2	22, 139	13.33 (8.04, 19.63)	0.78	NA
Australia	2	31, 124	23.47 (16.01, 31.75)	0.67	NA
Japan	12	854, 2494	35.89 (27.02, 45.26)	4.68	93.72% (P=0.00)
India	3	63, 216	25.25 (2.81, 59.01)	1.19	NA
Italy	11	1663, 5367	40.38 (25.65, 56.04)	4.55	99.12% (P=0.00)
Israel	6	272, 597	46.12 (35.66, 56.75)	2.39	84.00% (P=0.00)
Bangladesh	1	22, 56	39.29 (26.5, 53.25)	0.39	NA
Canada	1	8, 20	40.00 (19.12, 63.95)	0.32	NA
Argentina	1	14, 52	26.92 (15.57, 41.02)	0.38	NA
Egypt	2	18, 127	10.61 (5.53, 16.89)	0.73	NA
Singapore	1	97, 708	13.70 (11.25, 16.46)	0.43	NA
Dominican	1	2, 64	3.13 (0.38, 10.84)	0.39	NA
Iceland	1	9, 105	8.57 (3.99, 15.65)	0.41	NA
Mongolia	2	162, 513	31.54 (27.57, 35.64)	0.84	NA
Peru	1	27, 76	35.53 (24.88, 47.34)	0.40	NA
Slovenia	1	25, 104	24.04 (16.2, 33.41)	0.41	NA
Lithuania	1	2, 79	2.53 (0.31, 8.85)	0.40	NA
Algeria	3	107, 406	26.62 (21.42, 32.15)	1.21	NA

Russia	3	28, 333	13.34 (2.11, 30.9)	1.12	NA
Honduras	1	13, 116	11.21 (6.1, 18.4)	0.41	NA
Switzerland	2	145, 216	67.16 (60.71, 73.31)	0.81	NA
Cameroon	1	19, 140	13.57 (8.37, 20.38)	0.41	NA
Congo	1	24, 102	23.53 (15.69, 32.96)	0.41	NA

1

Figure 1

The study PRISMA flow diagram.

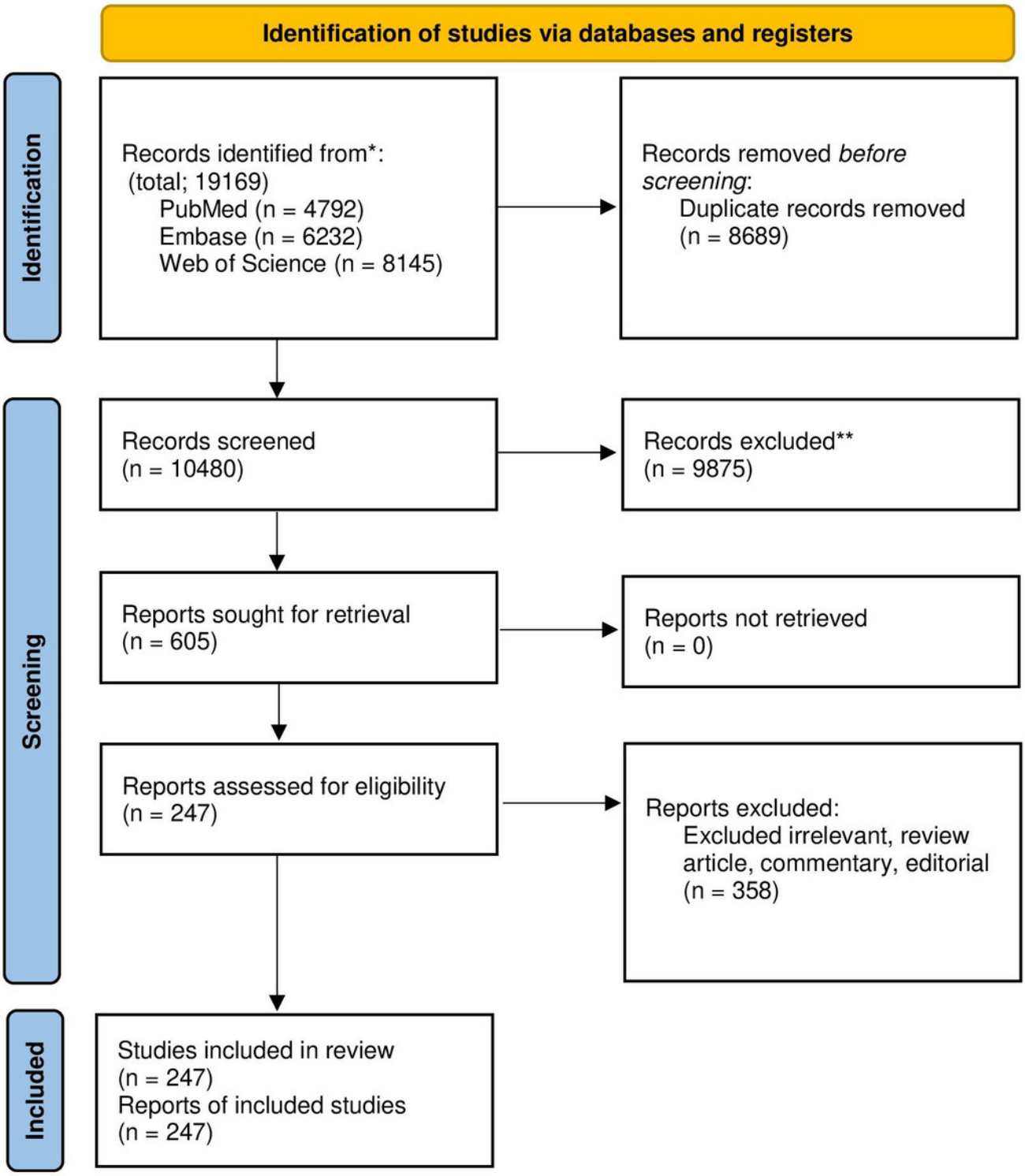
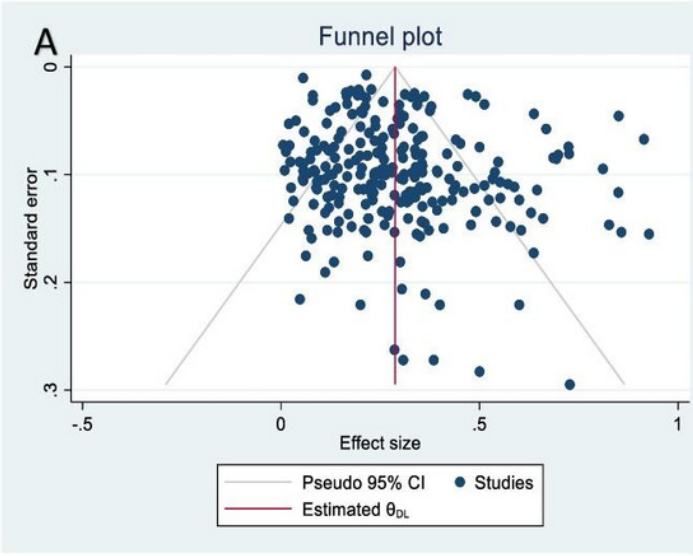
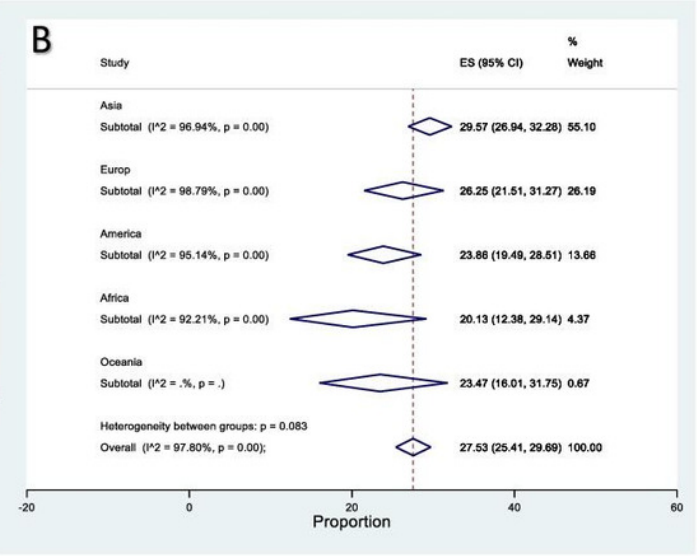

Identification of studies via databases and registers
Identification
Records identified from*:
(total; 19169)
PubMed (n = 4792)
Embase (n = 6232)
Web of Science (n = 8145)
Records removed *before screening*:
Duplicate records removed
(n = 8689)
Screening
Records screened
(n = 10480)
Records excluded**
(n = 9875)
Reports sought for retrieval
(n = 605)
Reports not retrieved
(n = 0)
Reports assessed for eligibility
(n = 247)
Reports excluded:
Excluded irrelevant, review article, commentary, editorial
(n = 358)
Included
Studies included in review
(n = 247)
Reports of included studies
(n = 247)

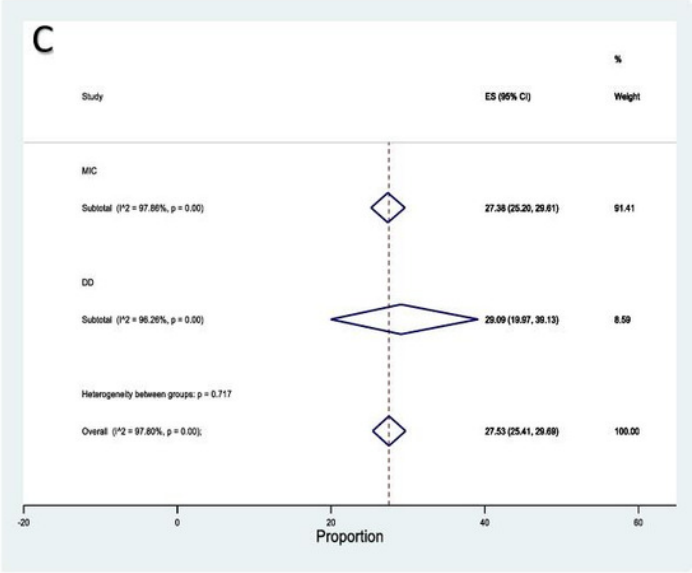
Figure 2

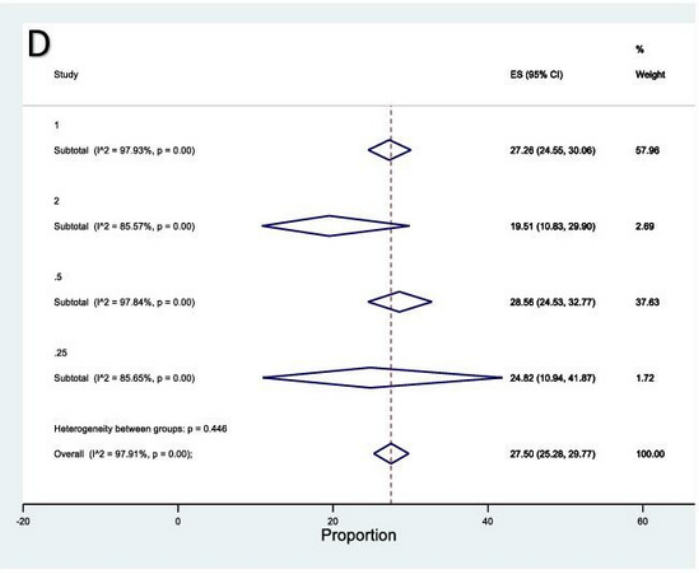
Meta-analysis charts

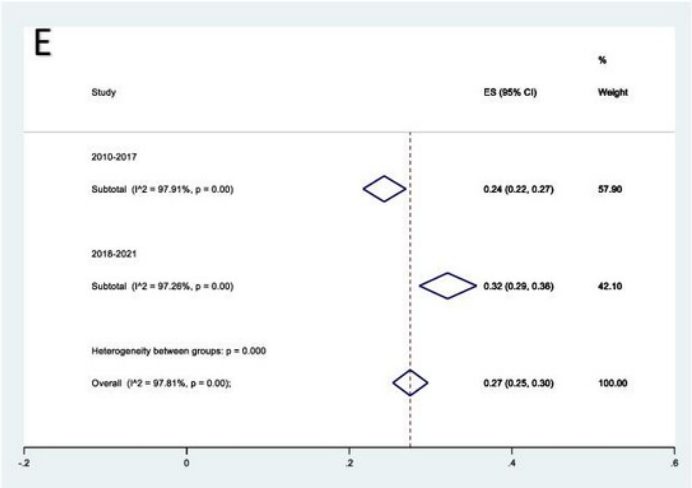
A: The funnel plot of clarithromycin-resistant *Helicobacter pylori* prevalence did not have significant evidence of publication bias; B: The subgroup analysis forest plot of clarithromycin-resistant *Helicobacter pylori* prevalence in different continents; C: The subgroup analysis forest plot of clarithromycin-resistant *Helicobacter pylori* prevalence using different AST methods; D: Subgroup analysis forest plot of clarithromycin-resistant *Helicobacter pylori* prevalence in different breakpoints to interpret antimicrobial susceptibility test data; E: Subgroup analysis forest plot of clarithromycin-resistant *Helicobacter pylori* prevalence in years; F: The regression analysis of clarithromycin-resistant *Helicobacter pylori* prevalence over years with 95% Confidence interval had a significant correlation 0.013 (95% CI; 0.01, 0.02) ($P < 0.001$).

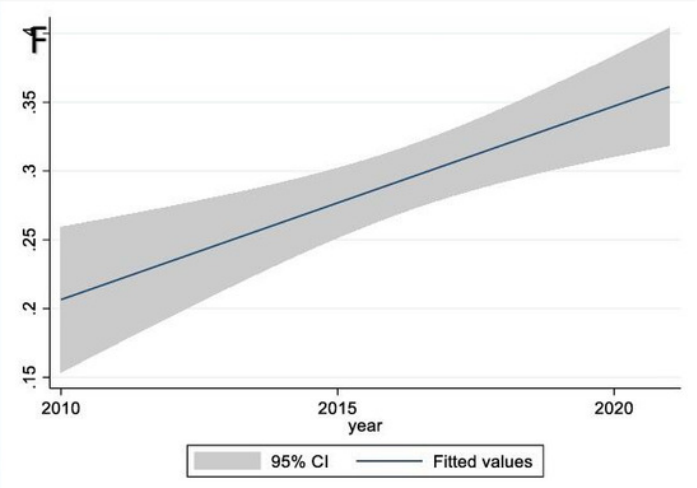

A
Funnel plot
Standard error
0
.1
.2
.3
-.5
0
.5
1
Effect size
Pseudo 95% CI
Studies
Estimated θDL


B
Study
ES (95% CI)
%
Weight
Asia
Subtotal (I^2 = 96.94%, p = 0.00)
29.57 (26.94, 32.28) 55.10
Europ
Subtotal (I^2 = 98.79%, p = 0.00)
26.25 (21.51, 31.27) 26.19
America
Subtotal (I^2 = 95.14%, p = 0.00)
23.86 (19.49, 28.51) 13.66
Africa
Subtotal (I^2 = 92.21%, p = 0.00)
20.13 (12.38, 29.14) 4.37
Oceania
Subtotal (I^2 = .%, p = .)
23.47 (16.01, 31.75) 0.67
Heterogeneity between groups: p = 0.083
Overall (I^2 = 97.80%, p = 0.00);
27.53 (25.41, 29.69) 100.00
-20
0
20
40
60
Proportion


C
Study
ES (95% CI)
%
Weight
MIC
Subtotal (I^2 = 97.86%, p = 0.00)
27.38 (25.20, 29.61)
91.41
DD
Subtotal (I^2 = 96.26%, p = 0.00)
29.09 (19.97, 39.13)
8.59
Heterogeneity between groups: p = 0.717
Overall (I^2 = 97.80%, p = 0.00);
27.53 (25.41, 29.69)
100.00
-20
0
20
40
60
Proportion


D
Study
ES (95% CI)
%
Weight
1
Subtotal (I^2 = 97.93%, p = 0.00)
27.26 (24.55, 30.06)
57.96
2
Subtotal (I^2 = 85.57%, p = 0.00)
19.51 (10.83, 29.90)
2.69
.5
Subtotal (I^2 = 97.84%, p = 0.00)
28.56 (24.53, 32.77)
37.63
.25
Subtotal (I^2 = 85.65%, p = 0.00)
24.82 (10.94, 41.87)
1.72
Heterogeneity between groups: p = 0.446
Overall (I^2 = 97.91%, p = 0.00);
27.50 (25.28, 29.77)
100.00
-20
0
20
40
60
Proportion


E
Study
ES (95% CI)
%
Weight
2010-2017
Subtotal (I^2 = 97.91%, p = 0.00)
0.24 (0.22, 0.27)
57.90
2018-2021
Subtotal (I^2 = 97.26%, p = 0.00)
0.32 (0.29, 0.36)
42.10
Heterogeneity between groups: p = 0.000
Overall (I^2 = 97.81%, p = 0.00);
0.27 (0.25, 0.30)
100.00
-.2
0
.2
.4
.6


F
.15
.2
.25
.3
.35
2010
2015
2020
year
95% CI
Fitted values