



PREVALENCE AND ANTIBIOTIC SUSCEPTIBILITY PATTERN OF HELICOBACTER PYLORI ISOLATES FROM GASTRIC BIOPSIES OF PATIENTS IN TERTIARY CARE HOSPITAL

FATIMA S<sup>1</sup>, ULLAH I<sup>\*2</sup>, AYAZ M<sup>3</sup>, MALIK K<sup>4</sup>, SHAIQA MNQ<sup>5</sup>, YAN X<sup>6</sup>, HAN L<sup>1</sup>, ZHAO L<sup>1</sup>

<sup>1</sup>Research Center, The Fourth Hospital of Hebei Medical University, Shijiazhuang, Hebei 050011. P. R. China

<sup>2</sup>Department of Microbiology, Government Degree College Madyan Swat, Pakistan

<sup>3</sup>Department of Immunology, Hebei Medical University, 361 East Zhongshan Road, Shijiazhuang (050017), Hebei Province, China

<sup>4</sup>Institute of Biological Sciences, Gomal University, D. I. Khan KP 29220, Pakistan

<sup>5</sup>Department of Pharmacology, Hebei Medical University, China

<sup>6</sup>Department of Clinical Laboratory, The Fourth Hospital of Hebei Medical University, Shijiazhuang, Hebei 050011. P. R. China

\*Corresponding author email address: [Inammicro@gmail.com](mailto:Inammicro@gmail.com)

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**Abstract:** Worldwide, *Helicobacter pylori* is prevalent and is strongly associated with causing numerous digestive tract infections. Combination therapy for this pathogen includes a combination of antimicrobials such as amoxicillin, metronidazole, clarithromycin, levofloxacin, and proton pump inhibitors. Even though the present therapy is effective, treatment failure has been observed. This failure has been observed to be mainly due to point mutation, which in *H. pylori* is considered the primary developed resistance mechanism. This study investigated the prevalence and drug susceptibility of *H. pylori* in patients in Mufti Mehmood Memorial Teaching Hospital, Dera Ismail Khan, Pakistan, from 2016 to 2017. A total of 100 gastric biopsies of patients were included in our study. All the samples were cultured and identified by biochemical testing for *H. pylori* to determine the prevalence. The disk diffusion method was used for the determination of the susceptibility pattern. Among 100 patients, *H. pylori* strains were isolated from 52 (52%) patient samples. To metronidazole (MTZ), maximum number of isolates (69.23%) shows resistance. Resistance to other antibiotics was also detected, including clarithromycin (CLR; 50%) and amoxicillin (AML; 57.69%). Comparatively low resistance was observed to tetracycline (TET; 7.69%) and ciprofloxacin (CIP; 15.38%) by a few isolates in our study. These data suggest that metronidazole should be used among Pakistani patients in first-line therapy with caution and ciprofloxacin in association. The clinician must know their area's resistance patterns when selecting an empiric antibiotic regimen for *H. pylori*.

**Keywords:** Prevalence; *Helicobacter pylori*; Antibiotic Susceptibility Pattern; Resistance

## Introduction

*Helicobacter pylori* (*H. pylori*) is a Gram-negative bacteria characterised as a class I carcinogen (NIH, 1994). Gastritis, gastric and duodenal ulcers, gastric adenocarcinoma, and mucosa-associated lymphoid tissue lymphoma have an association with this pathogen (Sipponen, 1994). Chronic gastritis in the long term due to *H. pylori* leads over 12 years to glandular atrophy and intestinal metaplasia (Corral et al., 2017). Gastritis due to *Helicobacter pylori* might progress to multifocal atrophy and intestinal metaplasia, steadily increasing from the antrum to the body. Almost 50% of the world's population is infected by *Helicobacter pylori*, which causes disease development like gastritis, peptic ulcer, and gastric cancer (Blaser and Atherton, 2004). *H. pylori* has developed high resistance to commonly used antibiotics. This development of resistance is the main factor in the failure of treatment. The reported antibiotic resistance pattern varies according to geographical location (Adamek et al., 1998; Glupczynski et al., 2001). Once acquired, *H. pylori* often last a lifetime unless it is eliminated by antimicrobial medication. Beginning in the early 1990s, treatment plans for *H. pylori* have changed. Treatment with antibiotics for *H. pylori* infection is a complex matter. Bismuth salt could be added to the existing regimen of two antimicrobial

agents and an anti-secretory medication, such as a proton pump inhibitor, to manage *H. pylori*. (Malfertheiner et al., 2005). Commonly prescribed antibiotics are metronidazole, clarithromycin, and amoxicillin (Malfertheiner et al., 2002), while tetracycline is used in rescue therapy (Gisbert and Pajares, 2001). *H. pylori* antimicrobial resistance is a significant issue that has contributed significantly to the infection's inability to be wholly eradicated. Antimicrobial susceptibility data is crucial for choosing the right course of therapy. Before selecting an optimum treatment regimen, knowing the resistance frequency to antimicrobial agents is compulsory. Effective infection cure by *H. pylori* not only helps eradicate this pathogenic microbe but also helps in the treatment and prevention of other associated diseases (Kuipers, 1997). However, the decrease in the rate of eradication, which causes economic losses and unhappy feelings for the patient, is mainly caused by the rising frequency of antibiotic resistance. There is variation in the reported resistance pattern to various commonly used antibiotics. For metronidazole 10-90%, clarithromycin 0-45%, amoxicillin 0-33%, and tetracycline 5-59%, resistance was reported in previous studies (Al-Qurashi et al., 2001; Boyanova et al., 2002; Kim et al., 2001; Thyagarajan et al., 2003; Wang et al., 2000). In different parts of the world,

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increasing resistance to metronidazole, clarithromycin, and amoxicillin has been reported for *H. pylori* (Megraud, 2004). The rise in *H. pylori* antibiotic resistance prevalence carries significant consequences. The single most significant risk factor that affects how well antibiotic therapy works is antimicrobial resistance. (Storskrubb et al., 2006). Numerous research conducted in Pakistan have focused on the clinical manifestations of gastric disorders, the identification of *Helicobacter pylori* infection, and the evaluation of the effectiveness of various treatment protocols in combating this pathogen. (Abbas et al., 2001; Khokhar, 2002; Yakoob et al., 2004). No information about resistance to widely used antibiotics for *H. pylori* eradication is available, based on our knowledge. Given the rising frequency of *H. pylori* infections and related complications, it is extremely concerning that there is a high degree of resistance to metronidazole (93.5%) and that resistance to additional antibiotics that are routinely used in or recommended for the management of *H. pylori* infections is growing. Mutations in a comparatively small number of nucleotide and amino acid sequences are responsible for antibiotic resistance. It has been reported that in the sequences of oxygen-independent NADPH nitroreductase (RdxA) and NADH flavin oxidoreductase (FrxA), metronidazole (MTZ) resistance is mainly associated with amino acid substitutions (Goodwin et al., 1998; Jeong et al., 2000). Resistance to amoxicillin (AML) and clarithromycin (CLR) is due to 23S *rRNA* point mutations and changes of amino acid in Pbp1, respectively (Gerrits et al., 2006; Paul et al., 2001; Ribeiro et al., 2003; Versalovic et al., 1996). A high prevalence of *H. pylori* has been observed in Pakistan, and there is also non-judicious use of commonly available antibiotics. Therefore, we designed a study to investigate *Helicobacter pylori* isolates' prevalence and antibiotic susceptibility pattern from gastric biopsies of patients in tertiary care hospitals.

### Methodology

One hundred patients who visited Mufti Mehmood Memorial Teaching Hospital, district Dera Ismail Khan, Khyber Pakhtunkhwa Pakistan, for upper endoscopy during 2016-2017 were enrolled in our study. Informed consent was provided by all subjects, and the hospital's Ethics Committee approved the study protocol. The study excluded patients who were prescribed antibiotics and bismuth compounds in the four weeks before to endoscopy. Malignancy and serious liver illnesses were among the other exclusion criteria, as was a regular intake of nonsteroidal anti-inflammatory medicines such as acetylsalicylic acid. Every patient in the research had an upper gastrointestinal endoscopy. All patients had gastric biopsy specimens taken, and each sample underwent an *H. pylori* culture test. In a 20% glucose solution, all the gastric antral biopsies were placed. They were then chopped with sterile blades. It was then inoculated on Columbia blood agar. Horse blood (7 %) and Dent's *H. pylori* selective medium were added to the Columbia blood agar. All the plates were incubated for up to 7 days at 37 °C. A campylobacter gas-generating kit provided moist microaerophilic conditions of 10% CO<sub>2</sub>, 5% O<sub>2</sub>, and 85% N<sub>2</sub>. On a daily basis, all the plates were checked for growth after three days. Plates were considered negative

for *H. pylori* when no growth was found after seven days of incubation. Positive growth and individual rounded, small, translucent colony-forming units were selected and sub-cultured to confirm pure cultures. Positive results of oxidase, catalase and urease tests and based on morphology and gram staining, the isolates were considered as *H. pylori*. Aliquots of the suspension were placed onto Muller Hinton agar comprising 5% defibrinated sheep blood and 7% fetal calf serum. Antibiotic discs were placed on the surface of the medium. At 37°C for 72 hours, all the plates were incubated in a microaerophilic condition. Zones of inhibition were measured according to the guidelines of the CLSI 2012 (Wayne, 2010).

### Results

In the present study, a total of 100 patients who visited Mufti Mehmood Memorial Teaching Hospital district Dera Ismail Khan, Khyber Pakhtunkhwa, Pakistan, for upper endoscopy during 2016-2017 were observed for *H. pylori*. The patients were between 18 and 83 years old. The samples were cultured on Columbia blood agar medium. Gram-negative bacteria with characteristic cell shape and biochemical assays were among the usual criteria used to identify colonies as *H. pylori*. The results of the biochemical test are given in table 1. An overall prevalence of 52% (52/100) was observed in our study. (Table 2) A high prevalence of *H. pylori* was observed in males in our study compared to females. Of 45 isolates, 36 (60%) were male while 16 were female (40%). Table 3

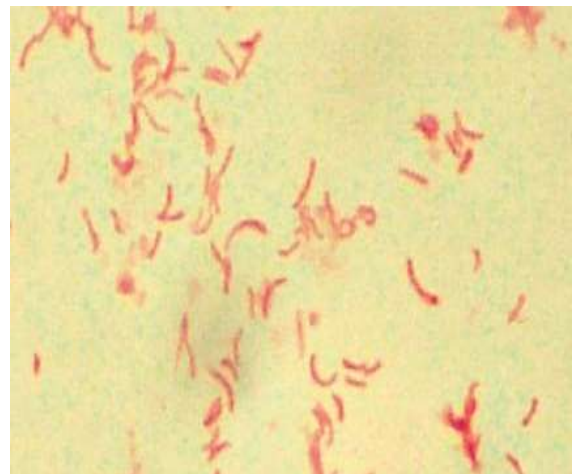


Figure 1: Gram staining of *H. pylori*

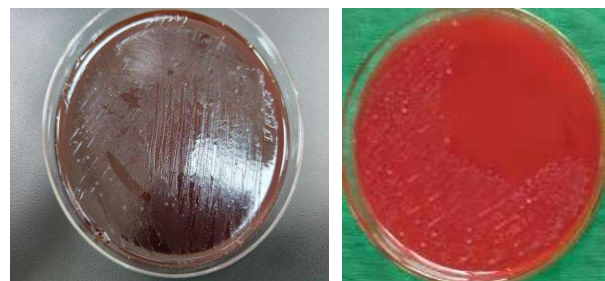


Figure 2: Growth of *H. pylori* on Columbia blood agar

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**Table 1: Biochemical tests for H. pylori**

Serial Number	Biochemical test	Result
1.	Catalase	Positive
2.	oxidase	Positive
3.	motility	Positive
4.	Nitrate reduction	Negative
5.	Urease	Positive
6.	Growth at 1.5% NaCl	Negative

The disk diffusion method was used for the determination of the susceptibility pattern of antibiotics. Metronidazole (MTZ), clarithromycin (CLR), amoxicillin (AML), tetracycline (TET) and ciprofloxacin (CIP) discs were used. To metronidazole (MTZ), maximum number of isolates (69.23%) shows resistance. Resistance to other

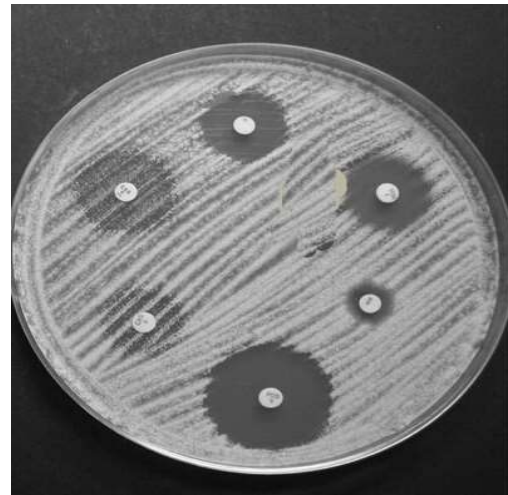
antibiotics was also detected, including clarithromycin (CLR; 50%) and amoxicillin (AML; 57.69%). Comparatively low resistance was observed to tetracycline (TET; 7.69%) and ciprofloxacin (CIP; 15.38%) by a few isolates in our study. (Table 4).

**Table 2: Overall prevalence of H. pylori in gastric biopsies sample**

Total sample	Positive for H. pylori n (%)	Negative for H. pylori n (%)
100	52 (52%)	48 (48%)

**Table 3: Gender-wise prevalence of H. pylori in gastric biopsies sample**

Gender	Total sample	Positive for H. pylori n (%)	Negative for H. pylori n (%)
Male	60	36 (60%)	24 (40%)
Female	40	16 (40%)	24(60%)



**Figure 3: : Antibiotic susceptibility testing**

**Table 4: Antibiotic susceptibility pattern of helicobacter pylori**

S.No	Antimicrobial drugs	Code	Drug susceptibility	H.pylori(n)%
1	Metronidazole	MTZ	Susceptible	16 (30.76)
			Resistant	36 (69.23)
2	Clarithromycin	CLR	Susceptible	26 (50)
			Resistant	26 (50)
3	Amoxicillin	AML	Susceptible	22 (42.30)
			Resistant	30 (57.69)
4	Ciprofloxacin	CIP	Susceptible	44 (84.61)
			Resistant	8 (15.38)
5	Tetracycline	TET	Susceptible	48 (92.30)
			Resistant	4 (7.69)

**Discussion**

While *H. pylori* infection is becoming less common in developed countries, *H. pylori* gastric colonisation is still common in developing nations; *H. pylori* infection can be diagnosed by a number of tests and is frequently

effectively treated with antibiotics (Kusters et al., 2006). The overall prevalence of *H. pylori* varies significantly between developed and developing nations, with adult prevalences typically between 80–90% and <40%, accordingly (Perez-Perez et al., 2004). In the present study, a total of 100 patients who visited Mufti Mehmood

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Memorial Teaching Hospital district Dera Ismail Khan, Khyber Pakhtunkhwa, Pakistan, for upper endoscopy during 2016-2017 were observed for h.pylori. The patients were between 18 and 83 years old. The samples were cultured on Colombia blood agar medium. Gram-negative bacteria with characteristic cell shape and biochemical assays were among the usual criteria used to identify colonies as *H. pylori*. The results of the biochemical test are given in table 1. An overall prevalence of 52% (52/100) was observed in our study. A high prevalence of h.pylori was observed in males compared to females in our study. Of 45 isolates, 36 (60%) were male while 16 were female (40%).

The degree of antibiotic use in various groups is thought to be connected to the regional diversity in *H. pylori* resistance to antibiotics (Graham, 1998). Antibiotics, particularly erythromycin, clarithromycin, metronidazole, amoxicillin, and tetracycline, are used indiscriminately in Pakistan for the management of a variety of diseases. Additionally, because such medicines are freely sold over-the-counter, open access to medications promotes self-medication. This may explain why the *H. pylori* isolates in this investigation showed enhanced resistance to amoxicillin, metronidazole, clarithromycin, tetracycline, clindamycin, and erythromycin as well as other antibiotics. The widespread administration of metronidazole for various intestinal conditions may possibly be the cause of the high frequency of metronidazole resistance. With the exception of tetracycline, where a greater resistance rate (48.4%) was noted in comparison to the 4.2% (Sengupta et al., 2002) and 28.5% reported by other investigators (Misra et al., 2006) that have been reported from India, the resistance pattern as described here is rather comparable to that reported there. Resistance to ofloxacin was extremely low (6.5%), suggesting that it might be employed in combination treatment, although resistance to the two associated antibiotics, clarithromycin and erythromycin, was comparable (38.7% and 42.0%, accordingly) (Schrauwen et al., 2009). Comparable to reports (Falsafi et al., 2004; Torres et al., 2001), a number of drug-resistant *H. pylori* isolates have been identified, which is indication of careless usage of antibiotics in Pakistan. The global prevalence of antibiotic resistance in *H. pylori* isolates makes the fight against infection more difficult. It has been reported that resistance differs based on the population under study, with resistance to clarithromycin ranging from 0-45% and to metronidazole from 10-90%. Since that metronidazole and clarithromycin are often used in combination as a therapy, associative resistance to these two medications is especially significant from a therapeutic standpoint. A perfect treatment plan should be easy to follow, have few adverse effects, and—above all—take local trends of antibiotic resistance into account. As a result, based on the patient's geographical area physicians may find it helpful to use culture and susceptibility testing before recommending the appropriate course of treatment. First, in Pakistan, the trend of antibiotic resistance amongst the *H. pylori* isolates was identified. The elevated resistance may be explained, most likely by the fact that we use more antibiotics than other nations do. Ultimately, research has shown that there is minimal resistance to ofloxacin, a high rate of resistance to metronidazole, and significant resistance to clindamycin, tetracycline, clarithromycin, erythromycin, and amoxicillin.

Future research endeavours aimed at comprehending the resistance pattern of *H. pylori* strains isolated from the Pakistani population might draw from the foundation established by this work. It emphasises how important it is to look for new antibacterial elements in order to effectively fight this extremely common illness. Studies showing the emergence of resistance in *H. pylori* isolates call for a thorough assessment of the advised treatment plans in local practice. When rescue and first-line therapy have failed and the patient has to be cured to undo the pathophysiological alterations brought on by an *H. pylori* infection, culture and susceptibility testing is advised.

## Conclusion

Our study concludes that *H. pylori* strains are highly prevalent in gastric biopsy samples of patients. Our study also observed considerable resistance to various antibiotics. A high percentage of resistance was observed in the case of metronidazole. These data suggest that metronidazole should be used among Pakistani patients in first-line therapy with caution. The clinician must be aware of the pattern of resistance in their area when they select an empiric antibiotics regimen for *H. pylori*. Reliable plans for checking drug resistance in *H. pylori* might be started. Studies in-depth might explore the relation to antibiotic resistance and its association with virulence genotypes in Pakistan. It is also noteworthy in Pakistan to explore the association of the circulating genotypes with the increase of severe forms of gastroduodenal diseases such as gastric cancer.

## Declarations

### Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

### Ethics approval and consent to participate

Approved by the department Concerned.

### Consent for publication

Approved

### Funding

Not applicable

## Conflict of interest

The authors declared absence of conflict of interest.

## Author Contribution

### SUMAYA FATIMA

Coordination of collaborative efforts.

### INAM ULLAH

Conception of Study, Development of Research Methodology Design, Study Design, Review of manuscript, final approval of manuscript

Coordination of collaborative efforts.

### MUHAMMAD AYAZ

Manuscript revisions, critical input.

Coordination of collaborative efforts.

### KHANSA MALIK

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Data acquisition, analysis.

**MOHAMMAD N.Q.SHAIEA**

Data entry and Data analysis, drafting article

**XI YAN**

Data acquisition, analysis.

Coordination of collaborative efforts.

**LINA HAN**

Manuscript revisions, critical input.

**LIANMEI ZHAO**

Coordination of collaborative efforts

## References

- Abbas, Z., Fareed, R., Baig, M., Khan, T., and Shah, M. (2001). Prevalence of histological reflux oesophagitis in H. pylori positive patients: effect of density of H. pylori and activity of inflammation. *JPMA. The Journal of the Pakistan Medical Association* **51**, 36-41.
- Adamek, R., Suerbaum, S., Pfaffenbach, B., and Opferkuch, W. (1998). Primary and acquired Helicobacter pylori resistance to clarithromycin, metronidazole, and amoxicillin—influence on treatment outcome. *The American journal of gastroenterology* **93**, 386-389.
- Al-Qurashi, A. R., El-Morsy, F., and Al-Quorain, A.-A. (2001). Evolution of metronidazole and tetracycline susceptibility pattern in Helicobacter pylori at a hospital in Saudi Arabia. *International journal of antimicrobial agents* **17**, 233-236.
- Blaser, M. J., and Atherton, J. C. (2004). Helicobacter pylori persistence: biology and disease. *The Journal of clinical investigation* **113**, 321-333.
- Boyanova, L., Mentis, A., Gubina, M., Rozynek, E., Gosciniak, G., Kalenic, S., Göral, V., Kupcinskas, L., Kantarçeken, B., and Aydin, A. (2002). The status of antimicrobial resistance of Helicobacter pylori in eastern Europe. *Clinical Microbiology and Infection* **8**, 388-396.
- Corral, J. E., Mera, R., Dye, C. W., and Morgan, D. R. (2017). Helicobacter pylori recurrence after eradication in Latin America: Implications for gastric cancer prevention. *World journal of gastrointestinal oncology* **9**, 184.
- Falsafi, T., Mobasheri, F., Nariman, F., and Najafi, M. (2004). Susceptibilities to different antibiotics of Helicobacter pylori strains isolated from patients at the pediatric medical center of Tehran, Iran. *Journal of clinical microbiology* **42**, 387-389.
- Gerrits, M. M., Godoy, A. P., Kuipers, E. J., Ribeiro, M. L., Stoof, J., Mendonça, S., Van Vliet, A. H., Pedrazzoli Jr, J., and Kusters, J. G. (2006). Multiple mutations in or adjacent to the conserved penicillin-binding protein motifs of the penicillin-binding protein 1A confer amoxicillin resistance to Helicobacter pylori. *Helicobacter* **11**, 181-187.
- Gisbert, J. P., and Pajares, J. M. (2001). Helicobacter pylori therapy: first-line options and rescue regimen. *Digestive Diseases* **19**, 134-143.
- Glupczynski, Y., Megraud, F., Lopez-Brea, M., and Andersen, L. (2001). European multicentre survey of in vitro antimicrobial resistance in Helicobacter pylori. *European journal of clinical microbiology & infectious diseases* **20**, 820-823.
- Goodwin, A., Kersulyte, D., Sisson, G., Veldhuyzen van Zanten, S. J., Berg, D. E., and Hoffman, P. S. (1998). Metronidazole resistance in Helicobacter pylori is due to null mutations in a gene (rdxA) that encodes an oxygen-insensitive NADPH nitroreductase. *Molecular microbiology* **28**, 383-393.
- Graham, D. Y. (1998). Antibiotic resistance in Helicobacter pylori: implications for therapy. *Gastroenterology* **115**, 1272-1277.
- Jeong, J.-Y., Mukhopadhyay, A. K., Dailidienė, D., Wang, Y., Velapatiño, B., Gilman, R. H., Parkinson, A. J., Nair, G. B., Wong, B. C., and Lam, S. K. (2000). Sequential inactivation of rdxA (HP0954) and frxA (HP0642) nitroreductase genes causes moderate and high-level metronidazole resistance in Helicobacter pylori. *Journal of bacteriology* **182**, 5082-5090.
- Khokhar, N. (2002). One-week therapy with omeprazole, clarithromycin and amoxicillin for eradication of Helicobacter pylori infection. *JOURNAL-COLLEGE OF PHYSICIANS AND SURGEONS OF PAKISTAN* **12**, 338-340.
- Kim, J. J., Reddy, R., Lee, M., Kim, J. G., El-Zaatari, F. A., Osato, M. S., Graham, D. Y., and Kwon, D. H. (2001). Analysis of metronidazole, clarithromycin and tetracycline resistance of Helicobacter pylori isolates from Korea. *Journal of Antimicrobial Chemotherapy* **47**, 459-461.
- Kuipers, E. (1997). Helicobacter pylori and the risk and management of associated diseases: gastritis, ulcer disease, atrophic gastritis and gastric cancer. *Alimentary pharmacology & therapeutics* **11**, 71-88.
- Kusters, J. G., Van Vliet, A. H., and Kuipers, E. J. (2006). Pathogenesis of Helicobacter pylori infection. *Clinical microbiology reviews* **19**, 449-490.
- Malfertheiner, P., Megraud, F., O'morain, C., Hungin, A., Jones, R., Axon, A., Graham, D., Tytgat, G., and Group, E. H. P. S. (2002). Current concepts in the management of Helicobacter pylori infection—The Maastricht 2-2000 Consensus Report. *Alimentary pharmacology & therapeutics* **16**, 167-180.
- Malfertheiner, P., Sipponen, P., Naumann, M., Moayyedi, P., Mégraud, F., Xiao, S.-D., Sugano, K., and Nyrén, O. (2005). Helicobacter pylori eradication has the potential to prevent gastric cancer: a state-of-the-art critique. *Official journal of the American College of Gastroenterology* | *ACG* **100**, 2100-2115.
- Megraud, F. (2004). H pylori antibiotic resistance: prevalence, importance, and advances in testing. *Gut* **53**, 1374-1384.
- Misra, R., Bhagat, M., and Ahmed, N. (2006). Helicobacter pylori in Dyspepsia—Antibiotic sensitivity and virulence patterns. *Medical Journal Armed Forces India* **62**, 22-26.
- NIH, C. C. (1994). Helicobacter pylori in peptic ulcer disease: NIH consensus development panel. *JAMA* **272**, 65-69.
- Paul, R., Postius, S., Melchers, K., and Schäfer, K. P. (2001). Mutations of the Helicobacter pylori genes rdxA and pbp1 cause resistance against metronidazole and amoxicillin. *Antimicrobial agents and chemotherapy* **45**, 962-965.
- Perez-Perez, G. I., Rothenbacher, D., and Brenner, H. (2004). Epidemiology of Helicobacter pylori infection. *Helicobacter* **9**, 1-6.
- Ribeiro, M. L., Vitiello, L., Miranda, M. C., Benvenuto, Y. H., Godoy, A. P., Mendonça, S., and Pedrazzoli, J. (2003). Mutations in the 23S rRNA gene are associated with clarithromycin resistance in Helicobacter pylori isolates in Brazil. *Annals of Clinical Microbiology and Antimicrobials* **2**, 1-4.
- Schrauwen, R., Janssen, M., and De Boer, W. (2009). Seven-day PPI-triple therapy with levofloxacin is very effective for Helicobacter pylori eradication.
- Sengupta, S., Saraswathi, K., Varaiya, A., De, A., and Gogate, A. (2002). HELICOBACTER IN DUODENAL ULCER DISEASE AND ITS ERADICATION. *Indian Journal of Medical Microbiology* **20**, 163-164.

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- Sipponen, P. (1994). Gastric cancer—a long-term consequence of *Helicobacter pylori* infection? *Scandinavian Journal of Gastroenterology* **29**, 24-27.
- Storskrubb, T., Aro, P., Ronkainen, J., Wreiber, K., Nyhlin, H., Bolling-Sternevald, E., Talley, N. J., Engstrand, L., and Agréus, L. (2006). Antimicrobial susceptibility of *Helicobacter pylori* strains in a random adult Swedish population. *Helicobacter* **11**, 224-230.
- Thyagarajan, S., Ray, P., Das, B. K., Ayyagari, A., Khan, A. A., Dharmalingam, S., Rao, U. A., Rajasambandam, P., Ramathilagam, B., and Bhasin, D. (2003). Geographical difference in antimicrobial resistance pattern of *Helicobacter pylori* clinical isolates from Indian patients: Multicentric study. *Journal of gastroenterology and hepatology* **18**, 1373-1378.
- Torres, J., Camorlinga-Ponce, M., Pérez-Pérez, G., Madrazo-De la Garza, A., Dehesa, M., González-Valencia, G., and Muñoz, O. (2001). Increasing multidrug resistance in *Helicobacter pylori* strains isolated from children and adults in Mexico. *Journal of Clinical Microbiology* **39**, 2677-2680.
- Versalovic, J., Shorridge, D., Kibler, K., Griffy, M. V., Beyer, J., Flamm, R. K., Tanaka, S. K., Graham, D. Y., and Go, M. F. (1996). Mutations in 23S rRNA are associated with clarithromycin resistance in *Helicobacter pylori*. *Antimicrobial agents and chemotherapy* **40**, 477-480.
- Wang, Wong, Mukhopadhyay, Berg, Cho, Lai, Fung, Hui, and Lam (2000). High prevalence of *Helicobacter pylori* infection with dual resistance to metronidazole and clarithromycin in Hong Kong. *Alimentary pharmacology & therapeutics* **14**, 901-910.
- Wayne, P. (2010). Clinical and Laboratory Standards Institute: Performance standards for antimicrobial susceptibility testing: 20th informational supplement. *CLSI document M100-S20*.
- Yakoob, J., Jafri, N., Jafri, W., Zaman, S., Bian, L. C., Islam, M., Hussainy, A. S., and Zaman, V. (2004). Polymerase chain reaction in the detection of *Helicobacter pylori* infection. *Journal of the College of Physicians and Surgeons--pakistan: JCPSP* **14**, 153-156.



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