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RESEARCH ARTICLE

Considering the clarithromycin resistance prevalence among *Helicobacter pylori* strains isolated from patients with Gastric complication

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Abstract: Objective: *Helicobacter pylori* is a major cause of gastric cancer. This study aimed to determine the frequency of clarithromycin resistance and its association with point mutations in the 23S rRNA gene. **Methods:** This study was conducted on 100 patients with gastric disorders who were referred to Valiasr Hospital in 2022. Two biopsy samples were obtained from each patient for pathological and microbiological examinations. Antimicrobial susceptibility testing was performed using the agar dilution method, and polymerase chain reaction (PCR) was used for molecular analysis. **Results:** Among the patients, 53% (53/100) were diagnosed as *H. pylori*-positive. Pathological findings indicated that 54.7% (29/53) of the *H. pylori*-positive patients had chronic gastritis, 37.7% (20/53) had severe active gastritis, and 7.5% (4/53) had intestinal metaplasia. Clarithromycin resistance was detected in 13.2% (7/53) of the patients. The MIC50 and MIC90 values were determined to be 0.125 mg/L and 2 mg/L, respectively. PCR results revealed that the A2142G point mutation in the 23S rRNA gene was present in all clarithromycin-resistant strains. **Conclusion:** Our findings indicate that the presence of the A2142G point mutation in the 23S rRNA gene may be associated with clarithromycin resistance in *H. pylori* strains. These results underscore the importance of routine screening for resistance genotypes to guide effective treatment strategies.

Keywords: *Helicobacter pylori*, gastric cancer, clarithromycin resistance, histopathological changes, minimum inhibitory concentration

Abbreviation

H. Pylori	Helicobacter pylori
CG	Chronic Gastritis
SAG	Sever Active Gastritis
IM	Intestinal Metaplasia
MIC	Minimal Inhibition Concentration

1 Introduction

The World Health Organization's International Agency for Research on Cancer (WHO-IARC) has classified Helicobacter pylori as a type I carcinogen. *H. pylori* infection is a primary risk factor for gastric cancer, which is the third leading cause of cancer-related death worldwide [1]. In addition, *H. pylori* is implicated in peptic ulcer disease, gastritis, and other gastrointestinal disorders [2]. Globally, *H. pylori* infection is widespread; it was estimated in 2015 that more than half of the world's population was infected [3]. This infection is particularly prevalent in developing countries [4]. In Iran, the prevalence of H. pylori is high, and the age of acquisition is relatively low [5]. Owing to the various complications associated with *H. pylori*, eradication is the primary treatment approach. Several drug regimens are available for its eradication, with clarithromycin being a critical component in many protocols [6, 7]. As a macrolide antibiotic, clarithromycin is effective against *H. pylori* by inhibiting protein synthesis through binding to the 50S ribosomal subunit [8]. However, resistance to clarithromycin has been increasing, primarily due to mutations at the A2143G, A2142G, and A2142C positions in the 23S rRNA gene [9, 10]. Given the widespread nature of the infection, continuous monitoring of *H. pylori*

prevalence and its antimicrobial resistance is essential [11]. The primary objective of this study is to assess the prevalence of clarithromycin resistance among Iranian patients with gastrointestinal disorders using the agar dilution method and PCR.

2 Materials and Methods

2.1 Patient Samples

This study was conducted in Iran at Valiasr Hospital in 2022 and included 100 patients with dyspepsia who underwent endoscopy. Patients who had recently taken medications were excluded. Demographic data were recorded using a standardized questionnaire. Two gastric biopsy samples were taken from the antrum of each patient: one for *H. pylori* isolation and the other for histopathological examination.

2.2 *H. pylori* Culture

Biopsy specimens were smeared onto supplemented Brucella agar medium containing lysed horse blood and antibiotics (Skirrow's supplement, which includes vancomycin, trimethoprim, and polymyxin B). Plates were incubated at 37°C under microaerobic conditions (85% N_2, 10% CO_2, 5% O_2) for 4 to 7 days. Suspected colonies were identified by cell morphology, Gram staining, urease, oxidase, and catalase assays, and confirmed by PCR using glmM primers, as described previously [12].

2.3 MICs Determination

The susceptibility of *H. pylori* strains to clarithromycin was determined by the agar dilution method in accordance with the latest guidelines from the European Committee on Antimicrobial Susceptibility Testing (EUCAST) [13]. Clarithromycin was added to Mueller-Hinton agar medium (Sigma-Aldrich, CAS-Number 70191) supplemented with 10% defibrinated horse blood at final concentrations ranging from 0.06 to 16 mg/L. *H. pylori* suspensions (approximately 10^8 CFU/mL, corresponding to a 3 McFarland standard) were used for testing. The minimum inhibitory concentration (MIC) was defined as the lowest concentration of antibiotic that inhibited bacterial growth after 72 hours of incubation at 37°C under microaerophilic conditions [14]. Strains were considered susceptible if MIC $\leq$ 0.25 mg/L, intermediate if MIC was 0.5 mg/L, and resistant if MIC $>$ 0.5 mg/L.

2.4 Molecular Identification and Mutation Analysis via PCR

Fresh *H. pylori* colonies were used for DNA extraction with a commercial DNA extraction mini kit (YTA Genomic DNA Extraction Mini Kit for Tissue, Yektatajhiz, Tehran, Iran). DNA extracts were stored at –20°C until further analysis. Species-level identification was confirmed by PCR targeting glmM and 16S rRNA genes. To detect mutations in the 23S rRNA gene (specifically A2143G and A2142G), a 25 μL PCR reaction mixture was prepared containing 1$\times$ PCR buffer, 0.3 μM of each primer, 1 μL genomic DNA, 200 μM dNTPs, 0.63 mmol $MgCl_2$, and 0.2 U/μL Taq DNA polymerase. PCR was carried out in an Eppendorf thermal cycler (Germany; AG 22331) under the following conditions: an initial denaturation at 94°C for 5 minutes, annealing at 36°C for 5 minutes, and extension at 72°C for 5 minutes; this was followed by 30 cycles of denaturation at 94°C for 1 minute, annealing at 36°C for 1 minute, and extension at 72°C for 2 minutes. PCR products were separated by electrophoresis on a 1.2% agarose gel and stained with ethidium bromide. Primer sequences and expected PCR product sizes are listed in Table 1. DNA extracts from three reference strains harboring A2142G and A2143G (accession numbers JQ765438, JQ765441) were used as controls.

Table 1 Primers sequences and PCR products size used in this study

Primer Name	Primer Sequence $5' \rightarrow 3'$	Product Size	Reference
16S rRNA	F:GGCTATGACGGGTATCCGGC R:GCCGTGCAGCACCTGTTTTC	764	[15]
glmM	F:GGATAAGCTTTTAGGGGTGTTAGGGG R:GCTTACTTTCTAACACTAACGCGC	296	[16]
A2142G	F: ACGGCGGCCGTAACTATA R: AGGTCCACGGGGTCTTC	175	[17]
A2143G	F: TCGAAGGTTAAGAGGATGCGTCAGTC R: CCGCGGCAAGACAGAGA	118	[18]

2.5 Ethics

The study received ethical approval (code IR.SBMU.RETECH.REC.1400.1189) from Shahid Beheshti University of Medical Sciences. Informed consent was obtained from all patients in accordance with the approved protocols.

2.6 Statistical Analysis

Data were analyzed using SPSS 22 and GraphPad Prism 6 software. Statistical significance was determined using Chi-square and Fisher's exact tests, with $p < 0.05$ considered statistically significant.

3 Results

Out of the 100 examined patients, 53 were positive for *H. pylori*. The age range of infected patients was 18–60 years, with 32 males (60.3%) and 21 females (39.6%). Based on pathological findings, patients were classified into three groups: 29 (54.7%) were diagnosed with chronic gastritis (CG), 20 (37.7%) with severe active gastritis (SAG), and 4 (7.5%) with intestinal metaplasia (IM) (see Figure 1).

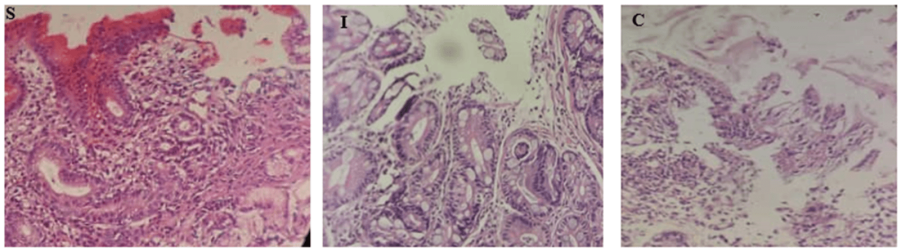

Figure 1 Pathological feature of *H. pylori* infected patient; S – Sever Active Gastritis, I – Intestinal Metaplasia, C – chronic Gastritis.

Demographic analysis revealed statistically significant differences related to alcohol consumption between the CG and IM groups ($p < 0.004$) and between the IM and SAG groups ($p < 0.02$) (Table 2). In addition, smoking showed a significant difference between the IM and SAG groups ($p < 0.03$).

Table 2 Demographic parameters of *H. pylori*-infected patients against pathological finding

Parameter	n	Pathological Finding (n = 53)		
		CG n = 29	SAG n = 20	IM n = 4
Gender				
Male	32	18 (56.2%)	11 (34.3%)	3 (9.3%)
Female	21	11 (52.3%)	9 (42.8%)	1 (4.7%)
Age				
Male		18-45	35-59	55-60
Female		22-48	30-57	52
smoking				
Male	7	4 (57.1%)	1 (14.2%)	2 (28.5%)
Female	2	1 (50%)	0 (0%)	1 (50%)
Alcohol consumption				
Male	6	1 (16.6%)	2 (33.3%)	3 (50%)
Female	1	0 (0%)	0 (0%)	1 (100%)
Blood group				
Male	32	A (n = 7, (38.8%)) B (n = 5, (27.7%)) O (n = 4, (22.2%)) Unknown(n = 2, (11.1%))	A (n = 7, (63.3%)) AB (n = 3, (27.2%)) O (n = 1, (9%))	A (n = 2, (66.6%)) B (n = 1, (33.3%))
Female	21	A (n = 5, (45.4%)) O (n = 6, (54.5%))	B (n = 3, (33.3%)) O (n = 5, (55.5%)) Unknown(n = 1, (11,1%))	A (n = 1, (100%))

Notes: CG – chronic Gastritis, SAG – sever active gastritis, IM – Intestinal Metaplasia

Clarithromycin resistance was evaluated in 53 *H. pylori* strains using the agar dilution method (Table 3). Analysis of the MIC values indicated that 7 (13.2%) strains were resistant to clarithromycin, while 39 (73.5%) strains were susceptible. One (1.8%) strain was classified as intermediate. The most common MIC value among resistant strains was 4 mg/L, and the MIC50 and MIC90 values were determined to be 0.125 mg/L and 2 mg/L, respectively. Furthermore, among the resistant strains, 57.1% were from the IM group, 28.5% from the SAG group, and 14.2% from the CG group. All strains with 100% sensitivity or intermediate resistance were from the CG group.

Table 3 MIC amount for clarithromycin among *H. pylori* isolates in different pathological finding

MIC (mg/L)	Gender	pathological finding		
	n = 53	CG n = 29	SAG n = 20	IM n = 4
0.06	M (n = 11) F (n = 10)	3 (27.2%) 6 (60%)	8 (72.7%) 4 (40%)	0 0
0.125	M (n = 8) F (n = 5)	7 (87.5%) 2 (40%)	1 (12.5%) 3 (60%)	0 0
0.25	M (n = 8) F (n = 3)	7 (87.5%) 2 (66.6%)	1 (12.5%) 1 (33.3%)	0 0
0.5	M (n = 0) F (n = 1)	0 1 (100%)	0 0	0 0
1	M (n = 1) F (n = 0)	0 0	1 (100%) 0	0 0
2	M (n = 0) F (n = 1)	0 0	0 1 (100%)	0 0
4	M (n = 3) F (n = 0)	1 (33.3%) 0	0 0	2 (66.6%) 0
8	M (n = 0) F (n = 1)	0 0	0 0	0 1 (100%)
16	M (n = 1) F (n = 0)	0 0	0 0	1 (100%) 0

Notes: CG – chronic Gastritis, SAG – sever active gastritis, IM – Intestinal Metaplasia, M – male, F – female, MIC – minimum inhibitory concentration.

For molecular analysis, PCR using specific primer sets (Table 1) was performed to detect point mutations in the 23S rRNA gene. The A2142G point mutation was identified in 8 out of 53 specimens (approximately 15%), while the A2143G mutation was not detected in any sample. The PCR results were consistent with the MIC findings (see Figure 2). According to pathological classification, strains HC34, HC30, HC27, and HC42 were in the IM group; HC23 and HC18 were in the SAG group; and HC14 was in the CG group. Strain HC5, which exhibited intermediate sensitivity, belonged to the CG group. Statistically significant differences in clarithromycin resistance rates were observed between the IM and CG groups ($p < 0.004$) and between the IM and SAG groups ($p < 0.02$).

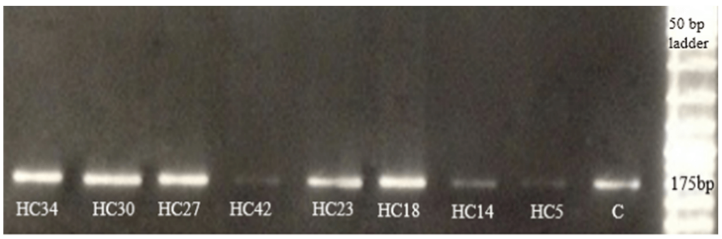

Figure 2 PCR amplification for the A2142G point mutation in 23S rRNA genes. C – control, HC – Helicobacter Pylori (34, 30 and so on are strain number.)

4 Discussion

H. pylori infection is the most common chronic bacterial infection, affecting nearly 50% of the world's population, with contamination rates exceeding 80% in developing countries [19]. This

study reported a 53% infection rate, which is consistent with previous studies in Iran that have reported rates ranging from 36% to 90% [20]. The administration of effective drug regimens is critical to achieving high eradication rates of *H. pylori*. The standard triple therapy, which includes a proton pump inhibitor (PPI), clarithromycin, and either amoxicillin or metronidazole, relies heavily on the efficacy of clarithromycin [21]. The occurrence of clarithromycin resistance varies geographically; while it is generally lower in developed countries, resistance rates in developing countries range from 25% to 50% [22]. In Iran, 21 studies have reported clarithromycin resistance rates varying from 0% to 75% [23]. One study in Iran reported MIC50 and MIC90 values of 0.25 mg/L and 16 mg/L, respectively [24]. In the present study, 13.2% of *H. pylori* strains were resistant to clarithromycin, with MIC50 and MIC90 values of 0.125 mg/L and 2 mg/L, respectively. A similar study in China reported MIC50 and MIC90 values of 0.0312 mg/L and 64 mg/L, respectively [25]. A European survey across 24 centers in 18 countries reported resistance rates ranging from 4.8% to 36.9% [26], and a study in Italy found a resistance rate of 13.5% [27]. Clarithromycin exerts its effect by binding to the peptidyl transferase domain V of the 23S rRNA subunit; consequently, point mutations in the 23S rRNA gene reduce clarithromycin binding, leading to resistance. The A2142G and A2143G mutations are the most prevalent [28]. Recent studies have shown variable prevalence rates for these mutations [29, 30]. In contrast, our study detected the A2142G mutation in 100% of the clarithromycin-resistant strains.

5 Conclusion

This study reveals an increasing trend of clarithromycin resistance among *H. pylori* strains in Iran. The findings also highlight the role of specific 23S rRNA gene mutations, particularly A2142G, in conferring antibiotic resistance. Routine screening for resistance genotypes in *H. pylori* is essential to guide clinicians in selecting appropriate therapeutic regimens.

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Author Contributions

Alireza Ahmadzadeh performed the primary experiments and drafted the initial manuscript.
Zhaleh Mohsenifar conducted all pathological examinations.
Behzad Hatami and Ali Pirsalehi provided the clinical samples.
Mostafa Rezaei-Tavirani contributed to the review and revision of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest

Availability of Data

All data generated during this study are included in this manuscript. There are no restrictions on data availability.

References

[1] Guo Y, Cao XS, Guo GY, et al. Effect of Helicobacter Pylori Eradication on Human Gastric Microbiota: A Systematic Review and Meta-Analysis. Frontiers in Cellular and Infection Microbiology. 2022, 12. https://doi.org/10.3389/fcimb.2022.899248

[2] Cho JH, Jin SY. Current guidelines for Helicobacter pylori treatment in East Asia 2022: Differences among China, Japan, and South Korea. World Journal of Clinical Cases. 2022, 10(19): 6349-6359. https://doi.org/10.12998/wjcc.v10.i19.6349

[3] Hooi JKY, Lai WY, Ng WK, et al. Global Prevalence of Helicobacter pylori Infection: Systematic Review and Meta-Analysis. Gastroenterology. 2017, 153(2): 420-429. https://doi.org/10.1053/j.gastro.2017.04.022

[4] Tran V, Saad T, Tesfaye M, et al. Helicobacter pylori (H. pylori) risk factor analysis and prevalence prediction: a machine learning-based approach. BMC Infectious Diseases. 2022, 22(1). https://doi.org/10.1186/s12879-022-07625-7

[5] Massarrat S, Saberi-Firoozi M, Soleimani A, et al. Peptic ulcer disease, irritable bowel syndrome and constipation in two populations in Iran. European journal of gastroenterology & hepatology. 1995, 7(5): 427-433.
https://pubmed.ncbi.nlm.nih.gov/7614105

[6] Goldberg L, Amrick TJ. Successful Eradication of Helicobacter pylori with 5-Day Concomitant Treatment. Aye TT, ed. GastroHep. 2022, 2022: 1-4.
https://doi.org/10.1155/2022/1211329

[7] Leung WK, Graham DY. Clarithromycin for Helicobacter pylori infection. Expert Opinion on Pharmacotherapy. 2000, 1(3): 507-514.
https://doi.org/10.1517/14656566.1.3.507

[8] Kocsmár É, Buzás GM, Szirtes I, et al. Primary and secondary clarithromycin resistance in Helicobacter pylori and mathematical modeling of the role of macrolides. Nature Communications. 2021, 12(1).
https://doi.org/10.1038/s41467-021-22557-7

[9] Hosseini RS, Rahimian G, Shafigh MH, et al. Correlation between clarithromycin resistance, virulence factors and clinical characteristics of the disease in Helicobacter pylori infected patients in Shahrekord, Southwest Iran. AMB Express. 2021, 11(1).
https://doi.org/10.1186/s13568-021-01310-9

[10] Albasha AM, Elnosh MM, Osman EH, et al. Helicobacter pylori 23S rRNA gene A2142G, A2143G, T2182C, and C2195T mutations associated with clarithromycin resistance detected in Sudanese patients. BMC Microbiology. 2021, 21(1).
https://doi.org/10.1186/s12866-021-02096-3

[11] Bordin D, Morozov S, Plavnik R, et al. Helicobacter pylori infection prevalence in ambulatory settings in 2017–2019 in RUSSIA: The data of real-world national multicenter trial. Helicobacter. 2022, 27(5).
https://doi.org/10.1111/hel.12924

[12] Gharibi S, Falsafi T, Alebouyeh M, et al. Relationship between histopathological status of the Helicobacter pylori infected patients and proteases of H. pylori in isolates carrying diverse virulence genotypes. Microbial Pathogenesis. 2017, 110: 100-106.
https://doi.org/10.1016/j.micpath.2017.06.023

[13] Kahlmeter G, Brown DFJ, Goldstein FW, et al. European Committee on Antimicrobial Susceptibility Testing (EUCAST) Technical Notes on antimicrobial susceptibility testing. Clinical Microbiology and Infection. 2006, 12(6): 501-503.
https://doi.org/10.1111/j.1469-0691.2006.01454.x

[14] Bińkowska A, Biernat MM, Łaczmański Ł, et al. Molecular Patterns of Resistance Among Helicobacter pylori Strains in South-Western Poland. Frontiers in Microbiology. 2018, 9.
https://doi.org/10.3389/fmicb.2018.03154

[15] Bohr URM, Primus A, Zagoura A, et al. A Group-Specific PCR Assay for the Detection of Helicobacteraceae in Human Gut. Helicobacter. 2002, 7(6): 378-383.
https://doi.org/10.1046/j.1523-5378.2002.00113.x

[16] Kauser F, Hussain MA, Ahmed I, et al. Comparative genomics of Helicobacter pylori isolates recovered from ulcer disease patients in England. BMC Microbiology. 2005, 5(1).
https://doi.org/10.1186/1471-2180-5-32

[17] Pan ZJ, Su WW, Tytgat GNJ, et al. Assessment of Clarithromycin-Resistant Helicobacter pylori among Patients in Shanghai and Guangzhou, China, by Primer-Mismatch PCR. Journal of Clinical Microbiology. 2002, 40(1): 259-261.
https://doi.org/10.1128/jcm.40.1.259-261.2002

[18] Furuta T, Soya Y, Sugimoto M, et al. Modified allele-specific primer–polymerase chain reaction method for analysis of susceptibility of Helicobacter pylori strains to clarithromycin. Journal of Gastroenterology and Hepatology. 2007, 22(11): 1810-1815.
https://doi.org/10.1111/j.1440-1746.2007.04919.x

[19] Alexander SM, Retnakumar RJ, Chouhan D, et al. Helicobacter pylori in Human Stomach: The Inconsistencies in Clinical Outcomes and the Probable Causes. Frontiers in Microbiology. 2021, 12.
https://doi.org/10.3389/fmicb.2021.713955

[20] Fakheri H, Saberi Firoozi M, Bari Z. Eradication of Helicobacter Pylori in Iran: A Review. Middle East Journal of Digestive Diseases. 2017, 10(1): 5-17.
https://doi.org/10.15171/mejdd.2017.84

[21] Kim SY, Chung JW. Best Helicobacter pylori Eradication Strategy in the Era of Antibiotic Resistance. Antibiotics. 2020, 9(8): 436.
https://doi.org/10.3390/antibiotics9080436

[22] Yilmaz Ö. Clinical role and importance of fluorescence in situ hybridization method in diagnosis of H pylori infection and determination of clarithromycin resistance in H pylori eradication therapy. World Journal of Gastroenterology. 2007, 13(5): 671.
https://doi.org/10.3748/wjg.v13.i5.671

[23] Khademi F, Poursina F, Hosseini E, et al. Helicobacter pylori in Iran: A systematic review on the antibiotic resistance. Iranian journal of basic medical sciences. 2015, 18(1): 2.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4366738

[24] Alavifard H, Mirzaei N, Yadegar A, et al. Investigation of Clarithromycin Resistance-Associated Mutations and Virulence Genotypes of Helicobacter pylori Isolated from Iranian Population: A Cross-Sectional Study. Current Microbiology. 2020, 78(1): 244-254.
https://doi.org/10.1007/s00284-020-02295-7

[25] Huang X, Liu Y, Lin Z, et al. Minimum inhibitory concentrations of commonly used antibiotics against Helicobacter Pylori: A multicenter study in South China. Siddique MH, ed. PLOS ONE. 2021, 16(9): e0256225.
https://doi.org/10.1371/journal.pone.0256225

[26] Megraud F, Bruyndonckx R, Coenen S, et al. Helicobacter pylori resistance to antibiotics in Europein 2018 and its relationship to antibiotic consumption in the community. Gut. 2021, 70: 1815–1822.
https://pubmed.ncbi.nlm.nih.gov/33837118

[27] De Francesco V, Zullo A, Fiorini G, et al. Role of MIC levels of resistance to clarithromycin and metronidazole in Helicobacter pylori eradication. Journal of Antimicrobial Chemotherapy. 2018, 74(3): 772-774.
https://doi.org/10.1093/jac/dky469

[28] Hussein RA, Al-Ouqaili MTS, Majeed YH. Detection of clarithromycin resistance and 23SrRNA point mutations in clinical isolates of Helicobacter pylori isolates: Phenotypic and molecular methods. Saudi Journal of Biological Sciences. 2022, 29(1): 513-520.
https://doi.org/10.1016/j.sjbs.2021.09.024

[29] Khashei R, Dara M, Bazargani A, et al. High rate of A2142G point mutation associated with clarithromycin resistance among Iranian Helicobacter pylori clinical isolates. APMIS. 2016, 124(9): 787-793.
https://doi.org/10.1111/apm.12567

[30] Seo SI, Do BJ, Kang JG, et al. Helicobacter pylori Eradication According to Sequencing-Based 23S Ribosomal RNA Point Mutation Associated with Clarithromycin Resistance. Journal of Clinical Medicine. 2019, 9(1): 54.
https://doi.org/10.3390/jcm9010054

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