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Adequacy of practice regarding *Helicobacter pylori* eradication in Al-madinah, Kingdom of Saudi Arabia: A cross-sectional study

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ABSTRACT

Background: H. pylori (*Helicobacter pylori*) is one of the most common infections worldwide, with a high prevalence in both developed and developing countries. *Objective:* This study aimed to assess the level of knowledge, attitudes and practices regarding *H. pylori* infection diagnosis and treatment among Primary Health Care Physicians in Al-Madinah, Saudi Arabia. *Methods:* A cross-sectional study design was employed at primary healthcare centers in Al-Madinah city between 2021-2022. Data were collected by distributing a self-administered questionnaire to primary healthcare physicians. Student's t-test and chi squared test were used to evaluate the differences in means and proportions, respectively. *Results:* In total, 100 participants were included in this study. The majority (91%) reported that the standard empirical treatment for *H. pylori* eradication was triple therapy. The treatment duration was reported to be 14 days in the majority of participants (73%). *Conclusion:* This study concluded that the current practice regarding *H. pylori* eradication in Al-Medinahis unsatisfactory. It is necessary to implement measures to increase the adequacy of practice by providing clear and updated guidelines on this important public health issue.

Keywords: Antibiotic resistance, Practice, Eradication, *Helicobacter pylori*, Infection, Peptic ulcer.

1. INTRODUCTION

H. Pylori (*Helicobacter Pylori*), is a slow-growing, spiral-shaped, highly motile, gram-negative bacterium discovered in 1983 in patients with chronic gastritis and peptic ulcer disease. *H. pylori* is now widely considered to be one of the most significant risk factors in the development of upper gastrointestinal diseases, mainly in developing countries (Mansour et al., 2011). *H. pylori* infection is estimated to affect almost half of the world's population. In Saudi

Arabia, 51–78 percent of the population is infected with *H. pylori* (Alsohaibani et al., 2015). In Almadinah City, the prevalence of *H. pylori* infection is estimated to be 28% (Hanafi and Mohamed, 2013).

Geographic location, ethnicity, socioeconomic status and age are known to influence the prevalence of *H. pylori* infection. In addition, the overall prevalence in developing countries is much higher than that in developed countries (Mansour et al., 2011). Adequate management of *H. pylori* infection may cure some consequences of infection, such as dyspepsia and peptic ulcers andmay prevent the development of gastric cancer (Alsohaibani et al., 2015; Alharth et al., 2022). Some evidence-based rules of thumb have been suggested for better management of *Helicobacter pylori* infection (Calvet, 2018). The first rule is use of quadrable therapy, rather than triple therapy. Second rule is the use of high-dose proton pump inhibitors. Third rule is the use of a prolonged course of treatment (two weeks). Fourth rule is to avoid repeating the same antibiotic if treatment fails. The final rule is to use the treatment if it is locally effective. In 2002, a study conducted in Peru highlighted that 60% of primary healthcare physicians used suboptimal regimens for *H. pylori* eradication (Montes, 2002). Saudi Arabia has reported a prevalence of 66% for *H. Pylori* infections (Hooi et al., 2017).

In 2015, there were an estimated 4.4 billion individuals globally infected with *H. Pylori* (Hooi et al., 2017). Owing to the high prevalence of infection, it is important to study the standard of treatment in Saudi Arabia and the reasons that contribute to treatment failure. To our knowledge, no previous studies have been conducted on primary healthcare physicians regarding their knowledge and practice of *H. pylori* infection in Saudi Arabia.

Our study aimed to evaluate the level of knowledge, attitudes and practices regarding *H. pylori* infection diagnosis and treatment among physicians in the primary health care centers in Al-Madinah, Saudi Arabia.

2. MATERIALS AND METHODS

This cross-sectional study was conducted at governmental primary healthcare centers in Al-Madinah Al-Munawarah city in the period between December 2021 and March 2022. The Al-Madinah Al-Munawarah region is one of the main regions in the Kingdom of Saudi Arabia. Al-Madinah City is divided into four geographic sectors: North, South, East and West. Each sector has several primary healthcare centers. After obtaining ethical approval, we contacted the managers of the primary healthcare centers to obtain permission to collect data. One hundred physicians who had practiced for more than six months were included in this study.

A self-administered questionnaire consisting of two sections was distributed to the physicians. The first section contained personal and educational data, such as age, sex, nationality, latest medical degree, years since graduation and years of experience. The second section measured practice data and the core component aimed to explore *H. pylori* treatment guidelines applied in practice and whether there is a consideration of the five empirical rules in *H. Pylori* eradication. The rules included using quadrable therapy, high doses of proton pump inhibitors, a prolonged course of treatment, avoiding repetition of the same antibiotic if the treatment failed and using the most effective treatment locally. The second section contains the following variables: Place of work, average number of *H. pylori* infections diagnosed monthly, knowledge and attitude of physicians regarding the failure of *H. Pylori* eradication, physician's satisfaction with current guidelines for treating *H. pylori* infection, knowledge regarding the prevalence of the diseases in the Saudi population and knowledge regarding the most common symptoms of *H. pylori* infection.

Data were managed and analyzed using the Statistical Package for Social Sciences (SPSS) and p-value is considered statistically significant when it is less than 0.05. For continuous variables, the Student's t-test was used to evaluate the differences in means between the groups. For categorical data, the chi-squared test was used to assess differences in proportions across categories.

3. RESULTS

Sociodemographic characteristics of participants

The majority were women (52%), Saudi nationality (64%) and aged ≤33 years (52%). Most had five or fewer years of experience (43%). More than half had a postgraduate certificate (53%). Sixty-two percent had less than five cases of *H. pylori* infection per month (Table 1).

Knowledge and practice of the participants regarding *H. Pylori* infection

The majority reported that the standard empiric treatment for *H. pylori* eradication was triple therapy (91%), whereas classic quadruple therapy was reported in 16%, levofloxacin quadruple therapy in 5%, concomitant quadruple therapy in 4% and rifabutin quadruple therapy in 0%. Regarding proton pump inhibitors used for the *H. pylori* eradication regimen, the use ofomeprazole and esomeprazole was reported to be 85% and 19%, respectively, whereas that of lansoprazole and pantoprazole was reported to be 3% and 4%, respectively. None of the participants reported using rabeprazole. Approximately, 73% of the participating physicians

reported that the treatment duration is 14 days. The dose and frequency were reported to be 20 mg, twice/day or 40 mg once/day by most of the participants (65%). If there is no response to the therapy, 27% stated that they would use the same protocol with different antibiotics, whereas 43% reported that they would use a different protocol (Table 2). The most common causesof *Helicobacter pylori* treatment failure reported by the participants were antibiotic resistance (68%) and poor adherence (71%). The most common symptoms of *Helicobacter pylori* infection reported by the participants were epigastria pain (89%), heartburn (78%), nausea (71%), vomiting (48%) and anorexia (46%). The following tests were used to diagnose the disease: Serology (56%), breath test (68%), fecal antigen (54%), histology (15%) and culture (13%). The following question was asked: "How long after *H. pylori* eradication treatment do you order a test to demonstrate eradication?" most participants chose "four to six weeks (54%)," while 31% and 12% chose "three to four weeks" and "one to two weeks," respectively (Table 2).

Table 1 Sociodemographic characteristics of the participants

		n	%
Sex	Male	48	48.0
	Female	52	52.0
Age (years)	≤33	52	52.0
	>33	48	48.0
Nationality	Saudi	64	64.0
	Non-Saudi	36	36.0
Latest Medical degree	Bachelor	47	47.0
	Postgraduate	53	53.0
Years since graduation	≤5	45	45.0
	6-10	21	21.0
	>10	34	34.0
Years of experience	≤5	43	43.0
	6-10	21	21.0
	>10	36	36.0
Number of cases with *H. Pylori* infection treated per month	< 5	62	62.0
	≥5	38	38.0

Table 2 Knowledge and practices of participants regarding *H. Pylori* infection

	n	%
What is the standard empiric treatment for *H. pylori* eradication		
Triple therapy	91	91.0
Classic quadruple therapy	16	16.0
Levofloxacin quadruple therapy	5	5.0
Hybrid therapy	0	0.0
Sequential therapy	4	4.0
Concomitant quadruple therapy	4	4.0
Rifabutin quadruple therapy	0	0.0
Reverse hybrid therapy	0	0.0
Which type of proton pump inhibitor do you include in your *Helicobacter pylori* eradication regimen		
Omeprazole	85	85.0
Lansoprazole (Prevacid)	3	3.0
Pantoprazole (Pantozol)	4	4.0
Esomeprazole (Nexium)	19	19.0
Rabeprazole (Aciphex)	0	0

Specify the treatment duration		
7 days	9	9.0
10 days	18	18.0
14 days	73	73.0
Dose and frequency		
20 mg, Bid or 40 mg, QD(correct answer)	65	65.0
In your practice, in case of *Helicobacter pylori* eradication failure, do you prefer to?		
Use the same protocol with different antibiotics	27	27.0
Use the same protocol with a longer duration	15	15.0
Use different protocol	43	43.0
Repeat same protocol, antibiotics, and duration	5	5.0
The most common reason of *H. pylori* treatment failure		
Antibiotic resistance	68	68.0
Host genetic polymorphism in the cytochrome (CYP2C19)	7	7.0
Poor adherence	71	71.0
Short duration of therapy	21	21.0
Smoking	12	12.0
Symptoms associated with *H. pylori* infection		
Halitosis	22	22.0
Pharyngitis	16	16.0
Nausea	71	71.0
Anorexia	46	46.0
Excessive burping	28	28.0
Chest pain	35	35.0
Diarrhea	11	11.0
Anemia	17	17.0
Epigastric pain	89	89.0
Vomiting	48	48.0
Dental erosion	8	8.0
Heartburn	78	78.0
Early Satiety	23	23.0
Constipation	6	6.0
Irritable bowel syndrome	20	20.0
Cough	16	16.0
Flatulence	23	23.0
Unintentional weight loss	16	16.0
Regurgitation	34	34.0
Bloating	34	34.0
How do you diagnose your patient presenting with *Helicobacter pylori* related symptoms?		
Serology	56	56.6
Breath test	68	68.7
Culture	13	13.1
Histology	15	15.2

Fecal antigen	54	54.5
When you wish to confirm eradication, what test do you use		
Serology	24	24.0
Breath test	61	61.0
Culture	5	5.0
Histology	7	7.0
Fecal antigen	46	46.0
How long after *H. Pylori* eradication treatment do you order a test to demonstrate eradication?		
One to two weeks	12	12.0
Three to four weeks	31	31.0
Four to six weeks	54	54.0

Practice and associated factors

The practices of participants were categorized as good or bad. Accordingly, 12% of the participants were classified as having good practice (Figure 1). A chi-squared test was used to assess the association between practice and participant characteristics (Table 3). There was no significant relationship between practices and participant characteristics.

Figure 1 Frequency of doctors who had good and bad practice

4. DISCUSSION

In our study, only 25% of the participants reported any type of quadruple therapy as the standard regimen for *H. pylori* eradication and most participants (91%) reported that the standard treatment regimen for *H. pylori* infections wasa triple therapy regimen, that is, clarithromycin-based triple therapy. Recent evidence shows a remarkable decline in the success of *H. pylori* infection eradication with the use of clarithromycin-based triple therapy (Jung et al., 2021). This decline can be attributed to several factors. However, the main reason for treatment failure is most likelythe increase in clarithromycin resistance (Kim et al., 2014). A study in Saudi Arabia conducted in 2002 to explore *H. pylori* resistance to different antibiotics found that 80% of the isolates were resistant to metronidazole, 4% to clarithromycin, 1.3% to amoxicillin and 0.4% to tetracycline (Eltahawy, 2002). A more recent study showed that clarithromycin resistance in *H. pylori* was 23%, whereas amoxicillin resistance was 15% (Alsohaibani et al., 2015). The observed rising levels of antibiotic resistance should be considered when selecting the most effective regimen against *H. pylori* infection in Saudi Arabia. The American College of Gastroenterology Clinical Guideline for Treatment of *Helicobacter pylori* Infection strongly recommends the use of bismuth quadruple therapy as a first-line regimen in regions with a high rate (>15%) of clarithromycin resistance (Chey et al., 2017). This recommendation was adopted locally in Saudi Arabia by the Saudi *H. pylori* working group and triple therapy is no longer recommended as first-line treatment (Alsohaibani et al., 2022).

Table 3 Factors associated with practice in univariate analysis

		Good practice n (%)	Bad practice n (%)	P value
Sex	Male	8 (66.7)	40 (45.5)	0.168
	Female	4 (33.3)	48 (54.5)	
Nationality	Saudi	10 (83.3)	54 (61.4)	0.137
	Non-Saudi	2 (16.7)	34 (38.6)	
Age	≤33	7 (58.3)	45 (51.1)	0.640
	>33	5 (41.7)	43 (48.9)	
Years since graduation	≤5	8 (66.7)	37 (42.0)	0.124
	6-10	3 (25.0)	18 (20.5)	
	>10	1 (8.3)	33 (37.5)	
Years of experience	≤5	5 (41.7)	38 (43.2)	0.123
	6-10	5 (41.7)	16 (18.2)	
	>10	2 (16.7)	34 (38.6)	
Number of patients with *H. pylori* seen per month	< 5	5 (41.7)	57 (64.8)	0.122
	≥5	7 (58.3)	31 (35.2)	
Latest medical degree	Bachelor	3 (25.0)	44 (50.0)	0.104
	Postgraduate	9 (75.0)	44 (50.0)	

One of the key management points for *H. pylori* eradication is antibiotic therapy duration. Based on evidence-based observed changes in infection eradication rates, the Maastricht V/Florence Consensus Report recommended extending standard triple therapy to 14 days (Malfertheiner et al., 2017). In our study, 73% of the participants were aware of the benefits of extending treatment duration. In our study, we found that the most common manifestation of *H. pylori* infection reported by the participants were epigastric pain (89%) and heartburn (78%). It is plausible that these complaints are complications of duodenal ulcers or gastric ulcers, of which *H. pylori* is responsible for 95% and 70% of the cases, respectively (Ford et al., 2016). These findings are consistent with evidence in the literature, which revealed that *H. pylori* infection can cause histological gastritis and the most common complaints are abdominal pain and heartburn (Kavitt et al., 2019; Barkun and Leontiadis, 2010).

The most common reasons of treatment failure, reported by the participants, were antibiotic resistance (68%) and poor adherence from the patients (71%). Most medical therapies require high adherence to achieve successful outcomes. Resistance of the pathogen to antibioticsis increasing globally, with a concomitant decline inthe eradication rate (Chey et al., 2017). A systematic review conducted to study the association between successful *H. pylori* eradication therapy and antibiotic resistance reported a substantial reduction in the cure rate of resistant strains (Houben et al., 1999).

Regarding acid inhibition, omeprazole was the most commonly used proton pump inhibitor in the *H. pylori* eradication regimen (85%), followed by esomeprazole (19%). Most participating physicians opted for a higher dose of PPI (65%) and prolonged duration of treatment (73%). It has been suggested in the literature that optimal acid inhibition may play a role in overcoming *H. pylori* antimicrobial resistance (Sugimoto et al., 2007). Proton pump inhibitors are metabolized in the liver by cytochrome P450 is enzyme 2C19. Different variants of this enzyme result in varying levels of activity. Individuals with a higher activity of this enzyme (extensive metabolizes) may be exposed to a lower level of PPI, requiring an increased dose to achieve a sufficient clinical response (Furuta et al., 2004). This has a significant and relevant application locally, as it was previously reported that extensive metabolizes are the most common (78%) CYP2C19 phenotype in Saudi Arabia (Saeed and Mayet, 2013).

Remarkably, not all PPI's were affected by variations in the CYP2C19 activity. A Meta-Analysis of Randomized Clinical Trials found that eradication rates of *H. pylori* infection with rabeprazole or esomeprazole did not change across all CYP2C19 variants (Tang et al., 2013). In our study, rabeprazole or esomeprazole was included in the treatment regimen in only 19% of participants. This highlights the importance of choosing the appropriate dose and PPI agent to achieve optimal management of *H. pylori* infection in Saudi Arabia. This study has several strengths. To the best of our knowledge, this is the first study to assess the adequacy of practices for the eradication of this infection in Saudi Arabia. In addition, we designed this study to be as representative as possible by achieving the precalculated sample size goal, selecting the centers and participants using a random sampling technique and

finally applying a few restrictions, thereby increasing the generalizability of the study as much as possible. The main limitation of our study was the use ofa self-designed questionnaire.

5. CONCLUSION

Our results showed that there is poor knowledge among physicians working in primary healthcare centers in Almadinah city regarding the best treatment regimen for *H. pylori* infections. There is average knowledge about the initial diagnosis and eradication confirmation of the disease. It is necessary to implement measures to increase the adequacy of practice regarding *H. pylori* eradication among primary healthcare physicians. Essentially, health authorities can help by providing Continuing Medical Education accredited programs and forming clear updated guidelines on this significant public health issue. In addition, studies on *H. pylori* eradication rates and drug resistance in Saudi Arabia are highly recommended.

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Authors' contributions

Sami A, Osama M and Abdulmajeed G contributed to the study design, Osama A, Hamza W, Zeyad K, Khaled T, Ahmed A and Mohamed H contributed to data collection and manuscript writing. Sami A performed the analysis. Osama M and Abdulmajeed G revised the manuscript. All authors have critically reviewed and approved the final draft and are responsible for the manuscript's content and similarity index.

Ethical approval

Ethical approval was obtained from the ethics committee of the General Directory of Health in Al-Madinah (Ethical Approval code 148-202, dated 15/08/2021).

Informed consent

Written & Oral informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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