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Knowledge Regarding *H.Pylori* Management Among Hospital Doctors in Benghazi, Libya

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Abstract:
Helicobacter pylori (H. pylori) affects almost half of the world population. The infection is more prevalent in developing countries (up to 90%) especially in societies with lower socioeconomic status. Doctors' knowledge about management of *H.Pylori* infection is a subject of continuous evaluation, given the worldwide high prevalence, and variations in diagnostic methods and treatment regimens. This is cross-sectional observational, questionnaire-based study that explored the knowledge background about managing *H.Pylori* infection among trainee doctors in Benghazi hospitals, where 150 doctors were asked to fill in the questionnaire. Hundred and eleven responded (74.0%). The most frequent symptoms thought by the participants to be caused by *H.Pylori* infection were epigastric pain (77.5%) and heartburn (62.2%). Forty-nine participants (out of 108 (45.3%)) preferred prescribing eradication for all patients with confirmed infection. Thirty-six (out of 94) (38.3%) participants preferred the antibiotic combination of amoxycillin and clarithromycin. The most preferred test for confirmation of *H.Pylori* eradication was fecal antigen test (82 out of 111(73.9%))**.** There is a clear knowledge gap among hospital doctors working in secondary care hospitals in Benghazi, regarding the symptomatology, and management of H.*Pylori* infection. Our findings are comparable to many similar observations worldwide.

Keywords: H.Pylori, Helicobacter Pylori, Peptic ulcer, MALT lymphoma, Dyspepsia.

المعرفة حول معالجة البكتيريا الحلزونية البوابية لدى أطباء المستشفيات ببنغازي، ليبيا

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الملخص
تصيب البكتيريا الحلزونية البوابية نحو نصف سكان العالم. تكون العدوى أكثر انتشارًا في البلدان النامية (تصل إلى 90%) خصوصًا في المجتمعات ذات الوضع الاقتصادي المنخفض. معرفة الأطباء معالجة عدوى البكتيريا الحلزونية البوابية هي موضوع تقييم مستمر، نظرًا للانتشار العالمي العالي لها، والاختلافات في طرق التشخيص وبرامج العلاج. هذه دراسة مستعرضة، قائمة على الاستبيان لاستكشاف الخلفية المعرفية حول عدوى البكتيريا الحلزونية البوابية بين الأطباء المتدربين في مستشفيات بنغازي، حيث طُلب من 150 طبيبًا ملء الاستبيان، ورد منهم 111 (74.0%). كانت أكثر الأعراض شيوعًا التي اعتقد المشاركون أنها ناتجة عن عدوى البكتيريا الحلزونية البوابية هي آلام البطن العلوية (77.5%) وحرقة المعدة (62.2%). كان 49 مشاركًا (من بين 108 (45.3٪)) يفضلون صرف العلاج لجميع المرضى المؤكدين بالإصابة. كان 36 من 94 (38.3%) يفضلون توليفة الأدوية المضادة للبكتيريا من الأموكسيسيلين والكلارثرومايسين. وكان اختبار البراز للتأكد من استئصال البكتيريا الحلزونية البوابية هو الاختبار الأكثر تفضيلًا (82 من 111 (73.9%)). هناك فجوة معرفية واضحة بين أطباء المستشفى الذين يعملون في مستشفيات الرعاية الصحية الثانوية في بنغازي، فيما يتعلق بالأعراض ومعالجة عدوى البكتيريا الحلزونية البوابية. نتائجنا مقاربة للعديد من الدراسات المماثلة على مستوى العالم.

الكلمات المفتاحية: البكتيريا الحلزونية البوابية، قرحة المعدة، الليمفوما MALT، عسر الهضم.

Introduction

Helicobacter pylori (H. pylori) is a gram-negative, microaerophilic bacterium. It's one of the most common pathogens affecting humans, as almost half of the world population are infected. (1)

The infection is more prevalent in developing countries (up to 90%) especially in societies with lower socioeconomic status, overcrowding and poor sanitation. (2)

H.Pylori infection can be responsible for non-specific upper gastrointestinal symptoms like abdominal pain, nausea, and vomiting. It should be considered in the differential diagnosis when evaluating patients with these complaints. The infection is also associated with development of chronic gastritis, peptic ulcer, type B gastric lymphoma (Mucosal Associated Lymphoid Tissue (MALT) lymphoma), and gastric adenocarcinoma. (3-7)
Testing for *H.Pylori* is indicated for patients with history of peptic ulcer disease, low grade MALT lymphoma or history of endoscopic resection of early gastric cancer. It's also indicated in patients with iron deficiency anemia; while in patients with gastroesophageal reflux disease, testing is not recommended unless there is history of peptic ulcer disease.(8)
Non-invasive testing with urea breath test is considered as the best initial diagnostic test for people under the age of 60 years with uninvestigated dyspepsia (test-and-treat approach). Gastric biopsies should be obtained to assess for *H.Pylori* infection when upper gastrointestinal endoscopy is performed in patients with dyspepsia. (8)
In the presence of alarm manifestations such as weight loss, anorexia, or gastrointestinal bleeding, or in older adults, gastroscopy is indicated to exclude upper gastrointestinal malignancy. Meanwhile, the diagnosis of *H.Pylori* infection can be made by biopsy and histopathology.
Test-and-treat approach in countries with high prevalence of *H.Pylori* infection, is supported by the evidence of decreased gastric cancer incidence following *H.Pylori* eradication. It allows doctors from different specialties to be involved managing *H.Pylori* infection (9,10)
Treatment is offered to all patients with positive test. It consists of a proton pump inhibitor with clarithromycin, and amoxicillin for 14 days, if the resistance against clarithromycin is < 15%, and in the absence of previous macrolide exposure. The National Institute for Health and Care Excellence (NICE) in the United Kingdom recommends treatment duration of 7 days, with PPI administered twice daily. (8,11)
Confirmation of eradication by a non-invasive test (urea breath test, or a stool antigen) is performed 4 weeks after completing antibiotic therapy and 2 weeks after PPI therapy (when PPI is continued after eradication regimen to control symptoms). (7,8,11)
There are gaps in the adherence to practice guidelines for the management of *H. pylori* worldwide, and the studies assessing doctors' awareness about *H.Pylori* diagnosis and management are limited. Many of these studies assessed primary care doctors, and not hospital doctors. (12)
In this study we tried to explore the knowledge background about managing *H.Pylori* infection among trainee doctors working in Benghazi hospitals.

Methods

Study design and setting

A questionnaire based cross-sectional study was conducted using a semi-structured questionnaire consisted of 16 questions. The questionnaire was designed to evaluate the trainee doctors' knowledge of the symptomatology and management of *H.Pylori* infection.

Data collection procedure

Trainee doctors working in secondary care hospitals in Benghazi (Benghazi Medical Center, Benghazi Cardiac Center, and Hawari General Hospital), Libya, with hospital practice experience of 5 years and less, were enrolled in the study.
All the study participants were exposed to patients with *H.Pylori* infection, and those who were posting in gastroenterology services were excluded.
Subjects were selected by availability during the period when the questionnaire was handed out (a non-probability, convenience sampling), and the questionnaire was filled in voluntarily and anonymously by doctors during their working hours.

Results

A total of 111 doctors (out of 150 (74.0%)) responded to the questionnaire.
Among the responders, male doctors were 30 (27.0%) and females were 81 (73.0%), with a mean age of 32.1 years (SD±2.23), and a range of 28-40 years.
The mean duration of the hospital practice experience of the participants was 3 years (SD±1.39). The response rate to different questions was variable. Not all questions were answered by all participants, and therefore non-responders for a particular question were excluded when the total percentage was calculated.
The most frequent clinical manifestations thought by the participants to be caused by *H.Pylori* infection were epigastric pain (77.5%), and heartburn (62.2%). Lesser number of participants thought that regurgitation, chest pain, halitosis, excessive burping, dental erosions, cough, and asthma were also manifestations of *H.Pylori* infection.
Eighty-seven (78.4%) of the study participants thought that *H.Pylori* infection can alter or produce gastroesophageal reflux symptoms, while 82 (74.5%) thought that *H.Pylori* infection is the main cause of dyspeptic symptoms (epigastric pain, nausea, early satiety, and gastric fullness).

Forty-nine participants (out of 108 (45.3%)) preferred prescribing eradication for all patients with confirmed infection, while 7 participants (6.5%) didn't prefer eradication therapy. Table (1).

Table (1) Participants' responses to when *H.Pylori* eradication therapy is indicated (multiple choices were allowed).

Indication for eradication	Number of responders (%)
Always	49 (45.3%)
Patients with history of ulcer	47 (43.5%)
Patients with dyspepsia	38 (35.2%)
Patients with reflux	33 (30.5%)
Patients with gastric cancer	20 (18.5%)
Patients with chronic NSAIDs use	16 (14.8%)
Patients with irritable bowel syndrome	14 (12.9%)
Patients with first degree relatives with gastric cancer	13 (12.0%)
Never	7 (6.5%)
Total	**237**

The most common specific indication for *H.Pylori* eradication as stated by the study participants was the presence of history of peptic ulcer (47 (43.5%)).
Sixty-nine (out of 108 (63.9%)) participants would order a diagnostic test for all patients with upper gastrointestinal symptoms. Fecal antigen test was the commonest diagnostic choice indicated by the study group (71/111 (63.9%)), and the most preferred test for confirmation of *H.Pylori* eradication was fecal antigen test (82 out of 111(73.9%)). Table (2)

Table (2) Participants' responses regarding the choice of initial diagnostic test(s) and test(s) for confirmation of eradication (multiple choices were allowed).

Test type	Number of responders (%)	
	Initial diagnostic test	Preferred test for confirmation of eradication
Serology	18 (9.6%)	10 (6.8%)
Histology	22 (11.8%)	8 (5.5%)
Breath Test	30 (16.0%)	30 (20.5%)
Fecal Antigen	71 (38.0%)	82 (56.2%)
ALL	46 (24.6%)	16 (11.0%)
Total	**187**	**146**

Thirty-six (out of 94 (38.3%)) participants preferred the antibiotic combination of amoxycillin and clarithromycin, while 18 (19.1%) preferred the combination of amoxycillin, clarithromycin, and metronidazole. Table (3).

Table (3) Participants' responses for antibiotic combination choice.

Antibiotic combination	Number of responders (%)
Amoxicillin + Clarithromycin	36 (38.3%)
Amoxicillin + Clarithromycin + Metronidazole	18 (19.1)
Amoxicillin + Metronidazole	5 (5.3%)
Amoxicillin + Clavulanic acid	7 (7.4%)
Amoxicillin	7 (7.4%)
Clarithromycin	1 (1.1%)
Clarithromycin + Metronidazole	13 (13.8%)
Amoxicillin + Clarithromycin + Ciprofloxacin	1 (1.1%)
Metronidazole + Ciprofloxacin	1 (1.1%)
Metronidazole + Tetracycline	1 (1.1%)
Amoxicillin + Clavulanic acid + Metronidazole	1 (1.1%)
Amoxicillin + Clarithromycin + Bismuth	2 (2.1%)

Metronidazole + Tetracycline + Bismuth	1 (1.1%)

Most of the participants (65 out of 109 (59.6%)) indicated 14 days as the recommended duration of eradication therapy. Ten (9.2 %) mentioned that duration of therapy is more than 30 days. Table (4).

Table (4) Participants' responses regarding the duration of *H.Pylori* eradication treatment.

Duration of eradication treatment	Number of responders (%)
7 days	15 (13.7%)
10 days	10 (9.2 %)
14 days	65 (59.6%)
20 days	5 (4.6%)
30 days	4 (3.7%)
>30 days	10 (9.2 %)
Total	**109**

Seventy-six of 110 (69.1%) preferred ordering tests to confirm *H.Pylori* eradication. Table (5).

Table (5) Participants' responses regarding which patients require a confirmation test for eradication after treatment.

Requirement for confirmation test for eradication	Number of responders (%)
In all patients	76 (69.1%)
In special cases	31 (28.2%)
None	3 (2.7%)
Total	**110**

The time period after which a test for confirmation of eradication following treatment is performed, was variable according to the participants' responses. Thirty-three (43.4%) thought that 4 weeks should elapse after treatment, before a test is performed. Twenty-two (29.0%) preferred 2 weeks, while the remaining participants (27.6%) gave wide range of responses, from 1 week to 24 weeks.

Discussion

Helicobacter Pylori infection prevalence is high in developing countries. The awareness about the diagnosis and treatment regimens remains a subject of continuous evaluation. The knowledge about *H.Pylori* is low among doctors, particularly non-gastroenterologists, according to many studies. This creates gaps in applying clinical management guidelines. (13–18)

Doctors working in different medical sub-specialties may have different knowledge backgrounds regarding the clinical manifestations and management of *H.Pylori* infection.

In this study we focused on the awareness of doctors, who have their training posts in different medical units, with a maximum of five years' experience following graduation.

Through the questionnaire, many participants didn't answer some questions, and we think this is self-recognition of knowledge gap.

H.Pylori infection usually causes no symptoms. If symptoms occur, they are attributed to gastritis or peptic ulcer disease. These include upper abdominal aching or burning pain (which may or may not be related to food intake), nausea, belching, bloating, and sometimes anorexia and weight loss. *H.Pylori* infected population develop peptic ulcer disease in about 20%. Chronic dyspepsia develops in 10 % and MALT lymphoma in 1 %. (3–5,19,20)

The majority of participant doctors (77.5%) agreed that epigastric pain is a common symptom of *H.Pylori* infection. Large proportion of participants thought that other symptoms are also common, including heartburn (62.2%) and abdominal distension (60.4%). Regurgitation is not a symptom related to *H.Pylori* infection, although 41.1% of the study participants thought *H.Pylori* may cause regurgitation. This may have negative impact on the proper selection of patients who need to be tested for *H.Pylori* infection. In the same time, symptoms that are more related to other gastrointestinal diseases or disorders may be wrongly attributed to *H.Pylori* infection, resulting in missing alternative etiologies. Compared to our results, from a Turkish study, dyspepsia was the main indication for a diagnostic test, followed by gastroesophageal reflux disease and PUD. (14)

According to these results, symptoms related to gastroesophageal reflux disease were selected by some participants as a manifestation of *H.Pylori* infection. Others (12.9%) mentioned that *H.Pylori* eradication therapy is indicated for patients with irritable bowel syndrome.

Other unrelated manifestations (chest pain, halitosis, dental erosions, cough, pharyngitis, and asthma) and even lower gastrointestinal symptoms (constipation) were thought to be related to *H.Pylori* infection by small

percentage of participants. The inaccuracy of analyzing gastrointestinal symptoms among the study participants is a major determinant of inappropriate work-up, which probably leads to over-testing for *H.Pylori* infection.

Non-invasive testing is recommended for the diagnosis of *H.Pylori* infection. Urea breath test is the best initial diagnostic test, and is the most commonly used non-invasive test worldwide with high accuracy and convenience, followed by fecal stool antigen, although there is no enough evidence to support the latter. (8,21)

Regarding which test is better to diagnose *H.Pylori* infection, fecal antigen was the most preferred test by the study group (38.0%), while only 9.6% recommended serology, despite its comparable sensitivity and specificity. The reason for preferring fecal antigen test was probably because of its wide local availability, compared with urea breath test.

Given the variation in cost and convenience among the available diagnostic tests, 24.6% of the participants selected all of them to be suitable for initial diagnosis or screening, which indicates knowledge defect in the properties of each test, as some of them may not be suitable for initial diagnosis if the testing is preceded by proton pump inhibitor or antibiotic therapy by 4 weeks or less. Furthermore, upper gastrointestinal endoscopy and gastric mucosal biopsies for histopathological diagnosis is not required for initial diagnosis of *H.Pylori* infection in the absence of other indications, given its cost and invasiveness.

The study participants opinion regarding the indication for eradication therapy was diverse. Treating all patients was the preferred approach by 45.3% participants. This is concordant with the American Gastroenterology Guidelines. (8)

Surprisingly, 7 participants (6.5%) preferred no therapy. In addition to PPI, the antibiotic combination clarithromycin and amoxycillin, was the most frequent first-line regimens given by the participants. Only 3 (3.2%) participants mentioned bismuth compound among their antibiotic combination of choice. Fifteen (15.9%) preferred only one antibiotic (amoxycillin, clavulanate potentiated amoxycillin, or clarithromycin). Since there are no local data about the sensitivity to antibiotics, the choice of the antibiotic regimen depends on either following international guidelines or doctors' personal preference. In our survey, some participants thought that clavulanate potentiated amoxycillin may be prescribed as alternative to amoxycillin, although it's not recommended in all published guidelines.

High dose PPI-amoxicillin dual therapy is recommended as first line treatment. But clarithromycin or clavulanate potentiated amoxycillin are not used as a part of dual therapy. (8)

The majority (59.6%) agreed that 14 days is the optimum duration of eradication therapy. Most of the *H.Pylori* eradication regimens duration is 10-14 days, while the recommended duration of therapy is 7 days according to NICE guidance. (8,11)

Unexpectedly, about 17.5% of the study participants would treat for 20 days or more, and most of them selected a duration of more 30 days. This will increase the cost and the incidence of side effects, without any proven extra benefit. None of the participants did specify the antibiotic dose or frequency of administration.

H.Pylori eradication should be confirmed in all patients. Out of our study group, 69.1% would test for eradication in all treated patients, although three (2.7%) participants preferred non-testing. The remainder will re-test in selected patients (the details of how to select cases for re-testing weren't mentioned in the questionnaire and were left to the participants' judgment.

The minimal recommended time interval to allow for re-testing for eradication is 4 weeks for antibiotics and 2 weeks for PPI (when PPI therapy is extended). (8)

Twenty participants didn't respond to the question related to the best time interval for testing for eradication. There were extremes in the responses from as early as 1 week and as late as 24 weeks. Thirty-three (43.4.3%) of the responders selected 4 weeks as the optimum time interval. Testing for eradication too early following eradication therapy will result in false negative results, which will falsely magnify the estimation of the eradication rate. None of the participants specified the time interval for PPIs or antibiotics, separately.

H.Pylori fecal antigen test was the most preferred test to confirm eradication as selected by the study participants (56.2%), followed by breath test (20.5%). Serology was selected by 6.8% of the participants which is not useful to confirm eradication, as antibodies may still be detectable years after eradication. Some of the study participants thought that all tests can be used to test for eradication. Based on these results, any local figures for the rate of successful eradication will be compromised by the inappropriate time of retesting and the choice of the test to confirm eradication. These results clearly reflect the lack of adequate knowledge among hospital trainee doctors who are posting in units or departments which are not directly dealing with gastrointestinal patients.

Similar observations worldwide also concluded that non-adherence to guidelines regarding *H.Pylori* management is widely prevalent among doctors. We compared our results with those of other similar studies assessing the knowledge and practice of primary care doctors, hospital doctors and internists as well.

In a Spanish survey, only 20% of doctors adhered to treatment recommendations. Many other surveys revealed non-adherence to management guidelines among doctors in developing countries. (22,23–26)

In a Peruvian study , it was shown that 60% of primary care doctors and 69% of internists prescribed inappropriate *H. pylori* eradication regimens. (27).

Several other studies showed inconsistent results regarding adherence to *H.Pylori* management guidelines. In a Chinese study, the most frequently preferred eradication therapy was bismuth quadruple therapy (47%), while the most commonly used antibiotic combination was amoxicillin and clarithromycin. (3,16,17,28,29,30)
Amoxicillin, clarithromycin, and PPI regimen was also the most commonly used regimen, in a study from Mexico High proportion (95%) of primary care doctors prescribe standard therapy despite the high prevalence of clarithromycin resistance (35%), according to studies from Italy, Turkey, South Korea, and South America. This figure was lower than those reported in studies from Pakistan (61%) and Mexico (64%), reflecting (14,16,17, 31-33).

Conclusion

We concluded that there is a clear knowledge gap among trainee hospital doctors working in secondary care hospitals in Benghazi, regarding the symptomatology, indication for testing, eradication regimens, duration of therapy, and retesting for *H.Pylori* infection. Our findings are comparable to many similar observations worldwide.

Disclaimer

The article has not been previously presented or published, and is not part of a thesis project.

Conflict of Interest

There are no financial, personal, or professional conflicts of interest to declare.

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