

## Helicobacter Pylori Infection among Dyspeptic Patients Referred for Endoscopy

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### ABSTRACT:

#### BACKGROUND:

Functional dyspepsia is one of the most common gastrointestinal symptoms and attributed to various causes including Helicobacter pylori infection.

#### AIM OF THE STUDY:

To correlate Helicobacter pylori infection to functional dyspepsia and to identify the possible risk factors for this infection.

#### PATIENTS AND METHODS:

Fifty patients who were referred to the endoscopy unit for dyspepsia symptoms, secondary gastric causes of dyspepsia were excluded during endoscopy, gastric biopsies were taken for histopathological study and for bedside urease test for detection of Helicobacter pylori infection.

#### RESULTS:

62% of non-ulcer dyspeptic patients were infected with Helicobacter pylori, 74.2% of the patients were above 30 years old, female gender patients were more than male patients ( 61.3% versus 38.7%). Using two standard methods of diagnosis of Helicobacter pylori infection, 31 patients had positive histopathology and urease test, 9 of them were positive for helicobacter pylori infection with single method (6 by histopathology and 3 by urease). Histopathology test has sensitivity 88% and specificity 76% in respect to rapid urease test for detection of Helicobacter pylori infection.

#### CONCLUSION:

The incidence of helicobacter pylori infection in patients with functional dyspepsia doesn't differ from what reported in general population in our locality which may argue the role of helicobacter pylori infection in non-ulcer dyspepsia. Female gender and age >30 years were the common risk factors for the infection. Smoking and alcohol consumption were not associated with increased risk of infection.

**KEY WORDS:** dyspepsia, H.pylori, endoscopy.

### INTRODUCTION:

Dyspepsia is a chronic or recurrent pain in the upper abdomen with a different variety of symptoms like bloating, early satiety, fullness, nausea or intermittent vomiting.<sup>1</sup> the prevalence of dyspeptic symptoms worldwide is nearly 25% but only 10-20% of the patients who have dyspepsia present to clinicians.<sup>(1)</sup>

The dyspepsia can be caused by other upper gastrointestinal diseases such as gastroesophageal reflux, peptic ulcer disease, and, gastric and esophageal malignancies<sup>1</sup>. Dyspepsia can also be the symptoms of systemic, or metabolic diseases (organic dyspepsia) or it may have no clear cause (functional dyspepsia or non-ulcer dyspepsia) which is the cause of >60% of dyspeptic patients.<sup>(2)</sup>

Dyspepsia is considered as functional (FD) when the symptoms are present for  $\geq 3$  months in the absence of organic cause (Rome III definition).<sup>(3)</sup>

The Rome III definition defined that heartburn is not a gastroduodenal symptom; despite that it commonly occurs in association with symptoms of functional dyspepsia, so this symptom does not exclude a diagnosis of functional dyspepsia.<sup>(4)</sup>

Regarding the pathogenesis of functional dyspepsia, different studies have shown the roles of gastric acid secretion, gastric dysmotility, psychosomatic factors, and Helicobacter pylori (H. pylori) infection in the development of functional dyspepsia. Among these possible pathogenic factors, H. pylori infection has been recently regarded as a most important one, as several investigators have published the results of clinical studies which showed successful responses of patients with functional dyspepsia after therapy for the eradication of H. pylori.<sup>(5,6,7)</sup>

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The association between FD and *H. pylori* infection has not been established clearly. In the Rome committee, *H. pylori* infection is not included as an organic cause of FD; thus, *H. pylori* -infected patients with dyspeptic symptoms can be considered to have FD. Recently, several studies have suggested that the relationship between *H. pylori* infection and FD may play a role in pathophysiology of dyspepsia.<sup>(8,9)</sup>

*H. pylori* infection increases gastric acid secretion by causing antral-predominant gastritis that is responsible for decreasing the somatostatin release in the antral gland area, which leads to increased gastrin level with subsequent rise in acid secretion, that may explain dyspepsia.<sup>(10)</sup>

*Helicobacter pylori* eradication leads to the resolution of the symptoms of dyspepsia in the minority of patients (from 0 to 7% in different studies) than placebo treatment.<sup>(12,13)</sup>

Tests for *Helicobacter pylori* can be classified to two groups: tests that require endoscopy and simpler tests without the need for endoscopy. Endoscopy is usually used to exclude gastric malignancy and make a positive diagnosis in older patients or those with "alarm" symptoms. If endoscopy is performed, the most simple biopsy-based test is the (urease test), in which one gastric biopsy specimen is placed into a gel containing urea and an indicator. The presence of *Helicobacter pylori* urease leads to a pH alteration and therefore to a color change, which often occurs within minutes, this test has sensitivity of 80-95 % and specificity of 95-100 % for diagnosing *H. pylori*.<sup>(14)</sup>

Histologic examination of biopsy specimens from antrum and corpus for *H. pylori* also is accurate with 80-90 % sensitivity and > 90% specificity, provided that a special stain (e.g. a modified Giemsa or silver stain) used for optimal visualization of the organism. Histologic study can give further information, including the degree of inflammation and the presence of any atrophy, metaplasia or dysplasia. Microbiologic culture is most specific but may be insensitive because of difficulty with *Helicobacter pylori* isolation.<sup>(15)</sup>

The best established accurate noninvasive test (> 90 % sensitivity) is the urea breath test. In this simple test, the patient drinks a solution of urea labeled with the nonradioactive isotope <sup>13</sup>C and then blows into a tube. If *Helicobacter pylori* urease is present, the urea is hydrolyzed, and labeled carbon dioxide is detected in breath samples.

The stool antigen test, a simple noninvasive accurate (> 90% sensitivity and specificity) test using monoclonal antibodies specific for *Helicobacter pylori* antigens, is more easy to use and potentially less expensive than the urea breath test. The simplest tests for detecting *Helicobacter pylori* status are serologic assays measuring specific IgG levels in serum by ELISA (enzyme-linked immunosorbent assay) with sensitivity and specificity of > 80%, 90% respectively.<sup>(15)</sup>

### **PATIENTS AND METHODS:**

A correlation study of 50 patients with dyspeptic symptoms whom ages range from 16-84 years who were referred to the endoscopy unit in Baghdad teaching hospital/ medical city. The study period was from February 2016 to November 2016. (44%) were males and (56%) were females.

Inclusion criteria:

1. Age  $\geq$  16 years.
2. Patients with functional dyspepsia based on history and endoscopic finding on oesophageogastroduodenoscopy.
3. Patients with no other intra-abdominal diseases based on abdominal ultrasound.

Exclusion criteria:

1. Age  $\leq$  16 years.
2. Patients on PPI, H<sub>2</sub> receptors blocker and antibiotics for the last 2 weeks.
3. Patients with single or multiple gastric and/or duodenal ulcers based on endoscopy findings.
4. Patients with gall bladder disease or diagnosed to have biliary colic based on history and abdominal ultrasound.

After a detailed history, the selected patients undergo gastroscopy with endoscopic finding of antral gastritis, multiple biopsies taken from the antral area of the stomach for histopathological and rapid urease kit testing for the presence of *H. pylori* infection. The rapid urease kit used in the study is HelicotecUT®Plus from (strong biotech corporation/Taiwan).

The rapid urease kit test reading is positive only if the color of the kit changes from yellow to light or bright pink in the first hour of the procedure and negative if the color remains yellow after the end of the first hour, if the color turned to pink after the first hour also was considered as negative as the manufacturer of the kit recommended in the guide. The biopsy samples sent histopathological examination of the gastric mucosa for microscopical detection of *H. pylori* infection using H&E stains.

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### Statistical analysis

The variables described using their number and percentage, chi square test was used to do analysis of these variables. T test used to do analysis of the differences in means between two groups. Binary logistic regression was used to calculate the odd ratio (OR) and their 95% confidence intervals. Cohen's kappa test was used to assess the possible agreement (or disagreement) and its magnitude for similarity between 2 variables.

### RESULTS:

Fifty patients were included in our study, 31 patients were positive for H. pylori infection, the mean age was  $39.6 \pm 16.3$  (range 16-84) years; 19(61.3%) patients were females and 12(38.7%) patients were males.

H. pylori infection was detected by rapid urease test and/or histopathology in 31(62%) patients out of 50. There was a significant difference in

age of the infected patients with age  $\geq 30$  years (23 patients (74.2%)), in comparison with age  $< 30$  years (8 patients (25.8%)). There was no significant difference between H. pylori infected group and the non-infected group in smoking (p-value 0.611) and alcohol consumption (p-value 0.582) as in table 1.

An agreement study was done between both types of diagnostic tests of H. pylori (urease and histopathology) and the result was 80-90% accuracy indicating both methods highly agree in detection of H.pylori infection P.value  $< 0.001$ . Of the 31 patients who were positive for H.pylori, 22 patients were positive in both two methods with 3 patients by rapid urease test and 6 only by histopathology only as shown in table 2.

Table 3 shows the contingency of histopathology test for detection of H. pylori in respect to urease test with sensitivity of 88%, specificity of 76%.

**Table 1: Association between possible risk factors and H pylori infection.**

Risk factors	H pylori		OR (95%CI)	P value
	Negative	Positive		
Age	$41.5 \pm 14.6$	$39.6 \pm 16.3$	0.99 (0.96 – 1.03)	0.691
Age group			0.77 (0.20 – 3.00)	0.703
<30 years	4 (21.1%)	8 (25.8%)		
$\geq 30$ years	15 (78.9%)	23 (74.2%)		
Gender			0.57 (0.18 – 1.80)	0.336
Female	9 (47.4%)	19 (61.3%)		
Male	10 (52.6%)	12 (38.7%)		
Smoking			1.4 (0.4 – 4.6)	0.611
Not smoker (32)	13 (68.4%)	19 (61.3%)		
Smoker (18)	6 (31.6%)	12 (38.7%)		
Alcohol			1.9 (0.2 – 20.0)	0.582
not (46)	18 (94.7%)	28 (90.3%)		
Alcoholic (4)	1 (5.3%)	3 (9.7%)		

OR: odd ratio, CI: confidence interval

**Table 2: Agreement between histopathology and urease test.**

Histopathology	Urease		Kappa	P value
	Positive (25)	Negative (25)		
Positive (28)	22	6	0.640	$< 0.001$
Negative (22)	3	19		

**Table 3: Validity of histopathology using urease as reference for diagnosis of H pylori.**

Sensitivity	Specificity	Accuracy	PPV	NPV
88%	76%	82%	78.6%	86.4%

### DISCUSSION:

Dyspepsia is a common symptom that affects the general population. H. pylori infection is also a common infection and estimated that 30-40% of western populations have the infection; while 60-70% of the population in the developing countries has H. pylori infection<sup>(16)</sup>. Epidemiological studies showed

the high infection rate in patients with non-ulcer dyspepsia but with variable figures<sup>17</sup>, therefore the majority recommends treating H. pylori infection in patients with functional dyspepsia before doing endoscopy.

This study result showed that 62% of the patients with functional dyspepsia have H. pylori

infection. Reports from other studies showed that the infection rate was 64% and 60%<sup>(18,19)</sup>.

The role of helicobacter pylori infection in dyspepsia is established by evidence of epidemiological studies compared to general population and from therapeutic trials of H. pylori eradication in dyspeptic patients, although our result (62%) doesn't support the possibility of the role of H. pylori infection in functional dyspepsia as the rate of infection in the whole population in our locality is nearly 77% which is more frequent than the patients in this study<sup>(20)</sup>.

This study results shows that the H. pylori infected group of non-ulcer dyspepsia has female predominance (61.3%) versus males (38.7%), this was similar to a study in 2010 by Dr. Mohammad A. Sheikhan et al which found the female percentage was 68.5% had H. pylori with dyspeptic symptoms<sup>(21)</sup>. Other study by Nibras S. Al-Ammar et al found the same difference in gender distribution of H. pylori infection<sup>(22)</sup> and in Thailand by Chariya Chomvarin et al, 54.8% of patients infected by H. pylori in non-ulcer dyspepsia where females<sup>(23)</sup>, other studies shows no significant difference in gender distribution of H. pylori infection as in Pakistan by Muhammad Kamran Hassan et al<sup>(24)</sup>, and in united kingdom by Patchett S. et al<sup>(25)</sup>.

The distribution of the age of the patients infected with H. pylori was significant as 74.2% were older than 30 years; this finding was in agreement with other study done in by Dr. Mohammad A. Sheikhan et al where they found that 59.8% of patients infected with H. pylori are between ages of 30-60 years<sup>(23)</sup>. In India, Salankar HV et al found that 56.66% of infected patients of non-ulcer dyspepsia are between 30-50 years of age<sup>(26)</sup>.

We studied also several factors that also could be attributed to dyspepsia and whether H. pylori infection is increased with these factors or not, these factors are smoking and alcohol consumption. This study found no significant association between these factors and H. pylori infection in the non-ulcer dyspepsia patients. A Study by haitham I. Baqir et al and Nibras et al found that the sero-prevalence of H. pylori infection was not different between current smokers and non-smokers<sup>(20,22)</sup>. In addition, other studies in Mexico by J.L. Rodríguez-García et al and in china by ching Cho Lo et al showed no significant difference between smoking, alcohol and the risk of H. pylori infection in non-ulcer dyspepsia<sup>(27,28)</sup>.

In this study we used two methods of detection of H. pylori infection using biopsy based rapid urease test kits and histopathological slide

examination and found there were 22 positive patients by the two methods with additional 9 (3 cases by urease and 6 by histopathology) patients by either one of the two methods of detection. After using agreement study for the two methods and found the result was 80-90% accuracy of the methods. Also this study showed 9 patients who were positive by only one of the methods were accepted to as positive patients. Single positive method may be due to technical issues during processing of the biopsy sample or not sufficient number of biopsies taken from each patient, or infection can be patchy in the stomach. Finding favors the histopathology method for diagnosis of H. pylori infection as positive cases with this method were more than the positive cases by urease method only but the little number of cases limits the significance of this finding.

In contrary to this study, another study done in Italy which found that the rapid urease test accuracy was greater than that of routine histology and the combination of the two tests increase the sensitivity of h. pylori detection to 100%<sup>(29)</sup>.

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### CONCLUSION:

The incidence of H. pylori infection in patients with functional dyspepsia doesn't differ from what was reported in the general population which may argue the role of H. pylori infection in non-ulcer dyspepsia. In addition, H. pylori infection in patients with non-ulcer dyspepsia is more common in females and more common in patients above 30 years and the frequency of H. pylori infection in non-ulcer dyspepsia is not affected by the consumption of alcohol or smoking.

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