Kurdistan Journal of Applied Research (KJAR) | Print-ISSN: 2411-7684 – Electronic-ISSN: 2411-7706 | kjar.spu.edu.iq
Volume 2 | Issue 2 | july 2017 | DOI: 10.24017/science.2017.2.12

# Clinical, Endoscopic and Urea Breath Test Among Dyspeptic Patients Referred to Kurdistan Center for Gastroenterology and Hepatology in Sulaimani

**Mohammed Omer Mohammed**
College of Medicine,
University of Sulaimani, Iraq
mohammed.raheem@univsul.edu.iq

**Hemn Hussein Bayz**
General Teaching Hospital,
General Directorate of Health of Sulaimani
hemn_hb@ yahoo.com

**Fenk Bakir Maarouf**
College of Medicine, Dept of Biochemistry,
University of Sulaimani, Sulaimani, Iraq
fenk.maarouf@univsul.edu.iq

**Abstract:** ***Objective is to assess patients with dyspepsia clinically and to find the relationship between endoscopic findings and Urea breathe test.***

***This is a cross-sectional descriptive study, was conducted during the period of October 2016 till April 2017 in Kurdistan Center for Gastroenterology and Hepatology in Sulaimani city. Eighty six patients were included, fifty eight of them underwent both OGD and Urea breath test, and twenty eight of them underwent Urea breath test only.***

***Patients who underwent OGD were prepared by overnight fasting, pre-procedure viral screening (Hepatitis B surface antigen, Hepatitis C virus antibody and Human immunodeficiency virus antibody), conscious sedation performed by midazolam at the time of procedure.***

***Patients underwent Urea breath test were prepared by overnight fasting and they were advised not to use antibiotics 4 weeks and proton pump inhibitors, or Bismuth compounds 2 weeks before the test. Results: The mean age of participants was 35.89 ±11.55.Fifty five cases 64% were female and 31 cases 36%were male. The mean Body Mass Index of studied patients was 24.83 kg/ $m^2$± 4.2, overweight patients were 31.4% and 8.1% were obese.***

***The main presenting symptom was epigastric discomfort 31%. Urea breath test for Helicobacter pylori was positive in51.2% with significant correlation with OGD findings.***

***Helicobacter pylori infection is common among dyspeptic patients; the infection is more common in the age group of 20-40 years. Urea breath test is a noninvasive test to detect Helicobacter pylori.***

**Key words:** Dyspepsia, Helicobacter pylori, Urea breath test, Sulaimani

## 1. INTRODUCTION

**Dyspepsia:** refers to a collection of upper gastrointestinal symptoms that is believed to be common world-wide that occur commonly in adults. It is a non-specific term to denote upper abdominal discomfort. It may encompass a variety of specific symptoms including chronic or recurrent epigastric pain or discomfort, bloating, anorexia, nausea, regurgitation, heart burn, or early satiety [1].

According to the Rome IV criteria, dyspepsia is defined as one or more of the following symptoms [2].

- Postprandial fullness (classified as postprandial distress syndrome).
- Early satiation (inability to finish a normal sized meal, also classified as postprandial distress syndrome).
- Epigastric pain or burning (classified as epigastric pain syndrome).

The prevalence of dyspepsia varies considerably between different populations. Although these may represent genuine epidemiological differences, it is also apparent that the varying definitions used in different population studies may have contributed to this discrepancy, in some studies using “upper abdominal pain” as the definition, while in other studies a broader definition of “upper gastrointestinal symptoms” is used to define dyspepsia[3] (Figure 1).

***Helicobacter pylori***: is a gram negative spiral bacteria that colonize the stomach, it is responsible for the most frequent and persistent bacterial infection world-wide [4, 5]

Although *H. pylori* infections are asymptomatic in most infected individuals, they are intimately related to malignant gastric conditions such as gastric cancer and gastric mucosa-associated lymphoid tissue (MALT) lymphoma and to benign diseases such as gastritis and duodenal and gastric peptic ulcers [6].

Members of the genus *Helicobacter* are all microaerophilic organisms and in most cases are catalase and oxidase positive, and many but not all species are also urease positive. [7].

Unlike most bacterial pathogens, *H. pylori* typically colonize the host for life unless specific treatment is given. Strain types that predominate within certain regions of the world correlate with human migration patterns [8].

Most infected individuals do not develop overt disease, leading to the hypothesis that some *H. pylori* strains are harmless or even beneficial; however, the list of diseases

potentially caused or worsened by *H. pylori* has been growing in recent years, making it premature to conclude that any strain is commensal [9].

*Helicobacter pylori* infection affects nearly half of world-wide population. There is marked disparity between developed and developing countries. In developing countries like sub-Saharan Africa, Latin America and the Middle East the prevalence is high as 90%, whereas in developed countries such as Australia, Switzerland, North America and Western Europe, excluding Japan, the prevalence is below 40% [10].

Gastritis is universally present in *H. pylori* infected patients and it is either acute or chronic. Gastritis may be antral-predominant, corpus-predominant, or diffuse. The risk of developing adenocarcinoma or MALT lymphoma varies depending on the type of pathology present [5].

Acute gastritis affects the entire stomach and is accompanied by loss of acid secretion [9]. Neutrophils are recruited to the lamina propria and epithelium and damage results from reactive oxygen species and other neutrophil products. The acute phase gives way to chronic gastritis as lymphocytes replace neutrophils [10].

Can be antrum-predominant, corpus-predominant, or diffuse (pangastritis or multifocal gastritis). In antrum-predominant gastritis, acid secretion usually remains intact and *H. pylori* colonization is limited to the antrum [11].

Antral gastritis favors development of duodenal ulcers, while corpus-predominant gastritis favors gastric ulcer formation, sometimes progressing to metaplasia and adenocarcinoma [12, 13].

Patients with diffuse gastritis typically have severely impaired acid secretion, which allows *H. pylori* to colonize the corpus. Chronic acid suppression mediated by proton pump inhibitors can lead to a switch from antral predominant to pangastritis, Interestingly antrum-predominant gastritis and duodenal ulcers do not increase the risk of cancer development [14].

*Helicobacter pylori* is an accepted cause of gastric adenocarcinoma and MALT lymphoma. Gastric adenocarcinoma is divided into two subtypes [15].

**Investigation**

There are many methods to investigate dyspeptic patients, some of these tests are invasive and need biopsy to perform Gram's stain, culture, rapid urease test, histological and cytological examination. Some non-invasive tests including UBT and ELISA [16].

Serological tests involve detection of antibodies against *H. pylori* and they are very accurate. These antibodies may remain positive for years after successful eradication of *H. pylori* and therefore they are not used for checking the success of treatment because the antibody levels in the blood decreases slowly [17].

**Urea Breath test**

There are two UBTs available and gained Food and Drug Administration approval: $^{13}C$ and $^{14}C$ tests. Both tests are affordable and can provide real-time results. The $^{13}C$ test as it is non-radioactive compared to $^{14}C$ which uses a radioactive isotope, especially in young children and pregnant women. UBT is indicated to confirm *H. pylori* colonization and to monitor its eradication. Positive UBT indicates an active *H. pylori* infection which requires treatment or further confirmation with invasive procedures [18].

Serological tests have suboptimal sensitivity and specificity in practice [19, 20].The value of noninvasive *H. pylori* tests (stool antigen test and UBT), are depend on the positive and negative predictive value, which in turn is related to the background prevalence of *H. pylori* infection. When *H. pylori* infection is very uncommon, a positive test is more likely to be a false positive, but if it is highly prevalent, a negative result is more likely to be a false negative [21].

**Aim of the study:** to assess:

**(1)** Patients with dyspepsia clinically.

**(2)** The relationship between endoscopic findings and UBT.

## 2. PATIENTS AND METHODS

This thesis is approved by scientific and ethical committee of Iraqi Board for Medical Specializations. Written consent taken from all patients. In a cross-sectional descriptive study was conducted during the period of Oct, 2016-April, 2017. Eighty six patients with dyspepsia were referred to Kurdistan Center for Gastroenterology and Hepatology (KCGH) in Sulaimani city were included, 58 of them underwent both OGD and UBT and 28 of them underwent UBT only.

A form designed to collect demographic data; name, age, gender, residency, BMI, dyspeptic elements, smoking and alcohol intake.

Investigations were asked including (Abdominal ultrasound, OGD and UBT).

Patients who underwent OGD were prepared by overnight fasting, pre-procedure viral screen (HBsAg, HCVAb, HIV Ab), and conscious sedation performed by midazolam at the time of procedure, using Olympus Eislucera (cv-260) video scope.

UBT was done by swallowing a capsule containing urea labeled with an isotope radioactive carbon-14 in 10 minutes. Samples of exhaled breath are collected, and the isotopic carbon in the exhaled carbon dioxide is measured. The dose of radiation is mini-dose (1 microCi) 14C-urea breath test equals (37 kbq), which has high diagnostic accuracy. It was done by a machine (Heliprobe® system, manufacture: Kibion AB, Sweden). Patients were prepared by overnight fasting and they were advised not to use antibiotics 4 weeks and PPIs, or Bismuth compounds 2 weeks before the test.

**Figure 1. Heliprobe® System** consists of three components:

Heliprobe®Analyzer, HeliCap™ – $^{14}$C-urea capsules and BreathCard™

If *H. pylori* is present in the stomach, the urea is broken up and turned into carbon dioxide. The carbon dioxide is absorbed across the lining of the stomach and into the blood. It then travels in the blood to the lungs, the detection of isotope labeled carbon dioxide in exhaled breath indicates the urea was split, this indicates urase present in stomach and hence *H. pylori* bacteria are present [22].

**The inclusion Criteria:**

All patients 18 years and older referred to KCGH with dyspeptic elements.

**Exclusion Criteria:**

**(1)** Patients below18 years of age **(2)** Pregnants **(3)** Those who had received antibiotics before 4 weeks and PPIs or Bismuth compounds in the last2 weeks [23]. **(4)** Patients who presented for reasons other than dyspeptic symptoms.

**Statistical analysis:**

All patients' data were analyzed by using the SPSS-22 (Statistical Package for Social Sciences).

Descriptive statistics presented as (mean ± SD) and frequencies as percentages.

Multiple contingency tables conducted and appropriate statistical tests performed, Chi-square used for categorical variables. Independence t-test was used to compare between means. In all statistical analysis, level of significance (p value) set ≤ 0.05 and the results presented as tables.

## 3. RESULTS

In this study 86 patients with dyspepsia who were referred to KCGH were enrolled. Fifty five cases 64% were female and 31cases 36% were male. As shown in (Table 1).

**Table 1. Characteristics of Studied Patients**

| | Frequency (%) |
|---|---|
| **Gender** | |
| Female | 55 (64) |
| Male | 31 (36) |
| Total | 86 (100) |
| **Age (Yrs.)** | |
| < 20 | 5 (5.8) |
| 20-39 | 61 (70.9) |
| 40-59 | 19 (22.1) |
| ≥ 60 | 1 (1.2) |
| Total | 86 (100) |
| **BMI** | |
| Below normal | 3 (3.5) |
| Normal | 49 (57) |
| Overweight | 27 (31.4) |
| Obese | 7 (8.1) |
| Total | 86 (100) |
| **Smoking** | |
| Smokers | 11 (12.8) |
| Non-smokers | 70 (81.4) |
| X-smokers | 5 (5.8) |
| Total | 86 (100) |
| **Alcohol** | |
| Yes | 4 (4.7) |
| No | 82 (95.3) |
| Total | 86 (100) |

The most common presenting symptom was epigastric discomfort 36%, and alarm features were found in 21% of cases, (Table 2).

UBT for *H. pylori* infection was positive in 51.2% of participants, Table 3.

The mean age of participants was 35.89 ± 11.55 Standard Deviation (SD) with a 95% confidence interval (CI) of 33.47-38.46. The age ranged between 18 and 74 years respectively. The mean BMI of studied patients was 24.83 kg/ $m^2$± 4.21 SD and a 95% CI of 23.94-25.73. BMI ranged between 17 and 36 respectively, Table 4.

A significant correlation was observed between abnormal OGD findings and UBT positive for *H. pylori* infection, as shown in Table 5.

Fifty eight patients 68% underwent upper endoscopy, results of OGD findings shown in Table 6.

Patients with negative past medical history were 28, 82.6%, and those with negative past surgical history were 90.7%, as shown in Table 7.

**Table 2. Dyspeptic Elements and Frequency of Alarm Features among Patients**

| | | Frequency (%) | |
|---|---|---|---|
| **Dyspeptic Elements** | | | |
| Epigastric Discomfort | | 31 (36) | |
| Combinations of Features | | 31 (36) | |
| Epigastric Burning | | 12 (14) | |
| Postprandial Fullness | | 9 (10.5) | |
| Early Satiety | | 3 (3.5) | |
| Total | | 86 (100) | |
| **Alarm Features** | | | |
| No | | 68 (79) | 68 (79) |
| Yes | Melena | 6 (7.0) | 18 (21) |
| | Anorexia | 2 (2.3) | |
| | Vomiting | 2 (2.3) | |
| | Anemia | 2 (2.3) | |
| | Dysphagia | 2 (2.3) | |
| | Family history of Gastric Cancer | 1 (1.2) | |
| | Personal History of Gastric Ca. | 1 (1.2) | |
| | Weight Loss | 1 (1.2) | |
| | Combinations | 1 (1.2) | |
| | Total | 86(100) | 86(100) |

**Table 3: Results of Urea Breath Test among Studied Patients**

| **UBT** | **Frequency** | **(%)** |
|---|---|---|
| **Positive** | 44 | 51.2 |
| **Negative** | 42 | 48.8 |
| **Total** | 86 | 100 |

**Table 4. Difference in Age and BMI between UBT Negative and UBT Positive Individuals**

| **Age** | **UBT Negative 42** | **UBT Positive** 44 | **P-value** |
|---|---|---|---|
| Mean | 37.28 Year | 34.56 year | 0.277 (unpaired t-test) |
| Std. Deviation | 12.78 | 10.20 | |
| **BMI** | **UBT Negative** 42 | 25.13 $kg/m^2$ | **P-value** |
| Mean | 24.52 $kg/m^2$ | 3.99 | 0.5047 (unpaired t-test) |
| Std. Deviation | 4.45 | 25.13 $kg/m^2$ | |

**Table 5. Outcomes of UBT among Studied Cases**

| | +ve UBT (%) | -ve UBT (%) | Total | P-Value |
|---|---|---|---|---|
| **Gender** | | | | |
| Male | 17 (19.7) | 14 (16.2) | 31 | 0.657 |
| Female | 27 (31) | 28 (32.5) | 55 | |
| Total | 44 | 42 | 86 | |
| **Residency** | | | | |
| Urban | 38 (44) | 34 (40) | 72 | 0.567 |
| Rural | 6 (7) | 8 (9) | 14 | |
| Total | 44 | 42 | 86 | |
| **Smoking** | | | | |
| Smokers | 4 (4.8) | 7 (8) | 11 | 0.338 |
| Non-smokers | 38 (44) | 32 (37.2) | 70 | |
| X-smokers | 2 (2.3) | 3 (3.4) | 5 | |
| Total | 44 | 42 | 86 | |
| **Alcohol** | | | | |
| Yes | 2 (2.3) | 2 (2.3) | 4 | 0.962 |
| No | 42 (49) | 40 (46.5) | 82 | |
| Total | 44 | 42 | 86 | |
| **Previous Eradication** | | | | |
| Yes | 3 (3.5) | 5 (5.8) | 8 | 0.478 |
| No | 41 (47.6) | 37 (43) | 78 | |
| Total | 44 | 42 | 86 | |
| **Alarm Features** | | | | |
| Yes | 6 (7%) | 12 (14) | 18 | 0.114 |
| No | 38 (44) | 30 (35) | 68 | |
| Total | 44 | 42 | 86 | |
| **OGD** | | | | |
| Normal | 5 (8.5) | 16 (27) | 21 | 0.015 |
| Abnormal* | 22 (37.2) | 16 (27) | 38 | |
| Total | 27 | 32 | 59 | |

*Abnormal OGD Findings in this Group include (Peptic ulcer disease, Antral gastropathy, erosive esophagitis and Hiatus hernia).

**Table 6. OGD and Abdominal Ultrasound in Patients With Dyspepsia**

| | Frequency (%) |
|---|---|
| **OGD** | |
| Normal | 21 (36) |
| Gastropathy | 11 (19) |
| DU | 11 (19) |
| GU | 7 (12) |
| Erosive GERD | 6 (10) |
| Hiatus Hernia | 2 (3.4) |
| Total | 58 (100) |
| **Abdominal Ultrasound** | |
| Normal | 78 (90.6) |
| Fatty Liver | 4 (4.7) |
| Gallstone | 4(4.7) |
| Total | 86 (100) |

**Table7. Past History of Studied Patients**

| | Frequency (%) | |
|---|---|---|
| **Past Medical History** | | |
| No | 71 (82.6) | 71 (82.6) |
| Hypertension | 8 (9.3) | 15 (17.4) |
| Gastric Cancer | 1 (1.2) | |
| Hypothyroidism | 1 (1.2) | |
| Inflammatory Bowel Disease | 1 (1.2) | |
| Other Malignancies | 2 (2.3) | |
| Ischemic Heart Disease | 1 (1.2) | |
| Diabetes Mellitus | 1 (1.2) | |
| Total | 86 (100) | 86 (100) |
| **Past Surgical History** | | |
| No | 78 (90.7) | 78 (90.7) |
| Thyroidectomy | 3 (3.5) | 8 (9.3) |
| Cholecystectomy | 3 (3.5) | |
| Gastric Surgery | 1 (1.2) | |
| Other Ca. Surgeries | 1 (1.2) | |
| Total | 86 (100) | 86 (100) |

## 4. DISCUSSION

Dyspepsia is a common complaint among individuals seeks medical care as well as in general population, it is diagnosed in the presence of symptoms thought to be originate from gastro-duodenal region ( early satiety, postprandial fullness, epigastric pain or burning) [1].

*Helicobacter pylori* infection is the most common chronic bacterial infection in the world, this bacterium colonizes human gastric mucosa and can elicit lifelong inflammatory and immune responses, with release of various bacterial and host dependent cytotoxic substances, it causes chronic and active gastritis, peptic ulcer disease and associated with increased risk of developing gastric cancer[24].

In the present study, Dyspepsia was predominant in young and middle age group, which is consistent to the result of. Shaikhani et al [25], probably because upper gastrointestinal tract diseases are prevalent in this population groups [26, 27].

Female gender was predominant in both the present of dyspepsia and *H.pylori* positivity. This is consistent to the result of Mohie Khalifa, et al [28] in Iran, and Salih BA [29]. A vast variety of results have been reported regarding the predominance of females; This may be explained by that females seeking health advice more than males at least in our region, but it is generally concluded that there is no significant association between the infection rate of *H. pylori* and sex.

Although there is no relation between symptoms of dyspepsia and body mass index in the study of Solhpour A. *et al* [30]. But in the study of Labiba Mohamed *et al* [31] A total of 489 patients were included (25.56%) were overweight (13.49%) were obese which can be comparable with our study (31.4%) were overweight and (8.1%) were obese.

In the present study, we explored the interaction between smoking status and *H. pylori* positivity in dyspeptic patients. We found that there was no statistically significant difference between smoking and the positivity rate of *H. pylori* by UBT, and this agree with the study of Mohie Khalifa et al. which was done in Saudi Arabia [28] and Shrma *et al* [32].

But findings were contrary to the findings of Rajashekhar et al [33] (80%) smokers and (43%) non-smokers were positive for *H. pylori* infection ($p < 0.001$)) who had found an association of smoking with *H. pylori* positivity in UD patients.

Several cross-sectional studies have investigated the relationship between alcohol consumption and *H. pylori* infection. Some studies reported a significantly inverse association with *H. pylori* infection such as in the study of Kuepper-Nybelen *et al* [34]. Although others found no significant association, but alcohol consumption appears to be associated with *H.pylori* infection. While in present study, there was no significant association between alcohol consumption and positive UBT.

Three mechanisms may explain the negative relationship. Firstly, alcohol may exert a bactericidal effect against new infection. Secondly, alcohol may be bactericidal against existing *H. pylori* infection, and finally, some alcoholic beverages are known to stimulate gastric acid secretion, which may eradicate *H. pylori* by lowering the pH in the stomach. In the other hand heavy alcohol consumption favored colonization of the gastric mucosa by *H.* pylori [35].

The most presenting feature among dyspeptic patients was epigastric discomfort (31%) followed by epigastric burning (12%) and postprandial fullness (9%), this can be comparable with the result of Sheikhani, *et al* [25].

There are different reports about the prevalence rate of this infection between countries, but interestingly, the results of this study (51.2%) which is compatible to the local study done in Hawler, Kurdistan by Bashdar M. Hussein *et al* [36] which is (55.8%) and showed the same prevalence of *H. pylori* in comparison with other reports from Asia and Middle East, such as the result of Alazmi *et al* [37]. research in Kuwait and Goh [38] in Malaysia, (49.7% and 49.0% respectively).

The present result nearly less than that of Sheikhani, *et al* [25] in Sulaimani, Kurdistan (62.7%), This may be due to different methodology as they used measurement of serum H. pylori immunoglobulin (IgG) antibody with ELISA for diagnosis of *H.pylori*.

In another report from India, Poddar U, *et al* [39] demonstrated that almost 80% of the populations in India were infected with *H. pylori*. But in USA by R. P. Jackman, *et al*. [40] was only (10.4%). The reason for the difference in the prevalence of *H. pylori* positivity is probably due to varying sample size; age groups, geographical locations, socioeconomical factors and time periods the studies were carried out. [(52)]

According to the present study, the most common endoscopic abnormality in dyspeptic patients was ulcerative lesion which was compatible with the result of Ramin Nikman et al. [41] in Shiraz, Iran, A significant association was found between OGD findings and *H.pylori* positivity, which can be seen in the study of Baban and Mohammed [5].

## 5. CONCLUSIONS

In conclusions: *H. pylori* infection is frequent among dyspeptic patients.

*H. pylori* infection is more common between the ages of 20-40 years. Patients with positive UBT for *H. pylori* infection have more endoscopic findings than those with negative UBT. No statistically significant difference between smoking and the positivity rate of *H. pylori* in dyspeptic patients. Urea breath test is a simple, non-invasive test to identify *H. pylori* infection.


## ACKNOELEDGMENT

We like to thank Mr. Abbas Osman Husein and Ms. Tavga Akrum in the KCGH for their cooperation .

**Conflict of interest:** None


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