



# Journal of Medical Sciences

ISSN 1682-4474

**science**  
alert

**ANSI***net*  
an open access publisher  
<http://ansinet.com>



## Research Article

# *Helicobacter pylori* Associated Psychiatric Disorders among Bahraini Adult Presenting with Function Dyspepsia

<sup>1</sup>Nada Ali Mohamed and <sup>2</sup>Nashwa Fawzy Abd El Moez Azzam

<sup>1</sup>Department of Neurology and Psychiatry, Faculty of Medicine, Alexandria University, Egypt

<sup>2</sup>Department of Microbiology, High Institute of Public Health, Alexandria University, Egypt

## Abstract

**Background and Objective:** The association between psychiatric disorders and *H. pylori* functional dyspepsia remains controversial. To determine the prevalence of psychiatric disorders in patients with *H. pylori* infections and assess the effect of antidepressant drugs on the relief of Functional Dyspepsia (FD) symptoms and eradication of *H. pylori*. **Materials and Methods:** The *H. pylori* diagnosis was done by using stool Ag detection and biopsies during endoscopic examination. The psychiatric status of *H. pylori* patients was evaluated using the Hamilton Anxiety Rating Scale (HAM). The effect of standard quadruple therapy was compared versus added antidepressant drugs in patients with psychiatric disorders. All patients' records were checked for *H. pylori* eradication and improvement of severity of FD symptoms for six months. **Results:** *H. pylori* was positive in 53 patients (55.2%). The majority of *H. pylori* patients were females  $\leq 50$  years old. About 52.8% of *H. pylori* patients had psychiatric disorders. The most common psychiatric disorder was anxiety in 19 patients (67.9%) and 9 patients (32.1%) were diagnosed with depression. Twenty-six out of twenty-eight patients (92.9%) who received antidepressant treatment plus the standard quadruple regimen, had successful treatment outcomes at 4 and 5 weeks. While only 14 out of 25 patients who received the standard quadruple regimen (56%) had successful treatment outcomes at 4 and 5 weeks. **Conclusion:** High prevalence of *H. pylori* infections in the Kingdom of Bahrain. There is a clear association between psychiatric disorder and *H. pylori* infection. Added antidepressant drugs to standard antibiotic regimen may have a role in the improvement of FD symptom and *H. pylori* eradication.

**Key words:** Functional dyspepsia, *H. pylori* infections, psychiatric disorders, antidepressant synergy, quadruple *H. Pylori* treatment, anxiety, depression

**Citation:** Mohamed, N.A. and N.F.A.E.M. Azzam, 2020. *Helicobacter pylori* associated psychiatric disorders among Bahraini adult presenting with function dyspepsia. J. Med. Sci., 20: 55-59.

**Corresponding Author:** Nashwa Fawzy Abd El Moez Azzam, Department of Microbiology, High Institute of Public Health, Alexandria University, Egypt

**Copyright:** © 2020 Nada Ali Mohamed and Nashwa Fawzy Abd El Moez Azzam. This is an open access article distributed under the terms of the creative commons attribution License, which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited.

**Competing Interest:** The authors have declared that no competing interest exists.

**Data Availability:** All relevant data are within the paper and its supporting information files.

## INTRODUCTION

Gut-brain axis is defined as the relationship of gastrointestinal with brain function and mental status. Mental stress is associated with personality-dependent gastric acid secretion changes. Moreover, gastric inflammation leads to anxiety and depression-like behaviors via the neuroendocrine pathways especially in female<sup>1</sup>.

One of the most common functional gastrointestinal disorders (FGIDs) in the world is FD. Most patients with FD develop anxiety and depression. In addition, patients with depression had a tendency to develop FD as well.<sup>2</sup> The FD is a common presenting symptom for *H. pylori* infection. It had been estimated that over half of the world's population is infected with *H. pylori*, which may give it a significant role in the brain-gut axis and links it with psychiatric disorders like depression<sup>3</sup>.

Moreover, it had been observed that the efficacy in ulcer treatment and *H. pylori* eradication is increased when antidepressants such as tricyclic antidepressant (TCA) or selective serotonin reuptake inhibitors (SSRIs) are added to the standard regimens against *H. pylori*. It had been suggested that receptors for serotonin were up-regulated when patients had *H. pylori* gastritis<sup>4</sup>.

This study aims to assess the relationship between psychiatric disorder and *H. pylori* gastritis and if antidepressant drugs play any role in treating patients with chronic *H. pylori* gastritis.

## MATERIALS AND METHODS

**Study area:** The study was conducted at a private hospital in the Kingdom of Bahrain. Data were collected retrospectively (from January 2016 to December 2019) from gastroenterology and hepatology center database.

**Subjects:** All patients who visited the gastroenterology and hepatology center for dyspeptic symptoms during the study period (n = 96). Dyspepsia was defined according to Rome III as the presence of at least one symptom of the followings: early satiation, postprandial fullness, epigastric pain or epigastric burning symptoms fulfilled for the last 3 months with onset at least 6 months before diagnosis<sup>5</sup>.

Stool Ag detection for *H. pylori* was done by commercially available Testmate Rapid Pylori Antigen (TRP) immunochromatography kit, according to the manufacturer's instructions (Testmate rapid pylori antigen [TRP]; Wakamoto Pharmaceutical Co., Ltd., Tokyo, Japan). The TRP is a sensitive,

cheap and easy method for the initial diagnosis of *H. pylori* infection. It is an immunochromatography based approach against *H. pylori* catalase. MAb 21G2 and anti-mouse IgG polyclonal antibody were immobilized onto nitrocellulose membranes. One drop of the stool sample suspension was placed on the specimen application region of the test strip. After 10 min, if native catalase *H. pylori* antigens were present in the samples, both the control and test lines were red<sup>6</sup>.

Patients had been examined endoscopically and two antral biopsies were taken during endoscopy within 2 cm of the pylorus with a standard 2.8 mm cup proved to perform rapid urease test *H. pylori*<sup>7</sup>.

Hamilton Anxiety Rating Scale (HAM-A) was used to evaluate and measure the severity of anxiety symptoms. The scale consists of 14 items; each item was defined by a series of symptoms. psychic anxiety (mental agitation and psychological distress) and somatic anxiety (physical complaints related to anxiety) were measured by using the scale.

Each item was scored on a scale of 0 (not present) to 4 (severe). The severity of anxiety was measured according to the total score range; mild severity = <17, mild to moderate=18-24, moderate to severe = 25-30<sup>8</sup>.

Hamilton Depression Rating Scale (HDRS) was the assessment scale for depression. The scale consists of 17 items related to symptoms of depression experienced over the past week and emphasis on melancholic and physical symptoms of depression.

A total score of 0-7 was considered as a normal range or clinical remission, while a score of 20 or more was considered moderate severity or more<sup>9</sup>.

All patients with *H. pylori* were given quadruple therapy (rabeprazole 20 mg+ amoxicillin 1.0 g+ clarithromycin 0.5 g+ colloidal bismuth subcitrate solution 10 mL, bid) for 2 weeks. Patients positive for *H. pylori* and had psychiatric disorders, in addition to quadruple therapy, were given TCA at night (tryptizol 20 mg) and one of SSRI drugs (escitalopram 10 mg once daily, sertraline 25 mg once daily, or paroxetine) in the morning time. All patients' records were checked for *H. pylori* eradication and improvement of severity of FD symptoms for six months. Follow up records were collected from the central database.

Follow up of persistent *H. pylori* infection after eradication therapy was monitored using Urea Breath Test (UBT) as it is the gold standard and by stool Ag detection (it needs at least 4 weeks after treatment due to delayed fecal elimination of *H. pylori* antigens or coccoid forms after successful eradication)<sup>10</sup>. After treatment courses were

completed, results were monitored starting at 4-5 weeks after treatment, then after 2 months and continued for 6 months post-treatment. Failure was defined as the persistence of FD symptoms that were not sufficiently controlled and positive *H. pylori* by urea breath test.

**Statistical analysis:** Data were collected and tabulated by using health electronic system and then analyzed using statistical software SPSS version 24 (IBM Corp., Chicago, Illinois, USA). Descriptive statistics of demographic variables were calculated including frequencies, percentages, means and ranges.

**RESULTS**

Out of 96 dyspeptic patients, *H. pylori* was positive in 53 patients by both stool Ag detection and rapid urease test (55.2%), with the most common complaints at initial presentation was epigastric burning. The majority of *H. pylori* patients were females 35 (66%), out of them 18 (51.4%) were ≤50 years old (Table 1).

By using the HADS questionnaire, psychiatric disorders were diagnosed in 60 patients of FD (62.5%). Females:Males ratio was 3:1.

Psychiatric status was evaluated in *H. pylori* patients and it was found that 25 of 53 *H. pylori* patients (52.8%) had psychiatric disorders. The most common psychiatric disorder was anxiety in 19 patients (67.9%) and 9 patients (32.1%) were diagnosed with depression (Fig. 1).

Both groups of *H. pylori* patients (with and without psychiatric disorders) had completed their treatment regimen. Twenty-six out of twenty-eight patients (92.9%) who received antidepressant treatment plus the standard quadruple regimen, had successful treatment outcomes with two consecutive negative UBT (<50 dpm) at 4 and 5 weeks following completion of treatment. Two of these UBT-negative patients (7.6%) had positive stool Ag at 1 month following treatment and became negative after 2 months (Fig. 2).

Out of the remaining 25 *H. pylori* patients (without psychiatric disorders) who received only the standard quadruple regimen, only 14 (56%) had successful treatment outcomes with two consecutive negative UBT (<50 dpm) at 4 and 5 weeks following completion of treatment. Five of these UBT-negative patients (35.7%) had positive stool Ag at 1 month following treatment and became negative after 3 months. Eradication rates increased to 88% (22 out of 25) after 2 months (Fig. 2).

The therapeutic efficacy of *H. pylori* eradication was significantly increased (p<0.05) in the patients group who

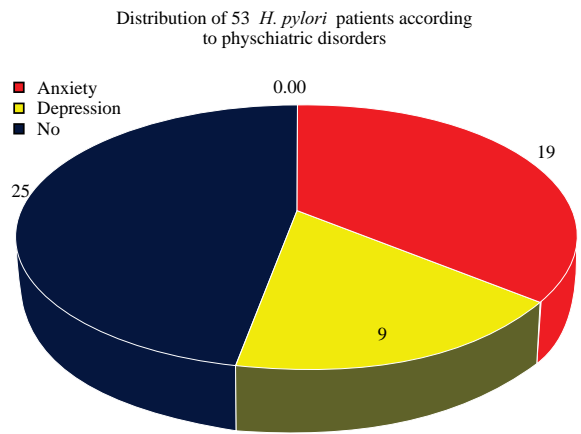


Fig. 1: Distribution of *H. pylori* patients according to psychiatric disorders  
25% shows psychiatric disorders patients

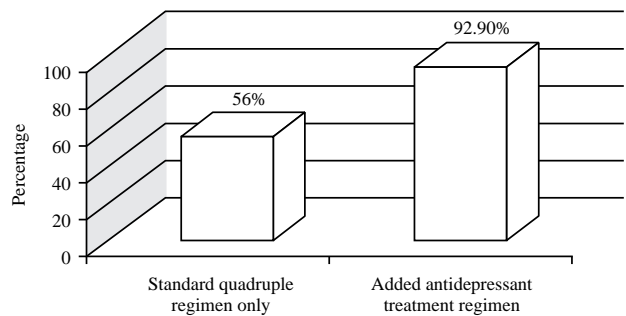


Fig. 2: Successful treatment outcomes at 4 and 5 weeks

Table 1: Demographic characteristic of *H. pylori* patients

Patients data	No (%)		Total
	≤50 year	> 50 year	
Age	29 (54.7%)	24 (45.3%)	53 (100%)
<b>Sex</b>			
Female	18 (51.4%)	17(48.5%)	35 (66%)
Male	11(61.1%)	7 (38.9%)	18 (34%)

received antidepressant treatment plus the standard quadruple regimen. The FD symptoms had declined dramatically after *H. pylori* eradication therapy and antidepressant treatment.

**DISCUSSION**

The prevalence of *H. pylori* infections varies in different populations and according to different socioeconomic groups<sup>11</sup>. In the developed countries the prevalence ranged between 10-30%<sup>12</sup>. High prevalence rates of *H. pylori*-associated gastritis among Bahraini dyspeptic adults had been

reported by Huerta-Franco *et al.*<sup>13</sup>, where it reached 75% and by Kabeer *et al.*<sup>14</sup> who found it to be 57% among Bahraini children presenting with recurrent abdominal pain. A similarly high prevalence was reported in this study among FD patients (55.2%). Epidemiological reports concluded male predominance of *H. pylori* infection. However, in the present study, the majority of *H. pylori* patients were females (66%) and more than half of them were  $\leq 50$  years old. This was in agreement with Kamath *et al.*<sup>15</sup>, who found that *H. pylori* infection was significantly associated with the female gender. The interconnection between psychiatric disorders and *H. pylori* gastritis and its association with failure of *H. pylori* eradication had been in consideration. Patients with functional dyspepsia commonly have *H. pylori* infection, anxiety and depression<sup>16</sup>. Piriyapong *et al.*<sup>17</sup> concluded that females below 50 years of age with seropositive *H. pylori* gastritis had a higher risk of psychological distress and depression. Shimoyama *et al.*<sup>18</sup> reported that 40.7% of functional dyspepsia and *H. pylori*-positive patients had at least one psychiatric illness; the most common was depression. Takeoka *et al.*<sup>19</sup> found the prevalence of *H. pylori* and depression in patients with functional dyspepsia was 29.2%. This study was parallel with previous studies, where *H. pylori* patients were evaluated for their psychiatric status using the HAM-A and HDRS questionnaire and it was found that 52.8% of them had either depression or anxiety.

Effect of combined medical treatment of *H. pylori* and psychiatric disorders had been studied and evidence of the synergistic effect of antidepressant drugs adjuvant therapy alongside standard antibiotics regimen (triplet or quadruplet drug therapy) to eradicate *H. pylori* is still not sufficiently strong. Moreover, the antibiotics regimen of *H. pylori* infection may develop neuropsychiatric symptoms that typically resolve after the discontinuation of the antibiotics<sup>20</sup>. Wang *et al.*<sup>21</sup> concluded that anxiolytic drugs and antidepressants have peculiar effects on functional dyspepsia of *H. pylori*. Wang *et al.*<sup>21</sup> found that using antipsychotic and TCA antidepressant (flupentixol and melitracen) combined with quadruple therapy in anxiety and depression patients led to a significant reduction in the recurrence rate of peptic ulcer and improvement of *H. pylori* eradication. A similar finding of improvement of *H. pylori* eradication in patients who received SSRIs agents and TCA in addition to quadruple therapy for 2 weeks. Zainaldeen *et al.*<sup>22</sup> showed similar results of the significant improvement in symptoms of FD in the group that received medical therapy along with cognitive behavioral therapy. On the other hand, Takeoka *et al.*<sup>19</sup> explained the poor improvement in the severity of dyspepsia in their psychiatric patients by lack of antidepressant drug treatment

and depending only on counseling therapy which may be inadequate or insufficient duration and lack of compliance. Despite the acceptable reliability of HAM-A, it could not discriminate between anxiolytic and antidepressant effects and somatic anxiety versus somatic side effects. Moreover, HDRS could not assess atypical symptoms of depression (hypersomnia and hyperphagia) that are not assessed.

## CONCLUSION

High prevalence of *H. pylori* infections in functional dyspepsia patients in the Kingdom of Bahrain. There is a clear association between psychiatric disorder and *H. pylori* infection. Added antidepressant drugs to standard antibiotic regimens may have a role in the improvement of FD symptom and *H. pylori* eradication. However, further studies should evaluate this finding due to the limited number of studied patients in this study.

## SIGNIFICANCE STATEMENT

This study discovered the correlation between psychiatric disorders and *H. pylori* infection that can be beneficial for psychiatrists to study psychosomatic disturbances in their patients. This study will help the researchers to uncover the critical areas of the brain-gut axis that many researchers were not able to explore. Thus a new theory on effective treatment of *H. pylori* using antidepressant drugs may be arrived at.

## REFERENCES

1. Agah, S., H. Khedmat, M.E. Ghamar-Chehred, R. Hadi and A. Aghaei, 2016. Female gender and Helicobacter pylori infection, the most important predisposition factors in a cohort of gastric cancer: A longitudinal study. *Caspian. J. Intern. Med.*, 7: 136-141.
2. Calvet, X., M.J.R. Lázaro, P. Lehours and F. Mégraud, 2013. Diagnosis and epidemiology of *Helicobacter pylori* infection. *Helicobacter*, 18: 5-11.
3. Chen, S.L., 2013. A review of drug therapy for functional dyspepsia. *J. Digestive Dis.*, 14: 623-625.
4. Drossman, D.A., 2006. The functional gastrointestinal disorders and the Rome III process. *Gastroenterology*, 130: 1377-1390.
5. Drumm, B., 1990. *Helicobacter pylori*. *Arch. Dis. Child.*, 65: 1278-1282.
6. Filipović, B.F., T. Randjelovic, T. Ille, O. Markovic, B. Milovanović, N. Kovacevic and B.R. Filipović, 2013. Anxiety, personality traits and quality of life in functional dyspepsia suffering patients. *Eur. J. Internal Med.*, 24: 83-86.

7. Fiedorek, S.C., H.M. Malaty, D.L. Evans, C.L. Pumphrey, H.B. Casteel, D.J. Evans Jr. and D.Y. Graham, 1991. Factors influencing the epidemiology of *Helicobacter pylori* infection in children. *Pediatrics*, 88: 578-582.
8. Gisbert, J.P. and J.M. Pajares, 2001. Diagnosis of *Helicobacter pylori* infection by stool antigen determination: a systematic review. *Am. J. Gastroenterol.*, 96: 2829-2838.
9. Haag, S., W. Senf, S. Tagay, M. Langkafel and U. Braun-lang *et al.*, 2007. Is there a benefit from intensified medical and psychological interventions in patients with functional dyspepsia not responding to conventional therapy? *Aliment. Pharmacol. Ther.*, 25: 973-986.
10. Hamilton, M., 1959. The assessment of anxiety states by rating. *Br. J. Med. Psychol.*, 32: 50-55.
11. Hamilton, M., 1960. A rating scale for depression. *J. Neurol. Neurosurg. Psychol.*, 23: 56-62.
12. Hooi, J.K.Y., W.Y. Lai, W.K. Ng, M.M.Y. Suen and F.E. Underwood *et al.*, 2017. Global prevalence of *Helicobacter pylori* infection: systematic review and meta-analysis. *Gastroenterology*, 153: 420-429.
13. Huerta-Franco, M.R., 2012. Effect of psychological stress on gastric motility assessed by electrical bio-impedance. *World. J. Gastroenterol.*, 18: 5027-5033.
14. Kabeer, K.K., N. Ananthkrishnan, C. Anand and S. Balasundaram, 2017. Prevalence of *Helicobacter pylori* infection and stress, anxiety or depression in functional dyspepsia and outcome after appropriate intervention. *J. Clin. Diagn. Res.*, 11: VC11-VC15.
15. Kamath, R., J. Alqumish, A. Yousif and A.R. Fakro, 1995. Prevalence of *Helicobacter pylori* among dyspeptic patients in Bahrain. *Bah. Med. Bull.*, 17: 50-52.
16. Neufeld, N.H., N.S. Mohamed, N. Grujich and K. Shulman, 2017. Acute neuropsychiatric symptoms associated with antibiotic treatment of *Helicobacter pylori* infections. *J. Psychiatr. Pract.*, 23: 25-35.
17. Piriyapong, K., A. Tangaroonsanti, V. Mahachai and R.K. Vilaichone, 2014. *Helicobacter pylori* infection impacts on functional dyspepsia in Thailand. *Asian Pacific J. Cancer Prev.*, 15: 10887-10891.
18. Shimoyama, T., M. Sawaya, A. Ishiguro, N. Hanabata, T. Yoshimura and S. Fukuda, 2011. Applicability of a rapid stool antigen test, using monoclonal antibody to catalase, for the management of *Helicobacter pylori* infection. *J. Gastroenterol.*, 46: 487-491.
19. Takeoka, A., J. Tayama, M. Kobayashi, I. Sagara and S. Ogawa *et al.*, 2017. Psychological effects of *Helicobacter pylori*-associated atrophic gastritis in patients under 50 years: A cross-sectional study. *Helicobacter*, 10.1111/hel.12445
20. Ünal, H.Ü., E. Akin, I. Aydin, M. Korkmaz, S. Özel, H. Selçuk and U. Yilmaz, 2013. Ongoing symptoms after eradication of *Helicobacter pylori*. psychiatric disorders may accompany. *Turk. J. Gastroenterol.*, 24: 15-21.
21. Wang, Z., B. Hu and B. Ding, 2015. Clinical observation on effect of flupentixol and melitracen combined with quadruple therapy on peptic ulcer patients with anxiety and depression. *Chin. J. Gastroenterol.*, 20: 366-368.
22. Zainaldeen, H.A. and H.M. Al-Faraj, 2010. *Helicobacter pylori* associated gastritis among Bahraini children presenting with abdominal pain. *J. Bah. Med. Soci.*, 22: 52-54.