Helicobacter Pylori Associated Depression among Patients Presenting with Epigastric Pain

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ABSTRACT

Background: Helicobacter pylori (H. pylori) infection is an extremely prevalent infection that has been connected to a number of illnesses, including stomach cancer and peptic ulcer disease. Additionally, depression has been listed as a widespread, expensive, and 13% prevalent public health concern. Despite the substantial link between depression and H. pylori gastritis, few studies have looked at the connection between H. pylori infection and depression.

Objective: In this study we aimed to assess the relation between depression and H. pylori infection.

Patients and methods: This was a case control study that included 150 patients with and without H. pylori infection, patients were diagnosed by detection of H. pylori antigen in the stool, with assessment of presence and severity of depression in all patients using depression score using PHQ-9 SCORE (Preliminary Psychiatric Assessment Using Patient Health Questionnaire).

Results: Comparing both groups revealed highly significant increase in PHQ-9 score in group 1 patients with positive H. pylori infection compared to group 2 patients with negative H. pylori infection with significant increase in the severity of depression among H. pylori positive group

Conclusion: H. pylori infection was significantly associated with depression and it is presence is related to the severity of depression making assessment of the presence of gastrointestinal symptoms or dyspepsia is very important in patient with depression.

Keywords: H. pylori infection, PHQ-9 score, Depression.

INTRODUCTION

H. pylori is gram-negative bacteria with spiral shape that is 3.5 microns long and 0.5 microns broad, Its two to seven unipolar sheathed flagella allow it to move through sluggish waters. With positive catalase, oxidase, and urease enzymes [1-2]which needed to live and colonise, it has to produce the plentiful urease enzyme, which makes up more than 5% of the bacteria's total protein weight [3-4]. Clinically, bacterial urease activity is essential because it serves as the foundation for conduct a number of invasive and non-invasive tests used to identify H.pylori infection , which is known to colonise in the antral area of the stomach mucosa [5].

H. pylori is a human gastrointestinal infection which is believed to be blamed for a number of gastric illnesses, from chronic gastritis to more catastrophic diseases such as stomach cancer. One of the most prevalent chronic bacterial illnesses affecting people is helicobacter pylori [6]. According to estimates of the most common illness, H. pylori infection, affects at least 50% of people worldwide [7].

H. pylori infection causes 75% of non-cardia stomach cancers globally [3]. Atrophic gastritis can result from gastritis brought on by H. pylori. Atrophic gastritis can then proceed to gastric adenocarcinoma and mucosa-associated lymphoid tissue lymphoma, intestinal metaplasia, dysplasia, and neoplasia [5,8,9].

Additionally, H. pylori may be responsible for unexplained ulcer risk in people with functional dyspepsia taking modest doses of aspirin or beginning treatment with non-steroidal anti-inflammatory drugs, unexplained anaemia from iron shortage, and idiopathic thrombocytopenic purpura [1]. According to various socioeconomic categories and populations, H. pylori infections are more common than others [10].

The emotional disorders in somatic diseases are frequent problems in internal medicine practice, numerous literature data suggest that there is strong relation of anxiety disorders, stress or depression to the somatic symptoms, the relation can undergo potentalisation in case of appearance of other pathogenic factors like H. pylori infection [12-15], this relation confirmed with many scientific reports, with common use of antidepressants and anxiety-relieving drugs in duodenal ulcers diseases therapy[13-15].

Depression is the second most prevalent cause of disability-adjusted life years lost. It is a very common, crippling, and expensive public health problem. It results in a persistent low mood and a sense of hopelessness and has a number of risk factors. The connection between digestive tract diseases and depression has been postulated for a very long time. In fact, depression was discovered to be a risk factor for digestive tract diseases [16].

It is also likely that the effect of numerous stress factors which injure the mucosa of the stomach, including also psychological stress, depression disorders and anxiety, modify the immunity of patients so that these patients become more sensitive to be infected with H. pylori. The infection becomes more aggressive and leads to the manifestations of gastritis or duodenitis and occurance of peptic ulcer disease [11].

The literature reports[17, 18] suggests that the presence of the chronic manifested H. pylori infection

can exacerbate or cause depression, the activity of stress agent itself can have an important effect on the clinical manifestation of the bacterial infection on stomach or duodenum walls because, according to **Levenstein *et al.*[19]** it modifies the immunological response of the system and contributes to the severity of H. pylori symptoms. Additionally, helicobacter pylori infection can alter the gastrointestinal (GI) flora's normal physiological condition in several ways. Few population studies have investigated the relationship between H. pylori infection and depressive symptoms in the general population, despite the fact that the physiological health of the GI tract is directly associated to mental diseases and disorders [18, 19].

Studies by **Levenstein *et al.*[20, 21]** showed that the risk of occurrence of duodenal ulcer disease is higher in patients with depression also the literature data suggest that the effect of psychological stress on the gastric and duodenal ulcer is controversial. So, according to the authors of the paper, the evaluation of relations of H. pylori infection to depression is interesting subject to study.

PATIENTS AND METHODS
Patients and study design
This was a prospective case-control study, which involved 150 patients with epigastric discomfort, examined the link between H. pylori infection and depression symptoms. Patients were chosen from the El-demerdash hospital's outpatient clinic at Ain Shams University.

Clinical assessment
One hudred and fifty patients aged 13 to 65 years with symptoms suggesting H. pylori infection which include epigastric pain, reflux symptoms, nausea, sense of early satiety, dyspepsia , repeated vomiting were included in the study and were subjected to detailed history taking and full clinical examination with full abdominal examination.

Patients were divided according to the presence or absence of H. pylori infection into two groups by detection of H. pylori in the stool [22]; group I, patients with H. pylori positive (75 patients) and group II (75 patients), patients with H. pylori negative infection as a control group. Patients with somatic diseases affecting occurrence of depression symptoms such as atypical enteritis, neoplasm diseases, ischemic heart disease, liver cirrhosis and endocrine diseases as well as patient with history of therapy to H. pylori infection. Also, pregnancy and neurological illness like dementia were excluded. Laboratory investigations included assessment of H. pylori antigen in the stool using qualititative immunochromatographic assay.

Psychological assessment:
Each patient was assessed using the preliminary psychiatric assessment using patient health questionnaire (PHQ-9)[23].Patient depression questionnaire done in outpatient clinic in Eldemerdash hospital and used to evaluate and measure the severity of depression. The scale consists of 10 items; each item was defined with a series of symptoms and each item was scored on a scale. The severity of depression was measured according to the total score. A total score of 1-4 was regarded as little depression, while scores of 5–9 were thought to be mild depression, 10–14 were thought to be moderate depression, 15–19 were thought to be moderately severe depression, and 20–27 were thought to be severe depression.

Ethical consent:
The protocol for this study was authorized by the Ain Shams University Ethics Committee (approval number FMASU R 43/2022). All study participants gave their written consent after being informed of the objectives of our investigation. The worldwide medical association's code of ethics, the Declaration of Helsinki for Humans, was adhered to throughout the course of this study.

Statistical Analysis
Utilizing MedCalc version 18.2.1, data input, processing, and statistical analysis were performed (MedCalc, Ostend, Belgium). Student's t, Chi square, tests, logistic regression analysis, and ROC Curve analysis were utilized as tests of significance. According to the kind of data (parametric and non-parametric) collected for each variable, data were presented, and an appropriate analysis was carried out. P value less than 0.05 was regarded as significant. Mean, Standard deviation (± SD), and range were used to describe parametric numerical data, whereas median and interquartile range (IQR), frequency, and the proportion of non-numerical data are used to describe non-parametric numerical data.

Logistic regression is helpful in predicting whether an event will occur based on a collection of independent factors. When the dependent variable is a qualitative variable, it is suitable and is equivalent to a linear regression model (categorical). The receiver operating characteristic (ROC) curve is a useful tool for measuring the sensitivity and specificity of quantitative diagnostic tests that split patients into two groups. 0.90 to 1 (%) is an excellent accuracy rate. Good accuracy is between 0.80 and 0.90 (%). Fair accuracy is 0.70–0.80 (percent). Poor accuracy is between 0.60 and 0.70 (%). Accuracy failure rate: 0.50 to 0.60 (%).

RESULTS
The present study included 150 patients with epigastric pain there mean age was(36.4 ± 13) years, and the mean BMI was (24.45 ± 2.86).Most of them were females (66.7%); while (33.3%) were males, all patients had epigastric pain (Table 1).

Table (1): Student's t and Chi square tests were used to compare basic clinical data between the two groups:

Variable		Negative H. pylori group (75)	Positive H. pylori group (75)	Student's t test
		Mean ± SD	Mean ± SD	P value
Age (years)		37.5 ± 13	35.3 ± 12.9	= 0.292
BMI		24.4 ± 2.9	24.45 ± 2.8	= 0.993
Variable		Negative H. pylori group (75)	Positive H. pylori group (75)	Chi square test
				P value
Gender	Female	54 (72%)	46 (61.3%)	= 0.1673
	Male	21 (28%)	29 (38.7%)	

Regarding depressive outcome data, the mean PHQ-9 score of all patients was (3.5 ± 3.98), with (34%) of patients had minimal depression, (20%) had mild depression, (9.3%) had moderate depression, (2.7%) had moderately severe depression, while nobody had severe depression (table 2, figure 1).

A comparison of the two groups' PHQ-9 scores showed a significant rise in the positive H. pylori group as compared to the negative H. pylori group (p < 0.01). Patients in group 1 had much more severe depression than patients in group 2 did (p < 0.01) (Figure 2, Table 2).

Table (2): Comparison between the 2 groups as regards depressive outcome data using Student's t and Chi square tests:

Variable		Negative H. pylori group (75)	Positive H. pylori group (75)	Student's t test
		Mean ± SD	Mean ± SD	P value
PHQ-9 score		1.1 ± 1.7	5.7 ± 4.2	< 0.001**
Variable		Negative H. pylori group (75)	Positive H. pylori group (75)	Chi square test
				P value
Depression Severity	No depression	42 (56%)	9 (12%)	< 0.001**
	Minimal depression	26 (34.7%)	25 (33.3%)	
	Mild depression	7 (9.3%)	23 (30.7%)	
	Moderate depression	0 (0%)	14 (18.7%)	
	Moderately severe depression	0 (0%)	4 (5.3%)	
	Severe depression	0 (0%)	0 (0%)	
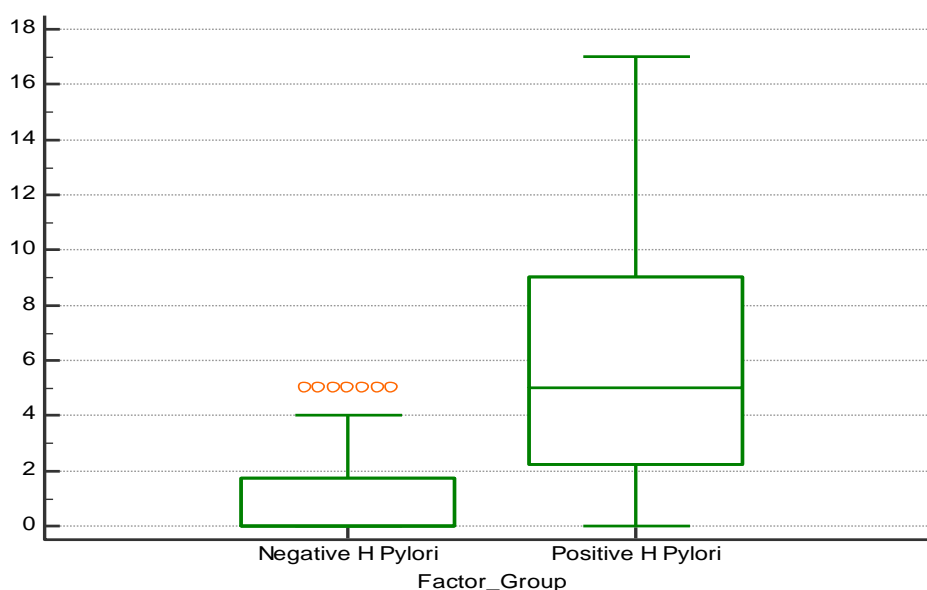
Figure (1): Comparison between the 2 groups as regardsPHQ-9 score.
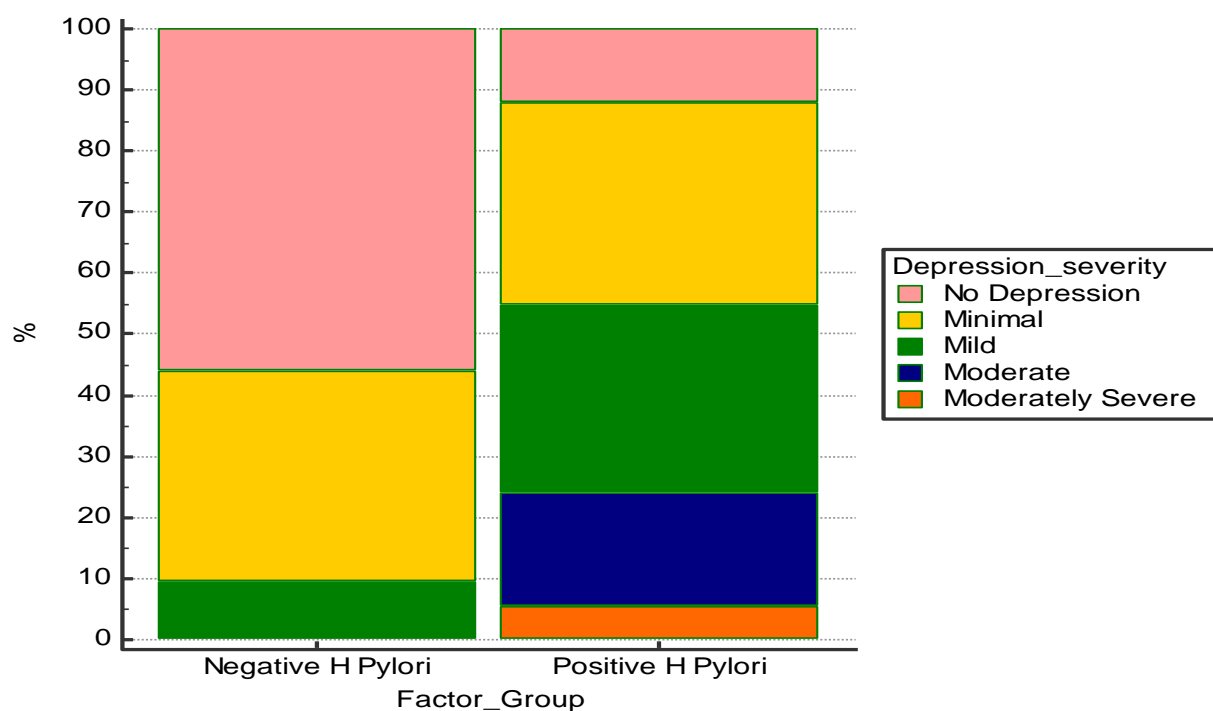
Figure (2): Comparison between the 2 groups as regards depression severity.

The increase in PHQ-9 score had an independent effect on increasing the likelihood of H. pylori infection occurrence (in symptomatic patients) after applying (Forward method) and entering some predictor variables, according to a Logistic regression analysis, with a statistically significant difference (p <0.01) (Table 3).

Table (3): Logistic regression model for the factors affecting H. pylori infection occurrence using Forward method:

Predictor Factor	Coefficient	OR	P value
(Constant)	-1.52990		
PHQ-9 score	0.54089	1.7175	<0.0001**

Other factors excluded from the model as (p value > 0.1). OR: odds ratio.

DISCUSSION

This case-control research, which inspected the link between H. pylori infection and depression symptoms, involved 150 patients with epigastric discomfort.

Since epigastric pain is the most prevalent H. pylori infection presenting symptom (H. pylori infection was found in up to 74% of patients with acid peptic ulcer disease symptoms.), all of our patients had this condition [24].

Akeel *et al.* [25] study found that age 30-39 had the greatest risk of H. pylori infection compared to other age groups. In the current investigation, the mean age of the patients included in the study was 36.4±13 years,

and almost 50% of patients were in this age range. A different research that found a greater incidence of H. pylori infection in patients under the age of 50 also stated that the prevalence among patients in the age group 13-29 years is 53.3% [26].

In terms of patient gender, women made up the bulk of patients (66.7%) while men made up 33.3%. This conclusion is consistent with some studies that found that females were more likely than males to have H. pylori infections [26-27], which accounted for 51.5% of patients with H. pylori seropositives. Females were more likely than men to have H. pylori infection (32.6% vs. 18.8%).

According to some authors[28-29], females are more likely than men to have H. pylori, while in another research, 66% of patients were female [26]. Another 2 sizable investigations revealed no gender differences in H. pylori infection rates, despite other authors reporting a high prevalence of infection in males [28, 30].

The majority of the patients in our study were average weight or overweight, and there were no obese patients included in our study. With regard to BMI, the mean BMI was (24.45±2.86), and there was no difference between the two groups that was not worthy. Previous studies reported that there was no discernible variation in BMI amongst the various BMI groups [25], and this is consistent with our finding.

In terms of depressed outcome data, all patients in our research had a mean PHQ-9 score of (3.5 3.98), with (34%) having minimum depression, (20%) mild depression, (9.3% moderate depression, (2.7%) moderately severe depression, and (0%) having severe depression.

A comparison of the two groups' PHQ-9 scores showed a significant rise in the positive H. pylori group as compared to the negative H. pylori group. This study's findings was supported by those of **Nguyen et al.**[11] who discovered a strong positive relationship between H. pylori presence and anxiety and depressive symptoms. They also supported those of **Kabeer et al.**[31] who found a significant association between H. pylori and depression in people with functional dyspepsia. Additionally, several trials have demonstrated relief in dyspeptic symptoms when H. pylori was eradicated [32-33].Another study found that females under 50 with seropositive H. pylori gastritis had the highest frequency of psychological discomfort and depression, as compared to H. pylori seronegatives [34].

Physicians should be aware of the neuropsychiatric symptoms associated with H. pylori infection, according to **Gu et al.**[35] They also discovered that symptoms often disappeared quickly after stopping medications and curing the H. pylori infection.

In addition, 54 patients with H. pylori infections were included by **Ünal et al.**[24] without knowledge of their psychological conditions. They discovered that 22 of them had at least one mental disorder, with depression accounting for around 13 of them. After eliminating H. pylori, they came to the conclusion that patients should be evaluated for psychiatric disorder since it would alter how they are treated.

Additional study revealed a strong correlation between H. pylori infection and psychiatric disease. Additionally, supplementing the conventional antibiotic course with antidepressant medications may aid in the relief of symptoms and the elimination of H. pylori [26].

Wang et al.[8] demonstrated that patients with peptic ulcers who also had anxiety and depression might boost therapy effectiveness and effectively reduce recurrence rates by using a combination of antidepressant treatment with H. pylori treatment utilising quadruple treatment in addition to flupentixol and melitracen, which reflects the close association between H. pylori infection and depression.

Intriguingly, we discovered that there was a highly significant increase in moderate and severe depression in the positive H. pylori group when compared to the negative H. pylori group. This finding is consistent with that of **Gu et al.**[35] who found that patients with H. pylori infection had elevated depressive symptoms.

CONCLUSION

H. pylori infection is very common worldwide infection which is significantly associated with depression especially with moderate to severe depression making assessment of presence of gastrointestinal symptoms and symptoms of dyspepsia very important in patients with depression Also, more studies are needed to evaluate the effect of addition of anti-depressant treatment to treatment of H. pylori infection.

REFERENCES

1. **Chey W, Leontiadis G, Howden C et al. (2017):** ACG Clinical Guidelines: Treatment of Helicobacter pylori infection. Am J Gastroenterol., 112: 212–238.
2. **Al-Akwaa A (2010):** Prevalence of Helicobacter pylori infection in a group of morbidly obese Saudi patients undergoing bariatric surgery: A preliminary report. Saudi J Gastroenterol., 16: 264-7.
3. **Rahman S, Ferwana M, Al-Qadhi I et al. (2014):** Adult depression screening in Saudi primary care: prevalence, instrument and cost. BMC Psychiatry, 14:1-9.
4. **Goodwin C, Worsley B (1993)**: Microbiology of Helicobacter pylori. Gastroenterol Clin North Am., 22:5-19
5. **Warren J, Marshall B (1983):** Unidentified curved bacilli on gastric epithelium in active chronic gastritis. The Lancet, 321(8336):1273-5.
6. **Cameron I, Crawford J, Lawton K et al. (2008):** Psychometric comparison of PHQ-9 and HADS for measuring depression severity in primary care. Br J Gen Pract., 58(546):32-6.
7. **Essawi T, Hammoudeh W, Sabri I et al. (2013):** Determination of Helicobacter pylori virulence gene in gastric biopsies by PCR. ISRN Gastroenteral., 13: 606258. doi: 10.1155/2013/606258
8. **Wang H, Cheng F, Wu M et al. (2015):**Genome sequences of three Helicobacter pylori strains from patients with gastric mucosa-associated lymphoid tissue lymphoma. Genom Announcement, 3(2):e00229-15.
9. **Souod N, Sarshart M, Dabiri H et al. (2015):** The study of the OIP A and DUP A genes in Helicobacter pylori strains and their relationship with different gastroduodenal disease. Gastroenteral Hepatol Bed Bench., 8(11):47-53.
10. **Khedmat H, Karbasi-Afshar R, Agah S et al. (2013):** Helicobacter pylori infection in the general population: A middle Eastern perspective. Caspian J Intern Med., 4(4):745-753.
11. **Nguyen N, Ramsey D, Graham D et al. (2015):** The prevalence of helicobacter pylori remains high in African American and Hispanic veterans. Helicobacrer., 20(4):305-11.
12. **Kadi R, Halawani E, Abdelkader H (2014):** Prevalence of H. pylori strains harbouring cagA and iceA virulence genes in Saudi patients with gastritis and peptic ulcer disease. Microbiology Discovery, 2(1): 2. doi: 10.7243/2052-6180-2-2.
13. **Cader J, Paradowski L, Rymaszewska J et al. (2007):** Is there any relation of Helicobacter pylori infection to anxiety and deprresive symptoms? Gastroenterologia Polska., 14 (6):397-401.

14. **Laghi-Pasini F (1977):** Action of the bromazepam-propantheline combination in patients with organic and functional gastrointestinal disorders.Clin.,83: 301-311.

15. **Noyes R, Clancy J, Hoenk P***et al.* **(1978):** Anxiety neurosis and physical illness. Compr Psychiatry, 19: 407-413.

16. **Reddy M (2010):** Depression: The Disorder and the Burden. Indian J Psychol Med., 32(1): 1–2.

17. **Murison R (2001):** Is there arole for psychology in ulcer disease? Integr Physiol Behav Sci., 36: 75-83.

18. **Jones M (2006):** The role of psychosocial factors in peptic ulcer disease: Beyond Helicobacter pylori and NSAIDS.J PsychosonRes.,60: 407-412.

19. **Levenstein S, Kaplan G, Smith M (1997):** psychological predictors of peptic ulcer incidence in the Alamenda country study. J Clin Gastroentero., 24: 140-142.

20. **Levenstein S, Ackerman S, Kiecolt-Glaser J***et al.* **(1999):** Stress and peptic ulcer disease.JAMA.,281: 10-11

21. **Levenstein S (2000):** The very model of a modern etiology. A biopsychosocial view of peptic ulcer. Psychoson Med., 62:176-185.

22. **O'Toole P, Logan S, Kostrzynska M** *et al.* **(1991):** Isolation, biochemical and molecular analysis of a species-specific protein antigen from the gastric pathogen Helicobacter pylori. J Bacteriol., 173(2):505-13.

23. **Cameron I, Crawford J, Lawton K** *et al***. (2008):** Psychometric comparison of PHQ-9 and HADS for measuring depression severity in primary care. Br J Gen Pract., 58(546):32-6.

24. **Ünal H, Akin E, Aydin I** *et al.* **(2013):** Ongoing symptoms after eradication of Helicobacter pylori: psychiatric disorders may accompany. Turk J Gastroenterol.,24:15–21

25. **Akeel M, Elmakki E, Shehata A** *et al.* **(2018):** Prevalence and factors associated with H. pylori infection in Saudi patients with dyspepsia. Electron Physician, 10(9): 7279–7286.

26. **Neufeld N, Mohamed N, Grujich N** *et al.* **(2017):** Acute neuropsychiatric symptoms associated with antibiotic treatment of helicobacter pylori infections: a review. J Psychiatr Pract., 23(1):25-35.

27. **Zhu Y, Zhou X, Wu J** *et al.* **(2014):** Risk Factors and Prevalence of Helicobacter pylori Infection in Persistent High Incidence Area of Gastric Carcinoma in Yangzhong City. Gastroenterol Res Pract., 14:481365. doi: 10.1155/2014/481365.

28. **Aminde J, Dedino G, Ngwasiri C** *et al.* **(2019):** Helicobacter pylori infection among patients presenting with dyspepsia at a primary care setting in Cameroon: seroprevalence, five-year trend and predictors. BMC Infect Dis., 19(1):30.doi: 10.1186/s12879-019-3677-0.

29. **PajavandH, Mohajeri P, Bakhtyari S** *et al.***(2015):**High Frequency of vacA s1m2 Genotypes Among Helicobacter pylori Isolates From Patients With Gastroduodenal Disorders in Kermanshah, Iran. Jundishapur J Microbiol., 8(11): e25425. doi:10.5812/jjm.25425.

30. **Ahmed S, Omar N, Azouz H** *et al.* **(2017):** Detection of Sutterella in the Stool of Egyptian Children with Autism Spectrum Disorders. MRJI., 22(2): 1-8.

31. **Kabeer K, Ananthakrishnan N, Anand C** *et al.* **(2017):** prevalence of H.pylori infection and stress, anxiety or depression in functional dyspepsia and outcome after appropriate intervention. J Clin Diagn Res., 11(8): 11-15.

32. **Tennant C, Goulston K, Langeluddecke P (1986)**: Psychological correlates of gastric and duodenal ulcer disease. Psychol Med., 16: 365-371.

33. **Kate V, Maroju N, Ananthkrishnan N (2013):** Helicobacter pylori infection and upper gastrointestinal disorders. Gastroenterol Res Pract., 2013: 896209.doi: 10.1155/2013/896209

34. **Lane J, Murray L, Noble S** *et al.* **(2006):** Impact of Helicobacter pylori eradication on dyspepsia, health resource use, and quality of life in the Bristol helicobacter project: randomized controlled trial. BMJ., 332(7535):199-204.

35. **Gu Y, Zheng L, Kumari S** *et al.* **(2019):** The relationship between Helicobacter pylori infection and depressive symptoms in the general in china: The TCLSIH cohort study. Helicobacter, 24(5):e12632. doi: 10.1111/hel.12632.