Biochemistry

Prevalence and Risk Factors of Helicobacter Pylori Infection among Patients with Peptic Ulcer Disease Attendeing Muhammad Abdullahi Wase Teaching Hospital

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Abstract	Original Research Article

Duodenal (DU) and gastric (GU) ulcers are both included in the category of peptic ulcer disease (PUD). The first section of the duodenum or the stomach's pre-pyloric region (antrum) are the most common sites for duodenal ulcers. Most cases of gastric ulcers occur in the stomach's lesser curvature, which connects to the body's antrum (angularis). The purpose of the study is to ascertain the prevalence and risk factors of Helicobacter pylori infections in Muhammad Abdullahi Wase Teaching Hospital patients suffering from peptic ulcer disease. Patients with PUD who had an H. pylori infection test performed between September and November 2019 at the Muhammad Abdullahi Wase Teaching Hospital in Kano, Nigeria, were included in the study. The One-step ANTI-HP in whole blood Rapid Screen Test was used to determine whether blood samples contained *H. pylori* infection. Seventy PUD patients had an overall prevalence rate of 80% for H. pylori infection; however, the percentage was higher in men (64.3%) than in women (35.7%). Patients with a house population of more than six (70%), those who drank pipe water (51.4%), those who took antiulcer drugs (67.1%), and those with a family history of PUD (55.7%) were the most common groups of patients with *H. pylori* infection. In conclusion, the age group with a male majority (31–50 years old) had the highest frequency of *H. pylori* infection. The main risk factors for *H. pylori* were using antiulcer drugs, drinking water in a particular way, and having a family history of PUD.

Keywords: Peptic ulcer disease (PUD)., ANTI-HP, *H. pylori* infection.

INTRODUCTION

Peptic Ulcer Disease or PUD, one of the most common ulcers, refers to ulcer of the gastrointestinal tract in the region of the stomach. It is characterized by high acidity resulting in mucosal erosions causing extreme pain and discomfort. By definition, mucosal erosions should be equal to or exceed 0.5 cm (Bhat *et al.,* 2013). It is the end result of an imbalance between the digestive fluids in the stomach and the duodenum. Most ulcers are caused by an infection, not spicy food, acid or stress. The stomach and the duodenal lining have several mechanisms that prevent ulcers from developing. A coating of mucus protects the stomach lining from the effects of acidic digestive juices. Food and other substances in the stomach neutralize acid. Certain chemicals produced by the stomach protect the cells lining the stomach.

Peptic Ulcers can be broadly classified into Gastric or stomach ulcer and Duodenal Ulcer. Gastric Ulcers occur mainly in the elderly, on the lesser curve. Ulcers elsewhere are often malignant. Duodenal Ulcers are four fold commoner than gastric ulcer. It is identified by the most common symptom i.e. the epigastric pain occurs typically before meals or at night which is relieved by eating or drinking milk (Murray Longmore *et al.,* 2010). Another type of PUD is the Idiopathic PUD (IPUD) is defined as a peptic ulcer without definite causes such as H. pylori infection, NSAIDs use or hypergastrinemia.

NSAIDs are widely used for a variety of conditions to help reduce pain and inflammation; however, many users develop gastrointestinal side effects. NSAIDs account for over 90% of all ulcers and approximately 25% of NSAID users will develop peptic ulcer disease. (Lydia B *et al.,* 2010) Aspirin users are also twice as likely to develop peptic ulcers as the general population. (Huang JQ *et al.,* 2015) Others develop a milder degree of topical injury, which is seen as mucosal hemorrhages and erosions and are referred to as NSAID

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gastropathy. These multiple small erosions are usually located in the antrum but may also be seen in the body (Chan FK *et al.,* 2002).

NSAIDs cause gastric injury by the damage of the gastric epithelium by intracellular accumulation of these drugs in an ionized state (Marry Longmore *et al.,* 2010). Then it reduces the hydrophobicity of the mucous gel layer by changing the action of surface active phospholipids followed by the suppression of the prostaglandin synthesis which is then followed by the injury due to neutrophils adherence to the endothelium of gastric microcirculation (Blaser and Atherton 2004). The risk of gastrointestinal bleeding increases steeply with age, and the excess risk from non-aspirin NSAIDs are much higher in the elderly than in young subjects, even when the relative risk is assumed to remain constant with age (Sheila E Crowe *et al.,* 2013).

For many years, excess acid was believed to be the major cause of ulcer disease. Accordingly, treatment emphasis was on neutralizing and inhibiting the secretion of stomach acid. While acid is still considered significant in ulcer formation, the leading cause of ulcer disease is currently believed to be infection of the stomach by a bacterium called "Helicobacter pyloridus" (*H. pylori*) accounting to about 70-90%. Other risk factors include anticoagulants, NSAIDs, corticosteroids, aspirin, ibuprofen, alcohol, diet (Spicy Food), H. Pylori, stress, past history of PUD and gender. Another cause of PUD is the excess acid production from tumors of the acid producing cells of the stomach which is also known as gastrinomas. It increases the gastric acid output (WebMd 2013).

Helicobacter pylori, a spiral-shaped pathogenic bacterium found on the human gastric mucosa, was first isolated by Warren and Marshall (Warren JR *et al.,* 1983) in 1982 and soon after was linked with chronic antral gastritis and peptic ulceration. Initially, this bacterium was classified as Campylobacter pylori but in 1989 was included in a new genus, Helicobacter, and renamed Helicobacter pylori (Goodwin CS *et al.,* 1989). Although it was "discovered" less than 20 years ago, thousands of articles have been written about *H. pylori*, one of the most common bacterial infections in the world (Cave DR *et al.,* 1997). Since a complete summary of the H. pylori literature is beyond the scope of this review, it briefly discusses the microbiologic characteristics of H. pylori, the diagnostic tests used in epidemiologic studies, and the association of H. pylori with gastric cancer and other diseases. The primary focus is on the epidemiology and transmission of *H. pylori* infection in adults, including reviews of the prevalence of *H. pylori* in various countries, risk factors for *H. pylori* infection, and hypothesized modes of transmission. Findings from studies of children have been added where appropriate to supplement the adult literature. The major emphasis is on scientific articles selected from the recent literature, but important scientific papers published in peer-reviewed journals prior to 1995 have also been included (Bhatia and Kulkarni 1997).

Epidemiology shows that PUD remains a relatively common condition worldwide with annual incidence ranging from 0.10% to 0.19% for physician-diagnosed PUD and from 0.03% to 0.17% for PUD diagnosed during hospitalization (Sung JJ *et al.,* 2009). The 1-year prevalence of physician diagnosed PUD was 0.12–1.5%, and the 1-year prevalence of PUD diagnosed during hospitalizations was 0.10–0.19% (Sung JJ *et al.,* 2009). The data show that the incidence of PUD has decreased over recent decades in many countries, most likely as a result of the decrease in H. pylori infection, particularly in Western populations. However, it is possible that the situation may be different in Asian countries; a recent study in Korea revealed that the prevalence of H. pylori infection in association with GU was increasing with time, whereas *H. pylori* infection in DU was decreasing (Jang HJ *et al.,* 2008). The most reliable study of physician-diagnosed prevalence was from Sweden, reporting cross-sectional data representative of the general population (Aro P *et al*., 2006); the study thus included both symptomatic and asymptomatic PUD. The overall prevalence of PUD observed in this study was 4.1%; 19.5% of all PUD cases identified were asymptomatic. Comparing this prevalence with the lower rates obtained from other studies of physician diagnosed PUD in primary care suggests that a proportion of individuals with PUD remain undiagnosed (Chey and Wong B. 2007). In individuals with asymptomatic PUD, severe complications, such as gastrointestinal hemorrhage, may be the first signs of the disease. Hemorrhage is associated with mortality approaching 10% and high recurrence (Christensen S *et al.,* 2007). Literature shows that the reported incidence and prevalence of PUD have decreased over time in recent decades. However, temporal trends in the rate of hospitalizations for complications of PUD varied, remaining unchanged or increasing in recent decades in two studies in Finland and the Netherlands (Paimela H *et al.,* 2002), but declining over time in one study in Scotland (Kang JY, *et al.,* 2006) The lifetime risk for peptic ulcer in infected individuals ranges from 3% in the United States to 25% in Japan (Suerbaum S *et al.,* 2002).

MATERIALS AND METHODS
This study was conducted in Muhammad Abdullahi Wase Specialist Hospital in Kano with a sample size of 70. A modified questionnaire was used to collect the information. A total of 70 patients were interviewed to collect the information regarding socio-demographic factors, lifestyle factors, risk factors and related variables. All the data were entered and analyzed by using statistical packages for social science (SPSS) software version 17.0.

MATERIALS

Questionnaire, syringe, test tube, centrifuge, pipette, *H. pylori* cassette, buffer, hand gloves.

METHODS

This is a study on patients who were to undergo H. pylori test at MUHAMMAD ABDULLAHI WASE HOSPITAL over a period of three months. Ethical clearance was requested from the Head of Department office, it was filled, and taking to the ministry of health together with consent foam for approval.

Muhammad Abdullahi Wase is a secondary health care facility located at Hospital road off Audu Bako way, Kano, which is own and run by Kano state government that provides general and specialized medical care.

During the study, a questionnaire was filled by the patients or their guardians, Data collected include; patient's demographic factors, lifestyle factors and associated risk factors.

TEST

One step ANTI-HP in whole blood Rapid Screen Test is a lateral flow, immunochromatographic screening test and was the test used at Muhammad Abdullahi Wase Teaching Hospital to detect the presence of helicobacter pylori in patient's blood sample.

PRINCIPLE

Recombinant antigen of HP are used in test band as capture materials and gold conjugates. If the antibody of HP is present in the sample in concentration above the labelled, complex will be formed. This complex is then captured by antigens immobilized in the Test zone of the membrane, producing a visible pink-rose colour band on the membrane. The colour intensity will depend on the concentration of the anti-HP present in the sample. This one step test is very sensitive and only takes about 15-20 minutes. Test results are read visually without any instrument.

SPECIMEN COLLECTION

Blood samples were collected in a syringe and were taken to microbiology laboratory, the samples/specimen were to be used within an hour. The specimen that were not tested within an hour, were stored at 4°C cold closet or refrigerator, but not freeze and then brought out to stay at room temperature before testing.

STATISTICAL ANALYSIS

All the data generated were entered and analyzed by using statistical packages for social science (SPSS) software version 17.0. Associations between categorical variables were tested using chi-squared test with reports of corresponding p values. The level of statistical significance for the study was set at P value of patients to be greater than of the control. In all the tests, p value less than that of control were used as statistical association for risk factors of *H. pylori* infection.

RESULTS

RESULT FOR SOCIODEMOGRAPHIC AND LIFESTYLE FACTORS OF THE PATIENTS

Table 1: Distribution of the patients by age (n=70)

Age (years)	Frequency	Percent (%)
10-30	25	35.7
31-50	35	50.0
51-70	8	11.4
70 and above	2	2.9
Total	70	100.0

Table 1 shows that 35%, 50%, 11.4%, and 2.9% of the patients belong to age group of 10-30 years, 31-50 years, 51-70 years, and 71 and above years, respectively.

There was no significant association of age group with the prevalence of *H. pylori* infection.

Table 2: Distribution of patients by marital status (n=70)

Marital status	Frequency	Percent
Never married	21	30.0
Widowed/Divorced	12	17.1
Currently married	37	52.9
Total	70	100.0

Table 2 shows that 30.0% of the patients were never married, 17.1% were widowed/divorced, and the majority of the patients (52.9%) were currently married.

Table 3: Distribution of patients by education (n=70)

Education	Frequency	Percent (%)
High institution +	18	25.7
Secondary graduate	15	21.4
Primary graduate	14	20.0
No education	23	32.9
Total	70	100.0

Table 3 shows that 25.7%, 21.4%, 20.0%, ad 32.9% were High institution+ graduates, Secondary graduate, Primary graduate and No education respectively.

Table 4: Distribution of patients by smoking habits

Smoking	Frequency	Percent (%)
Never	40	57.1
Tried at past, currently non smoker	10	14.3
Tried at past, currently occasional smoker	9	12.9
Regular smoker	11	15.7
Total		100.0

Table 4 shows that majority of the patients (57.1%) never smoke, 14.3% tried smoking at past and are currently nonsmokers, 12.9% of the patients tried smoking at past and are currently occasional smokers, and lastly, 15.7% were regular smokers.

Table 5: Distribution of patients by alcohol consumption

Alcohol	Frequency	Percent (%)
Never	67	95.7
Tried at past	03	4.3
Total	70	100.0

Table 5 shows that majority of the patients (95.7%) never consume alcohol, and 4.3% of the patients tried at past.

Table 6: Distribution of patients by housing tenure

Housing tenure	Frequency	Percent (%)
Owned by household members	40	57.1
Rented	18	25.7
Lodging/ no money paid	12	17.2
Total	70	100.0

Table 6 shows that 57.1% of the patient's hoses were owned by house members, 25.7% of the houses were rented, and 17.2% were lodging/ no money paid.

Table 7: Distribution of patients based on occupation

Occupation	Frequency	Percent (%)
Agriculture/animal husbandry	13	18.6
Industry	35	50.0
Construction	10	14.3
Retired/unemployed	12	17.1
Total	70	100.0

Table 7 shows that 18.6% of the patients were working in agriculture/animal husbandry, 50.0% were working in industries, 14.3% were construction workers, and 17.1% were retired/unemployed.

Table 8: Distribution of patients based on family income (naira/month)

Family income (N)	Frequency	Percent (%)
10,000-50,000	16	22.9
50,000-100,000	39	55.7
100,000 +	15	21.4
Total	70	100.0

Table 8 shows that 2.9%, 55.7%, and 21.4% has family income of 10-50, 50-100, and 100+ respectively.

RESULT FOR RISK FACTORS OF THE PATIENTS

Table 9: Distribution of patients by Gender

Sex	H pylori result (P)	H pylori result (N)	Total (%)	Chi square	P value
Male	37	8	45 (70%)	0.997a	0.318
Female	18	7	25 (30%)		

Table 10: Distribution of the patients based on House population

House population	H pylori result (P)	H pylori result (N)	Total (%)	Chi square	P value
1 to 5	16	4	20 (40%)	0.34	0.854
6+	39	11	50 (60%)		

Table 11: Distribution of patients based on Sources of drinking water

Sources of drinking water	H pylori result (P)	H pylori result (N)	Total (%)	Chi square	P value
Pipe water	29	7	36 (51.4%)		
Bottled water	13	3	16 (22.9%)	0.583a	0.747
Other	13	5	18 (25.7%)		

Table 12: Distribution of patients based on Dietary habit

		H pylori result (P)	H pylori result (N)	Total	Chi square	P value
VEGETABLES	Yes	20	10	30	4.419a	0.36
	No	35	5	40		
FRUITS	Yes	23	6	29	0.016a	0.899
	No	32	9	41		
SPICY FOODS	Yes	39	9	48	0.651	0.42
	No	16	6	22		
OTHERS	Yes	9	8	17	8.760a	0.003
	No	46	7	53		

Table 13: Distribution of patients based on Family history of PUD

Family history of PUD	H pylori result (P)	H pylori result (N)	Total (%)	Chi square	P value
Yes	29	10	39		
No	12	2	4	0.890a	0.641
Not aware	13	3	16		

Table 14: Distribution of the patients based on Antiulcer drug consumption

Antiulcer drug consumption	H pylori result (P)	H pylori result (N)	Total (%)	Chi square	P value
Once	14	2	16 (22.9%)		
Never	4	3	7 (10.0%)	2.667a	0.264
Most often	37	10	47 (67.1%)		

DISCUSION ON SOCIODEMOGRAPHIC AND LIFESTYLE FACTORS OF PATIENTS

This descriptive study was conducted from September to November 2019 to explore the prevalence of helicobacter pylori infection among patients with peptic ulcer diseases attending Muhammad Abdullahi Wase Teaching Hospital. In-depth data were collected from 70 patients and hospital files. A pretested modified questionnaire was used to collect the data. All the data were analyzed by using statistical package of social science (SPSS).

The current study shows that 35%, 50%, 11.4%, and 2.9% of the patients belong to age group of 10-30 years, 31-50 years, 51-70 years, and 71 and above years, respectively. There was no significant association of age group with the prevalence of h. pylori infection. 30.0% of the patients were never married, 17.1% were widowed/divorced, and the majority of the patients (52.9%) were currently married. 25.7%, 21.4%, 20.0%, ad 32.9% were High institution+ graduates, Secondary graduate, Primary graduate and No education respectively. Majority of the patients (70.0%) were Muslims, and 30.0% were Christians. Majority of the patients (57.1%) were Hausas, 28.6% were Yoruba, 10.0% were Igbos, and 4.3% were Fulani's. Majority of the patients (57.1%) never smoke, 14.3% tried smoking at past and are currently nonsmokers, 12.9% of the patients tried smoking at past and are currently occasional smokers, and lastly, 15.7% were regular smokers. Majority of the patients (95.7%) never consume alcohol, and 4.3% of the patients tried at past.

18.6% of the patients were working in agriculture/animal husbandry, 50.0% were working in industries, 14.3% were construction workers, and 17.1% were retired/unemployed. 2.9%, 55.7%, and 21.4% has family income of 10-50, 50-100, and 100+ respectively.

DISCUSSION ON RISK FACTORS OF PATIENTS AND CONTROL

Our male patients showed high prevalence of h pylori infection (64.3%) as compared to female patients (35.7%). For the control, (53.3%) were males and (46.7%) were females. This can give a clue that gender has no direct impact on h pylori infection. According to our p value of the patients (0.318) and that of the control (0.880), the statistical correlation between gender and *H. pylori* infection is insignificant. This trend was different from what was demonstrated in a similar study conducted at Saudi Arabia, were female patients showed high prevalence of h pylori (70%) compared to male patients (30%). According to this study, this female preponderance of h pylori infection could be coincidentally or may require another study with large sample size. The current study reveals that (30%) of the patients belong to house population number of 1 to 5, while (70%) of them belong to 6+. The p value of the patients (0.854) and that of the control (0.876) showed insignificant correlation between House population and h pylori infection. Additionally, in our controls, majority of them (73.3%) belong to 1 to 5, while 26.7% belong to 6+. The study also showed that, patients drinking pipe water (51.4%) were higher than those drinking bottled water (22.9), and other type of waters (25.7%). In contrast, our controls showed participant drinking bottled water (46.7%) and other type of waters (33.3%) were higher than those drinking pipe water (20%). There is significant correlation between mode of drinking water and *H. pylori* infection with p value approaching 1 (0.747) and that of control (0.010). As such it can be concluded that mode of drinking water may be a risk factor to h pylori infection.

In this study the respondents' dietary habit reveals that vegetables having the p value (0.36) of patients, and (0.003) of control showed insignificant correlation with h pylori infection. Fruits having the p value of patients (0.899) approaching1, and that of control (0.268) showed significant correlation with h pylori infection. Spicy foods showed significant correlation with *H. pylor*i infection by a p value of patients to be (0.42) and that of control (0.310), and other types of food showed insignificant correlation with h pylori infection with p value (0.003) of patients, and (0.010). This study showed significant correlation between *H. pylori* infection and vegetables, fruits, and spicy food, and reveals insignificant correlation with other type of foods.

In this study majority of the patients (55.7%) showed family history of PUD, (18.6%) patients were not aware, and (5.7%) patients showed no family history of PUD. In contrast, the result of the control showed majority of the patients (66.7%) to have no family history of PUD, (26.7%) of the respondents were not aware and (6.67%) have history of PUD. The p value of the patients (0.641) and that of the control (0.14) showed significant correlation between family history of PUD and h pylori infection. This trend was also supported by a similar studies conducted at Bangladesh, according to the study, majority of the patients (60.2%) had a family history of PUD and 39.8% did not have.

The study also reveals that majority of the patients (67.1%) took antiulcer drug most often, 22.9% took antiulcer drug once, and only 10.0% of the patients never took antiulcer drugs. From the control site, majority of them (86.7%) never took antiulcer drug, 13.3% once took it, and no control was found to be taking antiulcer drug most often. But, our patient's p value was found to be (0.264) and that of the control (0.919) showed insignificant correlation between antiulcer drug and h pylori infection which is not supported by any study that I came across. According to a similar study conducted at Bangladesh, were majority of the patients (57.7%) took aspirin and 42.3% did not. It can be concluded from the percentage of patients that took antiulcer drug and that of the controls that did not, that Antiulcer drug consumption is more likely to be a risk factor.

CONCLUSION

The prevalence of *H. pylori* infection among patients presenting with peptic ulcer complaints at Muhammad Abdullahi Wase Teaching Hospital was high (70%). Associated risk factors were sources of drinking water, type of foods, and family history of PUD.

The socio-economic conditions and educational levels of the patients with the disease were found to be under par. In addition, the patients having family history of the disease, stress, and those taking antiulcer dru6g most often were affected. This factors including possible lack of awareness about the diseases, its consequences and its available treatment options could be the main contributing elements in aggravating the burden of PUD in Kano.

REFERENCES

- Aro, P., Storskrubb, T., Ronkainen, J., Bolling-Sternevald, E., & Engstrand, L. (2006). Peptic ulcer disease in a general adult population: the Kalixanda study: a random population-based study. *American Journal of Epidemiology,* 163, 1025-1034.
- Bhat, S., Johannessen, T., Cullen, D. J., Hawkey, G. M., & Greenwood, D. C. Peptic Ulcer, (4th July 2013) Available at: http://en.wikipedia.org/wiki/Peptic_ulcer (Accessed:12th October, 2019).
- Bhatia S. J., & Kulkarni S. G. (1997). Cost-effectiveness of Helicobacter pylori eradication in India: to live and let live... expensively? *Indian Journal of Gastroenterology*, 16, S25-28.

- Blaser, M. J., & Atherton, J. C. (2004). Helicobacter pylori persistence: biology and disease. *Journal of Clinical Investigation,* 113, 321-333.
- Cave, D. R. (1997). How is Helicobacter pylori transmitted? *Gastroenterology*, 113, 9-14.
- Chan, F. K., To, K. F., Wu, J. C., Yung, M. Y., & Leung, W. K. (2002). Eradication of Helicobacter pylori and risk of peptic ulcers in patients starting long term treatment with non-steroidal anti-inflammatory drugs: a randomized trial. *Lancet*, 359, 9-13.
- Chey, W. D., & Wong, B. C. (2007). American College of Gastroenterology guideline on the management of Helicobacter pylori infection. *American journal of Gastroenterology*, *102*(8), 1808-1825.
- Christensen S., Riis A., Nørgaard M., Sørensen H. T., & Thomsen R. W. (2007). Short-term mortality after perforated or bleeding peptic ulcer among elderly patients: a population-based cohort study. *BMC Geriatrics*, 7, 8-11.
- Goodwin C. S., Armstrong J. A., & Chilvers T. (1989). Transfer of Campylobacter pylori and Campylobacter mustelae to Helicobacter gen. Nov. as Helicobacter pylori comb. Nov. and Helicobacter mustelae comb, Nov., respectively. *International Journal of Systematic and Evolutionary microbiology*, 39, 39-75.
- Huang J. Q., Sridhar S., & Hunt R. H. (2015). Role of Helicobacter pylori infection and non-steroidal anti-inflammatory drugs in peptic-ulcer disease: a meta-analysis. *Lancet*, 359, 14-22.
- Jang, H. J., Choi, M. H., Shin, W. G., Kim, K. H., & Chung, Y. W. (2008). Has peptic ulcer disease changed during the past ten years in Korea? A prospective multi-center study. *Digestive Diseases and Sciences*, 53, 1527-1531.
- Kang, J. Y., Elders, A., Majeed, A., Maxwell, J. D., & Bardhan, K. D. (2006). Recent trends in hospital admissions and mortality rates for peptic ulcer in Scotland 1982-2002. *Alimentary Pharmacology and Therapeutics,* 24, 65-79.
- Feinstein, L. B., Holman, R. C., Christensen, K. L. Y., Steiner, C. A., & Swerdlow, D. L. (2010). Trends in hospitalizations for peptic ulcer disease, United States, 1998–2005. *Emerging infectious diseases*, *16*(9), 1410-1418.
- Murray, L., Ian, B. W., Edward, H. D., Alexander, F., & Ahmad, R. M. (2010). Oxford Handbook of Clinical Medicine, 8th ed., New York: Oxford University Press Inc.
- Paimela, H., Paimela, L., Myllykangas-Luosujärvi, R., & Kivilaakso, E. (2002). Current features of peptic ulcer disease in Finland: incidence of surgery, hospital admissions and mortality for the disease during the past twenty-five years. *Scandinavian Journal of Gastroent*erology, 37, 399-403.
- Sheila E. Crowe, MD, FRCPC, FACP, FACG, AGAF, Peptic Ulcer disease (Beyond the basics), October 2011, Available at: http://www.uptodate.com/contents/peptic-ulcer-disease-beyond-the-basics (Accessed: 13th October, 2019).
- Suerbaum, S., & Michetti, P. (2002). Helicobacter pylori infection. *New England Journal of Medicine,* 347, 1175-1186.
- Sung, J. J., Kuipers, E. J., & El-Serag, H. B. (2009). Systematic review: the global incidence and prevalence of peptic ulcer disease. *Alimentary Pharmacology and Therapeutics*, 29, 938-946.
- Warren, J. R., & Marshall, B. (1983). Unidentified curved bacilli on gastric epithelium in active chronic gastritis. (Letter). *Lancet*, 1, 1273-1275.
- WebMd, Digestive Disorders Health Center, September 2012 Available at: http://www.webmd.com/digestive-disorders/digestivediseases-peptic-ulcerdisease (Accessed: 13th October, 2013).