

Is There Decreasing Prevalence of Helicobacter Pylori Infection in Patients with Dyspepsia ?

Irin Perveen^{1*} Madhusudan Saha² Md. Quamrul Hasan³

Abstract

Background: World-wide there is decreasing prevalence of Helicobacter pylori(H. Pylori) infection. As we are lacking in consistent data regarding H. Pylori infection in our population, we aimed to find out prevalence of H.pylori infection in patients with dyspepsia in North-East part of Bangladesh.

Material and methods: Clinical variables, stool antigen test result and endoscopic findings of consecutive patients with dyspepsia were recorded in a semi-structured questionnaire. Statistical analysis was done with SPSS programme 17.0(). Significance level was set at 0.05 or less.

Results: A total of 790 patients(male 549, female 241) were included in the study with higher mean age among female patients (41.46 VS. 39.19, p.008) than male patients. Three most common dyspeptic symptoms were abdominal pain (n=365, 46.2%), bloating (n=280, 35.4%) and vomiting (n=163, 20.6%). A total of 217(39.5%) male and 87(36.0%) female were positive for stool antigen test (n=308, 38.5%) for H. pylori. No significant association was found between Helicobacter pylori infection and presence of individual dyspeptic symptom, number of dyspeptic symptoms(OR 1.385, p .103), age (OR .998, p .668), sex (OR 1.157, p .362), rural/urban residence (OR 1.126, p .503) or socio-economic condition (OR .965, p .09). Around 81% (293/360) subjects had upper GI lesion (Gastritis/gastric ulcer, duodenitis/duodenalulcer, oesophagitis/ulcer) in endoscopy and stool antigen positivity in patients with duodenal and gastric lesions(37% VS. 36.6%)were comparable.

Conclusion: H. pylori infection rate among patients with dyspepsia is in favour of declining prevalence of H.pylori infection in comparison to previous studies. Majority of patients with dyspepsia had upperGI lesion in endoscopy. No significant difference was noted in H. pylori prevalence rate among gastric or duodenal lesion or among PPI takers or non-takers.

Key words: Dyspepsia; H. pylori; Prevalence.

Introduction

The prevalence of H pylori is highly variable in Asian countries depending on regions and countries. Estimated prevalence of H pylori is around 54.7% in Asia.¹ There are declining prevalence of H pylori in some South-East Asian countries like Japan due to changes in cohort and increased number of eradication of H pylori in younger population and improved socio-economic condition.² In Bangladesh there are lacking in consistent data regarding the decreasing trend of H pylori prevalence. Studies conducted in 1995 reported a prevalence H pylori of 92% among Bangladeshi population by ELISA and 67% among children of a lower socioeconomic area by urea breath test.³⁻⁵ Culture of H. Pylori from gastric biopsies is time-consuming and often difficult with low sensitivity values (55%-73%) in comparison to serology, stool antigen test, urea breath test or rapid urease test.⁶⁻⁹ More recent studies conducted among community population of Bangladesh and hospital based dyspeptic subjects showed prevalences of 59.1% and 47% respectively by H pylori culture.^{10,11} Prevalence at the community level was 92.7% when stool antigen test was used alone and the result is not different from that of serology-based study conducted in 1995.^{3,10} A PCR-based study from Chattogram in 2015 reported a H. pylori prevalence rate of approximately 49% among patients with dyspepsia.¹² This variation in H. Pylori prevalences may be due to use of different H. pylori detecting tests, region and population involved and non-compliance of patients (i.e. not refraining from taking PPI, antibiotics and other antiulcerants).

We have limited data regarding the recent prevalence of Helicobacter pylori infection in different parts of our country in patients with dyspepsia. Therefore this observational study was designed to find out the prevalence of H. pylori among dyspeptic patient in a tertiary care hospital in the North-East part of our country. We also aimed to find out whether there is any observable decline in H. Pylori infection rate among dyspeptic patients.

1. Professor of Gastroenterology
Enam Medical College, Dhaka.

2. Professor of Gastroenterology
North East Medical College, Sylhet.

3. Associate Professor of Gastroenterology
Enam Medical College, Dhaka.

*Correspondence: Dr. Irin Perveen

Cell : 01552 36 51 00

E-mail: irinperveen@yahoo.com

Submitted on : 04.05.2022

Accepted on : 29.05.2022

Materials and methods

This observational study was carried out in the Department of Gastroenterology, North East Medical College Sylhet and Enam Medical College during the period of 2019 to 2020. Consecutive patients aged 16 and above with dyspeptic symptoms irrespective of Proton Pump Inhibitor (PPI) or anti ulcerant intake were included in the study. Patients with significant comorbidity, mentally handicapped, unwilling to participate and patients with Upper Gastrointestinal (UGI) cancers and patients who failed to undergo stool antigen test for *Helicobacter pylori* were excluded from the study. Written informed consent was taken from the participants. Institute review board and ethics committee approved the study. Dyspeptic symptoms included epigastric pain/burning/discomfort, bloating, early satiety, anorexia, nausea, vomiting, acid eructation, heart burn and regurgitation. All the participants offered stool antigen (Stool samples were analyzed using a new polyclonal EIA stool antigen test (EZ-STEP H. pylori) test for *Helicobacter pylori* and upper GI endoscopy. Socio-demographic data, clinical features and investigation reports were recorded in a semi-structured questionnaire.

Statistical analysis was done with SPSS programme 17.0. Qualitative data were expressed as frequency and percentages and quantitative data as mean and standard deviation. Categorical data were compared with Chi-square test and quantitative data with Student's T test. p-value was set at .05 or less.

Results

Among 1095 subjects with dyspepsia 790 patients (Male 549, female 241) were finally included in the study (Table I). Mean age of female patients were higher (41.46 VS. 39.19, p .008) than male patients. Three most common dyspeptic symptoms were abdominal pain (n=365, 46.2%), bloating (n=280, 35.4%) and vomiting (n=163, 20.6%) (Table II). Distribution of dyspeptic symptoms (table 2) were similar between sexes. No significant association was found between *Helicobacter pylori* infection and presence of individual dyspeptic symptom, number of dyspeptic symptoms (OR 1.385, p .103), age (OR .998, p .668), sex (OR 1.157, P .362), rural/urban

residence (OR 1.126, p .503), socio-economic condition (OR .965, p .09) or body mass index.

A total of 217(39.5%) male and 87(36.0%) female were positive for stool antigen (n=308, 38.5%) for *H. pylori* (p .383) (Table III). Stool antigen test was positive in 52.5% males (n=114) and 64.4% females (n=56) in whom endoscopy was not done (n= 430, 54.6%). Among the 360 subjects underwent endoscopy, 55.7% had gastric lesion, 22.9% had duodenal lesion and 3.9% had oesophageal lesion (table III). No significant difference was found in stool antigen positivity in patients with duodenal and gastric lesion (37% VS. 36.6%) (Table III). Around 39.8%(n=114) males having any form of GI lesion were positive for stool antigen test and in female the rate is 28.7% (n=25) (p .087).

Among 790 subjects, 768(97.2%) used to take PPI and among them 298(38.8%) was positive for stool antigen (Table I), whereas among PPI non-intakers 27.3% (n=6) were positive for stool antigen (p .375) and 70% of *H. pylori* negative patients had gastritis/duodentitis or PUD in endoscopy.

H. pylori detected in 39.5% (n=170) subjects not undergoing endoscopy, 35.1% (n=20) subjects with normal endoscopic findings, 36.9% (n=104) subjects with PUD, 47.6% (n=10) subjects with other lesions (p .676). Among 120 subjects with History of NSAID intake, 43 underwent endoscopy and 35 had at least one UGI lesion. The most common lesions were non-erosive (n=12) and erosive gastritis (n=9).

Table I Socio-demographic profile of study population and *H. Pylori* infection Rate

Parameters	Values	H. Pylori +ve	p
Mean Age±SD	39.88±14.230 years	39.63±13.665 (H.pylori +ve)	.698*
Sex (n & %)	Male: 549(69.5%) Female: 241(30.5%)	Male: 217(39.5%) Female: 87(36.0%)	.383
Residence (n & %)	Rural:623 Urban: 167	Rural: 236(37.9%) Urban: 68 (40.7%)	.531
Socio-economic class (n & %)	Poor: 46(5.8%) Lower Middle class: 413(52.7%) Middle Class: 304(38.5%) Rich: 27(3.4%)	Poor: 21(45.7%) LMC: 154(37.3%) Middle class:123(40.5%) Rich: 6(2.0%)	.193
Education (n & %)	Illiterate: 123(13.6%) Primary: 337(42.7%) SSC & HSC: 212(26.8%) Graduate & above: 118(14.9%)	Illiterate: 50(40.7%) Primary: 122(36.2%) SSC & HSC: 87(41.0%) Graduate & above: 48(38.1%)	.665

Parameters	Values	H. Pylori +ve	p
PPI intake	Yes: 768(97.2%)	Yes: 298(38.8%)	.375
	No: 22(2.8%)	No: 6(27.3%)	
NSAID Intake	Yes: 120(15.2%)	Yes: 51(42.5%)	.359
	No:670(84.8%)	No: 253(37.8%)	

*p-Value for mean age of H. pylori positive and -ve patients (40.04±14.584).

Table II Dyspeptic symptoms among study population

Symptoms	Male n (%)	Female n (%)	p value
Pain abdomen	241(43.9)	124(51.5)	.059
Burning pain	43(12.0%)	19(7.9%)	1.00
Bloating	214(38.6%)	66(27.0%)	.007
Abdominal discomfort	10(1.8%)	10(4.1%)	.085
Vomiting	113(20.6%)	50(20.7%)	1.00
Weight loss	1(.2%)	2(.8%)	0.53

Table III Endoscopic findings and H. Pylori infection rate among subjects with UGI lesion

Endoscopy findings	Total (360, 100%) (n, %)	H. pylori +ve	p value
Normal	57(15.9%)	Male: 35(6.4%) Female: 22(9.1%)	Male: 14(40.0%) Female: 6(27.3%) .448
Gastritis/gastric ulcer	200(55.7%)	Male: 136(24.8%) Female: 64(26.6%)	Male: 55(40.4%) Female: 19(29.7%)
DUD	82(22.9%)	Male: 66(12.0%) Female: 16(6.6%)	Male: 27(40.9%) Female: 3(18.8%)
Oesophagitis/ulcer	11(3.1%)	Male: 8(1.5%) Female: 3(1.2%)	Male: 3(37.5%) Female: 2(66.6%)
Others	10(28.0%)	Male: 6(1.1%) Female: 4(1.7%)	Male: 1(10%) Female: 5(50%)

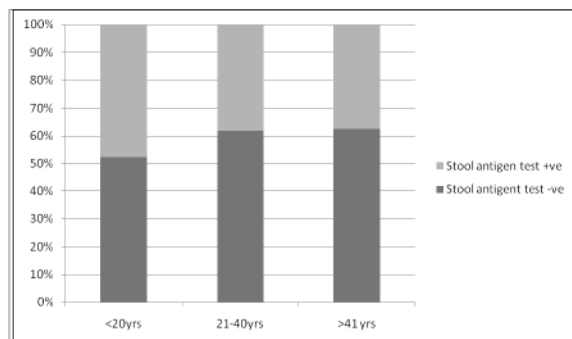


Figure 1 Stool antigen test according to age category

Discussion

A decreasing trend in prevalence of H. pylori is demonstrating in developed countries and some developing countries, though there is a wide variation in prevalence between regions and countries.¹ Communicable diseases are widely prevalent in Sout-East asian countries, and H. pylori infection is no exception. A Study from India reported lower prevalence (41.9%) of H.

pylori in patients with dyspepsia in 2010-2014, compared to study done in 1999 (70%) using same RUT test in dyspeptic patients.¹³ In 2013, Adlekha et al. from Kerela in southern India reported the prevalence of H. pylori to be 62% among 530 dyspeptic subjects.¹⁴

In Bangladesh we have limited data on prevalence of H. pylori infection among our population. Studies conducted in 1995, 2005-2007 , 2012-2013, 2015, 2015-2018 showed prevalences of 92%, 60.2%, 59.1-92.7%, 59.1%- 78% , 60.2% and 23% respectively using various diagnostic tools and population.^{3,4,14-18}

From 1995 to 2008 seroprevalence of H. pylori has decreased from 92% to 71.1%^{3,19}; in 2015 H. pylori prevalence was 30.1% (In dyspeptic patients) and in 2021 the reported rate was 38.9%.^{11,20} A study conducted in 2005-2007 reported stool antigen positivity around 93% in the community (both symptomatic and asymptomatic subjects).¹⁰ In 2012-2013, reported prevalence rate of H. pylori in the community level was 78% (by PCR, RUT and gastric biopsy) in patients with dyspepsia.¹⁶ In a hospital-based study stool antigen positivity rate was 51% in 2008-2009 among dyspeptic patients.²³ In our hospital- based study stool antigen positivity for H. pylori is 38.5% among dyspeptic patient. By RUT, H.pylori infection rates in dyspeptic patients were 78% in 2012-2013 and 43.6% in 2015.^{11,16} In a retrospective hospital-based study among dyspeptic patients H. pylori infection rate was 23% (By UBT) during the years of 2015-2018.¹⁸

Stool antigen specifically detects current ifection, whereas serological study detects both past and current infectin.^{21,22} Despite this, prevalence of H. pylori infection was similar in the study conducted in 1995 (Serology based) and 2005 (Stool antigen based) (92% vs. 92.7%).^{3,11}

Culture is the gold standard for detection of H. pylori though the sensitivity is low in comparison to serological tests, stool antigen test, UBT and RUT.⁶⁻⁹ In the culture-based studies in Bangladesh H. pylori detection rates were 53.3% in 2005-2007 and 42.1% in 2015.^{10,11} Despite adopting more sensitive test than H. pylori culture, a lower prevalence of H.pylori is found in the current study. From the above discussion it is apparent that despite variation in test methods and population involved, H. pylori prevalence rate is declining in our population.

Hafeza et al. in their hospital-based study meticulously sampled the study population and despite this, lower rate of *H. pylori* infection is consistent with our findings.¹¹ Authors suggested that non-compliance of patients (taking PPI within 14 days of test) may be responsible for this low rate of detection.¹¹ In our study *H. pylori* detection rate is similar between PPI intaker and PPI non-intaker ($p = .375$). This paradoxical data can not be explained properly. Low sample size of non PPI intakers and high resistant rate of *H. pylori* may be responsible. Further large scale study with meticulous detection of resistant pattern may help to resolve the unanswered question.

Age, gender, and socioeconomic conditions were found as important associated factor for *H. pylori* infection in the study of Malcolm et al.²² In the study of Nahar et al. no significant difference in prevalence of *H. pylori* was observed when compared to gender, income, and education in our population.¹⁰ However, in the culture-confirmed cases, a significant association of *H. pylori* infection with age and smoking habit was found.¹⁰ Mashud et al. also reported higher prevalence rate among 21 to 40 years age group.¹⁸ Hafeza found no relation between socio-economic condition and *H. pylori* infection.¹¹ On the other hand in the community-based study, study population was from lower socio-economic group.¹⁰ In our study no significant association was found between *H. pylori* infection and age, gender and socio-economic condition. This may be due to variation in region, study population (Community based Vs. hospital based, symptomatic Vs. asymptomatic, exclusion of subjects taking PPI) involved and diagnostic method involved. Studies from Thailand, Indonesia and Myanmar demonstrated that *H. pylori* prevalence varies in different geographical regions.²⁴⁻²⁷

Nahar reported 3.46 times higher probability of having dyspeptic symptoms (51.6% vs 23.6%) among *H. pylori* culture positive subjects (OR 3.46; 95% CI 1.99-5.99).¹⁰ We included only patients with dyspepsia and in our study no significant associations was found between the presence of individual dyspeptic symptom or number of dyspeptic symptoms with *H. pylori* infection.

Studies in dyspeptic patients in our population reported that 58 -77% of upper GI lesion were associated with *H. pylori* infection.^{10,12,26} Besides prevalence of *H. pylori* infection was more in patients with upper GI lesion than without lesion.^{10,11} Studies conducted in Asia among hospital or clinic-based dyspeptic patients reported a higher rate of organic lesions in endoscopy.²⁸⁻³⁰ In our study 81% of dyspeptic patients had UGI lesions and among these 45.5% esophageal lesions and equal percentage of gastric and duodenal lesions (37%) were associated with *Helicobacter* infection. Paradoxically around 70% of *H. pylori* negative patients had gastritis/duodenitis or PUD in endoscopy in the present study. As we did not include biopsy and other tests for detection of *H. pylori* we can not comment on the exact nature of these lesions or their type of association with *H. pylori* infection.

Limitation

Ours' is not a community-based survey, so our result is not representative of community prevalence of *H. pylori* infection. We did not exclude the subjects taking PPI within 14 days of stool antigen test, so prevalence may be lower than true prevalence of *H. pylori* infection. Other tests like *H. pylori* culture, serology and histopathology were not done due to lack of feasibility.

One strength of our study is that we included a good number of patients and this survey showed that most of our patients with dyspepsia are used to take PPI. Moreover this is the first report from North-Eastern part of Bangladesh regarding *H. pylori* infection. We included both PPI intakers and non-intakers and that helped us to observe the variation in prevalence of *H. pylori* among these two groups.

Conclusion

There is a decreasing trend in prevalence of *H. pylori* infection among patients with dyspepsia compared to studies conducted in 1995. Prevalence of *H. pylori* infection among patients with dyspepsia was approximately 39% and almost equal prevalence was found in gastric and duodenal lesion. Majority of dyspeptic patients had one or more upper GI lesion in endoscopy and takes PPI.

Recommendation

We recommend well designed multicentric or nationwide community –based studies in regular intervals to find out the true prevalence and antibiotic resistant pattern of *H. pylori* in our population to help or guide our future physicians for making uniform and proper decision in treating subjects with *H.pylori* infection.

Acknowledgement

We would like to thank all staffs of Endoscopy unit of North East Medical College, Sylhet, for their unconditional support and co-operation.

Contribution of authors

IP-Conception, data collection, data analysis, drafting & final approval.

MS-data collection, interpretation of data, critical revision & final approval.

MGH-Design, data collection, data analysis, critical revision & final approval.

Disclosure

All authors declared no competing interest.

References

- Hooi JKY, Lai WY, Ng WK, Suen MMY, Underwood FE, Tanyingoh D, et al. Global Prevalence of Helicobacter pylori Infection: Systematic Review and Meta-Analysis. *Gastroenterology*. 2017;153(2):420–429.
- Sugano K, Hiroi S, Yamaoka Y. Prevalence of Helicobacter pylori Infection in Asia: Remembrance of Things Past? *Gastroenterology*. 2018 ;154(1):257–258.
- Ahmad MM, Rahman M, Rumi AK, Islam S, Huq F, Chowdhury MF, et al. Prevalence of Helicobacter pylori in asymptomatic population--a pilot serological study in Bangladesh. *J Epidemiol*. 1997; 7(4): 251-254.
- Bardhan Pk. Epidemiological features of Helicobacter pylori infection in developing countries. *Clin Infect Dis*. 1997; 25(5): 973-978.
- Mahalanabis D, Rahman MM, Sarker SA, Bardhan PK, Hildebrand P, Beglinger C, Gyr K. Helicobacter pylori infection in the young in Bangladesh: Prevalence, socioeconomic and nutritional aspects. *International journal of epidemiology*. 1996; 25(4): 894-898.
- Savarino V, Zentilin P, Pivari M, Bisso G, Raffaella M M, Bilardi C, et al. The impact of antibiotic resistance on the efficacy of three 7-day regimens against Helicobacter pylori. *Aliment Pharmacol Ther*. 2000;14:893–900.
- Pilotto A, Rassa M, Leandro G, Franceschi M, Di Mario F. Prevalence of Helicobacter pylori resistance to antibiotics in Northeast Italy: A multicentre study. *GISU. Interdisciplinary Group for the Study of Ulcer. Dig Liver Dis*. 2000;32:763–768.
- Schwartz H, Krause R, Sahba B, Haber M, Weissfeld A, Rose P, et al. Triple versus dual therapy for eradicating Helicobacter pylori and preventing ulcer recurrence: A randomized, double-blind, multicenter study of lansoprazole, clarithromycin, and/or amoxicillin in different dosing regimens. *Am J Gastroenterol*. 1998;93:584–590.
- Chisholm SA, Owen RJ. Application of polymerase chain reaction-based assays for rapid identification and antibiotic resistance screening of Helicobacter pylori in gastric biopsies. *Diagn Microbiol Infect Dis*. 2008;61:67–71.
- Nahar S, Kibria KMK, Hossain ME, Sarker SA, Bardhan PK, Talukder KA, et al. Epidemiology of H. pylori and its relation with gastrointestinal disorders, a community-based study in Dhaka, Bangladesh. *J Gastroenterol Hepatol Res*. 2018 ;7(5):2709–2716.
- Aftab H, Yamaoka Y, Ahmed F, Khan AA, Subsomwong P, Miftahussurur M, et al. Validation of diagnostic tests and epidemiology of Helicobacter pylori infection in Bangladesh. *J Infect Dev Ctries*. 2018 ;12(05):305–312.
- Habib AM, Alam J, Rudra B, Quader A, Al-Forkan M. Analysis of Helicobacter pylori Prevalence in Chittagong, Bangladesh, Based on PCR and CLO Test. *Microbiol Insights*. 2016 ;9:MBI.S39858.
- Dutta AK, Reddy VD, Iyer VH, Unnikrishnan LS, Chacko A. Exploring current status of Helicobacter pylori infection in different age groups of patients with dyspepsia. *Indian J Gastroenterol*. 2017;36(6):509-513.
- Adlekha S, Chadha T, Krishnan P, Sumangala B. Prevalence of helicobacter pylori infection among patients undergoing upper gastrointestinal endoscopy in a medical college hospital in Kerala, India. *Ann Med Health Sci Res*. 2013;3:559–563.
- Matsuhisa T, Aftab H. Observation of gastric mucosa in Bangladesh, the country with the lowest incidence of gastric cancer, and Japan, the country with the highest incidence. *Helicobacter*. 2012;17: 396-401.
- Rahman MM, Ghoshal UC, Kibria MdG, Sultana N, Yusuf MA, Nahar S, et al. Functional Dyspepsia, Peptic Ulcer, and Helicobacter pylori Infection in a Rural Community of South Asia: An Endoscopy-Assisted Household Survey. *Clin Transl Gastroenterol*[Internet] 2021 Apr. 2021;12(4):e00334. Available from: <https://doi.org/10.14309/ctg.000000000000334> 17.
- Kibria KMK, Hossain ME, Sultana J, Sarker SA, Bardhan PK, Rahman M, et al. The Prevalence of Mixed Helicobacter pylori Infections in Symptomatic and Asymptomatic Subjects in Dhaka, Bangladesh. *Helicobacter*. 2015 ;20(5):397–404.
- Rahman A AM. Declining Prevalence of Helicobacter Pylori Infection- A 13C Urea Breath Test (UBT) Based Study in Symptomatic. *Anwer Khan Modern Medical College Journal* 2019;10(2):121-124.

19. Sumona AA, Hossain MA, Shamsuzzaman, AKM, Musa AKM, Mahmud MC, Ali MS, et al. Anti-Helicobacter pylori IgG in asymptomatic population. *Bangladesh J Med Microbiol.* 2008; 2(02): 31-34.
20. Rhaman MM, Rahman F, Mazumder S, Sayeed MA, Haq JA. Helicobacter pylori infection in asymptomatic rural Bangladeshi population. *IMC J Med Sci.* 2021;15(1):41–46.
21. Polk DB, Peek RM. Helicobacter pylori: Gastric cancer and beyond. *Nat Rev Cancer.* 2010 ;10(6):403–414.
22. Kusters JG, van Vliet AHM, Kuipers EJ. Pathogenesis of Helicobacter pylori Infection. *Clin Microbiol Rev.* 2006;19(3):449–490.
23. Islam MSU, Nahar S, Sarker MN, Salimullah ASM, Rahman MA, Ahmed DS, et al. Efficacy of Different Laboratory Tests to Diagnose Helicobacter pylori Infection. *Faridpur Med Coll. J* 2013;8(1):11-14.
24. Malcolm CA, MacKay WG, Shepherd A, Weaver LT. Helicobacter Pylori in Children is Strongly Associated with Poverty. *Scott Med J.* 2004 ;49(4):136–138.
25. Uchida T, Miftahussurur M, Pittayanon R, Vilaichone R, Wisedopas N, Ratanachu-ek T, et al. Helicobacter pylori Infection in Thailand: A Nationwide Study of the CagA Phenotype. *PLoS ONE* 2015. 2022;10(9):e0136775. Available from: <https://doi.org/10.1371/journal.pone.0136775>
26. Syam AF, Miftahussurur M, Makmun D, Nusi IA, Zain LH, Zulkhairi, et al. Risk Factors and Prevalence of Helicobacter pylori in Five Largest Islands of Indonesia: A Preliminary Study. *PLoS ONE* 2015. 2022;10(11):e0140186. Available from: <https://doi.org/10.1371/journal.pone.0140186>
27. Myint T, Shiota S, Vilaichone R, Ni N, Aye TT, Matsuda M, et al. Prevalence of Helicobacter pylori infection and atrophic gastritis in patients with dyspeptic symptoms in Myanmar. *World J Gastroenterol WJG.* 2015 ;21(2):629.
28. Siddique AR, Hossain L, Rana MA, Banerjee PK, Rahman A, Chowdhury MAU, et al. Prevalance and association of Helicobater Pylori with gastro-duodenal mucosal lesions in patients with dyspepsia. *J Dhaka Med Coll.* 2019;28(1):100–104.
29. Tack J, Talley NJ, Camilleri M, Holtmann G, Hu P, Malagelada Juan-R, et al. Functional gastroduodenal disorders. *Gastroenterology.* 2006;130(5):1466–1479.
30. Stanghellini V, Chan FKL, Hasler WL, Malagelada Juan-R, Suzuki H, Tack J, et al.. Gastroduodenal disorders. *Gastroenterology.* 2016;150(6):1380–1392.