Title

Comparison between vonoprazan-based triple therapy and esomeprazole-based triple therapy for eradication of *Helicobacter pylori* infection: An open-label randomized controlled trial

Document Date: 21.10.2026

Trial registration number: NCT07537634

Put tic (√) sign in the appropriate answer to each of the following

(If not Applicable write NA)

1	**Source of Population :**		
	a. Patients	√Yes	No
	b. Healthy Subjects	Yes	√No
	c. Minors or persons under guardianship	Yes	√No
2.	**Does the study involve:**		
	a. Physical risk to the subjects	√Yes	No
	b. Social Risks	Yes	√No
	c. Psychological risks to subjects	√Yes	No
	d. Discomfort to subjects	√Yes	No
	e. Invasion of the body	√Yes	No
	f. Invasion of Privacy	Yes	√No
	g.Disclosure of information damaging to object or others	Yes	√No
3.	**Does the study involve**		
	a. Use of records (Hospital, Medical, death, birth or other)	√Yes	No
	b. Use of fetal tissue or abortus	Yes	√No
	c. Use of organs or body fluids	Yes	√No
4.	**Are subjects clearly informed about**		
	a. Nature and purposes of study	√Yes	No
	b. Procedures to be followed including alternatives used	√Yes	No
	c. Physical risks	√Yes	No
	d. Private questions	√Yes	No
	e. Invasion of the Body	√Yes	No
	f. Benefits to be derived	√Yes	No
	g. Right to refuse to participate or to withdraw from study	√Yes	No
	h. Confidential handling of data	√Yes	No
	i. Compensation where there are risks or loss of working time or privacy is involved in any particular procedure	Yes	√No
5.	**Will signed consent form/verbal consent be required**		
	a. From Subjects	√Yes	No
	b. From parent or guardian (if subjects are minors)	Yes	√No
6.	**Will precautions be taken to protect the anonymity of subjects**	√Yes	No

Table of contents

Part-A	**Page no**
Title	1
Table of content	3
Abstract	4
Part-B	
Introduction	6
Rationale	9
Research question & hypothesis	10
Objective	11
Research Methodology	12
Sample Size	14
Operational definitions	15
List of variables	17
Study procedure	18
Data collection, processing and analysis	18
Utility of the study and ethical implications	19
Conflict of interest & quality assurance strategy	20
Confidentiality	21
References	22
Abbreviation	25
Appendix I: Study design by flow chart	26
Appendix II: Informed consent form	27
Appendix III: Data collection sheet	32

Abstract

Title: Comparison between vonoprazan-based triple therapy and esomeprazole-based triple therapy for eradication of *Helicobacter pylori* infection: An open-label randomized controlled trial

Background: *Helicobacter pylori* infection is one of the most common infections worldwide and is responsible for various upper gastrointestinal (GI) diseases. It is an important cause of dyspepsia. Eradication of *H. pylori* is a major challenge due to growing widespread anti-microbial resistance and a lack of effective anti-*H. pylori* eradication therapy. There are multiple regimens for *H. pylori* eradication, but the efficacy of these regimens depends on the local antibiotic resistance pattern. Among the different regimens studied in Bangladesh, levofloxacin-based triple therapy has shown the best efficacy. However, a recent study in Bangladesh showed clarithromycin, metronidazole, and levofloxacin resistance rates of 39.3%, 94.6%, and 66.1%, respectively. On the contrary, amoxicillin resistance is quite low, at 3.6%. In comparison to proton pump inhibitors (PPI), vonoprazan is superior in maintaining a neutral pH in the stomach over a 24-hour period and enhancing the bactericidal activity of amoxicillin on *H. pylori.* Among PPIs, esomeprazole has better potency in acid inhibition than other PPIs. So, a new treatment strategy to use vonoprazan in place of esomeprazole in levofloxacin- containing triple therapy may combat antimicrobial resistance.

Objective: To assess and compare the efficacy of vonoprazan-based triple therapy and esomeprazole -based levofloxacin-containing triple therapy for the eradication of *Helicobacter pylori*

Materials and methods: This open-label randomized controlled study will be carried out in the department of Gastroenterology, BSMMU. Patients with dyspepsia coming to the outpatient department fulfilling inclusion and exclusion criteria, being able to read and/or comprehend the questionnaire will be offered a stool antigen test for *H*. pylori detection. Stool antigen test-positive patients will be offered an upper GI endoscopy with a rapid urease test. Patients will be considered *H. pylori* positive if both tests are positive. Then these positive patients will be randomly assigned into two groups through computer software. One group will receive

vonoprazan-based levofloxacin containing triple therapy (VAL) containing amoxicillin 1 gm twice daily, levofloxacin 500 mg once daily, and vonoprazan 20 mg twice daily for 14 days. Another group will receive esomeprazole-based levofloxacin-containing triple (EAL) therapy (amoxicillin 1 gm twice daily, levofloxacin 500 mg once daily, and esomeprazole 20 mg twice daily) for 14 days. Patients will be declared infection-free if a repeat stool antigen test is negative one month after the completion of eradication therapy. Whoever had an endoscopic mucosal lesion at enrollment will be offered a follow-up endoscopy four weeks later for evaluation of the mucosal lesion. Drug compliance and side effects will be recorded. The dyspeptic symptoms score through a 5-point Likert scale will also be recorded at baseline and 1 month after completion of eradication therapy.

Duration of study: 15 April 2026- 14 September 2026

Data analysis: The data will be analyzed using SPSS version 27 software. Statistical analysis will be done by the student's t-test, Chi-square test, or Fisher's exact test, as appropriate. A P-value of < 0.05 will be considered statistically significant.

Ethical consideration: Every ethical issue will be discussed with the patient regarding the study, and informed written consent will be obtained. There will be no chance of disclosure of information that will have been harmful to the patients or others. Permission will be obtained from the concerned departmental ethical committee as well as the ethical review committee of BSMMU in order to carry out the study.

Introduction

Helicobacter pylori (*H. pylori*) is a slow-growing, microaerophilic, S-shaped, highly motile, gram-negative bacterium. It is located on the luminal surface of the gastric epithelium. It was first isolated by Warren and Marshall in 1982, and they were awarded the Nobel Prize in 2005 (Malfertheiner et al., 2023). *H. pylori* infection can cause gastritis, gastric and duodenal ulcers, and mucosa-associated lymphoid tissue lymphoma (McColl, 2010). Furthermore, *H. pylori* was classified as a group 1 carcinogen by the World Health Organization and the International Agency for Research on Cancer. Prompt removal of this primary risk factor for gastric carcinoma can reduce 75% of the risk (Savoldi et al., 2018; Kumar et al., 2020; and News release by Philadelphia, Pennsylvania, 2019).

According to Hooi et al. (2017), over 50% of people worldwide have *H. pylori* infection. The prevalence of the infection varies among populations and is more common in developing countries (Eusebi et al., 2014; Frenck and Clemens, 2003). Bangladesh has the highest frequency of *H. pylori* infection (86.3%) in South Asia (Kharel et al., 2020). A pilot study showed that 92% of participants had H. pylori infection (Ahmad et al., 1997). A semi-urban study close to Dhaka revealed that the prevalence of infection was 92.7% (Nahar et al., 2018).

H. pylori has been treated with various regimens, with varying results. Antibiotic resistance is the main concern for management and eradication of *H. pylori*. Suzuki et al. (2019) reported an increase in metronidazole and fluoroquinolone resistance globally, in addition to clarithromycin. A study conducted in Bangladesh found that 39.3% of people were resistant to clarithromycin, 94.6% to metronidazole, and 66.1% to levofloxacin. However, only 3.6% had amoxicillin resistance (Aftab et al., 2016).

According to Maastricht's VI recommendation, susceptibility testing should ideally be performed prior to giving first-line therapy. But it is not always practically, economically, or logistically feasible in Bangladesh. In areas of high (>15%) or unknown clarithromycin resistance, it is advised to treat *H. pylori* with bismuth quadruple or non-bismuth concomitant quadruple therapy. If it fails or is not available, levofloxacin triple or quadruple therapy is advised for 14 days (Malfertheiner et al., 2022).

Avoiding problems related to antibiotic resistance has become an important issue regarding the selection of a proper anti-H. pylori regimen. Bismuth salts decrease the bacterial load. Complex treatment regimens and adverse effects of bismuth-based or non-bismuth-based quadruple therapy lead to poor compliance and thus decrease the eradication rate (Kuo et al., 2009). Moreover, bismuth salts are not yet available in Bangladesh.

A double-blind randomized placebo-controlled clinical trial conducted in Bangladesh in 2016 in *H. pylori* eradication in functional dyspepsia showed that the efficacy of levofloxacin-based triple therapy was 56.5% (Arefin et al., 2023). The efficacy of levofloxacin-based triple therapy for *H. pylori* eradication in peptic ulcer disease was 78.6% in a study in Bangladesh (Ahmed et al., 2009). This rate was the highest eradication rate for *H. pylori* among previous studies conducted in Bangladesh using different regimens.

The efficacy rate of PPI-based regimens has progressively decreased in the past few years, and the inadequate acid suppression effect is deemed non-negligible (Yang et al., 2022). Antibiotic like amoxicillin can be more stable and concentrated when intra-gastric pH levels are raised; however, *H. pylori* can become drug-susceptible, replicative when acid suppression is prolonged and strong enough (Graham et al., 2008; Sugimoto et al., 2007). On the other hand, the prodrug PPI has a short half-life and a delayed commencement of action due to CYP2C19 polymorphisms and diet (Shin et al., 2011; Mori et al., 2019). So it is critically necessary to identify and employ excellent acid inhibitors in the *H. pylori* eradication technique. However, esomeprazole is reported to have higher potency in acid inhibition than other PPIs (Kalaitzakis & Bjornsson, 2007).

A potassium-competitive acid blocker, vonoprazan, reversibly inhibits H+/K+ ATPase without requiring acid activation, and its mechanism of action is similar to that of PPIs. Furthermore, compared to PPIs (eg. Esomeprazole), vonoprazan can reduce gastric acid output more quickly, strongly, and for a longer period of time due to several pharmacological properties (Shin et al., 2011; Mori et al., 2019). This prolonged action and effective acid suppression will allow the replication of *H. pylori* and thus result in more killing of bacteria and more effective eradication of H. pylori. Compared to esomeprazole, it is mainly metabolized by Cytochrome P450 (CYP) 3A4, and its efficacy is not hampered by CYP2C19 polymorphism (Abdelghani et al., 2023)

In a meta-analysis of Asian studies, PPI-based triple therapy achieved considerably lower eradication rates than the triple combination of vonoprazan, amoxicillin, and clarithromycin, even in patients with strains of antibiotic resistant to clarithromycin (Li et al., 2018). In Egypt, levofloxacin-based triple therapy involving either vonoprazan or esomeprazole showed that vonoprazan-based triple therapy had a better eradication rate than the esomeprazole-based one (97.7% vs. 68.5%, P = 0.031) (Abdelghani et al., 2023). So, the addition of vonoprazan to levofloxacin-based triple therapy in place of esomeprazole needs further research.

Rationale of the study

Due to the growing prevalence of anti-microbial resistance and the lack of an efficient anti- *H. pylori* regimen, eradicating *H. pylori* poses a significant challenge for health care professionals. High clarithromycin resistance precludes its use as a component of triple therapy. Bismuth component are not yet available in our country. Though levofloxacin resistance is also high in our country, levofloxacin-based triple therapy regimen has demonstrated satisfactory efficacy among different regimens of anti-*H. pylori* therapy in different clinical trials conducted in Bangladesh so far. Levofloxacin is well- tolerated and safe, with a mild to moderate side-effect profile. On the other hand, since its discovery, vonoprazan has been used in reflux esophagitis, peptic ulcer disease, and for *H. pylori* eradication. Like PPI, vonoprazan also suppresses gastric acid secretion. As vonoprazan is an active drug, vonoprazan is more rapid-acting than PPI. Vonoprazan is more potent and long-acting than PPI in suppressing gastric acid and so it enhances more time-dependent bactericidal action of antibiotic. Moreover, its efficacy is not hampered by diet and gene polymorphisms. Vonoprazan-based anti- *H. pylori* therapy has shown better efficacy than the PPI-based one. Eradication rate is also higher with vonoprazan in comparison to PPI even in clarithromycin-resistant *H. pylori* infection. So, replacing PPI with vonoprazan may improve the eradication rate of levofloxacin-based triple therapy. As esomeprazole has higher potency in acid inhibition, esomeprazole will be used among the PPIs. There was no study conducted in our country comparing the efficacy of vonoprazan-based triple therapy with esomeprazole-based triple therapy for the eradication of *H. pylori* infection. Therefore, this study will be conducted to compare the efficacy of vonoprazan-based versus esomeprazole-based levofloxacin-containing triple therapy for the eradication of *H. pylori* infection.

Research question

Is there any difference in the efficacy between vonoprazan-based triple therapy and esomeprazole-based triple therapy in the eradication of *Helicobacter pylori* infection?

Research hypothesis

Null hypothesis

There is no difference in the efficacy between vonoprazan-based triple therapy and esomeprazole-based triple therapy in the eradication of *Helicobacter pylori* infection.

Alternate hypothesis

There is difference in the efficacy between vonoprazan-based triple therapy and esomeprazole-based triple therapy in the eradication of *Helicobacter pylori* infection.

Objectives of the Study

General objective:

To compare the efficacy of vonoprazan-based levofloxacin-containing triple therapy with esomeprazole-based levofloxacin-containing triple therapy for the eradication of *Helicobacter pylori* infection

Specific objectives:

1. To identify *H. pylori* infection on the basis of both stool antigen test and rapid urease test among dyspeptic patients

2. To determine *H. pylori* status on the basis of stool antigen test 4 weeks after vonoprazan-based triple therapy

3. To determine *H. pylori* status on the basis of stool antigen test 4 weeks after esomeprazole-based triple therapy

4. To assess the efficacy of vonoprazan-based triple therapy for *H. pylori* eradication

5. To assess the efficacy of esomeprazole-based triple therapy for *H. pylori* eradication

6. To compare the efficacy between two groups for *H. pylori* eradication

7. To compare percentage of patients with healed endoscopic mucosal lesion between two groups 4 weeks after completion of treatment

8. To compare the improvement of dyspepsia symptoms score within and between the groups after 4 weeks of completion of treatment

9. To see the adverse effects between the groups

Research Methodology

Study design: Open-label randomized controlled trial

Place of study: Department of Gastroenterology, BSMMU, Dhaka.

Study period: 15 April 2026- 14 September 2026

Study population: Patients with dyspeptic symptoms attending the outpatient department of Gastroenterology, BSMMU, Dhaka

Sampling technique: Purposive sampling

Randomization method: Block randomization

Selection criteria for the patients

Inclusion criteria:

1. Age ≥ 18 years
2. Dyspeptic patients with positive for both rapid urease test and stool antigen test
3. Patients giving written informed consent

Exclusion criteria:

1. Treatment with a proton pump inhibitor, H_2-receptor antagonist within the last 2 weeks, prior to the study
2. Treatment with antibiotics or bismuth preparation within 4 weeks prior to the study
3. Previous *H. pylori* eradication therapy
4. Gastric or duodenal ulcer with current or recent bleeding on endoscopy
5. Significant upper or lower gastrointestinal bleeding within 4 weeks
6. Patients with regular intake of NSAIDs or steroids
7. Surgery that might affect gastric acid secretion e.g., upper GI resection or vagotomy
8. Known case of malignancy, including MALToma
9. Advanced co-morbidities (e.g., CLD, CKD, cardio-respiratory failure, known thyroid disease)
10. Chronic alcohol abuse, chronic illegal drug use, or drug addiction within the past 12 months
11. Pregnant, lactating woman or intend to become pregnant within the study period
12. History of hypersensitivity to vonoprazan, PPIs, amoxicillin, and/or levofloxacin
13. On colchicine
14. Subjects with abnormal laboratory test at the start of the screening period:

    S. creatinine > 2 mg/dl

    SGPT > 2 x Upper limit of normal
15. History of interstitial nephritis, prolonged QT interval on ECG

Sample size calculation

Formula:

$$\mathbf{n} = \left[\frac{P_1(1-P_1)+P_2(1-P_2)}{(P_1-P_2)^2}\right] x (Z_\alpha + Z_\beta)^2$$

n = sample size for each group

P_1= Outcome of intervention group (vonoprazan-based triple therapy) = 0.977 (Abdelghani et al., 2023).

P_2= Outcome of control group (esomeprazole-based levofloxacin-containing triple therapy) = 0.685 (Abdelghani et al., 2023).

Z_α=Z-value at 5% level of significance = 1.96

Z_β= Z-value at 95% power = 1.645

n= 36.3≈36

Calculated sample size in each group= 36

Assuming 10% drop out,

$\mathbf{N} = \left[\frac{36}{0.9}\right]$

= 40

n = 40 in each group

Total number of patients in the study =40+40 = 80

Operational definitions

Dyspepsia: Dyspepsia is derived from dys and pepse and literally means “difficult digestion.” In this study, dyspepsia will be defined as the presence of one or more of the following symptoms: epigastric pain, postprandial fullness, early satiation, anorexia, belching, nausea and vomiting, upper abdominal bloating, and even heartburn and regurgitation. (Tack et al., 2004).

***H. pylori* infection:** Patients will be considered *H. pylori* infection positive if both the rapid urease test and stool antigen test are positive at enrollment

H. pylori eradication: If the stool antigen test is negative 1 month after the completion of eradication therapy, patients will be considered cured of H. *pylori* infection (Malfertheiner et al. 2022).

Vonoprazan-based (levofloxacin-containing) triple therapy: Amoxicillin 1 gm twice daily, levofloxacin 500mg once daily & vonoprazan 20 mg twice daily for 14 days (Abdelghani et al., 2023)

Esomeprazole-based (levofloxacin-containing) triple therapy: Amoxicillin 1 gm twice daily, levofloxacin 500mg once daily & esomeprazole 20 mg twice daily for 14 days (Chey et al., 2017)

Rapid urease test (RUT): RUT will detect the urease enzyme of *Helicobacter pylori* in gastric mucosal biopsies. H-P TEST (Lenus Medicare & Research (OPC) Private Limited®) slide will be used for the study. After introduction of biopsy specimen to yellow media of H-P test slide and addition of one drop of sterile water, if color changes from yellow to pink or red at 2 minutes to 10 minutes, test will be considered *H. pylori* positive.

Stool antigen test: It is a rapid, immunochromatographic assay for the detection of *Helicobacter pylori* antigen in human feces sample. It is an appropriate test before and after anti-*H. pylori* therapy. ONE STEP H. pylori Ag Test (InTec PRODUCTS, INC®) kit will be used. After addition of feces sample in the sample pad, if formation of colored band occurs in the test region at 15-20 minutes, it will be considered as *H. pylori* positive.

Patient's dyspepsia symptom score: This is a patient-completed measure of disease. In this scoring system, impact of eight symptoms related to dyspepsia on quality of life is graded on 5-point Likert scale over the last two weeks. Score is graded from no problem (1 point) to very severe problem (5 point)

	No problem	Mild problem	Moderate problem	Severe problem	Very severe problem
Post prandial fullness					
Early satiety					
Epigastric pain (a sharp, easy to pinpoint pain after eating)					
Epigastric discomfort (an ache or discomfort after eating, poorly localized)					
Upper abdominal bloating					
Belching after meals					
Postprandial nausea					
Vomiting					

Talley et al., 2000

List of Variables:

Demographic variables

1. Age
2. Gender

Independent variables

1. Vonoprazan-based levofloxacin-containing triple therapy
2. Esomeprazole-based levofloxacin-containing triple therapy
3. Stool antigen test

Outcome variable

1. Percentage of negative stool antigen test for *H. pylori* 4 weeks after treatment completion
2. Percentage of patients with healed endoscopic mucosal lesion
3. Mean change of dyspepsia symptom score on 5-point Likert scale
4. Adverse drug reaction rates

Study procedure

Data collection:

Consecutive patients of both dyspepsia and symptoms of peptic ulcer disease will initially be evaluated from the patients who will attend the outpatient department of gastroenterology of BSMMU. Patients, with past history of PPI, H2-receptor blocker intake within last 2 weeks, or antibiotic or bismuth preparation intake within 4 weeks prior to study, or previous history of intake of anti- *H. pylori* therapy, will be excluded from the study. Who had history of gastric ulcer with significant bleeding, will be also excluded. Fresh stool sample will be sent for stool antigen test. A one-step chromatographic immunoassay (ONE STEP H. pylori Ag Test - InTec PRODUCTS, INC® kit) will be used to perform the stool antigen test. After proper evaluation and ensuring that the patient is fit for endoscopy, patients who test positive for stool antigen will proceed to have an upper GIT endoscopy. Informed written consent will be taken for upper GIT endoscopy. Endoscopy will be done by expert endoscopist of the department, and Olympus GIF-H190 endoscopy machine will be used. Patients with endoscopic finding of peptic ulcer with current bleeding, and history of upper or lower GIT bleeding within previous 4 weeks, will be excluded, and will be dealt according to guideline. Any mucosal lesion (such as erosion, gastritis, duodenal, or gastric ulcer) will be recorded in the data sheet, and biopsy (one from the antrum and one from the corpus) will be taken for a rapid urease test (H-P TEST- Lenus Medicare & Research® (OPC) Private Limited). If a lesion looks suspicious, an additional biopsy will also be taken. The study will eventually include patients who test positive for both the stool antigen test and rapid urease test. A 5-point Likert scale will be used to record dyspeptic symptoms at the time of enrollment.

Selected 80 patients will then be randomly assigned into two groups: Group A and Group B, with 40 patients in each group. Groups A and B will receive vonoprazan-based (VAL) and esomeprazole-based (EAL) levofloxacin-containing triple therapy for 14 days, respectively. In both groups, amoxicillin 1 gm twice daily and levofloxacin 500 mg once daily will be taken after meal. Vonoprazan or esomeprazole 20 mg twice daily will be taken 30 minutes before meal in groups A & B respectively for 14 days. Even in patients with uncomplicated ulcers, 14-day anti-secretory regimen will be given (Gisbert et al., 2005; Kamada et al., 2021). All the drugs will be supplied from same pharmaceutical. All the medicines will be stored at room temperature between 15 to 25 degree Celsius in a cool, dry place away direct sunlight. Patient will be asked for follow-up at the end of the therapy. Drug compliance and adverse effects will be noted at that

time. Patients will be asked for 2nd follow-up 4 weeks later. Then, all the patients will have a repeat stool antigen test to confirm eradication. Each group's *H. pylori* eradication will be documented. Repeat upper GIT endoscopy will be performed on patients who had mucosal lesions at enrollment in order to re-evaluate the lesions. One month following the end of therapy, each group's dyspeptic symptoms will also be recorded using a 5-point Likert scale to see if there has been any improvement.

Data collection tools:

1. Data collection form
2. 5 point Likert scale score for assessment of dyspepsia

Statistical analysis:

The following steps will be used to analyze the collected data:

- The entered data will be checked, verified and analyzed by IBM® SPSS® Statistics version 27 (Statistical Program for Social Science) software.
- The data will be presented in tables, figures and diagrammatical form.
- Appropriate statistical test will be applied for data analysis. Numeric data (e.g. age, Likert scale score for dyspepsia) will be expressed as mean ± standard deviation and median (range), qualitative data (e.g. sex, stool antigen test, endoscopy of upper GIT) will be expressed as frequency and percentage.
- Baseline characteristics of the study patients and outcomes will be evaluated using student's t-test, Chi-square test or Fisher's exact test, as appropriate.
- Factors influencing the efficacy of the eradication therapy were assessed by univariate & multivariate analysis
- A P-value less than 0.05 will be considered as significant at a 95% confidence interval (95% CI).

Utilization of the study results

The study will be able to assess the efficacy and adverse effects of vonoprazan-based and esomeprazole-based levofloxacin-containing triple therapy for the eradication of *H. pylori* Infection. So, this study enables clinicians to find a new alternative to existing eradication regime to improve individual patient care.

Ethical issue

Throughout the study, following factors will be taken into account:

- The patients and important family memberts will be fully aware of the objectives and limitations of the study.
- They will be informed that there is no risk to participatants' safety, either socially or physically.
- They will also be informed about the freedom to participate or not to participate at any time.
- Written consent will be obtained from the participants.
- No information about the patient would be shared with outside parties.
- The participants in the study will not receive any compensation for their participation.
- The Institutional Review Board (IRB) will be consulted for ethical clearance.

Conflict of interest

None declared

Quality assurance strategy

This will be an open-label randomized controlled trial. Extensive literature review will be done and investigator will be sufficiently trained. Inclusion and exclusion criteria will be strictly maintained. Every step of the study will be carried out under direct supervision of the guide. The completeness and quality of the collected data will be ensured by regular and routine supervision, checking and monitoring. Guide will randomly scrutinize the data collection procedure. Gathered information from patient will be checked and rechecked with medical record. Schedule meeting will be arranged with the guide regularly to discuss the progress of data collection. Data cleaning will be done before editing in the computer for analysis. After obtaining results of one quarter of the study subjects, review meeting will be arranged with the guide and emerged issue will be addressed properly. Before entering data in computer for analysis random checking of 10% of data will be done by the guide. Irrelevant and inconsistent data will be discarded. After collection of data, meeting will be arranged with guide at weekly interval to discuss about the progress of thesis writing and submission.

Confidentiality

All the information collected from the patients including the results of the laboratory tests will be kept as confidential under the responsibility of principal investigator. No one other than the investigators, regulatory authorities and institutional review board committee will have access to such information. Patient's identity will not be disclosed while analyzing or publishing the results of the study

References

Abdelghani, Y. A., Moussa, M. M. (2023) 'Vonoprazan-Based Versus Esomeprazole-Based Triple Therapy for Helicobacter pylori: A Randomized Trial', *Appli Microbiol Open Access,* 9, pp. 258.

Aftab, H., Miftahussurur, M., Subsomwong, P., Ahmed F., Azad Khan A. K. and Yamaoka Y. (2016) 'Helicobacter Pylori Antibiotic Susceptibility Patterns in Bangladesh: Emerging Levofloxacin Resistance', *Journal of Infection in Developing Countries,* 10 (3), pp. 245–53.

Ahmad, M. M., Rahman, M., Rumi, A. K., Islam, S., Hug, F., Chowdhury, M. F., Jinnah, F., Morshed, G., Hassan, S., Azad Khan, A. K. and Mahmud Hasan, M. (1997) 'Prevalence of Helicobacter Pylori in Asymptomatic Population- a Pilot Serological Study in Bangladesh', *Journal of Epidemiology*, 7, pp. 251-254.

Ahmed, E. U., Alam, R., Alam, F., Ghosh, C. K., Dey, S. K., Masud, H., Ahmed, D. S., Bhuiyan, M. M. R., Mia, Roy, P. K., and Raihan, A. S. M. A. (2009) 'Comparative study between Metronidazole, Amoxycilin, Omeprazole based therapy and Levofloxacin, Amoxycilin, Omeprazole based therapy for helicobacter pylori eradication in peptic ulcer disease', *Journal of Chittagong Medical College Teachers Association,* 20, pp. 29-32.

Arefin, M. S., Basak, S., Sarkar, M. A. M., Habib, M. R., Ahmed, F., Kanta, S. S., Alam, M. R. (2023) 'Efficacy of Helicobacter pylori Eradication in Helicobacter pylori positive Functional Dyspepsia Patients- A Double-Blind, Randomized, Placebo-Controlled Trial', *Med. Res. Chronicles*, 10(1), pp. 37-45

Chey, W. D., Leontiadis, G. I., Howden, C. W., Moss, S. F. (2017) 'ACG Clinical Guideline: Treatment of Helicobacter pylori Infection', *American Journal of Gastroenterology*, 112(2), pp. 212-239

Eusebi, L. H., Zagari, R. M., Bazzoli, F. (2014) 'Epidemiology of Helicobacter pylori infection', *Helicobacter*, 19(1), pp. 1-5

Frenck, R.W. Jr., Clemens, J. (2003) 'Helicobacter in the developing world', *Microbes Infect*, 5(8), pp. 705-13

Gisbert, J. P., & Pajares, J. M. (2005) 'Systematic review and meta-analysis: is 1-week proton pump inhibitor-based triple therapy sufficient to heal peptic ulcer?', *Alimentary pharmacology & therapeutics*, *21*(7), pp. 795–804.

Graham, D. Y., Shiotani, A. (2008) 'New concepts of resistance in the treatment of Helicobacter pylori infections', *Nat Clin Pract Gastroenterol Hepatol,* 5(6), pp. 321--331.

Hooi, J. K.Y., Lai, W. Y., Ng, W. K., Michael, M.Y., Suen, F. E., Underwood, T. D., Malfertheiner, P. et al. (2017) 'Global Prevalence of Helicobacter Pylori Infection: Systematic Review and Meta-Analysis', *Gastroenterology,* 153 (2), pp. 420–29.

Kalaitzakis, E., & Bjornsson, E. (2007) 'A review of esomeprazole in the treatment of gastroesophageal reflux disease (GERD)', *Therapeutics and Clinical Risk Management,* 3(4), pp. 653-663.

Kamada, T., Satoh, K., Itoh, T., Ito, M., Iwamoto, J., Okimoto, T., Kanno, T., Sugimoto, M., Chiba, T., Nomura, S., Mieda, M., Hiraishi, H., Yoshino, J., Takagi, A., Watanabe, S., & Koike, K. (2021) 'Evidence-based clinical practice guidelines for peptic ulcer disease 2020', *Journal of gastroenterology*, *56*(4), pp. 303–322.

Kharel, S., Anil, Shrestha, Suraj & Sushan, H. (2020) 'Helicobacter pylori healthy South Asians', *JGH Open*, 4, pp. 1037-46

Kumar, Shria, Metz, D. C., Ellenberg, S., David, E., Kaplan and Goldberg, D. S. (2020) 'Risk Factors and Incidence of Gastric Cancer after Detection of Helicobacter Pylori Infection: A Large Cohort Study', *Gastroenterology*, 158 (3), pp. 527-536.e7

Kuo C. H., Hu H. M., Kuo F. C., Hsu P. I., et al., (2009) 'Efficacy of levofloxacin-based rescue therapy for Helicobacter pylori infection after standard triple therapy: a randomized controlled trial', *The Journal of antimicrobial chemotherapy*, 63(5), pp. 1017-1024

Li, M., Oshima, T., Horikawa, T., Tozawa, K., Tomita, T., Fukui, H., Wtari, J., & Miwa, H. (2018) 'Systemic review with meta-analysis: Vonoprazan, a potent acid blocker, is superior to proton-pump inhibitors for eradication of chlarithromycin-resistant strains of Helicobacter pylori', *Helicobacter*, 23(4), pp. e12495

Malfertheiner, P., Megraud, F., Rokkas, T., Gisbert, J. P., Liou, J. M., Schulz, C., Gasbarrini, A. (2022) 'Management of *Helicobacter Pylori* Infection: The Maastricht VI/Florence Consensus Report', *Gut,* 71(9), pp. 1724–62.

Malfertheiner, P., Camargo, M. C., El-Omar, E., Liou, J. M., et al., (2023) 'Helicobacter pylori infection', *Nature Reviews. Disease primers*, 9(1), pp. 19

McColl, Kenneth, E. L. (2010) 'Clinical Practice. Helicobacter Pylori Infection', *The New England Journal of Medicine,* 362 (17), pp. 1597–1604.

Mori, H., Suzuki, H. (2019) 'Role of acid suppression in acid-related diseases: Proton pump inhibitor and potassium-competitive acid blocker', *J Neurogastroenterol Motil.* 25, pp. 6–14.

Nahar, s., Kibria, M. K., Hossain, M. E., Sarker, S. A., Bardhan, P. K., Talukder, K. A. and Rahman, M. (2018) 'Epidemiology of H. Pylori and Its Relation with Gastrointestinal Disorders, A Community-Based Study in Dhaka, Bangladesh', *Journal of Gastroenterology and Hepatology Research*, 7(5), pp. 2709–16.

News release by Philadephia, Pennsylvania, (2019). [online] Available at: http://pennmedicine.org/news/news-releases/2019/november/eliminating-common-bacterial-infection-significantly-decreases-gastric-cancer-risk [Accessed 17 Feb. 2024]

Savoldi, Alessia, Carrara, E., Graham, D. Y., Conti, M. and Tacconelli, E. (2018) 'Prevalence of Antibiotic Resistance in Helicobacter Pylori: A Systematic Review and Meta-Analysis in World Health Organization Regions', *Gastroenterology,* 155 (5), pp. 1372-1382.e17

Shin, J. M., Inatomi, N., Munson, K., Strugatsky, D., Tokhtaeva, E., Vagin, O., et al. (2011) 'Characterization of a novel potassium-competitive acid blocker of the gastric H,K-ATPase, 1-[5-(2-uorophenyl)-1-(pyridin-3-ylsulfonyl)-1H-pyrrol-3-yl]-N-methylmethanamine monofumarate (TAK-438)', *J Pharmacol Exp Ther,* 339, pp. 412–20.

Sugimoto, M., Furuta, T., Shirai, N., et al. (2007) 'Evidence that the degree and duration of acid suppression are related to Helicobacter pylori eradication by triple therapy', *Helicobacter*, 12(4), pp. 317--323.

Suzuki, S., Esaki, M., Kusano, C., Ikehara, H. and Gotoda, T. (2019) 'Development of Helicobacter Pylori Treatment: How Do We Manage Antimicrobial Resistance?', *World Journal of Gastroenterology*, 25 (16), pp. 1907–12.

Tack, J. 'Dyspepsia'. In: Feldman M., Friedman, L. S., Brandt, L. S. eds. (2021) 'Sleisenger And Fordtran's Gastrointestinal and Liver disease: Pathophysiology,diagnosis, management', 11th edition, Philadelphia, Elsevier Saunders; pp. 177-189.

Talley, N. J., Verlinden, M., Snape, W., et al. (2000) 'Failure of a motilin receptor agonist (ABT-229) to relieve the symptoms of functional dyspepsia in patients with and without delayed gastric emptying: a randomized double-blind placebo-controlled trial', *Aliment Pharmacol Ther,* 14, pp. 1653-1661.

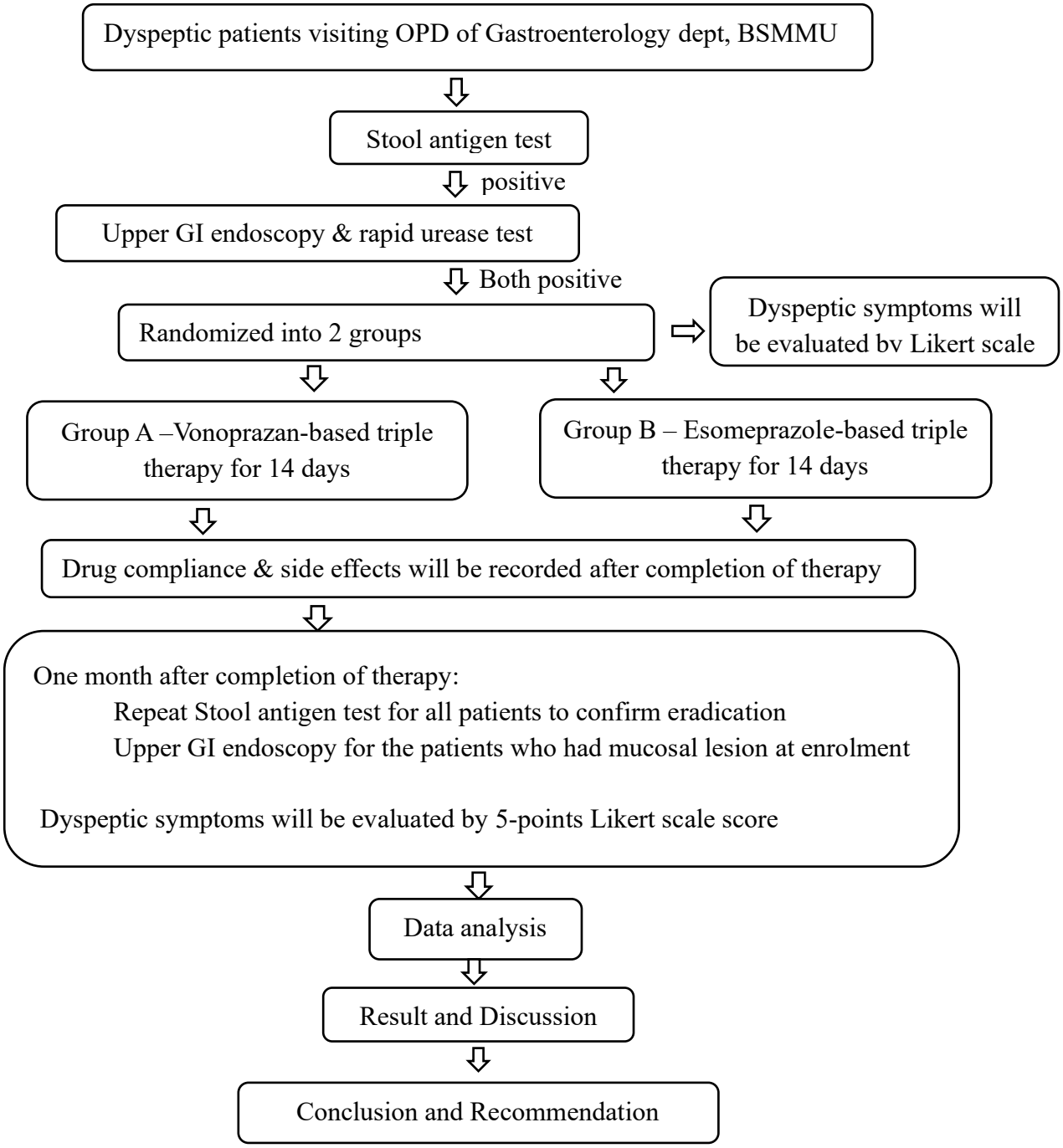
Yang, C., Li, S., Huang, T., et al. (2022) 'Effectiveness and safety of vonoprazan-based regimen for *Helicobacter pylori* eradication: A meta-analysis of randomized clinical trials', *J Clin Pharm Ther.,* 47, pp. 891-904

Abbreviations

Anti-HCV	Anti- Hepatitis C Virus
BP	Blood pressure
BSMMU	Bangabandhu Sheikh Mujib Medical University
CI	Confidence Interval
CKD	Chronic Kidney Disease
CLD	Chronic Liver Disease
CYP	Cytochrome P450
EAL	Esomeprazole-Amoxicillin-Levofloxacin
GIT	Gastrointestinal tract
HBsAg	Hepatitis B virus surface Antigen
IRB	Institutional Review Board
ITT	Intention-to-treat analysis
MALT	Mucosa Associated Lymphoid Tissue
NSAID	Non-steroidal Anti-inflammatory Drug
OPD	Outdoor Patient Department
PP	Per protocol analysis
PPI	Proton Pump Inhibitor
RUT	Rapid Urease Test
SAT	Stool Antigen Test
SGPT	Serum Glutamate Pyruvate Transaminase
SPSS	Statistical Package for Social Science
VAL	Vonoprazon-Amoxicillin-Levofloxacin
WHO	World Health Organization

Appendix I

Study flow chart



Appendix-II

Consent form –English

INFORMED CONSENT FORM FOR PARTICIPANTS

Title of research study: Comparison between vonoprazan-based triple therapy and esomeprazole-based triple therapy for eradication of *Helicobacter pylori* infection: An open-label randomized controlled trial

Principal investigator: [redacted]

Name of participant:_____

Place of study: Department of Gastroenterology, Bangabandhu Sheikh Mujib Medical University, Dhaka

Part 1: Information Sheet

Introduction: I am [redacted], working for the Department of Gastroenterology, BSMMU, Bangladesh. We are doing research on efficacy of 2 different drug regimens for *Helicobacter pylori* eradication. I am going to give you information and invite you to be part of this research. You do not have to decide today whether or not you will participate in the research. Before you decide, you can talk to anyone you feel comfortable with about the research.

There may be some words that you do not understand. Please ask me to stop as we go through the information and I will take time to explain. If you have questions later, you can ask them of me or the staff.

Objective of this consent form: The objective of this informed consent form is to give you necessary information that would help you to take decision on whether you will participate or not in this study.

Objective and procedure of this research: Lots of patients suffer from dyspepsia & *Helicobacter pylori* infection is an important cause of dyspepsia. There are multiple eradication regimens for *H. pylori* infection but the efficacy of these regimens is not satisfactory, moreover needs multiple antibiotics for prolonged period. Our plan is to give 2 different therapeutic regimens to 2 groups of patients & compare the efficacy between the 2 groups.

Type of Research Intervention: This research will involve stool antigen test & endoscopy with rapid urease test at baseline followed by *H. pylori* eradication regimen for 14 days. Repeat stool antigen test & endoscopy will be carried out one month after completion of eradication therapy to check success of therapy & for the evalution of mucosal lesion.

Participant selection: Patients with dyspepsia visiting the outpatient department of Gastroenterology, BSMMU.

Information on stool antigen test: This test will need fresh stool sample for detection of *H. pylori* infection & will be done in the microbiology department, BSMMU**.**

Information on upper GI endoscopy & rapid urease test: Upper GI Endoscopy involves passing a tube with camera into your stomach to see any abnormality. Anesthetic jelly & spray will be used to make the procedure comfortable. Endoscopy will be carried out by an experienced interventionist. Two biopsy will be taken for rapid urease test which can detect *H. pylori* infection. This procedure will be done in the department of Gastroenterology, BSMMU.

Information on drugs: Levofloxacin, amoxicillin and esomeprazole or vonoprazan will be used in this study in two different regimens with different doses & frequencies. All these medications are commonly used for various reasons for long time & well tolerated. Side effects like headache, nausea, vomiting, abdominal pain, and rash can occur but are usually not serious and will be managed accordingly.

Duration: The research will take place over 6 weeks in total.

Risk of the study: You may face some risk, but the chance is low. There is some risk of headache, nausea, vomiting, abdominal pain, diarhoea, rash after taking these medications. You may also face endoscopy related hazards like bleeding & perforation but chance of these complications are extremely low. We will take necessary precaution and other support to overcome the risk.

Benefits: If you participate in this study, you will get free investigation facility, free treatment, free follow-up during study period.

Alternatives: You have the right to participate in this study or not, or to withdraw from the study at any stage of this research.

Cost: You will not have to bear any extra cost or not be getting any financial benefit for participating in this study.

Confidentiality: Strict confidentiality will be maintained regarding the information of the patients during and after the study. Your identity will not be used in data analysis, reporting and publication. It will not be disclosed to anybody except the researcher. So, nobody will be able to know your personal information.

Voluntary participation: It is fully a voluntary activity to participate in this research. You may not admit participating in this study or you may withdraw yourself at any time of the study which will not hamper your treatment in the hospital at all. You will not lose any legal right if you put your signature in this form.

Questions: You can ask any question if you have. I shall try my best to answer your question (Mobile no: 01973-395139).

Declaration: I am informing you that this collected data sample will only be used for this study and no other study.

Part II: Certificate of Consent:

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this research.

Name of Participant_____

Signature of Participant _____

Date _____

Day/month/year

If illiterate

I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

Name of witness_____ AND Thumb print of participant

Signature of witness _____

Date _____

Day/month/year

Statement by the researcher/person taking consent

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that.

I confirm that the participant was given an opportunity to ask questions about the study, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this ICF has been provided to the participant.

Name of Researcher/person taking the consent

_____

[redacted]

Signature of Researcher /person taking the consent

_____

Date _____

Day/month/year

Appendix- III

DATA COLLECTION SHEET

Title: Comparison between vonoprazan-based triple therapy and esomeprazole-based triple therapy for eradication of *Helicobacter pylori* infection: An open-label randomized controlled trial

Principle Investigator: [redacted]

Place of study: Department of Gastroenterology, BSMMU

Section A: Particulars of the patient

GROUP:

• ID No: …… Date: …….

• Name:……

• Father's Name :

• Mother's Name:

• Address :

• Contact no:

• Hospital Reg. no : ……..

Section B: Socio-demographic profile

SL	Question	Answer	Code
1	Age	Full years	
2	Sex	1. Male 2. Female	
3	Residence	1. Urban 2. Rural	
3	Religion	3. Islam 4. Hinduism 5. Buddhism 6. Christian	
4	Educational qualification	1. No formal education 2. Primary [Class 1-5] 3. Secondary [Class 6-10] 4. HSC/Equivalent or above 5. Honours or above	
5	Marital status	1. Married 2. Unmarried 3. Other	
6	Occupation	1. Housewife 2. Cultivator 3. Businessman 4. Garment worker 5. Student 6. Day labourer 7. Teacher 8. Unemployed 9. Other	
7	Monthly income	Approximately (In taka)	
8	Smoking history	1. Current smoker 2. Former smoker 3. Non-smoker	

Section C: GI symptoms

• Epigastric pain:	Yes=1, No=2	
• Epigastric burning:	Yes=1, No=2	
.		
• Postprandial fullness:	Yes=1, No=2	
• Early satiation:	Yes=1, No=2	
• Anorexia:	Yes=1, No=2	
• Passage of black tarry stool:	Yes=1, No=2	
• vomiting:	Yes=1, No=2	
• Belching:	Yes=1, No=2	
• Nausea:	Yes=1, No=2	
• Weight loss:	Yes=1, No=2	
• Upper abdominal bloating:	Yes=1, No=2	
• Dysphagia:	Yes=1, No=2	
• Duration of symptoms (months)		

Section D: Co-morbidity

• Hypertension	Yes=1, No=2	
• Diabetes	Yes=1, No=2	
• Coronary artery disease	Yes=1, No=2	
• Others (please mention_____)	Yes=1, No=2	

Section E: Past medical history

• Any family history of gastric malignancy	Yes=1, No=2	
• Any history of abdominal surgery	Yes=1, No=2	
• History of antibiotic use in previous year	Yes=1, No=2	
• Any history of allergy (Food, drugs and environmental) :	Yes=1, No=2	

Physical Examination:

***General examination*:**

• Weight:……Kg

• Height: ……m

• BMI: ……Kg/m^2

• Anaemia: Present=1, Absent=2 |.……|

Systemic examination findings:

Laboratory findings at baseline:

• CBC:

Hb-…….gm/dl,

TC of WBC……/mm^3

ESR ……. mm in 1st hr.

• S. creatinine: ……..mg/dl

• ECG:

• **Upper GIT Endoscopy at baseline:**

Erosive gastritis	Present =1, Absent=2	|.……|
Non-erosive gastritis	Present =1, Absent =2	|.……|
Gastric ulcer	Present =1, Absent =2	|.……|
Duodenal ulcer	Present =1, Absent =2	|.……|
Others	Present =1, Absent =2	|.……|

• Rapid urease test at enrolment: Positive =1, Negative=2 |.……|

• SAT at enrolment: Positive =1, Negative=2 |.……|

• SAT 1 month after treatment: Positive =1, Negative=2 |.……|

• Endoscopic mucosal healing after treatment (if present initially): Yes =1, No=2 |.……|

Patient's dyspepsia symptom score at baseline |.....|

	No problem (কোন সমস্যা নেই)	Mild problem (অল্প সমস্যা)	Moderate problem (মোটামুটি সমস্যা)	Severe problem (বেশি সমস্যা)	Very severe problem (খুব বেশি সমস্যা)
Post prandial fullness (খাবারের পর অস্বস্তি ভাব)					
Early satiety (অল্প খেলে পেট ভরে যাওয়া)					
Epigastric pain (উপরের পেটে ব্যাথা)					
Epigastric burning(উপরের পেটে জ্বালা করা)					
Upper abdominal bloating (উপরের পেটে ফুলা ভাব)					
Belching (ঢেঁকুর তোলা)					
Nausea (বমি ভাব)					
Vomiting (বমি হওয়া)					

No problem : 1
(কোন সমস্যা নেই)

Mild problem : 2
(অল্প সমস্যা)

Moderate problem : 3
(মোটামুটি সমস্যা)

Severe problem : 4
(বেশি সমস্যা)

Very severe problem : 5
(খুব বেশি সমস্যা)

Follow up for drug adverse effects:

Anorexia	Yes=1, No=2	|……|
Nausea	Yes=1 , No=2	|……|
Vomiting	Yes=1, No=2	|……|
Taste disturbance	Yes=1, No=2	|……|
Dizziness	Yes=1, No=2	|……|
Abdominal pain	Yes=1, No=2	|……|
Diarrhea	Yes=1, No=2	|……|
Constipation	Yes=1, No=2	|……|
Headache	Yes=1, No=2	|……|
Skin eruption	Yes=1, No=2	|……|
Bloating	Yes=1, No=2	|……|
Dry mouth/ throat	Yes=1, No=2	|……|
Others: specify (…… ……)	Yes=1, No=2	|……|

Dyspepsia symptom score 1 month after eradication therapy |.....|

	No problem (কোন সমস্যা নেই)	Mild problem (অল্প সমস্যা)	Moderate problem (মোটামুটি সমস্যা)	Severe problem (বেশি সমস্যা)	Very severe problem (খুব বেশি সমস্যা)
Post prandial fullness (খাবারের পর অস্বস্তি ভাব)					
Early satiety (অল্প খেলে পেট ভরে যাওয়া)					
Epigastric pain (উপরের পেটে ব্যাথা)					
Epigastric burning (উপরের পেটে জ্বালা করা)					
Upper abdominal bloating (উপরের পেটে ফুলা ভাব)					
Belching (ঢেঁকুর তোলা)					
Nausea (বমি ভাব)					
Vomiting (বমি হওয়া)					

No problem : 1
(কোন সমস্যা নেই)

Mild problem : 2
(অল্প সমস্যা)

Moderate problem : 3
(মোটামুটি সমস্যা)

Severe problem : 4
(বেশি সমস্যা)

Very severe problem : 5
(খুব বেশি সমস্যা)