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PRESCRIPTION PATTERN OF DRUGS USED IN THE TREATMENT OF PEPTIC ULCER DISEASE IN THE DEPARTMENT OF GASTROENTEROLOGY IN A TERTIARY CARE HOSPITAL

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ABSTRACT: For more than a century Peptic Ulcer Disease (PUD) has been considered to be a major cause of morbidity and mortality. Most first line treatment for PUD involves use of acid suppressing drugs and target against the eradication of *Helicobacter pylori* (*H. pylori*) infection. However, the treatment strategy employed in India is not well studied. Hence, this study aims to provide insight into the prescription pattern of drugs used in PUD in India. The data was extracted from the medical records of all patients diagnosed with PUD from June 2011 to May 2012. A retrospective analysis was done to study the prescribing pattern of the drugs. The data was noted down on a pre-designed proforma and analysed. Records of 200 patients were assessed. About 91% of patients were prescribed anti *H. pylori* kit and the most commonly prescribed kit being Esomeprazole H.P kit (59.7%) followed by Pantoprazole H P kit. Following this, all patients were started on Proton pump inhibitors (PPI) for duration of about 6.89±2.25 weeks. On the basis of present study it was found that eradication of *H. pylori* is considered to be the most important treatment strategy in the management of PUD in India. Esomeprazole based HP kit was preferred, since several studies have shown them to be more efficacious. This was followed by a course of PPI to prevent recurrence.

INTRODUCTION: Peptic ulcer disease is defined as disruption of the mucosal integrity of the stomach and/or duodenum thereby resulting in a defect or excavation occurring locally due to the presence of an active inflammation. Ulcers occurring within the stomach and/or duodenum are often chronic in nature [1]. Studies have reported the point prevalence of active PUD at 3% with a lifetime prevalence of 9 per cent [2].

Helicobacter pylori (*H. pylori*) infection and usage of Non-Steroidal Anti Inflammatory Drugs (NSAID s) have been considered to be the most important causative factors in the development of PUD. Warren and Marshall's discovery of the association between *H. pylori* and development of PUD was a significant breakthrough in the pathogenesis and treatment of PUD [3].

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H. pylori is an ubiquitous, gram negative organism, known to have infected more than half of the world's population [4, 5]. However, in the Indian sub-continent the prevalence of *H. pylori* infection can go upto 80 percent especially in the rural setup. *H. pylori* infection in India most commonly presents as peptic ulcer disease, duodenal ulcer being more common than gastric ulcer [6].

Another important aspect in the management of PUD is the diagnosis. The physicians in India are faced with the problems of availability of the diagnostic tests and the cost factor. Upper Gastro Intestinal (UGI) endoscopy is usually performed to obtain a definitive diagnosis of PUD which is followed up with biopsy that can be examined by histology, Rapid Urease Testing (RUT), brush cytology, or even culture to determine infection with *H. pylori*. The current gold standard to diagnose *H. pylori* infection invasively is two positive tests and the ones most feasible in India could be a combination of RUT and brush cytology [7, 8].

Since *H. pylori* is considered to be an important factor in the causation of PUD, the most common treatment strategy involves the eradication of this organism from the gut. Different antimicrobial agents have been used to treat *H. pylori* infection. The most successful regimen consists of two or three antimicrobial agents and an anti-secretory agent preferably a proton pump inhibitor (PPI) [9, 10].

Some of the antibiotics used as a part of anti *H. pylori* medication in India are Amoxicillin, Bismuth compounds, Clarithromycin, Fluoro-quinolones, Furazolidone, Metronidazole/ Tinidazole, Nitazoxanide, Rifabutin, Secnidazole and Tetracycline [11].

The different regimens that are used vary in different parts of the world and are dependent on several factors such as prevalence of *H. pylori* infection, anti-microbial efficacy and resistance, along with genetic factors. The antibiotics need to be individualized based on these factors. However, the literature available regarding the pattern of drug usage in treatment of PUD in Indian population is lacking.

Hence, the present study aims to determine the treatment strategy in the management of PUD in Indian scenario.

OBJECTIVE: To determine the current trend in the usage of drugs in the treatment of confirmed cases of peptic ulcer disease.

MATERIALS AND METHODS: A retrospective analysis of the prescriptions was done of all PUD patients who had attended the Gastroenterology OPD of M.S. Ramaiah Hospitals, Bangalore, from June 2011 to May 2012. The data was extracted from the medical records department of the hospital. The data regarding age, gender, endoscopy findings, medications given along with their dose and duration, were noted down for each of these patients on a pre-designed proforma and analyzed. The diagnosis of PUD was made on the basis of UGI endoscopy. The infection with *H. pylori* was determined by performing Rapid urease test on the biopsy tissue.

The patients were included in the study only if they were a new case of PUD and had a definitive diagnosis of PUD based on upper GI endoscopy. The patients were excluded if they had associated secondary complications of PUD such as bleeding, perforation, gastric outlet obstruction, cancer, and if they were treated surgically. Patients with Non Ulcer Dyspepsia were excluded from the study. The study was approved by the Institutional ethics committee (IEC).

Statistical Analysis: The sample size was estimated to be 225 based on the previous literature [12] with a relative precision of 15% and desired confidence level of 95%.A descriptive analysis of the data was done to evaluate the proportion of patients receiving various types of medications. All the quantitative parameters such as age, gender were described as mean and standard deviation.

RESULTS: A total of 200 patients were included in the study. The sample size was estimated to be 225, but the total number of patients who were diagnosed with PUD during the study period from June 2011 to May 2012 was only 200. In the present study it was observed that PUD was more prevalent in men as shown in the baseline findings in **Table 1**.

It was found that history of alcohol intake was obtainable in only about 7(3.5%) and in the remaining patients either there was no history of alcohol intake or the information was not available in the case file. Most patients presented with complaints of pain abdomen 129(64.2%) and the other complaints being nausea, vomiting, bloating, loss of appetite as shown in **Table 2**. It was noted that only about 75(38%) patients were subjected to RUT, out of which a total of 36(18%) patients tested positive as shown in **Table 3**.

TABLE 1: DEMOGRAPHIC AND ENDOSCOPY FINDINGS

Gender (male)	148 (73.6%)
Age mean ± SD	51.86±17.5
H/o alcohol intake	7(3.5%)
H/o tobacco consumption	8(4%)
Endoscopy findings	
Gastric ulcer	103 (51.2%)
Duodenal ulcer	92 (45.8%)
Gastric & duodenal ulcer	6 (3%)

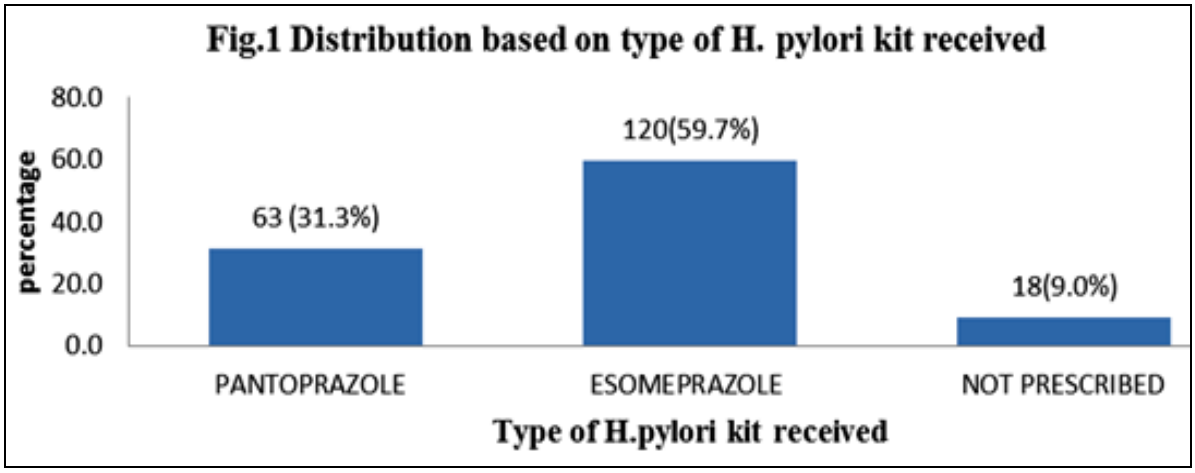
TABLE 2: PROMINENT PRESENTING COMPLAINTS OF THE PATIENT

Pain abdomen	129 (64.2%)
Nausea and vomiting	20 (10%)
Loss of appetite	4 (2%)
Bloating	2 (1%)
Pain abdomen with vomiting	29 (14.4%)
Others	11 (5.5%)
Not available	6 (3%)

TABLE 3: RAPID UREASE TEST FINDINGS

RUT positive	36(18 %)
Gastric ulcer	22 (11%)
Duodenal ulcer	13(6.5%)
Gastric and duodenal ulcer	1 (0.5%)

About 183 (91%) of the total patients were started on *H. pylori* kit, most common being Esomeprazole HP kit 120 (59.7%) followed by Pantoprazole HP kit 63(31.3%) as shown in **Fig. 1** on a twice daily dose. The constituents of the Esomeprazole kit being Esomeprazole 40mg, Clarithromycin 500mg, Amoxicillin 750mg and that of Pantoprazole HP kit being Pantoprazole 40mg, Clarithromycin 500mg and Amoxicillin 750mg.



The kit was administered for a mean duration of 12.09±2.19 days. It was also noted that 17(9%) patients did not receive HP kit. Out of those who did not receive the kit, gastric ulcer 12(6%) was the common finding and RUT was negative in only 6(3%) of the patients. All patients were started on a proton pump inhibitor for about 6.9±2.2 weeks depending on the prevalence of symptoms.

Most of the patients received a once daily dose of the proton pump inhibitor with the newer generation PPI, Esomeprazole being commonly used as shown in **Fig. 2**.

The other medications that were prescribed were Tab. Levosulpiride, Tab. Trifluoperazine and Antacid syrup as shown in **Table 4**.

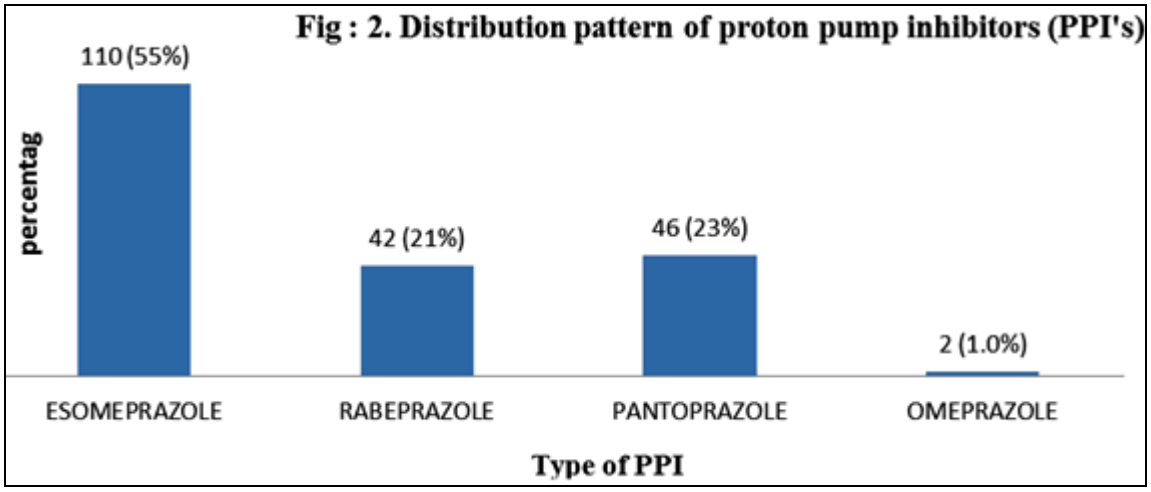


TABLE 4: MEDICATIONS PRESCRIBED TO THE PATIENTS

H. pylori kit prescribed	183 (91%)
Type of kit	
Pantoprazole HP kit	63 (31.3%)
Esomeprazole HP kit	120 (59.7%)
Levosulpiride	13 (6.5%)
Antacid syrup	16 (8%)
Trifluoperazine	5 (2.5%)

DISCUSSION: In the present study, it was observed that most patients with peptic ulcer disease were started on a fixed combination of Helicobacter pylori kit. The diagnosis of PUD was made on the basis of endoscopy and the definitive diagnosis for determination of *H. pylori* infection was based on biopsy and RUT. It was noted that these tests were done only in a small percentage of patients and the patients were started on an empirical treatment of anti *H. pylori* medication irrespective of the RUT results.

The rationality of such a treatment strategy is questionable. Some authors however favour the empirical treatment strategy for all patients with duodenal ulcer, even without confirmation of the infection [13, 14, 15, 16, 17, 18]. The argument saying that the cost of such confirmatory tests to determine *H. pylori* infection is high, and also that such results may be misleading in case of a false negative result. This justifies the empirical use of HP kits but the widespread use of antibiotics for *H. pylori* eradication may itself pose another public health problem in the form of antibiotic resistance.

The present study also showed that Esomeprazole based HP kit was more commonly prescribed. In a previous study conducted by Gisbert *et al*, it was found that Esomeprazole based triple therapy is more efficacious in the *H. pylori* eradication [19]. A similar finding was also obtained from a study conducted by Wang *et al* where Esomeprazole based kit was found to have good tolerance and efficacy comparable to Omeprazole based kit [20].

Following the completion of anti *H. pylori* medication, patients were started on a course of PPI for a mean period of 6.9±2.2 weeks. In a meta-analysis conducted by McNicholl *et al*, it was found that Esomeprazole was more efficacious in the eradication of *H. pylori* infection than the first generation proton pump inhibitors [21].

The other important cause for PUD is usage of NSAID's, but information regarding the history of NSAID usage was not obtainable from the medical records. However, data suggest that in patients with chronic NSAID usage, an underlying *H. pylori* infection itself acts as an additional risk factor for the development of PUD [22] and its complications such as bleeding [23]. On the other hand the treatment of *H. pylori* negative, NSAID negative PUD is highly controversial. However the current recommendation is to use long term anti secretory drugs [24].

CONCLUSION: The treatment strategy practised in India is primarily to start an empirical treatment for *Helicobacter pylori* eradication. The current guidelines strongly recommend eradication therapy for *H. pylori* in all patients with duodenal or gastric ulcers, which will result in cure for over 90% of these patients, so that treatment is cost-effective as well as clinically beneficial [25].

The inclusion of proton pump inhibitors with appropriate antibiotics has proven to maintain high eradication rates. Shorter courses of therapy with fixed combinations of *H. pylori* kits can improve compliance and decrease treatment failures. However the implication of such widespread use of antibiotics on antibiotic resistance needs to be borne in mind.

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