

# Expert Opinion on the Utilization of Proton Pump Inhibitors for the Treatment of Gastroesophageal Reflux Disease Among Indian Patients

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## Abstract:

Several studies have demonstrated that esomeprazole enhances the management of gastroesophageal reflux disease (GERD) patients by reducing the incidence of heartburn and epigastric pain, as well as relapse rates. But, there was a dearth of data regarding the preference of esomeprazole. So, this study was conducted to gather expert opinions on the routine use of proton pump inhibitors (PPIs) in clinical practice with a focus on the utilization of esomeprazole as a maintenance therapy for GERD in Indian settings. A cross-sectional, questionnaire based study was conducted to collect opinion among physicians involved in managing GERD symptoms across India between June 2022 and December 2022. The study enrolled 972 participants, and 63% of them noted the frequent occurrence of both erosive and non-erosive reflux disease in GERD patients. Approximately 47% of the respondents identified obesity as a significant GERD risk factor, with 32% attributing it to irregular and unhealthy eating habits. The majority of the clinicians preferred PPIs for the treatment of GERD (90%), particularly esomeprazole (87%). The typical duration of PPIs for GERD patients was reported to be 2-4 weeks by approximately 57% of the experts. Most respondents recommended a combination of PPIs and prokinetic drugs for GERD treatment. When dealing with PPI-resistant patients, 56% of physicians preferred maintaining the same PPI therapy twice daily, while 32% advised switching to another PPI. The majority of the respondents (71.81%) recommended making dietary and lifestyle adjustments for managing GERD, including consuming smaller, more frequent meals, refraining from lying down for at least two hours after eating and addressing excess weight around the midsection. It was noted that clinicians recommended PPIs, especially esomeprazole, as the primary approach for GERD management. Experts advise a regimen of twice-daily PPIs for patients who exhibit resistance to the treatment. They also underscore the importance of dietary and lifestyle adjustments in GERD management.

**Keywords:** Proton pump inhibitors, Gastroesophageal reflux, Esomeprazole, Erosive reflux diseases

## Introduction

The term "gastroesophageal reflux disease" (GERD) refers to esophageal and extraesophageal syndromes brought on by the reflux of stomach contents. GERD adversely affects patients' quality of life by causing frequent discomfort, disrupting sleep, and impairing daily activities [1]. Due to its association with an elevated risk of esophageal cancer, Barrett's esophagus also imposes a substantial burden on affected subjects [2]. The prevalence of GERD in India was estimated in the range between 7.6% and 30% [3]. The global prevalence of acid peptic disorders is on the rise due to evolving dietary and lifestyle trends. Studies among clinicians estimated the prevalence of peptic ulcer disease, non-ulcer dyspepsia, and GERD to be 37.1%, 25.2%, and 39.2% respectively [4-6].

Proton pump inhibitors (PPIs) have been recognized as the most popular class of medications for reducing stomach acid output due to their effectiveness in healing oesophageal lesions, relieving heartburn symptoms, and preventing symptomatic and endoscopic relapses. Prior clinical trials have reported that PPIs were superior to histamine 2 receptor antagonists (H2RAs) in managing these conditions [5,7]. In India, there were variety of PPIs available in the market, including rabeprazole, pantoprazole, omeprazole, esomeprazole, lansoprazole, dexlansoprazole, dexrabeprazole, and ilaprazole [8]. Numerous studies have demonstrated that esomeprazole was a promising therapeutic agent that enhances the management of GERD patients by reducing the incidence of heartburn and epigastric pain, as well as relapse rates, significantly in the esomeprazole-treated group when compared to the other PPI group, specifically omeprazole [9,10].

However, there was no data available regarding the prescribing pattern or preference of PPIs in determining the superiority of one PPI over another in the treatment of GERD or peptic ulcer disease-related symptoms. This knowledge gap was particularly important in India, where resources are limited, and only a small percentage of the population has health insurance. Therefore, the cost of various PPIs can significantly influence treatment decisions, making it a pivotal factor in the choice of medication [11]. The appropriateness of PPIs has been the subject of substantial research in Western nations, and there was a dearth of evidence from Indian clinical settings. Determining the prescribing patterns has warranted to enhance rationale and cost-effectiveness in the future. This cross-sectional survey aimed to gain expert opinion regarding the commonly prescribed PPIs in clinical practice, with a specific focus on the use of esomeprazole as a treatment for GERD maintenance therapy in Indian settings.

## Methodology

We carried out a cross sectional, questionnaire based survey among clinicians specialized in treating GERD patients in the major Indian cities from June 2022 to December 2022.

## Questionnaire

The questionnaire booklet titled GEMINI (GERd Management In iNdian patIents) study was sent to the physicians who were interested to participate. The GEMINI study questionnaire included questions on the current practices, preferences, clinical observations, and experiences related to the use of oral PPIs in routine settings, particularly esomeprazole, for the management of GERD. The study was conducted after receiving approval from Bangalore Ethics, an Independent Ethics Committee which is recognized by the Indian Regulatory Authority, Drug Controller General of India.

**Participants**

An invitation was sent to leading doctors in managing GERD in the month of March 2022 for participation in this Indian survey. 972 doctors from major cities of all Indian states representing the geographical distribution shared their willingness to participate and provide necessary data. Physicians were asked to complete the questionnaire without discussing with peers. A written informed consent was obtained from each physician prior initiation of the study.

**Statistical Methods**

Descriptive statistics were used for the analysis, with percentages representing categorical variables. Bar charts were created using Excel 2013 (version 16.0.13901.20400) to depict the frequency and percentage distributions for each variable.

**Results**

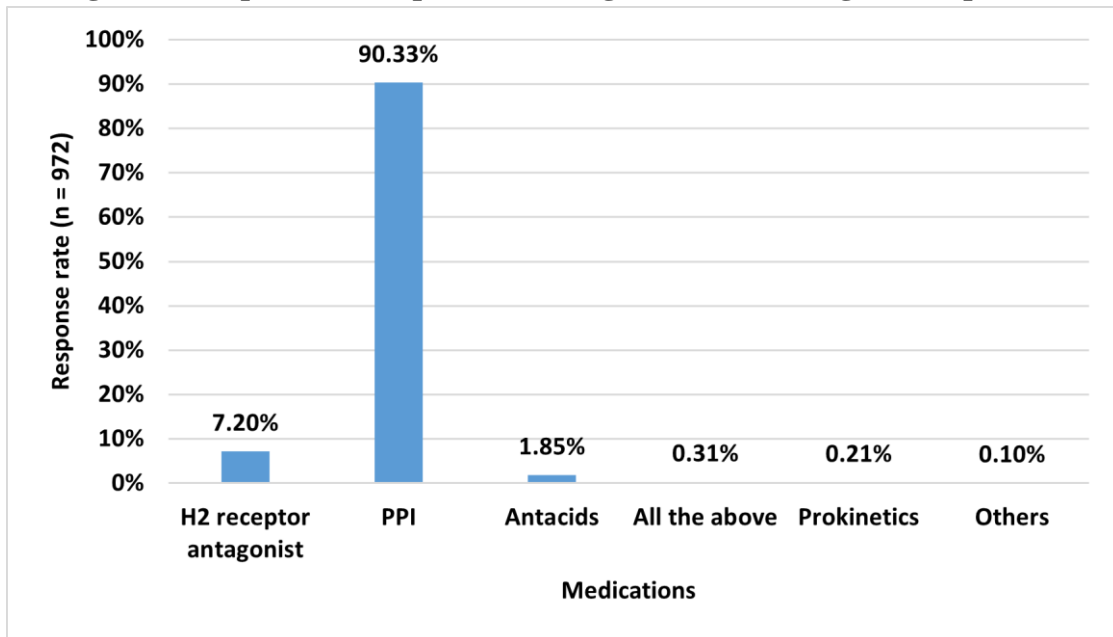
Out of 972 participants in this study, 63% indicated that both erosive reflux disease and non-erosive reflux disease were commonly encountered in GERD patients in clinical practice (Table 1). Approximately 65% of the experts noted that GERD was more prevalent among individuals aged 40-50 years whereas it was nearly 18% in the age group of 30-40 years, 16% in 50-60 year’s group and only 1.95% in above 60 year’s age group. Irregular and unhealthy eating habits were identified as major risk factors for GERD by 47% of the experts, while 32% attributed to obesity, 6% for smoking or alcohol, nearly 3% each for family history of GERD and connective tissue disorders, and 11% of physicians reported all the factors. About 62% of the respondents identified lower esophageal sphincter abnormalities as the most common cause of GERD in clinical practice, whereas 31% reported it as abnormal esophageal contractions and 6% of them highlighted hiatal hernias.

**Table 1: Response to the common type of GERD observed in clinical practice**

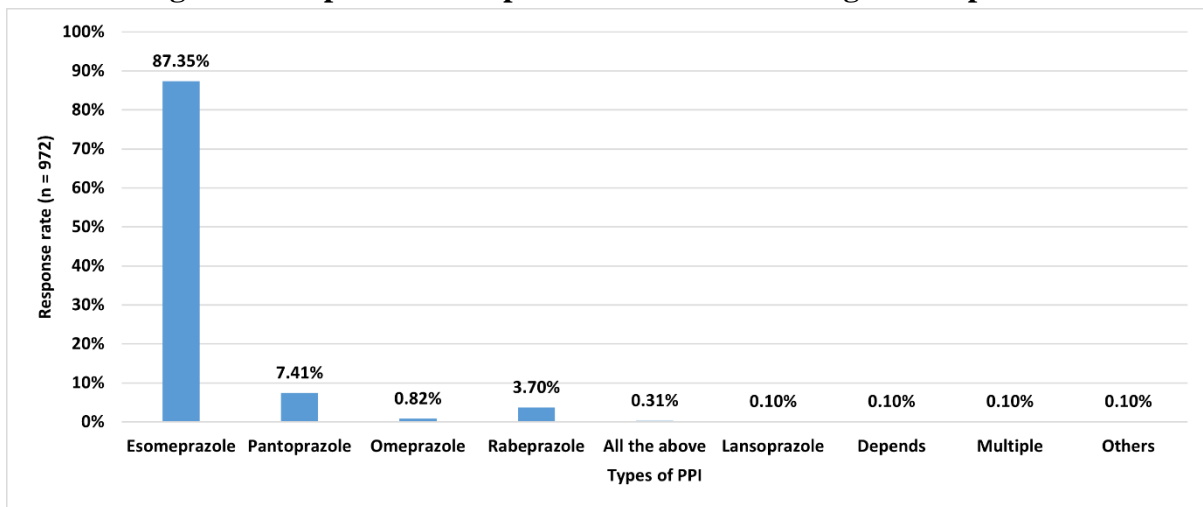
<b>Types of GERD</b>	<b>Response rate (n = 972)</b>
Erosive reflux disease	192 (19.75%)
Non-erosive reflux disease	163 (16.77%)
Both	615 (63.27%)
No endoscopic facilities	1 (0.1%)
Others	1 (0.1%)

The majority of the respondents (90.33%) indicated PPIs as the preferred medications for treating GERD patients (Figure 1). Esomeprazole was the preferred choice for 87% of the experts for treating GERD (Figure 2). An average duration of 2-4 weeks was reported for PPI therapy in GERD patients according to 57% of experts, whereas 4-8 weeks for 27% of physicians and only 1-2 weeks for 16% of clinicians. Most respondents (95%) stated that they would prescribe PPIs in combination with prokinetic agents for GERD treatment, but 5% of the clinicians denied it.

**Figure 1: Response to the preferred drug class for treating GERD patients**



**Figure 2: Response on the preferred PPI for treating GERD patients**



To manage patient’s refractory to PPI therapy, 56% of the respondents preferred the same PPI therapy twice daily, while 32% suggested switching to other PPIs (Table 2). The majority of the experts (71.81%) recommended lifestyle and dietary changes for GERD patients. This included avoiding foods that might trigger reflux and heartburn, consuming smaller, more frequent meals, refraining from lying down for at least two hours after eating, and addressing excess weight around the midsection (Table 3).

**Table 2: Response on the preferred management strategy for cases refractory to PPI therapy**

Management strategies	Response rate (n = 972)
Twice daily PPI therapy	541 (55.66%)
Switch over to other PPI	310 (31.89%)
Refer to a tertiary centre for further management	107 (11.01%)

Combination, diet, and exercise changes	2 (0.21%)
Constipation treatment	1 (0.1%)
Add prokinetics and increase PPI doses	1 (0.1%)
Manometers to confirm compliance	1 (0.1%)
Further evaluation	1 (0.1%)
As per condition	3 (0.31%)
Use antacid with PPI	1 (0.1%)
Add antidepressant	1 (0.1%)
Other measures	1 (0.1%)
H2 antagonist	1 (0.1%)
Not attempted	1 (0.1%)

**Table 3: Response to the recommendation of lifestyle/diet changes for GERD patients**

Recommendation of lifestyle/diet changes for GERD patients	Response rate (n = 972)
Avoiding foods that may precipitate reflux episodes and heartburn	114 (11.73%)
Eating smaller and more frequent meals each day instead of a few large meals	131 (13.48%)
Avoiding lying down for at least two hours after a meal	20 (2.06%)
Reducing excess weight around the midsection	8 (0.82%)
All the above	698 (71.81%)
Others	1 (0.1%)

Around 91% of the experts preferred levosulpiride, a prokinetic agent, for treating diabetic gastroparesis since only 9% opted for itopride. However, in patients receiving levosulpiride, about 51% of the experts noted occurrences of amenorrhea, galactorrhea, abnormal movements, and parkinsonism in 1-5% of cases, 39% of them noted in more than 1% of cases and nearly 10% of clinicians in 5-10% cases. For the treatment of functional dyspepsia, 67% of the respondents preferred PPIs in combination with prokinetic agents, 28% of them opted PPIs only and 4% of them recommended prokinetics.

### Discussion

This study also emphasizes the significance of tailoring treatment options to specific patient characteristics to optimize treatment outcomes. The majority of the current participants noted that both erosive reflux disease and non-erosive reflux disease are common in GERD patients. Studies by Fass and Frazier (2007 and 2017) found that non-erosive reflux disease was the most common phenotype in 60–70% of GERD patients, followed by Barrett's esophagus (30%) and erosive esophagitis (6-12%) [12,13]. Increased risk of developing GERD was associated with anatomical variables such as the development of hiatal hernia and increased intra-abdominal pressure, often seen in obesity [14]. A meta-analysis by Hampel et al. concluded that obesity was linked to an elevated risk of developing GERD symptoms, erosive esophagitis, and esophageal cancer [15]. Additionally, Malfertheiner et al., involved over 6000 GERD patients and found that the odds ratio for erosive reflux disease increases with body mass index [16]. In line with these findings, the majority of the current survey participants identified irregular and unhealthy eating habits as

a major risk factor for GERD. Notably, a significant number of respondents also recognized obesity as a major risk factor.

The current survey findings also highlighted a significant preference for PPIs, particularly esomeprazole, as a reliable and effective treatment option for GERD patients. In four randomized cross-over studies, esomeprazole 40 mg demonstrated superior intragastric acid management compared to lansoprazole 30 mg, omeprazole 20 mg, pantoprazole 40 mg, and rabeprazole 20 mg in patients with GERD symptoms [17]. On the other hand, a randomized clinical trial concluded that rabeprazole 20 mg was non-inferior to esomeprazole 20 mg in treating heartburn and regurgitation symptoms in GERD patients [18]. However, a randomized single-blinded study reported that rabeprazole 40 mg has better efficacy when compared to esomeprazole 40 mg in mild-to-moderate GERD patients [19].

The American College of Gastroenterology recommended optimizing PPI medication as the first step in treating refractory GERD [20]. As a result, increasing compliance with PPI treatment was a crucial step in optimizing PPI treatment. In the present study, experts preferred PPI therapy twice daily for the management of refractory cases unresponsive to PPI therapy. A crucial aspect of PPI optimization involves adhering to the recommended timing for PPI ingestion. Gunaratnam et al. reported an increased prevalence of sub-optimal PPI dosing in patients with poorly controlled gastro-oesophageal reflux disease. The authors noted that approximately 54% of patients received PPIs in a manner that did not optimize acid suppression, while only 12% received them in a way that maximized acid suppression [21]. It was imperative to educate patients on the optimal timing for PPI intake to ensure they derive the maximum benefit.

Most experts recommended avoiding foods that could cause reflux episodes and heartburn, eating smaller, more frequent meals throughout the day rather than a few large ones, avoiding lying down for at least two hours following a meal, and losing excess weight around the midsection for GERD patients. Newberry C et al. highlighted the significance of customizing diets for patients according to their specific symptoms, and the need to consider reintroducing certain foods and habits, if symptoms remain uncontrolled. They also reported that adjusting meal size, timing, and macronutrient composition was more effective than eliminating foods altogether, with a particular focus on reducing meal size, carbohydrates (especially simple sugars), and late-night eating [22].

The survey findings underscored the importance of personalized therapeutic approaches to improve patient outcomes and shed light on the most effective management strategies for GERD and its associated comorbidities. The key strengths of the study include a substantial sample size, the incorporation of expert insights from experienced GERD practitioners, and a comprehensive evaluation of esomeprazole's effectiveness. It was critical to recognize some of the limitations of the current survey. Relying on expert judgment in the study introduces the potential for bias, as various perspectives and preferences may have influenced the reported results. It is essential to consider these limitations when interpreting the findings and to conduct further research to validate the survey conclusions.

## Conclusion

Most of the specialists preferred the use of PPIs, especially esomeprazole, for managing GERD. Experts recommend twice-daily PPIs use for patients who are resistant to PPI treatment. Further, patients with GERD are strongly advised to make lifestyle changes, including avoiding foods that may trigger reflux and heartburn, consuming smaller, more frequent meals, refraining from lying down for at least two hours after eating, and addressing excess weight around the waist.

**Conflict of Interest:**

None

**Acknowledgement**

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