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# Expert Opinion on the Effectiveness of Proton Pump Inhibitors Therapy in Gastroesophageal Reflux Disease in Indian Settings

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***Authors' contributions***

*This work was carried out in collaboration between both authors. Authors MS and KKM contributed equally in managing literature search, designing the study, performed the statistical analysis, wrote the protocol, and the first draft of the manuscript. Both authors read and approved the final manuscript.*

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## ABSTRACT

**Objective:** To gather expert opinion regarding the commonly prescribed proton pump inhibitors (PPIs) in clinical practice, with a specific focus on the use of pantoprazole as a treatment for gastroesophageal reflux disease (GERD) in Indian settings.
**Methodology:** The questionnaire-based survey, comprised of 19 questions, collected perspectives of experts across various regions of India regarding the usage of PPI therapy for the management of GERD in their clinical practice.
**Results:** The present survey included 238 participants. The majority (84%) of the clinicians recommended PPIs as the first-line therapy for gastritis. According to 85% of clinicians, there were no significant side effects associated with PPI use in GERD treatment. Most of the experts (92%)

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recommended pantoprazole as the most frequently prescribed PPI. Approximately 46% of experts preferred pantoprazole 20 mg for pediatric use, while 41% preferred prescribing pantoprazole 80 mg for adults. A significant portion (63%) of clinicians suggested pantoprazole as an adjuvant therapy alongside other medications. The benefits of using pantoprazole include a quicker onset of action, safety, good tolerance, and extended acid suppression, as reported by 71%, 14%, and 13% of experts, respectively.

**Conclusion:** As per the expert consensus, PPI was the preferred first-line therapy for gastritis and GERD with negligible side effects. Pantoprazole emerged as the most favorable PPI for GERD treatment and was also regarded as a valuable adjuvant therapy when combined with other medications. Experts have shown a preference for prescribing 20 mg and 80 mg doses of pantoprazole for children and adults, respectively. With its rapid onset of action, safety profile, excellent tolerability, and sustained acid suppression, pantoprazole presented significant advantages, making it a valuable therapeutic option for GERD treatment.

*Keywords: Proton pump inhibitors; pantoprazole; gastroesophageal reflux disease; Indian setting; survey.*

## 1. INTRODUCTION

Gastroesophageal reflux disease (GERD) is one of the most prevalent complaints in general medicine, and it can manifest as a debilitating condition requiring lifelong medication, invasive surgery, and lifestyle adjustments. Over time, it has evolved into the most common diagnosis in gastroenterology practices and has become a widespread ailment affecting populations in nearly every country [1,2]. Additionally, due to its chronic nature and high incidence, GERD imposed a significant economic burden on patients, their families, healthcare providers, and society [3].

The prevalence of GERD has been estimated to be approximately 15% globally [4]. According to the latest Global Burden of Disease Study (GBD) the entire burden of GERD has increased by 77.53%, from 441.57 million in 1990 to 783.95 million in 2019 [4]. Although the overall incidence in Asia was reported to be lower, there were regional variations, and India stands out with a higher prevalence [5]. Major population-based studies conducted in India suggest a GERD prevalence of around 10%, a figure likely to be growing due to changing lifestyles and increasing obesity rates [4]. A meta-analysis of Indian studies conducted by Rai et al. reported a pooled prevalence of 15.6 (95% CI 11.046 to 20.714) for GERD in the Indian population [6].

Proton pump inhibitors (PPIs) have been used since the early 1990s and have remained the cornerstone of medical therapy for GERD for the past three decades due to their significant and constant acid-suppressive properties [7,8]. The Indian Society of Gastroenterology, the Association of Physicians of India (API-ISG), and American College of Gastroenterology (ACG) recommend the use of PPIs as an empiric treatment of GERD [9]. Pantoprazole has been demonstrated to be more effective than histamine-2 receptor antagonists in alleviating acid reflux symptoms, healing esophagitis, and improving health-related quality of life. Pantoprazole has demonstrated greater effectiveness compared to histamine-2 receptor antagonists in relieving acid reflux symptoms, healing esophagitis, and enhancing health-related quality of life. Backed by over 100 clinical studies, pantoprazole boasts a favorable safety profile, was as effective as other PPIs, and showed a low incidence of drug interactions. It has also been shown to be safe and effective across various patient demographics, including the elderly and individuals with mild to moderate liver disease [10]. Oral pantoprazole has been shown to improve the quality of life for GERD patients and was associated with high levels of treatment satisfaction among patients [11].

GERD will remain a substantial public health burden and a leading cause for primary care consultation. Hence appropriate management of GERD was extremely important to improve quality of life. The current survey-based study was intended to gather expert opinion regarding the commonly PPIs in clinical practice, with a specific focus on the use of pantoprazole as a treatment for gastroesophageal reflux disease (GERD) in Indian settings.

## 2. MATERIALS AND METHODS

We carried out a cross sectional, multiple-response questionnaire-based study involving

clinicians with expertise in managing GERD patients in the major Indian cities from June 2022 to December 2022.

## 2.1 Questionnaire

The questionnaire booklet named PRISM (Proton Pump Inhibitors usage in GERD management and Its lateSt advanceMents) study was sent to the clinicians who were interested to participate. The PRISM study questionnaire comprising 19 questions, was focused on the prevalence, symptoms, causes, clinical characteristics, management of GERD, and the utilization of PPI therapy in clinical practice. The study was conducted after getting approval from Bangalore Ethics, an Independent Ethics Committee which was recognized by the Indian Regulatory Authority, Drug Controller General of India.

## 2.2 Participants

An invitation was sent to leading gastroenterologists in treating GERD in the month of March 2022 for participation in this Indian survey. 238 doctors from major cities of all Indian states representing the geographical distribution shared their willingness to participate and provided necessary data. Participants were asked to complete the questionnaire without discussing with their peers. A written informed consent was obtained from each gastroenterologists before initiation of the study.

## 2.3 Statistical Methods

The data were analyzed using descriptive statistics. Categorical variables were presented as percentages to provide a clear understanding of their distribution. The frequency of occurrence and the corresponding percentage were used to represent the distribution of each variable. To visualize the distribution of the categorical variables, pie, and bar charts were created using Microsoft Excel 2013 (version 16.0.13901.20400).

## 3. RESULTS

The current survey-based study included a total of 238 clinicians. Among the respondents, 45% considered the Asia Pacific consensus as the preferred guideline for managing GERD patients, while 34% and 16% respectively favored the ACG recommendations and Montreal definition and global consensus. According to 43% of the clinicians, 25-50% of GERD patients were managed in their routine practice. Regarding the prevalence of GERD, nearly 89% of participants identified patients aged 21-35 years as the most affected group, while 8% estimated those above 50 years to be predominant. Concerning GERD-related symptoms, approximately half of the respondents reported a prevalence of 11-20% for cough or hoarseness of voice, while 27% and 18% indicated rates of 10% and 21-30% respectively. The majority of the participants (89%) stated that smokers have a high incidence of GERD.

According to the respondents, heartburn was the most common symptom of GERD observed in clinical practice (67%), followed by acid regurgitation (23%), and epigastric pain (8%). About 45% of respondents noted that the majority of the patient's experience reflux symptoms primarily at nighttime, while 36% indicated symptoms occurring both during the day and nighttime. Approximately 59% of the clinicians reported heartburn and regurgitation symptoms as the most significant indicators for diagnosing GERD, while 29% of participants favored a questionnaire assessing GERD symptoms. As for the causes of GERD, 54% of respondents attributed it to a sedentary lifestyle, while 33% and 9% pointed to improper diet and medication respectively.

The majority of the clinicians (84%) recommended PPIs as the first-line treatment for gastritis. For GERD therapy, nearly 79% of respondents favored domperidone as their preferred gastroprokinetic when used in conjunction with a PPI. Regarding dosage forms, 52% of respondents opted for pellets/capsules for PPIs, while gastro-resistant tablets were preferred by 36%. For managing hyperacidity, 68% of respondents recommended liquid antacids, while 25% did not endorse their use. Nearly 85% of clinicians observed no significant side effects reported from using PPIs for GERD, while 14% of respondents did report key side effects (Table 1). Most of the clinicians (92%) reported pantoprazole as the most often prescribed PPI in routine practice (Fig. 1).

**Table 1. Distribution of response to any key side effects reported from using PPI in GERD**

| Response | Response rate (n= 238) |
|---|---|
| No | 202 (84.87%) |
| Yes | 33 (13.86%) |
| Not attempted | 3 (1.26%) |

Nearly 46% of clinicians reported pantoprazole 20 mg as the preferred pediatric dose and 41% of clinicians stated 80 mg as the preferred dose for adults (Table 2).

Majority of the clinicians (63%) reported using pantoprazole as an adjuvant therapy in conjunction with other medications (Table 3). Approximately 71% of the clinicians selected 'faster onset of action' as the key advantage of using pantoprazole whereas 14% and 13% selected 'safe and well tolerable' and 'prolonged acid suppression' respectively (Fig. 2).

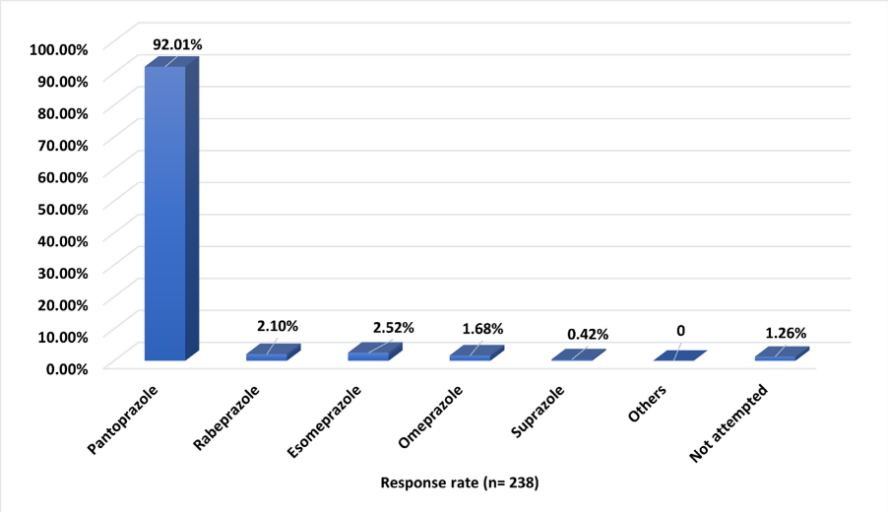


**Fig. 1. Distribution of response to most recommended PPI by clinicians**

**Table 2. Distribution of response to probability of prescribing pantoprazole 20 mg for pediatric subjects and 80 mg for adults**

| Likelihood | Response rate (n= 238) | |
|---|---|---|
| | Pantoprazole 20 mg pediatric subjects | Pantoprazole 80 mg for adults |
| Likely | 110 (46.21%) | 98 (41.17%) |
| Very likely | 51 (21.42%) | 55 (23.10%) |
| Unlikely | 54 (22.68%) | 57 (23.94%) |
| Not sure | 20 (8.40%) | 25 (10.50%) |
| Not attempted | 3 (1.26%) | 3 (1.26%) |

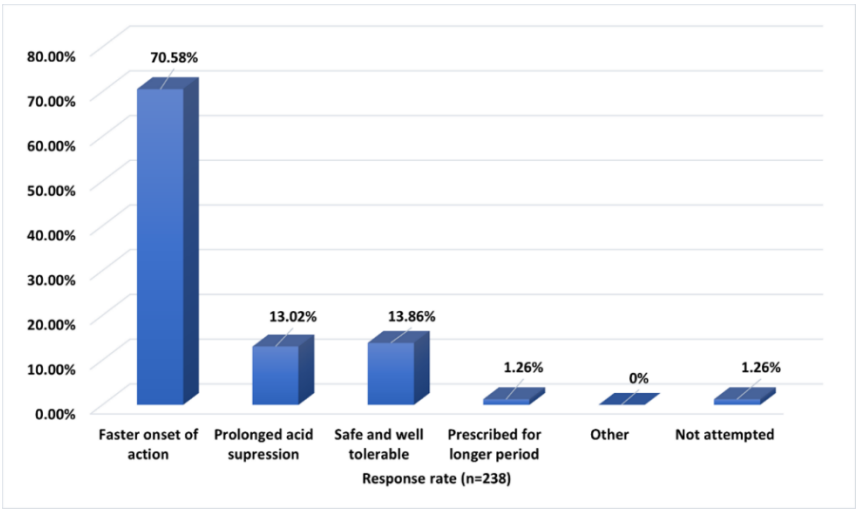


**Fig. 2. Distribution of response to advantages of using pantoprazole**

**Table 3. Distribution of response to prescribing pantoprazole as an adjuvant therapy along with other medication**

| Response | Response rate (n= 238) |
|---|---|
| No | 85 (35.71%) |
| Yes | 150 (63.02%) |
| Not attempted | 3 (1.26%) |

## 4. DISCUSSION

In the current survey, experts suggested PPIs as the primary treatment for gastritis and did not identify significant adverse effects linked to PPI use in GERD. The prevailing pathogen found in gastritis cases, *Helicobacter pylori* (*H. pylori*), was widely recognized. PPIs act by reducing both the urease activity and bioactivity of *H. pylori*, which are essential for its survival in an acidic environment [12,13]. Several studies have reported the effectiveness of PPIs in eradicating *H. pylori* infection [14-17]. Rostom et al. examined the impact of PPIs on preventing NSAID-induced upper gastrointestinal damage in six randomized controlled trials, involving 1,259 individuals. In comparison to placebo, PPIs significantly reduced the risk of endoscopic duodenal ulcers (RR = 0.20; 95% confidence interval) as well as stomach ulcers [18]. A review by de la Coba et al. concluded that PPIs can be considered as safe with minimal, often minor side effects [19]. A study by Vakil et al. reported esomeprazole maintains erosive esophagitis healing while being safe and well-tolerated, with just minor side effects [20].

In the present study, experts recommended pantoprazole as the most preferred PPI. Additionally, they reported that pantoprazole can be used as an adjuvant therapy in combination with other medications. The PAN-STAR meta-analysis indicated that for majority of the patients with erosive reflux disease (ERD) and non-erosive reflux disease (NERD), pantoprazole 40 mg was associated with complete alleviation of GERD-related symptoms. Even among those who did not experience complete symptom relief, the intensity of their symptoms was significantly reduced. Over an 8-week treatment period, pantoprazole consistently improved the quality of life for GERD patients and was well-tolerated throughout the study [21]. Pantoprazole, studied in over 100 clinical trials, boasted a low rate of medication interactions, a favorable safety profile, and comparable efficacy to other PPIs. Moreover, it has been demonstrated to be safe and effective in specific patient populations, including the elderly and those with mild hepatic or renal impairment [10]. Pilotto et al. reported that pantoprazole was significantly more effective than omeprazole in treating esophagitis. Additionally, it outperformed omeprazole and lansoprazole in alleviating symptoms among older individuals [22].

Pantoprazole was one of the few PPIs that may be administered intravenously or orally for the treatment of GERD in patients who cannot tolerate the delayed-release capsule form [23]. Several studies have reported that when used as adjuvant therapy after endoscopic treatment for peptic ulcer bleeding, intravenous pantoprazole lowers the likelihood of ulcer rebleeding, surgical intervention, transfusion requirements, and total length of hospital stay [24,25].

The experts recommended prescribing 20 mg of pantoprazole for pediatric subjects and 80 mg for adults. Children with endoscopically confirmed GERD symptoms can benefit from pantoprazole 20 mg, as it has been shown to significantly reduce symptoms after just one week [26]. In Madrazo-de la et al., pantoprazole was found to be well-tolerated and safe. After 28 days of therapy, oral pantoprazole 20 mg daily controlled stomach acid in 15 pediatric patients with reflux esophagitis, albeit only partially improving their clinical symptoms [27]. According to a review article by van et al., administering an 80 mg bolus dose of pantoprazole followed by an 8 mg/hour infusion for 72 hours can control intragastric pH and prevent rebleeding following endoscopic treatment. The 80 mg dose was both effective and tolerable in healing erosive esophagitis [28].

In the present study, experts highlighted the benefits of using pantoprazole, including its rapid onset of action, safety, excellent tolerability, and prolonged acid suppression. Dammann et al. reported that, compared to omeprazole, pantoprazole exhibited a quicker onset of action and was more effective in reducing acid production after meals [29]. PAN-STAR meta-analysis study revealed that over 90% of patients throughout the study experienced no side effects while receiving pantoprazole treatment, indicating high tolerability [21]. Several other studies have similarly reported the safety and excellent tolerability of pantoprazole [10,30-32].

The current study provides valuable insights regarding clinicians' perspectives on the usage of PPIs in the management of GERD within an

Indian context. The findings were derived from a meticulously designed and validated questionnaire-based survey. This information can aid in making informed decisions regarding the optimal treatment options, thus enhancing patient outcomes in GERD management. However, it was important to acknowledge some limitations of the study. Relying on expert judgments increases the risk of bias, as individual perspectives and preferences may have influenced the reported conclusions. It was crucial to interpret the results while considering these limitations and to contemplate further research to validate and expand upon the findings.

## 5. CONCLUSION

The current study adds to the existing literature evidence on the use of PPIs for the management of GERD in clinical practice. As per expert consensus, PPIs were recommended for the management of gastritis and GERD with minimal side effects. Pantoprazole was suggested as the most prescribed PPI in GERD management and could be used as an adjuvant therapy with other medications. Pantoprazole 20 mg was indicated for children and 80 mg for adults. Pantoprazole offered significant advantages due to its faster onset of action, safety, excellent tolerability, and sustained acid suppression, rendering it a valuable therapeutic option for GERD treatment.

## CONSENT

A written informed consent was obtained from each gastroenterologists before initiation of the study.

## ETHICAL APPROVAL

The study was conducted after getting approval from Bangalore Ethics, an Independent Ethics Committee which was recognized by the Indian Regulatory Authority, Drug Controller General of India.

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## COMPETING INTERESTS

Authors have declared that they have no known competing financial interests or non-financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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