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RESEARCH ARTICLE
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THE IMPACT OF PROTON PUMP INHIBITORS ON LARYNGOPHARYNGEAL REFLUX DISEASE

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ABSTRACT:

Background: Laryngopharyngeal reflux (LPR) is an extraesophageal manifestation of gastroesophageal reflux characterized by throat symptoms (hoarseness, chronic cough, globus). Proton pump inhibitors (PPIs) are first-line therapy, but evidence for their efficacy in LPR is mixed.

Objective: We evaluated the clinical impact of a PPI regimen on LPR symptoms and findings in a prospective interventional study.

Methods: One hundred adult patients with confirmed LPR (Reflux Symptom Index (RSI) ≥13 and Reflux Finding Score (RFS) >7) were enrolled. All received Rabeprazole 20 mg twice daily for 6 weeks. RSI and RFS were recorded before and after therapy. Secondary analyses assessed the influence of lifestyle factors (smoking, alcohol, diet). Data were analyzed using paired t-tests for RSI (normally distributed) and Wilcoxon signed-rank tests for RFS (non-normally distributed). A p-value <0.05 was considered statistically significant.

Results: Treatment yielded marked improvements. Mean RSI fell from 21.28 to 9.38 and mean RFS from 10.2 to 3.2 (both $p<0.001$). All individual RSI and laryngoscopic findings improved ($p<0.001$). Smokers experienced significantly less RFS improvement than non-smokers ($p<0.05$); alcohol use and diet did not significantly alter outcomes.

Conclusion: 6 weeks of high-dose rabeprazole significantly alleviated LPR symptoms and laryngeal findings in this study. The data support PPIs as an effective component of LPR management, though residual symptoms in some patients – especially smokers – highlight the importance of lifestyle modification and adjunctive therapies.

Keywords: Laryngopharyngeal reflux, gastroesophageal reflux, proton pump inhibitors, rabeprazole, reflux symptom index, reflux finding score.

INTRODUCTION

Laryngopharyngeal reflux (LPR) is characterized by the retrograde flow of gastric contents into the laryngopharynx, causing throat and voice-related symptoms. It often presents with chronic cough, hoarseness, throat clearing, and a foreign body sensation in the throat. In contrast to classic GERD, LPR frequently lacks heartburn, which can delay diagnosis [1]. The condition is believed to arise when transient relaxations of the upper and lower esophageal sphincters allow acidic or non-acidic gastric contents including acid, pepsin and bile to reach the larynx, where the mucosa is more vulnerable to injury due to lack of protective mechanisms [1,2].

Diagnosis of LPR is based on symptom indices and laryngoscopic findings. The Reflux Symptom Index (RSI) is a patient-reported questionnaire assessing the severity of typical LPR symptoms (hoarseness, throat clearing, cough, swallowing difficulty, globus, heartburn, etc)[3]. The Reflux Finding Score (RFS) is an objective scoring system applied during laryngoscopy to quantify signs of reflux-related laryngeal irritation (erythema, edema, granulation, etc) [3]. These tools are widely used in clinical practice to identify patients for anti-reflux therapy.

Proton pump inhibitors (PPIs), which suppress gastric acid secretion, are the mainstay of medical treatment for LPR, as they are for GERD. Rabeprazole is a second-generation PPI with potent acid suppression and relatively rapid onset of action. Its efficacy in GERD is well documented, and it is increasingly studied in LPR [4]. However, clinical response in LPR has been variable. Meta-analyses have shown that PPI therapy often leads to significant symptom relief in LPR patients [1, 5], but may have limited impact on objective laryngeal findings [6]. For example, Guo et al found that PPIs significantly improved subjective reflux symptoms (RSI) compared to placebo, but did not produce a statistically significant change in RFS [6]. In contrast, Bhargava et al reported significant improvements in both RSI and RFS after three months of PPI therapy in an Indian study [7]. These mixed results highlight that PPI effectiveness in LPR remains debated.

Lifestyle and dietary factors (smoking, alcohol use, dietary triggers) are also thought to influence LPR. Avoiding acidic and fatty foods, reducing caffeine and alcohol, and smoking cessation are often recommended, but the independent effect of these modifications on treatment outcomes is unclear [8,9]. Given the prevalence of LPR and its impact on quality of life, it is critical to obtain robust evidence on optimal therapy. Many prior studies have been limited by small sample sizes or short follow-up.

This study aims to assess the impact of rabeprazole (20 mg twice daily for 6 weeks) on LPR symptoms and laryngeal findings in a larger patient study. We hypothesized that PPI therapy would significantly reduce both RSI and RFS scores, and that lifestyle factors might modulate treatment response. By systematically evaluating pre- and post-treatment scores and analyzing patient characteristics, this research seeks to clarify the therapeutic benefits of PPIs in LPR and inform comprehensive management strategies.

MATERIALS AND METHODS

This prospective interventional study was conducted in the Department of ENT at Adichunchanagiri Hospital and Research Centre (tertiary care center, Mandya, India) over 18 months (July 2023 – January 2025). The institutional review board approved the protocol and informed consent was obtained from all patients prior to enrolment.

PARTICIPANTS: Adults aged 18–80 years presenting with symptoms suggestive of LPR were screened. Inclusion criteria required an RSI ≥13 and RFS >7. Patients were excluded if they had used PPIs within the past month, had prior esophageal or laryngeal surgery, significant comorbid laryngeal pathology, known PPI hypersensitivity, or were pregnant. After screening, 100 eligible patients were enrolled consecutively using purposive sampling.

STUDY INTERVENTION: All participants received rabeprazole 20 mg twice daily (before breakfast and dinner) for a duration of 6 weeks. No placebo or alternative treatment was included; the study employed a before-and-after design.

ASSESSMENTS: At baseline and after 6 weeks of therapy, patients completed the validated RSI questionnaire (total score range 0–45) and underwent flexible laryngoscopy to determine the RFS

(score 0–26). The RSI consists of nine symptom items (e.g. hoarseness, throat clearing, excess throat mucous, breathing difficulty, cough, swallowing difficulty, lump sensation, heartburn) scored by the patient on a 0–5 scale [3]. The RFS is determined by a single experienced otolaryngologist evaluating laryngeal signs such as edema, erythema, and post-cricoid hypertrophy during endoscopy [3]. Demographic data and lifestyle factors (smoking, alcohol, tobacco chewing, dietary habits regarding fried/fatty/spicy foods and caffeine) were recorded at baseline.

STATISTICAL ANALYSIS: Continuous variables are presented as means ± standard deviation or medians. Categorical variables are frequencies (percentages). The primary outcomes were the change in mean RSI and RFS from baseline to post-treatment. Data were analyzed using paired t-tests for RSI (normally distributed) and Wilcoxon signed-rank tests for RFS (non-normally distributed). A p-value <0.05 was considered statistically significant.

RESULTS

One hundred patients completed the study. The mean age was 54.3 years; 42.4% were >60 years. Females comprised 63% of the study. Lifestyle data showed 20% were current smokers, 19% regularly consumed alcohol, and 15% chewed tobacco. Common dietary habits included frequent consumption of fried foods (70% of patients), fatty foods (72%), spicy foods (52%), and tea/coffee (65%).

AGE (Years)	FREQUENCY	PERCEN
< 30	4	4.0
31-40	15	15.2
41-50	16	16.2
51- 60	22	22.2
>60	42	42.4
TOTAL	100	100.0

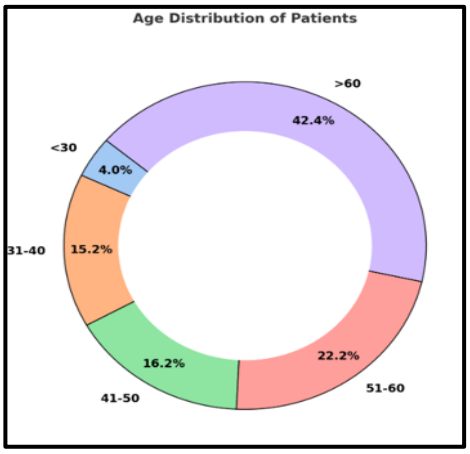

Table 1 and figure 1: Age Distribution of Patients with Laryngopharyngeal Reflux Disease (LPRD)

	FREQUENCY	PERCENT
FEMALE	63	63.0
MALE	37	37.0

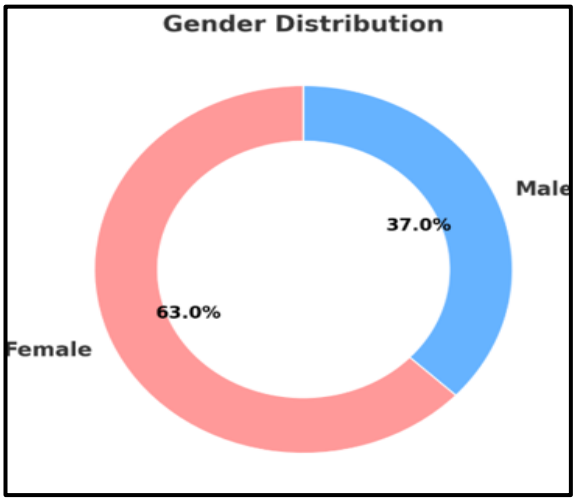

Table 2 and figure 2: Gender Distribution of Patients with Laryngopharyngeal Reflux Disease (LPRD)

Symptom and Laryngeal Scores: At baseline, mean RSI was 21.28 ± 3.9 and mean RFS was 10.24 ± 2.5. After 6 weeks of rabeprazole therapy, significant improvements were observed in both measures. The mean RSI decreased to 9.38 ± 3.3(mean reduction ~12 points, p<0.001), and the mean

RFS decreased to 3.2 ± 1.9 (mean reduction ~7 points, p<0.001). These changes indicate marked relief of reflux symptoms and decreased laryngeal inflammation.

REFLUX SYMPTOM SCORE	PRE TREATMENT	POST TREATMENT	p-value
MINIMUM	13	3	<0.001
MAXIMUM	31	19	
MEAN	21.28	9.38	
MEDIAN	21.5	9	
SD	3.95	3.30	

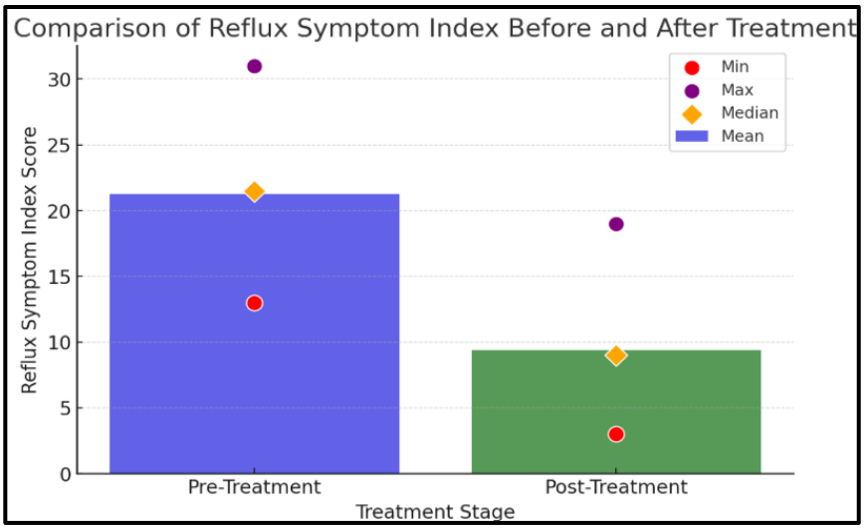

Table 3 and figure 3: Comparison Of Reflux Symptom Index Between Pre Treatment And Post Treatment Group

REFLUX FINDING SCORE	PRE TREATMENT	POST TREATMENT	p-value
MINIMUM	7	0	<0.001
MAXIMUM	18	8	
MEAN	10.24	3.2	
MEDIAN	10	3.5	
SD	2.55	1.94	

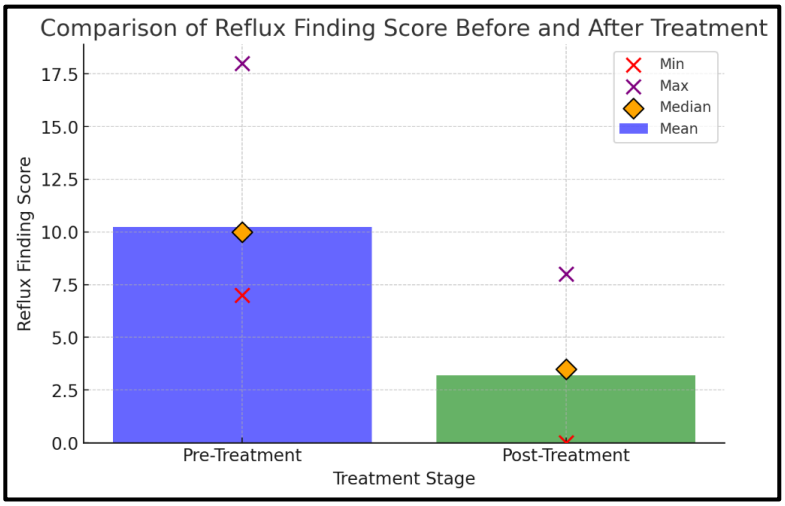

Table 4 and figure 4: Comparison Of Reflux Finding Score Between Pre Treatment and Post Treatment Group

Analysis of individual symptom indices (components of the RSI) showed consistent improvement across all items. For example, the percentage of patients reporting no hoarseness increased from 15% pre-treatment to 41% post-treatment Similarly, throat clearing, excess mucus, swallowing difficulty, and cough-after-eating all demonstrated significant shifts toward lower severity categories (each $p<0.001$).

Effects of Lifestyle Factors: Subgroup analysis evaluated the influence of smoking, alcohol, tobacco, and dietary habits on treatment outcomes. Smokers (n=20) had a smaller mean reduction in RFS compared to non-smokers (5.9±2.7 vs. 7.3±2.3; $p=0.04$), indicating less improvement in laryngeal findings. In contrast, mean RSI reduction did not differ significantly by smoking (12.6±3.6 vs. 13.5±3.9; $p>0.05$). Alcohol use (n=19) and tobacco chewing (n=15) were not associated with significant differences in RSI or RFS improvement. Likewise, dietary habits (consumption of fried, fatty, spicy foods, or caffeine) did not significantly affect the magnitude of symptom or RFS score reduction (*all* $p>0.05$).

HABITS		FREQUENCY	MEAN REDUCTION IN SYMPTOM INDEX		p VALUE
			MEAN	SD	
SMOKING	YES	20	12.6	3.6	0.37
	NO	80	11.7	3.5	
ALCOHOL	YES	19	12.8	3.3	0.75
	NO	81	11.7	3.6	
TOBACCO CHEWING	YES	15	13.5	3.3	0.59
	NO	84	11.6	3.6	

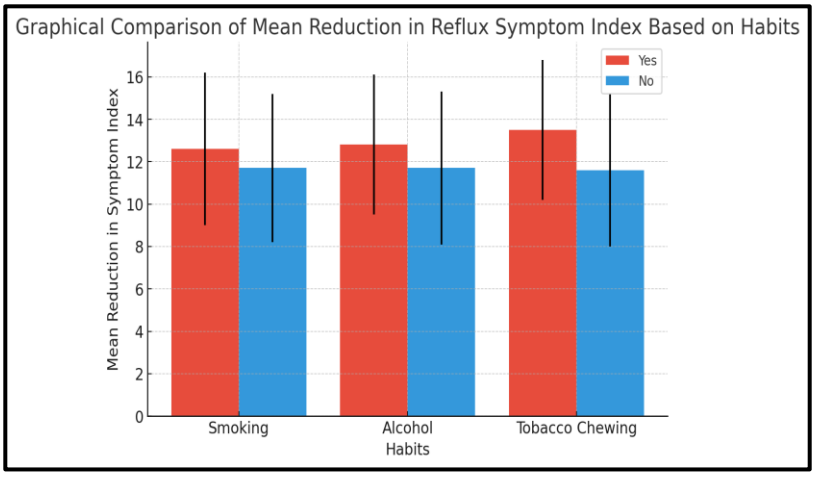

Table 5 and figure 5: Comparison Of Mean Reduction In Reflux Symptom Index Based On Addictive Habits

HABITS		FREQUENCY	MEAN REDUCTION IN SYMPTOM INDEX		p VALUE
			MEAN	SD	
FRIED FOODS	YES	70	11.7	3.4	0.77
	NO	30	12.4	3.9	
FATTY FOODS	YES	72	12.1	3.5	0.75
	NO	28	11.5	3.6	
TEA/ COFFEE	YES	65	12.2	3.7	0.79
	NO	35	11.4	3.3	
SPICY FOOD	YES	52	11.5	3.4	0.29
	NO	48	12.3	3.7	

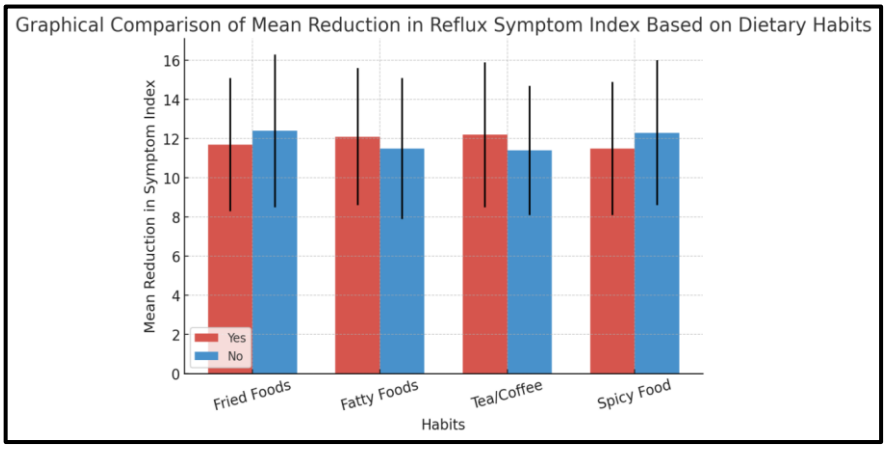

Table 6 and figure 6: Comparison Of Mean Reduction In Reflux Symptom Index Based On Dietary Habits

SAFETY: No serious adverse events were reported. Minor side effects (headache, mild nausea) occurred in <5% and did not necessitate discontinuation.

DISCUSSION

This prospective study found that rabeprazole 20 mg twice daily for 6 weeks significantly improved both subjective and objective markers of LPR. The mean RSI dropped by ~45% and mean RFS by ~39% after treatment. These findings suggest that aggressive acid suppression can effectively alleviate LPR symptoms and reduce laryngeal inflammation.

Our results align with several prior reports. For example, Lam et al [8] conducted a randomized trial of rabeprazole (20 mg BID) versus placebo and found a significant reduction in RSI scores with rabeprazole ($p<0.01$) after 12 weeks [8]. Likewise, Bhargava et al [7], observed significant decreases in both RSI and RFS after 3 months of PPI therapy in an Indian population. A meta-analysis by Guo et al [6] also demonstrated that PPI therapy yields superior symptom relief compared to placebo (pooled effect favouring PPI, $p=0.03$), although that analysis did not show a significant difference in laryngeal signs between groups [6]. In our study, in contrast to Guo's meta-analysis, both symptom scores and laryngeal findings improved significantly. The discrepancy may relate to differences in patient selection, PPI dosing, or treatment duration. Our finding of improved RFS suggests that, at least in this study, acid suppression led to visible healing of laryngeal irritation.

It is noteworthy that nearly all individual symptoms measured by the RSI showed marked improvement. The proportion of patients free of specific symptoms (e.g. hoarseness, throat clearing, cough) increased substantially post-treatment. This broad symptomatic benefit is consistant with other studies indicating that PPIs can improve the spectrum of LPR complaints. For instance, Pokharel et al [9] compared rabeprazole vs an alternative regimen and reported significant symptom relief in the PPI group. Recent evidence also suggests twice-daily PPI regimens (as used here) may be more effective for LPR symptoms than standard once-daily dosing [10].

Lifestyle factors appeared to play a modifying role. Smokers in our study had a significantly smaller reduction in RFS than non-smokers, implying reduced laryngeal healing despite PPI therapy. Tobacco smoking has been associated with impaired upper esophageal sphincter function and increased reflux events[11], which may explain the attenuated response. Alcohol and diet (fatty/spicy foods, caffeine) did not significantly alter outcomes in our analysis, suggesting that while avoiding triggers is advisable, PPI efficacy remained consistent irrespective of these habits. This finding is consistent with some prior reports indicating that pharmacologic acid suppression is the primary driver of improvement, whereas the impact of dietary modification is less clear[12].

The overall results support a combined management approach: aggressive PPI therapy to suppress reflux, plus counselling on modifiable habits. The significant symptomatic and endoscopic improvements highlight PPIs as first-line treatment for LPR [8]. However, the variable response (e.g. by smoking status) underscores that treatment should be individualized. In cases of refractory

symptoms or incomplete healing, further evaluation (e.g. impedance testing, consideration of adjunctive therapies) may be warranted.

Limitations: This study lacked a placebo control due to ethical concerns regarding withholding treatment and did not randomize treatment. It was also single-center and limited to short-term outcomes (6 weeks). Longer follow-up would help assess symptom recurrence. Nonetheless, the large sample and systematic assessment strengthen confidence in the observed effects.

Conclusion

Rabeprazole 20 mg twice daily for 6 weeks significantly reduced both symptom scores and laryngeal findings in patients with laryngopharyngeal reflux disease. These findings indicate that high-dose PPI therapy is effective in managing LPR. Treatment response was somewhat influenced by lifestyle factors: smokers benefited less in terms of laryngeal healing, suggesting that adjunctive measures (e.g. smoking cessation) may optimize results.

A comprehensive treatment plan combining medical therapy with behavioral modifications is recommended to achieve the best outcomes. Future randomized trials with longer follow-up are needed to confirm these results and evaluate long-term management strategies.

References

1. Spantideas N, Drosou E, Bougea A, AlAbdulwahed R. Proton pump inhibitors for the treatment of laryngopharyngeal reflux. *J Voice.* 2020;34(6):918–929.
2. Gatta L, Vaira D, Sorrenti G, et al. Meta-analysis: efficacy of proton pump inhibitors for laryngeal symptoms attributed to gastro-oesophageal reflux disease. *Aliment Pharmacol Ther.* 2007;25(4):385–392.
3. Qadeer MA, Phillips CO, Lopez AR, et al. Proton pump inhibitor therapy for suspected GERD-related chronic laryngitis: a meta-analysis of RCTs. *Am J Gastroenterol.* 2006;101(11):2646–2654.
4. Jin X, Zhou X, Fan Z, Qin Y, Zhan J. Meta-analysis of proton pump inhibitors in the treatment of pharyngeal reflux disease. *Comput Math Methods Med.* 2022;2022:9105814.
5. Waxman J, Yalamanchali S, Valle ES, et al. Effects of proton pump inhibitor therapy for laryngopharyngeal reflux on posttreatment symptoms and hypopharyngeal pH. *Otolaryngol Head Neck Surg.* 2014;150(6):1010–1017.
6. Guo H, Ma H, Wang J. PPI therapy for laryngopharyngeal reflux: a meta-analysis of RCTs. *J Clin Gastroenterol.* 2016;50:295–300.
7. Bhargava A, Faiz SM, Srivastava M, et al. Role of proton pump inhibitors in laryngopharyngeal reflux: evaluation in a North Indian population. *Indian J Otolaryngol Head Neck Surg.* 2018;70(1):1–7.
8. Lam PKY, Ng ML, Cheung TK, et al. Rabeprazole is effective in treating laryngopharyngeal reflux in a randomized placebo-controlled trial. *Clin Gastroenterol Hepatol.* 2010;8(9):770–776.
9. Pokharel A, Mayya JP, Upadhyay H. Comparison of PPI and triple therapy regimen for laryngopharyngeal reflux. *J Nepal Health Res Counc.* 2020;18(3):513–519.
10. Ji JY, Huh G, Ji E, et al. Impact of twice-daily versus once-daily PPI dosing on laryngopharyngeal reflux symptoms: a prospective RCT. *J Neurogastroenterol Motil.* 2024;30:459–467.
11. Smit C.F. et al., *"Effect of cigarette smoking on gastropharyngeal and gastroesophageal reflux"* (*Ann Otol Rhinol Laryngol.* 2001;110(2):190–193)
12. Min C. et al., *"Dietary modification for laryngopharyngeal reflux: systematic review"* (*J Laryngol Otol.* 2019;133(2):80–86)