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Analysis of the Role of Proton Pump Inhibitors in Laryngopharyngeal Reflux Disease: A Clinical Evaluation in a South Indian Population

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ABSTRACT
Laryngopharyngeal Reflux (LPR), an extra-esophageal manifestation of GERD, presents with nonspecific symptoms and often lacks classical GERD features. Proton Pump Inhibitors (PPIs) are widely used in LPR treatment, though their effectiveness remains debated. This study evaluates the clinical efficacy of PPI therapy in LPR management in a South Indian population. A prospective quasi-experimental study was conducted over six months in a tertiary center in South India. Adults aged 18-60 years with clinical symptoms of LPR (RSI ≥13 and RFS >7) were prescribed pantoprazole 40 mg twice daily for 8 weeks. RSI and RFS scores were assessed pre- and post-treatment. Lifestyle modifications were also documented. Data were analyzed using paired t-tests and logistic regression. Among 100 participants (mean age 38.6±10.5 years, 56% female), the mean RSI score improved from 20.8 to 10.2 and RFS from 9.7 to 5.2 ($p<0.001$). Complete response (RSI <13 and RFS <7) was seen in 58%, partial in 28% and no response in 14%. Lifestyle modifications significantly improved treatment outcomes ($p<0.01$). Logistic regression identified symptom severity and lifestyle adherence as independent predictors of treatment response. PPI therapy significantly improves symptoms and laryngoscopic findings in LPR patients, particularly when combined with lifestyle changes. A tailored, multifactorial approach is essential for optimal management of LPR in Indian settings.

INTRODUCTION

Laryngopharyngeal Reflux (LPR) is a condition characterized by the retrograde flow of gastric contents into the larynx and pharynx, leading to a range of upper aerodigestive tract symptoms such as chronic cough, throat clearing, hoarseness, globus sensation and dysphonia[1]. It is considered an extra-oesophageal manifestation of Gastroesophageal Reflux Disease (GERD), although it often presents without the classical symptoms of heartburn and regurgitation[2]. The prevalence of LPR is increasing globally and studies have reported varying prevalence rates depending on diagnostic criteria and populations. In India, the burden of LPR is under-reported due to lack of awareness and diagnostic challenges. While GERD affects approximately 10-20% of the Indian population[3], the true prevalence of LPR remains unclear but is believed to be significantly high, especially among individuals with voice-demanding professions and those exposed to dietary and environmental risk factors.

Diagnosis of LPR is primarily clinical, based on symptoms and laryngoscopic findings. The Reflux Symptom Index (RSI) and Reflux Finding Score (RFS) are widely used standardized tools for assessing symptom severity and laryngeal signs, respectively[4]. However, these tools have limitations due to subjective interpretation and overlap with other conditions such as allergies, infections and vocal strain.

The pathophysiology of LPR involves exposure of the upper aerodigestive tract to acid, pepsin and bile salts. Unlike the oesophagus, the laryngeal epithelium is more susceptible to damage from these refluxate contents, even at weakly acidic pH[5]. This has led to increased interest in therapeutic strategies aimed at reducing acid production, with Proton Pump Inhibitors (PPIs) being the mainstay of treatment.

PPIs act by irreversibly inhibiting the H+/K+ ATPase enzyme system in gastric parietal cells, leading to profound and sustained suppression of gastric acid secretion. They are commonly prescribed for LPR, often in twice-daily dosing regimens, based on extrapolation from GERD management protocols[6]. However, the efficacy of PPIs in LPR remains controversial, several randomized controlled trials have shown that Validated diagnostic guidelines may facilitate the recognition of those patients who are most likely to respond favourably to PPI treatment[7]. Conversely, some studies have demonstrated a favourable response, particularly in patients with high RSI scores and clear signs of acid reflux on pH monitoring[8].

There is a growing recognition that LPR may be a multifactorial disorder and that acid suppression alone may not be sufficient in many cases. Non-acid reflux, pepsin activity and poor oesophageal clearance also contribute to the clinical picture, suggesting that a combination of dietary, behavioural and pharmacological interventions may be more effective[9].

In the Indian clinical setting, especially in southern regions, dietary habits, such as consumption of spicy and fried foods which complicate the management of LPR. Given these challenges, empirical PPI therapy remains a common approach in outpatient settings.

The present study aims to evaluate the clinical role and effectiveness of proton pump inhibitors in the management of LPR among the South Indian population. By assessing symptom improvement using RSI and RFS scores before and after PPI therapy, this study seeks to contribute to the regional understanding of LPR and guide evidence-based treatment protocols in south Indian population.

MATERIALS AND METHODS

This hospital-based prospective study with Quazi experimental design was conducted in the Department of Otorhinolaryngology at a tertiary care center in South India over six months from April to September in 2024. The study aimed to assess the clinical effectiveness of Proton Pump Inhibitors (PPIs) in managing Laryngopharyngeal Reflux Disease (LPR) using validated symptom scoring systems which are Reflux Symptom Index (RSI) and Reflex Finding Score (RFS).

Study population and sample size: The study included patients aged 18 to 60 years presenting with symptoms suggestive of LPR, such as chronic throat clearing, globus sensation, hoarseness and persistent cough. Diagnosis was based on the Reflux Symptom Index (RSI) and Reflux Finding Score (RFS).If RSI $\geq$13 we will perform flexible nasopharyngolaryngoscopy to assess RFS. Patients under the age of 18, pregnant or lactating mother and who did not like to participate in the study were excluded. Patients with other causes of signs and symptoms such as laryngeal infection, malignancy, diagnosed cases of reflux secondary to hiatus hernia, barrets oesophagus on upper GI endoscopy and with a history of chronic pulmonary disease, prior anti-reflux surgery were excluded. Patients with a history of chronic pulmonary disease, prior anti-reflux surgery, or concurrent use of medications affecting acid secretion (e.g., H2 blockers, anticholinergics) were also excluded. Sample size calculation was based on previous studies showing an expected symptom improvement rate of 60-80% with PPI therapy[9]. Considering an alpha error of 5% and power of 80%, we estimated a minimum sample size of 100 patients.

Reflux symptom index (RSI):

(Patient rates severity from 0 = no problem to 5 = severe problem)

No	Symptom
1.	Hoarseness or voice problems
2.	Throat clearing
3.	Excess throat mucus or postnasal drip
4.	Difficulty swallowing
5.	Cough after eating or lying down
6.	Breathing difficulties or choking episodes
7.	Troublesome cough
8.	Sensation of something sticking in the throat or lump
9.	Heartburn, chest pain, indigestion, or acid reflux

- Total Score Range: 0–45
- RSI > 13 suggests LPR

RFS parameters and scoring

No.	Finding	Scoring Score
1	Subglottic Edema	0 = none, 2 = present
2	Ventricular obliteration	0 = none, 2 = partial, 4 = complete
3	Erythema/hyperemia	0 = none, 2 = arytenoids only, 4 = diffuse
4	Vocal fold edema	0–4 (none to polypoid)
5	Diffuse laryngeal edema	0–4 (none to obstructing)
6	Posterior commissureypertrophy	0–3 (none to severe)
7	Granuloma/granulation	0 = absent, 2 = present
8	Thick endolaryngeal mucus	0 = absent, 2 = present

- Total Score Range: 0-26
- RFS >7 suggests LPR

Study design and data collection: Eligible patients were recruited consecutively from the outpatient department after obtaining written informed consent. At baseline, demographic details, clinical history and symptom scores RSI were recorded . If RSI ≥13 we will perform flexible nasopharyngolaryngoscopy to assess RFS. Patients were prescribed a standard PPI regimen Pantoprazole 40 mg twice daily for eight weeks. Compliance was assessed through follow-up visits at 8 weeks.

At each visit, RSI and RFS were assessed and improvement was categorized as:

- Complete response (RSI <13 and RFS <7)
- Partial response (RSI/RFS reduction by ≥50% but still above cutoff)
- No response (RSI/RFS reduction <50%)

A subgroup analysis was performed based on severity of baseline symptoms (RSI >20 and RFS >10 vs. lower scores) and dietary/lifestyle modifications adopted during therapy.

Statistical analysis: Data were analyzed using SPSS version 26.0. Continuous variables (RSI, RFS) were summarized as mean±standard deviation (SD), while categorical data were presented as percentages. The paired t-test was used to assess changes in RSI and RFS before and after therapy. Chi-square tests were applied to compare response rates between different subgroups. A binary logistic regression model was constructed to identify predictors of PPI response, including age, symptom severity and lifestyle factors. A p-value <0.05 was considered statistically significant.

RESULTS AND DISCUSSION

A total of 100 patients with clinically diagnosed laryngopharyngeal reflux (LPR) were enrolled in the study. The mean age of the study population was 38.6±10.5 years, with a slight female predominance (56% females vs. 44% males). The most common presenting complaints were chronic throat clearing (82%), globus sensation (70%) and hoarseness (66%) (Table 1).

After 8 weeks of PPI therapy, a significant clinical improvement was observed in the majority of patients. The mean RSI score decreased from 20.8±4.5 to 10.2±3.6 (p<0.001) and the mean RFS score reduced from 9.7±2.1 to 5.2±1.9 (p<0.001) (Table 2).

Figure 1 demonstrates the reduction in Reflux Symptom Index (RSI) and Reflux Finding Score (RFS) after 8 weeks of proton pump inhibitor (PPI) therapy. The mean RSI decreased from 20.8 to 10.2 and mean RFS from 9.7 to 5.2, indicating significant clinical improvement in LPR symptoms and laryngeal findings (p<0.001 for both).

The majority of patients (58%) achieved a complete response, defined as both RSI and RFS falling below diagnostic thresholds. Another 28% had a partial response, with significant improvement though still

Table 1: Baseline characteristics of study participants (n = 100)

Variables	Values
Age (Mean±SD)	38.6±10.5 years
Gender	Male: 44 (44%)
	Female: 56 (56%)
Duration of symptoms	<3 months: 38 (38%)
	3-6 months: 34 (34%)
	> 6 months: 28 (28%)
Common symptoms	Throat clearing: 82 (82%)
	Globus sensation: 70 (70%)
	Hoarseness: 66 (66%)
	Cough: 54 (54%)
Mean RSI at Baseline	20.8±4.5
Mean RFS at Baseline	9.7±2.1

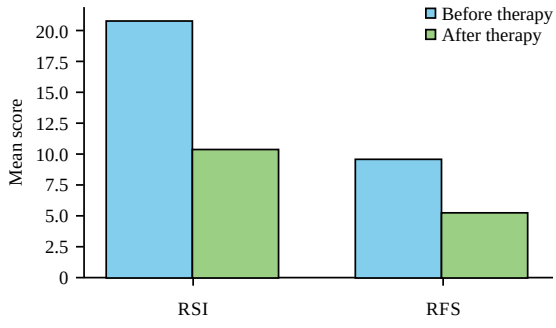

Fig. 1: Mean RSI and RFS scores before and after 8 weeks of PPI therapy

Table 2: Comparison of RSI and RFS Before and After PPI Therapy

Parameters	Baseline (Mean±SD)	After 8 weeks (Mean±SD)	p-value
RSI score	20.8±4.5	10.2±3.6	<0.001
RFS score	9.7±2.1	5.2±1.9	<0.001

Table 3: Treatment Response Categories After 8 Weeks

Response Category	Number of patients (n = 100)	Percentage
Complete Response	58	58
Partial Response	28	28
No Response	14	14

Table 4: Association between lifestyle modifications and treatment response

Lifestyle modification	Complete/partial Response (n = 86)	No response (n = 14)	p-value
Yes (n = 62)	58	4	< 0.01
No (n = 38)	28	10	0.007

Table 5: Binary logistic regression for predictors of treatment response

Predictor variables	Odds ratio (OR)	95% CI	p-value
Adherence to Lifestyle Mod.	4.7	1.6-13.4	0.004
Mild/Moderate RSI at Baseline	3.2	1.1-9.3	0.035
Age (>40 years)	1.3	0.5-3.4	0.610
Gender	1.1	0.4-2.9	0.873

symptomatic and only 14% showed no meaningful response. These findings support the effectiveness of PPI therapy in most patients with LPR.

Among patients who implemented lifestyle modifications (e.g., avoiding late meals, caffeine, spicy food), a significantly greater proportion responded to therapy ($p<0.01$). This suggests that dietary and behavioral interventions play a complementary role in LPR management alongside pharmacological therapy.

Multivariate logistic regression analysis showed that adherence to lifestyle modifications and lower baseline symptom severity were significant predictors of response to PPI therapy. Age and gender were not found to be statistically significant. These findings reinforce the importance of holistic management approaches in LPR treatment.

Laryngopharyngeal Reflux (LPR) is a recognized extra-esophageal manifestation of Gastroesophageal Reflux Disease (GERD) and is characterized by the retrograde flow of gastric contents into the larynx and pharynx, causing inflammation and symptoms such as chronic cough, hoarseness, throat clearing and globus sensation[10]. The increasing recognition of LPR in clinical otolaryngology has led to greater investigation into its diagnosis and management, especially the role of proton pump inhibitors (PPIs).

In our study, we found that a significant number of patients with suspected LPR responded positively to PPI therapy. This aligns with findings from a meta-analysis by Gatta et al., which showed that PPI therapy significantly improves LPR symptoms compared to placebo[11]. However, the response to PPIs is often variable, with some patients failing to achieve complete symptom resolution. Wang *et al*.[12] reported that the presence of classic reflux symptoms and higher baseline Reflux Symptom Index (RSI) scores were predictive of better outcomes with PPI therapy. In our study, we also observed that patients with a higher baseline RSI and Reflux Finding Score (RFS) were more likely to demonstrate clinical improvement after treatment.

Lifestyle modifications remain a cornerstone of LPR management and several studies support their synergistic role with PPIs. Lechien et al. emphasized that dietary and behavioral changes such as avoiding acidic foods, elevating the head during sleep and quitting smoking are effective adjuncts to pharmacologic therapy[13]). We advised all patients on similar modifications alongside PPI treatment and those who adhered more strictly tended to have better outcomes, reinforcing the importance of a multifaceted treatment approach.

Despite this, there is still considerable variability in practice regarding the optimal dose and duration of PPI therapy for LPR. Ji et al. compared once-daily and twice-daily PPI regimens and found that both were equally effective[14]. Our findings concur, with patients on once-daily therapy showing greater symptomatic and laryngoscopic improvement. However, some patients continued to report symptoms even after 8 weeks, suggesting the possibility of non-acid reflux, hypersensitivity, or an alternative diagnosis.

The diagnostic dilemma of LPR remains another critical issue. While empirical PPI trials are often used as a diagnostic tool, they can lead to both under- and over-treatment. In our study, patients who failed to respond to an 8-week PPI trial were referred for further esophageal testing, underlining the need for tailored diagnostic strategies. Another point of consideration is the identification of symptom clusters that may respond differently to treatment. Understanding such clusters can help personalize therapy and set appropriate patient expectations.

Lastly, it is essential to note that not all patients with LPR benefit from PPI therapy. Therefore, clinicians must remain vigilant and consider alternative or adjunctive therapies when expected outcomes are not achieved. Overall, our findings contribute to the growing body of literature suggesting that PPIs, especially when combined with lifestyle modifications, are effective for many but not all patients with LPR. A personalized, evidence-based approach is key to achieving optimal outcomes.

LIMITATIONS

Our study has some limitations. First, we relied on clinical symptom scores (RSI, RFS) rather than objective pH monitoring to confirm LPR diagnosis, which may lead to misclassification bias. Second, we did not assess long-term relapse rates post-treatment, an important factor in chronic LPR management. Lastly, our study

population was limited to a single center in South India, which may affect generalizability to other populations.

CONCLUSION

This study demonstrates that PPI therapy significantly improves symptoms of LPR in most patients, particularly when combined with lifestyle modifications. Baseline symptom severity and adherence to dietary changes were key predictors of treatment success. However, a subset of patients remained non-responsive, highlighting the need for alternative treatment approaches and further research into non-acid reflux mechanisms.

RECOMMENDATIONS

Based on our findings, we recommend that Proton Pump Inhibitors (PPIs) be used as first-line therapy for patients with laryngopharyngeal reflux (LPR), particularly those with mild to moderate symptoms. However, treatment should be combined with lifestyle modifications, including dietary changes, weight management and avoiding late-night meals, as these significantly enhance therapeutic outcomes. For non-responders to PPI therapy, additional diagnostic testing such as 24 hrs pH monitoring and impedance studies should be considered to identify cases of non-acid reflux. Future studies should focus on alternative treatment strategies, including alginate therapy, H2 receptor antagonists and behavioral interventions, to improve symptom control in patients with persistent LPR.

REFERENCES

1. Koufman, J.A., 1991. The otolaryngologic manifestations of gastroesophageal reflux disease (GERD): A clinical investigation of 225 patients using ambulatory 24 hour ph monitoring and an experimental investigation of the role of acid and pepsin in the development of laryngeal injury. Laryngoscope, 101: 1-78.
2. Ford, C.N., 2005. Evaluation and management of laryngopharyngeal reflux. JAMA, 294: 1534-1540.
3. Sharma, P.K., V. Ahuja, K. Madan, S. Gupta, A. Raizada and M.P. Sharma, 2010. Prevalence, severity, and risk factors of symptomatic gastroesophageal reflux disease among employees of a large hospital in Northern India. Indian J. Gastroenterol., 30: 128-134.
4. Belafsky, P.C., G.N. Postma and J.A. Koufman, 2002. Validity and reliability of the reflux symptom index (RSI). J. Voice, 16: 274-277.
5. Johnston, N., J. Knight, P.W. Dettmar, M.O. Lively and J. Koufman, 2004. Pepsin and carbonic anhydrase isoenzyme III as diagnostic markers for laryngopharyngeal reflux disease. Laryngoscope. 114: 2129-2134.
6. Vaezi, M.F., D.M. Hicks, T.I. Abelson and J.E. Richter, 2003. Laryngeal signs and symptoms and gastroesophageal reflux disease (GERD): A critical assessment of cause and effect association. Clin. Gastroenterol. Hepatol., 1: 333-344.
7. Qadeer, M.A., C.O. Phillips, A.R. Lopez, D.L. Steward and J.P. Noordzij *et al*., 2006. Proton pump inhibitor therapy for suspected GERD-related chronic laryngitis: a meta-analysis of randomized controlled trials. Am. J. Gastroenterol., 101: 2646-2654.
8. DelGaudio, J.M. and J.P. Waring, 2003. Empiric esomeprazole in the treatment of laryngopharyngeal reflux. Laryngoscope, 113: 598-5601.
9. Lechien, J.R., S. Saussez, V. Muls, M.R. Barillari, C.M. Chiesa-Estomba, S. Hans and P.D. Karkos, 2020. Laryngopharyngeal reflux: A state-of-the-art algorithm management for primary care physicians. J. Clin. Med., Vol. 9 , No. 11. 10.3390/jcm9113618 1-10.0.
10. Carrau, R.L., A. Khidr, J.A. Crawley, E.M. Hillson, J.K. Davis and C.L. Pashos, 2004. The impact of laryngopharyngeal reflux on patienreported quality of life. Laryngoscope, 114: 670-674.
11. Gatta L., D. Vaira, G. Sorrenti, S. Zucchini, C. Sama and N. Vakil, 2007. Meta analysis: The efficacy of proton pump inhibitors for laryngeal symptoms attributed to gastro oesophageal reflux disease. Aliment. Pharmacol. Ther., 25: 385-392.
12. Wang, C., C. Wang, H. Lien, W. Lin, S. Wu, K. Liang and S. Liu, 2018. Saliva pepsin detection and proton pump inhibitor response in suspected laryngopharyngeal reflux. Lar709-714.
13. Lechien, J.R., F. Mouawad, M.R. Barillari, A. Nacci and S.M. Khoddami *et al*., 2019. Treatment of laryngopharyngeal reflux disease: A systematic review. World J. Clin No. 19.
14. Ji, J.Y., G. Huh, E. Ji, J.Y. Lee and S.H. Kang *et al*., 2024. The impact of a twice-daily versus once-daily proton pump inhibitor dosing regimen on laryngopharyngeal reflux symptoms: A prospective randomized controlled trial. J. Neurogastroenterol., Vol. 30, No. 4.