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The importance of laryngoscopic findings as predictors of the treatment outcomes of laryngopharyngeal reflux: a retrospective review of 143 cases

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Abstract

Background: Laryngopharyngeal reflux can be described as even a single episode of reflux of gastric acid peptic contents into the larynx and hypopharynx. A large number of new researches show non-acid reflux to be an important cause of LPR symptoms. The present study explores the role of laryngoscopic findings in predicting the treatment outcomes of empirical PPI therapy for LPR.

Methods: A total of 143 patients diagnosed clinically with LPR were evaluated by rigid laryngoscopy and classified into 3 groups based on the Belafsky reflux findings score, as normal (0–7), mild to moderate (8–16), and moderate to severe (17–26).

Results: Twelve out of 39 patients in the normal group, 44 out of 61 patients in the mild to moderate group, and 31 out of 43 patients in the moderate to severe group reported symptomatic improvement after 3 months of PPI therapy and lifestyle modifications. The results were statistically significant.

Conclusion: Pretherapy laryngoscopic findings can be an important predictor of successful treatment outcomes of empirical PPI therapy for LPR.

Keywords: Laryngopharyngeal reflux, LPR, Reflux laryngitis, Reflux finding score

Background

Gastro-esophageal reflux disease (GERD) and its various manifestations such as chronic cough and hoarseness are fairly common conditions accounting for as much as 10% of patients in an otolaryngologist's clinic. Gastroesophageal reflux (GPR) is a physiologic condition characterized by the reflux of stomach acid contents into the esophagus with a drop in pH below 4. Up to 50 GPR episodes per day are considered as normal. GERD is diagnosed when there are more than 50 GPR episodes per day with a drop in pH below 4. GERD is a fairly common condition present in up to 30% of the adult population.

In the past, a number of terms such as reflux laryngitis, extra-esophageal reflux (EER), and supra-esophageal reflux (SPR) have been advocated for various upper airway manifestations such as chronic cough, hoarseness, throat clearing, and globus sensation with the assumption that such conditions form a spectrum of GERD manifestations. However, with the gradual recognition of the distinct pathology of such manifestations, found often in absence of classic GERD symptoms, the more recent term laryngopharyngeal reflux (LPR) has been adopted by otolaryngologists for this condition.

A large body of research has been published which has brought to focus the distinct etiopathogenesis of LPR.

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The commonly accepted hypothesis has been the role of acidic reflux into the hypopharyngeal and laryngeal mucosa. While up to 50 episodes of GPR can be considered normal in a day, even a single episode of acid reflux into the larynx and laryngopharynx is considered abnormal. Whereas the stomach mucosa has an internal defense mechanism against acid and pepsin, the presence of the latter in the esophagus and larynx can precipitate mucosal injury. The resultant symptoms have been hypothesized to be due to either direct mucosal injury or vagally mediated cough reflexes causing chronic laryngeal trauma.

The role of non-acid and weakly acidic reflux has been brought to light by an increasing body of research. Tutuian et al [1]. have shown that episodes of proximal reflux episodes in the causation of symptoms to be significant irrespective of the pH of the refluxate. Furthermore, a number of publications by Johnston et al. [2, 3] have elucidated the receptor-mediated uptake of pepsin by laryngeal epithelial cells at neutral pH and subsequent cell damage by intracellular expression in low-pH Golgi organelles and mitochondrial damage, as well as by expression of pro-inflammatory cytokines.

More recent researches have also brought to light the role of intrinsic defense mechanisms of the laryngeal mucosa in protection from LPR and how abnormal expression of these can result in mucosal injury. Carbonic anhydrase isoenzyme III is present in the normal laryngeal mucosa and produces bicarbonate from atmospheric CO_2 which protects against acid refluxate. A study by Gill et al. [4] has demonstrated this enzyme to be deficient in the laryngeal mucosa in 64.2% of LPR patients.

Another study by Eckley et al. [5] has demonstrated that patients with LPR have lower levels of salivary epidermal growth factor (EGF) than healthy controls.

Laryngopharyngeal reflux has also been under investigation for an ever-increasing list of conditions relevant to the otolaryngologists practice, such as vocal nodules and polyps, chronic cough, globus pharyngeus, laryngomalacia, laryngotracheal stenosis, intubation-related injuries and complications, and laryngeal cancer (Fig. 1).

Proton pump inhibitors have been the mainstay of treatment of LPR with operative procedures such as fundoplication being reserved for patients not responding to PPI after 3 months of therapy. Controversies related to the treatment of laryngopharyngeal reflux range from issues such as if LPR is at all a real entity to the optimum use of PPIs based on different symptoms and appropriate use of laryngoscopic examinations as markers for prognostication and treatment. While failure to diagnose or treat LPR can be dangerous, overtreatment may result in unnecessary waste of resources and expenditure on the part of the patient.

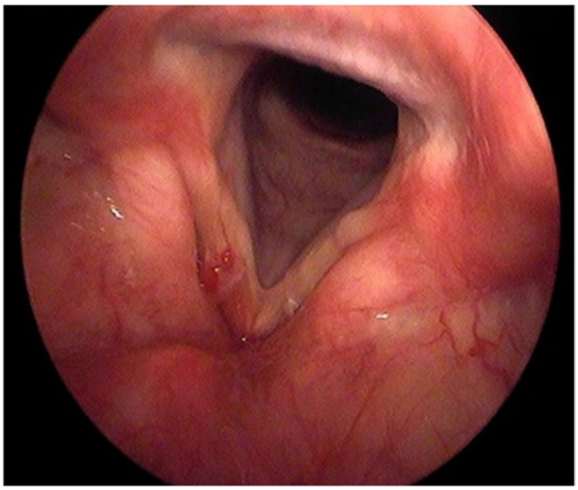

Fig. 1 Laryngoscopic picture showing moderate to severe LPR associated with right vocal polyp

The present study aims to explore the role of laryngoscopic exam findings as pretherapy predictors of response to treatment with PPIs and in guiding the optimum selection of investigation and treatment in LPR patients.

Methods

For the purpose of this study, 143 patients who were evaluated between February 2021 and January 2022 and diagnosed with LPR based on clinical features and laryngoscopic findings and other ancillary tests wherever indicated were reviewed and recalled for follow-up at the end of this period and selected for the study. The inclusion criteria for the study included (1) age > 12 years, (2) patients who were clinically diagnosed with LPR, and (3) laryngoscopic features suggestive of LPR and/or any concomitant benign disease, such as vocal nodules, related to LPR and amenable to conservative treatment protocol described below. The exclusion criteria included (1) pediatric age group patients of age < 12 years; (2) patients with laryngeal lesions not amenable to the conservative treatment protocol as described, or those requiring surgery; (3) patients with lesions suggestive of malignancy as diagnosed by laryngoscopy, barium swallow radiography, or upper GI endoscopy; and (4) patients with known diagnoses of concomitant allergic rhinitis, sinusitis, and obstructive sleep apneas which can produce confounding laryngeal manifestations.

Of the 143 patients selected for the study, 81 were male and 62 were female. The mean age of the study population was 40.5 years with a standard deviation of ± 13.8 years. All the patients diagnosed with LPR were then treated with PPIs and advised lifestyle modifications as detailed below. Patients not responding to 3 months of

conservative therapy were referred for further surgical and other interventions as required.

Clinical work-up

All patients were subjected to a thorough interview along with documentation of classic LPR symptoms such as chronic cough, hoarseness, sensation of a lump in the throat, throat clearing, episodes of choking, reflux of stomach contents, heartburn, and dysphagia. Patients with such suggestive symptoms were diagnosed clinically as LPR and referred for further investigations like rigid laryngoscopy and radiologic evaluation.

Rigid laryngoscopy

All patients in the study were subjected to rigid laryngoscopy with an 8-mm 70-degree rigid rod lens endoscope for a thorough evaluation and photodocumentation of the larynx. Rigid laryngoscopy is considered paramount in the diagnosis of LPR, with classic findings being posterior laryngitis and posterior commissure hypertrophy and pachydermia (Figs. 2, 3, and 4). The findings of rigid laryngoscopy were graded in this study according to the Belafsky reflux finding score (Table 1) [6] and classified, for the purpose of this study, as normal study (scores 0–7), mild to moderate (scores 8–16), and moderate to severe (scores 17–26).

Barium swallow study

A modified barium swallow study can be helpful in demonstrating various structural abnormalities of the esophagus such as rings, slings, and strictures. Esophagopharyngeal reflux can also be demonstrated by videofluoroscopic studies. Patients with a normal study on laryngoscopy or not responding to conservative therapy were evaluated by a barium swallow study.

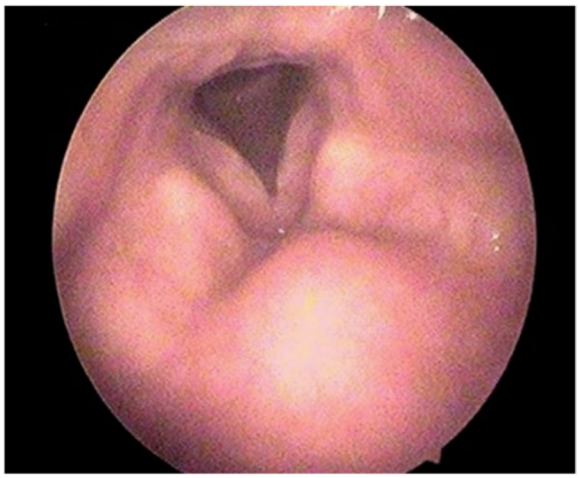

Fig. 3 Severe LPR showing edematous vestibular folds, arytenoids, and obliteration of ventricles as well as Reinke's space edema of the bilateral vocal cords

Upper gastrointestinal endoscopy

Upper gastrointestinal (UGIE) is useful in the diagnosis of esophagitis, esophageal erosions and ulcers, and Barret metaplasia. Selective patients with prominent symptoms of acid reflux and heartburn were referred for an UGIE in this study.

In our study, we did not opt for experimental procedures such as 24-h pH monitoring as the appropriate instruments, diagnostic criteria for such tests, and the

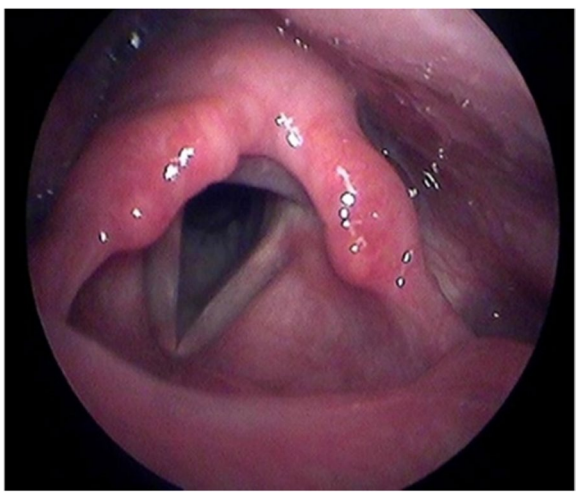

Fig. 2 Mild to moderate LPR showing erythematous arytenoids and posterior commissure hypertrophy

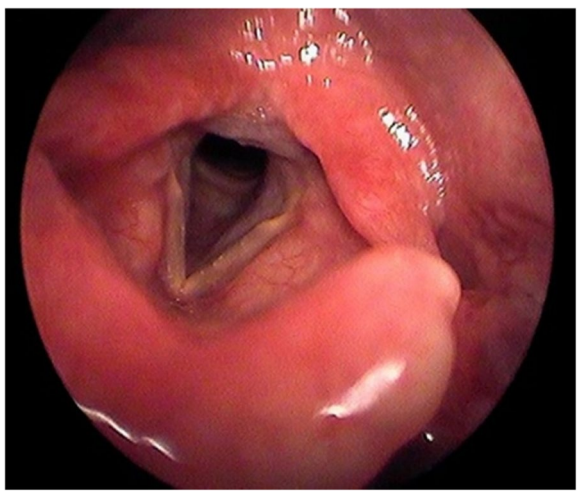

Fig. 4 A case of severe LPR showing edematous arytenoids and vestibular folds with prominent interarytenoid pachydermia

Table 1 Belafsky reflux finding score

Subglottic edema	0 = absent 2 = present
Ventricular obliteration	2 = partial 4 = complete
Erythema/hyperemia	2 = arytenoids only 4 = diffuse
Vocal fold edema	1 = mild 2 = moderate 3=Severe 4=polypoid
Diffuse laryngeal edema	1 = mild 2 = moderate 3 = severe 4 = obstructing
Posterior commissure hypertrophy	1 = mild 2 = moderate 3 = severe 4 = obstructing
Granuloma/granulation	2 = present 0 = absent
Thick endolaryngeal mucus	2 = present 0 = absent

role of non-acid reflux in the pathogenesis of LPR are under extensive research and are controversial at present [7].

Treatment

All patients in our study underwent empirical treatment with proton pump inhibitors along with lifestyle modifications such as avoidance of smoking and caffeinated drinks, avoidance of spicy and deep-fried foods, maintenance of hydration, and proper rest and sleep. Patients were conservatively treated in this way for 3 months and followed up, and improvements in symptoms were documented. Patients who failed to improve were investigated further and referred for surgery as required.

Results

A total of 143 patients were selected for this study conducted over a period of 1 year in a tertiary care institution and treated as per protocol described above. All patients were diagnosed with LPR on clinical grounds and separated into 3 groups based on laryngoscopic findings as normal (flux finding scores 0–7), mild to moderate (reflux finding scores 8–16), and moderate to severe (reflux finding scores 17–26). All patients then conservatively treated for 3 months were evaluated for self-reported symptomatic improvement. The data from the study thus obtained are summarized in Table 2 along with their statistical significance which was determined by using the chi-square test with a p-value < .05 as a cutoff for statistical significance.

Of a total of 143 patients included in this study, 39 patients who were clinically diagnosed as LPR had a normal study on laryngoscopy, whereas 61 patients were classified as mild to moderate and 43 patients classified as moderate to severe. Symptomatic improvement after 3 months of medical therapy was noted in 12 patients in the normal study group, 44 patients in the mild to moderate group, and 31 patients in the moderate to severe group. It can be clearly discerned from the above data that the presence of laryngoscopic findings along with a clinical diagnosis of LPR correlates with better symptomatic improvement after 3 months of conservative medical therapy. The results were found to be statistically significant (p-value < .05) by the chi-square test.

In this study, 44 patients were referred for an upper GI endoscopy of which 9 patients showed the presence of esophageal erosions suggestive of GERD, and 4 patients showed the presence of duodenal ulcers. Two patients showed the presence of both esophageal erosions and duodenal ulcers, and 1 patient reported an upper esophageal web.

Furthermore, 29 patients were subjected to a modified barium swallow study. Three patients were positive for motility disorders, including 1 patient with achalasia.

As the sample sizes for both UGIE and barium swallow studies are very small, no statistically meaningful conclusion can be obtained from these data, and therefore, these data have not been used for any further analyses or interpretations.

Table 2 Results of the study

Laryngoscopic findings	Symptoms improved			Symptoms not improved			Row total
	Observed	Expected	Chi-square statistic	Observed	Expected	Chi-square statistic	
Normal	**12**	23.73	*5.80*	**27**	15.27	*9.00*	**39**
Mild to moderate	**44**	37.11	*1.28*	**17**	23.89	*1.99*	**61**
Moderate to severe	**31**	26.16	*.90*	**12**	16.84	*1.39*	**43**
Column total	**87**			**56**			**143** (grand total)

The chi-square statistic is 20.3515. The p-value is .000038. The result is significant at $p < .05$

Discussion

The results of this study highlight some very interesting aspects of the diagnosis as well as the treatment of LPR. Of the 39 patients clinically diagnosed with LPR but having normal laryngoscopic findings, only 12 patients comprising 30.8% reported symptomatic relief. It is noteworthy that there may be an issue of overdiagnosis of LPR among ENT physicians as the same types of symptoms may also be found in various other conditions such as esophageal rings, webs, and strictures; allergic laryngitis; and obstructive sleep apnea. Voice changes may also be due to various infective, allergic, and other non-LPR pathologies.

However, of the 61 patients classified as having mild to moderate reflux findings on laryngoscopy, 44 patients comprising 72% reported improvement after 3 months of therapy. Also, of the 43 patients classified as having moderate to severe laryngoscopic findings, 31 comprising 72% reported symptomatic improvement after 3 months of medical therapy.

Historically, a number of studies have been published by various authors on the effectiveness of medical therapy in LPR giving widely varying results. A study by Shaw et al. [8] in 1996 showed symptomatic improvement in two-thirds of LPR patients after 3 months of omeprazole therapy. However, a prospective multicentre randomized study by El Serag et al. [9] in 2001 found no difference in the response of LPR patients to PPIs in comparison with placebo. Reichel et al. [10] in 2008 however demonstrated improvement in both symptoms and reflux findings after 12 weeks of omeprazole treatment in comparison with placebo.

The use of empirical PPI therapy in the initial treatment of LPR has been questioned by many authors in recent studies, especially in view of adverse effects related to the long-term use of many proton pump blockers. A recent review by Lechien et al. [11] found that more than one-third of the patients treated with PPIs for LPR remained non-responders and hence suggested careful exclusion of related conditions that may mimic the same symptoms. The authors suggested the use of hypopharyngeal-esophageal multichannel intraluminal impedance-pH monitoring (HEMII-pH) for the evaluation and further treatment of non-responders.

Furthermore, a study by Zalvan et al. [12] has also shown that a plant-based Mediterranean diet along with alkaline water intake can be as good as, and perhaps better than, empirical PPI therapy in the control of LPR. While further studies may be required into the dietary aspect, it may be a good idea to incorporate the same into standard empirical treatment protocols for LPR.

The present study has made use of the Belafsky reflux finding score (RFS) for the gradation of laryngoscopic findings in the treatment of LPR. The validity and the reliability of the Belafsky RFS have been proven by a number of studies [6, 13]. A study by Eckley et al. [13] found that a statistically significant difference was observed in the mean RFS between patients with LPR (10.26 ± 3.58) and controls (5.52 ± 1.34) ($p < 0.001$), and the interclass correlation coefficient comparing test and retest for both raters was high ($R1 = 0.956$; $R2 = 0.948$). The authors concluded that the Brazilian Portuguese version of the RFS proved to be a reliable and reproducible instrument for the diagnosis of LPR with a sensitivity of 82.08%, a specificity of 93.94%, a positive predictive value of 95.60%, and a negative predictive value of 76.54%. This and other validation studies on the Belafsky RFS system have proved beyond doubt the reliability of laryngoscopic findings in the diagnosis of LPR and also forms the basis for patient classification in the present study.

The present study has also taken a symptomatic improvement on the part of the patient to be the signifier for a successful treatment outcome, rather than an improvement in laryngoscopic findings. This is also in accordance with a number of research works which have shown that symptomatic improvements precede the resolution of laryngoscopic signs, as has also been shown by Belafsky et al. [14].

Finally, it may also be noted that the diagnosis of LPR, its probable relation to GERD, and the optimal treatment for the same remain a contentious issue. Many of the studies by various authors have historically suffered from disadvantages like weak inclusion criteria and lack of a true gold standard diagnostic test.

A study by Shilpa et al. [15] recently concluded that LPR may or may not be associated with GERD, and PPI therapy can be an effective first-line therapy for both types of LPR and that the use of both RFS and reflux symptom index (RSI) is useful in the diagnosis and treatment of LPR.

The present study thus corroborates many of the already published works on the topic and clearly demonstrates that the presence or absence of laryngoscopic diagnostic features can have an impact on the outcome of the treatment of the patient with LPR.

Conclusion

The diagnosis and treatment of LPR are best done by a multidisciplinary team consisting of an ENT physician, gastroenterologist, voice therapist, pulmonologist, and laparoscopic surgeon. Gastroenterologists have traditionally relied more on upper gastrointestinal symptoms like heartburn and endoscopic findings of GERD along with symptoms such as throat irritation for diagnosis, while ENT specialists rely more on throat symptoms and laryngoscopic findings for the diagnosis of LPR. PPIs generally

form the first line of empirical treatment for a suspected case of LPR. While a number of studies have demonstrated the effectiveness of PPIs in the empirical therapy of LPR, the shortcomings of most studies include small sample size, weak diagnostic criteria, short treatment duration, and lack of control groups.

The present study suffers from many of the same disadvantages. Inclusion of pretherapy and post-therapy phonetic assessment in terms of acoustic voice parameters would have certainly provided better quality data for a study of this type, and non-inclusion of these criteria is a shortcoming for this study. However, in spite of these shortcomings, this study is able to adequately demonstrate that the presence of more prominent laryngoscopic findings of reflux predicts a better outcome after the medical treatment of LPR.

Abbreviations

LPR: Laryngopharyngeal reflux; GERD: Gastroesophageal reflux disease; RFS: Reflux finding score; RSI: Reflux symptom index; PPI: Proton pump inhibitor; HEMII-pH: Hypopharyngeal-esophageal multichannel intraluminal impedance-pH; UGIE: Upper gastrointestinal endoscopy.

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Authors' contributions

All the authors of the study made significant contributions with special responsibilities as follows. JS supervised the whole study process and made critical revisions to the final manuscript. DB was responsible for the study design and critical review of the final manuscript. RC as the corresponding author was involved in the conceptualization and design of the study, data collection, patient evaluation and follow-up, manuscript preparation, and final manuscript submission. AC was involved with the data collection, data analysis, and patient follow-up. AD was responsible for patient evaluation and follow-up and data collection. All the authors have reviewed and approved the final manuscript. This manuscript has not been published or submitted for publication in any other journal.

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None.

Availability of data and materials

All data related to the study are available from the corresponding author and will be shared on reasonable request.

Declarations

Ethics approval and consent to participate

The study was approved by the institutional Ethics Committee of R. G. Kar Medical College and Hospital in February 2021. Informed written consent was obtained from all patients participating in the study. For subjects who were under 16 years, informed written consent for participation in the study was obtained from their parents or legal guardians.

Consent for publication

Informed written consent was obtained from all patients for publication of studies done on them including clinical photographs wherever applicable. For subjects under 16 years, informed written consent for publication was obtained from their parents or legal guardians.

Competing interests

The authors declare that they have no competing interests.

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