e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2024; 16(5); 161-170

Original Research Article

Efficacy of Proton Pump Inhibitors in Laryngopharyngeal Reflux: A Tertiary Care Experience in Erode District, Tamil Nadu

G. Satheesh Kumar[1], R. Kalaimani[2], M. Rajesh Kumar[3]

[1]Senior Resident, Department of Otorhinolaryngology (ENT), Government Erode Medical College & Hospital, Perundurai, Erode, Tamilnadu.
[2]Assistant Professor, Department of Otorhinolaryngology (ENT), Government Erode Medical College & Hospital, Perundurai, Erode, Tamilnadu.
[3]Senior Resident, Department of Otorhinolaryngology (ENT), Government Theni Medical College, Theni, Tamilnadu

Received: 25-02-2024 / Revised: 23-03-2024 / Accepted: 26-04-2024
Corresponding Author: Dr. G. Satheesh Kumar
Conflict of interest: Nil

Abstract:

Background: The otorhinolaryngology clinics have seen an increase in patients with symptoms of Laryngopharyngeal reflux disease (LPRD) as a result of changes in lifestyle and food.

Aim: The study aimed to observe various signs and symptoms of Laryngopharyngeal reflux and evaluate its management and result using proton pump inhibitor medication.

Methodology: This prospective study was carried out at Government Erode Medical College Hospital in the department of Otorhinolaryngology, from January 2023 to February 2024. The study included 30 patients who sought medical attention at the hospital due to symptoms and signs of Laryngopharyngeal reflux illness. A study was conducted to examine the distinct indicators and manifestations of Laryngopharyngeal reflux, as well as the effectiveness of proton pump inhibitors in its treatment, utilising the Reflux Finding Score (RFS) and Reflux Symptom Index (RSI).

Result: The average age group was 43.5 years. The most prevalent symptoms reported by patients with Laryngopharyngeal reflux were a sensation of a foreign object in the throat and frequent throat cleaning. Video laryngoscopy revealed common findings of erythema of the arytenoids, combined with hypertrophy of the posterior commissure and obliteration of the ventricles. The use of proton pump inhibitors resulted in a notable enhancement in both the reflux symptom index and reflux finding score.

Conclusion: Proton pump inhibitors are a highly successful therapy option for managing laryngopharyngeal reflux. The reflux finding score and reflux symptom index developed by Wake Forest University are highly helpful diagnostic tools for identifying laryngopharyngeal reflux (LPR).

Keywords: Proton Pump Inhibitors, Laryngopharyngeal Reflux, GERD.

Introduction

Laryngopharyngeal reflux is the backward movement of stomach contents towards the larynx and pharynx, causing them to come into touch with the upper aerodigestive tract [1]. Conversely, gastroesophageal reflux disease refers to the regurgitation of stomach acids into the oesophagus. Acid reflux illnesses, such as GERD and LPR, are widespread and have reached epidemic proportions [2–5]. EL-Serag [2] reported that the occurrence of reflux illnesses (LPR and GERD) has been steadily rising at a rate of 4% per year since 1976. Additionally, data from the National Cancer Institute of the United States reveals a significant 600% increase in the prevalence of esophageal cancer since 1975. Altman et al. documented a fivefold surge in the number of visits to the otolaryngologist as a result of laryngopharyngeal reflux (LPR) from 1990 to 2001. Furthermore, it has been estimated that more than 50% of patients with dysphonia have laryngopharyngeal reflux (LPR) [6]. Laryngopharyngeal reflux disease is a type of gastroesophageal reflux disease that specifically affects the larynx and pharynx. The given text is a list containing the elements 3 and 4. Other synonymous terminology used in the field of otorhinolaryngology for this condition include 'extra esophageal reflux', 'chronic laryngitis', and 'above esophageal complication of gastroesophageal reflux'. The user's text is "[7]". Recent research in this area clearly demonstrates that laryngopharyngeal reflux encompasses a range of intricate abnormalities. Therefore, it is crucial to

comprehend the fundamental scientific principles related to this condition and provide appropriate clinical treatment for patients with laryngopharyngeal reflux.

Refluxed material from the stomach, which includes acid and pepsin, can cause chemical injuries and inflammation of the mucosa in the laryngopharyngeal structures. It can also indirectly stimulate vagal afferents in the oesophagus, leading to symptoms such as a feeling of a lump in the throat, hoarseness, a sore or burning throat, difficulty swallowing, changes in voice, coughing, and frequent throat clearing [8]. Koufman [9] emphasises the significance of distinguishing LPR and GERD as separate entities. In a study conducted by Kaufman involving 899 individuals, it was found that throat clearing was detected in 87% of patients with laryngopharyngeal reflux (LPR) compared to only 3% of patients with gastroesophageal reflux disease (GERD). In contrast, only 20% of patients diagnosed with Laryngopharyngeal Reflux (LPR) reported experiencing heartburn or a burning sensation, but 83% of patients in the Gastroesophageal Reflux Disease (GERD) group had these symptoms.

The diagnosis of LPR can be made by conducting patient interviews and inquiring about specific symptoms, doing a video laryngoscopic assessment of the larynx, or using double probe pH monitoring [10-12]. Ambulatory 24-hour dual probe (pharyngeal and esophageal) pH monitoring is a highly accurate and specific method for diagnosing Laryngopharyngeal Reflux (LPR) [13]. Although pH monitoring is not commonly accessible in clinical practice due to its discomfort and cost, video laryngoscopic examination is more readily available.

Belafsky et al. [14] created cost-effective, non-invasive devices called the Reflux Symptom Index and Reflux Finding Score [15]. The video laryngoscopic examination was the main diagnostic method for identifying laryngopharyngeal reflux. Feng et al. [16] have determined that both laryngopharyngeal pH monitoring and RSI scoring are equally effective in identifying laryngopharyngeal reflux disease (LPRD).

The Reflux Symptom Index (RSI) [14] is a self-administered outcome measure consisting of nine items. It has been asserted that it precisely records symptoms exhibited by patients with LPR. This index seems to be valid and exhibits a good level of reproducibility. A Relative Strength Index (RSI) over 13 is regarded as indicative of Laryngopharyngeal Reflux (LPR). The score can vary from 0 and 45, with 45 being the lowest possible result. The Reflux Finding Score (RFS) [15], in contrast, is a clinical severity rating scale consisting of 8 items that assess endoscopic findings. The scale encompasses the typical laryngeal observations associated with LPR. It has been determined that individuals with an RFS score exceeding 7 have a likelihood of over 95% of having LPR [15]. Belafsky et al. determined that RFS provides a reliable record of therapy effectiveness in patients with LPR. The range spans from 0 to 26.

Using a proton pump inhibitor as a therapy trial is recommended as a practical and economical method for determining patients with genuine laryngopharyngeal symptoms caused by reflux [17]. Research has shown that using a single daily dose of the PPI has resulted in high failure rates. To improve effectiveness, it is recommended to employ a regimen of two daily doses, as suggested by most research [18, 19]. In Park et al.'s study [20], it was noted that 50% of patients reacted to the treatment regimen of two daily doses of PPI after 2 months, but only 28% of patients who received a single daily dose responded to the treatment. Among the patients who had not experienced any improvement, 54% of those in the single dose group had symptom improvement after receiving two daily doses of therapy for an additional 2 months.

The prevalence of individuals seeking treatment from an Otolaryngologist for GERD is believed to range from 4% to 10%.[21] However, Laryngopharyngeal reflux problem is frequently overlooked, misdiagnosed, or neglected due to the lack of a formal diagnosis. The incidence of laryngopharyngeal reflux disease is significantly elevated.[22,23] However, there is a lack of epidemiological studies providing data on the prevalence of laryngopharyngeal reflux illness specifically in India. There are now five commonly marketed proton pump inhibitors (PPIs): Pantoprazole, Omeprazole, Lansoprazole, Esomeprazole, and Rabeprazole. This study was to assess the clinical characteristics of Laryngopharyngeal Reflux (LPR) and investigate the effectiveness of Proton Pump Inhibitors (PPIs) in treating LPR. Additionally, the study aimed to compare the effects of different PPIs in LPR. The objective of the study is to assess the efficacy of Proton pump inhibitors in the treatment of Laryngopharyngeal reflux disease.

Materials and Methods

A prospective study was carried out at the Department of ENT in Government Erode Medical College and Hospital, Perundurai, Erode, Tamil Nadu, following clearance from the Institutional Ethical Committee.

The study spanned from January 2023 to February 2024 and involved a sample size of 30 patients. Patients were enrolled based on their Reflux Symptom Index (RSI) and Reflux Finding Score (RFS). Included patients ranged in age from 18 to

65 years and presented with symptoms of laryngopharyngeal reflux (LPR) persisting for at least one month, with RSI scores exceeding 13 and RFS scores surpassing 7. Exclusion criteria encompassed patients exhibiting evident alternative causes for their symptoms and signs, such as infections, malignancies, and chronic diseases. Every patient who met the specified requirements filled out a questionnaire at the beginning of the study. The questionnaire comprised sections on demographic status, socio-economic position, educational qualification, tobacco usage, smoking and alcohol use, and the presence of symptoms as per the RSI.

Patients were instructed to indicate whether they had symptoms such as hoarseness, throat clearing, coughing, a sensation of a lump in the throat, heartburn, regurgitation, difficulty swallowing, chest pain, and excessive throat mucus. Additionally, assess the intensity of the issue using a range from 0 to 5, where 0 represents no difficulty and 5 represent a serious problem. Every patient received a comprehensive examination of the ear, nose, and throat, followed by a procedure called laryngeal endoscopy. The diagnosis of Laryngopharyngeal Reflux (LPR) was established based on the assessment of Reflux Symptom Index (RSI) and Reflux Finding Score (RFS). Patients with a Repetitive Strain Injury (RSI) score higher than 13 and a Repetitive Force Strain (RFS) score higher than 7 were prescribed Proton Pump Inhibitors (PPI) to be taken twice daily for a duration of 12 weeks. Additionally, they were provided guidance on making lifestyle modifications. Laryngeal endoscopy was performed at 4, 8, and 12 weeks, and the values for RSI and RFS were recalculated. Patients continued to receive monthly follow-up appointments for lifestyle adjustment counselling and treatment, if necessary, even after 12 weeks. The study utilised Proton Pump Inhibitors such as Omeprazole at a dosage of 20 mg taken twice daily, or Pantoprazole at a dosage of 40 mg taken twice daily. In each category, demographic variables were presented in frequency with percentages. $P \leq 0.05$ is considered statistically significant.

The data were analyzed using Statistical Package for Social Sciences for Windows, Version 22 (IBMSPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. IBM Corp.).

Results

In our study most of cases were in the age categories of 41-50 years. The mean age was 44.3 years, with the youngest patient being 19 years old and the oldest patient being 72 years old.

Table 1: Demographic data of study participants

Demographic data	Mean ± SD
Age (year)	44.3 ± 12.15
Sex (male: female)	4:6

Table 1 presents the demographic characteristics of the study participants. The mean age of the participants was 44.3 years with a standard deviation of 12.15 years, indicating a relatively wide age range among the subjects. In terms of gender distribution, the study included a ratio of 4 males to 6 females, suggesting a slightly higher representation of female participants in the study cohort.

Table 2: socio economic status of study participants

Socio economic status	Number (%)
Lower	30.5%
Lower middle	41%
Upper lower	11%
Upper middle	17.5%

Table 2 outlines the socioeconomic status distribution among the study participants.

The majority of participants fell into the lower middle socioeconomic category, comprising 41% of the total participants. Lower socioeconomic status accounted for 30.5% of the participants, while upper middle socioeconomic status represented 17.5%. A smaller proportion of participants, 11%, belonged to the upper lower socioeconomic category.

These findings suggest a diverse representation of socioeconomic backgrounds within the study population, with a notable concentration in the lower and lower middle socioeconomic strata.

Table 3: Addiction history of study participants

Addiction history	Number (%)
Tobacco	26%
Smoking	14.5%
Alcohol	10%

Table 3 provides an overview of the addiction history among the study participants. Approximately 26% of the participants reported a history of tobacco use, indicating a significant portion of the study population with this addiction. Smoking was reported by 14.5% of the participants, representing another notable subgroup with a smoking habit. A smaller proportion, 10%, disclosed a history of alcohol consumption.

These findings underscore the prevalence of addictive behaviors within the study cohort, particularly concerning tobacco use, followed by smoking and alcohol consumption, albeit to a lesser extent.

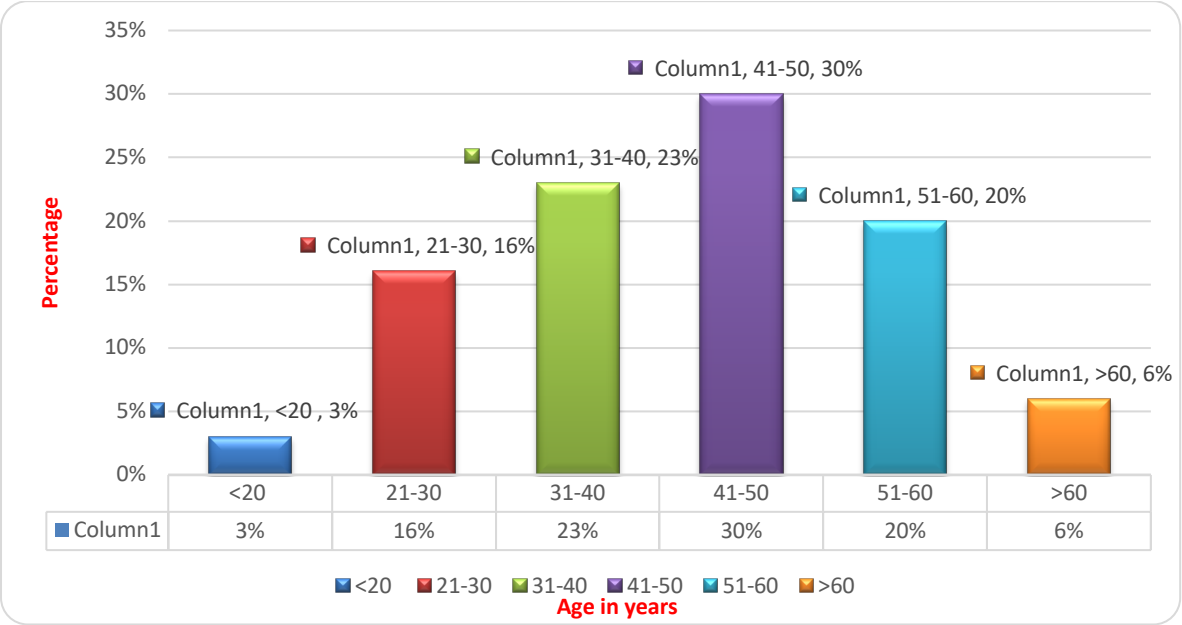

Figure 1: Age distribution of study participants

The Figure 1 chart depicts age distribution of study participants. Age groups are listed on the x-axis, and percentages are on the y-axis.

The largest age group is 41-50 years old, at 30%. The next largest age group is 31-40 years old, at 23%. The following age groups are 51-60 years old (20%), 21-30 years old (16%), less than 20 years old (3%), and over 60 years old (6%).

Gender Distribution: The Figure 2 confirms that females make up the majority of the study participants. The pie chart shows that 60% of the participants were female, while 40% were male. This aligns with the text that states that out of 30 patients, 18 were female and 12 were male. In total, there were 30 participants according to the text.

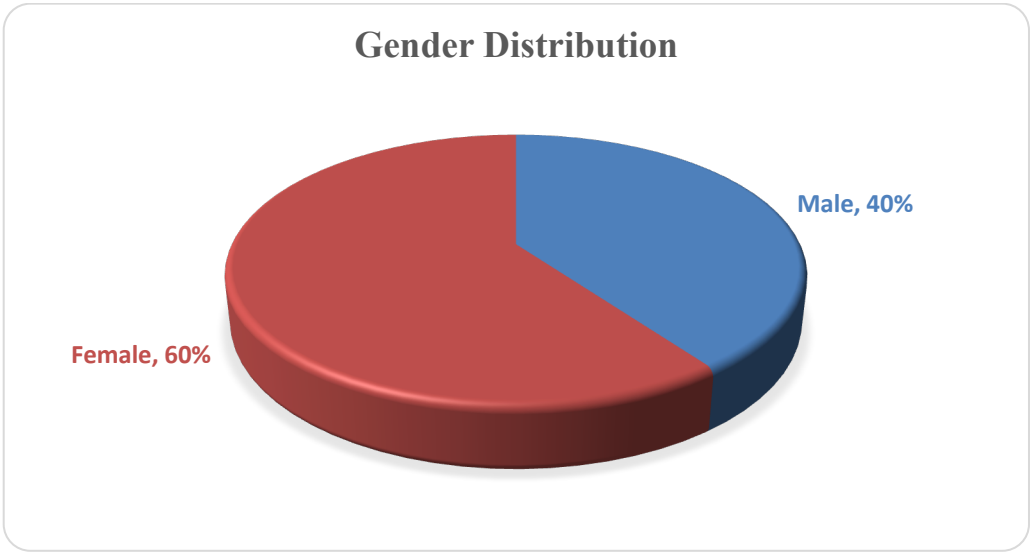

Figure 2: Gender distribution of study participants

The average RSI of all patients was 24.80 before to treatment with PPIs. Following 8 weeks of therapy with proton pump inhibitors (PPI), the average reflux symptom index (RSI) declined to 14.53. After 16 weeks of PPI therapy, the mean RSI further dropped to 12.96.A notable shift in RSI was observed within the initial 8 weeks of therapy across all age groups, followed by another substantial change in the subsequent 8 weeks.

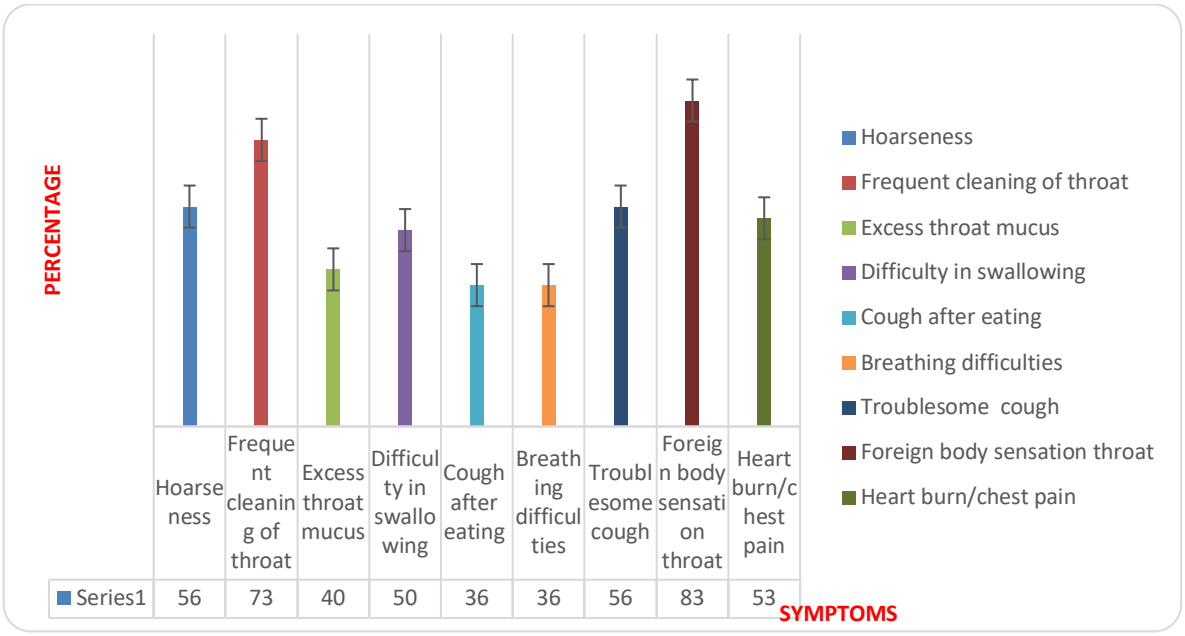

Figure 3: Percentage distribution of symptoms (RSI)

The mean RSI of all patients was 24.80 prior to treatment with PPIs. After undergoing 8 weeks of treatment with proton pump inhibitors (PPI), the average reflux symptom index (RSI) decreased to 14.53. Following 16 weeks of proton pump inhibitor (PPI) treatment, the average Reflux Symptom Index (RSI) decreased even further to 12.96.An evident change in RSI occurred during the first 8 weeks of treatment in all age groups, followed by another significant shift in the following 8 weeks (figure 3).

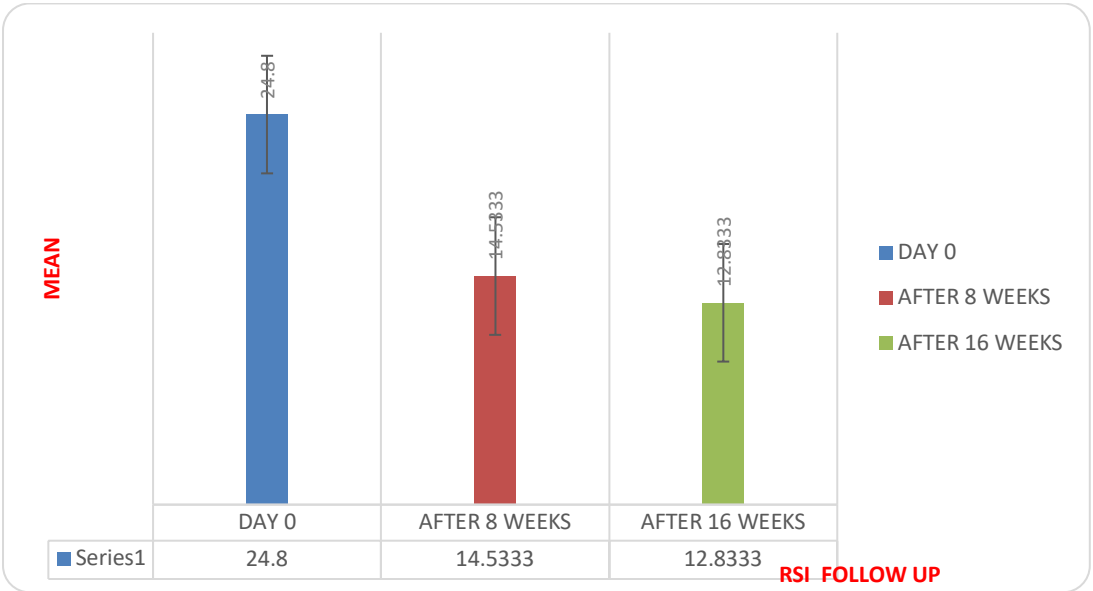

Figure 4: RSI pre and post PPI therapy

Before treatment with proton pump inhibitors (PPI), the patients exhibited a mean Reflux Finding Score (RFS) of 12.66, as depicted in Figure 4. Following an 8-week course of PPI therapy, the mean RFS decreased to 9.46, indicating an improvement in reflux-related findings. Subsequently, after 16 weeks of PPI therapy, the mean RFS further declined to 6.80, suggesting a continued reduction in reflux-related symptoms and findings over the treatment period (figure 4).

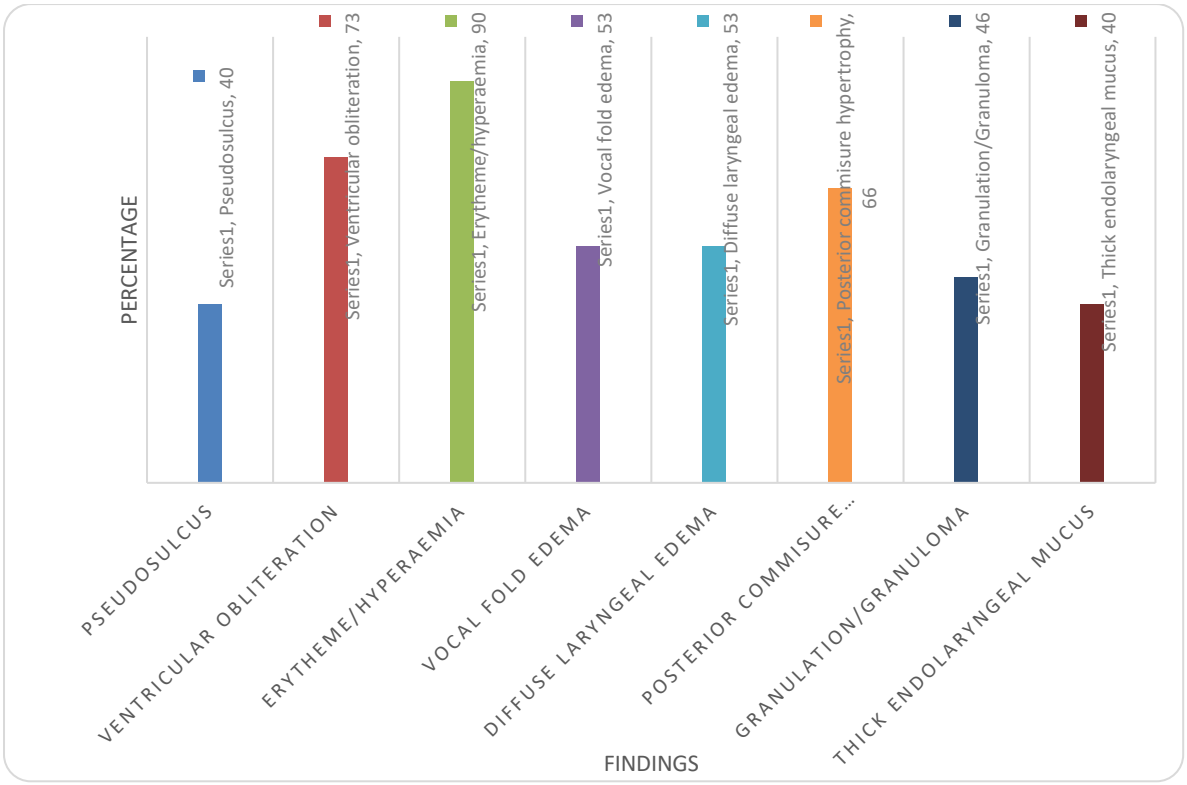

Figure 5: RFS findings

Reflux Finding Score is a scoring system used to assess the presence and severity of laryngopharyngeal reflux (LPR). LPR is a condition where stomach acid flows back up into the throat, causing symptoms like hoarseness, chronic cough, and throat irritation (Figure 5).

Percentage distribution of symptoms (RSI): The most prevalent laryngeal finding among the study participants was erythema or hyperemia, observed in 90% of the cases, indicating a widespread occurrence of mucosal inflammation or increased vascularity within the larynx. Following closely, ventricular obliteration was identified as the next common finding, present in 73% of the cases. This finding suggests a narrowing or closure of the laryngeal ventricles, possibly indicative of chronic irritation or inflammation affecting the laryngeal structures. Additionally, posterior commissure hypertrophy was noted in 66% of the cases, highlighting a significant proportion of participants exhibiting enlargement or swelling of the posterior laryngeal region. These findings collectively suggest a spectrum of laryngeal abnormalities associated with laryngopharyngeal reflux (LPR) in the study population, with erythema/hyperemia, ventricular obliteration, and posterior commissure hypertrophy being the most frequently observed manifestations.

Figure 6: RFS pre and post PPI therapy

Prior to initiating treatment with proton pump inhibitors (PPIs), the patients exhibited a mean Reflux Finding Score (RFS) of 12.66, indicating the severity of reflux-related findings. As depicted in Figure 6, following an 8-week course of PPI therapy, there was a noticeable decrease in the mean RFS to 9.46. This reduction suggests an initial improvement in the reflux-related symptoms and findings among the patients. Subsequently, after continuing the PPI therapy for a total duration of 16 weeks, the mean RFS further decreased to 6.80. This significant drop in the RFS underscores a continued amelioration of reflux-related symptoms and findings over the course of treatment. The progressive decline in the mean RFS values at both time points highlights the efficacy and sustained benefit of PPI therapy in managing laryngopharyngeal reflux (LPR) in the study population(figure 6).

Discussion

The prevalence of LPR disorders has significantly increased due to the continually evolving modern lifestyle. The symptoms of LPRD are thought to result from the irritating effects of gastric refluxate on the sensitive mucosa of the esophagus and pharynx [24]. Patients diagnosed with laryngopharyngeal reflux (LPR) should receive information about the characteristics of their condition and be advised on making lifestyle adjustments and dietary modifications [25].

In addition to guidance on lifestyle and dietary adjustments, the majority of patients will necessitate some type of medical treatment. The objective of medical care is to neutralize the acidity of gastric juice and improve the motility of the gastrointestinal system. Proton pump inhibitor treatment is necessary to resolve laryngeal symptoms and physical findings in people with LPR. PPIs are benzimidazoles that have been replaced with other substances. Upon oral administration, these substances are absorbed in the small intestine as prodrugs and concentrate in the acidic environment of the parietal cells. In this milieu, they undergo protonation and are transformed into an active and rather stable sulfonamide form. This molecule forms an irreversible bond with certain subunits on the outer surface of the luminal H+/K+-ATPase. The activation of this enzyme is the last step in acid secretion. Treatment with PPIs will decrease both the production of stomach acid in its resting state and the production of stomach acid when stimulated [26].

Our investigation revealed that 27 individuals (22.5%) were tobacco chewers, 15 individuals (12.5%) were smokers, and 12 individuals (10%) were alcoholics. The study included a larger population from rural areas, with a higher percentage from the lower middle socio-economic group. Our main focus was to raise awareness about the mild signs of LPR and promote early identification at the primary level using RFS and RSI. The treatment of LPR involves the use of four groups of drugs: Proton Pump inhibitors, H2-receptor antagonists, Prokinetic medicines, and Mucosal cytoprotectants. Proton pump inhibitors are often regarded as the primary form of medical treatment [27]. The medical literature still recommends empirical treatment with PPIs for 2-3 months as a cost-effective and beneficial therapy for the initial diagnosis of LPR [28]. The advice is to administer the complete dosage of PPIs for a minimum duration of 2-3 months during empirical therapy [28, 29]. Typically, the administration of PPIs occurs prior to meals in the majority of studies. Typically, a dose schedule of twice a day is used to effectively manage and regulate the amount of acid in the esophagus throughout both night-time and daytime. In our trial, we provided PPI (proton pump inhibitor) twice daily for duration of 12 weeks. The results showed a notable reduction in both the symptoms and signs associated with LPR (laryngopharyngeal reflux). The use of proton pump inhibitors (PPI) for a duration of 12 weeks resulted in a significant reduction in both reflux symptom frequency (RFS) and reflux severity index (RSI). In our study, we observed that patients who received a dosage of 20 mg of omeprazole twice daily for duration of 8 weeks experienced a significant improvement of 82% in their laryngeal symptoms, as well as a 74% improvement in laryngeal results. Weber [30] demonstrated complete (100%) symptom-free healing of LPR after a 4-week treatment with 40 mg omeprazole per day, as also shown in our study. Kamel and Hanson [31] found a 92% response rate. Wo and Hunter [32], Hanson et al. [33], Pieter Noordzij and Khidir [34], Tauber and Gross [35], and Williams and Szczesniak [36] reported response rates of 47% and 63% at 6 and 12 weeks, respectively, with omeprazole. Delgaudio and Waring [37], Issing and Karkos [38], Bilgem and Ogut [39], Toros and Toros [40], and Zelenik [41] also reported on this topic. In order to reduce the subjective nature of these evaluations, a team of researchers suggested the implementation of a scoring system called the RFS. This system is based on the endolaryngeal inflammatory results that are believed to indicate the presence of reflux. The English validation of this index was conducted in 2001 by Belafsky et al. and has since been extensively utilized in the literature as a diagnostic measure for LPR. The rating score assigns levels of severity to inflammatory symptoms and indicates the presence or absence of lesions that indicate the condition. The Reproducibility and Reliability of the RFS have been shown to be high. A patient with scores above 7 points has a 94% probability of having

LPR. This tool has also been utilized to monitor the progression of diseases and evaluate the effectiveness of treatment [42]. The majority of patients exhibited positive results for both RSI and RFS. This demonstrates that the RSI (Respiratory Severity Index) is a crucial clinical indicator that should be taken into account during the diagnosing process. Physicians can independently assess it and determine whether or not to conduct additional tests, based on the strong association between these symptomatic and endoscopic characteristics [13,14,42].

The gender distribution of the subjects in our study showed a 60% majority of females, which aligns with the findings of a study conducted by Patigaroo et al (2012) where females also accounted for 60% of the participants [13].However, a study conducted by Belafsky et al. (2002)[15] demonstrated a male predominance of 56%.The average reflux symptom index for the pretreatment group in our study was 24.80, and it decreased to 12 in the posttreatment group.

The Wilcoxon signed rank test was conducted on the pretreatment and post-treatment groups, yielding a p-value of less than 0.000, indicating a very significant result. Niran Hunchaisri and colleagues in Bangkok, Thailand conducted a comparison between the combination of Domperidone and omeprazole, and omeprazole alone. The overall RSI scores were compared between the groups prior to therapy. Following a three-month treatment period, there was a statistically significant moderate improvement in both the total RSI score and the specific sub scores for each group ($p<0.001$ each).The user's text is "[43]".

In 2014, Nasir A. Khan and his colleagues conducted a prospective study on patients with LPR. The most often observed laryngeal finding was redness or increased blood flow. The average Reflux Finding Score (RFS) of all patients was 13 before to treatment with proton pump inhibitors (PPI). There was a minimal reaction in physical findings after the initial 10 weeks of therapy, followed by a substantial improvement after 20 weeks of therapy. The user's text is "[44]". The results of our investigation did not indicate any disparity between genders in terms of the decrease in reflux symptom index or reflux finding score.

Conclusion

Laryngopharyngeal reflux (LPR) is a disease frequently identified in otorhinolaryngology practice when a range of non-specific signs and symptoms affecting the larynx are present. The use of Proton Pump Inhibitors (PPIs) as empirical therapy has been extensively acknowledged as both a diagnostic test and treatment for Laryngopharyngeal Reflux (LPR).

The most prevalent symptoms seen in patients with laryngopharyngeal reflux were a sensation of a foreign object in the throat and frequent throat clearing. The videolaryngoscopy revealed frequent findings of erythema of the arytenoids, posterior commisure hypertrophy, and ventricular obliteration. The use of proton pump inhibitors resulted in a notable enhancement in both the reflux symptom index and reflux finding score.

Combining proton pump inhibitors with lifestyle change offers significant alleviation to the patient. According to our study, omeprazole was determined to be more effective than other proton pump inhibitors. This conclusion was based on the observation that patients treated with omeprazole experienced greater reductions in RFS and RSI scores.

However, additional research is required to produce a conclusive diagnostic test for LPR and to ascertain the underlying mechanism of mucosal injury. This would aid in the development of novel treatments and enhance our understanding of the physiopathology of LPR.

Limitations: As this was a single center study with a comparatively short sample size, results of this study cannot be generalized. Generalization requires the support of results from similar large studies

Acknowledgments: The authors would like to thank all of the study participants and the administration of Department of ENT Government Erode Medical College, Perundurai, Tamilnadu, India for granting permission to carry out the research work.

Authors' contributions:

Dr G Satheesh kumar - conceptualization, data curation, investigation, methodology, project administration, visualization, writing—original draft, writing—review and editing; Dr R.Kalaimani -conceptualization, methodology, writing—original draft, writing—review and editing; Dr.M.Rajesh Kumar - conceptualization, visualization, supervision, writing—original draft, methodology, writing review and editing.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work. All authors have read and agreed to the published version of the manuscript**.**

Informed Consent: Informed consent was obtained from all individual participants included in the study.

Ethical Approval: All procedures performed involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964

Helsinki declaration and its later amendments or comparable ethical standards.

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