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Original Article

Ear, Nose and Throat Section

Acoustic Changes in Patients with Laryngopharyngeal Reflux Disease without Voice Complaints: A Cross-sectional Study

TULASI KOTA KARANTH[1], MANOJ KUMAR[2], SUPREET NAYYAR[3], RAHUL GUPTA[4], INDRAJEET CHAUHAN[5], LEKHRAJ SONKAR[6]

ABSTRACT

Introduction: In Laryngopharyngeal Reflux (LPR), refluxate rich in acid, pepsin, and bile regurgitates above the upper oesophageal sphincter onto the laryngeal mucosa. However, not all patients with LPR present with subjective voice changes. This may be due to a gradual change in voice that remains unnoticed. The clinical subtlety is important for diagnosis or at least awareness for better treatment and care.

Aim: To objectively determine preclinical acoustic changes in patients with LPR who have not reported any voice complaints.

Materials and Methods: This cross-sectional study was conducted on adult patients visiting the Out-patient department of a Tertiary Care Teaching Institute in Northern India, from September 2022 to October 2022. Patients with LPR but without voice changes were included in the study. They underwent multidimensional voice analysis during the phonation of the vowel /a/. Mean fundamental frequency (MF0), absolute jitter, absolute shimmer, and Soft Phonation Index (SPI) were analysed for the sample and compared to the gender-specific mean values provided by the software used. Statistical significance was determined using the one-sample t-test.

Results: A total of 27 participants (20 females, 7 males) completed the study. In the female group, the mean MF0 (204.30±32.49 Hz) was significantly lower, absolute jitter (92.41±87.93 μs), absolute shimmer (0.38±0.31 dB), and SPI (25.62±15.24) were significantly higher than the reference mean. In the male group, the mean MF0 (138.03 Hz), absolute jitter (104.01±84.28 μs), and absolute shimmer (0.34±0.16 dB) were not significantly different from the reference mean. However, SPI (25.09±16.95) remained significantly higher than the reference mean.

Conclusion: Increased jitter, shimmer, and SPI are primary acoustic changes observed in patients with LPR. These changes appear even before patients experience any voice changes.

Keywords: Dysphonia, Laryngitis, Oesophageal sphincter, Voice analysis

INTRODUCTION

LPR is a disease in which there is a backflow of gastric contents over the oesophageal sphincter into the larynx and hypopharynx [1]. LPR is seen in 1% of primary care practice [2], 10% of patients seeking outpatient otolaryngology consultation [3], and in about 50% of patients presenting with laryngeal or voice complaints [4]. It produces symptoms such as throat pain, coughing, hoarseness of voice, and globus sensation [1]. Laryngoscopic changes in severe reflux include congestion of the posterior larynx, retroarytenoid oedema, pseudo-sulci of vocal cords, presence of endolaryngeal mucus, contact ulcers, and granulomas. These changes do not always correlate with symptom severity. Dual-channel 24-hour pH monitoring is considered the gold standard for diagnosing LPR. In practice, this is reserved for patients who do not respond to oral anti-reflux therapy [5].

Treatment options are varied and usually include a combination of lifestyle modifications (elevation of the head end when supine, avoidance of alcohol, avoidance of diets rich in sour or oily foods) and medical management. The use of proton pump inhibitors and prokinetic agents is the primary mode of management. Surgical treatment options like laparoscopic fundoplication are reserved for patients with underlying hiatal hernia [2].

In LPR, refluxate rich in acid, pepsin, and bile regurgitates above the upper oesophageal sphincter onto the laryngeal mucosa. Copious and continuous exposure of the mucosa to this noxious refluxate induces inflammation, resulting in mucosal oedema and erythema [6]. Inflammation produced in the larynx secondary to LPR results in changes in voice quality evaluations [7]. However, not all patients with LPR present with subjective voice changes. This study was planned as there was no study in the literature that assessed the voice quality of patients with LPR but no subjective speech complaints. The aim was to objectively determine preclinical acoustic changes in patients with LPR who have never had a voice complaint.

MATERIALS AND METHODS

This cross-sectional study was conducted on adult patients visiting the out-patient department of a Tertiary Care Teaching Institute in Northern India, during the months of September and October 2022. Approval for this study was obtained from the institutional ethical committee (No: IEC-03/2022/55).

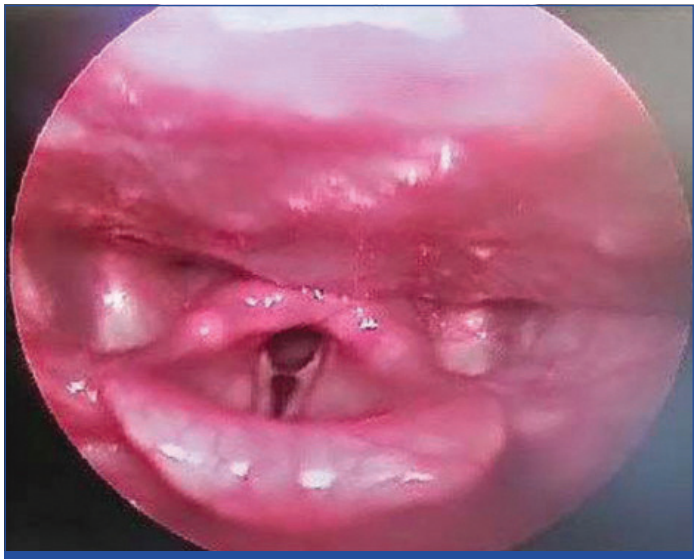
Inclusion criteria: Patients with LPR but without voice changes were included in the study after obtaining written informed consent.

Exclusion criteria: Those who had consumed alcohol, had a history of daily smoking, had a history of allergic rhinitis or bronchial asthma, or had undergone laryngeal surgery or thyroidectomy in the past and those patients who were on long-term medication such as aspirin or steroids were excluded from the study.

Procedure

Adult patients attending the outpatient department with symptoms of throat pain, foreign body sensation in the throat, burning sensation in the throat, or throat discomfort underwent evaluation by video laryngoscopy [Table/Fig-1]. The health of the laryngeal mucosa was

assessed using the Reflux Finding Score (RFS). It was concluded by Belafsky PC et al., that any individual with an RFS greater than seven had more than a 95% probability of having LPR [8]. Therefore, a cutoff of seven was used to objectively diagnose LPR [Table/Fig-2].



[Table/Fig-1]: Videolaryngoscopy image showing diffuse laryngeal hyperemia, vocal cord oedema, and mucous string across the vocal cord in a case of Laryngopharyngeal Reflux (LPR).

Findings	Score
Sub-glottis oedema	0=absent; 2=present
Ventricular obliteration	2 = partial; 4=complete
Erythema/hyperemia	2=arytenoids only; 4=diffuse
Vocal fold oedema	1=mild; 2=moderate
	3=severe; 4=obstructing
Diffuse laryngeal oedema	1=mild; 2=moderate
	3=severe; 4=obstructing
Granuloma/granulation of tissue	0=absent; 2=present

[Table/Fig-2]: Reflux finding score as adapted from Belafsky PC et al., [8].

The patient was taken to a noise-proof room and asked to phonate the vowel /a/ for ten seconds at their most comfortable pitch and loudness using a high-quality handheld microphone. The recorded voice was analysed using Visi-Pitch, Model 3950C (Pentax Medical, Hoya Inc., Japan). Multidimensional voice analysis was performed, and data were retrieved for mean fundamental frequency (MF0) (average of extracted fundamental frequency in a sustained vowel measurement), absolute jitter (random cycle-to-cycle variation of frequency), absolute shimmer (random peak-to-peak variation of loudness), and SPI. SPI is a parameter of a multidimensional voice program that reflects the approximation of vocal folds and is known to alter in cases of vocal cord oedema or nodular changes [9]. This is of particular interest to us as it helps determine vocal cord anatomical changes that may not be apparent on videolaryngoscopy or significant enough for patients to notice any voice change.

For the purpose of comparison, the study group was initially divided into males and females, as the normal ranges f or the parameters being measured are different for each gender and the reference ranges considered for comparison of each parameter (mean F0 for males: 145.223 Hz and females: 243.973 Hz; absolute jitter for males: 41.663 µs and females: 26.927 µs; absolute shimmer for males: 0.219 dB and females: 0.176 dB; SPI for males: 6.770 and females: 7.534).

STATISTICAL ANALYSIS

The mean with standard deviation was calculated for mean fundamental frequency, absolute jitter, absolute shimmer, and SPI for the two groups. The software used for voice analysis provided the normal range for these parameters for each gender.

Statistical significance was determined using a one-sample t-test. The Statistical Package for the Social Sciences (SPSS) version 21.0 was used for data analysis. A statistically significant association was considered to exist if the p-value was less than 0.05.

RESULTS

Twenty-seven patients participated in the study. The mean age of LPR patients was 45.6±14.3 years, with 7 (25.9%) being male and 20 (74.1%) being female. In the female group, the mean MF0 was 204.30±32.49 Hz, which was significantly lower than the reference mean of 243.97 Hz ($p<0.05$). Both absolute jitter and absolute shimmer were significantly higher than the reference mean of 26.927 µs and 0.176 dB, respectively ($p<0.05$).

In the male group, the mean SPI in the LPR group (25.09±16.95) was statistically higher than the reference mean of 6.770 ($p<0.05$) [Table/Fig-3].

Variables	Gender	Mean	SD	Reference mean	Mean difference	One sample t-test p-value
Mean fundamental frequency (Hz)	Female	204.30	32.49	243.973	-39.67	**<0.001**
	Male	138.03	25.14	145.223	-30.44	0.478
Absolute jitter (µs)	Female	92.41	87.93	26.927	65.48	0.004
	Male	104.01	84.28	41.663	62.35	0.098
Absolute Shimmer (dB)	Female	0.38	0.31	0.176	0.2010	0.010
	Male	0.34	0.16	0.219	0.119	0.096
Soft Phonation Index (SPI)	Female	25.62	15.24	7.534	18.085	**<0.001**
	Male	25.09	16.95	6.770	18.324	**0.029**

[Table/Fig-3]: Comparison of voice analyses of male and female groups with reference mean.

DISCUSSION

LPR is considered one of the main aetiological factors for patients presenting with voice disorders, with 85% of patients with LPR complaining of dysphonia, and 20% considering it their primary complaint [10].

Ross JA et al., conducted a study on 49 patients with LPR, divided into three groups based on their willingness to undergo 24-hour pH probe testing and the results of the test. Voice analysis was performed and compared to a healthy control group. They found that there was no significant difference in mean fundamental frequency (MF0) between the LPR groups and the control group, but percentage jitter and percentage shimmer were significantly higher in the LPR group [11].

Similar findings were demonstrated in a study conducted by Pribuisiene R et al. In this study, 108 patients with LPR were compared to 90 healthy individuals for various parameters including video stroboscopy, Voice Handicap Index (VHI), Grade of hoarseness, Roughness, Breathiness, Asthenia, and Strain (GRABS), and acoustic analysis. The results showed slight hoarseness on the GRABS scale and increased mean jitter, shimmer, and VHI in patients with LPR [12].

Another interesting study from Turkey compared 48 patients with LPR to 64 control subjects. The LPR group was further subdivided into those with objective LPR and subjective LPR based on the results of 24-hour ambulatory pH monitoring. The study revealed that LPR patients had significantly higher jitter and shimmer compared to the control group. However, there was no significant difference in jitter and shimmer between the objective LPR and subjective LPR groups [7].

In addition to the above, an exquisite study by Lechien JR et al., included 80 patients diagnosed with LPR and compared them to 80 healthy controls for various parameters such as Grade, Roughness, Asthenia, Breathiness, Strain, and Instability (GRABSI), VHI, percentage jitter, and percentage shimmer. Consistent with

other studies, they found that patients with LPR had worse scores for all parameters [13]. They also attempted the first large-scale comparison between male and female groups and found that females with LPR had stronger values of lower fundamental frequency and aerodynamic measurements like maximum phonation time. The rigorous use of inclusion and exclusion criteria and the large sample size recruited strengthens the significance of these findings.

Mean F0 represents the average value of all extracted period-to-period fundamental frequency values in a sustained vowel measurement [14]. In this study, the mean F0 for females was significantly lower than the normal mean, possibly indicating vocal cord thickening secondary to LPR. Jitter refers to the random cycle-to-cycle variations of F0, while shimmer refers to the variability of peak-to-peak amplitude in a voice sample. Jitter is typically attributed to structural asymmetries of the vocal folds, unpredictable effects of laryngeal mucus and airflow, muscle noise related to abnormal integration between motor units in the laryngeal muscles, and blood flow across laryngeal vessels [15]. Similar factors may also contribute to shimmer. An increase in jitter and shimmer corresponds to the "grade of hoarseness" and "roughness" aspects of the GRABS scale [15,16]. The increase in absolute jitter and absolute shimmer was observed across most studies in the literature, including the present study [7,12]. The only difference was the non-significant difference observed in the male group, which may be due to present study participants consisting of LPR patients without voice complaints and the smaller size of the male group.

In addition to these parameters, this study also evaluated SPI in the LPR group. SPI is one of the parameters analysed by multidimensional voice analysis programes. It reflects the average ratio of low-frequency harmonic energy to higher-frequency harmonic energy for the voiced area in the analysed signal. SPI indicates how well the vocal cords approximate and correlates with the "breathiness" and "asthenia" aspects of the GRABS scale [9]. It is known to detect small alterations in vocal cord mucosa and their impact on phonation. In LPR, there is oedema of the mucosa of the subglottis, posterior cords, and arytenoids, which can alter voice quality. These changes likely resulted in significantly higher SPI values for both males and females, even in the absence of noticeable symptoms. This suggests very subtle changes in the vocal cords.

Acoustic analysis can be performed on patients with perplexing throat symptoms to diagnose LPR [17], with a sensitivity as high as 76% [18]. Additionally, treating LPR with anti-reflux measures and proton-pump inhibitors can improve acoustical voice quality in these patients [19-21]. Furthermore, adding voice therapy to the standard LPR treatment can further improve acoustical voice quality [22]. Therefore, performing acoustic analysis in patients with LPR, regardless of the presence of voice complaints, is of paramount importance.

Limitation(s)

There are two limitations to this study. Firstly, the small sample size for the male group is a limitation. LPR is more commonly diagnosed in females [23], as higher levels of oestrogen and progesterone can reduce lower oesophageal sphincter pressure and decrease gastric motility, leading to prolonged gastric emptying time [24]. Additionally, this study included LPR patients without voice complaints, which represents a smaller subset of the LPR population.

Secondly, a comparison was made to the mean values provided by the software developed in Japan. Although various studies have shown that race does not significantly affect normal voice parameters [25-26], it would have been ideal to have a separate control group of age and gender-matched individuals from the general population. However, performing video laryngoscopy, an invasive procedure with associated financial costs, to rule out reflux disease is not recommended for the normal population. Therefore, the mean values for each gender and parameter as provided by the software were used for comparison instead.

CONCLUSION(S)

An increase in jitter, shimmer, and SPI are primary acoustic changes observed in patients with LPR. These changes can occur even before a patient experiences any noticeable voice changes, and they tend to appear earlier in females. This study opens up new possibilities for conducting more sophisticated clinical studies on the pathogenesis of voice changes in LPR patients. In clinical practice, this study highlights the usefulness of voice analysis in diagnosing LPR in patients with ambiguous throat complaints when a definitive diagnosis has not yet been made.

Author declaration: The views expressed in this paper are those of the authors and do not represent the views or positions of the Indian Armed Forces.

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PARTICULARS OF CONTRIBUTORS:
1. Specialist, Department of ENT-HNS, Army Medical Corps, Delhi, India.
2. Professor, Department of ENT-HNS, Army Medical Corps, Delhi, India.
3. Professor, Department of ENT-HNS, Army Medical Corps, Delhi, India.
4. Associate Professor, Department of ENT-HNS, Army Medical Corps, Delhi, India.
5. Specialist, Department of ENT-HNS, Army Medical Corps, Delhi, India.
6. Audiologist and Speech, Language Pathologist, Department of ENT-HNS, Army Medical Corps, Delhi, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Manoj Kumar,
Professor, Department of ENT-HNS, Army Medical Corps, Delhi-110010, India.
E-mail: manojkanzhuly@gmail.com

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