Soni *et al.*
The Egyptian Journal of Otolaryngology (2024) 40:116
https://doi.org/10.1186/s43163-024-00686-2

The Egyptian Journal of Otolaryngology

ORIGINAL ARTICLE Open Access

Does reflux symptom index and reflux finding score have clinical utility in the diagnosis of laryngopharyngeal reflux disease?

Annanya Soni[1*], Ankit Gupta[2], Arijit Jotdar[1], Amit Kumar Gupta[3] and Manoj Yadav[2]

Abstract

Background Reflux symptom index(RSI) and reflux finding score (RFS) are widely used scoring systems used to diagnose laryngopharyngeal reflux disease(LPRD). However many patients do visit the outpatient department with minimal symptoms not sufficient to fit the criteria described by Belafsky et al. for diagnosing LPRD. Most of these patients are provisionally diagnosed and treated for LPRD. Reflux symptom index(RSI) and reflux finding score (RFS) are widely used scoring systems used to diagnose(LPRD) (Belafsky PC et al., J Voice 16(2):274–7, 2002, Belafsky PC et al, Laryngoscope 111(8):1313–7, 2001).

RSI has nine questions that the patient must grade from 0 to 5. An abnormal score is greater than 13. Laryngopharyngeal reflux (LPR) may or may not be diagnosed using the RSI and RFS especially when patients present with minimum symptoms not sufficient to score more than 13 and 7 respectively. These patients may miss the diagnosis and have to be treated empirically. Pepsin's presence in the saliva is indicative of reflux as pepsin is a gastric enzyme (NICE advice on Peptest for diagnosing gastro-oesophageal reflux, 2015, Wood JM et al., J Laryngol Otol 125(12):1218–24, 2011). Patients with minimum symptoms may be missed if diagnosis relies only on RSI AND RFS. The present study aims to see the correlation of pepsin-proven LPRD and RSI and RFS.

Methods This is a prospective study, 49 patients with symptoms suggestive of LPRD who tested positive for the pepsin test were further analysed for RSI and RFS. A cut-off value of > 25 ng/mL was considered diagnostic of LPRD (Dhillon VK et al., Curr Gastroenterol Rep 18(8):44, 2016).

Result The average RSI and RFS were respectively 10 and 4. The mean age of the patients in the study was 39 years and the mean weight was 60 kg. The association between RSI and PEPSIN detection is considered to be not statistically significant. Chi-squared equals 0.086 with 1 degree of freedom. The two-tailed *P* value equals 0.7698. Chi-squared equals 0.233 with 1 degree of freedom. The two-tailed *P* value equals 0.6295. The association between RFS and PEPSIN detection is considered to be not statistically significant.

In terms of correlation analysis, neither the RSI nor the RFS had Pearson's correlation coefficient that was statistically significant.

Conclusion Since salivary pepsin detection and the RSI do not have any significant correlation, the RSI is not a valid diagnostic method for LPR and should not be used exclusively.

Level of evidence 4.

Keywords Saliva, Reflux symptom index, Reflux finding score, Laryngopharyngeal reflux, Pepsin

*Correspondence:
Annanya Soni
annanyasoni2004@gmail.com
Full list of author information is available at the end of the article

Background

Laryngopharyngeal reflux disease(LPRD) is often diagnosed based on symptoms after other illnesses have been ruled out. Reflux symptom index(RSI) and reflux finding score (RFS) are widely used scoring systems used to diagnose laryngopharyngeal reflux disease(LPRD) [1, 2]. Table 1 list a symptom-based questionnaire called the RSI which is frequently used to identify LPRD. It has nine questions that the patient must grade from 0 to 5. An abnormal score is one that is greater than 13. Table 2 mentions reflux finding score where a score more than 7 is considered diagnostic for LPRD. Laryngopharyngeal reflux (LPR) may or may not be diagnosed using the RSI and RFS especially when patients present with minimum symptoms not sufficient to score more than 13 and 7 respectively. These patients may miss the diagnosis and have to be treated empirically.

LPRD patients make up a significant section of the outpatient otolaryngology department and usually treated empirically.

The salivary pepsin test is one of the novel LPR diagnostic techniques that stands out. An immunological in vitro test called PEP-test (RD Biomed, Hull, UK) can determine whether saliva contains pepsin at concentrations of at least 16 ng/mL [3]. Pepsin's presence in the saliva is indicative of reflux as pepsin is a gastric enzyme [4, 5].

Patients with minimum symptoms may be missed if diagnosis relies only on RSI AND RFS. The present study aims to see the correlation of pepsin proven LPRD and RSI and RFS.

Method

This was a hospital-based descriptive cross-sectional study conducted in outpatient department of otorhinolaryngology and surgery, after approval from institute's Ethics Committee and informed consent was taken from all the patients. The study was funded by institute research cell [IM006].

Inclusion and exclusion criteria

Patients aged 18 to 50 years who presented with symptoms suggestive of LPRD for more than 1 month were included. All eligible patients were subjected to pepsin estimation in saliva. Forty-nine eligible patients who tested positive for pepsin in saliva were considered for further evaluation and analysis. Patients with voice and throat symptoms lasting less than a month or those with

Table 1 Reflux symptom index(RSI) [1]. Finding within the last month, how did the following problems affect you? 0 = No problem 5 = Severe Problem

1. Hoarseness or a problem with your voice	0	1	2	3	4	5
2. Clearing your throat	0	1	2	3	4	5
3. Excess throat mucus or postnasal drip	0	1	2	3	4	5
4. Difficulty swallowing food, liquids or pills	0	1	2	3	4	5
5. Coughing after you ate or after lying down	0	1	2	3	4	5
6. Breathing difficulties or choking episodes	0	1	2	3	4	5
7. Troublesome or annoying cough	0	1	2	3	4	5
8. Sensations of something sticking in your throat or a lump in your throat	0	1	2	3	4	5
9. Heartburn, chest pain, indigestion or stomach acid coming up	0	1	2	3	4	5
Total						

Table 2 Reflux finding score (RFS) [2]

Findings	Score
Subglottic edema	0 = Absent, 2 = Present
Ventricular erythema	0 = None, 2 = Partial, 3 = Complete hyperemia
Vocal fold edema	0 = None, 2 = Mild, 3 Severe, 4 = Obstructive
Diffuse laryngeal edema	0 None, 2 = Mild, 3 = Severe, 4 = Obstructive
Posterior commissure	0 = None, 2 = Mild, 3 = Severe, 4 = Obstructive hypertrophy
Granuloma/granulation	0 = Absent, 2 = Present of tissue
Thick endolaryngeal mucus	0 = Absent, 2 = Present

additional potential underlying causes of voice changes, such as tumours or long-term laryngeal irritants like smoking cigarettes, were eliminated. Patients who had received antireflux medication within the last 15 days were excluded. Patients with history of allergy, hypothyroidism were excluded.

All patients with symptoms suggestive of laryngopharyngeal reflux, after ruling out allergic symptoms, organic lesions, and infective conditions, were subjected to pepsin estimation in saliva. The patients with symptoms suggestive of LPRD underwent salivary pepsin estimation and were analyzed in terms of RSI and RFS scoring. A 4-h fasting unstimulated salivary sample was taken and transferred to the lab for pepsin detection using the peptest kit. Positive pepsin detection indicated laryngopharyngeal reflux. A cut-off value of > 25 ng/mL was considered diagnostic of LPRD [6, 7].

Patients with positive pepsin detection and symptoms consistent with LPRD may be considered as having reflux since pepsin is not present in the upper airways. RSI and RFS scoring were analysed.

Results

A total of 49 symptomatic Patients with positive salivary pepsin were enrolled in the study for further analysis. the patients were grouped in two groups on the basis of diagnostic cut-off value of pepsin.RSI and RFS were estimated in both the groups. The mean age of the patients in the study was 39 years and the mean weight was 60 kg. The mean RSI was 10 and the mean RFS was 4. On correlation analysis, Pearson's correlation coefficient was not statistically significant for both RSI and RFS as cited in Figs. 1 and 2.

According to Table 3, Chi-squared equals 0.086 with 1 degree of freedom. The two-tailed *P* value equals 0.7698. The association between RSI and PEPSIN detection is considered to be not statistically significant.

According to Table 4, Chi-squared equals 0.233 with 1 degree of freedom. The two-tailed *P* value equals 0.6295. The association between RFS and PEPSIN detection is considered to be not statistically significant.

Discussion

According to previous studies, 10% of otolaryngology consults are for LPR [8, 9]. In the field of otolaryngology, laryngopharyngeal reflux is a common but sometimes misdiagnosed condition. Although RSI and RFS are practical, easy-to-use scales, they cannot be regarded as diagnostic tools in and of themselves. Although RSI questionnaire is helpful in ordinary clinical practise, it does not rule out other inflammatory pharyngolaryngeal illnesses because none of the laryngeal symptoms it includes are pathognomonic of LPR neither its low score rule out LPR. Similarly RFS scoring can miss a lot of symptomatic reflux patients.

Friedman et al. noted that a diagnosis of LPR cannot be made solely on the basis of the presence of symptoms [10]. Multichannel intraluminal impedance test and the 24-h dual-channel pH-metry are now regarded as the gold standard for the diagnosis of LPR, but are invasive and expensive procedures that cannot be done on all patients who have a clinical suspicion of LPR [11].

Salivary pepsin detection is a relatively new technique that is gaining popularity. Salivary pepsin test can be a worthwhile, reliable alternative diagnostic tool

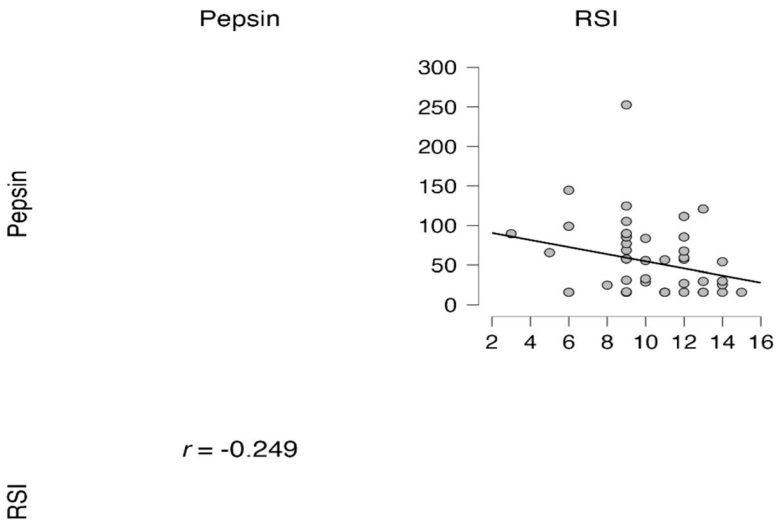

Fig. 1 Correlation plot between RSI and pepsin

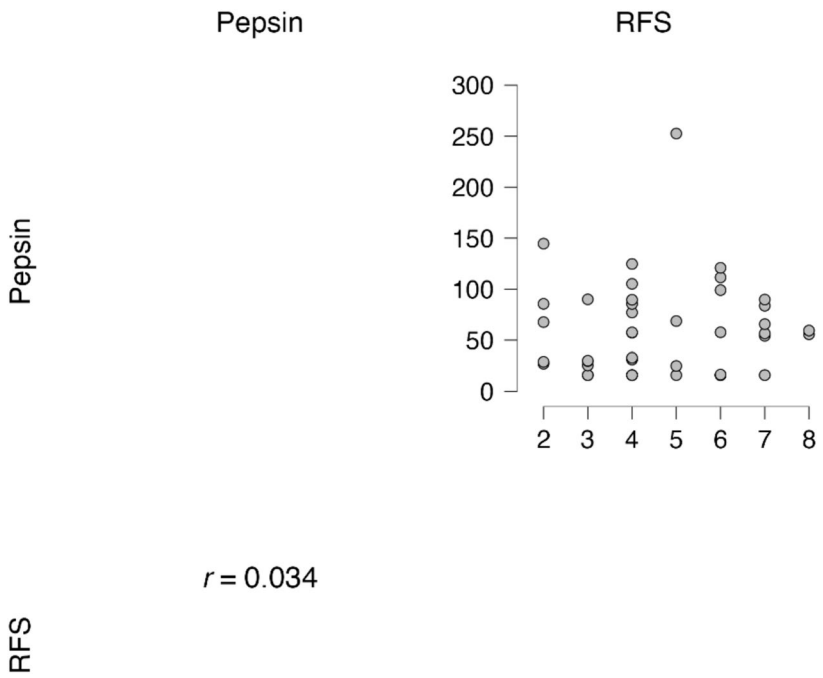

Fig. 2 Correlation plot between RFS and pepsin

Table 3 Contingency table between RSI and pepsin

	Pepsin > 25 ng/ml	Pepsin < 25 ng/ml
RSI > = 13	5	4
RSI < 13	27	13

Table 4 Contingency table between RFS and pepsin

	Pepsin > 25 ng/ml	Pepsin < 25 ng/ml
RFS > = 7	7	2
RFS < 7	25	15

in a patient having symptoms of LPRD, with the added advantage of simplicity of usage and office-based test.

In a study by Barona-Lleo L et al., the peptest's specificity was 98% [12]. There is a limited chance of false positive results when the test yields a positive result, which might be regarded as diagnostic of LPR. A negative test result in patients who have a clinical suspicion of LPR does not, however, rule out the possibility of disease. Similarly in another study, the results of 24-h pH monitoring were contrasted with those from in vitro pepsin detection tests. The presence of pepsin in saliva in a patient suspected of LPR can be a strong indicator of LPRD, according to the study's high specificity rate. The pepsin detection test had a high specificity of 100%, though sensitivity is low. pH values of the study group and the pepsin-positive patients were compared, it was found to be more acidic in the pepsin-positive patients [13].

The Peptest demonstrated a modest diagnostic value for GERD/LPRD in a meta-analysis, with pooled sensitivity of 62%, pooled specificity of 74%, and an area under the curve of 0.70. The study, which comprised 897 controls and 2401 patients, found no statistically significant difference in diagnostic value between the cut-off values of over 25 ng/ml and below 25 ng/ml [14].

In a study by Wang et al., RSI demonstrated low sensitivity, a low positive predictive value, and a low negative predictive value. Only 0.133 was the kappa value, indicating poor consistency between the RSI and 24-h pH monitoring. The RSI and pH monitoring, the two LPR diagnosis techniques, do not yield reliable results. The study concluded that, the RSI cannot be used in place of reflux monitoring as an LPR diagnostic tool. However, the negative predictive value of RSI is very large. Patients who might benefit more from pH monitoring can be identified using RSI in nations or locations with limited reflux monitoring conditions [15]. RSI, and RFS were discovered to have weak correlations with LPR detection in another investigation employing the Dx-pH system [16]. Similar results are derived in our study.

Whereas, study by Weitzendorfer et al., found a significant correlation between the values of salivary pepsin and the RSI score in patients with LPR diagnosed by 24 HOUR pH monitoring [17].

There are many studies which demonstrate a substantial correlation between positive salivary pepsin and both RSI > 13 and RFS > 7. Likewise, favourable correlations were identified for positive pepsin and a mix of RFS > 7 and RSI > 13. But all these studies included patients on the basis of RFS and RSI scoring so there are chances that many patients with low scores may have been excluded [18]. All symptomatic patients irrespective of their RSI and RFS scores had been included in this study.

Small sample size is a limitation in this study, further studies with larger sample size is needed to support the findings.

Conclusion

Salivary pepsin is an alternative, cost-effective, noninvasive measurement tool to assist in the diagnosis of LPR. The RSI and salivary pepsin monitoring, the two LPR diagnosis techniques, do not yield reliable results. Therefore RSI cannot be used as an LPR diagnostic tool. However, RSI can be reliably used as a screening test to exclude LPRD.

Since there was inadequate agreement in the diagnosis of LPR between the RSI and Salivary pepsin detection, the RSI is not a reliable initial screening technique for LPR and should not be relied upon exclusively. The RSI could not be compared to a gold standard investigation since our institute does not offer 24-h pH monitoring, which is one of the study's shortcomings. To support our findings, additional research with a bigger sample size is required.

Acknowledgements
None.

Authors' contributions
AS: contributed to data gathering, clinical evaluation and management of the patient, and supervision of the project. AG: Conducting the tests and writing manuscript in consultation with Annanya Soni. AKG: contributed to data gathering, clinical evaluation and management of the patient and and preparing for submission. AJ: contributed to data gathering, clinical evaluation and management of the patient and editing the manuscript. MY: contributed to data gathering and conducting the tests. All authors read and approved the final manuscript.

Funding
The study was funded by All India Institute Of Medical Sciences, Raebareli. [IM006].

Availability of data and materials
Data included in the manuscript is available with the author and can be submitted on request.

Declarations

Ethics approval and consent to participate
The study has been approved by institute ethics committee. AIIMS ethics committee 2021–2-IM-1. Informed consent was taken from all the patients.

Consent for publication
Informed written consent obtained for participation and publication from all participants.

Competing interests
The authors declare that they have no competing interests.

Author details
[1]Department of ENT, AIIMS, Uttar Pradesh, Raebareli, India. [2]Department of Biochemistry, AIIMS, Raebareli, India. [3]Department of Surgery, AIIMS, Raebareli, India.

Received: 21 November 2023 Accepted: 13 September 2024
Published online: 27 September 2024

References

1. Belafsky PC, Postma GN, Koufman JA (2002) Validity and reliability of the reflux symptom index (RSI). J Voice 16(2):274–277. https://doi.org/10.1016/s0892-1997(02)00097-8. PMID: 12150380
2. Belafsky PC, Postma GN, Koufman JA (2001) The validity and reliability of the reflux finding score (RFS). Laryngoscope 111(8):1313–1317. https://doi.org/10.1097/00005537-200108000-00001. PMID: 11568561
3. NICE (2015) Peptest for diagnosing gastro-oesophageal reflux. Available from: https://www.nice.org.uk/guidance/mib31/resources/peptest-for-diagnosing-gastrooesophageal-reflux-63499100556229
4. Wood JM, Hussey DJ, Woods CM et al (2011) Biomarkers and laryngopharyngeal reflux. J Laryngol Otol 125(12):1218–1224. https://doi.org/10.1017/S0022215111002234. Epub 2011 Sep 14 PMID: 21914248
5. Dhillon VK, Akst LM (2016) How to approach laryngopharyngeal reflux: an otolaryngology perspective. Curr Gastroenterol Rep 18(8):44. https://doi.org/10.1007/s11894-016-0515-z. PMID: 27417389
6. Bozzani A, Grattagliano I, Pellegatta G et al (2020) Usefulness of pep-test for laryngo-pharyngeal reflux: A pilot study in primary care. Korean J Fam Med 40(4):250–255. https://doi.org/10.4082/kjfm.18.0207. Epub 2020 May 28. PMID: 32460472; PMCID: PMC7385291
7. Hayat JO, Yazaki E, Moore AT et al (2014) Objective detection of esophagopharyngeal reflux in patients with hoarseness and endoscopic signs of laryngeal inflammation. J Clin Gastroenterol 48(4):318–327. https://doi.org/10.1097/MCG.0000000000000011. PMID: 24172180
8. Hammer HF (2009) Reflux-associated laryngitis and laryngopharyngeal reflux: a gastroenterologist's point of view. Dig Dis 27(1):14–17. https://doi.org/10.1159/000210098. Epub 2009 May 8 PMID: 19439955
9. Campagnolo AM, Priston J, Thoen RH et al (2014) Laryngopharyngeal reflux: diagnosis, treatment, and latest research. Int Arch Otorhinolaryngol 18(2):184–91. https://doi.org/10.1055/s-0033-1352504. Epub 2013 Nov 5. PMID: 25992088; PMCID: PMC4297018
10. Friedman M, Hamilton C, Samuelson CG et al (2012) The value of routine pH monitoring in the diagnosis and treatment of laryngopharyngeal reflux. Otolaryngol Head Neck Surg 146(6):952–958. https://doi.org/10.1177/0194599812436952. Epub 2012 Feb 2 PMID: 22301104
11. Calvo-Henríquez C, Ruano-Ravina A, Vaamonde P et al (2017) Is pepsin a reliable marker of laryngopharyngeal reflux? A systematic review. Otolaryngol Head Neck Surg 157(3):385–391. https://doi.org/10.1177/0194599817709430. Epub 2017 Jun 6 PMID: 28585488
12. Barona-Lleo L, Barona-De Guzman R, Krstulovic C (2019) The diagnostic usefullness of the salivary pepsin test in symptomatic laryngopharyngeal reflux. J Voice 33(6):923–928. https://doi.org/10.1016/j.jvoice.2018.07.008. Epub 2018 Oct 9 PMID: 30314932
13. Ocak E, Kubat G, Yorulmaz İ (2015) Immunoserologic pepsin detection in the saliva as a non-invasive rapid diagnostic test for laryngopharyngeal reflux. Balkan Med J 32(1):46–50. https://doi.org/10.5152/balkanmedj.2015.15824. Epub 2015 Jan 1. PMID: 25759771; PMCID: PMC4342137

14. Guo Z, Jiang J, Wu H, Zhu J, Zhang S, Zhang C (2021) Salivary peptest for laryngopharyngeal reflux and gastroesophageal reflux disease: A systemic review and meta-analysis. Medicine (Baltimore) 100(32):e26756. https://doi.org/10.1097/MD.0000000000026756
15. Wang JY, Peng T, Zhao LL et al (2021) Poor consistency between reflux symptom index and laryngopharyngeal pH monitoring in laryngopharyngeal reflux diagnosis in Chinese population. Ann Transl Med 9(1):25. https://doi.org/10.21037/atm-20-4783.PMID:33553318;PMCID:PMC7859794
16. Wang G, Qu C, Wang L et al (2019) Utility of 24-hour pharyngeal pH monitoring and clinical feature in laryngopharyngeal reflux disease. Acta Otolaryngol 139(3):299–303. https://doi.org/10.1080/00016489.2019.1571280. PMID: 31056040
17. Weitzendorfer M, Antoniou SA, Schredl P, Witzel K, Weitzendorfer IC, Majerus A, Emmanuel K, Koch OO (2020) Pepsin and oropharyngeal pH monitoring to diagnose patients with laryngopharyngeal reflux. Laryngoscope 130(7):1780–1786. https://doi.org/10.1002/lary.28320
18. Divakaran S, Rajendran S, Thomas RM, Jacob J, Kurien M (2021) Laryngopharyngeal reflux: symptoms, signs, and presence of pepsin in saliva - a reliable diagnostic triad. Int Arch Otorhinolaryngol 25(2):e273–e278. https://doi.org/10.1055/s-0040-1709987

Publisher's Note