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The association between the reflux symptoms index and nasal symptoms among patients with non-allergic rhinitis

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Abstract

Background. Laryngopharyngeal reflux symptoms assessed with the reflux symptom index can overlap with non-allergic rhinitis symptoms. This study aims to explore the association between the reflux symptom index and nasal symptoms in non-allergic rhinitis patients.

Methods. A cross-sectional study was conducted on consecutive adults with non-allergic rhinitis. The reflux symptom index (score of more than 13 = laryngopharyngeal reflux) and nasal symptoms (categorised as mild (total score of 0–3), moderate (4–7) or severe (8–12)) were assessed.

Results. The study included 227 participants (aged 58.64 ± 12.39 years, 59.5 per cent female). The reflux symptom index scores increased with total nasal symptom scores (mild *vs* moderate *vs* severe, 8.61 ± 6.27 *vs* 12.94 ± 7.4 *vs* 16.40 ± 8.10; $p < 0.01$). Logistic regression indicated that laryngopharyngeal reflux is more likely in patients with severe nose block (odds ratio 5.47 (95 per cent confidence interval = 2.16–13.87); $p < 0.01$).

Conclusion. Laryngopharyngeal reflux symptoms are associated with nasal symptom severity, and nasal symptoms should be primarily treated. Those with predominant nose block and laryngopharyngeal reflux symptoms are more likely to have laryngopharyngeal reflux.

Introduction

Non-allergic rhinitis is a non-immunoglobulin E mediated disease with various underlying pathologies.[1] Laryngopharyngeal reflux (LPR) has been associated as an underlying pathology.[2] Laryngopharyngeal reflux is a chronic inflammatory condition of the larynx caused by exposure to gastric content and presents with chronic throat symptoms. It is assessed using the reflux symptom index, and a score of more than 13 predicts this diagnosis.[3]

Non-allergic rhinitis patients with chronic throat symptoms and high reflux symptom index scores will raise suspicion of LPR. Clinicians treating non-allergic rhinitis may initiate a trial of high-dose proton pump inhibitors to both diagnose and treat LPR.[4] However, throat symptoms may also be caused by nasal pathologies.[5] The severity of nasal symptoms may contribute to a high reflux symptom index score. This study aimed to assess the reflux symptom index among non-allergic rhinitis patients and determine its relationship with nasal symptom severity. It is hoped that the findings will aid clinicians in the careful selection of patients who need reflux therapy.

Methods

This was a cross-sectional study. Appropriate ethics approval from the institutional review board was obtained prior to study commencement, and participants provided informed consent.

Study population

Consecutive adult patients (aged 18 years or more) with chronic rhinitis symptoms and negative skin prick test results were recruited. All patients complained of experiencing at least one of the following nasal symptoms for the previous six months: nasal obstruction, runny nose, nasal itching and sneezing. A skin prick test was performed within one year of recruitment. Those with negative skin prick test results were defined as non-allergic rhinitis patients. We excluded individuals who had received treatment with a proton pump inhibitor within the previous four weeks.

Nasal symptoms

All patients completed a self-administered questionnaire, which included assessment of nasal symptom severity and the reflux symptom index. The severity of individual nasal

Main Article

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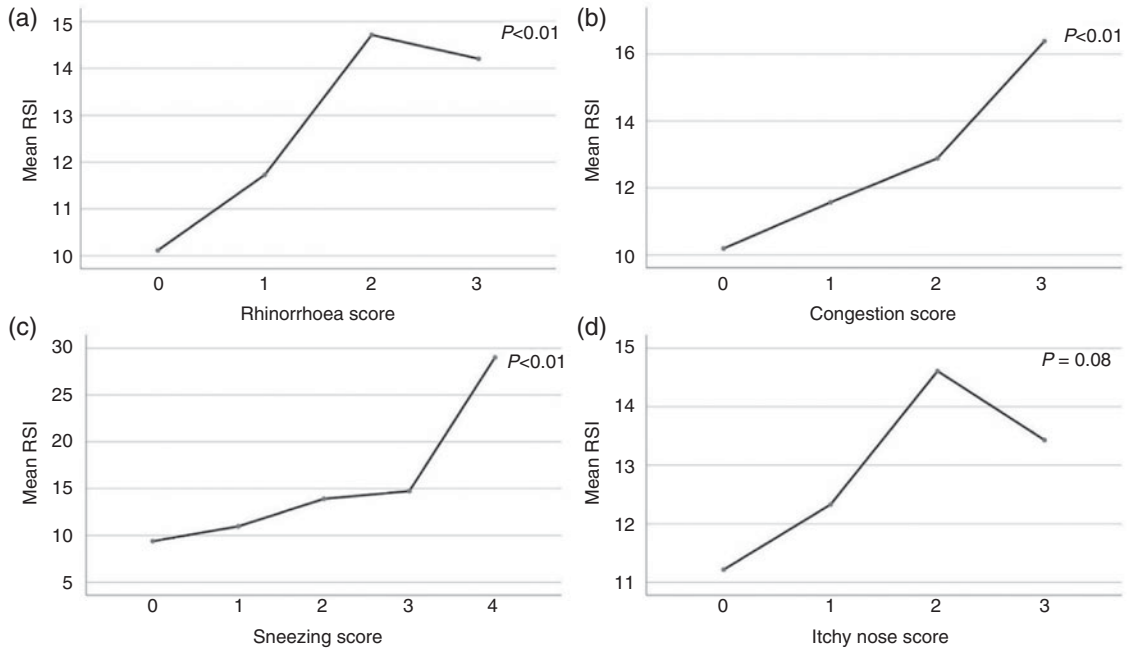

Fig. 1. The association between mean reflux symptom index score (RSI) and individual nasal symptom scores (0–3) for: (a) rhinorrhoea ($p < 0.01$), (b) congestion ($p < 0.01$), (c) sneezing ($p < 0.01$) and (d) itchy nose ($p = 0.08$).

symptoms – nasal obstruction, runny nose, nasal itching and sneezing – were scored on a scale from 0 to 3. Participants gave a score of 0 (none) if there were no symptoms; 1 (mild) for tolerable symptoms causing minimal awareness; 2 (moderate) if there was definite awareness of symptoms that were bothersome but tolerable; and 3 (severe) if the symptoms were hard to tolerate and interfered with activities and/or sleeping. These scores give a total nasal symptom score ranging from 0 to 12. Total nasal symptom scores were categorised into mild (0–3), moderate (4–7) or severe (8 or more).

Reflux symptoms index

The reflux symptom index[3] assessed nine LPR-related symptoms (hoarseness, clearing of throat, excess throat mucus, difficulty in swallowing, coughing out mucus, breathing difficulties, troublesome cough, sensation of something sticking in the throat, and heartburn). These symptoms were scored on a scale of 0 (no problem) to 5 (severe problem). A score of more than 13 was defined as LPR.

Skin prick test

A skin prick test was performed to assess sensitisation to a panel of allergens in a 50 per cent glycerine solution. The allergens tested included common aeroallergens in Malaysia (dust mite (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae* and *Blomia tropicalis*),[6,7] cockroach, mixed mould, mixed grass and cat). Participants did not use oral antihistamines for at least 72 hours prior to testing. Both a negative glycerine control and a positive histamine control were used. The wheal size was measured 15 minutes after application. A wheal diameter of 3 mm or more with a non-reactive negative control was defined as a positive test. Non-allergic rhinitis patients were defined as those who tested negative for all allergens on the skin prick test.

Statistical analysis

All statistics performed and graphic representations were generated using SPSS software, version 25 (IBM, Armonk, New York, USA). The total nasal symptom score (score range of 0–12) and the individual symptom score (range of 0–3) were treated as ordinal data. The reflux symptoms index data were treated as both continuous and categorical (LPR was defined as a reflux symptom index score of more than 13, and non-LPR was defined as a reflux symptom index score of 13 or lower). The relationship between reflux symptom index and nasal symptoms was assessed with one-way analysis of variance and Spearman's rho. The nasal symptom scores were compared between patients with and without LPR. Categorical data were analysed using the chi-square test, ordinal data were analysed with Kendall's tau-b test and continuous data were analysed with student's *t*-test. Binary logistic regression was used to assess the probability of LPR based on the nasal symptom score.

Results

The study included 227 participants, with a mean ± standard deviation (SD) age of 58.64 ± 12.39 years, of whom 59.5 per cent were female. The total nasal symptom score was moderate (score 4–7) in 48.9 per cent and severe (score of 8 or higher) in 22.9 per cent of participants. The most frequent individual nasal symptoms scored as moderate or severe (score of 2 or higher) were sneezing (50.2 per cent) and congestion (49.8 per cent), followed by rhinorrhoea (44.1 per cent) and itchy nose (31.7 per cent). The mean ± SD reflux symptom index score was 12.51 ± 7.6, and the median was 12 (interquartile range, 6–18). Of the participants, 45.4 per cent were determined as having LPR.

Individual reflux symptom index scores among the non-allergic rhinitis patients were highest for excess throat mucus (mean ± SD = 2.35 ± 1.69) and throat clearing (2.25 ± 1.59). This was followed by heartburn, chest pain or indigestion (1.57 ± 1.57), troublesome or annoying cough (1.49 ± 1.58),

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Table 1. Characteristics of patients with non-allergic rhinitis with and without LPR

Characteristic	LPR group (RSI score > 13)	Non-LPR group (RSI score ≤ 13)	*P*-value
Patients (*n*)	103	124	
Females (%)	60.5	58.2	0.73
Age (mean ± SD; years)	60.77 ± 11.50	56.87 ± 12.85	0.02*
TNSS (*n*)			
– 0–3	14.6	39.5	<0.01*
– 4–7	52.4	46.0	
– ≥8	33.0	14.5	
Rhinorrhoea score (*n*)			
– 0	19.4	33.1	0.01*
– 1	28.2	29.8	
– 2	28.2	21.8	
– 3	24.3	15.3	
Nasal congestion score (*n*)			
– 0	21.4	37.1	<0.01*
– 1	20.4	28.2	
– 2	25.2	22.6	
– 3	33.0	12.1	
Sneezing score (*n*)			
– 0	7.8	16.1	<0.01*
– 1	31.1	41.9	
– 2	33.0	24.2	
– 3	28.2	17.7	
Itchy nose score (*n*)			
– 0	35.0	41.9	0.20
– 1	28.2	30.6	
– 2	28.2	17.7	
– 3	8.7	9.7	

*Indicates statistical significance. LPR = laryngopharyngeal reflux; RSI = reflux symptom index; SD = standard deviation; TNSS = total nasal symptom score

Table 2. Binary logistic regression model to predict high RSI scores among non-allergic rhinitis patients*

Variables	OR (95% CI)	*P*-value
Constant	0.01	<0.01†
Sinus grades (base: score of 0)		
Rhinorrhoea score		0.51
– 1	1.58 (0.71–3.53)	0.26
– 2	1.78 (0.75–4.24)	0.19
– 3	1.89 (0.69–5.13)	0.21
Nasal congestion score		<0.01†
– 1	1.17 (0.52–2.65)	0.71
– 2	1.82 (0.82–4.14)	0.15
– 3	5.47 (2.16–13.87)	<0.01†
Sneezing score		0.18
– 1	1.47 (0.53–4.08)	0.46
– 2	2.52 (0.88–7.20)	0.08
– 3	2.88 (0.90–9.27)	0.08
Itchy nose score		0.36
– 1	1.43 (0.66–3.09)	0.36
– 2	1.32 (0.56–3.14)	0.53
– 3	0.49 (0.14–1.66)	0.25
Age	1.04 (1.02–1.07)	<0.01†

*Chi-square < 0.01; log-likelihood ratio = 272.42; Nagelkerke R^2 = 0.22; Cox and Snell R^2 = 0.16; Hosmer–Lemeshow test p = 0.39; and classification accuracy = 66.5 per cent. †Indicates statistical significance. RSI = reflux symptom index; OR = odds ratio; CI = confidence interval

coughing after eating or lying down (1.33 ± 1.57), breathing difficulty or choking episodes (1.21 ± 1.52), sensation of something sticking or a lump (0.99 ± 1.41), hoarseness (0.94 ± 1.46) and, least severe of all, difficulty swallowing food, liquids or pills (0.41 ± 1.00).

Reflux symptom index scores were higher in the moderate to severe total nasal symptom score group (mean ± SD scores for mild *vs* moderate *vs* severe groups were 8.61 ± 6.27 *vs* 12.94 ± 7.4 *vs* 16.40 ± 8.10, respectively; $p < 0.01$). The reflux symptom index was associated with all severe individual nasal symptoms except itchy nose (Figure 1).

There was weak correlation between the reflux symptom index and total nasal symptom score (Spearman's rho = 0.37; $p < 0.01$), rhinorrhoea (Spearman's rho = 0.290; $p < 0.01$), nasal congestion (Spearman's rho = 0.246; $p < 0.01$), sneezing (Spearman's rho = 0.251; $p < 0.01$) and itchy nose (Spearman's rho = 0.137; $p < 0.05$).

Among those with LPR, there were more individuals with a moderate to severe total nasal symptom score. Laryngopharyngeal reflux was also associated with rhinorrhoea, nasal congestion and sneezing, but not itchy nose (Table 1). Logistic regression analysis indicated that LPR was more likely in older age (odds ratio = 1.04 (95 per cent confidence interval (CI) = 1.02–1.07)). Among the nasal symptoms, nasal congestion was predictive of LPR (odds ratio = 5.47 (95 per cent CI = 2.16–13.87—)) (Table 2).

Discussion

Among patients with non-allergic rhinitis, 45 per cent had a reflux symptom index score of more than 13, defined as LPR. However, they did not necessarily have true LPR, as nasal symptoms contribute to a high reflux symptom index, and more severe nasal symptoms lead to higher reflux symptom index scores. Patients with non-allergic rhinitis tend to complain of excess throat mucus and throat clearing, which is also associated with post-nasal drip or chronic throat irritation due to backflow of nasal secretions. Therefore, moderate to severe nasal symptoms contribute to LPR symptoms and need to be addressed first. Patients with mild nasal symptoms and/or predominance of nasal congestion with a high reflux symptom index score may be considered for early LPR intervention.

In this study, the mean ± SD reflux symptom index score was 12.51 ± 7.6, and, as stated above, 45 per cent of patients had a reflux symptom index score of more than 13. This is similar to the findings of a study that compared asthmatics (50 per cent of whom had concomitant allergic rhinitis) with healthy controls (mean ± SD reflux symptom index

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scores = 12.03 ± 8.3 *vs* 6.64 ± 6.08; $p < 0.05$); 42 per cent of the asthmatic group had positive reflux symptom index.[8] Another study on chronic rhinosinusitis documented that more patients with chronic rhinosinusitis had a high reflux symptom index compared with controls (19.8 per cent *vs* 4 per cent; $p < 0.01$), and demonstrated a moderate correlation between the Sino-Nasal Outcome Test 22 score and reflux symptom index ($r = 0.67$).[9]

The reflux symptom index score for determining patients with rhinitis symptoms is not well established. Brauer *et al.*[10] reported a mean ± SD score of 18.3 ± 9.8 among patients seen in an allergy clinic without a clinical diagnosis of LPR. In that study, the authors suggested a cut-off score of 19 to determine LPR among allergy patients. However, LPR was not determined by the 'gold standard' multichannel intraluminal impedance with 24-hour pH monitoring.

Among the individual reflux symptom index scores, throat clearing is a prominent LPR symptom, and this may be caused by post-nasal drip. Throat clearing is a non-specific symptom of pharyngeal irritation. This is supported by another study, which reported that throat clearing and post-nasal drip did not differ among LPR patients with and without concomitant allergy.[11] In the current study, it is surprising that hoarseness was not among the most bothersome symptoms in patients with non-allergic rhinitis. This is because rhinitis itself is a risk factor for hoarseness.[12] This association may be stronger among allergy patients, as aeroallergen deposition leads to allergic laryngitis.[13] Therefore, among rhinitic individuals without proven allergy (non-allergic rhinitis), hoarseness could be a potential clinical clue to indicate reflux. Hoarseness has been associated with high reflux symptom index,[14] and about half of patients with voice disorder have LPR,[15] but this requires further study.

Laryngopharyngeal reflux is closely related to nasal pathologies, with overlapping symptoms.[16] Studies on the predominant nasal symptoms associated with LPR are lacking. Nasal symptoms of LPR will likely resemble those of non-allergic rhinitis. Sneezing, nasal congestion and runny nose may be due to mucosal irritation from exposure to gastric refluxate or may be a reflex mechanism.[17] Nasal itchiness was not found to be associated with LPR in this study and is unlikely to contribute to laryngeal symptoms. It is also a symptom with a stronger association to allergic rhinitis.[18] In this study, only severe nasal congestion was predictive of LPR (odds ratio = 5.47 (95 per cent CI = 2.16–13.87)). This would suggest that patients with predominant nasal blockage and chronic throat symptoms are more likely to have LPR, but this requires further study.

Identifying the primary pathology for patients with concomitant throat and nasal symptoms remains a treatment dilemma. This may have led to overuse of proton pump inhibitors and increased medical cost. Although studies have shown that treatment of LPR symptoms also decreased nasal symptoms in chronic rhinosinusitis[19] and decreased nasal resistance on rhinomanometry,[20] proton pump inhibitors should not be initiated in all non-allergic rhinitis patients with a high reflux symptom index. Clinicians should treat moderate to severe nasal symptoms first. Failure to control the nasal symptoms may be an indication of LPR. Zelenik *et al.* found that patients with chronic rhinosinusitis in whom surgery and medical treatment failed were more likely to have pathological LPR.[21] Other factors to consider are a reflux symptom index score of 19 or more, and non-allergic rhinitis patients with relatively mild nasal symptoms and predominantly nasal congestion but with a reflux symptom index score of 13 or higher.

- The reflux symptom index is worse with more severe nasal symptoms
- Moderate to severe nasal symptoms should be primarily treated
- Laryngopharyngeal reflux should be suspected in non-allergic rhinitis patients with predominant nasal congestion

This study is limited by the lack of objective measurement to diagnose LPR among patients with non-allergic rhinitis. The reflux finding score was also not determined to support the diagnosis of LPR. However, the reflux finding score may be high even in asymptomatic individuals with low reflux symptom index.[22] This is an observational study linking the symptoms of rhinitis and reflux using the reflux symptom index. Unfortunately, LPR remains a ubiquitous disease without an established gold standard. Further studies using the current objective measures for LPR (such as mucosal impedance, presence of pepsin or oropharyngeal pH probe) are needed in order to further assess the causal link between rhinitis and LPR.

Conclusion

Moderate to severe nasal symptoms contribute to high reflux symptom index scores and should be primarily addressed. Patients with predominant nasal congestion and throat symptoms may be more likely to have LPR as the underlying cause, and are candidates for early anti-reflux intervention. Further studies are needed to establish the causal link between rhinitis and LPR using current objective tests.

Competing interests. None declared

References

1 Hamizan AW, Azer M, Alvarado R, Earls P, Barham HP, Tattersall J *et al.* The distinguishing clinical features of nonallergic rhinitis patients. *Am J Rhinol Allergy* 2019;**33**:524–30
2 Torresan F, Ioannou A, Schiavon P, Mancini M, Cimatti MC, Pirodda A *et al.* P.08.8 Causal effect association between gastroesophageal reflux disease and nonallergic rhinitis with neutrophils. *Dig Liver Dis* 2016;**48**(suppl 2):E167–8
3 Belafsky PC, Postma GN, Koufman JA. Validity and reliability of the reflux symptom index (RSI). *J Voice* 2002;**16**:274–7
4 Masaany M, Marina M, Ezat WS, Sani A. Empirical treatment with pantoprazole as a diagnostic tool for symptomatic adult laryngopharyngeal reflux. *J Laryngol Otol* 2011;**125**:502–8
5 Uno K, Saito K, Yabe H, Kono T, Ogawa K. Clinical review of globus patients with a focus on GERD cases [in Japanese]. *Nihon Jibiinkoka Gakkai Kaiho* 2016;**119**:1388–96
6 Zahedi FD, Gendeh BS, Husain S. Sensitisation to common allergens in children with allergic rhinitis. *Brunei Int Med J* 2011;**7**:200–6
7 Samiah Yasmin A, Karim A, Rohani M, Pathak R, Aye Mon A, Doustjalali SR *et al.* Skin prick test reactivity to common aeroallergens among patients with rhinitis. *Am J Res Commun* 2013;**1**:18–26
8 Hamdan AL, Jaffal H, Btaiche R, Turfe ZA, Bawab I, Kanj N *et al.* Laryngopharyngeal symptoms in patients with asthma: a cross-sectional controlled study. *Clin Respir J* 2016;**10**:40–7
9 Ren JJ, Zhao Y, Ren X, Wang J. Is reflux symptom index reliable to assess the reflux status of chronic rhinosinusitis patients? *Kaohsiung J Med Sci* 2017;**33**:318–19
10 Brauer DL, Tse KY, Lin JC, Schatz MX, Simon RA. The utility of the reflux symptom index for diagnosis of laryngopharyngeal reflux in an allergy patient population. *J Allergy Clin Immunol Pract* 2018;**6**:132–8.e1
11 Eren E, Arslanoglu S, Aktas A, Kopar A, Ciger E, Onal K *et al.* Factors confusing the diagnosis of laryngopharyngeal reflux: the role of allergic rhinitis

https://doi.org/10.1017/S0022215120002492 Published online by Cambridge University Press

and inter-rater variability of laryngeal findings. *Eur Arch Otorhinolaryngol* 2014;**271**:743–7
12 Turley R, Cohen SM, Becker A, Ebert CS Jr. Role of rhinitis in laryngitis: another dimension of the unified airway. *Ann Otol Rhinol Laryngol* 2011;**120**:505–10
13 Randhawa PS, Mansuri S, Rubin JS. Is dysphonia due to allergic laryngitis being misdiagnosed as laryngopharyngeal reflux? *Logoped Phoniatr Vocol* 2010;**35**:1–5
14 Alanazi R, Alrahim A, Bayounos S, Al-Ghuwainem A, Al-Bar MH. Association between voice handicap index and reflux symptom index: a cross-sectional study of undiagnosed general and teacher cohorts in Saudi Arabia. *Sultan Qaboos Univ Med J* 2018;**18**:e350–4
15 Maldhure S, Chandrasekharan R, Dutta AK, Chacko A, Kurien M. Role of PH monitoring in laryngopharyngeal reflux patients with voice disorders. *Iran J Otorhinolaryngol* 2016;**28**:377–83
16 Alharethy S, Baqays A, Mesallam TA, Syouri F, Al Wedami M, Aldrees T *et al.* Correlation between allergic rhinitis and laryngopharyngeal reflux. *Biomed Res Int* 2018;**2018**:2951928
17 Barrett CM, Patel D, Vaezi MF. Laryngopharyngeal reflux and atypical gastroesophageal reflux disease. *Gastrointest Endosc Clin N Am* 2020;**30**: sr]361–76
18 Bernstein JA. Characteristics of nonallergic vasomotor rhinitis. *World Allergy Organ J* 2009;**2**:102–5
19 Anzic SA, Turkalj M, Zupan A, Labor M, Plavec D, Baudoin T. Eight weeks of omeprazole 20 mg significantly reduces both laryngopharyngeal reflux and comorbid chronic rhinosinusitis signs and symptoms: randomised, double-blind, placebo-controlled trial. *Clin Otolaryngol* 2018;**43**:496–501
20 Dagli E, Yuksel A, Kaya M, Ugur KS, Turkay FC. Association of oral anti-reflux medication with laryngopharyngeal reflux and nasal resistance. *JAMA Otolaryngol Head Neck Surg* 2017;**143**:478–83
21 Zelenik K, Formanek M, Matousek P, Kominek P. Chronic rhinosinusitis and extraesophageal reflux: who is the candidate for antireflux treatment? *Am J Rhinol Allergy* 2016;**30**:e5–9
22 Chen M, Hou C, Chen T, Lin Z, Wang X, Zeng Y. Reflux symptom index and reflux finding score in 91 asymptomatic volunteers. *Acta Otolaryngol* 2018;**138**:659–63

https://doi.org/10.1017/S0022215120002492 Published online by Cambridge University Press