Prevalence of Laryngopharyngeal Reflux Related Symptoms in Patients With Allergy

*Abdul Latif Hamdan, *Christophe Abi Zeid Daou, *Nader Nawfal, and †Jerome R. Lechien, *Beirut, Lebanon, and †Paris, France

Summary: Objective. To describe the prevalence of laryngopharyngeal reflux (LPR)-related symptoms in allergy patient using the Reflux Symptom Index (RSI) by Belafsky et al and the Reflux Symptom Score (RSS) by Lechien et al.

Subjects and Methods. A total of 84 patients were enrolled in this study. Fifty-two consecutive patients were asked to fill RSI. Similarly, 32 patients were asked to fill RSS. Demographic data included age, gender, history of smoking, family history for eczema, atopy, asthma, food and drug allergy.

Results. Fifty-seven of the 84 patients were positive for at least one allergen and hence were diagnosed with allergy. Of the 52 patients who received the RSI, 36 patients were allergic to at least one allergen (36/52). Of the 32 patients who filled the RSS, 21 tested positive for at least one allergen (21/32). There was no significant difference in the number of positive RSI scores (>13) between patients with allergy to at least one allergen in comparison to patients with no allergy ($P = 0.329$). There was a significant difference in the number of positive RSS scores (>13) between patients with allergy to at least one allergen in comparison to patients with no allergy (*P*-value 0.0345). The odds of having RSS >13 in an allergic patient was significant (OR = 5.6, CI 95% = 1.15-27.37).

Conclusion. The results of this study provide evidence that patients with allergy have increased incidence of LPR related symptoms using the RSS. The cross-cutting in the clinical picture of patients with allergy and LPR stresses the need for objective testing such as double probe Ph-metry and impedance to diagnose this latter. Future studies are needed to explore further the cause-effect relationship between allergy and LPR.

Key Words: Otolaryngology—Allergy—Laryngopharyngeal reflux disease—Screening—Reflux—Laryngology.

INTRODUCTION

Allergic disorders are part of everyday medical practice. Their prevalence is increasing with more than 50% of the United States (US) population testing positive to at least one allergen.[1-4] One of the highlights of allergic disorders is the presence of systemic sensitization manifested by multiple comorbidities, among which is allergic laryngitis.[5,6] Brook et al reported than half (51.8%) of patients with laryngeal symptoms tested positive for one inhalant allergen at least. More so, the odds of having a positive allergy in patients with laryngeal symptoms was comparable to those with nasal symptoms.[7] Similarly, Koc et al studied the prevalence of vocal symptoms in 30 patients with allergic rhinitis and showed a higher VHI (Voice Handicap Index) score and s/z ratio in the allergic group in comparison to the non-allergic group.[8] In an investigation by Randhawa et al involving 70 patients presenting for skin testing, the mean VHI score was found to be higher in patients with positive testing for 4 or more allergens.[9] In another study by Hamdan et al singers with vocal symptoms were 15% more likely to have allergic rhinitis than singers with no vocal complaints.[10]

The high prevalence of vocal symptoms in patients with allergy can be ascribed to the location of the larynx between the upper and lower airways, which makes it susceptible to environmental allergens and inflammatory changes. Based on the unified airway concept described by Krouse et al,[11] atopic diseases of the airway are the manifestation of one inflammatory process which requires an integrated unified approach for management.[12] Local inflammation in one part of the airway induces systemic signaling that results in inflammatory cell release into different sites of the airway. Common inflammatory mediators such as interleukins (IL-4, IL-5, IL-13) and others "crosstalk" between different parts of the respiratory tract[13] leading to inflammatory changes. Other causes of laryngeal inflammation include downstream trafficking of the mucus via postnasal drip and mouth breathing secondary to nasal congestion. This latter can lead to vocal fold dryness which in turn is associated with an increase in phonatory effort.[14-16] Changes in voice timber have also been described in patients with allergies as a result of alterations in the wall and configuration of the vocal tract. These in turn can lead to changes in vocal tract resonance.[17]

Few studies have examined the prevalence of laryngopharyngeal reflux (LPR) in patients with allergy.[18-21] The refluxed contents from the stomach into the upper aerodigestive tract causes a wide-spectrum of symptoms and signs that can overlap with those of patients with allergy. To that end, Lechien et al, stressed the lack of a standardized objective diagnostic criteria for LPR and the need to

Accepted for publication December 8, 2021.
Funding: No funding was needed.
From the *American University of Beirut Medical Center, Department of Otolaryngology and Head & Neck Surgery, Beirut, Lebanon; and the †Laryngopharyngeal Reflux Study Group of Young-Otolaryngologists of the International Federations of Oto-rhino-laryngological Societies (YO-IFOS), Department of Otolaryngology-Head and Neck Surgery, Foch Hospital, School of Medicine, University Paris Saclay, Paris, France.
Address correspondence and reprint requests to Abdul Latif Hamdan, American University of Beirut Medical Center, Department of Otolaryngology and Head & Neck Surgery, 11-0236, Riad El Solh 1107 2020, Beirut, Lebanon. E-mail: ah77@aub.edu.lb
Journal of Voice, Vol. ■■, No. ■■, pp. ■■–■■
0892-1997

https://doi.org/10.1016/j.jvoice.2021.12.007

establish a multiparametric diagnostic approach to better identify and manage LPR in the clinic.[21,22] The aim of this study is to cast more information on the prevalence of LPR-related symptoms in allergy patient using the Reflux Symptom Index (RSI) by Belafsky et al[23] and the more comprehensive questionnaire, the Reflux Symptom Score (RSS) by Lechien et al.[24] The hypothesis set forth is that patients with allergy are more likely to score higher on reflux (LPR) symptom surveys than patients without positive allergy skin test.

SUBJECTS AND METHODS

After having read and signed the informed consent approved by the Institution review board, patients who presented to the allergy clinic of a tertiary medical referral center for skin testing between June 2019 and December 2019 were invited to participate in this study. Patients on medications for rhinitis and/ or gastro-esophageal reflux disease at the time of investigation were excluded from the study. Similarly, patients with a recent history of upper respiratory tract infection, history of laryngeal manipulation or surgery, history of central or peripheral neurologic disorder causing throat symptoms or vocal changes were also excluded. Demographic data included age, gender, history of smoking, family history for eczema, atopy, asthma, food and drug allergy.

All the patients included in this study underwent the skin prick test, which is a minimally invasive test with a sensitivity of 80%-97%, specificity of 70%-95%, and positive predictive value of 95%-100%.[25,26] When coupled with history taking in patients with allergic rhinitis, the PPV (Positive Predictive Value) ranges between 97% and 99%.[26] The advantage of the skin prick test is that it can tailored to cover the most common allergens in a specific area/region in order to increase its sensitivity. In our study, patients were tested for common tree allergens (ash, cypress, olive tree, eastern oak, privet, birch mix, pine mix), grasses (bermuda, timothy, ryegrass, 7 grass mix), weeds (chenopodium, russian thistle, ragweed and weed mix), mold mix, household inhalants (D. Farinae and D. pteronyssinus) and pet allergens (cat and dog).[27] The tests were done on the back of participants (the allergens tested were provided from DIATER Laboratories). A test was considered positive when it contained a wheal larger than 3 mm.[28]

A total of 84 patients were enrolled in this study. Fifty-two consecutive patients were asked to fill RSI, where a score >13 or more was considered as abnormal.[23] Similarly, 32 patients were asked to fill RSS.[24] This latter is divided into three sections with symptoms relating to the ear/nose/throat in one, symptoms related to the abdomen in two, and symptoms related to chest in three. Each item was rated from 0 to 5 for severity, frequency, and interference with quality of life. For each item, the severity score is multiplied by the frequency score to obtain a symptom score (0-25). The sum of these symptom scores is calculated to obtain the RSS final score (0-550). Patients with an RSS >13 were considered as highly suspect of LPR.[24]

STATISTICAL ANALYSIS

Means (± standard deviation) and frequencies were calculated to describe continuous and categorical variables, respectively. Mann-Whitney *U* test was used to compare the means of the continuous variables between patients with allergy and patients without. Data was analyzed using SPSS version 24 (SPSS Inc, Chicago, IL).

RESULTS

Demographic data and clinical symptoms of the study group

A total of 84 patients (41 males, 43 females) were recruited for this study. Thirty-eight percent of the participants were smokers and 52% had a positive history of alcohol consumption. In the total group, patient's history was positive for eczema or urticaria, asthma and food/drug allergy in 49%, 14%, and 12% of the cases, respectively. There was a family history of atopy in 73% of patients. The most common allergic symptoms were nasal congestion (72.3%), sneezing (47%), and rhinorrhea (43.4%). Less common symptoms included cough and postnasal drip in 22.9%, dyspnea in 18.1% and ocular symptoms of redness or itching and lacrimation in 15.7% of the cases.

Thirty-two filled the RSS, and 52 patients filled RSI. There was no statistically significant differences between the group of patients who filled the RSS and RSI questionnaires in regards to gender and gender. Similarly, there was no statistically significant difference in family and personal history for eczema, atopy, asthma, food and drug allergy between those who filled the RSI and RSS questionnaire. There were no statistically significant differences in RSI or RSS scores between normal-weight, overweight and obese patients ($P > 0.05$) (Table 1).

Allergy skin testing results

Fifty-seven of the 84 patients were positive for at least one allergen and hence were diagnosed with allergy. Of the 57 patients with positive skin testing to at least one allergen, 25 (44%) tested positive for trees, 18 (32%) for Grasses, 15 (26%) for Weeds, 5 (9%) for Molds, 47 (82%) for in house inhalants and 27 (47%) for pets (Table 2). Of the 52 patients who received the RSI, 36 patients were allergic to at least one allergen (36/52), and 23 patients tested positive to at least three allergens. Of the 32 patients who filled the RSS, 21 tested positive for at least one allergen (21/32), and 17 tested positive to at least three allergens.

Prevalence of LPR related symptoms using the RSI in patients with allergy vs. patients with no allergy

A total of 52 patients filled the RSI, among whom 69.23% (N = 36) tested positive to at least one allergen. Of the 36

TABLE 1.
Demographics Information

Category	RSI Group	RSS Group	*P*-value	N (% of total)
Sex				
Male	15 (47%)	26 (50%)		41 (49%)
Female	17 (53%)	26 (50%)	0.784	43 (51%)
Smokers	12 (38%)	20 (39%)	0.931	32 (38%)
Alcohol consumption	16 (50%)	28 (55%)	0.736	44 (52%)
Body Mass Index (BMI)				
BMI < 25	16 (50%)	34 (67%)		50 (60%)
BMI > 25	17 (53%)	17 (33%)	0.167	34 (40%)
Family history of atopy	23 (72%)	38 (75%)	0.906	61 (73%)
Personal history of eczema/urticaria	18 (56%)	23 (45%)	0.832	41 (49%)
Personal history of asthma	2 (6%)	10 (20%)	0.101	12 (14%)
Personal history of food allergy	2 (6%)	8 (16%)	0.214	10 (12%)
Personal history of drug allergy	4 (13%)	8 (16%)	0.718	12 (14%)

patients who tested positive to at least one allergen, seven had an RSI >13 and the mean RSI score was 8.05. Of the 16 non-allergic patients, four had an RSI >13 and the mean RSI score was 9.93. There was no significant difference in the number of positive RSI scores (>13) between patients with allergy to at least one allergen in comparison to patients with no allergy ($P = 0.329$). Similarly, there was no significant difference in the mean score of RSI in patients with allergy to at least one allergen in comparison to patients with no allergy ($P = 0.764$).

A sub-category analysis was also performed comparing the RSI mean scores in patients testing positive for at least three allergens compared to non-allergic patients. There was no significant difference in the mean score of RSI in patients with allergy to at least three allergens in comparison to patients with no allergy (8.203 vs. 8.963, respectively, $P = 0.849$). Similarly, there was no significant difference in the number of positive RSI scores (>13) between the two groups (6/23 vs. 5/29, respectively, $P = 0.224$) (Table 3).

In summary, there was no significant difference in the prevalence of LPR related symptoms using RSI in patients with allergy vs. patients with no allergy. There was also no significant difference in the mean score of RSI among the two groups. The odds of having RSI >13 in an allergic patient was non-significant (OR = 0.72, CI 95% = 0.18-2.94).

TABLE 2.
Number of Patients (N) Testing Positive for Each of the Tested Allergens

Positive Skin Test for:	N
Trees	25
Grasses	18
Weeds	15
Molds	5
Household inhalants	47
Pets	27

Prevalence of LPR related symptoms using the RSS in patients with allergy vs. patients with no allergy

A total of 32 patients filled the RSS questionnaire, 65.62% (n = 21) tested positive for at least one allergen. Among the 21 patients positive to at least one allergen, 14 (66.66%) had a RSS >13 and the mean RSS score was 25.91. Of the 17 non-allergic patients, three (17.64%) had an RSS >13 and the mean RSS score was 14.18. There was a significant difference in the number of positive RSS scores (>13) between patients with allergy to at least one allergen in comparison to patients with no allergy (*P*-value 0.0345). However, there

TABLE 3.
Frequency of Reflux Disease and Mean Reflux Symptoms Index (RSI) in Patients Allergic to at Least One, and at Least Three Allergens and Patients Who are not Allergic

	Allergic to at Least One Allergen (n = 36)	Non-allergic (N = 16)	*P*-value	Allergic to at Least Three Allergens	Non-allergic	*P*-value
Number of patients with RSI above 13	7/36	4/16	0.329	6/23	5/29	0.224
Mean score RSI	8.056	9.933	0.764	8.208	8.963	0.849

TABLE 4.
Frequency of Reflux Disease and Mean Reflux Symptoms Score (RSIS) in Patients Allergic to at Least One, and at Least Three Allergens and Patients Who are not Allergic

	Allergic to at Least One Allergen (n = 21)	Non Allergic	*P*-value	Allergic to at Least Three Allergens	Non- allergic	*P*-value
Frequency with RSS > 13	14/21	3/11	0.0345	12/17	5/15	0.0178
Mean RSS	25.91	14.18	0.47	29.07	13.39	0.21

was no significant difference in the mean score of RSS in patients with allergy to at least one allergen in comparison to patients with no allergy ($P = 0.47$).

A sub-category analysis was also performed comparing the RSS mean scores in patients testing positive for at least three allergens compared to non-allergic patients. There was also a significant difference in the number of positive RSS scores (>13) between the two groups (12/17 vs. 5/15, respectively, $P = 0.0178$). There was no significant difference in the mean score of RSS in patients with allergy to at least three allergens in comparison to patients with no allergy (29.07 vs. 13.39, respectively, $P = 0.21$) (Table 4).

In summary, there was a significant difference in the prevalence of LPR related symptoms using RSS in patients with allergy vs. patients with no allergy. The odds of having RSS >13 in an allergic patient was significant (OR = 5.6, CI 95% = 1.15-27.37).

DISCUSSION

Since the introduction of the unified airway concept, allergic laryngitis has become an increasingly frequent diagnosis in patients with non-specific laryngeal symptoms and signs. ~~Common~~ Endoscopic findings commonly encountered in patients with LPR and allergy include mucosal edema, hyperemia, and presence of thick mucus. Note that this later has a high positive predictive value for allergy whereas pseudosulcus vocalis is mostly diagnostic of LPR.[29,30] Patients with allergy may complain of symptoms that are congruent with those reported by patients with history of LPR, including throat clearing, globus, dysphonia…[31-33] Multiple studies have looked at the prevalence of allergy in patients with LPR, but only few examined the prevalence of LPR in patients with allergy. In our study group, one out of five of patients tested positive for at least one allergen had LPR using RSI (>13) and three out of four patients had LPR using RSS.

The higher prevalence of LPR related symptoms using the RSS questionnaire in comparison to the RSI can be ascribed to the more extensive nature of this questionnaire which screens for 22 symptoms instead of 9, and looks at severity and frequency of each. Moreover, the odds of having RSS >13 in an allergic patient was significant particularly (OR = 5.6, CI 95% = 1.15-27.37). The decrease specificity of the RSI questionnaire in patients with allergy has been investigated by Brauer et al. The authors looked at the RSI scores in a population of allergic adults and found that score cut-off of 19 instead of 13 had a better specificity in diagnosing LPR. The cut-off of 19 was chosen based on the ROC (receiver operating characteristic) analysis and yielded a sensitivity of 0.8333 and a specificity of 0.5556 with a PPV of 0.5102.[34] However, in our study, there was no significant difference in the number of positive RSI scores (>13) between patients with allergy to at least one allergen in comparison to patients with no allergy. Bringing the threshold of the RSI up to 19 in our study group would decrease the number of positive RSI scores from 11 to 4. The prevalence is very low to draw any statistically significant analysis.

The higher prevalence of LPR related symptoms in patients with allergy in our study population is in accord with previous studies. Feng et al showed an increase hazard ratio of developing GERD in allergic rhinitis (AR) patients in comparison to non-AR, particularly in children younger than six. In their study, patients with allergy were 91% more likely to develop GERD (Gastro-esophageal Reflux Disease) than non-allergic patients (adjusted HR 1.91, 95% CI, $P < 0.001$).[18] In another study, Kung et al evaluated the presence of GERD in allergic rhinitis (AR) in 96,905 participants. The authors found that AR is significantly correlated with the onset of newly diagnosed GERD in adults. AR by itself was found a risk factor for developing GERD as well as when it is present with asthma.[19] The results of these studies are in alignment with the results of our investigation

The higher prevalence of LPR-related symptoms in patients with allergy can be ascribed to several factors. Throat itching and postnasal drip in allergic patients cause an increased frequency of swallowing that is associated with increased frequency of transient lower-esophageal sphincter relaxations.[8,35] Although LPR is characterized by dysfunction in the upper esophageal sphincter not the lower-esophageal sphincter (LES), transient lower esophageal relaxations exacerbated by the frequent swallowing may promote reflux into the esophagus and possibly into the pharyngeal and laryngeal inlet in patients with concomitant UES dysfunction. This can be ascribed to the fact that reflux disease is often a spectrum that includes both GERD and LPR.[36]

Symptoms of reflux may also be the result of alterations in LES contractions secondary to the release of histamine

from mast cells.[37] Histamine has been shown to play an important role in LES tone in a dose-dependent manner. Furthermore it increases the production of gastric acid by acting on H2 receptors in the stomach and therefore promotes reflux and its symptoms.[38] It is also speculated that reflux can be aggravated by the presence of eosinophils in the esophageal mucosa in the setting of atopic airway disease.[39] Eosinophils, which play an important role in the pathogenesis of allergy, have also been discovered in esophageal mucosa of GERD patients.[40] Eosinophils are important inflammatory mediators, they secrete significant amount of IL-4 that promotes goblet cell production and hence mucus accumulation. They can further up-regulate integrins and adhesion molecules to recruit further inflammatory mediators and potentiate the inflammatory response and eventually aggravate GERD symptoms.[40,41]

Our study has limitations including small sample size and a non-randomized sample as the first fifty-two all received the RSI with subsequent patients taking the RSS. Moreover, the study results are based on a subjective questionnaire with no objective evaluation of LPR such as laryngoscopy, double-probe pH monitoring and esophageal impedance testing. The cross-cutting in the clinical picture of patients with allergy and LPR stresses the need for objective testing such as double probe Ph-metry and impedance to diagnose this latter. Another limitation to our study is the high prevalence of smoking, which is a confounding factor that can mask the laryngeal symptoms of allergy and reflux disease. Nevertheless, it is important to note that the high prevalence of smoking in our study group, is commensurate with the prevalence of smoking in Lebanon, which has been shown to be 36.9%.[42] The prevalence is higher in adults aged above 40 with a value of 35.9%-51.9%.[43] Another limitation worth mentioning is the fact that allergen test panels are finite and do not test for all possible allergens to rule out allergy. Nevertheless, as was mentioned above, the patients were tested for the most common allergens encountered in our region.[27]

CONCLUSION

The results of this study provide further evidence that patients with allergy are more likely to exhibit LPR symptoms assessed on the RSS questionnaire. Objective diagnostic tests can aid in differentiating these two entities. This study also highlights the need for future studies to explore whether the presence of allergy can be responsible for causing the LPR symptoms identified on the RSS questionnaire.

REFERENCES

1. Alharethy S, Baqays A, Mesallam T, et al. Correlation between allergic rhinitis and laryngopharyngeal reflux. *Biomed Res Int*. 2018;2018:2951928.
2. Cecil, Goldman, Schafer. *Goldman's Cecil Medicine*. 24th ed. Philadelphia, PA: Elsevier/Saunders; 2011.
3. Rakel D. *Integrative Medicine*. 4th ed. Philadelphia, PA: Elsevier; 2018.
4. Mabry RL. The importance of allergy in the practice of otolaryngology. *Otolaryngol Clin North Am*. 2003;36:781–787. v.
5. Shin YS, Jung CG, Park HS. Prevalence and clinical characteristics of local allergic rhinitis to house dust mites. *Curr Opin Allergy Clin Immunol*. 2018;18:10–15.
6. Licari A, Caimmi S, Bosa L, et al. Rhinosinusitis and asthma: a very long engagement. *Int J Immunopathol Pharmacol*. 2014;27:499–508.
7. Brook CD, Platt MP, Reese S, et al. Utility of allergy testing in patients with chronic laryngopharyngeal symptoms is it allergic laryngitis? *Otolaryngol Head Neck Surg*. 2016;154:41–45.
8. Koç EAÖ, Koç B, Erbek S. Comparison of acoustic and stroboscopic findings and voice handicap index between allergic rhinitis patients and controls. *Balkan Med J*. 2014;31:340–344.
9. Randhawa P, Nouraei S, Mansouri S, et al. Allergic laryngitis as a cause of dysphonia: a preliminary report. *Logopedics Phoniatr Vocol*. 2010;35:169–174.
10. Hamdan AL, Sibai A, Youssef M, et al. The use of a screening questionnaire to determine the incidence of allergic rhinitis in singers with dysphonia. *Arch Otolaryngol Head Neck Surg*. 2006 May;132:547–549.
11. Krouse JH, Altman KW. Rhinogenic laryngitis, cough, and the unified airway. *Otolaryngol Clin North Am*. 2010;43:111–121. ix-x.
12. Licari A, Castagnoli R, Denicolo C, et al. The nose and the lung: united airway disease? *Front Pediatr*. 2017;5:44.
13. Braunstahl GJ, Overbeek S, Kleinjan A, et al. Nasal allergen provocation induces adhesion molecule expression and tissue eosinophilia in upper and lower airways. *J Allergy Clin Immunol*. 2001;107:469–476.
14. Verdolini K, Titze IR, Fennell A. Dependence of phonatory effort on hydration level. *J Speech Hear Res*. 1994;37:1001–1007.
15. Solomon NP, Glaze LE, Arnold RR, et al. Effects of a vocally fatiguing task and systemic hydration on men's voices. *J Voice*. 2003;17:31–46.
16. Hamdan AL, Al-Barazi R, Kanaan A, et al. The effect of snoring on voice: a controlled study of 30 subjects. *Ear Nose Throat J*. 2012;91:28–33.
17. Sundberg J. (2017). Vocal tract resonance. In: R. Sataloff, Professional Voice: The Science and Art of Clinical Care (4th ed., 309-328). San Diego, CA. Plural.
18. Feng M, Tsai Y, Chang Y, et al. Allergic rhinitis as a key factor for the development of gastroesophageal reflux disease in children. *J Microbiol Immunol Infect*. 2020. https://doi.org/10.1016/j.jmii.2020.08.008.
19. Kung Y, Tsai P, Chang Y, et al. Allergic rhinitis is a risk factor of gastro-esophageal reflux disease regardless of the presence of asthma. *Scientific Rep*. 2019;9. https://doi.org/10.1038/s41598-019-51661-4.
20. Koufman JA. Laryngopharyngeal reflux is different from classic gastroesophageal reflux disease. *Ear Nose Throat J*. 2002;81(9 suppl 2):7–9. PMID: 12353431.
21. Alharethy S, Baqays A, Mesallam TA, et al. Correlation between allergic rhinitis and laryngopharyngeal reflux. *Biomed Res Int*. 2018;2018:2951928.
22. Lechien JR, Akst LM, Hamdan AL, et al. Evaluation and management of laryngopharyngeal reflux disease: state of the art review. *Otolaryngol Head Neck Surg*. 2019;160:762–782.
23. Belafsky P, Postma G, Koufman J. Validity and reliability of the Reflux Symptom Index (RSI). *J Voice*. 2002;16:274–277. https://doi.org/10.1016/s0892-1997(02)00097-8.
24. Lechien JR, Bobin F, Muls V, et al. Validity and reliability of the reflux symptom score. *The Laryngoscope*. 2019;130. https://doi.org/10.1002/lary.28017.
25. Frati F, Incorvaia, Cavaliere, et al. The skin prick test. *J Biol Regul Homeost Agents*. 2018;32(1 suppl 1):19–24.
26. Crobach MJ, Hermans, Kaptein, et al. The diagnosis of allergic rhinitis: how to combine the medical history with the results of radioallergosorbent tests and skin prick tests. *Scand J Prim Health Care*. 1998;16:30–36.
27. Hamdan AL, Abi Zeid Daou C, Nawfal N, et al. Prevalence of self-reported dysphonia and dysphagia in patients with allergy. *J Voice*. 2021. S0892-1997(21)00082-5.

28. van der Valk JP, van Wijk G, Hoorn E, et al. Measurement and interpretation of skin prick test results. *Clin Transl Allergy*. 2015(6). p. 8.
29. A Eren E, Arslanoğlu S, Aktaş A, et al. Factors confusing the diagnosis of laryngopharyngeal reflux: the role of allergic rhinitis and interrater variability of laryngeal findings. *Eur Arch Otorhinolaryngol*. 2014;271:743–747.
30. A Hickson C, Simpson CB, Falcon R. Laryngeal pseudosulcus as a predictor of laryngopharyngeal reflux. *Laryngoscope*. 2001;111:1742–1745.
31. Khan DA. Allergic rhinitis and asthma: epidemiology and common pathophysiology. *Allergy Asthma Proc*. 2014;35:357–361. https://doi.org/10.2500/aap.2014.35.3794.
32. Campagnolo A, Benninger MS. Allergic laryngitis: chronic laryngitis and allergic sensitization. *Br J Otorhinolaryngol*. 2019;85:263–266. https://doi.org/10.1016/j.bjorl.2019.02.001.
33. Stachler RJ, Dworkin-Valenti JP. Allergic laryngitis: unraveling the myths. *Curr Opin Otolaryngol Head Neck Surg*. 2017;25:242–246. https://doi.org/10.1097/MOO.0000000000000354.
34. Brauer DL, Tse K, Lin J, et al. The utility of the reflux symptom index for diagnosis of laryngopharyngeal reflux in an allergy patient population. *J Allergy Clin Immunol Pract*. 2018;6:132–138. e1.
35. Krouse JH, Altman KW. Rhinogenic laryngitis, cough, and the unified airway. *Otolaryngol Clin North Am*. 2010;43:111–121.
36. Babaei A, Venu M, Naini SR, et al. Impaired upper esophageal sphincter reflexes in patients with supraesophageal reflux disease. *Gastroenterology*. 2015;149:1381–1391.
37. Kravitz JJ, Snape Jr WJ, Cohen S. Effect of histamine and histamine antagonists on human lower esophageal sphincter function. *Gastroenterology*. 1978;74:435–440. 2 Pt 2PMID: 620912.
38. Fernandez Rojas C, Wichrowska-Rymarek K, Pavlic A, et al. Oral health needs of athletes with intellectual disability in Eastern Europe: Poland, Romania and Slovenia. *Int Dent J*. 2016;66:113–119.
39. Hamdan AL, Ashkar J, Sibai A, et al. Effect of fasting on voice in males. *Am J Otolaryngol*. 2011;32:124–129.
40. Mahdavinia M, Carter R, Ocampo C, et al. Basophils are elevated in nasal polyps of patients with chronic rhinosinusitis without aspirin sensitivity. *J Allergy Clin Immunol*. 2014;133:1759–1763.
41. Kia L, Hirano I. Distinguishing GERD from eosinophilic oesophagitis: concepts and controversies. *Nat Rev Gastroenterol Hepatol*. 2015;12:379–386. https://doi.org/10.1038/nrgastro.2015.75.
42. Haddad C, Lahoud N, Akel M, et al. Knowledge, attitudes, harm perception, and practice related to waterpipe smoking in Lebanon. *Environ Sci Pollut Res*. 2020;27:17854–17863.
43. El-Hajj M, Salameh P, Rachidi S, et al. Cigarette and waterpipe smoking are associated with the risk of stroke in Lebanon. *J Epidemiol Global Health*. 2019;9:62–70.