# Laryngopharyngeal reflux: knowledge, attitudes, and practices among primary healthcare physicians

Sultan Bin Obaid<sup>1</sup>, Shahad Bin Obaid<sup>2</sup>, Mohammed Mesfer Alessa<sup>1</sup>, Mohammed Alnajeim<sup>1</sup>, Rakan Almetary<sup>1</sup>, Khalid H. Malki<sup>3</sup>, Tamer Mesallam<sup>3</sup>, Daniele Farneti<sup>4</sup>, Mohamed Farahat<sup>3</sup>

<sup>1</sup> King Saud University, College of Medicine, Riyadh, Saudi Arabia; <sup>2</sup> King Saud bin Abdulaziz University for Health Sciences, College of Medicine, Riyadh, Saudi Arabia; <sup>3</sup> Department of Otolaryngology, College of Medicine, King Saud University, Riyadh, Saudi Arabia; <sup>4</sup> Audiology Phoniatrics Service, ENT Division, Infermi Hospital, AUSL Romagna, Italy



Cover figure. Endoscopic picture of the larynx showing signs of laryngopharyngeal reflux.

#### Summary

**Objective**. The aim of this study was to estimate the level of knowledge, attitudes, and practices regarding laryngopharyngeal reflux (LPR) among primary healthcare (PHC) physicians in Saudi Arabia.

**Methods**. This quantitative cross-sectional study used an online-based questionnaire distributed to physicians in PHC facilities and hospitals in Saudi Arabia. The questionnaire consisted of four sections that provided data on demographics, knowledge, attitudes, and practices.

**Results**. Of the 473 physicians included in the study, one-third were unaware of LPR, and twothirds were unfamiliar with the reflux symptom index (RSI). The most common sources of LPR knowledge were textbooks and literature (49.8%). The most recognised risk factor, symptom, and complication were high body mass index (75.8%), voice problems (82.4%), and laryngeal cancer (70.6%), respectively. The most recognised diagnostic and treatment options were laryngoscopy (73.5%) and lifestyle modifications (87.3%), respectively, while only 60.4% of participants recognised proton pump inhibitors as a treatment option. Most PHC physicians believed that LPR is underdiagnosed and that primary prevention and awareness among the general population need to be improved.

**Conclusions**. One in three PHC physicians knew nothing about LPR, and two in three were unfamiliar with the RSI. More than half could not recognise all major symptoms of LPR, which might be

Received: October 11, 2023 Accepted: March 4, 2024

#### Correspondence

Mohamed Farahat E-mail: mfarahat@ksu.edu.sa

How to cite this article: Obaid SB, Obaid ShB, Alessa MM, et al. Laryngopharyngeal reflux: knowledge, attitudes, and practices among primary healthcare physicians. Acta Otorhinolaryngol Ital 2024;44:306-312. https://doi. org/10.14639/0392-100X-N2776

© Società Italiana di Otorinolaringoiatria e Chirurgia Cervico-Facciale



This is an open access article distributed in accordance with the CC-BY-NC-ND (Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International) license. The article can be used by giving appropriate credit and mentioning the license, but only for non-commercial purposes and only in the original version. For further information: https://creativecommons.org/licenses/by-ncnd/4.0/deed.en a cause for concern, as recognising these symptoms is crucial for proper diagnosis. We recommend increasing the education of physicians about LPR, its signs and symptoms, and the RSI, all of which provide valuable clues for diagnosis.

Key words: laryngopharyngeal reflux, gastric reflux, larynx, primary care physicians, reflux symptoms index

## Introduction

Laryngopharyngeal reflux (LPR) is a retrograde flow of acidic stomach content and pepsin into the larynx and pharynx where they contact the upper aerodigestive tract <sup>1</sup>. LPR is highly prevalent and has reached the scale of an epidemic in the past few years <sup>1,2</sup>. In Saudi Arabia, primary healthcare (PHC) clinics are widely distributed across the kingdom and are the first locations visited by patients to address any new complaints that need to be treated or assessed by specialists. PHC physicians are therefore usually the first to encounter patients complaining of LPR. Patients with LPR are commonly misdiagnosed and have complications that usually go unrecognised. It is estimated that 50% of patients with dysphonia have symptoms of LPR <sup>1</sup>. LPR awareness among physicians is the most important factor contributing to its diagnosis.<sup>3</sup>

LPR risk factors include a history of gastro-oesophageal reflux disease (GERD), high body mass index (BMI), and unhealthy dietary habits, whereas *Helicobacter pylori* (H. *pylori*) infection is not correlated with LPR risk.<sup>4</sup> The most common symptoms of LPR are excessive throat clearing and mucus, sore throat, coughing, voice problems, and globus pharyngeus (sensation of a lump in the throat) <sup>5,6</sup>. Changes in the voice, or dysphonia, typically appear in the morning and improve throughout the day <sup>6</sup>. Heartburn may suggest GERD, as it is an uncommon presentation in LPR. Epigastric pain may suggest gastric ulcers, which are rarely associated with LPR.

The reflux symptom index (RSI) is a widely used, validated, self-administered, nine-item scoring system of symptoms suggestive of LPR; an RSI score of more than 13 is abnormal and suggestive of LPR 7. The reliability of laryngoscopy in diagnosing LPR has been a subject of debate in the literature, although it remains one of the methods used alongside hypopharyngeal-oesophageal impedance pH testing or proton pump inhibitor (PPI) trials. The RSI, which can demonstrate improvement following PPI trials, is currently the most recommended method for first-line assessment of LPR by PHC physicians<sup>8</sup>. There are many treatment options for LPR, including lifestyle modifications to reduce the risk of gastric reflux (e.g. waiting at least 3 hours after a meal before going to sleep), medications such as PPIs and liquid alginate, and surgery (e.g. laparoscopic fundoplication) in certain cases <sup>6</sup>. LPR can result in several complications, including vocal process granuloma, subglottic stenosis, otitis media, exacerbation of asthma, and chronic bronchitis <sup>9-12</sup>.

Physicians should be knowledgeable on this subject, as LPR is the most common cause of chronic and recurrent larvngitis <sup>13</sup>, and awareness is necessary to diagnose the condition. The aim of this study was to estimate the knowledge of LPR, attitude types, and common practices among PHC physicians in Saudi Arabia stratified by years of experience. We hypothesised that the level of knowledge regarding LPR was low to moderate, with LPR being underrecognised and underdiagnosed. Studies have assessed LPR awareness and practices among PHC physicians across several nations 3,14-<sup>17</sup>. Most did not anticipate that the physicians would be uninformed about LPR; therefore, they focused on management while overlooking major symptoms, risk factors, and complications. In this study, we aimed to obtain a proper, wide, and comprehensive view of the knowledge, attitudes, and practices of PHC physicians with a large sample to represent the whole population by using a modified questionnaire that focused on LPR awareness rather than management.

## Materials and methods

The study was performed using an online questionnaire adapted from the literature <sup>14</sup>. The questionnaire was piloted on 10 otorhinolaryngology consultants to obtain their opinions and suggestions. Thirty data collectors were recruited from the cities of Riyadh, Dammam, Mecca, Medina, Taif, Abha, and Tabuk in October and November 2021. Primary care clinics were chosen randomly and visited by data collectors, who provided physicians with access to the online questionnaire via a QR code. All participants provided their consent to participate and were asked not to consult others or access related information before submission of the questionnaire. The questionnaire included 50 items, both multiple choice and checkbox questions. We collected demographic data and tested knowledge with eight questions about participants' sources of LPR knowledge; LPR's differences from GERD, symptoms, risk factors, and management options; and participants' familiarity with the RSI. Finally, we included two large checkbox questions to evaluate attitudes and practices, respectively. This study included general practitioners who were not yet active in any

residency and not board certified, but were working in PHC clinics, family physicians, internal medicine physicians, and other physicians working as PHC practitioners in Saudi Arabia. Medical interns and physicians who did not work in the PHC field were excluded.

With approximately 3,000 PHC practitioners in Saudi Arabia, the minimum sample size required with a 95% confidence level and 5% margin of error was 434. Spreadsheets with questionnaire responses were imported from Google Forms and coded using Excel version 16.0 (Microsoft, Redmond, WA, USA). Coded data were analysed using IBM SPSS Statistics for Windows, version 24.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics (means, standard deviations, frequencies, and percentages) were used to describe quantitative and categorical variables. A chi-squared test was used for comparison. Statistical significance was set at p < 0.05.

# **Results**

We obtained 498 completed questionnaires. Twenty-five were excluded, as they were submitted by medical interns. The participants included family physicians (45.4%), general practitioners (38.5%), general internal medicine physicians (7.8%), and other physicians (8.2%). The participants' characteristics are shown in Table I. More than half the participants (51.2%) had under 5 years of work experience, 17.1% had 5-10 years, and 31.7% had over 10 years. Table II displays the frequency of responses to questions regarding the sources of information on LPR and the risk factors and symptoms of LPR. The knowledge sources were primarily textbooks and scientific literature (49.8%), postgraduate education (residency program) (23.4%), and scientific conferences (12.4%). Of the cohort, 30.8% did not know about LPR, while 16.3% mistakenly thought that GERD and LPR were the same disease. Participants recognised the following risk factors for LPR: high BMI (75.8%), history of GERD (72.7%), unhealthy dietary habits (65.7%), and H. pylori infection (41.6%). Physicians identified the symptoms of LPR as voice problems (82.4%), chronic cough (73.3%), globus pharyngeus (60.4%), excessive throat mucus (60%), and heartburn (50.9%). The preferred method of LPR diagnosis was through use of a laryngoscope, according to 73.5% of the participants, while 62.3% thought clinical assessment could be sufficient for diagnosis; a PPI trial was the least preferred method of LPR diagnosis (35.9%). The most preferred treatment option for LPR was lifestyle modifications (87.3%), whereas PPI was recognised as a treatment option by only 60.4% of the PHC

	N (%)	
Specialty	General internal medicine	37 (7.8)
	General practitioner	182 (38.5)
	Family medicine	215 (45.4)
	Other	39 (8.3)
Years of experience	0-5 years	242 (51.2)
	5-10 years	81 (17.1)
	Over 10 years	150 (31.7)

**Table I.** Participants' specialties and experience (N = 473).

physicians, and surgery to prevent gastric reflux was recognised as an option by 44.6% of participants.

Table III presents levels of knowledge of the RSI and LPR-associated complications. Only 34.2% of the participants knew about the RSI. Laryngeal cancer was the most frequently recognised complication of LPR (70.6%), followed by asthma exacerbation (66.4%) and chronic bronchitis (65.3%). Physicians associated LPR with otitis media (44.6%), vocal fold paralysis (57.1%), and subglottic stenosis (63.8%).

Table IV presents data on the attitudes and practices of the participants regarding LPR. Of the participants, 61.1% agreed that LPR could lead to complications of high concern, and 66.4% agreed that LPR was underdiagnosed in Saudi Arabia. Most participants (82.5%) thought that primary prevention of LPR was crucial, and 79.1% agreed that public awareness of LPR should be increased. According to 83.7% of respondents, the first line of LPR management was lifestyle changes. Only 49.9% of participants always informed and educated patients about LPR at the time of diagnosis.

No association was found between the knowledge of whether GERD and LPR were the same disease and a physician's number of years of experience or specialty (Tab. V). The number of years of experience was positively correlated with a physician's knowledge of the RSI (p = 0.001), but was not associated with the physician's specialty.

## Discussion

Since its description by Koufman in 1991<sup>18</sup>, LPR has been widely investigated and described extensively in textbooks, systematic reviews, and meta-analyses that have covered its clinical presentation, risk factors, and complications. Despite its importance, knowledge and awareness of LPR among PHC family physicians and general practitioners have been at low to moderate levels and have remained insufficient; consequently, LPR is considered to be underdiagnosed <sup>15-17</sup>.

Table II. Knowledge regarding the source of LPR-region	lated information, symptoms, risk factors, and d	iagnostic and treatment options (N = 473).		
Item		N (%)		
Source of information regarding LPR	Textbooks and scientific literature	236 (49.8)		
	Postgraduate education	111 (23.4)		
	Scientific conferences	59 (12.4)		
	Patient complaints	2 (0.4)		
	Online	4 (0.8)		
	I do not know anything about LPR	146 (30.8)		
Are GERD and LPR the same disease?	Yes	77 (16.3)		
	No	396 (83.7)		
Risk factors for LPR	History of GERD	344 (72.7)		
	High BMI	359 (75.8)		
	Helicobacter pylori infection	197 (41.6)		
	Type-2 diabetes mellitus	106 (22.4)		
	Unhealthy dietary habits	311 (65.7)		
Symptoms of LPR	Voice problems	390 (82.4)		
	Excess throat mucus	284 (60)		
	Chronic cough	347 (73.3)		
	Epigastric pain	118 (24.9)		
	A sensation of a lump in the throat	286 (60.4)		
	Heartburn	241 (50.9)		
	Post-nasal drip	194 (41)		
Diagnostic options for LPR	Laryngoscopy	348 (73.5)		
	PPI trial	170 (35.9)		
	Clinical diagnosis	295 (62.3)		
	24 h pH monitoring	201 (42.5)		
Treatment options for LPR	PPI	286 (60.4)		
	Lifestyle modifications	413 (87.3)		
	Surgery	211 (44.6)		

A recent study assessing LPR awareness and practices among Saudi PHC practitioners found that approximately one-third of practitioners were knowledgeable about LPR<sup>19</sup>. In contrast, our study, which boasted a sample size of over 100 participants, indicated that around two-thirds of practitioners were aware of LPR. The larger sample size of our study enhanced its representativeness and reliability compared to those of the recent study <sup>19</sup>. However, both studies concluded that the number of years of experience correlated positively with knowledge of LPR. Moreover, our study evaluated the risk factors, association with laryngeal cancer, and primary prevention of LPR, while these topics were not discussed in the related study <sup>19</sup>.

Across countries, awareness of LPR has been improving over time. The percentage of physicians who did not know about LPR was 70% in 2005<sup>15</sup>, 55% in 2013<sup>16</sup>, and 30%

## Table III. Familiarity with RSI and LPR-related complications (n = 473).

Knowledge section	Yes, n (%)	No, n (%)
Are you familiar with the RSI?	162 (34.2)	311 (65.8)
Is there an association between LPR and laryngeal cancer?	334 (70.6)	139 (29.4)
Is there an association between LPR and otitis media?	211 (44.6)	262 (55.4)
Is there an association between LPR and chronic bronchitis?	309 (65.3)	164 (34.7)
Is there an association between LPR and vocal fold paralysis?	270 (57.1)	203 (42.9)
Is there an association between LPR and subglottic stenosis?	302 (63.8)	171 (36.2)
Is there an association between LPR and asthma exacerbation?	314 (66.4)	159 (33.6)

RSI: reflux symptom index; LPR: laryngopharyngeal reflux.

Table IV. Attitudes and practices toward LPR (N = 473).							
	Agree N (%)	Neutral N (%)	Disagree N (%)				
Attitude							
LPR leads to complications of major concern	289 (61.1)	152 (32.1)	32 (6.8)				
LPR is underdiagnosed in Saudi Arabia	314 (66.4)	123 (26)	36 (7.6)				
Primary prevention of LPR is important	390 (82.5)	73 (15.4)	10 (2.1)				
PHC centers are suitable for LPR diagnosis and treatment	200 (42.3)	173 (36.6)	100 (21.1)				
Population awareness of LPR needs to be improved	374 (79)	68 (14.4)	31 (6.6)				
Practice							
I start with lifestyle modifications as a treatment for LPR	396 (83.7)	68 (14.4)	9 (1.9)				
I always refer patients with LPR to otolaryngology	163 (34.5)	194 (41)	116 (24.5)				
The first medication I prescribe for LPR is an antacid	201 (42.5)	158 (33.4)	114 (24.1)				
I advise patients to use herbal medicine to relieve LPR symptoms	70 (14.8)	149 (31.5)	254 (53.7)				
I have always educated patients about LPR	236 (49.9)	142 (30)	95 (20.1)				

Table	V. Correlation	between year	s of experience	and level of	f education o	on RSI and	GERD (N =	= 473).
-------	----------------	--------------	-----------------	--------------	---------------	------------	-----------	---------

		Are GERD and LPR	the same disease?	р	p Knowledge about the RSI		р
		Yes	No		Yes	No	
Years of experience	0-5	39 (16.1)	203 (83.9)	0.683	70 (29)	172 (71)	0.001
	5-10	11 (13.6)	70 (86.4)		23 (28.4)	58 (71.6)	
	Over 10	27 (18)	123 (82)		69 (46)	81 (54)	
Data are presented as N (%)							

Data are presented as N (%).

LPR: laryngopharyngeal reflux; GERD: gastro-esophageal reflux disease; RSI: reflux symptom index.

in the current study, although these results are for different geographic locations. However, these results were insufficient to reduce the disease burden; this information makes these types of studies highly valuable.

The current study adopted a previously used survey to study the knowledge, attitudes, and practices of PHC physicians regarding LPR in one of the regions of Saudi Arabia<sup>14</sup>. We replicated this study to increase the sample size by including almost all regions of Saudi Arabia; our study can be used as a foundation for future LPR studies.

Responses to the knowledge section of the questionnaire revealed that the source of information on LPR's symptoms, diagnostic methods, and treatment modalities was mostly scientific literature rather than medical schools or postgraduate education (family and internal medicine residency programs). Less than one-quarter of participants learned about LPR during their training, and familiarity with the RSI was correlated with amount of experience rather than physician specialty or postgraduate education. This could be a cause of the insufficient knowledge about the disease. Thus, we highly recommend educating medical students and PHC physicians about LPR in postgraduate education programs.

Our study found that 83.7% of participants understood that GERD and LPR are two different disorders. In contrast, a study conducted in Turkey concluded that only 6.9% of participants could differentiate GERD from LPR, which is alarming<sup>3</sup>. Physicians who are not able to recognize LPR or to differentiate it from GERD might also be prone to conducting needless testing and assuming these patients have viral or bacterial laryngitis, as these conditions have similar symptoms to those of LPR. Such mistakes might lead to delays in LPR diagnosis and treatment. One of the confusing presenting symptoms of LPR is heartburn. Almost half our participants thought that heartburn was a symptom of LPR. However, heartburn is not usually a symptom of LPR, as it is experienced by only 43% of LPR patients <sup>20</sup>. Absence of heartburn might lead physicians to exclude acid reflux and LPR from the most likely diagnoses, frequently resulting in misdiagnoses. However, in our study, we included symptoms mentioned in the RSI as a reference for testing the knowledge of PHC physicians.

Diagnosing LPR is still the most controversial aspect of the disease and has proven to be a challenge for many physicians. Among the diagnostic options, pH monitoring, laryngoscopy, and PPI trials have been investigated for their reliability over the past three decades. More than half the questionnaire respondents did not consider 24-h pH monitoring to be a diagnostic option, although it has been shown to be useful. However, its use is still controversial <sup>20</sup>. Familiarity with the RSI was lower than expected, at almost onethird of the participants; however, only 15% of participants were familiar with the RSI in a related study <sup>16</sup>. The RSI can aid in correct clinical diagnosis by allowing a review of the important clinical features associated with LPR <sup>21</sup>. Amount of experience and familiarity with the RSI were positively correlated in our study, highlighting how experience plays an important role in the proper use of related tools. In addition, we found that more than half the respondents did not think otitis media was linked to LPR, which is contradictory to general knowledge, since the relationship between otitis media and LPR is well established <sup>22</sup>. Moreover, as many as 70% of physicians demonstrated knowledge of the association between laryngeal cancer and LPR, although there is ongoing uncertainty in the literature, particularly due to the confounding effects of smoking habits and alcohol consumption. Other LPR-related complications had agreement by the participants, which was also noted in a previous study 14.

The attitudes section of the questionnaire revealed that nearly two-thirds of participants concurred that LPR is often underdiagnosed in Saudi Arabia. Most respondents also considered it vital to focus on primary prevention and to raise public awareness about LPR. This places a responsibility on healthcare providers to act in this regard.

Responses to the practices section of the questionnaire indicated that physicians typically acknowledged the importance of lifestyle modifications and antacids as treatments for LPR, as they are considered mainstays for reducing chronic reflux of stomach acid and pepsin into the larynx and pharynx <sup>23</sup>. However, only one-third of the participants refer patients with LPR to otolaryngologists, which could be because many physicians feel comfortable treating LPR patients and see no need for referrals. PPIs were considered effective medications for LPR, as they reduce stomach acid production. Theoretically, PPIs can reduce pepsin levels; while pepsin activity is optimal at a low pH, pepsin is denatured at neutral pH <sup>24</sup>. However, PPI therapy only does not reduce reflux or the incidence of microaspirations. Patients resistant to PPI therapy, for whom there is objective evidence (via reflux monitoring) confirming persistent reflux as the source of symptoms, should be evaluated for supplementary anti-reflux interventions. This may involve the consideration of transient lower oesophageal sphincter relaxation inhibitors or surgical options <sup>25</sup>.

While the findings of this study could be generalised, as it covered almost all regions of Saudi Arabia, the study also had limitations. The self-reported data from PHC physicians could have been subject to recall bias or social desirability bias.

# Conclusions

Most findings of this study indicated that PHC physicians' awareness of LPR was poor, as one in three had no knowledge of it, and two in three were unfamiliar with the RSI. More than half the participants did not recognise all major symptoms of LPR, which is concerning, given that clinical symptoms are crucial for correct diagnosis. Most PHC physicians thought that LPR was underdiagnosed and that primary prevention and awareness among the general population should be improved. Consequently, we recommend educating physicians, specifically PHC physicians, about LPR and its clinical presentation, diagnostic methods, and treatment options through courses, workshops, scientific conferences, residency programs, and medical schools. Knowledge of the RSI is important, as it could lead to fewer errors in the diagnosis of LPR.

## Acknowledgements

The authors extend their appreciation to the Deputyship for Research & Innovation, Ministry of Education in Saudi Arabia for funding this research (IFKSUOR3-614-1).

#### Conflict of interest statement

The authors declare no conflict of interest.

## Funding

Deputyship for Research & Innovation, Ministry of Education, in Saudi Arabia.

#### Author contributions

SBO, MMA, MA, MF: study conception, design, and material preparation; SBO, ShBO: data collection; MMA: statistical analysis; SBO, RA: writing of the first draft of the manuscript, management of the analyses of the study, and management of the literature searches; KHM, TM, ShBO, RA, DF, MF: review and editing. All authors commented on previous versions of the manuscript, read and approved the final manuscript. The study was supervised by MF.

#### Ethical consideration

This study was approved by the Institutional Review Board (IRB) (Approval Research Project No. E-21-60710) of the College of Medicine, King Saud University.

The research was conducted ethically, with all study procedures being performed in accordance with the requirements of the World Medical Association's Declaration of Helsinki.

Written informed consent was obtained from each participant/patient for study participation and data publication.

## References

- <sup>1</sup> Campagnolo A, Priston J, Thoen R, et al. Laryngopharyngeal reflux: diagnosis, treatment, and latest research. Int Arch Otorhinolaryngol 2014;18:184-191. https://doi.org/10.1055/s-0033-1352504
- <sup>2</sup> El-Serag HB. Time trends of gastroesophageal reflux disease: a systematic review. Clin Gastroenterol Hepatol 2007;5:17-26. https://doi. org/10.1016/j.cgh.2006.09.016
- <sup>3</sup> Eryilmaz A, Basal Y, Gunel C, et al. Awareness and daily practices of family physicians and trainees towards laryngopharyngeal reflux. Eur Arch Otorhinolaryngol 2016;273:4377-4384. https://doi.org/10.1007/ s00405-016-4180-5
- <sup>4</sup> Saruç M, Aksoy EA, Vardereli E, et al. Risk factors for laryngopharyngeal reflux. Eur Arch Otorhinolaryngol 2012;269:1189-1194. https:// doi.org/10.1007/s00405-011-1905-3
- <sup>5</sup> Belafsky PC, Postma GN, Amin MR, et al. Symptoms and findings of laryngopharyngeal reflux. Ear Nose Throat J 2002;81:10-13.
- <sup>6</sup> 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. https://doi. org/10.1177/0194599819827488
- <sup>7</sup> Farahat M, Malki KH, Mesallam TA. Development of the Arabic version of reflux symptom index. J Voice 2012;26:814.e15-814.e19. https://doi.org/10.1016/j.jvoice.2012.03.010
- <sup>8</sup> Pontes P, Tiago R. Diagnosis and management of laryngopharyngeal reflux disease. Curr Opin Otolaryngol Head Neck Surg 2006;14:138-142. https://doi.org/10.1097/01.moo.0000193193.09602.51
- <sup>9</sup> Lechien JR, Saussez S, Nacci A, et al. Association between laryngopharyngeal reflux and benign vocal folds lesions: a systematic review. Laryngoscope 2019;129:E329-E341. https://doi.org/10.1002/ lary.27932
- <sup>10</sup> Blumin JH, Johnston N. Evidence of extraesophageal reflux in idiopathic subglottic stenosis. Laryngoscope 2011;121:1266-1273. https://doi.org/10.1002/lary.21776
- <sup>11</sup> Doğru M, Kuran G, Haytoğlu S, et al. Role of laryngopharyngeal reflux in the pathogenesis of otitis media with effusion. J Int Adv Otol 2015;11:66-71. https://doi.org/10.5152/iao.2015.642

- <sup>12</sup> Nowak KM. Laryngopharyngeal reflux as a major cause of chronic respiratory symptoms and asthma mimic among community health center patients. J Allergy Clin Immunol 2009;123:S85. https://doi. org/10.1016/j.jaci.2008.12.298
- <sup>13</sup> Stein DJ, Noordzij JP. Incidence of chronic laryngitis. Ann Otol Rhinol Laryngol 2013;122:771-774. https://doi. org/10.1177/000348941312201207
- <sup>14</sup> Alanazy SM, Alawaji RI, Alsager AH, et al. Knowledge, attitudes and practices of primary health care physicians with regard to laryngopharyngeal reflux in the Qassim Region of Saudi Arabia. J Adv Med Med Res 2021;33:98-103. https://doi.org/10.9734/jammr/2021/ v33i930904
- <sup>15</sup> Karkos PD, Thomas L, Temple RH, et al. Awareness of general practitioners towards treatment of laryngopharyngeal reflux: a British survey. Otolaryngol Head Neck Surg 2005;133:505-508. https://doi. org/10.1016/j.otohns.2005.06.013
- <sup>16</sup> Chorti MS, Prokopakis EP, Lahanas VA, et al. Knowledge of primary care doctors about laryngopharyngeal reflux disease. B-ENT. 2013;9:53-56.
- <sup>17</sup> Fisichella PM. Hoarseness and laryngopharyngeal reflux. JAMA 2015;313:1853-1854. https://doi.org/10.1001/jama.2015.10045
- <sup>18</sup> Koufman JA. The otolaryngologic manifestations of gastroesophageal reflux disease (GERD): a clinical investigation of 225 patients using ambulatory 24-hour pH monitoring and an experimental investigation of the role of acid and pepsin in the development of laryngeal injury. Laryngoscope 1991;101:1-78. https://doi.org/10.1002/lary.1991.101. s53.1
- <sup>19</sup> Alrayah M, Alzahrani R, Alghamdi M, et al. Assessment of the current knowledge and practice of general practitioners towards laryngopharyngeal reflux in Saudi Arabia. Cureus 2023;15:E38043. https:// doi.org/10.7759/cureus.38043
- <sup>20</sup> Baudouin R, Calvo-Henriquez C, Mayo-Yanez M, et al. The importance of 24-h hypopharyngeal-esophageal impedance-pH monitoring for the treatment of laryngopharyngeal reflux. Eur Arch Otorhinolaryngol 2022;279:5481-5482. https://doi.org/10.1007/s00405-022-07623-0
- <sup>21</sup> Belafsky PC, Postma GN, Koufman JA. 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
- <sup>22</sup> Al-Saab F, Manoukian JJ, Al-Sabah B, et al. Linking laryngopharyngeal reflux to otitis media with effusion: pepsinogen study of adenoid tissue and middle ear fluid. J Otolaryngol Head Neck Surg 2008;37:565-571.
- <sup>23</sup> Martinucci I, de Bortoli N, Savarino E, et al. Optimal treatment of laryngopharyngeal reflux disease. Ther Adv Chronic Dis 2013;4:287-301. https://doi.org/10.1177/2040622313503485
- <sup>24</sup> Campos LA, Sancho J. The active site of pepsin is formed in the intermediate conformation dominant at mildly acidic pH. FEBS Lett 2003;538:89-95. https://doi.org/10.1016/s0014-5793(03)00152-2
- <sup>25</sup> Katz P, Gerson L, Vela M. Guidelines for the diagnosis and management of gastroesophageal reflux disease. Am J Gastroenterol 2013;108:308-328. https://doi.org/10.1038/ajg.2012.444