



Review Article

The assessment of children with suspected laryngopharyngeal reflux: An Otorhinolaryngological perspective



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ABSTRACT

The assessment of pediatric laryngopharyngeal reflux (LPR) is controversial. Otorhinolaryngologists may play a role in the evaluation of children with suspected LPR detecting typical airway endoscopic findings and/or associated diseases and may help in the selection of children to be subjected to further instrumental tests. In this perspective the present review aims at examining the available evidence in the literature regarding the assessment of LPR in children. After careful literature search there are no current validated symptoms assessment questionnaires for LPR evaluation in children; flexible fiberoptic nasopharyngolaryngoscopy remains controversial as a diagnostic tool in suspect LPR cases; even though the multichannel intraluminal impedance with pH monitoring has been proposed as the instrumental gold standard, further evidence need to be found for validation in children with typical features of LPR.

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Contents

1. Introduction	1613
2. Symptoms	1614
3. Upper airways endoscopic findings	1614
4. Instrumental diagnostic tools	1616
5. ENT associated diseases	1617
6. Conclusions	1617
References	1617

1. Introduction

Laryngopharyngeal reflux disease (LPR) is defined as the reflux of either gastric acid or refluxate (containing pepsin) beyond the esophagus into larynx, oropharynx, and/or nasopharynx [1]. Although it has been initially considered an extension of gastroesophageal reflux disease (GERD) [2], recently pediatric LPR tends to be identified as a unique and distinct disease process as it is expressed in different reflux patterns, symptoms presentation and response to treatment [1,3]. Nonetheless, the terms pediatric LPR and extraesophageal manifestations of GERD in children are almost used to describe the same reflux related disease.

The prevalence of GERD in children has been estimated to be between 1.8% and 22% [4]. It affects approximately fifty percent of infants younger than three months old [5] and it is generally a self-limiting condition that improves with age, only five percent continue to have symptoms after infancy [6]. The prevalence of LPR disease in children is still unknown [3].

The etiology of GERD is multifactorial and is incompletely understood. Pediatric population at risk for GERD including mainly preterm infants, children with neurologic impairment, repaired esophageal atresia or achalasia, hiatal hernia, lung transplantation, chronic respiratory disorders [7] and obesity [8]. Population trends hypothesized to contribute to an increase in the prevalence of GERD include global epidemics of both asthma and obesity [9].

Clinical manifestations of LPR are usually present with a different set of symptoms depending on age; in particular children

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tend to demonstrate adult like symptoms such as regurgitation, heartburn, hoarseness and globus sensation [1].

There is, at present, no ideal diagnostic test for LPR detection in children. In addition to the multichannel impedance with pH monitoring (MII-pH) that has become the new gold standard due to its ability to document both acid and non acid reflux [10–12], flexible fiberoptic nasopharyngolaryngoscopy has been recently indicated to find upper airways signs and/or associated diseases of LPR. For this reason, otorhinolaryngologists are increasingly involved in the management of children with suspected LPR. The present comprehensive review aims at examining the available evidence in the literature regarding the assessment of pediatric LPR analyzing symptoms, endoscopic findings, instrumental diagnosis and associated diseases in an otorhinolaryngological perspective.

2. Symptoms

LPR disease is characterized by a broad set of symptoms that vary according to age at presentation and severity of disease [1,10,13,14]. Table 1 describes the main characteristics of available studies concerning pediatric LPR. They are retrospective or prospective studies, none of them was randomized. The number of patients included ranges from 16 to 337, age varies from 0 to 21 years and the majority were males. Data regarding symptoms describes mainly laryngotracheal and pharyngeal complaints (chronic cough, hoarseness, sore throat and throat clearing, and dyspnea) [12,15–21] and/or gastrointestinal symptoms (nausea, regurgitation/vomiting, chest or abdominal pain, heartburn and chronic respiratory disease) [22–25], rarely also rhinologic symptoms (sinusitis, post nasal discharge) and/or otitis [26–29].

Overall, those data show that there are typical gastroesophageal symptoms of reflux and a variety of extra-esophageal symptoms that could be related to a reflux-mediated damage of the larynx, oropharynx, and/or nasopharynx. This pathological relationship has been previously documented in a systematic review on 18 cross-sectional controlled trials. Tolia et al. have concluded that, regardless of age, there is a possible association between GERD and asthma, pneumonia, bronchiectasis, acute life-threatening event (ALTE), laryngotracheitis, sinusitis and dental erosion but causality or temporal association were not established [30]. In this perspective Banaszekiewicz et al. in a prospective study including 21 children with difficult-to-treat asthma (mean age 12.7 years, range 7–17) have found that 13/21 (61.9%) subjects had LPR and that there was a positive correlation between LPR and the degree of asthma control [31].

Moreover, it should be considered an age dependent symptom because, as some authors have observed, it seems that children less than two years old presented with airway flow problems and feeding problems significantly more often than children older than two years of age [10,32]. Accordingly, infants typically have regurgitation/vomiting, dysphagia, growth failure, apnea or life-threatening events (ALTE), abnormal crying, recurrent croup, laryngomalacia, subglottic stenosis or recurrent respiratory issues, while children tend to show adult-like symptoms.

In order to characterize the clinical evaluation of children with suspected GERD, symptom assessment questionnaires have been recommended. Boiler et al. in a systematic review found that 65 types of questionnaires have been described for both adults and children with a variety of characteristics that value symptoms, response to treatment, diagnosis and burden on quality of life. Eight out of 65 are specific questionnaires for the assessment of GERD in infants and/or children [33]. Among them, the Infant Gastroesophageal Reflux Questionnaire Revised (I-GERQ-R) is the most thoroughly evaluated questionnaire to screen infant for burden symptoms. It consists of 12 items measuring: the

frequency, amount, and discomfort attributable to spit up; the refusal or stopping feeding, crying and fussing, hiccups, arching back, and stopping breathing or changing color. The total score range from 0 to 42, the higher scores represent greater symptom burden [34]. I-GERQ-R has been translated into multiple languages with cultural adaptation, however its diagnostic validity is limited because of poor specificity [35]. Considering GERD-specific extra-esophageal symptom questionnaires, three validated questionnaires were found for adults: the most widely accepted and validated is the Reflux Symptom Index (RSI) developed by Belafsky et al. [36,37]. It has been proved to be very useful in the diagnosis and treatment of LPR in adults [38], but its used in children has not been validated. Simons et al. have been the first to use RSI as a parent-proxy instrument in children. In a retrospective study including 36 children with dysphonia or cough reported a significant correlation between Pediatric Voice Index score (PVOS) and Reflux Symptom Index (RSI) score suggesting a relationship between LPR and pediatric voice disorders. [39] However currently, there are no current validated symptom assessment questionnaires specific for detection laryngopharyngeal reflux in children.

3. Upper airways endoscopic findings

Flexible fiberoptic nasopharyngolaryngoscopy is a diagnostic tool that allows to study the upper airway in children with LPR symptoms. It may detect endoscopic signs presumably related with LPR and/or potential LPR associated diseases.

Previous studies have described a variety of endoscopic airway findings commonly associated with chronic inflammation in children with GERD [23,40–42], in this context, we consider specifically endoscopic data of children with diagnosis of LPR. As it is reported in all studies listed in Table 1, the most frequent endoscopic findings are arytenoid, interarytenoid, and postglottic edema and erythema. Some authors also describe ventricle obliteration [16–18,22,26], large lingual tonsil [19,23], hypopharyngeal and/or tracheal cobblestoning mucosa [19,23]. Moreover, it is possible to detect associated diseases, by frequency: vocal folds nodules [12,16–25], laryngeal granulomas or polyp [16,18,20,24], vocal palsy [16,22,24], subglottic stenosis [22,26], recurrent papillomatosis [22,26], pseudosulcus [43] and laryngomalacia [26].

The debated issue is the possible correlation between these typical endoscopic findings and the presence of reflux in children with clinical suspected LPR. May et al. in a systematic review including eight articles aims at demonstrating this assumption. Especially, they reported a statistically significant correlation between the presence of GERD or LPR and arytenoid edema and erythema (RR = 2.46), lingual tonsil hypertrophy (RR = 2.24), posterior glottic edema and erythema (RR = 3.19), trachea edema (RR = 1.86), vocal folds edema and nodules (RR = 12.15), and subglottic stenosis (RR = 2.5) [44]. Moreover, a moderated risk ratio analysis demonstrated that children with those endoscopic findings (except lingual tonsil hypertrophy) had more than 70% chance of having GERD.

Taken together, these results confirm the role of flexible fiberoptic nasopharyngolaryngoscopy as a diagnostic tool to detect signs or associated diseases of pediatric LPR. In this context Ozmen et al. in a retrospective trial on 49 patients with respiratory complaints, aged between 1 and 16 years (7.26 ± 2.8 years), found that twelve of 30 patients diagnosed with LPR and GERD or GERD had positive laryngeal findings on fiberoptic laryngoscopy, most frequently arytenoid erythema [29]. Baudoin et al. in a retrospective study on 89 children, aged 1–18 years (median age was 11.2), have also found a sensitivity of 92% and specificity of 10.26% of endoscopic findings in detecting LPR. Overall published studies report varying positive fiberoptic laryngoscopic rates, ranging from 40% to 90% [25].

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