Li C, et al., HSOA J Altern Complement Integr Med 2025, 11: 648
DOI: 10.24966/ACIM-7562/100648

HSOA Journal of
Alternative, Complementary & Integrative Medicine

Review Article

The Bidirectional Relationship between Adenoid Hypertrophy and Laryngopharyngeal Reflux: A Comprehensive Review of Epidemiological and Mechanistic Evidence

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Abstract

Adenoid Hypertrophy (AH) and Laryngopharyngeal Reflux (LPR) are prevalent and interconnected pediatric otolaryngological conditions. While their clinical association is widely recognized, the underlying causality remains debated. This review synthesizes epidemiological data from recent meta-analyses with deep mechanistic insights from molecular and pathophysiological studies to elucidate the complex, bidirectional relationship between AH and LPR. Epidemiological evidence robustly demonstrates a significantly higher prevalence of LPR in children with AH (OR ≈ 10.53), and LPR is identified as a key risk factor for AH recurrence post-adenoidectomy (RR ≈ 9.43). Mechanistically, AH can exacerbate LPR through anatomical obstruction and by inducing obstructive sleep apnea (OSA), which alters intrathoracic pressure and autonomic neural regulation of the esophageal sphincters. Conversely, LPR contributes to AH pathogenesis through pepsin-mediated inflammatory pathways, disrupting epithelial barriers (e.g., E-cadherin degradation) and activating inflammatory cascades such as the NLRP3 inflammasome, leading to chronic inflammation and lymphoid tissue hyperplasia. A neuroinflammatory axis involving the Nucleus Tractus Solitarius (NTS) and vagal pathways may represent a unifying mechanism that perpetuates a vicious cycle between airway obstruction, sleep disturbance, and reflux. This review underscores the necessity of an integrated diagnostic and therapeutic approach, suggesting that managing LPR may be crucial for the effective long-term treatment of AH in children. Future research should focus on standardizing diagnostic criteria for pediatric LPR and validating non-invasive biomarkers like salivary pepsin.

Keywords: Adenoid Hypertrophy; Bidirectional Comorbidity; Laryngopharyngeal Reflux; Obstructive Sleep Apnea; Pathophysiology; Pediatric Otolaryngology; Pepsin

Introduction

Adenoid Hypertrophy (AH) and Laryngopharyngeal Reflux (LPR) are two of the most common clinical entities in pediatric otorhinolaryngology, with prevalence rates of AH reaching up to 70% among pediatric outpatients [1-7]. LPR, the retrograde flow of gastroduodenal contents into the laryngopharynx, is also highly prevalent in children and is associated with a spectrum of upper aerodigestive tract disorders, including chronic sinusitis, otitis media with effusion, and laryngeal pathologies [8]. A growing body of evidence suggests a significant comorbidity and a potential bidirectional causal relationship between these two conditions. However, the precise nature of this interplay—whether AH mechanically induces LPR, or LPR inflammatory mediators drive adenoid tissue hyperplasia, or both—remains a subject of intensive investigation [1]. This review aims to consolidate the current understanding by integrating large-scale epidemiological findings with detailed molecular and physiological evidence to provide a comprehensive overview of the AH-LPR bidirectional axis, discussing its underlying mechanisms, clinical implications, and future research directions.

Epidemiological Evidence for a Bidirectional Association

Recent meta-analytic data has provided robust quantitative evidence supporting a strong, bidirectional link between AH and LPR.

High Prevalence of LPR in Children with AH

A systematic meta-analysis by Li et al. (2025) involving over 39,000 participants revealed a pooled LPR prevalence of 47% among children with AH. More strikingly, children with AH exhibited a significantly increased risk of having LPR, with a calculated odds ratio (OR) of 10.53 (95% CI: 1.36–81.32) compared to their non-AH counterparts [1]. This strong association highlights that LPR is not an incidental finding but a highly significant comorbidity in the AH population. The study also noted substantial heterogeneity ($I^2 = 80.9\%$), primarily attributed to variations in diagnostic methodologies for LPR (e.g., 24-hour pH monitoring, pepsin assays, symptom scores), underscoring a critical need for standardized diagnostic criteria in future research [1].

The Impact of Adenoidectomy on LPR Symptoms

The relationship is further nuanced by the outcomes of adenoidectomy (AT). The same meta-analysis showed that AT can lead to a

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Citation: Li C, Wang C (2025) The Bidirectional Relationship between Adenoid Hypertrophy and Laryngopharyngeal Reflux: A Comprehensive Review of Epidemiological and Mechanistic Evidence. HSOA J Altern Complement Integr Med 11: 648.

Received: November 02, 2025; **Accepted:** November 12, 2025; **Published:** December 15, 2025

significant short-term (<1 year) improvement in LPR symptoms, with a pooled risk ratio (RR) of 0.08, suggesting that relieving the mechanical obstruction alleviates reflux [1]. This supports the hypothesis that AH contributes to LPR. However, paradoxically, a long-term follow-up study (>10 years) included in the analysis found an increased susceptibility to LPR (RR = 2.03) post-AT compared to the general population [1,9]. This suggests that while surgery addresses the mechanical component, it may not resolve the underlying inflammatory or neurological predispositions, or perhaps alters pharyngeal mechanics in the long run.

LPR as a Risk Factor for AH Recurrence

Evidence for the other direction of causality (LPR causing AH) is strongly supported by data on revision AT. The meta-analysis found that pediatric patients requiring revision AT had a dramatically elevated risk of concurrent LPR, with an RR of 9.43 (95% CI: 4.88–18.21) compared to those undergoing primary surgery [1]. This finding powerfully suggests that persistent, untreated LPR acts as a chronic inflammatory stimulus that can drive the regrowth of adenoid tissue, leading to surgical failure [1,10].

Pathophysiological Mechanisms

Mechanisms by which AH May Exacerbate LPR

The primary mechanism is believed to be mechanical obstruction leading to Obstructive Sleep Apnea (OSA) or sleep-disordered breathing. AH significantly reduces the volume of the upper airway, leading to increased negative intrathoracic pressure during inspiration to overcome the resistance [2]. This exaggerated negative pressure gradient between the chest and abdomen can lower the pressure barrier of the Lower Esophageal Sphincter (LES), thereby promoting the reflux of gastric contents [3,11]. Studies using nasal continuous positive airway pressure (nCPAP) in OSA patients have shown a reduction in reflux events, supporting the role of airway pressure dynamics [12].

Furthermore, the frequent arousals from sleep caused by OSA can Trigger Transient LES Relaxations (TLESRs), which are a primary mechanism for reflux events [13]. The associated autonomic nervous system dysfunction in OSA, characterized by sympathetic overactivity, may also impair esophageal motility and sphincter function, further predisposing the child to LPR [6].

Mechanisms by which LPR Drives AH Pathogenesis

The damaging effects of LPR on nasopharyngeal mucosa are not solely due to acid but are significantly mediated by non-acidic components, particularly the enzyme pepsin [4]. Pepsin retains its proteolytic activity at higher pH levels found in the nasopharynx and can be internalized by epithelial cells, where it remains stable and can be reactivated by subsequent acid reflux events [14].

At the molecular level, pepsin exposure triggers a cascade of inflammatory events. It has been shown to disrupt epithelial barrier integrity by promoting the degradation of E-cadherin, a key cell adhesion molecule, via the upregulation of matrix metalloproteinases (MMPs) like MMP-7 [5,15]. This breach allows refluxate to penetrate deeper into the tissue, initiating a robust inflammatory response. Recent studies have implicated the activation of the nucleotide-binding oligomerization domain, leucine-rich repeat and pyrin domain-containing 3 (NLRP3) inflammasome by pepsin. This leads to the production of Reactive Oxygen Species (ROS) and the release of potent pro-inflammatory cytokines like IL-1β and TNF-α, which recruit immune cells (e.g., CD4+ T cells) and promote the chronic inflammation and lymphoid hyperplasia characteristic of AH [4,16].

The Neuroinflammatory Axis: A Unifying Pathway?

A compelling hypothesis is the existence of a self-perpetuating neuroinflammatory cycle. Both respiratory and esophageal functions are regulated by vagal nerve pathways that converge in the brainstem, particularly the nucleus tractus solitarius (NTS) [6]. Chronic irritation of the laryngopharynx by LPR can sensitize vagal afferent C-fibers. Simultaneously, the intermittent hypoxia and sleep fragmentation from AH-induced OSA activates peripheral chemoreceptors that also signal to the NTS [17]. This convergence could lead to a state of central sensitization and dysregulated autonomic output, impairing both upper airway muscle tone and esophageal sphincter control, thus perpetuating both OSA and LPR in a vicious cycle.

Clinical Implications and Future Directions

The bidirectional nature of the AH-LPR relationship has significant clinical implications. The high failure rate of revision adenoidectomy in the context of LPR suggests that surgeons should consider screening for and treating LPR in children with recurrent or severe AH. An integrated management approach that combines surgical intervention with anti-reflux therapy (e.g., lifestyle modifications, medication) may improve long-term outcomes and reduce the need for repeat surgeries [1,10]. A major hurdle in clinical practice is the difficulty in diagnosing pediatric LPR, as current gold-standard methods like 24-hour MII-pH monitoring are invasive and poorly tolerated. There is an urgent need to validate and implement non-invasive diagnostic tools, such as salivary pepsin assays, which have shown promise as specific biomarkers for LPR [1,18]. Future research should focus on large-scale, prospective longitudinal studies with standardized diagnostic criteria to definitively elucidate causality and to evaluate the efficacy of combined treatment strategies.

Conclusion

In conclusion, the relationship between adenoid hypertrophy and laryngopharyngeal reflux is not a simple one-way association but a complex, bidirectional interplay. Robust epidemiological data confirms that each condition significantly increases the risk for the other. This interplay is driven by a combination of mechanical obstruction, sleep-disordered breathing, pepsin-mediated molecular inflammation, and potentially a unifying neuroinflammatory axis. Acknowledging this intricate relationship is paramount for clinicians to move towards a more holistic and effective management strategy for children suffering from these common and impactful conditions.

References

1. Li C, Ye J, Huang S, Wang C, Yin G (2025) Bidirectional risk association between adenoid hypertrophy and laryngopharyngeal reflux: A systematic meta-analysis. Medicine (Baltimore) 104: 44376.

2. Mohamed AS, Habumugisha J, Cheng B, Zhao M, Bu W, et al. (2023) A cone-beam computed tomography study of hyoid bone position and airway volume in subjects with obstructive and nonobstructive adenotonsillar hypertrophy. Angle Orthod 93: 467-475.

3. Sagar M, Sagar P, Kabra SK, Kumar R, Mallick S (2020) The concatenation of association between gastroesophageal reflux and obstructive adenotonsillar hypertrophy. Int J Pediatr Otorhinolaryngol 139: 110439.

4. Tan JJ, Dai YF, Wang F, Lv ZH, Huang LJ, et al. (2024) Pepsin-mediated inflammation in laryngopharyngeal reflux via the ROS/NLRP3/IL-1β signaling pathway. Cytokine 178: 156568.

5. Im NR, Lee DY, Kim B, Kim J, Jung KY, et al. (2019) Role of matrix metalloproteinases 7 in the pathogenesis of laryngopharyngeal reflux: decreased E-cadherin in acid exposed primary human pharyngeal epithelial cells. Int J Mol Sci 20: 5276.

6. King TL, Heesch CM, Clark CG, Kline DD, Hasser EM (2012) Hypoxia activates nucleus tractus solitarii neurons projecting to the paraventricular nucleus of the hypothalamus. Am J Physiol Regul Integr Comp Physiol 302: 1219-1232.

7. Pereira L, Monyror J, Almeida FT, Almeida FR, Guerra E, et al. (2018) Prevalence of adenoid hypertrophy: a systematic review and meta-analysis. Sleep Med Rev 38: 101-112.

8. Johnston N, Knight J, Dettmar PW, Lively MO, Koufman J (2004) Pepsin and carbonic anhydrase isoenzyme III as diagnostic markers for laryngopharyngeal reflux disease. Laryngoscope 114: 2129-2134.

9. Dearking AC, Lahr BD, Kuchena A, Orvidas LJ (2012) Factors associated with revision adenoidectomy. Otolaryngol Head Neck Surg 146: 984-990.

10. Johnston J, Mahadevan M, Douglas RG (2017) Incidence and factors associated with revision adenoidectomy: a retrospective study. Int J Pediatr Otorhinolaryngol 103: 125-128.

11. Wasilewska J, Kaczmarski M, Debkowska K (2011) Obstructive hypopnea and gastroesophageal reflux as factors associated with residual obstructive sleep apnea syndrome. Int J Pediatr Otorhinolaryngol 75: 657-663.

12. Green BT, Broughton WA, O'Connor JB (2003) Marked Improvement in Nocturnal Gastroesophageal Reflux in a Large Cohort of Patients With Obstructive Sleep Apnea Treated with Continuous Positive Airway Pressure. Arch Intern Med 163: 41-45.

13. Shepherd K, Ockelford J, Ganasan V, Holloway R, Hillman D, et al. (2020) Temporal Relationship Between Night-Time Gastroesophageal Reflux Events and Arousals From Sleep. Am J Gastroenterol 115: 697-705.

14. Johnston N, Wells CW, Samuels TL, Blumin JH (2010) Rationale for targeting pepsin in the treatment of reflux disease. Ann Otol Rhinol Laryngol 119: 547-558.

15. Kim B, Lee HJ, Im NR, Lee DY, Kang CY, et al. (2018) Effect of matrix metalloproteinase inhibitor on disrupted E-cadherin after acid exposure in the human nasal epithelium. Laryngoscope 128: 1-7.

16. Souza RF, Huo X, Mittal V, Schuler CM, Carmack SW, et al. (2009) Gastroesophageal reflux might cause esophagitis through a cytokine-mediated mechanism rather than caustic acid injury. Gastroenterology 137: 1776-1784.

17. Fawley JA, Hegarty DM, Aicher SA, Beaumont E, Andresen MC (2021) Dedicated C-fiber vagal sensory afferent pathways to the paraventricular nucleus of the hypothalamus. Brain Res 1769: 147625.

18. Zeleník K, Hránková V, Vrtková A, Staníková L, Komínek P, et al. (2021) Diagnostic value of the PeptestTM in detecting laryngopharyngeal reflux. J Clin Med 10: 2996.

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