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Microbiological And Immunological Aspects Of Chronic Tonsillitis In Children: A Review

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Abstract

Chronic tonsillitis (CT) remains one of the most common conditions in pediatric otorhinolaryngology, with reported prevalence ranging from 10-15% up to 37-63% in some populations, compared with 2.8-4.1% reported in the mid-20th century. This review summarizes current evidence on the microbiological and immunological aspects of CT in children, with particular attention to the role of group A beta-hemolytic Streptococcus (GABHS), local cytokine dysregulation, recently identified inflammatory biomarkers, and diagnostic and complication-related implications. The clinical and research directions for developing an integrated, evidence-based diagnostic algorithm are discussed.

Keywords: chronic tonsillitis, children, group A Streptococcus, cytokines, biomarkers, immunopathogenesis, tonsillogenic complications.

Introduction

Chronic tonsillitis (CT) continues to occupy a leading position in the structure of pharyngeal diseases in childhood, despite continuous improvement of diagnostic and therapeutic approaches. Historical data indicate that the prevalence of CT has increased markedly since the mid-20th century, from 2.8-4.1% to 10-15% of the general population, with some authors reporting figures as high as 37-63% depending on the population studied and diagnostic criteria applied [1]. This persistent and, in many regions, rising burden underscores the need for a deeper understanding of the microbiological and immunological mechanisms underlying the disease, as well as of their diagnostic and prognostic value.

2. Global epidemiology and the resurgence of group A Streptococcus

Recent regional data illustrate the heterogeneous burden of tonsillar pathology in children. A cross-sectional study in Rabak City, Sudan, found chronic tonsillitis in 25.9% of patients presenting to ENT clinics, with a male predominance (67.5%)



and peak occurrence among 11-20-year-olds [2]. A retrospective analysis in the Al-Baha region of Saudi Arabia similarly reported a male predominance (60%) among 348 tonsillitis patients examined between 2019 and 2023 [8]. A nine-year retrospective analysis in Saudi Arabia identified recurrent and chronic tonsillitis as the leading indications for pediatric tonsillectomy among 361 patients, most frequently combined with adenoidectomy, consistent with current clinical practice guidelines on surgical indications [10,11].

A regional Italian survey involving 3,580 children reported that 20.3% had a GAS-associated infection, with the highest incidence in the 3-6-year age group (42.3%); the most frequent symptoms were sore throat, fever, and tonsillar exudate [3]. A multicenter French study covering September 2022-April 2024 documented an increase in severe GAS infections among children, predominantly manifesting as upper and lower respiratory tract disease, with the emm1 genotype accounting for 73.0% of isolates and the M1_UK sublineage representing half of emm1 strains [4]. Similar increases in invasive GAS disease among children have been reported in Cyprus, where half of confirmed cases occurred in children aged 0-4 years [5], and in Colorado (USA), where an outbreak between October 2022 and March 2023 was associated with pediatric intensive care admission in 33% of cases and two fatalities [6]. Taken together, these findings confirm a global resurgence of GAS-related disease in the pediatric population since the post-COVID-19 period, which has direct relevance for the epidemiology of chronic and recurrent tonsillitis.

3. Microbiological features: the role of group A *Streptococcus* and other pathogens

Bacteriological investigation remains among the most widely used diagnostic approaches for tonsillar pathology, and group A beta-hemolytic *Streptococcus* (GABHS, *Streptococcus pyogenes*) is consistently identified as playing a leading role in the pathogenesis of chronic tonsillitis [9]. However, culture-based diagnosis has notable limitations: throat culture sensitivity has been reported between 50% and 85%, with results available only after 48 hours [25]. Rapid antigen detection tests (RADTs), by contrast, offer same-visit results; a Cochrane review of RADT accuracy reported a pooled sensitivity of 86% and specificity of 95%, meaning that among 100 children with true GAS pharyngitis, approximately 14 would be missed by RADT alone [25].

Comparative studies indicate that RADT sensitivity is broadly similar between younger children (81%) and adolescents (75%), with specificity above 89% in both groups [26]. A multicenter study of 785 children found that GAS prevalence was 36% and that RADT accuracy was significantly affected by clinical spectrum (McIsaac score) and bacterial inoculum size,

although negative predictive value remained stable at approximately 92% [27]. Test performance also depends on the operator: sensitivity has been shown to range from 56% to 90% depending on whether testing was performed by trained laboratory personnel or other staff [28]. Newer-generation rapid tests have demonstrated a negative predictive value as high as 99.6%, supporting their use for same-visit exclusion of GAS pharyngitis and more judicious antibiotic prescribing [29].

Beyond GABHS, culture of the tonsillar surface may substantially underestimate the true microbial burden. A study of Tanzanian children undergoing (adeno)tonsillectomy for recurrent chronic tonsillitis and obstructive sleep apnea found that combined surface and core tonsillar sampling identified *Neisseria meningitidis* (86.1%), *Haemophilus influenzae* (74.9%), *Streptococcus pneumoniae* (42.6%), and *Staphylococcus aureus* (28.7%), indicating that superficial swabbing alone may be insufficient and potentially misleading for guiding therapy [19]. Nevertheless, the diagnostic value of GABHS isolation for determining the severity and clinical form of chronic tonsillitis remains debated, since this pathogen is also detected in a substantial proportion of asymptomatic carriers.

4. Immunopathogenesis and cytokine dysregulation

Chronic inflammation of the palatine tonsils is associated with disruption of local protective and adaptive mechanisms of tonsillar tissue, with bacterial invasion contributing to the initiation and maintenance of the inflammatory process. Scarring changes at the crypt orifices, tonsillar capsule, and tonsillar pillars impair lacunar drainage, which in turn sustains chronic intoxication and perpetuates the inflammatory cycle [1]. The palatine tonsils, as paired lymphoid organs at the entrance of the upper aerodigestive tract, play a central role in mucosal immune defense, with extrafollicular T cells contributing prominently to this function [17]. Dysregulated cytokine gene expression in tonsillar tissue has similarly been implicated in the pathogenesis of habitual tonsillitis and tonsillar focal infection [16].

A study measuring salivary cytokines in 92 children aged 6-15 years with chronic tonsillitis, compared with 17 healthy controls, found elevated TNF-alpha, IL-1beta, and IL-6, with a statistically significant difference confirmed only for IL-6 (median 12.5 vs 6.72 units, $p=0.01$) [14]. This finding supports salivary IL-6 as a candidate, minimally invasive biomarker of tonsillar inflammation, although the lack of significance for other cytokines highlights the limitations of any single marker used in isolation.

Analyses of cytokine production in tonsillar tissue and blood from children with recurrent acute tonsillitis have shown predominance of a Th1-type response (TNF-alpha, IFN-gamma,



IL-2) over a Th2-type response (IL-4, IL-10), a pattern also confirmed in adenoid and tonsil comparisons in children aged 4-15 years [17]. In tonsillar hypertrophy related to obstructive sleep apnea, a lower proportion of IL-10-producing regulatory B cells (Bregs) has been observed compared with tonsils removed for chronic tonsillitis, suggesting immunologically distinct pathogenic pathways between infectious and obstructive tonsillar disease [15]. Further immunohistochemical work in children with chronic tonsillitis has linked vitamin D status with CD68 macrophage polarization and proinflammatory cytokine expression, pointing to a possible systemic metabolic contribution to local tonsillar inflammation [18].

At the molecular level, transcriptomic analyses have identified an interferon-related host response specific to severe GAS-related tissue infections, in which the chemokines CXCL9, CXCL10, and CXCL11 have been proposed as potential diagnostic biomarkers, alongside inflammasome activation, IL-1 β release, and T-cell hyperactivation as key components of the pathogenic cascade [7]. Extrapolating these mechanisms to pediatric chronic tonsillitis may offer new avenues for objective, immunologically based diagnostic markers to complement traditional clinical assessment.

5. Tonsillogenic and immune-mediated complications

The clinical significance of GABHS-related chronic and recurrent tonsillitis is further underscored by its association with suppurative and non-suppurative complications. Suppurative complications include peritonsillar, parapharyngeal, and retropharyngeal abscess or cellulitis, while non-suppurative complications include scarlet fever, acute rheumatic fever, and post-streptococcal glomerulonephritis [22,24]. Acute GABHS tonsillitis can occasionally precipitate rheumatic fever and acute glomerulonephritis, complications that are largely preventable with timely penicillin therapy; although rare in resource-rich settings, they remain clinically significant in several populations worldwide [21].

An increasingly recognized, though still debated, immune-mediated complication is pediatric autoimmune neuropsychiatric disorder associated with streptococcal infections (PANDAS), characterized by abrupt onset or exacerbation of obsessive-compulsive disorder and/or tic disorder following GABHS infection, thought to result from cross-reactive anti-neuronal antibodies [20]. A rare but life-threatening suppurative complication is Lemierre's syndrome, involving internal jugular vein thrombophlebitis following an oropharyngeal infection, which despite being uncommon in the antibiotic era can progress rapidly and carries significant mortality risk if unrecognized [23]. Conservative antibiotic management of pediatric peritonsillar abscess has been shown to

be effective in the majority of cases (up to 87% in one retrospective cohort), although older age and severe presentation are associated with higher rates of treatment failure requiring surgical intervention [33].

6. Emerging non-antibiotic and adjunctive approaches

Given concerns regarding antibiotic overuse and resistance, adjunctive and microbiome-modulating strategies have attracted growing interest. A prospective study of 98 children aged 5-15 years with recurrent throat and tonsil infections found that paraprobiotic lozenges containing heat-killed *Lactobacillus helveticus* MIMLh5 were associated with significant reductions in infection frequency, enlarged submandibular glands, and positive throat cultures, alongside decreased antibiotic and corticosteroid prescriptions over three months [30]. Similarly, incorporation of probiotic strains such as *Bifidobacterium adolescentis* and *Streptococcus salivarius* BLIS K12 into conservative management protocols has been associated with improved sanitation of chronic oropharyngeal infection foci and stimulation of innate immune responses [31]. While promising, these approaches require further controlled evaluation before routine adoption in pediatric CT management.

7. Diagnostic implications and directions for future research

Existing diagnostic approaches to chronic tonsillitis - including quantitative salivary interleukin assays, cytological analysis of tonsillar surface smears, lacunar content examination, mucosal electrical impedance measurement, infrared spectroscopy of saliva, exhaled gas analysis, fine-needle aspiration biopsy, and rheotonsillography - each provide partial information but share common limitations: technical complexity, dependence on non-standard equipment, invasiveness in some cases, and susceptibility to confounding by comorbid conditions such as laryngopharyngeal reflux or postnasal drip syndrome. Clinical scoring systems such as the original Centor score and its McIsaac modification, alongside national diagnostic guidance recommending rapid testing in patients with sore throat [12,13], likewise show limited standalone accuracy: in one pediatric cohort, a Centor score of 3 or more had a sensitivity of only 22.3% and specificity of 79.0% relative to rapid antigen testing, and C-reactive protein did not reliably differentiate viral from bacterial pharyngitis [32].

Consequently, clinical assessment - history taking, symptom evaluation, and mesopharyngoscopy - continues to play the leading role in everyday diagnostic practice, despite the absence of clearly defined criteria for the transition of the tonsil from a functionally beneficial immune organ to a focus of chronic infection. Integrating microbiological data (culture and rapid



testing), emerging immunological biomarkers (salivary IL-6, CXCL9/10/11), and standardized clinical criteria into a unified, stepwise diagnostic algorithm represents a priority direction for future research and for improving the management of chronic tonsillitis in children, particularly in regions such as Central Asia where dedicated epidemiological and diagnostic data remain limited.

Conclusion

Current evidence confirms the central role of group A Streptococcus and of local immune dysregulation, particularly Th1-skewed cytokine responses and elevated salivary IL-6, in the pathogenesis of chronic tonsillitis in children, while also revealing the limitations of isolated microbiological, biochemical, or clinical-score-based testing. The risk of suppurative and non-suppurative tonsillogenic complications further reinforces the clinical importance of accurate diagnosis. The development of a comprehensive, evidence-based diagnostic algorithm that integrates clinical, microbiological, and immunological parameters is warranted to improve early detection, guide conservative therapy, and reduce the risk of tonsillogenic complications.

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