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REVIEW ARTICLE

Bronchiectasis in pediatrics

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ABSTRACT

Bronchiectasis in children is a long-term respiratory condition defined by a persistent productive cough, airway infection, and inflammation, with visible bronchial dilatation on chest computed tomography. It has a profound impact on children's well-being, daily life, and family economy. Prompt diagnosis is crucial, as early treatment can prevent progression and even reverse some changes. The condition's presentation and outcomes vary depending on the underlying causes, disease severity, and social or economic background. Thorough investigations to identify the underlying etiology are essential for optimizing treatment and preventing further lung damage. Pediatric bronchiectasis differs significantly from the adult form, with differences in diagnostic criteria, etiology, and treatment strategies. Although it is a substantial burden, bronchiectasis in children remains an underresearched area, highlighting the need for more focused efforts to improve care and reduce disparities. This narrative review explores the pathophysiology, diagnosis, and management of bronchiectasis in children.

Keywords: Bronchiectasis. Children. Pediatrics. Infection. Inflammation.

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INTRODUCTION

Bronchiectasis in children is a long-term respiratory disease characterized by chronic wet cough, airway inflammation and infection, and bronchial dilatation, which is visible on chest computed tomography (CT) scans[1,2]. Bronchiectasis is increasingly recognized as a common yet neglected disease, impacting in children's health, quality of life, and family finances. Despite its significant burden, disparities in care and outcomes remain, particularly in low and middle-income countries and among Indigenous populations. Detecting the condition early is crucial, for ensuring timely diagnosis and management, as they can potentially be reversed with appropriate intervention[2-5].

PATHOPHYSIOLOGY

The pathophysiology of bronchiectasis is complex, multifactorial, and influenced by etiologies and modifying factors, often specific to the population or setting under study. Despite these variations, the vortex diagram captures the key elements of bronchiectasis pathophysiology, where impaired mucociliary clearance, infection, inflammation, and airway damage interact between them perpetuating and promoting the progression of the disease (Fig. 1). Conditions such as cystic fibrosis (CF) and primary ciliary dyskinesia (PCD) exemplify this paradigm, as both inherently disrupt mucociliary function. Similarly, immunodeficiencies and airway injuries (e.g., from severe infections, toxic inhalation, or chronic aspiration) contribute by increasing susceptibility to infection and sustaining inflammation. The vortex model underscores the limitations of treatments that target only specific disease components, such as antibiotics or anti-inflammatory therapies. It emphasizes the need for comprehensive treatment strategies that address all aspects of the disease[6-8].

SPECTRUM OF CHRONIC COUGH

Bronchiectasis is part of a continuum of respiratory conditions characterized by chronic inflammation, endobronchial infection, and a persistent wet cough (Fig. 2). At the mild end of this spectrum is persistent bacterial bronchitis, characterized by a wet cough lasting more than 4 weeks without an alternative cause, typically resolving with a 2-week course of antibiotics[9]. While persistent bacterial bronchitis is a transient condition if left untreated, it can lead to ongoing infection-inflammation, eventually progressing to chronic suppurative lung disease and, in more severe cases, bronchiectasis[10-12].

Chronic suppurative lung disease is recognized as a syndrome involving persistent endobronchial symptoms but without radiographic evidence of bronchiectasis on chest CT[13,14]. These three conditions – persistent bacterial bronchitis, chronic suppurative lung disease, and bronchiectasis – share common underlying pathological mechanisms, and represent different stages of disease severity within the same spectrum[10].

RADIOLOGICAL INSIGHTS

In suspected pediatric bronchiectasis, a bronchoarterial ratio (BAR) > 0.8 (calculated

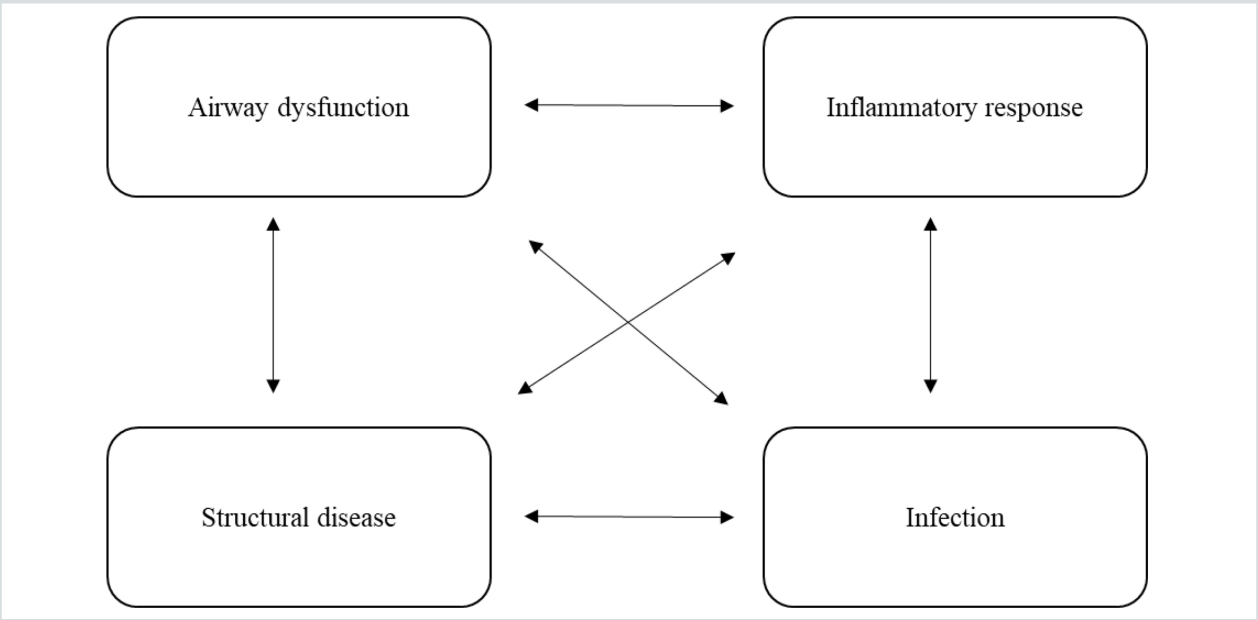

Figure 1. Vortex diagram *(adapted from Kantar et al.[8])*.

with the airway's inner diameter relative to the adjacent artery's outer diameter) is recommended over the adult cut-off of > 1-1.5 (Fig. 3)[1]. This adjustment accounts for children's smaller airway size relative to vessels, as applying adult criteria risks underestimating disease presence. While the pediatric cut-off improves diagnostic sensitivity, it may lower specificity. Given the typically milder presentation in children, prioritizing sensitivity is essential to minimize underdiagnosis in this population[15,16].

Other findings on the CT scan include the absence of progressive bronchial tapering toward the periphery, making peripheral bronchi visible. Additional CT features may involve bronchial wall thickening, mucus plugging, mosaic attenuation, and expiratory air trapping[17].

The radiological severity of bronchiectasis is determined using the modified Reiff score, which evaluates disease extent by grading each of the six lung lobes (including the lingula) and bronchiectasis morphology based on the BAR: cylindrical (BAR > 0.8- < 2), varicose (BAR ≥ 2- < 3), and cystic (BAR ≥ 3)[18,19].

Bronchiectasis, traditionally considered irreversible, is now recognized as a potentially reversible condition in some pediatric cases. Although historically defined by permanent bronchial dilatation, pediatric studies suggest that early diagnosis and optimal management can interrupt the infection-inflammation relation, potentially restoring normal airway structure on chest high-resolution CT (HRCT)[20,21].

Bronchiectasis in children may evolve over time but with appropriate medical treatment, most

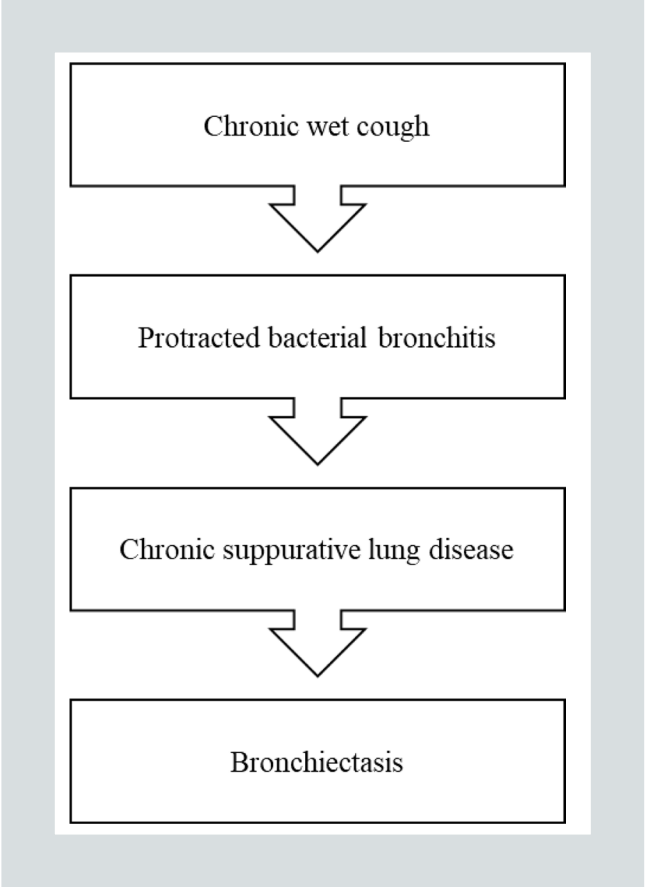

Figure 2. Spectrum of chronic wet cough, protracted bacterial bronchitis, chronic suppurative lung disease and bronchiectasis *(adapted from Chang et al.[10]).*

children without progressive conditions -such as CF - have the potential to improve[20]. This has been observed in cases like foreign body aspiration[22]. Moreover, bronchiectasis secondary to primary immunodeficiency in childhood is not inherently progressive, suggesting that timely and effective treatment could slow or even prevent disease progression[23].

Younger children with less extensive radiographic disease are more likely to experience reversibility, emphasizing the importance of early detection and timely treatment. In contrast, the presence of *Pseudomonas*

$$\text{BAR} = \frac{\text{Airway's inner diameter}}{\text{Adjacent artery's outer diameter}} > 0{,}8$$

Figure 3. Interpretation of the bronchoarterial ratio for the diagnosis of bronchiectasis in the pediatric population.

aeruginosa decreases the likelihood of reversibility, underscoring the need for microbiological monitoring and aggressive management of *P. aeruginosa*[20].

Magnetic resonance imaging (MRI) has been explored as a diagnostic and monitoring tool for bronchiectasis in various studies. It avoids radiation exposure, making it particularly suitable for pediatric patients who may require repeated imaging during long-term follow-up. MRI has demonstrated efficacy in evaluating soft tissue and can detect airway wall thickening and bronchial dilatation in certain cases, although MRI accuracy is generally lower than that of HRCT. Despite this, MRI holds promise as a valuable alternative for monitoring bronchiectasis progression, especially in situations where minimizing radiation exposure is a priority[24,25].

UNDERLYING ETIOLOGY

Bronchiectasis often arises from various underlying causes. When suspected, a thorough evaluation is crucial, involving a core set of investigations to identify potential factors and guide clinical management, with the aim of preventing further lung damage. The clinical presentation of bronchiectasis is influenced by the underlying etiology, disease severity, and

various factors, including geographical location and socioeconomic conditions. While not always directly correlated with disease severity, comorbidities are frequently observed and may include asthma, malnutrition, cardiac dysfunction, sleep disorders, gastro-esophageal reflux disease, and psychosocial disorders. These factors can have a significant impact on quality of life, highlighting the need for a comprehensive, multidisciplinary approach to patient care[1,2].

The most common etiologies are[26,27]:

- CF: This genetic disorder results from mutations in the CF transmembrane conductance regulator gene, which leads to abnormal mucus production and impaired mucociliary clearance, creating an environment conducive to chronic respiratory infections and progressive bronchial damage. CF often results in bronchiectasis from an early age, with infections like *P. aeruginosa* exacerbating the condition over time.

- Post-infectious bronchiectasis: Post-infectious bronchiectasis can follow severe respiratory infections, such as pneumonia, with immune dysregulation playing a key role. Elevated airway inflammation markers (interleukin-1 β, interleukin-6) and reduced systemic interferon-γ (IFN-γ) in response to non-typeable *H. influenzae* are observed, along with decreased Toll-like receptor expression, impairing bacterial clearance. Genetic studies suggest that specific human leukocyte antigens (HLA), such as HLA-DR1 and DQ5, may increase susceptibility to respiratory infections and bronchiectasis[28,29].

- Immunodeficiencies: Primary and acquired immunodeficiencies are contributors to bronchiectasis. Conditions such as common variable immunodeficiency, immunoglobulin G (IgG) deficiency, and agammaglobulinemia impair immune function, increasing susceptibility to infections. Affected individuals often exhibit reduced levels of IgG subclasses, particularly IgG2 and IgG3, impaired antibody responses to polysaccharide antigens, and polymicrobial infections, all of which contribute to bronchiectasis development[27].

- PCD: PCD is a rare genetic disorder where defective ciliary motility impairs the mucociliary clearance system. This results in the accumulation of mucus and pathogens in the airways, leading to chronic respiratory infections and progressive airway damage, ultimately causing bronchiectasis. The most common manifestations of PCD include persistent cough, chronic sinusitis, and hearing loss. Early diagnosis is crucial to manage symptoms and prevent severe bronchiectasis[30–33].

- Chronic pulmonary aspiration: In children with confirmed aspiration, studies show that 66% developed bronchiectasis, with the highest prevalence in those under 2 years of age. The right lower lobe, left lower lobe, and right upper lobe are most commonly affected. Risk factors for chronic aspiration include severe neurological impairment and gastro-esophageal reflux disease. In some cases, bronchiectasis may improve or resolve with appropriate treatment[34].

– Endobronchial obstruction: Bronchiectasis can result from endobronchial obstruction due to foreign body aspiration, endobronchial tuberculosis, or tumors. The obstruction disrupts normal airflow, resulting in recurrent infections, chronic inflammation, and progressive structural damage to the airways promoting the development of bronchiectasis. Radiological features of bronchial obstruction include lung collapse, air trapping, and involvement of adjacent lobes.

– Syndromes associated with tracheobronchomalacia: Tracheobronchomalacia can lead to obstruction, air trapping, and bronchiectasis. It is commonly associated with syndromes and genetic disorders affecting airway integrity and lung development[35].

– Systemic inflammatory diseases: Conditions, such as rheumatoid arthritis can also contribute to the development of bronchiectasis. Although these diseases may not directly cause airway damage, systemic inflammation can contribute to airway remodeling and bronchiectasis over time.

The location and distribution of bronchiectasis, whether focal or diffuse, can vary widely depending on the cause and may provide clues to the underlying etiology[17]. In PCD, bronchiectasis predominantly affects the middle lobe, lingula, and lower lobes, a pattern also observed in immunodeficiencies. In contrast, CF typically involves the upper lobes, while aspiration-related bronchiectasis is more common in the lower lobes and the right upper lobe. Although certain patterns are more frequently associated with specific etiologies – such as basal predominance in idiopathic cases; middle lobe involvement in PCD; and middle, lingular, and lower lobe involvement in hypogammaglobulinemia – there is considerable overlap in CT findings, making it challenging to determine the underlying etiology based on distribution alone[36].

MICROBIOLOGY

The most common bacterial pathogens in children with bronchiectasis include *H. influenzae*, *Streptococcus pneumoniae*, *Moraxella catarrhalis*, *Staphylococcus aureus*, and *P. aeruginosa*. Non-typeable *H. influenzae* is the predominant pathogen in this group, followed by *S. pneumoniae*. Children with bronchiectasis often show impaired immune responses, such as reduced IFN-γ production, which contributes to increased airway inflammation. *P. aeruginosa* is more commonly found in older children with advanced disease and in adults, where it is linked to more severe progression and accelerated pulmonary decline. While *P. aeruginosa* is typically an opportunistic pathogen in immunocompromised individuals, it becomes a significant pathogen in non-CF bronchiectasis in adults, often coexisting with *H. influenzae*[26,28].

Non-tuberculous mycobacteria are rarely found in children with bronchiectasis, and their clinical significance in this population remains unclear. In addition, culture methods have identified numerous anaerobic organisms in bronchiectasis patients, such as α-hemolytic *Streptococcus*, which are typically considered normal oral or upper airway flora.

It remains unclear whether these organisms are pathogenic or contaminants[36–38].

Viral infections, especially influenza, respiratory syncytial virus, and adenovirus, contribute to bronchiectasis physiopathology and exacerbations by impairing immune responses, particularly macrophage and neutrophil function, increasing susceptibility to bacterial infections. *In vitro* and experimental studies suggest viruses enhance bacterial adherence to pulmonary epithelial cells and impair clearance. Moreover, a study of children with chronic wet cough revealed that viral-bacterial co-infection enhances the neutrophilic airway response, suggesting that viral infections not only facilitate bacterial colonization but also aggravate airway inflammation, worsening bronchiectasis[39].

Respiratory viruses are frequently detected in clinically stable children with bronchiectasis, often alongside bacterial co-infections, highlighting viral-bacterial interactions[37,38]. A Canadian retrospective study found that 8% of children with adenovirus infections developed chronic pulmonary changes, and 30% had bronchiectasis on chest CT[40]. Adenovirus is recognized as a risk factor for persistent bacterial bronchitis. While clinical evidence is still limited, these findings support influenza vaccination as a recommended measure for both children and adults with bronchiectasis. The role of antibiotics during viral-related exacerbations remains uncertain, particularly when concurrent bacterial data are lacking[37,38].

Exacerbations of bronchiectasis in children are characterized by increased respiratory symptoms, primarily increased cough frequency, with or without increased sputum production or purulence, lasting for at least 3 days. Given that obtaining bacterial data from the lower airways is often challenging in young, non-expectorating children, a pragmatic approach of treating these exacerbations with antibiotics targeting common pathogens such as *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis* may be warranted[1].

DIAGNOSTIC ASSESSMENT

For suspected or confirmed bronchiectasis, a structured diagnostic workup is recommended, including a chest HRCT, sweat test to exclude CF, spirometry (if feasible by age), complete blood count, immunological tests for total IgG, IgA, IgM, IgE and specific antibodies to vaccine antigens to identify immune disorders, and lower airway bacteriology (Fig. 4). Spirometry, routinely performed from age four, can help identify and monitor lung function, although it is not used to diagnose or assess disease severity. Lower airway bacteriology is important for guiding antibiotic therapy during exacerbations. Sputum cultures should be obtained from patients who can expectorate, while induced sputum and bronchoalveolar lavage can be used for those unable to expectorate. Tuberculosis or human immunodeficiency virus testing should be included if suspected. Additional evaluations may be required depending on the clinical presentation and initial test results. These may include bronchoscopy to assess structural anomalies, rule out foreign body aspiration, or perform a comprehensive microbiological analysis through bronchoalveolar lavage. In selected cases, further

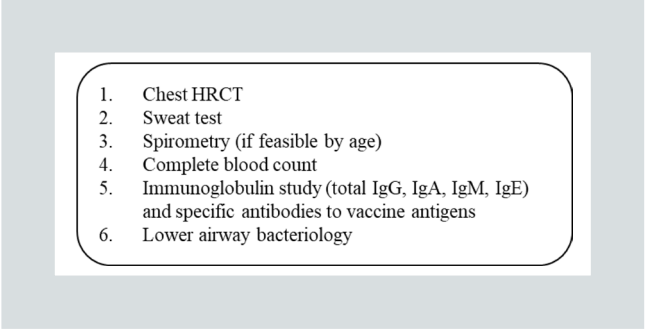

Figure 4. Minimum set of investigations *(adapted from Chang et al.[1]).*

investigations may be warranted, such as studies for gastro-esophageal reflux disease, expanded genetic testing for CF, comprehensive immunological assessment, or diagnostic evaluation for PCD[1,41,42].

When diagnosing PCD, the approach varies based on the guidelines followed. The European Respiratory Society (ERS) recommends evaluating patients with a combination of typical symptoms, potentially aided by predictive tools like the PCD diagnostic algorithm rule (PICADAR) score[32]. In contrast, the American Thoracic Society (ATS) advises testing patients presenting with at least two of the following four clinical features: Early-onset chronic wet cough, early-onset chronic nasal congestion, unexplained neonatal respiratory distress, or an organ laterality defect[33].

The diagnosis of PCD is usually based on a combination of tests, including nasal nitric oxide measurement (often reduced in PCD patients), electron microscopy to examine ciliary ultrastructure, high-speed optical microscopy to assess ciliary motility, and genetic testing for mutations linked to PCD. The PICADAR questionnaire is also commonly used to aid clinical assessment[43]. Efforts are underway to develop unified guidelines from both the ERS and ATS to establish consistent and accurate diagnostic criteria for PCD, enhancing standardization in the diagnostic process.

THERAPEUTIC APPROACH

The management of bronchiectasis in children primarily aims to reduce inflammation and infection, with the following therapeutic goals: prompt treatment of respiratory exacerbations, prevention of future exacerbations, addressing identifiable underlying causes, and managing comorbidities such as malnutrition, vitamin D deficiency, and chronic lung aspiration (Fig. 5)[1].

Respiratory exacerbations in bronchiectasis are often characterized by excessive bronchial secretions, impaired mucociliary clearance, and mucous plugging. As a result, airway clearance techniques are a crucial part of the treatment strategy. Furthermore, airway clearance techniques have been demonstrated to be safe for individuals with stable bronchiectasis, both in adults and children. They contribute to improved sputum expectoration, better lung function parameters, symptom relief, and enhanced quality of life[44,45]. Hypertonic saline can improve pulmonary function and reduce morbidity associated with bronchiectasis[46]. However, the ERS guidelines advise against the routine use of hypertonic saline and inhaled mannitol in children with bronchiectasis, highlighting the importance of personalized treatment approaches.

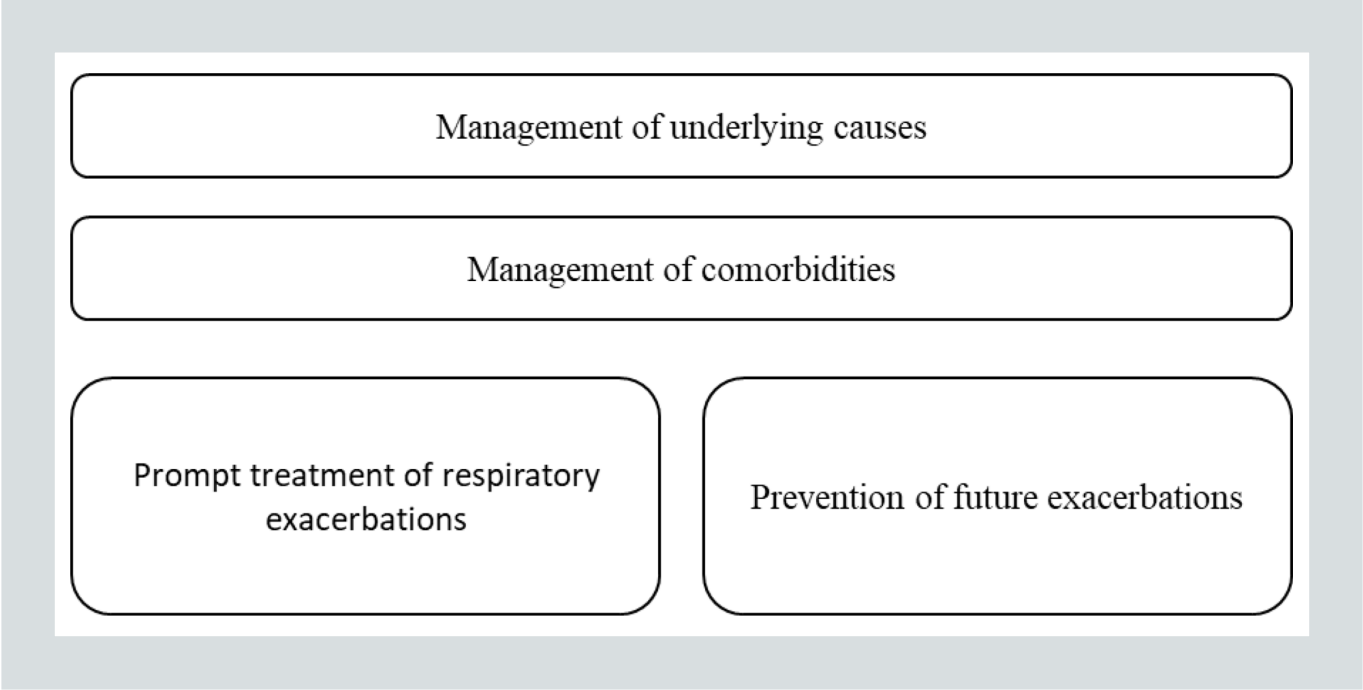

Figure 5. Treatment strategies.

Bronchodilators and inhaled corticosteroids are indicated in the presence of bronchial hyperreactivity[1,41]. There is insufficient evidence to support the routine use of inhaled corticosteroids in bronchiectasis, either as monotherapy or in combination with long-acting β-agonists[47-49].

Antibiotics are essential in managing bronchiectasis in children, they reduce bacterial load and disrupt the infection-inflammation relation. During acute exacerbations, they are critical for controlling the infection and preventing symptom progression[41,50].

The management of bronchiectasis exacerbations involves personalized antibiotic therapy based on the severity of the episode and the cultures obtained. For mild-to-moderate exacerbations, oral antibiotics such as amoxicillin-clavulanic acid are typically prescribed. A randomized controlled trial for treating protracted bacterial bronchitis in children used amoxicillin-clavulanic acid at a dose of 25-35 mg/kg twice daily[51]. In clinical practice, this dosage can be adjusted based on local resistance patterns[41]. For severe exacerbations and when there is no improvement with oral treatment, intravenous antibiotics are preferred. The recommended initial duration of antibiotic therapy is 14 days, with treatment extended for an additional 2 weeks with the appropriate antibiotic if symptoms persist[41]. Antibiotic selection should be based on microbiological results, a targeted treatment approach that optimizes therapeutic outcomes and minimizes the risk of bacterial resistance[1].

The ERS guidelines advocate for the eradication of *P. aeruginosa* in bronchiectasis due to its strong association with poor clinical

outcomes. While chronic endobronchial infections are common, there is limited evidence supporting the eradication of non-*P. aeruginosa* pathogens, as they are not consistently associated with worse outcomes[1].

In long-term management, antibiotics reduce bacterial load, enhance mucociliary clearance, and modulate inflammatory responses, all crucial for controlling chronic airway infection and inflammation. The goal of treatment is to reduce exacerbation frequency and slow the decline in lung function. Macrolides are effective particularly in children who experience frequent exacerbations (≥ 3 exacerbations per year) or have had more than one hospitalization[1]. A randomized controlled trial showed that a once-weekly azithromycin dose of 30 mg/kg for 12–24 months significantly reduced the frequency of respiratory exacerbations in children with chronic suppurative lung disease or bronchiectasis[52]. Alternatively, a common clinical practice is to prescribe 10 mg/kg 3 times/week, either on Monday-Wednesday-Friday or any other set of 3 days. A treatment course of at least 6 months is recommended, with periodic reassessments to evaluate the effectiveness[1,53,54].

Vaccination plays a crucial role in managing bronchiectasis by preventing respiratory infections. Guidelines recommend fully immunization according to their national immunization programs, including vaccines against influenza and pneumococcus[1,41]. Evidence supports the routine use of 23-valent pneumococcal vaccination in children with bronchiectasis, with some recommending a repeat dose after 5 years[55]. However, as pneumococcal vaccination recommendations may vary, it is important to adhere to local guidelines.

In cases of significant, life-threatening hemoptysis, more invasive treatments such as bronchial artery embolization or surgery may be necessary, especially if conservative management fails[1]. Surgical treatment is rarely indicated in pediatric bronchiectasis but may be considered in highly selected cases with localized lesions not associated with an underlying disease and recurrent severe infections refractory to optimal medical management. Surgery for diffuse bronchiectasis is exceptionally rare and generally not recommended.

New anti-inflammatory therapies, such as reversible inhibitors of dipeptidyl peptidase 1, have shown promising results in adults with bronchiectasis. In particular, treatment with brensocatib significantly prolonged the time to the next exacerbation, reduced the risk of exacerbations, and lowered sputum neutrophil elastase levels compared to placebo[56,57]. However, these therapies have not yet been approved for use in children, and further studies are needed to assess their safety and efficacy in the pediatric population.

CONCLUSION

This overview highlights the present understanding and management strategies for bronchiectasis in children. However, further research is essential to enhance our characterization of the pediatric population with bronchiectasis, establish optimal management protocols, and deepen our understanding of the specific characteristics of bronchiectasis in children that distinguish it from the adult form[58,59]. In addition, there is a need to explore novel therapeutic options, refine diagnostic tools, and focus on

preventive strategies to reduce the burden of this chronic condition in the pediatric population.

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CONFLICTS OF INTEREST

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ETHICAL CONSIDERATIONS

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The study does not involve patient personal data nor requires ethical approval. The SAGER guidelines do not apply.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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