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Non-cystic fibrosis bronchiectasis: An updated review

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Abstract

Non-cystic fibrosis bronchiectasis is a chronic and heterogeneous respiratory disease characterized by irreversible dilation of the bronchi, persistent inflammation, and recurrent respiratory infections. Its global prevalence varies widely, from 52.3 to more than 1000 cases per 100,000 individuals, with a progressive increase attributed to improved diagnostic techniques and greater clinical awareness. The condition mainly affects older adults and is currently recognized as the third most frequent chronic inflammatory airway disease, after chronic obstructive pulmonary disease and asthma. The causes are diverse and include post-infectious damage, particularly after tuberculosis or pneumonia, immune deficiencies, autoimmune disorders, congenital malformations, and chronic aspiration.

The pathophysiological basis of the disease is a self-perpetuating cycle of infection and inflammation, driven by chronic bacterial colonization especially by Pseudomonas aeruginosa and neutrophilic inflammation that progressively destroys the bronchial wall. Alterations in the bronchial microbiome and structural remodeling aggravate mucus retention and infection. Clinically, patients present with a persistent productive cough and frequent exacerbations that impair lung function, reduce quality of life, and increase mortality. Diagnosis is established through high-resolution computed tomography, lung function tests, and microbiological cultures. Prognostic indices such as the Bronchiectasis Severity Index, the FACED score, and the E-FACED score allow objective assessment of severity and risk of mortality.

Treatment aims to reduce bacterial load, prevent exacerbations, and improve symptoms through prolonged antibiotic therapy, macrolides, respiratory physiotherapy, and pulmonary rehabilitation. Managing comorbidities and maintaining vaccination coverage are also essential. Despite therapeutic advances, this disease entails a significant physical and psychological burden, requiring a multidisciplinary approach that integrates medical, functional, and psychosocial care to improve adherence, prognosis, and quality of life.

Keywords: Bronchiectasis; Chronic Inflammation; Bacterial Colonization; Airway Remodeling; Exacerbations; Multidisciplinary Management

1. Introduction

Bronchiectasis is a chronic respiratory disease characterized by the permanent dilation of the bronchi, leading to persistent symptoms such as chronic cough, sputum production, and recurrent respiratory infections. Unlike cystic

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fibrosis, a genetic disorder primarily affecting the lungs and digestive system, bronchiectasis can result from various causes, including prior infections, immune system dysfunctions, and other pulmonary diseases. This distinction is essential, as both conditions differ in their underlying mechanisms and management approaches. The global and regional epidemiological relevance of bronchiectasis is considerable and continues to rise, partly due to advances in diagnostic methods and increased clinical awareness (1; 2).

The prevalence of bronchiectasis varies widely, with estimates ranging from 52.3 to more than 1,000 cases per 100,000 people, with methodological differences between studies being a determining factor in this variability (1). It is currently recognized as the third most common chronic inflammatory disease of the airways, after chronic obstructive pulmonary disease (COPD) and asthma (2). Mortality rates in patients with bronchiectasis range from 16% to 24.8% over a period of four to five years, highlighting the severity of this condition (1).

From a clinical perspective, the most common symptoms include dyspnea, cough, wheezing, and frequent exacerbations, all of which have a considerable impact on patients' quality of life. Furthermore, the disease is associated with a significant increase in healthcare utilization, both in hospitalizations and outpatient consultations, reflecting the high healthcare burden it represents (3).

Economically and socially, bronchiectasis generates substantial medical costs from repeated hospital admissions and prolonged treatments (Chalmers et al., 2024). Added to this are the indirect costs associated with lost income and productivity, which further aggravate its socioeconomic impact (3).

Although bronchiectasis has been increasingly recognized as a significant health problem, it remains underdiagnosed and under researched compared to other chronic respiratory diseases. The creation of international registries and guidelines has contributed to improving understanding and management of the disease; however, significant gaps in care and available therapeutic options remain, underscoring the need to continue promoting research and investment in this field (3; 4).

The objective of this article is to provide an updated analysis of non-cystic fibrosis bronchiectasis, addressing its epidemiological relevance, clinical burden, economic and social impact, as well as recent advances in its diagnosis, management, and prognosis.

2. Methodology

For the development of this review on non-cystic fibrosis bronchiectasis, a comprehensive literature analysis was conducted with the objective of examining its epidemiology, etiological spectrum, pathophysiological mechanisms, clinical manifestations, diagnostic strategies, therapeutic approaches, and current challenges in management. Particular attention was given to the clinical burden, quality-of-life impact, treatment optimization, and recent advances in pharmacological and non-pharmacological interventions for affected patients.

The review was based on the consultation of well-established scientific databases, including PubMed, Scopus, and Web of Science, selected for their relevance in respiratory medicine, pulmonology, and infectious disease research. Strict inclusion and exclusion criteria were applied to ensure the quality and pertinence of the selected studies. Articles published between 2020 and 2025, in English or Spanish, were included if they addressed essential aspects such as the epidemiology of bronchiectasis, pathogenesis, microbiological profiles, diagnostic imaging, treatment strategies, and patient outcomes. Studies lacking peer review, with incomplete data, or presenting duplicated content were excluded. Keywords used in the search strategy included: Bronchiectasis, chronic inflammation, bacterial colonization, airway remodeling, exacerbations, multidisciplinary management.

The initial search identified 36 relevant sources, including original research articles, systematic reviews, meta-analyses, and clinical practice guidelines published by recognized respiratory medicine and thoracic societies. These documents were critically analyzed to extract data related to epidemiological trends, underlying causes, microbiological patterns, prognostic indicators, and recent advances in both pharmacological and supportive management.

Additionally, artificial intelligence tools were employed as complementary aids for information synthesis, thematic categorization, and identification of conceptual relationships among the studies reviewed. This methodological support improved the efficiency of literature organization and contributed to maintaining coherence and clarity in the structural development of the review.

The analysis followed a qualitative and comparative approach, categorizing findings thematically to identify current management practices, gaps in clinical care, limitations of existing evidence, and future directions for research and guideline development. This structured, evidence-based approach provided an updated and integrative overview of non-cystic fibrosis bronchiectasis, emphasizing the importance of early diagnosis, individualized therapy, multidisciplinary follow-up, and continuous evaluation of emerging therapeutic strategies to improve patient outcomes.

3. Epidemiology

The prevalence of bronchiectasis varies considerably worldwide, with estimates ranging from 52.3 to more than 1000 cases per 100,000 individuals, depending on methodological and regional differences (1). In China, epidemiological data show an increase from 75.48 per 100,000 inhabitants in 2013 to 174.45 per 100,000 in 2017, particularly affecting individuals over 50 years of age (5). Currently, bronchiectasis is recognized as the third most common chronic inflammatory airway disease, following COPD and asthma (2).

There is marked heterogeneity in the geographic distribution of bronchiectasis, influenced by local etiologies, comorbid conditions, and microbiological characteristics (1; 6). In Asian populations, patients tend to be younger and exhibit milder disease compared with those in Western countries, where unique endophenotypes such as post-tuberculosis bronchiectasis are more prevalent (6). The presence of non-tuberculous mycobacteria (NTM) among patients with bronchiectasis also shows regional variability, with an estimated global prevalence of approximately 10% (7).

Age is another key determinant in the distribution of bronchiectasis. The condition predominantly affects older adults, with a notable increase in both prevalence and disease burden observed in individuals over 50 years (5). Mortality risk likewise escalates with age, as older patients experience higher mortality rates than younger cohorts (8).

Significant disparities also exist between developed and developing countries. In high-income nations, advanced diagnostic tools and stronger healthcare systems contribute to more accurate detection and management of the disease. Conversely, in low- and middle-income countries, limited healthcare access and diagnostic resources lead to underdiagnosis, greater disease severity, and higher mortality (1). The socioeconomic burden is particularly pronounced in developed regions, where the costs associated with chronic disease management and recurrent hospitalizations are substantial (9).

Underdiagnosis remains a major global concern. Insufficient recognition of bronchiectasis often results in delayed or inappropriate treatment, worsening disease outcomes. Historically, limited awareness and low research investment have contributed to its classification as an orphan disease; however, growing interest and recent initiatives are helping to reverse this trend (2; 3). The expansion of international registries and collaborative research networks is essential to improve diagnostic accuracy, optimize management strategies, and reduce the global burden of bronchiectasis (2).

4. Etiology and predisposing factors

Previous respiratory infections play a fundamental role in the development of bronchiectasis. Tuberculosis and pneumonia are among the most significant contributors, as both can induce chronic inflammation and irreversible damage to the bronchial walls (10). Likewise, viral infections may also precipitate the disease by causing persistent airway inflammation and obstruction, which promote long-term structural alterations in the bronchi (11).

Inflammatory diseases and immunodeficiencies represent another important etiological group. Common variable immunodeficiency (CVID) is frequently associated with a high prevalence of bronchiectasis due to recurrent infections and immune dysregulation (11). Similarly, primary antibody deficiencies can contribute to the condition through a cycle of infectious and non-infectious mechanisms, highlighting the need for multidisciplinary management that integrates pulmonology, immunology, and infectious disease care (12).

Congenital disorders may also predispose individuals to bronchiectasis. Syndromes such as Williams-Campbell, characterized by deficient bronchial cartilage, result in structural airway weakness that promotes recurrent collapse and subsequent bronchial dilation (13).

Autoimmune diseases are likewise recognized contributors. Conditions such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) can lead to bronchiectasis through chronic inflammation and immune-mediated injury to the bronchial architecture (11).

Other contributing factors include chronic aspiration and bronchial obstruction, both of which can cause localized inflammation and structural damage that ultimately lead to bronchiectasis (10). In addition, hypersensitivity responses such as allergic bronchopulmonary aspergillosis represent a distinct pathway, in which bronchopulmonary fungal allergies trigger inflammation, mucus plugging, and progressive airway dilation (13).

5. Physiopathology

The pathophysiology of bronchiectasis is fundamentally sustained by a self-perpetuating infection–inflammation cycle. Chronic bacterial colonization, particularly by Pseudomonas aeruginosa, triggers persistent neutrophilic inflammation characterized by the release of neutrophil serine proteases, such as neutrophil elastase, which promote progressive tissue destruction and airway remodeling (3; 14). Neutrophil extracellular traps (NETs) further exacerbate this process by releasing proteolytic enzymes that intensify airway injury, and their presence has been correlated with greater disease severity and unfavorable clinical outcomes (14).

The bronchial microbiome plays a crucial role in this pathophysiological cascade. In patients with bronchiectasis, microbial diversity is significantly reduced, with a predominance of pathogenic species that contribute to sustained inflammation and infection (15; 16). This dysbiosis reinforces the infection–inflammation cycle, aggravating airway damage and clinical deterioration. Integrative microbiomics studies have revealed that the interactions within microbial communities, rather than the abundance of individual pathogens, determine the risk of exacerbations, underscoring the therapeutic potential of targeting microbial network dynamics rather than single organisms (16).

Structural remodeling of the airways is a defining feature of bronchiectasis, characterized by irreversible bronchial dilatation and wall destruction. These structural changes are compounded by impaired mucociliary clearance due to ciliary dysfunction, a hallmark of the disease (14; 17). Mucus hyperconcentration and obstruction further impair airway patency, facilitating microbial persistence. Overexpression of mucins such as MUC5B and MUC5AC contributes to mucus plugging and defective clearance, perpetuating infection and inflammation (17, 18).

The immunological landscape of bronchiectasis is dominated by neutrophilic inflammation, although an eosinophilic component has been identified in a subset of patients, suggesting underlying heterogeneity that may influence treatment response (14; 19). Dysregulated immune responses, including excessive production of pro-inflammatory cytokines such as interleukin-1β (IL-1β), enhance mucus hypersecretion and perpetuate airway inflammation, thereby accelerating disease progression (17).

6. Clinical manifestations and diagnosis

Clinical manifestations of non-cystic fibrosis bronchiectasis are dominated by chronic respiratory symptoms and recurrent exacerbations. The most characteristic symptom is a persistent productive cough, resulting from impaired mucociliary clearance and airway dilation, which leads to continuous sputum production and bacterial colonization (20). Exacerbations represent a major clinical challenge, particularly among patients with severe disease phenotypes such as those chronically colonized by Pseudomonas aeruginosa (19). These exacerbations are frequently precipitated by infections, including viral pathogens such as SARS-CoV-2, which have been shown to increase both the frequency of exacerbations and hospitalization rates (21).

A comprehensive clinical evaluation is fundamental for diagnosis and disease characterization. A detailed medical history and thorough physical examination are essential to identify key symptoms and potential etiological factors, such as prior infections or systemic inflammatory diseases (19; 22). Functional respiratory tests, including spirometry and lung volume assessments, provide quantitative data on the degree of airway obstruction and lung function decline, parameters that are critical for assessing disease severity and monitoring progression (23).

Imaging studies and microbiological analyses constitute the cornerstone of diagnostic confirmation. High-resolution computed tomography (CT) remains the gold standard for diagnosis, revealing hallmark features such as bronchial dilation, wall thickening, and architectural distortion. CT imaging is also valuable in identifying structural abnormalities in patients with a history of smoking or other chronic pulmonary conditions (24). Microbiological cultures of sputum or bronchoalveolar samples are indispensable for identifying key pathogens including Pseudomonas aeruginosa, Haemophiles influenzae, and nontuberculous mycobacteria (NTM) that contribute to disease progression and guide antibiotic selection (10; 25).

Biomarker evaluation and sputum analysis provide additional diagnostic and prognostic information. Elevated blood eosinophil counts have been associated with a distinct bronchiectasis phenotype characterized by more severe disease and increased exacerbation frequency (22). Sputum analyses can detect atypical pathogens and contribute to understanding the underlying microbiological environment, including potential CFTR dysfunction in patients with non-cystic fibrosis bronchiectasis (25).

Differential diagnosis is a critical step in the diagnostic process, as several chronic respiratory diseases share overlapping clinical and radiological features. Differentiating non-cystic fibrosis bronchiectasis from conditions such as COPD, severe asthma, and cystic fibrosis requires integration of clinical presentation, imaging findings, microbiological results, and, when necessary, genetic testing (25; 26).

7. Stratification of severity and prognosis

Prognostic assessment in non-cystic fibrosis bronchiectasis relies on multifactorial scoring systems that integrate clinical, functional, and microbiological parameters to estimate disease severity and mortality risk. The Bronchiectasis Severity Index (BSI) and the FACED score are the most widely validated tools, both demonstrating strong predictive value for long-term outcomes. Higher scores in these indices have been consistently correlated with an increased risk of mortality and frequent exacerbations. The E-FACED score, an extended version of the FACED index that incorporates the frequency of exacerbations and the presence of bacterial colonization, offers an enhanced prognostic perspective by emphasizing the impact of recurrent infections on disease progression (27).

Several clinical factors contribute to disease progression and mortality in bronchiectasis. Among the most significant are impaired lung function, advanced age, and the extent of bronchial involvement observed on imaging studies. The modified Medical Research Council (mMRC) dyspnea scale, a simple patient-reported measure of breathlessness, has also been identified as a valuable predictor of mortality, underscoring the relevance of incorporating patient-reported outcomes into clinical evaluation and follow-up (27).

Colonization by Pseudomonas aeruginosa is one of the most critical prognostic determinants in bronchiectasis. The presence of this pathogen is associated with poorer lung function, increased rates of hospitalization, and higher mortality (28). It serves as a marker of advanced disease severity and chronic infection, which complicates treatment and often necessitates prolonged or suppressive antibiotic therapy (29). Moreover, patients chronically colonized with Pseudomonas aeruginosa frequently exhibit more extensive radiographic bronchiectasis and significantly lower quality-of-life scores compared with non-colonized patients (28).

8. Therapeutic management

Pharmacological management of non-cystic fibrosis bronchiectasis focuses on reducing bacterial load, preventing exacerbations, and alleviating symptoms, while minimizing treatment-related complications. Antibiotic therapy remains the cornerstone of pharmacological treatment. Long-term use of inhaled antibiotics is recommended for patients with chronic Pseudomonas aeruginosa infection, as these agents have been shown to decrease exacerbation frequency and bacterial burden; however, their effects on lung function and quality of life remain variable (3; 30). Oral macrolides are another effective option, demonstrating reductions in exacerbation rates and improvements in quality of life, though their long-term use carries risks of adverse events and the development of bacterial resistance (31).

Inhaled corticosteroids (ICS) and bronchodilators are used selectively in bronchiectasis management. The clinical evidence supporting ICS for improving lung function is limited, and high-dose use has been linked to an increased risk of Staphylococcus aureus infection, necessitating cautious application (32). Bronchodilators may provide symptomatic relief in patients with coexisting airway hyperreactivity, although their routine use is not universally recommended (3).

Non-pharmacological interventions are fundamental components of bronchiectasis management. Airway clearance techniques, including respiratory physiotherapy and postural drainage, are strongly recommended for most patients to facilitate mucus expectoration, alleviate symptoms, and reduce exacerbation frequency. Physical exercise and pulmonary rehabilitation are indicated for individuals with reduced exercise tolerance, as they improve physical conditioning and enhance overall quality of life. Preventive strategies such as vaccination play an essential role in minimizing the risk of respiratory infections that can trigger exacerbations (3).

Comprehensive management also requires addressing underlying causes and comorbid conditions. The control of gastroesophageal reflux, chronic sinusitis, asthma, or COPD is vital to prevent exacerbation triggers and optimize

respiratory function. In cases related to specific etiologies such as primary ciliary dyskinesia or immunodeficiencies, tailored treatments should be implemented to target the underlying pathophysiological mechanisms (3; 18).

For patients with advanced or refractory disease, surgical intervention may be considered. Lung resection is reserved for those with localized disease unresponsive to medical therapy, while lung transplantation remains an option for selected patients with end-stage diffuse bronchiectasis and respiratory failure (3; 13).

9. Prognosis and quality of life

Non-cystic fibrosis bronchiectasis (NCFB) is associated with a substantial treatment burden, as patients often require complex therapeutic regimens that involve multiple medications and airway clearance techniques. These demanding treatment schedules, along with medication side effects, contribute to a negative impact on health-related quality of life (Houl). Psychological comorbidities are also frequent; depression and anxiety affect approximately one-third of patients, complicating disease management, reducing adherence to therapy, and further diminishing overall well-being (33). The European Respiratory Society guidelines underscore the importance of controlling daily symptoms and preventing exacerbations as key strategies for improving clinical outcomes and patient quality of life (3).

From a functional perspective, long-term respiratory impairment is a major concern in NCFB. Lung function can be effectively monitored using impulse oscillometer, particularly in patients unable to perform conventional spirometry due to advanced disease or limited effort capacity (34). In pediatric populations, early detection and comprehensive management are critical to preserving lung function and preventing irreversible structural damage over time (35).

Optimal prognosis requires a multidimensional approach that integrates clinical, functional, and psychosocial domains. Regular assessment of therapeutic adherence and treatment effectiveness is essential to ensure the success of multidimensional interventions (36). Moreover, incorporating mental health evaluation into routine respiratory care is strongly recommended to identify and address psychological challenges that negatively influence adherence and disease perception (33).

Adherence to prescribed therapy remains a significant challenge, with only about 16% of patients reported to follow all components of their treatment plan (36). Poor adherence correlates with higher exacerbation rates, accelerated lung function decline, and reduced quality of life. Strategies to improve adherence include patient education, regular clinical follow-up, individualized care plans, and addressing emotional and cognitive barriers to treatment participation (33; 36).

10. Conclusion

Non-cystic fibrosis bronchiectasis presents wide epidemiological variability influenced by regional, demographic, and socioeconomic factors. Its global prevalence is increasing, particularly among older adults, largely due to improved diagnostic capabilities and heightened clinical awareness. Infectious, immunological, congenital, and autoimmune mechanisms interact as predisposing factors, demonstrating that bronchiectasis is a heterogeneous condition requiring individualized etiological assessment and management strategies.

The disease is driven by a chronic infection–inflammation cycle perpetuated by neutrophilic activity, microbiome dysbiosis, and structural airway remodeling, resulting in progressive bronchial damage and recurrent exacerbations. Prognosis depends on disease severity, extent of functional impairment, and microbial colonization, especially by Pseudomonas aeruginosa, which markedly worsens clinical outcomes. Validated prognostic tools such as BSI, FACED, and E-FACED enable risk stratification and guide therapeutic decisions based on objective parameters.

Therapeutic management combines pharmacological treatments primarily antibiotics and macrolides with non-pharmacological strategies including airway clearance, pulmonary rehabilitation, and vaccination. Addressing comorbidities and psychological health is crucial, as complex therapeutic regimens and treatment burden significantly impair quality of life and adherence. A multidimensional, patient-centered approach that integrates clinical, functional, and psychosocial components, along with improved adherence support and mental health care, remains essential to optimize outcomes and reduce the long-term burden of bronchiectasis.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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