

Scientific letter

Longitudinal Dynamics in the Airway Bacterial Profile in Bronchiectasis



Dinámica longitudinal del perfil bacteriano de las vías respiratorias en las bronquiectasias

Dear Editor,

Infection is undeniably one of the most critical factors influencing the prognosis and severity of various diseases affecting the airways.¹ Although it is well established that the respiratory tract is never sterile, even in healthy individuals, the composition of the airway microbiome undergoes complex and dynamic alterations in diseases such as chronic obstructive pulmonary disease (COPD) and bronchiectasis.^{2,3}

In recent years, there has been a substantial increase in studies examining the lung microbiome and its shifts, which will undoubtedly lay the groundwork for future assessments of microbiological changes in patients affected by airway diseases, potentially enabling more personalized therapeutic strategies.⁴ Nevertheless, traditional respiratory culture techniques remain the most commonly employed tool in routine clinical practice and are currently the only method available for evaluating microbiological changes in historical patient cohorts.

Bronchiectasis is characterized by irreversible bronchial dilations caused by over a hundred pulmonary and extrapulmonary conditions. It involves mixed inflammation of the bronchial tree, ultimately leading to destruction of the mucociliary clearance system and, almost invariably, to chronic bacterial bronchial infection (CBI). CBI is defined as the repeated detection of the same pathogenic bacterium in respiratory secretions over time.^{1,5}

Over time, the composition of pathogenic microorganisms present in the airways of these patients evolves, affecting clinical presentation, treatment, and prognosis.⁶ The aim of the present study is to assess the temporal dynamics of pathogenic bacterial appearance in respiratory samples – typically sputum – as chronic bronchial infection (in bronchiectasis).

This longitudinal study of historical cohorts. Bronchiectasis patients data were extracted from the Spanish Bronchiectasis Registry (RIBRON),^{5,6} which includes 2631 patients also followed for seven years with at least one annual microbiological evaluation. All ethics committees in the participating centers approved the registry, and all patients signed an informed consent to include their data in the registry. The recommendations of the Helsinki Declaration, good clinical practice guidelines, and currently applicable data protection laws were followed at all times.

The registry is sponsored by SEPAR and for this analysis, only bacterial isolates – whether single or consistent with CBI – were considered.

Each patient was instructed to provide three valid morning sputum samples annually, either spontaneously or induced. Patients were trained to follow the most sterile home-collection methods and to deliver samples to the hospital laboratory within 3 h of expectoration. Sputum samples were deemed acceptable if they contained fewer than 10 squamous epithelial cells per low-power field and more than 25 leukocytes per high-power field. Samples were separated from saliva, Gram-stained, homogenized, and plated on blood, chocolate, MacConkey, and Sabouraud agars. Culture results were quantified as colony-forming units (CFU) per milliliter. A bacterial load $\geq 10^6$ CFU/mL was considered significant for abnormal positivity. The bacterial strains analyzed included *Haemophilus influenzae* (HI), *Streptococcus pneumoniae* (Sp), *Staphylococcus aureus* (SA), *Pseudomonas aeruginosa* (PA), and other Gram-negative bacilli. Microbiological cultures were processed by technicians blinded to the patients' clinical data.

In the evolution of bacterial infections over time in patients with bronchiectasis (Fig. 1), CBI due to *P. aeruginosa* (PA) predominates throughout the 7-year follow-up, persisting with a continuous course. In contrast to PA, CBI due to HI shows a gradual decline over time. CBI caused by other pathogenic bacteria, such as SA: Sp, and Enterobacteriaceae, rarely exceeds 5% of samples, except for SA, which may show a resurgence in the very advanced stages of the disease.

This study provides valuable insights into the longitudinal evolution of bacterial colonization in bronchiectasis. By employing a large dataset with a 7-year follow-up period, it has been elucidated the diverging microbial trajectories of this condition, emphasizing the clinical importance of tailoring therapeutic approaches accordingly. A noteworthy contribution of the study is the characterization of pathogenic dynamics over time in a standardized microbiological context.

The data indicate that in bronchiectasis, despite aggressive antibiotic and anti-inflammatory therapy initiated from the first detection of PA (the so-called “initial infection”), its prevalence continued to rise. This early and intensive treatment approach stems from the well-established link between PA infection and rapid disease progression, increased exacerbation frequency, and early mortality especially in patients with multiple comorbidities.^{7,8}

Interestingly, the temporal decline of HI may suggest a microbial succession model, where early colonizers potentially modulate the airway environment in ways that facilitate subsequent colonization by more virulent or resistant organisms, such as PA.⁹ The late emergence of SA and Enterobacteriaceae, especially in advanced disease stages, likely reflects cumulative antibiotic pressure and the selective expansion of resistant strains.

The principal strength of this study lies in its novel analysis of the temporal dynamics of bacterial colonization in bronchiectasis as well as the prospective nature of sputum sampling and standardized culture techniques,

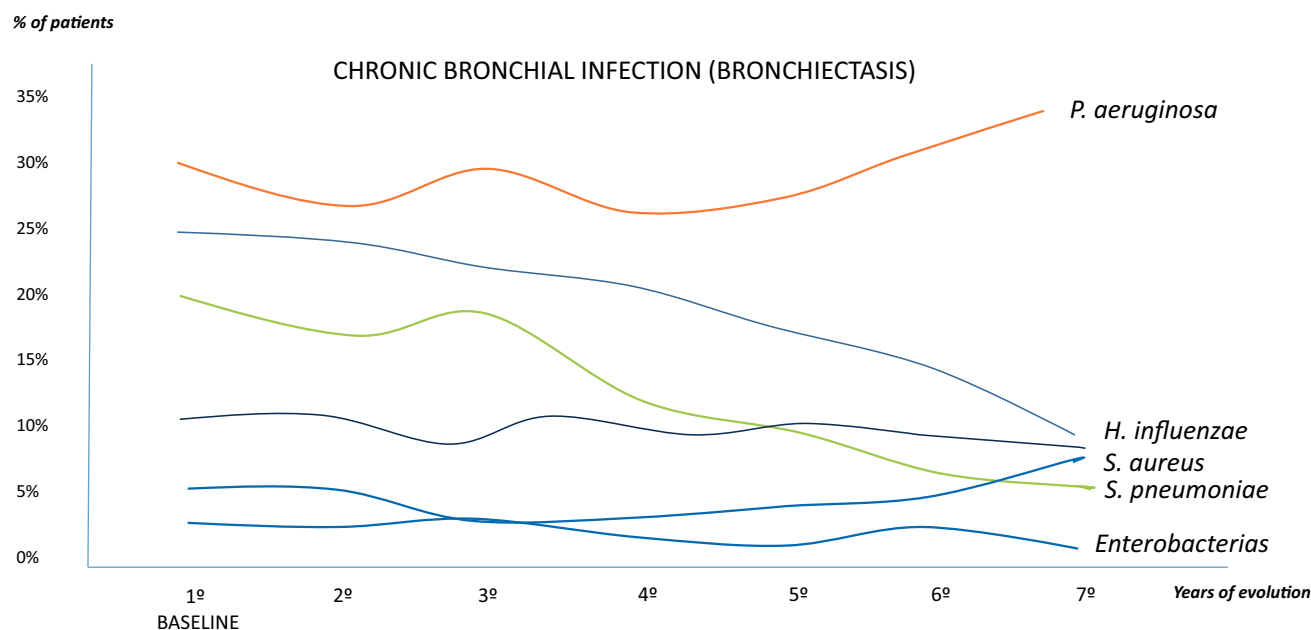


Fig. 1. Microbiology bacterial evolution in 2631 patients with bronchiectasis during 7 years follow-up.

A key limitation of the study is that only CBI was analyzed rather than all single bacterial isolates. However, given the significantly higher number of isolates typically found in bronchiectasis compared to other airways diseases such as COPD, the authors consider this approach more clinically relevant. Another potential limitation is that approximately 25% of patients – typically those with more severe disease – died during the 7-year follow-up period which may introduce a selection bias toward milder forms of the diseases.

Overall, this research enhances our understanding of microbiological shifts in bronchiectasis and supports a more personalized, pathogen-specific management approach. Future studies integrating culture-independent microbiome analyses may further refine these findings and offer therapeutical¹⁰ new targets for intervention.

In conclusion, in bronchiectasis, PA emerges as the dominant pathogen throughout the natural course of the disease, despite intensive treatment. However, HI tends to decline over time, while SA and Enterobacteriaceae – often multidrug-resistant – become more prevalent in late disease stages, likely as a result of accumulated antibiotic pressure. Understanding these distinct microbial trajectories has undeniable clinical utility in guiding therapeutical strategies to prevent future exacerbations.

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Conflicts of interest

None declared.

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