Bronchiectasis in Italy: an analysis of the EMBARC registry

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Abstract

Background Bronchiectasis is a complex disease with geographical variability in its presentation and management. Despite the growing contribution of international registries, real-world data on the Italian bronchiectasis population remain limited. The objective of the present study was to describe the demographic, clinical, microbiological, functional and treatment characteristics of Italian patients with bronchiectasis and to compare them with those of patients from other Southern European countries.

Methods This was a secondary analysis of adults from 18 Italian centres included in the European Multicentre Bronchiectasis Audit and Research Collaboration (EMBARC) registry, with comparisons made to patients in Spain, Greece, Portugal, Turkey, Israel and Malta (Southern European countries). Demographics, comorbidities, exacerbation history, spirometry, microbiology and treatment patterns were evaluated.

Results Among 1657 Italian patients, the majority were female (70.5%) with a median age of 65 years, with high rates of idiopathic bronchiectasis (55.4%) and preserved lung function. Compared with other Southern European countries (n=2638), Italian patients had lower disease severity (median Bronchiectasis Severity Index: 6 *versus* 7; p<0.001), less frequent isolation of *Pseudomonas aeruginosa*, and lower prevalence of daily sputum production and purulence, despite identical quality of life (median Quality of Life Questionnaire-Bronchiectasis Respiratory Symptom Score: 70.4 in both groups). Treatment patterns differed, with lower use of inhaled antibiotics (1.1% *versus* 13.1%) and macrolides (6.0% *versus* 14.3%), but more widespread use of airway clearance (48.4% *versus* 35.9%) among patients from Italy *versus* other Southern European countries.

Conclusions These findings may reflect earlier referral, diagnostic preferences or structural differences in care delivery in Italy compared with other Southern European countries. This work lays the foundation for tailored national strategies and future longitudinal studies. The largest bronchiectasis cohort ever studied in Italy reveals unique clinical traits and highlights key differences from other Southern European countries, and provides real-world data to shape better care models and guide future research.

Introduction

Bronchiectasis is a chronic and progressive respiratory disease characterised by irreversible bronchial dilation, persistent productive cough and recurrent exacerbations, which together drive a self-perpetuating cycle of airway inflammation and infection [1, 2]. In recent years, major advances in bronchiectasis management have been achieved, largely supported by translational research and data from large international registries [3–5]. These registries have significantly informed clinical practice and highlighted the heterogeneity of the disease with respect to aetiology, severity and associated comorbidities [3, 6, 7]. Pronounced regional differences in disease presentation have also been documented worldwide, likely influenced by a complex interplay of factors, including disparities in healthcare infrastructure and underlying genetic susceptibility [3, 6–8].

The epidemiology of bronchiectasis also varies within continents, with Southern Europe showing distinct clinical and microbiological features compared with other European regions, as indicated by data from the European Multicentre Bronchiectasis Audit and Research Collaboration (EMBARC) registry [3]. For instance, idiopathic and post-tuberculosis bronchiectasis are more prevalent in Southern Europe, along with a higher frequency of *Pseudomonas aeruginosa* and a lower prevalence of *Haemophilus influenzae*. Treatment patterns likewise differ, with Southern and Western Europe reporting lower use of macrolides and mucoactive agents [9].

It is reasonable to assume that differences also exist among Southern European countries. In Italy, the time from symptom onset to a diagnosis of bronchiectasis is ∼3.5 years, which may contribute to disease progression and worsen patients' outcomes [10]. A retrospective study using a large primary care database reported a progressive increase in both the prevalence and incidence of bronchiectasis in Italy over time [11]. Detailed data specifically describing the Italian bronchiectasis population in terms of epidemiology, clinical characteristics and treatment practices remain limited [12]. Nonetheless, these estimates provide only a partial picture, and robust, nationally representative data are still required to comprehensively assess the bronchiectasis burden in Italy. Such information is crucial for identifying unmet healthcare needs, support the development of structured care pathways and inform national, evidence-based guidelines aimed at improving outcomes and optimising healthcare resource allocation.

To address this knowledge gap, we performed a secondary analysis of the EMBARC registry to characterise the Italian bronchiectasis population in terms of disease severity, microbiological profiles and treatment strategies, and to explore potential differences compared with patients from other Southern European countries.

Methods

Study design and setting

This study represents a secondary analysis of the EMBARC registry, a multicentre, observational, prospective study that collects data from adults with bronchiectasis across Europe and Israel [13]. For the present analysis, we included all patients enrolled across 18 Italian centres (IT group) between 1 January 2015 and 1 May 2022, and compared them with patients from other Southern European countries, including Spain, Greece, Turkey, Portugal, Malta and Israel (SEC group). Data collection and patient management adhered to international guidelines and local clinical practices, without any interference from the registry team, consistent with the non-interventional design of the EMBARC registry [14–17].

Study population

Patients were eligible if they had a primary diagnosis of bronchiectasis confirmed by high-resolution computed tomography, demonstrating bronchial dilation in at least one lobe, together with a clinical history of chronic cough, persistent sputum production or recurrent respiratory infections. Exclusion criteria included a diagnosis of cystic fibrosis (CF), traction bronchiectasis secondary to interstitial lung disease or prior heart–lung transplantation. Patients aged <18 years and those unable or unwilling to provide informed consent were also excluded.

Data collection

Data were collected during periods of clinical stability, defined as the absence of exacerbations requiring antibiotic therapy within the preceding 4 weeks, to ensure consistency in baseline assessments. Information

was gathered at enrolment and at annual follow-up visits using standardised data collection forms. Collected variables included demographics (age, sex, ethnicity, body mass index and smoking history), as well as comorbidities such as cardiovascular disease, COPD, asthma, rhinosinusitis, osteoporosis, diabetes and psychiatric disorders. Comprehensive aetiological testing was performed according to consensus guidelines and included screening for allergic bronchopulmonary aspergillosis, CF, alpha-1 antitrypsin deficiency, primary ciliary dyskinesia and immunodeficiencies. All evaluations were conducted and documented by the treating clinicians. Lung function was assessed by spirometry, including forced expiratory volume in 1 s (FEV_1) expressed as a percentage of the predicted value, forced vital capacity (FVC) and the FEV_1/FVC ratio. Pulmonary function patterns were categorised as obstructive, preserved ratio impaired spirometry (PRISm) or normal. Radiological severity was assessed using the modified Reiff score, which considers the number of affected lobes and the presence of cystic changes. Microbiological data were obtained from sputum and bronchial lavage samples collected during periods of clinical stability or exacerbations, and included identification of key pathogens such as *P. aeruginosa*, *H. influenzae*, *Staphylococcus aureus* and other potentially pathogenic microorganisms. Exacerbations were defined as acute worsening of respiratory symptoms requiring antibiotic therapy, as judged by the treating physician, and their frequency in the 12 months preceding inclusion was recorded. Health-related quality of life was assessed using the Quality of Life Questionnaire-Bronchiectasis Respiratory Symptom Score (QOL-B-RSS), a validated patient-reported outcome measure [18]. Data on long-term treatments, including inhaled corticosteroids, long-acting β_2-agonists, inhaled antibiotics, long-term macrolides, mucoactive agents and airway clearance techniques, were also collected.

Statistical analysis

Descriptive statistics were used to summarise the baseline characteristics. Continuous variables were expressed as median and interquartile range (IQR), and categorical variables as absolute frequency and percentage. Differences between the IT and SEC groups were measured using the Chi-squared test for categorical variables and the Mann–Whitney U-test for continuous variables. Exacerbation rates were analysed using a negative binomial regression model to account for data overdispersion, adjusting for potential confounders such as age, sex, comorbidities and baseline lung function. For subgroup analyses, patients with co-diagnoses of COPD or asthma were excluded to minimise confounding, in accordance with EMBARC methodology.

Ethical considerations

The EMBARC registry received central ethical approval from the UK Multicentre Research Ethics Committee on 8 January 2015 (14/SS/1101). All participating sites, including those in Southern Europe, obtained local ethical approval as required. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. Written informed consent was obtained from all participants prior to enrolment.

Results

The IT group comprised 1657 patients (median (IQR) age: 65.0 (52.5–73.0) years; 70.5% female) enrolled across 18 centres between 1 January 2015 and 1 May 2022 (figure 1). Most patients were of Caucasian ethnicity (97.6%). The majority of patients (85.1%) were recruited from centres located in Northern Italy (figure 1). The IT group was compared with 2638 individuals from the SEC group (median (IQR) age: 65.0 (52.0–74.0) years; 60.5% female) (table 1). Compared with the SEC group, the IT group included a significantly higher proportion of females and a lower prevalence of current smokers. Comorbidity profiles differed across groups. Italian patients had a higher prevalence of cardiovascular diseases (34.7% *versus* 31.2%; p=0.015) and chronic rhinosinusitis (25.2% *versus* 16.5%; p<0.001), and lower rates of COPD (16.8% *versus* 20.8%; p<0.001), anxiety (10.0% *versus* 18.8%; p<0.001), depression (9.9% *versus* 12.5%; p=0.010), osteoporosis (9.1% *versus* 11.8%; p=0.005) and diabetes (6.2% *versus* 11.4%; p<0.001).

Radiological assessments in the IT group showed a median (IQR) Reiff score of 4 (2–6), with cylindrical bronchiectasis being the predominant morphological type (53.7%), followed by cystic (15.6%) and varicoid (8.4%) forms. Daily sputum production was reported by 58.0% of patients, with a median (IQR) volume of 5 (0–15) $mL \cdot day^{-1}$. Sputum consistency was most frequently mucoid (23.6%) or mucopurulent (23.2%). Major haemoptysis requiring hospitalisation was observed in 8.1% of patients. Overall, 411 (24.8%) patients had a modified Medical Research Council dyspnoea score ⩾2. Pulmonary function tests indicated significantly better lung function in the IT group, with higher median (IQR) FEV_1 % pred (84.2% (65.3–100.8%) *versus* 75.9% (54.9–95.5%); p<0.001) and a lower prevalence of airflow obstruction (33.6% *versus* 44.2%; p<0.001). Aetiological profiles varied significantly between groups. Idiopathic bronchiectasis was more frequent in the IT group (55.4% *versus* 24.4%), whereas post-infective

FIGURE 1 Geographical distribution of patient enrolment across Italian centres participating in the EMBARC registry. Circle size is proportional to the percentage of total patients enrolled per region.

(12.2% *versus* 29.6%) and tuberculosis-related (3.9% *versus* 11.3%) aetiologies were more prevalent in the SEC group (figure 2).

In the overall IT group (n=1657), *P. aeruginosa* was the most frequently isolated pathogen (18.8%). Other common isolates from stable-phase samples included Enterobacterales (10.3%), *H. influenzae* (9.4%) and *S. aureus* (7.5%), with similar distributions observed when considering all available samples. Microbiological findings differed significantly between the IT and SEC groups. *P. aeruginosa* was less frequently isolated in Italian patients (18.8% *versus* 24.2%; p<0.001), as were Enterobacterales, *Streptococcus pneumoniae*, *Stenotrophomonas maltophilia* and *Moraxella catarrhalis*. Conversely, *S. aureus* was more commonly detected in the IT group (7.5% *versus* 5.1%).

The median (IQR) number of exacerbations in the year prior to enrolment was 2 (1–3) in the IT group. Specifically, 256 (15.4%) patients experienced one, 250 (15.1%) two and 416 (25.1%) three or more exacerbations. Hospitalisations for exacerbations within the preceding year were reported in 335 (20.2%) patients. No statistically significant differences in exacerbation frequency were observed between the IT and SEC groups.

Disease severity was lower in the IT group, as reflected by a median (IQR) Bronchiectasis Severity Index (BSI) of 6 (4–9) compared with 7 (4–11) in the SEC group (p<0.001). Similarly, the proportion of patients classified as having severe disease (BSI ⩾9) was significantly lower among the IT group (27.2% *versus* 36.2%; p<0.001).

Regarding pharmacological treatment, the IT group showed significantly lower usage rates of long-acting β_2-agonists (41.7% *versus* 53.6%; p<0.001), inhaled corticosteroids (33.9% *versus* 49.9%; p<0.001), inhaled antibiotics (1.1% *versus* 13.1%; p<0.001), macrolides (6.0% *versus* 14.3%; p<0.001), other oral antibiotics (0.5% *versus* 3.4%; p<0.001) and mucolytics (2.8% *versus* 6.1%; p<0.001). Among Italian patients receiving macrolides, azithromycin was the most frequently prescribed (75.8%), while tobramycin (35.3%) and colistin (29.4%) were the most used inhaled antibiotics. Airway clearance strategies were more widely employed in Italy, with 48.4% of the IT group performing airway clearance techniques and

TABLE 1 Comparison of demographic, clinical, functional, microbiological and treatment characteristics between bronchiectasis patients enrolled in Italian centres (IT group) and those from other Southern European countries[#] (SEC group)

	IT group (n=1657)	SEC group (n=2638)	p-value
Age (years)	65.0 (52.5–73.0)	65.0 (52.0–74.0)	0.386
Sex			
Female	1169 (70.5)	1597 (60.5)	<0.001
Male	488 (29.5)	1041 (39.5)	
Ethnicity			
Caucasian	1617 (97.6)	2225 (84.3)	<0.001
Smoking history			
Current smoker	72 (4.3)	286 (10.8)	<0.001
Former smoker	651 (39.3)	850 (32.2)	
Never-smoker	934 (56.4)	1502 (56.9)	
Comorbidities			
Cardiovascular disease	575 (34.7)	822 (31.2)	0.015
Stroke	28 (1.7)	51 (1.9)	0.563
Diabetes	102 (6.2)	301 (11.4)	<0.001
Osteoporosis	150 (9.1)	310 (11.8)	0.005
Chronic renal failure	73 (4.4)	100 (3.8)	0.318
Neoplastic disease	152 (9.2)	283 (10.7)	0.100
COPD	278 (16.8)	550 (20.8)	<0.001
Asthma	329 (19.9)	482 (18.3)	0.197
Rhinosinusitis	418 (25.2)	435 (16.5)	<0.001
Anxiety	165 (10.0)	495 (18.8)	<0.001
Depression	164 (9.9)	329 (12.5)	0.010
Clinical status			
Daily sputum production	961 (58.0)	1736 (65.8)	<0.001
Sputum volume (mL·day^{-1})	5 (0–15)	10 (0–20)	<0.001
Sputum colour			
Mucoid	391 (23.6)	677 (25.7)	<0.001
Mucopurulent	385 (23.2)	818 (31.0)	
Purulent	167 (10.1)	310 (11.8)	
Severe mucopurulent	22 (1.3)	22 (0.8)	
Major haemoptysis requiring hospital admission	134 (8.1)	339 (12.9)	<0.001
Severity			
BSI	6 (4–9)	7 (4–11)	<0.001
Mild (0–4)	589 (35.5)	851 (32.3)	<0.001
Moderate (5–8)	575 (34.7)	832 (31.5)	
Severe (⩾9)	451 (27.2)	955 (36.2)	
Exacerbations (n)	2 (1–3)	2 (1–3)	0.077
1 exacerbation	256 (15.4)	585 (22.2)	0.199
2 exacerbations	250 (15.1)	576 (21.8)	
⩾3 exacerbations	416 (25.1)	838 (31.8)	
Lung function			
FEV_1 % pred	84.2 (65.3–100.8)	75.9 (54.9–95.5)	<0.001
FEV/FVC <0.7	557 (33.6)	1167 (44.2)	<0.001
PRISm[¶]	660 (39.8)	1323 (50.2)	<0.001
Normal spirometry[+]	38 (2.3)	0 (0)	<0.001
Quality of life			
QOL-B-RSS	70.4 (54.2–85.2)	70.4 (51.9–81.5)	0.073
Underlying cause			
Idiopathic	918 (55.4)	643 (24.4)	<0.001
Post-infective	202 (12.2)	781 (29.6)	
Tuberculosis	65 (3.9)	299 (11.3)	
NTM	15 (0.9)	22 (0.8)	
ABPA	17 (1.1)	33 (1.3)	
Rheumatoid arthritis	13 (0.8)	48 (1.8)	
Primary ciliary dyskinesia	48 (2.9)	96 (3.6)	
Asthma	59 (3.6)	145 (5.5)	
COPD	118 (7.1)	247 (9.4)	
GORD	11 (0.7)	54 (2.0)	

Continued

TABLE 1 Continued

	IT group (n=1657)	SEC group (n=2638)	p-value
Immunodeficiency	117 (7.1)	143 (5.4)	
Alpha-1 antitrypsin deficiency	11 (0.7)	13 (0.5)	
Connective tissue disease	17 (1.0)	36 (1.4)	
Inflammatory bowel disease	17 (1.0)	27 (1.0)	
Obstructive	1 (0.1)	9 (0.3)	
ILD	6 (0.4)	20 (0.8)	
CFTR-related disorder	12 (0.7)	3 (0.1)	
Other causes	10 (0.6)	19 (0.7)	
Drug treatment			
Inhaled corticosteroid	562 (33.9)	1317 (49.9)	<0.001
Long-acting β_2-agonists	691 (41.7)	1413 (53.6)	<0.001
Long-acting muscarinic antagonist	476 (28.7)	802 (30.4)	0.242
Long-term treatments			
Inhaled antibiotic	19 (1.1)	346 (13.1)	<0.001
Macrolide	99 (6.0)	376 (14.3)	<0.001
Other oral antibiotic prophylaxis	9 (0.5)	90 (3.4)	<0.001
Carbocisteine or *N*-acetylcysteine	46 (2.8)	162 (6.1)	0.005
Airway clearance			
Partaking in airway clearance	802 (48.4)	947 (35.9)	<0.001
Airway clearance devices	642 (38.7)	379 (14.4)	<0.001
Manual airway clearance	342 (20.6)	910 (34.5)	<0.001
Microbiology			
Pseudomonas aeruginosa	312 (18.8)	638 (24.2)	<0.001
Haemophilus influenzae	156 (9.4)	289 (11.0)	0.107
Moraxella catarrhalis	15 (0.9)	74 (2.8)	<0.001
Enterobacterales	171 (10.3)	486 (18.4)	<0.001
Staphylococcus aureus	125 (7.5)	135 (5.1)	0.001
Streptococcus pneumoniae	57 (3.4)	184 (7.0)	<0.001
Stenotrophomonas maltophilia	20 (1.2)	61 (2.3)	0.010
Aspergillus fumigatus	17 (1.0)	61 (2.3)	0.559

Data are presented as median (interquartile range) or n (%), unless otherwise stated. BSI: Bronchiectasis Severity Index; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; PRISm: preserved ratio impaired spirometry; QOL-B-RSS: Quality of Life Questionnaire-Bronchiectasis Respiratory Symptom Score; NTM: non-tuberculous mycobacteria; ABPA: allergic bronchopulmonary aspergillosis; GORD: gastro-oesophageal reflux disease; ILD: interstitial lung disease; CFTR: cystic fibrosis transmembrane conductance regulator. [#]: Southern European countries include Spain, Greece, Turkey, Portugal, Malta and Israel; [¶]: FEV_1 % pred <80% but FEV_1/FVC >0.7; [+]: FEV_1 % pred >80% and FEV_1/FVC >0.7. Statistical comparisons were performed using the Mann–Whitney U-test for continuous variables and the Chi-squared test for categorical variables.

38.7% using dedicated devices (*versus* 35.9% and 14.4% in the SEC group, respectively; p<0.001) (figure 3). In the IT group, 106 (6.4%) patients were on long-term oxygen therapy, 25 (1.5%) on non-invasive ventilation and 484 (29.2%) had received the pneumococcal polysaccharide vaccine; additionally, 690 (41.6%) had received the pneumococcal conjugate vaccine and 978 (59.0%) had received influenza vaccination in the previous year. Despite comparable scores on the QOL-B-RSS (median 70.4 in both groups), patients from the SEC group exhibited greater clinical severity, as indicated by higher BSI scores, worse lung function and a higher prevalence of chronic *P. aeruginosa* colonisation.

Discussion

Our study demonstrates that patients with bronchiectasis in Italy exhibit a milder disease phenotype compared with those from other Southern European countries. This was reflected by better preserved lung function, a lower prevalence of daily and purulent sputum production, reduced prevalence of *P. aeruginosa*, higher isolation rates of *S. aureus*, and lower BSI scores. Furthermore, Italian patients were less frequently treated with bronchodilators and inhaled corticosteroids, consistent with the lower prevalence of COPD and asthma, and potentially contributing to the marked female predominance observed in the cohort. They also received long-term macrolides and inhaled antibiotics less often, while reporting greater use of airway clearance techniques. The lower disease severity observed in Italian patients reflects the reduced prevalence of different individual components of the BSI (*e.g.* impaired lung function and chronic *P. aeruginosa* colonisation), consistent with lower disease activity in terms of sputum volume, sputum purulence and major haemoptysis.

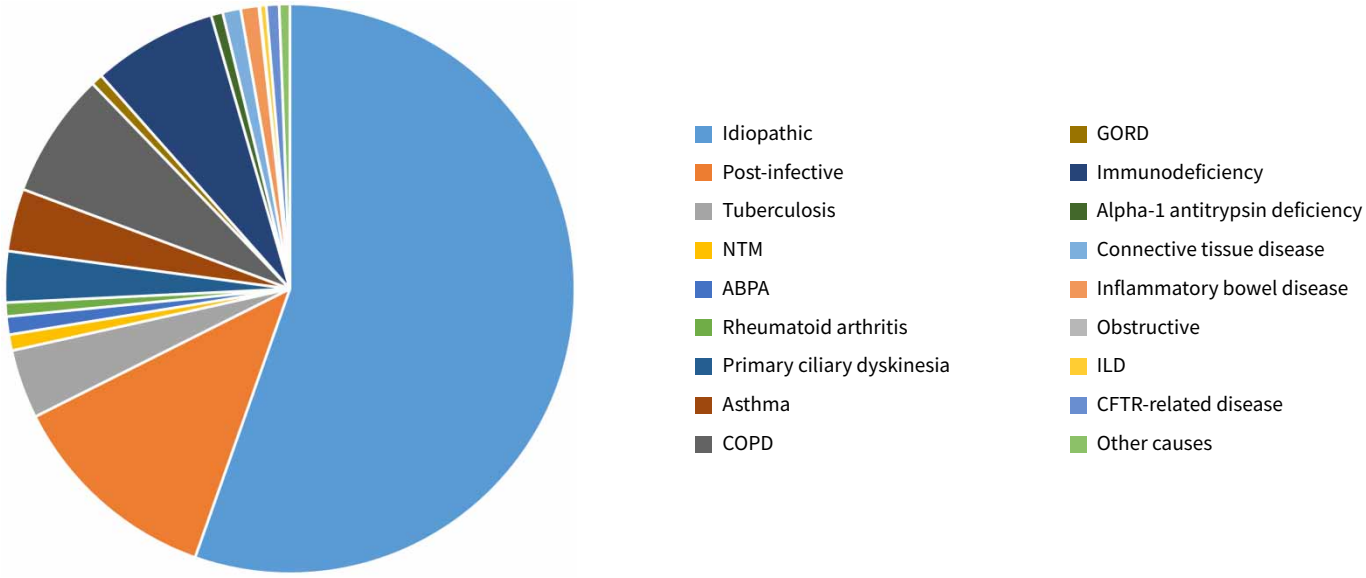

FIGURE 2 Distribution of underlying aetiologies in the Italian bronchiectasis population. The pie chart illustrates the aetiological breakdown, with idiopathic bronchiectasis accounting for the largest proportion, followed by post-infective and tuberculosis-related causes. NTM: non-tuberculous mycobacteria; ABPA: allergic bronchopulmonary aspergillosis; GORD: gastro-oesophageal reflux disease; ILD: interstitial lung disease; CFTR: cystic fibrosis transmembrane conductance regulator.

The overall milder clinical profile of the Italian cohort may result from a combination of healthcare organisation, environmental exposures, microbiology and genetic background. First, the high proportion of patients undergoing airway clearance (nearly half of the cohort) may contribute to more effective mucus

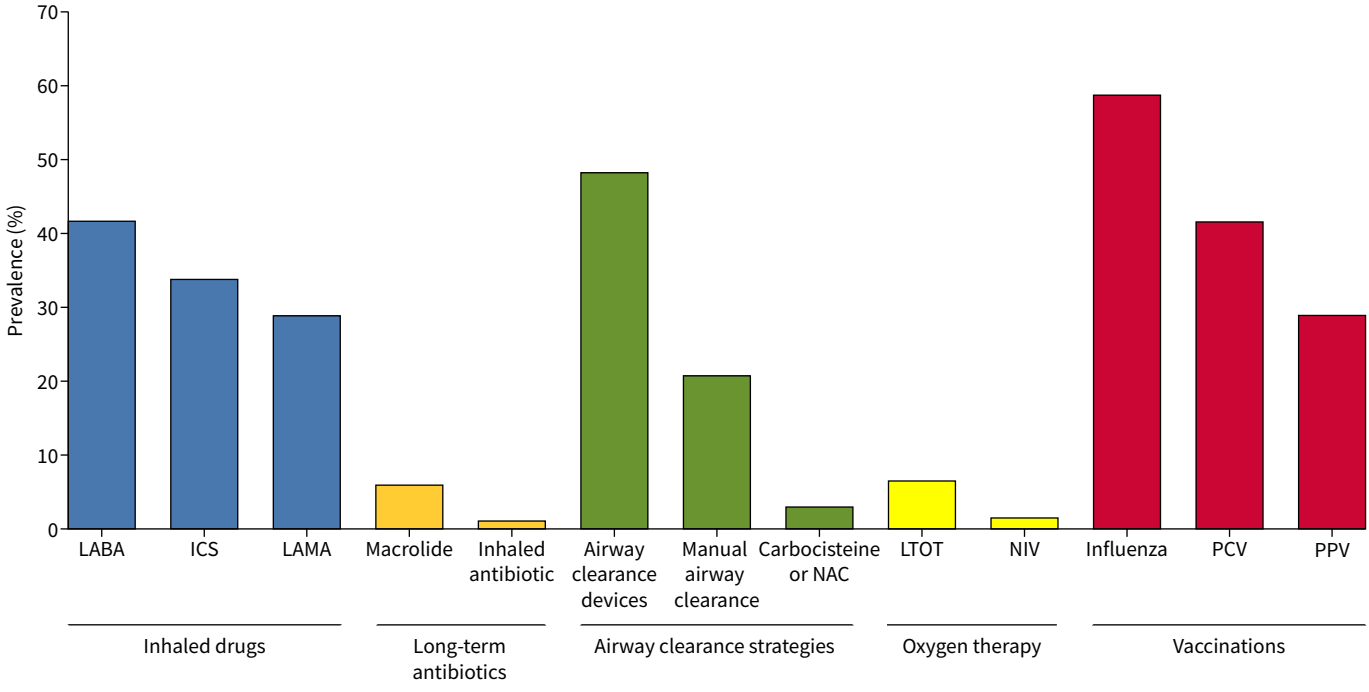

FIGURE 3 Prevalence of treatments in the EMBARC Italian bronchiectasis cohort: bar chart illustrating the proportion of patients receiving different treatment strategies (n=1657). Airway clearance techniques and vaccinations were the most frequently reported interventions. LABA: long-acting β_2-agonist; ICS: inhaled corticosteroid; LAMA: long-acting muscarinic antagonist; NAC: *N*-acetylcysteine; LTOT: long-term oxygen therapy; NIV: non-invasive ventilation; PCV: pneumococcal conjugate vaccine; PPV: pneumococcal polysaccharide vaccine.

elimination, thereby reducing symptoms and chronic bacterial infection. Second, the lower prevalence of *P. aeruginosa* infection in Italy likely contributes to the reduced disease activity and severity, given its well-established association with accelerated lung function decline and increased morbidity [19–21]. Nevertheless, although the prevalence is lower, it remains substantial: *P. aeruginosa* still accounts for a considerable proportion of pathogens in the Italian cohort, and its frequency is high compared with Northern European cohorts [3]. Third, differences in referral patterns to tertiary care centres may have influenced our findings: general practitioners in Italy tend to refer bronchiectasis patients earlier in their disease course, and disparities in healthcare access across countries could have shaped the disease presentation of patients enrolled in the registry. Importantly, despite the apparently milder phenotype observed in Italian patients, exacerbation rates were comparable with those of the Southern European countries cohort. This underscores the dual significance of symptom burden and exacerbations as measures of disease activity, which may not always evolve in parallel and can even diverge. Further investigation is warranted to clarify these relationships and their implications for patient management. Idiopathic bronchiectasis was more prevalent in the Italian cohort, whereas post-infective and tuberculosis-related bronchiectasis were significantly more frequent in other Southern European countries, reflecting historical and regional differences in tuberculosis burden. According to the European Centre for Disease Prevention and Control, TB notification rates in 2023 remained higher in Portugal (14.3 per 100 000), Turkey (10.9 per 100 000) and Spain (7.5 per 100 000) compared with Italy (4.1 per 100 000) and Israel (3.3 per 100 000) [22, 23].

The striking female predominance in the Italian cohort may reflect the lower prevalence of COPD, more common in men, as well as sex-based differences in healthcare utilisation, diagnostic practices and referral dynamics [24]. Further research is warranted to explore whether these differences reflect true epidemiological patterns or potential biases in diagnosis and enrolment.

Microbiological profiles also differed between groups. While *P. aeruginosa* was the most frequently isolated pathogen overall, its prevalence was significantly lower in Italy, whereas *S. aureus* was more commonly isolated in the Italian cohort. Although the role of *S. aureus* in bronchiectasis remains uncertain, evidence (primarily from CF) suggests that it may be more frequent in early-stage or less severe disease, a hypothesis that warrants further investigation in non-CF bronchiectasis [25]. Recent EMBARC registry data support this view, showing that *S. aureus* infection was associated with younger age and a lower prevalence in smokers, without significant associations with exacerbations, hospitalisations or mortality over a 5-year follow-up [26].

Long-term treatment patterns were also consistent with the milder clinical profile observed in Italy, and reflect characteristics of the Italian healthcare system and its structural barriers. Use of macrolides and inhaled antibiotics was significantly lower, likely due to their off-label status and lack of full reimbursement by the national health system, which transfers the financial burden to patients. Despite robust evidence of efficacy, this likely contributes to their underuse. Beyond the lower prevalence of asthma and COPD, which explains the reduced use of bronchodilators, there is also growing awareness of the potential risks associated with inhaled corticosteroid overuse, including pneumonia, non-tuberculous mycobacterial infection, exacerbations and mortality [9, 27–29]. This awareness has fostered a culture of inhaled corticosteroid de-prescription, particularly in specialised centres. Overall, these differences in treatment patterns appear to result from a combination of clinical factors, medication accessibility and local prescribing practices. In contrast, the broader adoption of airway clearance strategies, both manual and device-based, may represent an effective and accessible alternative to pharmacological prophylaxis. The widespread adoption of airway clearance in Italy is facilitated by the presence of rehabilitation hospitals and multidisciplinary bronchiectasis clinics, particularly in northern regions, where respiratory physiotherapists play a central role in both outpatient and inpatient care. This is further supported by the Italian Association of Respiratory Physiotherapists, which promotes standardised implementation of non-pharmacological strategies.

Our study has several practical implications. First, the widespread use of airway clearance in Italy appears to contribute to improved symptom control and reduced need for long-term antibiotic or corticosteroid treatment. This supports investment in structured physiotherapy services and training. Second, our findings highlight a dissociation between disease activity as measured by symptom burden and by exacerbation risk, consistent with recent evidence showing that symptom-defined activity independently predicts future exacerbations and response to macrolide therapy, even in patients without a history of frequent events [30]. This aligns with the treatable traits framework, in which symptoms and exacerbation risk are considered distinct but actionable domains [31, 32]. Despite comparable QOL-B RSS scores, patients in other Southern European countries exhibited objectively more severe disease, underscoring the importance of addressing both dimensions independently in therapeutic decision making. Third, the underuse of long-term macrolides and inhaled antibiotics in Italy, likely driven by regulatory and reimbursement

constraints, represents a substantial treatment gap. Collaborative initiatives with healthcare authorities and patient associations will be essential to ensure equitable access to evidence-based therapies.

Several research questions remain open. First, the impact of structured physiotherapy programmes on clinical outcomes in bronchiectasis requires confirmation in large, prospective studies. Second, national health economic analyses are needed to evaluate the cost-effectiveness of airway clearance techniques and long-term pharmacological strategies. Third, potential genetic or environmental determinants of the milder Italian phenotype should be explored using multi-omic studies. Finally, further registry analyses should stratify outcomes by centre, geographic region and healthcare model, both within Italy and across Europe.

This study has limitations. As a registry-based study, results depend on the accuracy, completeness and consistency of site-level data entry, which may vary across centres and countries. Moreover, differences in diagnostic practices, such as the extent of testing for immunodeficiencies, CF transmembrane conductance regulator-related disorders or other rare aetiologies, may have contributed to heterogeneity in reporting underlying causes. Third, most patients were enrolled from Northern Italy, potentially limiting geographical representativeness. However, cohorts from northern centres do not exclusively include local residents. This likely reflects the concentration of specialised bronchiectasis centres in the north of Italy and the well-documented phenomenon of healthcare migration from Southern to Northern Italy, whereby patients seek care in tertiary referral hospitals outside their region of residence [33]. Microbiological data were collected based on routine clinical sampling rather than standardised protocols, which may under-represent some pathogens. Residual confounding, including socioeconomic status, education level and access to care, was not captured but may have influenced disease burden. This cross-sectional analysis may be subject to selection bias related to referral and enrolment patterns, and does not include longitudinal outcomes, which will be addressed in future analyses of the Italian EMBARC cohort.

Despite these limitations, our study has several important strengths. It represents the largest and most comprehensive prospective characterisation of bronchiectasis in Italy to date, encompassing clinical, radiological, microbiological and therapeutic domains. It also provides the first real-world comparison between Italy and other Southern European countries located at similar latitudes, leveraging standardised data from a multinational registry. Its multicentre design (18 centres across Italy) and large sample size enhance generalisability and robustness. Furthermore, the inclusion of detailed treatment data, particularly on off-label and non-pharmacological therapies, offers valuable insights into real-world practice. Collectively, these findings provide a foundation for future planning efforts, from the development of national guidelines to the organisation of regional services and the design of respiratory care models, such as hub-and-spoke systems.

In conclusion, bronchiectasis in Italy is characterised by a milder phenotype, reduced use of long-term pharmacological treatments and greater adoption of airway clearance strategies compared with other Southern European countries. These findings highlight the need to tailor clinical pathways and national guidelines to local epidemiology and healthcare infrastructure. Future initiatives should prioritise equitable access to treatment, expansion of physiotherapy services, and dedicated research into disease heterogeneity and progression in the Italian population.

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