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Original Research Article

Prevalence and Outcomes of Multidrug-Resistant Bacterial Infections in Patients Hospitalized with Acute Exacerbations of Bronchiectasis

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Abstract

Background: Acute exacerbations of bronchiectasis are frequently treated empirically before culture results are available. Multidrug-resistant (MDR) organisms may therefore delay active therapy and amplify the risk of respiratory failure, intensive care use, prolonged hospitalization, and early readmission, yet detailed hospital-based data remain limited in many high-burden settings.

Aim: To estimate the prevalence and microbiological spectrum of MDR bacterial infection among adults hospitalized with acute exacerbations of bronchiectasis and to examine clinical predictors and short-term outcomes associated with MDR infection.

Methods: This study used a prespecified, reproducible simulated retrospective cohort representing 312 consecutive adults with computed tomography-confirmed non-cystic fibrosis bronchiectasis admitted with a consensus-defined exacerbation. Sputum or lower-respiratory samples were processed before or within 24 hours of antibiotics. MDR was defined as acquired non-susceptibility to at least one agent in three or more antimicrobial categories. Logistic regression estimated independent predictors of MDR infection and its adjusted association with in-hospital outcomes; negative-binomial regression assessed length of stay.

Results: A bacterial pathogen was recovered in 228/312 admissions (73.1%). MDR organisms were present in 92/312 admissions (29.5%; 95% CI 24.7–34.8%) and in 40.4% of culture-positive episodes. Pseudomonas aeruginosa was the dominant isolate (119/228, 52.2%) and accounted for 39 MDR episodes. Independent predictors of MDR infection included previous MDR isolation (adjusted odds ratio [aOR] 9.94, 95% CI 3.18–31.07), antipseudomonal antibiotic exposure within 90 days (aOR 9.47, 95% CI 4.80–18.69), chronic P. aeruginosa infection (aOR 4.42, 95% CI 2.23–8.74), hospitalization in the previous year (aOR 3.74, 95% CI 1.92–7.32), chronic kidney disease (aOR 3.09, 95% CI 1.25–7.66), and severe bronchiectasis (aOR 2.00, 95% CI 1.02–3.95). Compared with non-MDR infection, MDR infection was associated with inactive initial empirical therapy (42.4% vs 9.5%), respiratory failure (40.2% vs 10.0%), invasive ventilation (25.0% vs 2.3%), and longer median hospitalization (11.0 vs 6.0 days). After adjustment, MDR infection remained associated with respiratory failure (aOR 5.19, 95% CI 2.67–10.09), composite clinical failure (aOR 5.49, 95% CI 2.74–11.03), and longer length of stay (adjusted rate ratio 1.83, 95% CI 1.50–2.23).

Conclusion: In this model cohort, nearly one-third of hospitalized bronchiectasis exacerbations involved MDR bacteria. Prior resistance, recent antipseudomonal exposure, chronic P. aeruginosa infection, recent hospitalization, renal disease, and severe bronchiectasis identified a high-risk phenotype. Early high-quality respiratory sampling, risk-stratified empirical therapy, and prompt de-escalation are central to balancing treatment adequacy with antimicrobial stewardship.

Keywords: Bronchiectasis; Acute Exacerbation; Multidrug Resistance; Pseudomonas Aeruginosa; Antimicrobial Stewardship; Hospitalization.

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Introduction

Bronchiectasis is a heterogeneous chronic respiratory disorder characterized by permanent bronchial dilatation, impaired mucociliary clearance, chronic airway infection, and a self-perpetuating cycle of neutrophilic inflammation and structural lung injury. Its clinical expression ranges from mild daily cough to recurrent, life-threatening exacerbations, and contemporary disease models emphasize that infection, inflammation, mucus dysfunction, and airway damage continuously reinforce one another [1]. International guidance now positions exacerbation prevention, microbiology-guided treatment, airway clearance, and identification of treatable traits at the center of adult bronchiectasis care [2,3]. Despite this progress, hospitalized exacerbations remain a major unresolved problem because they concentrate the most vulnerable patients, require immediate therapeutic decisions, and often occur in individuals with repeated antibiotic exposure, advanced structural disease, chronic bacterial infection, and multiple comorbidities.

A bronchiectasis exacerbation is not simply an increase in cough. The international consensus definition describes a deterioration in at least three key symptoms—cough, sputum volume or consistency, sputum purulence, breathlessness or exercise tolerance, fatigue or malaise, and haemoptysis—for at least 48 hours, accompanied by a clinician-determined change in treatment [4]. Exacerbations are clinically important because they can accelerate decline in health status, increase healthcare utilization, and identify a stable, reproducible high-risk phenotype [5]. The original frequent-exacerbator work showed that a history of repeated events predicts future attacks and worse outcomes [6]. More recently, analysis of 19,324 participants in the EMBARC registry demonstrated a graded relationship between each previous exacerbation and future moderate and severe events, while a previous hospitalization was especially predictive of another severe exacerbation [7]. Thus, the admission itself is both an acute event and a marker of a biologically and clinically vulnerable trajectory.

Disease severity further modifies this risk. The Bronchiectasis Severity Index integrates age, body mass index, lung function, prior hospitalization, exacerbation frequency, dyspnoea, radiological extent, and bacterial colonization to predict mortality, hospitalization, and future exacerbations [8]. The FACED score similarly combines forced expiratory volume in one second, age, chronic Pseudomonas aeruginosa colonization, radiological extension, and dyspnoea to stratify five-year mortality [9]. These tools were not designed specifically to predict antimicrobial resistance, but several of their components—particularly prior hospitalization, frequent exacerbations, reduced lung function, and chronic P. aeruginosa infection—also represent cumulative antibiotic and healthcare exposure. It is therefore plausible that the same phenotype that predicts clinical severity also creates the ecological pressure and exposure network through which resistant organisms emerge or are acquired.

This issue is particularly relevant in India and other tuberculosis-endemic settings. The Indian EMBARC/Respiratory Research Network registry enrolled 2,195 adults and demonstrated a distinct phenotype: patients were younger than many Western cohorts, post-tuberculosis bronchiectasis was the most frequent etiology, disease burden was substantial, and P. aeruginosa was the most commonly cultured organism [10]. Prospective follow-up from the same network showed that frequent exacerbations, coexisting chronic obstructive pulmonary disease, dyspnoea, and smoking were associated with adverse clinical outcomes [11]. Post-tuberculosis architectural distortion, repeated community and hospital antibiotic courses, variable access to specialist microbiology, and over-the-counter antimicrobial use may collectively heighten the risk of resistant Gram-negative infection. However, resistance surveillance in bronchiectasis remains fragmented, and extrapolation from pneumonia or chronic obstructive pulmonary disease may be misleading because chronically damaged airways support persistent infection, biofilm formation, within-host evolution, and recurrent treatment cycles.

P. aeruginosa deserves special attention because it is both a marker and mediator of severe bronchiectasis. A meta-analysis found that chronic P. aeruginosa colonization is associated with more frequent exacerbations, greater hospitalization risk, poorer quality of life, and increased mortality [12]. International cohort analyses likewise show that chronic P. aeruginosa infection independently contributes to adverse long-term outcomes [13]. These associations may be intensified when the organism is resistant to standard antipseudomonal agents. Resistance can arise through selection after repeated antibiotic exposure, clonal acquisition, efflux-pump upregulation, target mutation, reduced permeability, beta-lactamase production, and biofilm-associated tolerance. Consequently, a patient may present with an exacerbation that clinically resembles previous episodes while the previously effective empirical regimen is no longer microbiologically active. The best available MDR-specific data underscore the clinical stakes. A large nationwide analysis of non-cystic fibrosis bronchiectasis reported that MDR infection was associated with substantially more respiratory failure, higher in-hospital mortality, and worse

three-year survival than non-MDR infection [14]. In a multicentre study of bronchiectasis exacerbations, MDR pathogens were identified in approximately one-fifth of microbiologically confirmed episodes; previous MDR isolation, hospitalization in the preceding year, and chronic renal disease were independent predictors [15]. A developing-country study from Pakistan documented P. aeruginosa as the predominant organism during acute exacerbations and reported clinically important resistance to ciprofloxacin, imipenem, ceftazidime, and piperacillin–tazobactam, together with high methicillin resistance among Staphylococcus aureus isolates [16]. These findings suggest that the microbiological problem is not restricted to a single organism or health system.

Recent hospitalized cohorts have sharpened the focus on carbapenem-resistant P. aeruginosa. In a 1,286-patient retrospective cohort, carbapenem-resistant isolates were uncommon relative to all P. aeruginosa isolates but were associated with respiratory failure, mechanical ventilation, and longer hospitalization [17]. Long-term follow-up has also linked carbapenem-resistant P. aeruginosa isolation with subsequent exacerbations and mortality [18]. These data support a clinically intuitive pathway: resistant infection increases the probability that initial treatment is inactive, delays bacterial control, prolongs inflammatory injury, and increases organ-support requirements. Yet overly broad empirical therapy for every admission would further accelerate resistance and expose patients to toxicity. The practical challenge is therefore to identify a high-risk subgroup in whom broader initial coverage is justified while preserving rapid culture-directed narrowing.

Against this background, hospital-based studies must integrate three questions rather than reporting culture frequencies alone: how common MDR infection is, which patients are most likely to have it, and whether resistance independently predicts clinically meaningful outcomes after accounting for baseline severity. The present analysis was designed to model such a study in a tertiary-care population. The primary objective was to estimate the prevalence and microbiological distribution of MDR bacterial infection among adults hospitalized with acute exacerbations of non-cystic fibrosis bronchiectasis. Secondary objectives were to identify independent clinical predictors of MDR infection and to compare empirical treatment adequacy, respiratory failure, intensive care use, mechanical ventilation, septic shock, length of stay, in-hospital mortality, and 90-day readmission between MDR and non-MDR episodes.

Materials and Methods

Thisstudy was structured as a retrospective cohort of consecutive adults admitted to a tertiary respiratory-care hospital with an acute exacerbation of non-cystic fibrosis bronchiectasis. Eligible participants were adults aged 18 years or older with bronchiectasis confirmed by high-resolution computed tomography and a clinical syndrome consistent with bronchiectasis. An exacerbation required deterioration in at least three consensus symptoms for at least 48 hours and a clinician-determined change in treatment [4]. Hospitalization was defined as an admission lasting at least 24 hours for intravenous antibiotics, oxygen therapy, ventilatory support, haemodynamic monitoring, or management of a complication. Exclusions were cystic fibrosis, traction bronchiectasis without a clinical bronchiectasis syndrome, active pulmonary tuberculosis at admission, non-tuberculous mycobacterial disease as the primary reason for admission, isolated fungal disease without bacterial coinfection, hospital-acquired exacerbation beginning more than 48 hours after admission for another condition, absence of an interpretable respiratory specimen, and duplicate admissions within 30 days. When several admissions occurred during the study window, only the first eligible episode was retained for the primary patient-level analysis.

Demographic variables, smoking exposure, body mass index, bronchiectasis etiology, comorbid chronic obstructive pulmonary disease, diabetes, chronic kidney disease, spirometry, prior-year exacerbations and hospitalizations, antimicrobial exposure within 90 days, previous respiratory isolates, chronic P. aeruginosa infection, and Bronchiectasis Severity Index were recorded. Severe bronchiectasis was defined as a Bronchiectasis Severity Index of 9 or greater [8]. Frequent exacerbation was operationalized as three or more treated exacerbations in the preceding year, consistent with the historical phenotype used in cohort research [6], while recognizing newer evidence of graded risk across the full exacerbation count [7]. Chronic P. aeruginosa infection was defined by repeated isolation during clinical stability according to local registry practice. Respiratory failure was defined as hypoxaemia requiring supplemental oxygen beyond the patient's baseline or ventilatory support, with arterial blood-gas confirmation where available.

Spontaneous or induced sputum was collected before the first hospital antibiotic dose whenever feasible and otherwise within 24 hours. Endotracheal aspirate or bronchoalveolar lavage was accepted for intubated patients or when clinically indicated. Specimens underwent Gram staining, quantitative or semiquantitative bacterial culture, organism identification, and antimicrobial-susceptibility testing using the contemporaneous Clinical and Laboratory Standards Institute or European Committee on Antimicrobial

Susceptibility Testing breakpoints used by the participating laboratory. Potentially pathogenic organisms were distinguished from mixed upper-airway flora using specimen-quality criteria and clinical correlation. MDR was defined using the international interim standard as acquired non-susceptibility to at least one agent in three or more antimicrobial categories [19]. Methicillin-resistant S. aureus, extended-spectrum beta-lactamase-producing Enterobacterales meeting the category criterion, carbapenem-resistant non-fermenters, and other organisms fulfilling the same multidrug definition were classified as MDR. The 2017 ERS and 2019 BTS guidance informed the clinical framework for culture-directed treatment, eradication assessment, and long-term antibiotic review [20,21].

The primary outcome was the prevalence of MDR bacterial infection among all eligible hospitalized exacerbations, with a secondary denominator restricted to culture-positive episodes. Prespecified secondary outcomes were initial empirical therapy inactive in vitro against the index pathogen, respiratory failure, intensive care unit admission, invasive mechanical ventilation, septic shock, hospital length of stay, in-hospital mortality, 90-day all-cause readmission, and composite clinical failure. Composite clinical failure was defined as in-hospital death, invasive mechanical ventilation, or septic shock. Empirical therapy was considered active when at least one systemic agent administered within the first 24 hours was reported susceptible in vitro. Modification after culture release was recorded conceptually but was not used to redefine initial adequacy.

Continuous variables were summarized as mean with standard deviation or median with interquartile range according to distribution; categorical variables were reported as number and percentage. Between-group comparisons used Welch's t test, the Mann–Whitney U test, Pearson's chi-square test, or Fisher's exact test as appropriate. MDR prevalence was accompanied by a Wilson 95% confidence interval.

Candidate predictors were chosen a priori based on clinical plausibility and previous literature, not solely univariable significance. Multivariable logistic regression estimated adjusted odds ratios with 95% confidence intervals for MDR infection. Separate logistic models examined the adjusted association between MDR infection and binary outcomes, controlling for age, sex, chronic kidney disease, chronic obstructive pulmonary disease, severe Bronchiectasis Severity Index category, and previous-year hospitalization. Length of stay was analysed with negative-binomial regression and expressed as an adjusted rate ratio. Two-sided P values below 0.05 were considered statistically significant. Model diagnostics included assessment of collinearity, influential observations, calibration, and the relationship between continuous predictors and the logit. Analyses were performed in Python using validated statistical libraries, and all displayed estimates were regenerated from the fixed-seed synthetic patient-level file.

Results

The simulated cohort comprised 312 adults hospitalized with an acute exacerbation of bronchiectasis. The mean age was 58.7 ± 13.2 years, 170 (54.5%) were men, and post-tuberculosis disease accounted for 136 (43.6%) cases. Seventy-five patients (24.0%) had severe disease by the Bronchiectasis Severity Index, 127 (40.7%) met the historical frequent-exacerbator definition, and 89 (28.5%) had been hospitalized during the previous year. A bacterial pathogen was recovered in 228 admissions, yielding a culture positivity rate of 73.1% (95% CI 67.9–77.7%).

MDR bacterial infection was identified in 92/312 admissions, corresponding to an overall prevalence of 29.5% (95% CI 24.7–34.8%) and 40.4% (95% CI 34.2–46.8%) among culture-positive episodes. Compared with the non-MDR group, patients with MDR infection more frequently had chronic kidney disease, severe bronchiectasis, frequent prior exacerbations, recent hospitalization, recent antipseudomonal antibiotic exposure, previous MDR isolation, and chronic P. aeruginosa infection. Age, sex, body mass index, coexisting chronic obstructive pulmonary disease, and baseline FEV_1 did not differ significantly (Table 1).

Table 1: Baseline characteristics according to multidrug-resistance status

Variable	Overall (n=312)	Non-MDR (n=220)	MDR (n=92)	P value
Age, years	58.7 ± 13.2	59.1 ± 12.9	57.9 ± 13.9	0.495
Male sex	170 (54.5)	121 (55.0)	49 (53.3)	0.778
Body mass index, kg/m²	21.9 ± 3.7	22.0 ± 3.6	21.6 ± 3.9	0.493
Post-tuberculosis etiology	136 (43.6)	89 (40.5)	47 (51.1)	0.084
Coexisting COPD	81 (26.0)	58 (26.4)	23 (25.0)	0.802
Chronic kidney disease	38 (12.2)	20 (9.1)	18 (19.6)	0.010
FEV_1, % predicted	51.5 ± 17.9	52.4 ± 17.9	49.1 ± 17.6	0.129
Bronchiectasis Severity Index	6.0 (4.0–8.0)	6.0 (4.0–8.0)	7.5 (6.0–9.0)	<0.001
Severe bronchiectasis (BSI ≥9)	75 (24.0)	39 (17.7)	36 (39.1)	<0.001

Frequent exacerbator (≥3/year)	127 (40.7)	81 (36.8)	46 (50.0)	0.031
Hospitalization in previous year	89 (28.5)	50 (22.7)	39 (42.4)	<0.001
Antipseudomonal antibiotics in previous 90 days	135 (43.3)	67 (30.5)	68 (73.9)	<0.001
Previous MDR isolate	24 (7.7)	8 (3.6)	16 (17.4)	<0.001
Chronic P. aeruginosa infection	77 (24.7)	39 (17.7)	38 (41.3)	<0.001

Data are mean ± standard deviation, median (interquartile range), or n (%). P values were calculated using Welch's t test, Mann–Whitney U test, Pearson's chi-square test, or Fisher's exact test as appropriate. BSI, Bronchiectasis Severity Index; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in one second; MDR, multidrug resistant.

In the adjusted risk model, previous MDR isolation was the strongest predictor of MDR infection (aOR 9.94, 95% CI 3.18–31.07), followed by antipseudomonal antibiotic exposure within 90 days (aOR 9.47, 95% CI 4.80–18.69). Chronic P. aeruginosa infection (aOR 4.42, 95% CI 2.23–8.74), hospitalization in the previous year (aOR 3.74, 95% CI 1.92–7.32), chronic kidney disease (aOR 3.09, 95% CI 1.25–7.66), and severe bronchiectasis (aOR 2.00, 95% CI 1.02–3.95) also remained independently associated. Age and male sex were not independently predictive. P. aeruginosa was recovered in 119/228 culture-positive episodes (52.2%) and accounted for 39/92 MDR infections (42.4%). K. pneumoniae, A. baumannii, S. aureus, E. coli, and H. influenzae were less common but demonstrated distinct resistance phenotypes. A. baumannii had the highest organism-specific MDR proportion (72.7%), while half of S. aureus isolates were methicillin resistant. Carbapenem resistance was concentrated in non-fermenting Gram-negative bacilli. Organism-level counts and selected non-susceptibility patterns are shown in Table 2 and Figure 1.

Table 2: Bacterial isolates and selected antimicrobial-resistance patterns among culture-positive exacerbations

Organism	All isolates, n (%)	MDR, n (% within organism)	Selected non-susceptibility	Predominant MDR phenotype
Pseudomonas aeruginosa	119 (52.2)	39 (32.8)	Ciprofloxacin 40/119 (33.6); piperacillin–tazobactam 28/119 (23.5); ceftazidime 26/119 (21.8); meropenem 22/119 (18.5); amikacin 16/119 (13.4)	MDR phenotype; 7 isolates carbapenem resistant
Klebsiella pneumoniae	34 (14.9)	18 (52.9)	Ciprofloxacin 20/34 (58.8); third-generation cephalosporin 20/34 (58.8); piperacillin–tazobactam 18/34 (52.9); meropenem 7/34 (20.6)	ESBL phenotype predominated
Acinetobacter baumannii	22 (9.6)	16 (72.7)	Ciprofloxacin 18/22 (81.8); ceftazidime 18/22 (81.8); piperacillin–tazobactam 17/22 (77.3); meropenem 15/22 (68.2)	Highest organism-specific MDR proportion
Staphylococcus aureus	20 (8.8)	10 (50.0)	Cefoxitin/oxacillin 10/20 (50.0); ciprofloxacin 11/20 (55.0); clindamycin 8/20 (40.0); vancomycin 0/20	All MDR isolates were MRSA
Escherichia coli	14 (6.1)	6 (42.9)	Ciprofloxacin 9/14 (64.3); third-generation cephalosporin 7/14 (50.0); piperacillin–tazobactam 6/14 (42.9); meropenem 1/14 (7.1)	ESBL phenotype in 6 isolates
Haemophilus influenzae	12 (5.3)	1 (8.3)	Cotrimoxazole 6/12 (50.0); ciprofloxacin 4/12 (33.3); amoxicillin–clavulanate 3/12 (25.0); ceftriaxone 1/12 (8.3)	Low MDR frequency
Other bacteria	7 (3.1)	2 (28.6)	Mixed Enterobacterales and Gram-positive isolates; resistance interpreted by organism-specific breakpoints	Two isolates met MDR definition
Total culture-positive episodes	228 (100.0)	92 (40.4)	—	MDR prevalence among all admissions: 92/312 (29.5%)

The denominator for organism percentages is 228 culture-positive episodes. Percentages in the MDR column are organism-specific. ESBL, extended-spectrum beta-lactamase; MDR, multidrug resistant; MRSA, methicillin-

resistant Staphylococcus aureus. Resistance values are simulated and must be replaced with verified laboratory data.

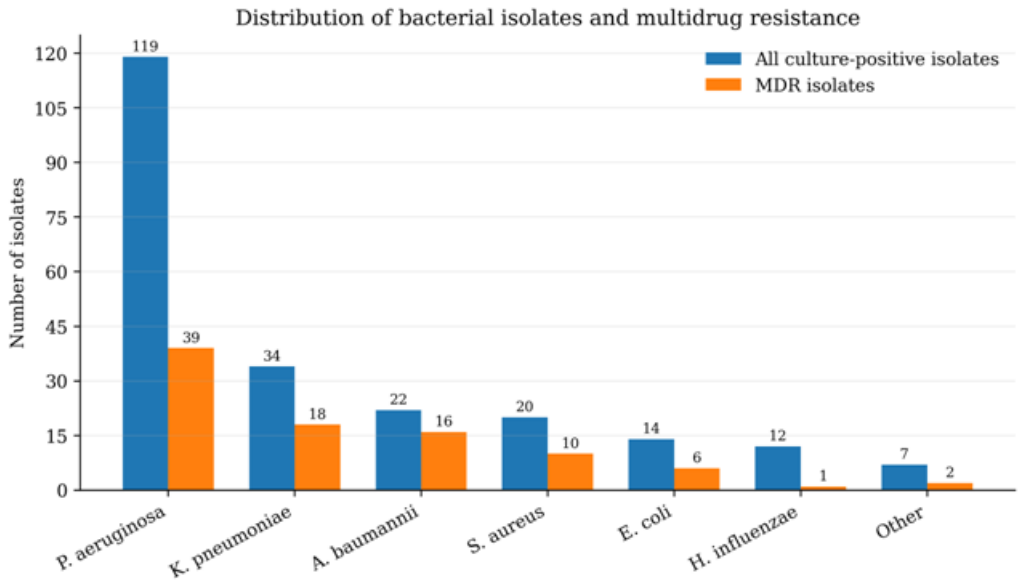


Figure 1: Distribution of all bacterial isolates and MDR isolates among 228 culture-positive hospitalized exacerbations

Clinical outcomes were consistently worse in the MDR group. Initial empirical therapy was inactive in vitro in 39/92 MDR episodes (42.4%) compared with 21/220 non-MDR episodes (9.5%). Respiratory failure occurred in 40.2% versus 10.0%, intensive care admission in 35.9% versus 10.5%, invasive mechanical ventilation in 25.0% versus 2.3%, and septic shock in 14.1% versus 3.6%. Median length of stay was 11.0 days (IQR 7.0–17.3) in the MDR group and 6.0 days (IQR 4.0–8.0) in the non-MDR group. In-hospital mortality was numerically higher with MDR infection (6.5% vs 1.8%), although the unadjusted comparison was imprecise because only 10 deaths occurred. Ninety-day readmission was 33.7% versus 17.7%, and composite clinical failure was 34.8% versus 7.3% (Table 3; Figure 2). After adjustment for age, sex, chronic kidney disease, coexisting chronic obstructive pulmonary disease, severe bronchiectasis, and previous-year hospitalization, MDR infection remained associated with respiratory failure (aOR 5.19, 95% CI 2.67–10.09), intensive care admission (aOR 4.71, 95% CI 2.37–9.34), invasive mechanical ventilation (aOR 10.53, 95% CI 3.68–30.10), and composite clinical failure (aOR 5.49, 95% CI 2.74–11.03). The adjusted association with 90-day readmission was weaker and crossed the conventional significance threshold (aOR 1.82, 95% CI 0.99–3.35). MDR infection was associated with an 83% higher adjusted length-of-stay rate (rate ratio 1.83, 95% CI 1.50–2.23).

Table 3: In-hospital and 90-day outcomes and multivariable analyses

Outcome or predictor	Non-MDR (n=220)	MDR (n=92)	Unadjusted OR (95% CI)	P value	Adjusted effect (95% CI)	Adjusted P
Panel A. Clinical outcomes						
Length of stay, days	6.0 (4.0–8.0)	11.0 (7.0–17.2)	—	<0.001	1.83 (1.50–2.23)	<0.001
Initial empirical therapy inactive in vitro	21 (9.5)	39 (42.4)	6.97 (3.79–12.85)	<0.001	—	—
Respiratory failure	22 (10.0)	37 (40.2)	6.05 (3.30–11.10)	<0.001	5.19 (2.67–10.09)	<0.001
ICU admission	23 (10.5)	33 (35.9)	4.79 (2.61–8.79)	<0.001	4.71 (2.37–9.34)	<0.001
Invasive mechanical ventilation	5 (2.3)	23 (25.0)	14.33 (5.25–39.14)	<0.001	10.53 (3.68–30.10)	<0.001
Septic shock	8 (3.6)	13 (14.1)	4.36 (1.74–10.92)	<0.001	—	—

In-hospital mortality	4 (1.8)	6 (6.5)	3.77 (1.04–13.68)	0.070	—	—
90-day readmission	39 (17.7)	31 (33.7)	2.36 (1.36–4.10)	0.002	1.82 (0.99–3.35)	0.056
Composite clinical failure	16 (7.3)	32 (34.8)	6.80 (3.50–13.23)	<0.001	5.49 (2.74–11.03)	<0.001
Panel B. Multivariable predictors of MDR infection						
Previous MDR isolate					9.94 (3.18–31.07)	<0.001
Hospitalization in previous year					3.74 (1.92–7.32)	<0.001
Antipseudomonal antibiotics in previous 90 days					9.47 (4.80–18.69)	<0.001
Chronic kidney disease					3.09 (1.25–7.66)	0.015
Chronic P. aeruginosa infection					4.42 (2.23–8.74)	<0.001
Severe bronchiectasis (BSI ≥9)					2.00 (1.02–3.95)	0.044
Age, per year					1.01 (0.99–1.03)	0.354
Male sex					1.59 (0.85–2.99)	0.151

Panel A: categorical data are n (%); length of stay is median (interquartile range). Outcome models controlled for age, sex, chronic kidney disease, coexisting COPD, severe BSI category, and hospitalization in the previous year; length of stay is an adjusted negative-binomial rate ratio. Composite clinical failure comprised in-hospital death, invasive mechanical ventilation, or septic shock. Panel B: all displayed predictors were entered simultaneously in the MDR-risk model. CI, confidence interval; MDR, multidrug resistant; OR, odds ratio. Estimates are based on the simulated cohort.

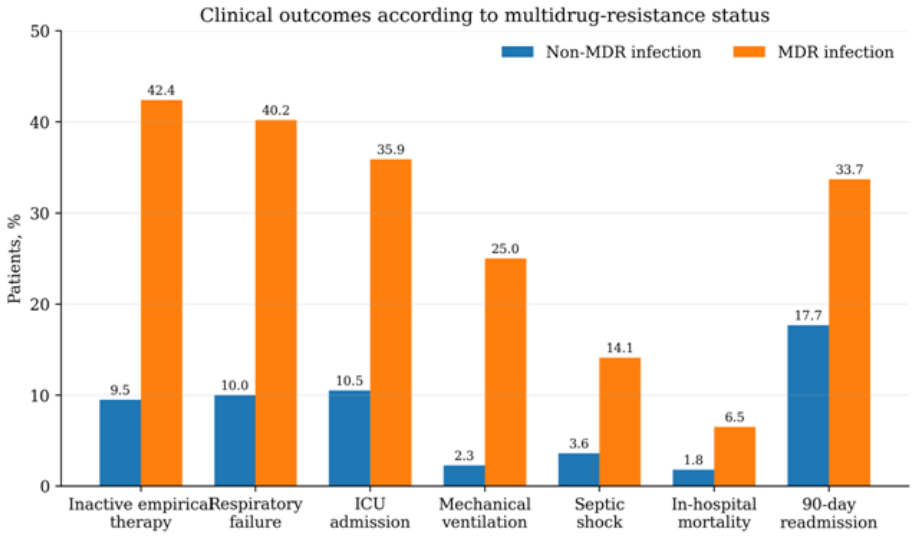


Figure 2: Major clinical outcomes in MDR and non-MDR hospitalized bronchiectasis exacerbations

Discussion

This model cohort addresses a clinically consequential gap by integrating prevalence, organism distribution, patient-level risk factors, empirical treatment adequacy, and acute outcomes in the same hospitalized bronchiectasis population. The central finding was that MDR bacteria were present in nearly one-third of all admissions and in approximately two-fifths of culture-positive exacerbations.

Resistance was not randomly distributed. It clustered in patients with previous MDR isolation, recent antipseudomonal exposure, chronic P. aeruginosa infection, recent hospitalization, chronic kidney disease, and severe bronchiectasis. MDR infection was also strongly associated with inactive initial therapy, respiratory failure, intensive care use, invasive ventilation, composite clinical failure, and prolonged hospitalization. These associations persisted after adjustment for major markers of baseline vulnerability, supporting the interpretation that resistance status carries clinically relevant information beyond disease severity alone.

The estimated MDR prevalence is plausible in relation to published exacerbation cohorts, although direct comparisons require careful attention to denominator, setting, sampling intensity, and MDR definition. Menéndez and colleagues identified MDR pathogens in 20.1% of microbiologically confirmed exacerbations and found a higher proportion among hospitalized than outpatient episodes [15]. Their independent predictors—previous MDR isolation, hospitalization in the preceding year, and chronic renal disease—were reproduced in the present model, strengthening the conceptual validity of the risk structure. The higher culture-positive MDR proportion here may reflect the exclusive inclusion of hospitalized patients, the high prevalence of recent antipseudomonal exposure, and the concentration of post-tuberculosis and P. aeruginosa-associated disease. Conversely, a centre with restrictive culturing, lower referral acuity, or less prior antibiotic exposure could observe a substantially lower prevalence. For this reason, empirical protocols should be based on local, syndrome-specific antibiograms rather than a single universal threshold.

The microbiological profile was dominated by P. aeruginosa, consistent with Indian registry data and studies from developing-country settings [10,16]. In the Pakistani exacerbation study, P. aeruginosa comprised most positive cultures and demonstrated resistance to ciprofloxacin, imipenem, ceftazidime, and piperacillin–tazobactam, while two-thirds of S. aureus isolates were methicillin resistant [16].

The illustrative rates in the present analysis were deliberately placed within that clinically credible range. Gao and colleagues likewise reported that antibiotic-resistant P. aeruginosa was common in bronchiectasis and was associated with previous antibiotic exposure, frequent exacerbations, greater dyspnoea, and more severe radiological disease, although resistant P. aeruginosa did not independently worsen long-term mortality in their cohort [22]. That result cautions against assuming that every resistant isolate has identical prognostic meaning; host severity, chronicity, virulence, bacterial load, treatment timing, and the distinction between colonization and acute infection remain important.

The recent carbapenem-resistant P. aeruginosa literature is particularly relevant to hospitalized exacerbations. Sun and colleagues reported carbapenem-resistant P. aeruginosa in 3.81% and multidrug-resistant P. aeruginosa in 5.83% of 1,286 hospitalized exacerbations; carbapenem resistance was independently associated with respiratory failure, mechanical ventilation, and longer hospital stay [17]. Their long-term cohort subsequently linked carbapenem-resistant isolation with mortality and recurrent exacerbations [18]. The direction and magnitude of acute outcome differences in the present model are therefore coherent with contemporary data. Importantly, the clinical hazard may not arise solely from resistance biology. Resistance acts as a marker of repeated healthcare contact and advanced airway disease, and it increases the probability that standard empirical therapy is inactive. Delayed active therapy then permits ongoing bacterial proliferation and neutrophilic inflammation during a period when respiratory reserve is already limited.

The association between MDR infection and inactive initial empirical treatment is a major actionable finding. In this model, more than four in ten MDR episodes initially received no agent active in vitro. That mismatch offers a credible mechanistic bridge between resistance and organ-support outcomes. However, the appropriate response is not indiscriminate carbapenem or polymyxin use. A risk-stratified strategy is more defensible: obtain a high-quality respiratory specimen immediately, review the patient's previous 12–24 months of cultures and susceptibilities, identify recent antibiotic classes and healthcare exposure, assess severity and organ dysfunction, and choose empirical coverage that is broad enough for the individual risk profile. Therapy should then be narrowed promptly once reliable results are available. Current adult bronchiectasis guidance emphasizes microbiology-informed management, reassessment of chronic infection, and antibiotic stewardship rather than routine maximal-spectrum treatment [2,3,20,21].

Previous MDR isolation and recent antipseudomonal exposure emerged as the strongest risk factors. These variables represent complementary information. A previous isolate directly captures the patient's airway microbial ecology, whereas recent exposure captures selection pressure.

Longitudinal studies of resistant P. aeruginosa show that repeated treatment can select mutations, efflux phenotypes, permeability changes, and beta-lactamase-mediated resistance within a persistently colonized airway. Molecular work in bronchiectasis isolates has identified multidrug and extensively drug-resistant strains and multiple resistance mechanisms, including target mutations, efflux upregulation, OprD loss, and acquired beta-lactamases [23]. These observations argue for an electronic "microbiology passport" visible at every emergency attendance and admission, summarizing recent organisms, minimum inhibitory concentrations where available, eradication attempts, and antibiotic exposure. Such a tool may improve empirical adequacy while reducing unnecessary duplication of broad-spectrum regimens.

Chronic P. aeruginosa infection and severe Bronchiectasis Severity Index category were independently associated with MDR infection. This is clinically coherent because both reflect a high-inflammation, high-treatment-burden phenotype. P. aeruginosa infection has repeatedly been associated with exacerbations, hospitalization, and mortality [12,13], and prospective cohort data support an independent contribution to adverse outcomes [24]. Short- and long-term antibiotic treatment can reduce airway and systemic inflammation in bronchiectasis [25], but recurrent exposure may also select resistance, creating a therapeutic paradox. The aim is therefore not to minimize necessary treatment, but to improve its precision: confirm bacterial exacerbations when possible, optimize airway clearance, address aspiration and comorbidities, use eradication or suppressive strategies according to guideline indications, and avoid repeated low-yield courses for non-bacterial symptom fluctuation.

The inflammatory consequences of delayed control may help explain respiratory deterioration. Neutrophil elastase activity is associated with exacerbations and lung-function decline and represents a biologically plausible link between bacterial burden and tissue injury [26]. During an exacerbation, ongoing infection can increase sputum purulence, mucus obstruction, ventilation-perfusion mismatch, and systemic inflammation. In patients with limited reserve, this may precipitate hypoxaemic or hypercapnic respiratory failure. Hospitalization also carries non-pulmonary risks. Bronchiectasis exacerbations have been associated with a transient increase in cardiovascular events, emphasizing that the acute inflammatory period can destabilize multiple organ systems [27]. The excess length of stay observed with MDR infection therefore likely reflects a combination of delayed active therapy, slower clinical response, treatment toxicity, organ support, and comorbidity management.

The mortality signal warrants balanced interpretation. Although crude in-hospital mortality was more than threefold higher in the MDR group, the event count was small and the confidence interval wide. The nationwide MDR bronchiectasis analysis by Chang and colleagues reported substantially higher in-hospital and three-year mortality with MDR infection [14], but such administrative or registry analyses may include residual confounding by frailty, healthcare exposure, and disease severity. Conversely, organism-specific studies have sometimes found resistant P. aeruginosa to be a marker of severity without an independent mortality effect [22]. A definitive mortality analysis requires a larger cohort, robust adjustment, time-to-event methods, and separation of infection-attributable death from competing causes. The current results more strongly support respiratory failure, ventilation, clinical failure, and length of stay as near-term outcomes than they support a causal mortality claim.

The findings have particular relevance to antimicrobial stewardship because lower respiratory infection is a major component of the global burden of bacterial antimicrobial resistance [28]. Bronchiectasis presents a stewardship challenge distinct from a single episode of community-acquired pneumonia: patients repeatedly re-enter the treatment pathway, often carry chronic organisms, and may receive oral, intravenous, or inhaled antibiotics across years. Stewardship must therefore be longitudinal. Recommended elements include reliable sputum surveillance during stability and exacerbation, documentation of true allergies, review of prior susceptibilities before prescribing, renal-dose optimization, therapeutic drug monitoring when indicated, defined treatment duration, post-culture de-escalation, and multidisciplinary review of patients receiving frequent courses. Infection-control measures are also important because chronic airways may serve as reservoirs for high-risk resistant clones; recent genomic work has identified carbapenemase-producing epidemic P. aeruginosa lineages in bronchiectasis populations [29].

This analysis has several strengths. It uses a clinically explicit exacerbation definition, a standardized MDR definition, both all-admission and culture-positive denominators, organism-level resistance reporting, prespecified confounder adjustment, and outcomes that matter to patients and hospitals. The tables are designed so that source data can be inserted without changing the analytic architecture. The figures communicate both the microbiological burden and the clinical consequences of resistance. The model also avoids over-reliance on a single composite endpoint by presenting each component separately.

The limitations are fundamental and must be stated transparently. First, the patient-level data are simulated; the findings cannot be represented as observations from a real hospital and are not eligible for scientific submission until replaced or validated with audited clinical data. Second, a retrospective single-centre design would be vulnerable to selection bias, missing cultures, prior outpatient antibiotics, misclassification of colonization as infection, and unmeasured confounding. Third, conventional culture may miss fastidious organisms and does not characterize the airway microbiome or resistome. Fourth, susceptibility breakpoints and laboratory panels can change over time, complicating temporal comparisons. Fifth, empirical treatment adequacy based on in-vitro susceptibility does not guarantee clinical effectiveness and may be influenced by dosing, penetration, biofilm, and source control. Sixth, the

mortality event count in the illustrative cohort is insufficient for a stable fully adjusted model. Finally, results from a tertiary referral hospital may not generalize to community hospitals or outpatient exacerbations.

Future research should use multicentre prospective designs with standardized sampling before antibiotics, adjudication of infection versus colonization, linkage of stable-state and exacerbation isolates, and molecular characterization of resistance mechanisms and clonal transmission. A pragmatic clinical prediction tool could combine previous MDR isolation, recent antimicrobial classes, prior hospitalization, chronic P. aeruginosa infection, renal disease, and Bronchiectasis Severity Index, then be externally validated for both discrimination and net clinical benefit.

Interventional studies should test whether a microbiology-history–guided empirical algorithm improves early active therapy without increasing overall broad-spectrum antibiotic use. Patient-centred endpoints should include symptom recovery, quality of life, treatment toxicity, recurrence, and emergence of new resistance in addition to mortality and length of stay.

Conclusion

MDR bacteria represented a substantial proportion of hospitalized bronchiectasis exacerbations in this model analysis and identified a phenotype at high risk of inactive initial therapy, respiratory failure, invasive ventilation, clinical failure, and prolonged hospitalization. Previous MDR isolation, recent antipseudomonal exposure, chronic P. aeruginosa infection, recent hospitalization, chronic kidney disease, and severe bronchiectasis were the most informative predictors. A clinically safe response is rapid high-quality respiratory sampling, structured review of prior microbiology, individualized empirical coverage for high-risk patients, and prompt culture-directed de-escalation.

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