

ORIGINAL ARTICLE

Risk Factors for Multidrug Resistant Organisms in Exacerbation of Bronchiectasis

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Abstract:

Background & Objective: Bronchiectasis is a chronic debilitating airway disease. Patients with bronchiectasis are prone to repetitive infective exacerbations. Antibiotics are considered the cornerstone in the management of exacerbations. Frequent treatment with antibiotics makes the organism much more susceptible to acquire antibiotic resistance that account for a substantial number of excess deaths and catastrophic healthcare spending. Attention in focusing the risk factors for antibiotic resistance is necessary to take steps to reduce the development of resistant organisms and framing antibiotic policy.

Patients & Methods: This cross-sectional observational and analytical study was conducted in the Inpatient Department of Respiratory Medicine in National Institute of Diseases of the Chest and Hospital from April 2019 to April 2020. A total of 202 adult patients with exacerbation of bronchiectasis were enrolled. Early morning Sputum were examined for bacteriological culture and sensitivity. Multidrug-resistance was determined according to European Centre of Disease Prevention and Control classification.

Result: Two hundred and two exacerbations were included and microorganisms were isolated in 155 cases. Pseudomonas aeruginosa 87(55.8%) and Klebsiella pneumoniae 53(34.0%) were more frequent. Multidrug-resistant pathogens were found in 90(58.1%) cases. In multivariate analysis, recent hospitalization (Odds ratio (OR)2.42,95% CI 1.03-5.71), frequent antibiotic use (OR 2.650, 95% CI 1.21-5.80) and chronic kidney disease (5.98,95%CI 1.57-22.81) were found to be independent predictors for MDR pathogens.

Conclusion: Recent hospitalization, frequent antibiotic use and chronic kidney disease were seemed to be the risk factor for multidrug resistant bacteria. Identification of the factors associated with antibiotic resistance helps in rational prescription of antibiotics.

Key words: Multidrug Resistant Organism, exacerbation of Bronchiectasis, risk factors

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Introduction:

Bronchiectasis is defined as an abnormal and permanent dilatation of one or more bronchi.¹ It is a chronic respiratory disease presenting with chronic cough and sputum production, some have hemoptysis and shortness of breath. Increased production of mucous together with impaired mucociliary clearance leads to accumulation of secretion in dilated bronchi and causes recurrent respiratory infections. A vicious cycle is established involving persistent bacterial colonization, chronic inflammation of the bronchial mucosa, airway damage and remodeling. In most cases, infection is the primary force behind this ongoing cycle.²

Patients with bronchiectasis are prone to frequent exacerbations which have traditionally been viewed as being exclusively bacterial, evidenced by epidemiological data. So, identification and appropriate treatment of these organisms is an essential part of the management of bronchiectasis. Bacteria most commonly isolated from the airways of patients with bronchiectasis include *Haemophilus influenzae*, *Pseudomonas aeruginosa*, *Streptococcus pneumoniae*, *Staphylococcus aureus* and *Moraxella catarrhalis*.³ Dominant bacteria are *Pseudomonas aeruginosa* and *Haemophilus influenzae* worldwide.⁴

Antibiotics aiming to treat bacterial infections of the respiratory tract, or to control bacterial colonization, or both, represent a central component of the treatment of bronchiectasis. Those having frequent exacerbations causing significant morbidity, antibiotic therapy appears to decrease the frequency and severity of exacerbations at the expense of emerging drug resistance.⁵

Optimal antibiotic use is crucial, especially in an era of rising antibiotic resistance and lack of new antimicrobial development.⁶ Over-prescribing and mal-prescribing of antibiotics are undoubtedly contributing to the growing challenges posed by antibiotic resistant bacteria, and epidemiological studies have clearly demonstrated direct relationships between antibiotic consumption and the emergence and dissemination of resistant strains.⁷

Leaders in world health have described antimicrobial-resistant bacteria as “nightmare bacteria” that account for a substantial number of

excess deaths and catastrophic healthcare spending⁸. The impact of antibiotic resistant bacteria is suggested to be far more serious in low- and middle-income countries (LMICs) than in well-resourced countries.

Routine screening is vital due to the circulation of resistant organisms in the community. Attention to identify the risk factors for antibiotic resistance is necessary to take steps to prevent the development of resistant organisms and framing antibiotic policy.

Materials and Methods:

This cross-sectional analytical study was carried out in the Department of Respiratory Medicine, National Institute of Diseases of the Chest & Hospital (NIDCH), Mohakhali, Dhaka over a period of one year between April 2019 to April 2020. Adult patients presented with exacerbation of bronchiectasis admitted to the inpatient Department of Respiratory Medicine were the study population. Patients with concomitant pulmonary tuberculosis were excluded from the study. A total of 202 cases were taken in the study. Study samples were selected by purposive sampling.

Having obtained ethical clearance from the Ethical Committee and verbal consent from the patients, the data collection was commenced. Statistical analyses were carried out using Statistical Package for Social Sciences, version 23.0. Data were presented in frequency, percentage and mean and standard deviation as applicable. Chi square test was used for categorical variables. Univariate and Multivariate logistic analysis were used for risk factors. For all analytical tests, the level of significance was set 5% and p-value < 0.05 was considered significant. The findings obtained from data analyses are presented below:

Results:

A total of 202 patients with exacerbation of bronchiectasis including 126 males (62.4%) and 76 females (37.6%) with a mean age of 47.2 years (range 19 - 83 years) who were admitted in department of respiratory medicine, NIDCH entered the study.

Among study population, 92(45.5%) were Diabetic, 34(16.8%) had chronic kidney disease, 97(48.0%) were smoker and 178(88.1%) from rural area. 178(88.1%) cases had previous exacerbation,

103(51.0%) had history of recent hospitalization, frequent antibiotic user were 122(60.4%), 87(43.1%) had history of previous I/V antibiotics, 16(7.9%) had previous ICU admission, 30(14.9%) had previous isolation of resistant organism and use of immunosuppressive drugs were 6(3.0%) .

Sputum for C/S showed bacterial growth in 155(76.7%) with multidrug-resistant organism in 90 (58.1%) cases.

In univariate analysis, previous exacerbation, recent hospitalization, frequent antibiotic use, diabetes mellitus and chronic kidney disease were found to be independent predictors for MDR pathogens.

In multivariable analysis, recent hospitalization, frequent antibiotic use and chronic kidney disease were found to be independent predictors for MDR pathogens.

Table I.
Demographic Characteristics of the Study Cases (n=202)

Demographic characteristic	Number of patients	Percentage
Sex		
Male	126	62.4
Female	76	37.6
Mean age (years)	47.2	±16.3
Range (min-max)	19.0	-83.0
Residence		
Rural	178	88.1
Urban	24	11.9
Smoker		
Yes	97	48.0
No	105	52.0

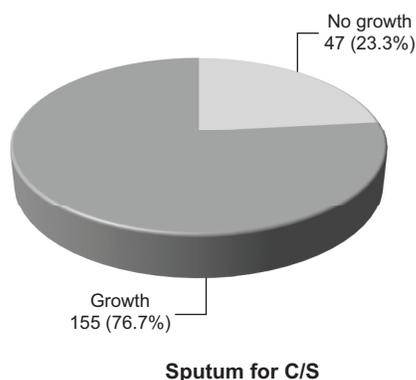


Fig.-1: *Distribution of the Study Cases According to Culture of Bacteria*

Table-II
Distribution of the Study Cases According to Growth of the Bacteria (n=155)

Name of the bacteria	Number of patients	Percentage
<i>Pseudomonas aeruginosa</i>	87	56.1
<i>Klebsiella pneumoniae</i>	53	34.1
<i>Streptococcus pneumoniae</i>	7	4.5
<i>Staphylococcus aureus</i>	4	2.6
<i>Escherichia coli</i> (E.coli)	3	1.9
<i>Haemophilus influenzae</i>	1	0.6

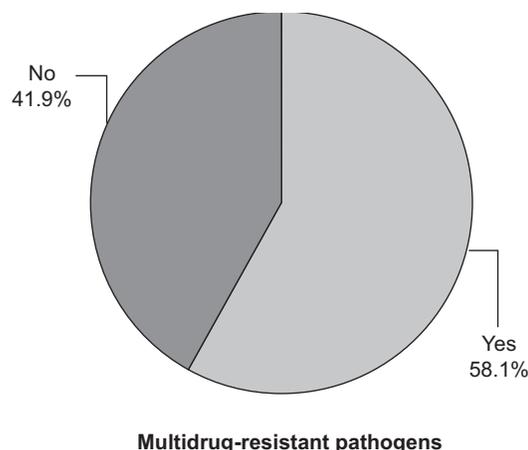


Fig.-2: *Distribution of Multidrug-resistant Pathogens of the Study Cases (n=155)*

Table-III
Distribution of the Study Cases According to Risk Factors for Antibiotic Resistance (n=202)

Risk factors	Number of patients	Percentage
Previous exacerbation	178	88.1
Frequent antibiotic use	122	60.4
Recent hospitalization	103	51.0
Previous use of I/V antibiotics	87	43.1
Previous resistant organisms	30	14.9
Previous ICU admission	16	7.9
Use of immunosuppressive drugs	6	3.0

Table IX shows previous exacerbation 86(95.6%), recent hospitalization 63(70.0%), frequent antibiotic use 69(76.7%), previous I/V antibiotic user 49(54.4%), previous resistant organisms 21(23.3%), diabetes mellitus 56(62.2%) and chronic kidney disease 27(30.0%) in multi-drug resistance, which were statistically significant ($p < 0.05$) when compared between multidrug-resistant and non-multidrug resistant pathogen

In univariate analysis, previous exacerbation, recent hospitalization, frequent antibiotic use, diabetes mellitus and chronic kidney disease were found to be independent predictors for MDR pathogens

In multivariate analysis, recent hospitalization, frequent antibiotic use and chronic kidney disease were found to be independent predictors for multidrug resistant pathogens.

Table-IV
Association between MDR Pathogens with Risk Factors (n=155)

Risk factors	Multidrug-resistant pathogens				P value
	Yes (n=90)		No (n=65)		
	n	%	n	%	
Previous exacerbation	86	95.6	54	83.1	0.010 ^s
Recent hospitalization	63	70.0	25	38.5	0.001 ^s
Frequent use of antibiotics	69	76.7	29	44.6	0.001 ^s
Previous I/V antibiotics	49	54.4	26	40.0	0.076 ^{ns}
Previous resistant organisms	21	23.3	7	10.8	0.045 ^s
Previous ICU admission	11	12.2	4	6.2	0.207 ^{ns}
Use of immunosuppressive drugs	2	2.2	1	1.5	0.621 ^{ns}
Diabetes mellitus	56	62.2	21	32.3	0.001 ^s
Chronic kidney disease	27	30.0	3	4.6	0.001 ^s

(s= significant, ns= not significant, p value reached from chi-square test)

Table V
Univariate Regression Analysis for MDR Pathogens (n=90)

	Adjusted OR	95% CI		P value
		Lower	Upper	
Previous exacerbation	4.380	1.327	14.452	0.015 ^s
Recent hospitalization	3.733	1.905	7.318	0.001 ^s
Frequent antibiotic use	4.079	2.043	8.142	0.001 ^s
Diabetes mellitus	3.451	1.762	6.759	0.001 ^s
Chronic kidney disease	8.857	2.555	30.707	0.001 ^s

(s= significant, p value reached from univariate analysis by binary logistic regression analysis, OR= Odds Ratio)

Table-VI
Multivariate Regression Analysis for MDR Pathogens (n=90)

	Adjusted OR	95% CI		P value
		Lower	Upper	
Age (>60 years)	0.614	0.255	1.477	0.276ns
Male	1.005	0.418	2.412	0.992ns
Rural	0.965	0.296	3.146	0.953ns
Smoker	1.519	0.623	3.701	0.358ns
Previous exacerbation	1.420	0.367	5.503	0.612ns
Recent hospitalization	2.423	1.028	5.711	0.043s
Frequent antibiotic use	2.650	1.209	5.808	0.015s
Diabetes mellitus	1.649	0.732	3.715	0.227ns
Chronic kidney disease	5.988	1.572	22.806	0.009s

(s= significant, ns= not significant, *p* value reached from multivariate analysis by binary logistic regression analysis, OR=Odds Ratio)

Discussion:

This cross sectional observational and analytical study was carried out with the aim to identify the possible risk factors for the development of multidrug resistant pathogens. In this study, the age of the patients ranged from 19 years to 83 years with a mean of 47.2±16.3 years. While the mean age was 58.44 and 48 years found in another studies.^{9,10,11}

This study observed that a significant number of patients (45.5%) had diabetes mellitus and 16.4% cases had chronic kidney disease. A study¹² showed MDR exacerbations occurred in elderly patients with a higher proportion of comorbid conditions. Diabetes mellitus was found in 7(21.9%) cases among total 32 MDR isolates and chronic renal disease was in 7(21.9%) cases.

This study also explored that majority of the patients had previous exacerbation 178(88.1%).Recent hospitalization was 103(51.0%), frequent antibiotic user was 122(60.4%), previous I/V antibiotic users 87(43.1%), previous ICU admission 16 (7.9%) and previous resistant organism was 30 (14.9%).These findings are consisted with the study findings¹² during the period of 2011 to 2015 among 233 patients.

This study showed bacterial growth found in significant number of cases 155(76.7%). These results are comparable with previous studies^{9,13,14,15} and are not supported by the

study¹⁰ where bacteriological isolation was found in 35% of cases.

In this study multidrug-resistance was found in 90 (58.1%) while it was 20.1% in another study.¹²

This study also showed previous exacerbation 86(95.6%), recent hospitalization 63(70.0%), frequent antibiotic use 69(76.7%), previous resistant organism 21(23.3%), diabetes mellitus 56(62.2%) and chronic kidney disease 27(30.0%) were found in multi-drug resistance, which were statistically significant ($p<0.05$) when compared between multidrug-resistant and non multi drug-resistant pathogens. Another study¹² reported that exacerbation in last year was 87.5%, hospitalization in previous year was 81.2%, long term oral antibiotics use was 12.5%, Diabetes mellitus was 21.9%, Renal disease was 21.9 %. Hospitalization in previous year and renal disease was statistically significant ($p<0.05$) between groups.

This study observed that in univariate analysis, previous exacerbation, recent hospitalization, frequent antibiotic use, diabetes mellitus and chronic kidney disease were found to be independent predictors for MDR pathogens. Another study¹² documented MDR pathogens were more frequently encountered in patients with more chronic conditions and in those with higher FACED and BSI scores.

In multivariate analysis, recent hospitalization (Odds ratio (OR)2.42, 95% CI 1.03-5.71), frequent

antibiotic use (OR 2.650, 95% CI 1.21-5.80) and chronic kidney disease (OR 5.98, 95%CI 1.57-22.81) were found to be independent predictors for MDR pathogens. Another similar study¹² found three independent MDR risk factors: chronic renal disease (Odds ratio (OR), 7.60, 95% CI 1.92-30.09), hospitalization in the previous year (OR, 3.88 95% CI 1.37-11.02) and prior multidrug-resistant isolation (OR, 5.58, 95% CI 2.02-15.46).

Prior hospitalization is a fairly widely recognized independent MDR risk factor and specifically for MRSA and for Enterobacteriaceae mainly related to exposure to 3rd/4th generation Cephalosporin or broad-spectrum Penicillin.^{17,18}

Limitations of the study:

Present study was conducted for a short period of time. Sample was taken purposively, so there may be chance of bias. Pathogen identification relied mainly on conventional microbiological tests and extended antibiogram was not possible to conduct in every patient.

Conclusion:

Multidrug resistant bacteria were found in 90 (58.1%) cases. Recent hospitalization, frequent antibiotic use and chronic kidney disease were seemed to be the risk factor for multidrug resistant bacteria.

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