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Original Research Article

Pattern of bacterial infection in acute exacerbation of bronchiectasis according to the lobar distribution

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ABSTRACT

Background: The pattern of bacterial infection in acute exacerbation of bronchiectasis is varied with geographical area and lobar distribution of bronchiectasis. The exact pattern of bacterial infection in acute exacerbation of bronchiectasis according to lobar distribution is not known in our country. This study aimed to investigate the pattern of bacterial infection in acute exacerbation of bronchiectasis according to lobar distribution.
Methods: A total of eighty-four patients diagnosed with acute exacerbation of bronchiectasis were included in this cross-sectional study in the department of respiratory medicine, Bangabandhu Sheikh Mujib Medical University. Sputum culture and real-time polymerase chain reaction were used to characterize the bacterial profile and high-resolution computed tomography scans for the location of the bronchiectasis. Before enrolment, informed written consent was obtained from the participants.
Results: The mean (SD) age of this study population was 47.89 (±14.95) years, 29.8% were female and 60.7% were a non-smoker. Bronchiectasis was more common in the right middle lobe (63.1%), followed by the right lower lobe (44%), and the left lower lobe (42%). Bacteria were isolated in 66% of patients and Gram-negative bacteria were predominant (78.6%). *Pseudomonas aeruginosa* (25%) and *Klebsiella pneumoniae* (17.9%) were the most common bacteria.
Conclusions: *Pseudomonas aeruginosa* was identified predominantly in the right upper lobe, right middle lobe, left upper lobe, and bilateral upper lobe and *Klebsiella pneumoniae* was in the right lower lobe, left lower lobe, and bilateral lower lobe.

Keywords: Bacterial profile, Bronchiectasis, Lobar distribution

INTRODUCTION

Bronchiectasis is a heterogeneous disease characterized by a clinical syndrome of cough, sputum production, bronchial infection, and radiologically abnormal and permanent dilatation of the bronchi.[1] The post-tubercular disease is the predominant cause of bronchiectasis in the Indian subcontinent.[2]

A combination of a defect in host defence and bacterial infection allows microbial colonization of the airways resulting in chronic inflammation and lung damage. Pathophysiological mechanisms of bronchiectasis include persistent bacterial infections, dysregulated immune responses, impaired mucociliary clearance, and airway obstruction.[3]

Acute exacerbation of bronchiectasis is defined by: a person with bronchiectasis with a deterioration in three or

more of the following key symptoms for at least 48 hours: cough; sputum volume and/or consistency; sputum purulence; breathlessness and/or exercise tolerance; fatigue and/or malaise; hemoptysis and a clinician determine that a change in bronchiectasis treatment is required.[4]

Recurrent exacerbation and hospital admission are associated with a decline in pulmonary function, morbidity, and mortality. Identification of microorganisms and appropriate choice of antibiotics in acute exacerbation of bronchiectasis is essential for the management and reduce mortality.

Sputum culture is a non-invasive and inexpensive procedure. However, no definite organism was identified in a larger proportion of patients even after repeated cultures. In this condition, a culture-independent molecular method (RT-PCR) might be helpful to detect pathogenic bacteria. PCR is more sensitive for the detection of multiple microorganisms and delivers fast results. Bronchiectasis is a radiological diagnosis and it may be unilateral or bilateral and upper/middle/lower /lingual/multilobar in distribution. Different pathogens may be associated with different lobar distributions.

There is a cross-country variation of bacterial profile and antibiotic susceptibility pattern. Limited research was found internationally on bacterial patterns according to the lobar distribution of bronchiectasis. Bangladesh is a high tuberculosis burden country, and many patients are suffering from post-tuberculosis long-term complications like bronchiectasis.

There was no digitally available study in Bangladesh on this problem. So, this study was conducted to find out the bacterial pattern in acute exacerbation of bronchiectasis according to lobar distribution.

METHODS

We conducted this cross-sectional study on a patient with acute exacerbation of bronchiectasis in the respiratory medicine department of BSMMU from 3rd April 2021 to 31st August 2021. A total of 150 patients were screened for this study and eighty-four were included finally.

Early morning sputum samples were taken in a sterile wide-mouth pot and then sent to the BSMMU microbiology laboratory for culture and sensitivity. Those patients who became culture-negative were performed RT-PCR of the sputum bacterial panel. Sputum for ZN stain, gene X-pert, sputum RT-PCR for COVID-19, FBS, 2HABF, and serum creatinine was done to exclude pulmonary tuberculosis, diabetes, COVID-19, and renal impairment. HRCT chest was performed to confirm bronchiectasis. Demographical and clinical data were collected in a structured data sheet. Informed consent was taken from the participants. Before starting, the study's ethical approval was taken from the institutional review board (IRB).

After the collection of data, all data were checked for proper entry of all desired variables, tabulated, and coded for statistical analysis. Then statistical analysis was done using the computer program SPSS (Statistical Package for the social sciences) version 26. The quantitative data obtained from the study were age, BMI, and categorical data were clinical variables, type and lobar distribution of bronchiectasis, and sputum isolated bacteria. Continuous variables were analyzed as mean value±standard deviation. Categorical variables were tested as counts and percentages. To investigate the association between sputum-isolated bacteria with types and lobar distribution of bronchiectasis Chi-square test was used. The logistic regression model was done for predicting sputum bacterial positivity (dependent variables) from types and lobar distribution (independent variables) of bronchiectasis. A p value of less than 0.05 was considered statistically significant.

Inclusion criteria

Patients with acute exacerbation of bronchiectasis were included.

Exclusion criteria

Patients with pre-existing pulmonary diseases including active pulmonary tuberculosis and COVID-19, known malignancy, long-term (>3 months) intake of oral steroids, organ transplantation, cytotoxic drugs, DM, CKD, and patients who took antibiotics within the last 4 weeks were excluded from this study.

RESULTS

In our study, the mean (SD) age and BMI of the participants were 47.89 (±14.95), and 18.99 (±1.70) respectively, and male predominant (70.2%). The majority of the participants 51 out of 84 (60.7%) were non-smokers. 39 out of 84 (46.4%) was low BMI. Cough (90.5%), increased sputum volume (73.8%), and purulence (63.1%) were the predominant presenting complaints. 67.8% of participants had a previous history of exacerbation and 48.8% of participants had a history of hospitalization. Post-infection (tuberculosis 72.6% and pneumonia 16.7%) was this study's predominant etiology of bronchiectasis. The sociodemographical and clinical features of the study subject were shown in Table 1.

Table 2 displayed the lobar distribution of bronchiectasis, bronchiectasis was more frequently observed in the right middle lobe (25.6%), right lower lobe (21.2%), left lower lobe (20%), and right upper lobe (16.4%). The bilateral upper lobe and lower lobe distribution had 47.1% and 52.9% respectively.

Table 1: Socio-demographic and clinical features of the study patients (n=84).

Socio-demographic characteristics	Frequency	Percentage
Age (years) Mean±SD	47.89±14.95	
Sex		
Male	59	70.2
Female	25	29.8
Smoking status		
Non-smoker	51	60.7
Ex-smoker	29	34.5
Current smoker	4	4.8
Body mass index (kg/m^2) Mean±SD		18.99±1.70
Presenting complaints		
Cough	76	90.5
Increase sputum volume	62	73.8
Increase sputum purulence	53	63.1
Fever	47	56.0
Haemoptysis	30	35.7
Shortness of breath	42	50.0
Fatigue	62	73.8
Number of exacerbations last year		
No exacerbation	27	32.2
<2 in last year	50	59.5
≥2 in last year	7	8.3
History of prior hospitalization	41	48.8
History of prior PTB	61	72.6
History of prior pneumonia	14	16.7

In our study, 56 out of 84 (66%) bacteria were isolated from sputum among them 78.6% and 21.4% were Gram-negative and Gram-positive correspondingly.

Table 3 showed that among the isolated bacteria *Pseudomonas aeruginosa* (P.A) was the predominant bacteria followed by *Klebsiella pneumoniae* (K.P). *Staphylococcus aureus* (S.A), *Streptococcus pneumoniae* (S.P), *E. coli*, *Haemophilus influenza* (H.I), *Moraxella catarrhalis* (M.C), and *Acinetobacter* were 8.3%, 6%, 3.6%, 2.4%, 2.4%, and 1.2% correspondingly.

Table 2: Lobar distribution of the bronchiectasis of the participants.

Lobar distribution	Frequency	Percentage
Right upper lobe (RUL)	34	16.4
Right middle lobe (RML)	53	25.6
Right lower lobe (RLL)	44	21.2
Left upper lobe (LUL)	19	9.1
Lingula	15	7.2
Left lower lobe (LLL)	42	20.0
Total	207	100%
Bilateral upper lobe (BUL)	24	47.1
Bilateral lower lobe (BLL)	27	52.9
Total	51	100%

Table 3: Distribution of isolated bacteria of the participants.

Type of bacteria	Frequency	Percentage
Pseudomonas aeruginosa	21	25.0
Klebsiella pneumoniae	15	17.9
Staphylococcus aureus	7	8.3
Streptococcus pneumoniae	5	6.0
E. coli	3	3.6
Haemophilus influenzae	2	2.4
Moraxella catarrhalis	2	2.4
Acinetobacter	1	1.2

Table 4: Distribution of bacteria according to the lobe involvement of bronchiectasis.

Lobe	Total	P. A	K. P	S. P	S. A	M.C	*Acinetobacter*	*E. coli*	H. I
RUL	23	17 (73.9%)	0 (0.0%)	3 (13.0%)	1 (4.3%)	0 (0.0%)	1 (4.3%)	1 (4.3%)	0 (0.0%)
RML	29	21 (72.4%)	0 (0.0%)	2 (6.9%)	2 (6.9%)	0 (0.0%)	0 (0.0%)	2 (6.9%)	2 (6.9%)
RLL	28	1 (3.6%)	15 (53.6%)	14 (14.3%)	2 (7.1%)	2 (7.1%)	0 (0.0%)	3 (10.7%)	1 (3.6%)
LUL	17	12 (70.6%)	0 (0.0%)	3 (17.6%)	0 (0.0%)	0 (0.0%)	1 (5.9%)	0 (0.0%)	1 (5.9%)
Lingula	8	5 (62.5%)	2 (25.0%)	1 (12.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
LLL	20	5 (5.0%)	11 (55.0%)	3 (15.0%)	1 (5.0%)	1(5.0%)	0 (0.0%)	2 (10.0%)	1 (5.0%)
BUL	18	12 (66.7%)	1 (5.6%)	3 (16.7%)	1 (5.6%)	0 (0.0%)	1 (5.6%)	0 (0.0%)	0 (0.0%)
BLL	20	4 (20.0%)	8 (40.0%)	4 (20.0%)	1 (5.0%)	1 (5.0%)	0 (0.0%)	2 (10.0%)	0 (0.0%)

The distribution of bacteria according to the lobe of the lung showed in Table 4. *Pseudomonas aeruginosa* was predominantly in the right upper lobe, right middle lobe, left upper lobe, and bilateral upper lobe bronchiectasis, whereas *Klebsiella pneumoniae* was in the right lower lobe, left lower lobe, and bilateral lower lobe. The Association of sputum bacterial positivity with the lobar distribution of bronchiectasis showed that the left upper and lower lobe, bilateral upper and lower lobe had a statistically significant association (Table 5).

The antibacterial drug sensitivity and resistance pattern of *Pseudomonas aeruginosa* showed that it had 100% sensitive to ticarcillin and colistin sulfate, 95.2% to

amikacin, 75% to ceftazidime, 73.7% to meropenem, and 66.7% to gentamicin. On the other hand, Pseudomonas was 94.7% resistant to amoxicillin, 72.2% cotrimoxazole, 83.3% azithromycin, 64.3% cefuroxime, 61.1%, ceftriaxone.

Table 5: Association of sputum bacterial positivity with the lobar distribution of bronchiectasis.

Lobar distribution	Total	Negative		Positive		P value
		n	%	n	%	
RUL	34	9	26.5	25	73.5	0.271^{ns}
RML	53	19	35.8	34	64.2	0.522^{ns}
RLL	44	13	29.5	31	70.5	0.440^{ns}
LUL	19	1	5.3	18	94.7	0.003*
Lingula	15	6	40.0	9	60.0	0.546^{ns}
LLL	42	20	47.6	22	52.4	0.005*
BUL	24	4	16.7	20	83.3	0.040*
BLL	27	5	18.5	22	81.5	0.047*

*=significant at p value <0.05; ns=not significant

On the other hand, the antibacterial sensitivity and resistant pattern of *Klebsiella pneumoniae* demonstrated that klebsiella was 100% sensitive to amikacin and colistin sulfate, 80% to meropenem, 60% to gentamicin, 53.3% to tazobactam, and 85.7% resistant to azithromycin. 84.6% to cotrimoxazole, 80% to ceftriaxone and cefotaxime, 76.9% to cefuroxime, and 66.7% to ciprofloxacin.

DISCUSSION

This cross-sectional study was conducted to assess the pattern of bacterial infection concerning the lobar distribution in acute exacerbation of bronchiectasis. A total of 84 subjects were enrolled, where the majority were male (70.2%), and the mean age of the participants was 47.89±14.95. The average BMI of this study population is concordant with the Indian population.[5]

The common presenting symptoms of the participants were cough, increased sputum volume, sputum purulence, and fatigue which was comparable to the study by Byun et al.[6] 67.5% of patients had 1 or more prior exacerbations in our study which corresponds to the study by Dimakou et al.[7] A systemic review by Lonni et al reported that previous pulmonary tuberculosis was the cause of bronchiectasis in 40-80% of patients which correlates with the current study finding.[8]

The current study showed that increased sputum volume, sputum purulence, history of prior exacerbation, and hospitalization were significantly associated with sputum pathogen identification. A study conducted by Izhakian et al displayed that 25.9% in the right middle lobe, 20.7% in the right lower lobe, 20.4% in the left lower lobe, 13.8% in the lingula,13% in the right upper lobe, 6.2% in left upper lobe were involved according to lobar distribution of bronchiectasis which was quite similar to our study.[9]

According to Shoemark et al study's report, 59% of the participants exhibited positive sputum bacteriology.[10] Our study demonstrated that the predominant sputum-isolated organism was Gram-negative (78.6%), which was similar to the of Shahid et al.[11] The most frequently detected Gram-negative organism was *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae* and Gram-positive pathogens were *Staphylococcus aureus* and *Streptococcus pneumoniae*. The commonest pathogen isolated from the sputum of this study was *Pseudomonas aeruginosa* which was consistent with previous studies.[12-14]

The present study showed Klebsiella was the second commonest sputum isolated pathogen in the exacerbation state of bronchiectasis which differs from the study conducted in Europe, the US, Canada, and other Asia-Pacific regions, where organisms like *Haemophilus influenzae* and NTM were common findings.[2] This study detected Haemophilus in 2.4% of cases, which was lower than in prior studies.

Saha et al explored the cause of the low detection rate of *Haemophilus influenzae* in a developing country and found that the fastidious pathogen needs the addition of isovitalex to agar media, this was possibly the reason for the low rate of *Haemophilus influenzae* isolation in the current study.[15]

According to a study by Izhakian et al in the left lower lobe, right lower lobe, and right middle lobe of the lung common pathogen was *Haemophilus influenzae* and in the right upper lobe, *Pseudomonas aeruginosa* was a prevalent organism.[9] In our study, *Pseudomonas aeruginosa* was seen more in the right upper lobe, right middle lobe, left upper lobe, and *Klebsiella pneumoniae* was detected more often from the right lower lobe and left lower lobe. The major difference between the present study and the previous was *Haemophilus influenzae* was found frequently in the lower lobes of the preceding study while *Klebsiella pneumoniae* was distinctly found in the lower lobes of the current study. In addition, bilateral upper lobes had further isolation of *Pseudomonas aeruginosa* and bilateral lower lobes had a predilection for *Klebsiella pneumoniae*.

Antibiotic sensitivity and resistance pattern of the isolated pathogen were also assessed in this study. *Pseudomonas aeruginosa* was highly sensitive to colistin (100%), ticarcillin (100%), and amikacin (95%), nonetheless marked resistance to amoxicillin, co-trimoxazole, ciprofloxacin, azithromycin, cefuroxime, ceftriaxone which reflect injudicious use of antibiotics in this study population.

The sensitivity of *Klebsiella pneumoniae* was quite high to colistin (100%), amikacin (100%), and meropenem (80%) and significant resistance to azithromycin (85.7%), ceftriaxone (80%), cefotaxime (80%) cefuroxime (76.9%), and ciprofloxacin (66.7%).

Limitations of the study were single center study with a small sample and lack of follow up whether sputum isolated pathogen was chronically colonized in the airway or it was truly an infectious cause for acute exacerbation of bronchiectasis.

CONCLUSION

Our study revealed that *Pseudomonas aeruginosa* was predominant in the upper and middle lobes and *Klebsiella pneumoniae* in the lower lobe. The right middle lobe, lower lobe, and left lower lobe had more tendencies to develop bronchiectasis. *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* were highly sensitive to colistin and amikacin but significantly resistant to azithromycin and cephalosporins.

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