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Original Article

Antibiogram of Sputum Collected from Patients with Acute Exacerbation of Asthma

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Abstract

Background: *Despite optimal guideline-directed treatment and irrespective of underlying disease severity, patients with asthma experience exacerbations due to variety of reasons including infections. Exacerbations continue to occur and impose considerable morbidity and mortality on patients and constitute a significant burden on healthcare resources. This study aimed to assess bacterial etiology in acute exacerbation of asthma and their antibiotic resistance pattern isolated from sputum samples.*

Materials and methods: *A cross-sectional study was conducted from September 2018 to February 2019, including 70 patients with acute exacerbation asthma from the Department of Medicine of Chittagong Medical College Hospital. Sputum samples were collected from the patients and analyzed by Gram staining, microscopy and culture.*

Results: *Sputum culture positivity was observed in 18 cases (25.7%) and all of them were gram negative bacteria. E. coli was the most common organism isolated (44.4%), followed by Klebsiella (33.3%) and Pseudomonas (22.2%). Isolated bacteria were resistant to Ceftriaxone, Ceftazidime, Doxycycline and Tetracycline while sensitive to amikacin, ciprofloxacin, meropenem, and colistin. Patients with positive culture were older than their counterparts (51.22±7.29 vs. 40.00±13.35, p=0.001). Smoking status, presence of comorbidities and steroid use had no association with culture positivity.*

Conclusion: *Sputum culture and sensitivity testing can be rational in patients with acute exacerbation of asthma to know its role in exacerbation as well as to know the antibiotic sensitivity as regularly used antibiotics were found resistant in most isolates.*

Key words: Asthma; Culture; Exacerbation; Sputum.

INTRODUCTION

Asthma is a significant global health issue affecting millions of people worldwide resulted in the loss of about 21.6 million Disability-Adjusted Life Years in 2019.[1] Limited epidemiological data on recent asthma prevalence in Bangladesh are available, however, between 1999 and 2010, the prevalence was around 7%.[2,3] In 2020, Bangladesh reported approximately 8893 asthma-related deaths among an estimated 7million affected individuals, underscoring asthma as a significant public health concern in the country and globally.[4,5]

Asthma exacerbations are a major cause of disease morbidity, increases in health care costs, and in some patients, a greater progressive loss of lung function.[6] The frequency of exacerbations can be reduced, but not always fully prevented, with adequate inhaled corticosteroid (ICS) treatment or combination ICS/Long-Acting β-Agonists (LABA).[7] Because asthma exacerbations can break through standard treatment regimens, identifying at-risk patients and having a plan of management can improve disease control and patient well-being.

Usually viral infections are common triggers for acute exacerbations of bronchial asthma. As a result, the routine use of antibiotics is not recommended unless there is clear evidence of a bacterial infection. Most asthma exacerbations are caused by viral infections, such as rhinovirus, Respiratory Syncytial Virus (RSV) and influenza.[8,9] Current guidelines generally advise against the routine use of antibiotics for asthma exacerbations to avoid over prescription and the development of antibiotic resistance.[10]

Antibiotic prescription practices in Low- and Middle-Income Countries (LMICs) show a high prevalence of antibiotic use, even in conditions where they may not be necessary including asthma.[11] This study aimed to determine the associations between bacterial infections and adult asthma exacerbations, together with detection of antibiotic resistance patterns in our clinical practice.

MATERIALS AND METHODS

A cross-sectional study was conducted in the Department of Medicine of Chittagong Medical College Hospital from September 2018 to February 2019. The Ethical Review Committee of Chittagong Medical College approved this study. Oral and written informed consent was obtained from each participant.

Patients who had a clinical diagnosis of asthma supported by one or more other characteristics including variability in peak expiratory flow of more than 20%, airway reversibility by inhaled β2 agonist and recurrent dyspnea episodes with wheezing, ages 18 and above were included in this study.[12] Assessment of asthma severity was performed according to previously published criteria.[13] The exclusion criteria were critically sick patients for whom spirometry could not be performed and who did not provide written consent for the study. Other exclusion criteria were pregnant ladies, patients with severe psychiatric disease and patients who could not produce induced sputum and who received antibiotics before hospitalization.

A spontaneous or provoked sputum sample was obtained and sent promptly for culture and sensitivity. Two weeks after hospital discharge, spirometry was performed, presuming acute aggravation had subsided. The data of patients whose diagnoses were verified by spirometry and reversibility tests were analyzed.

The computer program SPSS (Statistical Package for Social Sciences) version 23.0 was used to process and look at the data. The mean (Standard deviation) and median (Interquartile range) were used to describe the quantitative data, and the frequency and percentage were used for the qualitative data. A chi-square test was used to examine discrete or qualitative variables, and an independent sample t-test and Mann-Whitney U test was used to examine continuous variables. A p-value of <0.05 was considered statistically significant.

RESULTS

The study included 70 patients with a mean age of 42.89±13.01 years (Range: 18-69 years). More than half of them (54.3 percent) came from rural areas. Patients with a family income of more than 15000 BDT per month numbered only six (0.86%). Most of them had at least an elementary or secondary education, although not all of them (Table I).

Table I Sociodemographic chracteristics of the patients (n=70)

Variables	Frequency	Percentage (%)
Sex		
Male	32	45.7
Female		
Residence	38	54.3
Urban and semi-urban	32	45.7
Rural		
Occupation	38	54.3
Service	11	15.7
Business	4	5.7
Student	8	11.4
Housewife	35	50.0
Farmer	11	15.7
Others	1	1.4
Monthly income		
<5000 BDT	28	40.0
5000-10000BDT	24	34.3
10000-15000 BDT	12	17.1
>15000 BDT		
Education	6	8.6
Primary	47	67.1
Secondary	16	22.9
Higher secondary	4	5.7
Degree and above	3	4.3

Different clinical characteristics are shown in Table II. More than half of the patients (64.3%) had an asthma exacerbation in the past. The most common symptom, breathlessness, was reported by 70 (100%) patients, followed by cough by 66 (94.3%) patients, chest tightness by 43 (61.4%) patients, and wheezing by 28 (40%) patients. In addition, 53 individuals (75.7%) had sputum production. Patients had symptoms present for a significant duration, ranging from hours to ten days before admission. The cough lasted an average of 36 hours, whereas the other symptoms lasted 72 hours. Most patients (90 percent) were receiving inhaled short-acting 2-agonists. Oral corticosteroids were being used by more than half of the patients (52.9%).

Table II Clinical characteristics of the patients (n=70)

Characteristics	Frequency	Percentage (%)
Family history of asthma	27	38.6
Family history of allergy	51	72.9
Smoking	27	38.6
Co-morbidity	17	24.3
H/O Previous exacerbation	45	64.3
Presenting symptoms		
Breathlessness	70	100.0
Cough	66	94.3
Sputum production	53	75.7
Chest tightness	43	61.4
Wheeze	28	40.0
Medication use		
LABA inhaler		90.0
SABA inhaler	37	52.9

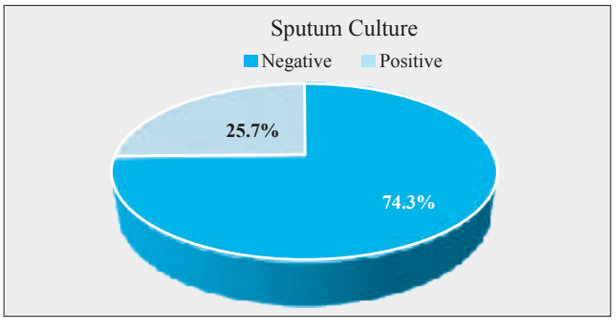

Figure 1 Sputum culture results (n=70)

Sputum culture was positive in 18 patients (25.7%) (Figure 1) all of which were gram-negative bacilli.

Table III Pattern of organisms in sputum culture (n=18)

Name of bacteria	Frequency	Percentage (%)
Escherichia coli	8	44.4
Klebsiella species	6	33.3
Pseudomonas species	4	22.2

Among the 18 patients who had positive sputum culture, the most frequently isolated organism was E. coli, identified in 8 cases, accounting for 44.4% of the isolates. Klebsiella species were found in 6 cases (33.3%), while Pseudomonas species were isolated in 4 cases (22.2%) (Table III). Among the 8 isolated E. coli strains, 100% were sensitive to Amikacin and Piperacillin, followed by high sensitivity to Ciprofloxacin and Colistin (87.5%). Moderate sensitivity was observed to Imipenem (62.5%) Meropenem (37.5%) Nitrofurantoin (50.0%) and Linezolid (50.0%). Sensitivity to other antibiotics such as Co-amoxiclav, Azithromycin, Cefuroxime and Gentamycin ranged between 12.5% and 25.0%, while no sensitivity was observed to Ceftriaxone, Ceftazidime, Cefotaxime, Cefpirome, Cloxacillin, Doxycycline, or Tetracycline (Table IV).

Table IV Sensitivity of the isolated E. coli (n=8)

Antibiotic	Frequency	Percentage (%)
Co-amoxiclav	1	16.7
Amikacin	8	100.0
Azithromycin	1	16.7
Cefuroxime	1	16.7
Ceftriaxone	0	0.0
Ceftazidime	0	0.0
Cefixime	1	12.5
Cefotaxime	0	0.0
Cefepime	1	12.5
Cefpirome	0	0.0
Ciprofloxacin	7	87.5
Cloxacillin	0	0.0
Levofloxacin	1	12.5
Cotrimazole	2	25.0
Doxycycline	0	0.0
Tetracycline	0	0.0
Gentamycin	2	25.0
Imipenem	5	62.5
Meropenem	3	37.5
Nitrofurantoin	4	50.0
Colistin	7	87.5
Piperacillin	8	100.0
Chloramphenicol	1	12.5
Linezolid	4	50.0

Among the 6 isolated Klebsiella species, all (100%) were sensitive to Colistin and Piperacillin, while high sensitivity was observed to Amikacin (83.3%) Ciprofloxacin, Meropenem and Nitrofurantoin (Each 66.7%). Moderate sensitivity was noted for Linezolid (50%) and several antibiotics including Co-amoxiclav, Azithromycin, Levofloxacin and Cotrimazole (each 33.3%). Minimal sensitivity (16.7%) was found for Cefepime, Cefpirome, Gentamycin and Imipenem, whereas no sensitivity was observed to Cefuroxime, Ceftriaxone, Ceftazidime, Cefixime, Cefotaxime, Cloxacillin, Doxycycline, Tetracycline and Chloramphenicol (Table V).

Table V Sensitivity of the isolated Klebsiella species (n=6)

Antibiotic	Frequency	Percentage (%)
Co-amoxiclav	2	33.3
Amikacin	5	83.3
Azithromycin	2	33.3
Cefuroxime	0	0.0
Ceftriaxone	0	0.0
Ceftazidime	0	0.0
Cefixime	0	0.0
Cefotaxime	0	0.0
Cefepime	1	16.7
Cefpirome	1	16.7
Ciprofloxacin	4	66.7

Antibiotic	Frequency	Percentage (%)
Cloxacillin	0	0.0
Levofloxacin	2	33.3
Cotrimazole	2	33.3
Doxycycline	0	0.0
Tetracycline	0	0.0
Gentamycin	1	16.7
Imipenem	1	16.7
Meropenem	4	66.7
Nitrofurantoin	4	66.7
Colistin	6	100.0
Piperacillin	6	100.0
Chloramphenicol	0	0.0
Linezolid	3	50.0

Among the 4 isolated Pseudomonas species, all (100%) were sensitive to Meropenem and Colistin, while high sensitivity was observed to Ciprofloxacin (75%) and moderate sensitivity to Amikacin (50%). Limited sensitivity (25%) was seen with Ceftazidime, Imipenem and Piperacillin. No sensitivity was observed to the remaining antibiotics, including Co-amoxiclav, Azithromycin, cephalosporins, Gentamycin, Levofloxacin, and others (Table VI).

Table VI Sensitivity of the isolated Pseudomonas species (n=4)

Antibiotic	Frequency	Percentage (%)
Co-amoxiclav	0	0.0
Amikacin	2	50.0
Azithromycin	0	0.0
Cefuroxime	0	0.0
Ceftriaxone	0	0.0
Ceftazidime	1	25.0
Cefixime	0	0.0
Cefotaxime	0	0.0
Cefepime	0	0.0
Cefpirome	0	0.0
Ciprofloxacin	3	75.0
Cloxacillin	0	0.0
Levofloxacin	0	0.0
Cotrimazole	0	0.0
Doxycycline	0	0.0
Tetracycline	0	0.0
Gentamycin	0	0.0
Imipenem	1	25.0
Meropenem	4	100.0
Nitrofurantoin	0	0.0
Colistin	4	100.0
Piperacillin	1	25.0
Chloramphenicol	0	0.0
Linezolid	0	0.0

Patients whose sputum cultures showed growth were much older than those whose cultures showed no growth (p=0.001). There was no significant difference in the culture positivity rate between smokers and non-smokers. Similarly, positive sputum culture was found to have no significant association with the presence of comorbidities. The culture positivity rate was similar among oral steroid users and non-users, and the duration of oral steroid administration was similar between the two groups (Table VII).

Table VII Association of demographic and clinical characteristics with sputum culture positivity

Characteristics	Sputum culture results		
	Positive (n=18)	Negative (n=52)	p value
Age, years	51.22±7.29	40.00±13.35	0.001†
Gender			
Male	7 (38.9)	25 (48.1)	0.589*
Female	11 (61.1)	27 (51.9)	
Residence			
Urban and semiurban	5 (27.8)	27 (51.9)	0.076*
Rural	13 (72.2)	25 (48.1)	
Smoking			
Yes	11 (61.1)	32 (61.5)	0.974*
No	7 (38.9)	20 (38.5)	
Comorbidity			
Present	13 (72.2)	13 (25.0)	0.951*
Absent	5 (27.8)	39 (75.0)	
Oral steroid use			
Yes	11 (61.1)	26 (50.0)	0.419*
No	7 (38.9)	26 (50.0)	
Duration of steroid use, years	1.50 (0.50-3.00)	1.50 (0.50-3.50)	0.896‡

Data were expressed as mean ±SD, n (%) or median (IQR). †Independet sample t test, *Chi- square test, ‡Mann-Whitney U test.

DISCUSSION

The study included 70 asthmatic patients with a mean age of 42.89±13.01 years. Similar data from the NIS National Asthma Education and Prevention Guidelines demonstrates that all age groups experienced hospitalization at similar rates,with 35–54 years representing

31.7 percent of admissions for asthma exacerbation.[14] The average age of all participants in the Asthma Insights and Reality in Asia-Pacific (AIRIAP) study was 31.4 years old, with ages ranging from 22.8 (In the Philippines) to43.9 (in China).[15] There were 45.7% male and 54.3% female patients in the present study. Like our study, the previously cited study had a female majority. Female patients comprised 51.5% in China, 36.8% in Hong Kong, 59.1%in Korea, and 57.5% in Vietnam, according to the AIRIAP study.[15]

Only 6 (8.6%) patients had a monthly family income of more than 15000 BDT, most had either an elementary or secondary education, which might not reflect the actual scenario as the present study was conducted in a public tertiary-level hospital. However, as previously stated, the prevalence of asthma attacks in the 2002 Bangladesh National Survey was significantly greater among lower-income social classes, such as the population containing 'deficient' and illiterate groups. These findings have been published in agreement with research conducted in New York City, where rates of Asthma hospitalizations were generally more excellent in the poor, unemployed, and illiterate groups.[16] A family history of asthma and allergy was present in 38.6% and 72.9% of the patients, respectively, which are known risk factors for asthma.[17]

Exacerbations are responsible for much of the mortality, morbidity and expense of asthma.[6,7] Our data showed that acute exacerbation of asthma was associated with infection in 25.7%. Study highlighted that both viral and bacterial agents can be present, with bacterial co- infections worsening the prognosis in hospitalized asthma patients with acute exacerbation.[8] However, the culture positivity rates for bacterial isolates in asthma patients varied widely (32%- 78%) in previous studies.[18,19]

In the present study, all of the bacterial isolates were gram-negative bacilli and E.coli was the commonest organisms (44.4%) followed by Klebsiella (33.3%) and Pseudomonas (22.2%). Previous study findings were inconsistent regarding the types of bacterial isolates in asthma patients. Gram-negative bacilli growth was seen in majority of the patients in the study of Nagaraja et al.[18] In contrast, S. pneumoniae was the most commonly isolated bacteria in the study of Ahmed et al and Iikura et al.[19,20] Differences in sample size, selection criteria and study populations can lead to varying results. Moreover, variations in diagnostic criteria and laboratory methods used to identify bacterial infections can result in different reported prevalences.

In our study, we examined the susceptibility of various bacterial strains to various antibiotics.

E. coli were particularly sensitive to Amikacin, Ciprofloxacin, Meropenem, Colistin and Piperacillin but resistant to Ceftriaxone, Ceftazidime, Cefotaxime, Cloxacillin, Doxycycline and Tetracycline. Klebsiella was most sensitive to Amikacin, Ciprofloxacin, Nitrofurantoin, Meropenem, Colistin and Piperacillin. Al lof them were resistant to Cefuroxime, Ceftriaxone, Ceftazidime, Cefotaxime, Cloxacillin, Tetracycline and Chloramphenicol. In our study, Meropenem, Ceftriaxone and Gentamicin were the most active antibacterial agents. More studies are required to be conducted on antibiotic susceptibility pattern at regular interval to formulate the antibiotic policy for improvement in patients conditions.

Patients with positive cultures were significantly older than those with negative cultures. Similarly, Zhang et al. discovered that patients with a positive culture tend to be older.[21] Similar to the preponderance of females in the study group, positive bacterial growth in sputum cultures was more prevalent in females than in males, but the difference was not statistically significant. The same was true for urban and rural connectedness. While the proportion of rural patients with a positive sputum culture was higher, the comparison between the subgroups was not statistically significant. Smokers and nonsmokers had similar ratesofculturepositivity. In one systematic review, it was found that smokers are more likely to get bacterial pneumonia than former smokers or non-smoker.[22] Recently, Losol et al. reported that the genera Corynebacterium, Propionibacterium, Streptococcus, Haemophilus, and Rothia were correlated with smoking exposure in adult asthmatics.[23] Culture positivity rate was similar among those who used oral steroids and those who did not use them. The duration of oral steroid use did not make a significant difference either, which agreed with previous study.[21]

LIMITATIONS

The present study's sample size was small and selected from a single tertiary- level public hospital. Therefore, this will not reflect the country as a whole. Numerous atypical bacteria could not be cultured because they require uncommon cell culture media.

CONCLUSION

Bacterial isolates were not common in the sputum of asthma patients admitted with acute exacerbation. Gram-negative organisms were found in positive cultures. Older age was found to be associated with positive sputum culture. There is no correlation between culture positivity and oral or inhaled steroid use.The routine use of antibiotics in hospitalized patients with acute asthma exacerbation is not rational. More research incorporating the isolation of atypical bacteria and anaerobes is recommended to fulfill best management.

DISCLOSURE

All the authors declared no competing interest.

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