A COMPARATIVE STUDY OF CLINICAL CHARACTERISTICS AND BACTERIOLOGICAL SENSITIVITY PATTERN OF SPUTUM IN ACUTE EXACERBATIONS OF COPD

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ABSTRACT

BACKGROUND

Chronic Obstructive Pulmonary Disease (COPD) is an important cause of disability and death globally and scenario has worsened. Acute Exacerbation of COPD (AECOPD) is associated with airway inflammation resulting in increased air trapping, further obstruction of airways and deterioration of gas diffusion. We wanted to determine the bacteriological pathogens causing acute exacerbation of COPD and their microbial sensitivity pattern.

METHODS

This is a cross sectional study comprising of 103 patients diagnosed with AECOPD. Before starting antibiotics, sputum samples of all patients were sent for culture and sensitivity.

RESULTS

Out of a total of 103 cases, 67% were males and 33% were females. *Streptococcus pneumoniae* was the commonest bacterium isolated (32.6%) followed by *Klebsiella* species (18.6%) and *E. coli* (16.3%). Highest sensitivity was found to be of Colistin and Polymyxin-B (100.0%) followed by carbapenems (86.0%) and Amikacin (74.4%) while the highest resistance patterns was of Azithromycin (32.6%) followed by Oxacillin (65.1%) and Tobramycin (62.8%).

CONCLUSIONS

AECOPD is more common in adult males above the age of fifty-five years secondary to smoking practices. There were no statistically significant correlation of age group, gender and smokers with positive sputum culture. Out of 103 patients, 41.7% had positive sputum culture and rest 58.3% had negative sputum culture report. Antimicrobials effective against gram-positive bacteria were Amikacin, Moxifloxacin, Carbapenems, Colistin and Polymyxin-B and therefore, the drugs of choice in treating AECOPD in our setting.

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BACKGROUND

Chronic Obstructive Pulmonary Disease (COPD) is defined as a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway or alveolar abnormalities usually caused by significant exposure to noxious particle and gases.¹ COPD is a spectrum of airway diseases, on the one end of which is chronic bronchitis while the other end belongs to emphysema. In the reality, majority of patients have both the components.²

COPD is a major cause of morbidity and mortality which varies across countries. In the United States of America alone, approximately 24 million people suffer with COPD and have emerged as the third leading cause of death.³ COPD is the fourth leading cause of death in the world and it is expected to be the third leading cause of death worldwide by 2020.⁴

Acute exacerbation of COPD (AECOPD) is defined as a sustained worsening of the patient's condition, from the stable state and beyond normal day-to-day variations, that is acute in onset and necessitates a change in regular medication in a patient with underlying COPD.⁵ Frequent exacerbations are associated with an accelerated decline of lung function, reduced physical activity,^{6,7} poorer quality of life, and an increased risk for mortality. To diagnose the patients and grade the severity of acute exacerbation of COPD, clinical guidelines have included the, Winnipeg criteria⁸ based on increased breathlessness, sputum volume and purulence.

Type of Exacerbations	Criteria
Type 1	All the 3 symptoms described above.
Type 2	Any 2 of the above symptoms.
Type 3	Any 1 of the above plus at least 1 of the following: Upper respiratory tract infection lasting ≥ 5 days, fever, increase in wheezes, increase in cough, and increase in heart rate 20%.
The Winnipeg Criteria	

Infections are the most common cause of AECOPD, three classes of pathogens have been implicated as a cause of COPD exacerbation: respiratory viruses, atypical bacteria, aerobic gram positive and gram-negative bacteria. Approximately

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50% of COPD acute exacerbations are associated with the bacteria from lower respiratory tract.^{9,10} The dominant bacteria isolated are *H. influenzae*, *S. pneumoniae* and *M. catarrhalis*. In advanced cases, *P. aeruginosa* becomes prevalent.¹⁰

It has been observed that use of antibiotics used to treat AECOPD has an impact on the failure rate.¹¹ More than 90% of patients with AECOPD are treated with antibiotics, due to emergence of resistant strains of most common respiratory pathogens, effectiveness of many is uncertain in past 15 years.¹² Exacerbations may also contribute to irreversible progression of COPD.¹³

Now a days, investigators need culture studies for proper selection of antibiotics, but it is time consuming process and the facility is not available in most of the institutions. The choice of the antibiotic should be based on the local bacterial resistance pattern.¹⁴

In view of very limited data about bacteriological profile in AECOPD patients in India, the present study was undertaken to identify the common aerobic bacterial agents responsible for COPD exacerbation and to study the antibiotic sensitivity pattern of isolates. Moreover, clinical and haematological profile of the patients was correlated with the bacterial growth in sputum to analyse whether these parameters can give a hint of bacterial infection prior to availability of culture reports.

METHODS

The present study was initiated in the Department of Respiratory Medicine after the approval of the Ethical Clearance Committee of the SRMS Institute of Medical Sciences, Bareilly, U. P. It is a cross sectional study conducted for a period of one year from May 2017 to April 2018.

Inclusion Criteria

1. All patients above 40 years of age with or without smoking history.
2. Patients who are diagnosed to have Chronic bronchitis (Presence of cough and sputum production for at least 3 months in each of two consecutive years), now presenting with increased sputum quantity, purulence and dyspnoea with or without fever and leukocytosis.

Exclusion Criteria

1. Patients who are already on antibiotic treatment.
2. Patients who had evidence of bronchiectasis on a chest radiograph-PA view.
3. Patients with pulmonary tuberculosis on antitubercular medications.
4. Patients with restrictive lung disease.
5. Patients with lung malignancy.

After taking consent form from all eligible patients' details about age, gender, smoking history or exposure to indoor smoke, vitals including SPO₂ and blood pressure (BP) at presentation and nature of sputum were recorded on prescribed proforma. All patients were subjected to detailed history and both general and systemic examination. After clinical examination all patients underwent a chest radiography, complete blood counts, differential blood counts, oxygen saturation by pulse oximetry.

Sputum Specimen Collection

Before starting on antibiotics all patients' sputum was sent for culture and sensitivity. All patients were instructed to collect early morning, deep coughed sputum into a sterile sputum container (Preferably two), thick, mucoid, purulent sputum was considered valid by microbiology department. Patients were asked to rinse the mouth with tap water. Samples were sending to laboratory after being labelled and numbered.

Specimens were transported and processed within two hours in the Department of Microbiology of our institute. Sputum samples were examined for physical appearance, gram stain, acid fast bacilli smear, pyogenic culture for bacterial organism and drug sensitivity testing.

Statistical Analysis

The collected data was analyzed using the statistical package SPSS (Statistical Package for Social Sciences) version 16.0 for Windows. Chi square tests of significance were carried out to test the association between proportions. Association between variables was considered statistically significant if *p*-value was <0.05.

RESULTS

A total of 103 patients fulfilling the inclusion and exclusion criteria were included in the present study, with 69 (67%) males and 34 (33%) females. In terms of age, the study group belonged to a wide range from 40 years to >80 years with maximum patients (41.7%) belonging to the age group of 50–60 years followed by 60–70 years (29.1%) and 40–50 years (14.6%). Majority of patients belonged to rural areas (86.4%).

History of smoking was present in 86.4% (*n* = 139) of patients in our study. Majority of patients (37.9%) gave a pack year history of ≤50 followed closely by pack years of 51–75 in 30.1% patients and 76–100 in 22.3% patients. While smoking history was more prevalent in male patients, exposure to household biomass fuel smoke was prevalent in females. Table 1 depicts the general profile of the patients along with the sputum culture bacterial growth positivity.

Out of 103 patients, sputum culture revealed positive bacterial growth in 43 cases (41.7%). As depicted in Table 1, culture positivity was maximum (32%) in the age group of 51–60 years, followed closely and equally by age group 61–70 and 41–50 years. However, the comparison between age groups was found to be statistically insignificant (*p*>0.05) in all age groups. Just like the male preponderance in the study group, positive bacterial growth in sputum culture was preponderant in males (67%) as compared to females (33%) but statistically insignificant (*p* = 0.421). Similar was the case with urban and rural belonging, smoking status of patients and pack years history. While sputum culture positivity was higher in patients belonging to rural areas with positive smoking history and pack year history of <50 and >75, the comparison between the subgroups was found to be statistically insignificant (*p*>0.05).

Out of the 43 case of AECOPD where sputum culture revealed growth of a bacterial organism, *Streptococcus pneumoniae* was the most common (32.6%) organism isolated. *H. influenzae* and *M. catarrhalis* were isolated in 4.7% cases each.

Age Group (Years)	Frequency (n=103)	Percent	Culture Positive Case (n=43)	Percent	P Value
41-50	15	14.6	10	23.4	0.295
51-60	43	41.7	13	30.2	0.217
61-70	30	29.1	11	25.6	0.743
71-80	12	11.7	6	13.9	0.708
>80	3	2.9	3	6.9	0.262
Gender					
Male	69	67	31	74.4	0.421
Female	34	33	11	25.6	
Demographics					
Rural	89	86.4	38	88.4	0.748
Urban	14	13.6	5	11.6	
Smoking					
Yes	89	86.4	39	90.5	0.472
No	14	13.6	4	9.5	
Pack Years					
≤50	39	37.9	13	30.2	0.380
51-75	31	30.1	15	34.9	0.570
76-100	23	22.3	11	25.6	0.671
>100	10	9.7	4	9.3	0.938
Table 1. General Characteristics Correlation with Sputum Culture Positivity					

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Organism	Frequency (n=43)	Percentage
Acinetobacter calcoaceticus	5	11.6
Klebsiella pneumonia and Klebsiella oxytoca	8	18.6
Pseudomonas aeruginosa	5	11.6
E. coli	7	16.3
Streptococcus pneumoniae	14	32.6
H. influenzae	2	4.7
M. catarrhalis	2	4.7

Table 2. Distribution of Various Bacterial Organisms Isolated

	Acinetob.	Klebsiella Species	P. aerug.	E. coli	Strept. Pneumo.	H. influenz.	M. catarr
Amikacin	1 (20.0)	5 (62.5)	4 (80.0)	4 (57.1)	14 (100.0)	2 (100.0)	2 (100.0)
Levofloxacin	1 (20.0)	5 (62.5)	3 (60.0)	2 (28.6)	12 (85.7)	2 (100.0)	2 (100.0)
Amoxy-clavulanic acid	1 (20.0)	1 (12.5)	2 (40.0)	0 (0.0)	13 (92.9)	2 (100.0)	2 (100.0)
Moxifloxacin	2 (40.0)	5 (62.5)	4 (80.0)	1 (28.6)	14 (100.0)	2 (100.0)	2 (100.0)
Piperacillin-Tazobactam	2 (40.0)	5 (62.5)	3 (60.0)	4 (57.1)	11 (84.6)	2 (100.0)	1 (50.0)
Cephalosporin	2 (40.0)	3 (37.5)	2 (40.0)	1 (57.1)	11 (78.6)	1 (50.0)	2 (100.0)
Carbapenems	5 (100.0)	8 (100.0)	5 (100.0)	7 (100.0)	14 (100.0)	2 (100.0)	2 (100.0)
Colistin and Polymyxin-B	5 (100.0)	8 (100.0)	5 (100.0)	7 (100.0)	14 (100.0)	2 (100.0)	2 (100.0)
Oxacillin	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	13 (92.6)	1 (50.0)	1 (50.0)
Ofloxacin	1 (20.0)	4 (50.0)	2 (40.0)	5 (71.4)	11 (78.6)	2 (100.0)	1 (50.0)
Ciprofloxacin	0 (0.0)	7 (87.5)	3 (60.0)	4 (57.1)	10 (71.4)	2 (100.0)	1 (50.0)
Gentamicin	3 (60.0)	4 (50.0)	3 (60.0)	4 (57.1)	14 (100.0)	1 (50.0)	1 (50.0)
Tobramycin	1 (20.0)	4 (50.0)	4 (80.0)	4 (57.1)	0 (0.0)	2 (100.0)	0 (0.0)
Azithromycin	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	11 (78.6)	1 (50.0)	1 (50.0)
Clindamycin	2 (40.0)	0 (0.0)	0 (0.0)	0 (0.0)	13 (92.6)	0 (0.0)	1 (50.0)
Vancomycin	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	14 (100.0)	2 (100.0)	2 (100.0)

Table 3. Sensitivity and Resistance Pattern of Etiological Bacterial Organisms to Antibiotics

Collectively, Gram Negative Bacteria (GNB) were the predominant etiological agent responsible for AECOPD in 58.1% patients. Among GNB, E. coli (16.3%) was the most common isolated organism followed by Klebsiella (18.6%). Acinetobacter and P. aeruginosa were isolated in 11.6% cases each as depicted in Table 2.

Antibiogram of isolated organisms revealed that usual organisms considered responsible for AECOPD, like S. pneumoniae, H. Influenzae and M. catarrhalis, were sensitive to commonly used antibiotics fluoroquinolones, cephalosporin, amino glycoside and Piperacillin-tazobactam. However, GNB showed significant resistance to the above antibiotic groups. Colistin and Polymyxin-B were the only effective antibiotics against all the isolated organisms. Table 3 depicts the sensitivity and resistance pattern of various organisms isolated in sputum culture to antibiotics.

Among gram negative organisms, E. coli which was the most common isolate were mainly sensitive to carbapenems, colistin and Polymyxin-b, all showing 100% sensitivity followed by ofloxacin, Piperacillin-tazobactam, Aminoglycosides, Ciprofloxacin, Gentamycin and Tobramycin all of them having the same sensitivity of 57.1%. E. coli were found to be significantly resistant to levofloxacin and moxifloxacin with sensitivity of 28.6 for both. Acinetobacter species were sensitive to mainly carbapenems, colistin and polymyxin-b with significant in vitro resistance to fluoroquinolones, cephalosporin and Piperacillin-tazobactam. Streptococcus Pneumoniae showed >70% sensitivity to all antibiotics except tobramycin. Poorest association was of Oxacillin, Clindamycin and Vancomycin antibiotics as these have shown 0.0% association with majority of the organisms.

DISCUSSION

COPD is a leading cause of mortality and morbidity both immediate and long term. Episodes of exacerbation add to the burden of the disease and are major reason for healthcare utilization including hospitalizations and intensive care admissions. Most exacerbations are associated with infective triggers, either viral or bacterial, although non infective triggers like air pollution may also be important.

The maximum number of cases in our study belonged to the age group of 51–60 years which can be explained by the fact that chronic bronchitis has maximum prevalence in the same age group.¹⁵

Sputum culture was positive in 41.7% of patients who presented with AECOPD. Similar frequency of bacterial isolation in sputum of patients of AECOPD has been reported in several Indian and foreign based studies.^{16,17,18} In our study Streptococcus pneumoniae (32.6%) was found to be still the most common sole bacterial agent responsible for COPD exacerbations followed by Klebsiella species isolated at in 18.6% of the cases. The least observed bacterial organism was H. influenza and M. catarrhalis causing complications in 4.7% of study patients each. This finding was similar to study Sharma P et al¹⁹ reported sputum culture was positive in 48.7% of patients who presented with AECOPD. In his study, Streptococcus pneumoniae was the most common (13%) organism isolated. H. influenzae and M. catarrhalis were isolated in 2% cases each.

In our study, Colistin and Polymyxin-B antibiotics had 100% sensitivity followed by carbapenems (86%), Amikacin (74.4%), Moxifloxacin (69.8%), levofloxacin (62.8%), Ciprofloxacin (62.8%), Piperacillin-tazobactam (62.8%) and the least was in Azithromycin (32.6%). It was also found that antibiotics Carbapenems, Colistin and Polymyxin-B were most effective against all bacterial organism found in this study with 100% of sensitivity. Moxifloxacin antibiotic also had highly significant sensitivity ranges-40% to 100% against various bacterial organisms. Moreover, Amikacin, levofloxacin, Piperacillin-tazobactam are also observed to be potentially higher sensitivity against bacteria organism with varying sensitivities.

CONCLUSIONS

Acute Exacerbation of COPD is associated with bacterial infections, profile of which varies in various geographical areas. Sputum culture is a good and simple diagnostic tool to study the aetiology due to bacteria in AECOPD. Antibigram helps in the correct treatment protocol during the management of AECOPD. It also helps in screening resistant pathogens and identifying the appropriate drug for treatment, thereby helping to reduce mortality and morbidity. In future, more elaborated studies are required, incorporating additional laboratory interpretations with personal, local socio-economical and epidemiological markers. Further, the interaction among different etiologic factors such as environment, bacteria, viruses and atypical pathogens should be better understood to treat exacerbations and develop novel as well as cost effective preventive and therapeutic strategies.

Limitations

1. Spontaneously expectorated sputum was analysed microbiologically in our study. Though sufficient efforts were taken to avoid upper airway contamination, accuracy can be increased by taking sample bronchoscopically.
2. Adequate past treatment history of patients was not available due to lack of records. It was necessary to evaluate the reason for such high antibiotic resistance pattern observed in our study.

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