

EPIDEMIOLOGICAL STUDY OF BACTERIAL MICROBIOLOGY IN AECOPD PATIENTS OF KOLKATA, INDIA

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Received: 15 October 2012, Revised and Accepted: 7 December 2012

ABSTRACT

The aim of our study is to analyze the hospital data on AECOPD in patients with special reference to the pathogens involved and their antibiotic susceptibility pattern of Kolkata, India. 50 patients were included in the study. The sputum specimen was collected using sterile sputum cups and subjected to Gram's stain, culture and biochemical reactions. Our study showed 21 positive sputum cultures and 76.20% were males and 23.80% were females. The prevalence of Gram negative bacteria was 71.42% and Gram positive bacteria were 28.58%. *Klebsiella pneumoniae* was the commonest bacteria isolated (33.33%) followed by *P. aeruginosa* (19.05%) and *Staphylococcus aureus* (14.30%). In a developing country like India AECOPD is more common in adults more than 55 years of age due to smoking habits and high indoor pollution. AECOPD cases are a major cause of hospital admission and health care utilization.

Keywords: AECOPD, Co-morbidities, Sputum, Antibiogram.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is associated with significant morbidity and mortality, with the World Health Organization estimating its rise from being the fifth to the third leading cause of death by 2030 ¹.

COPD is a slow and progressive disease, with patients experiencing episodes of acute deterioration known as exacerbations ², which increase in frequency and severity with disease progression. COPD is a chronic, slowly progressive disorder characterized by airways obstruction (FEV1/FVC ratio <70%) which does not change markedly over several months. One of the spectrums of COPD is chronic bronchitis, which is characterized by airway inflammation, mucus hyper secretion and airway reactivity. The spectrum emphysema, characterized by alveolar destruction and small airway abnormalities. Air trapping and hyperinflation are common at both ends of the spectrum. Most COPD patients have the both features ³.

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 ².

The causes of acute exacerbations of COPD (AE-COPD) are multifactorial. Half of the AECOPD cases are attributed to respiratory infections (50%), but exacerbations are also associated with pollution, temperature changes, allergens (30%), and other comorbidities (26%) such as heart failure and pulmonary thromboembolism ⁴. In several studies, the presence of bacteria in AECOPD has been associated with purulence of the sputum and the presence of inflammatory markers ^{5,6}.

Presenting Features of Acute Exacerbations

- Worsening of previously stable condition
- Increased sputum purulence
- Increased sputum volume
- Increased dyspnea
- Increased wheeze
- Chest tightness
- Fluid retention

Type of Exacerbations Criteria

Type 1 All the 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% ⁷.

Chronic obstructive pulmonary disease (COPD) is the most common respiratory disorder encountered in clinical practice. It constitutes 30% of cases seen in chest clinics and accounts for 1-2.5% admissions in hospitals all over India ⁸.

In 50%-70% of acute exacerbations of COPD, the pathophysiological basis is usually infectious. Acute exacerbation of COPD showed a hospital mortality rate of 24% if the patient required ICU admission. This mortality rate increased to 30% if the patient was above 65 years ⁹. Several lines of evidence now implicate bacteria as an important cause of exacerbation of AECOPD. Bronchoscopic sampling of the distal airways of the lung has demonstrated the presence of pathogenic bacteria in 50% of exacerbation. Acquisition of a new strain is associated with more than two-fold increase in the risk of exacerbation ¹⁰.

MATERIALS AND METHODS

We studied patients admitted with AECOPD over a period of three months. Patients with COPD were diagnosed as per the criteria of World Health Organization-Government of India (WHO-GOI) guidelines-2003 for the management COPD ¹¹.

Source of Data

All the patients of Acute Exacerbation of Chronic Obstructive Pulmonary disease admitted in different wards of different tertiary care hospitals including OPD departments in Kolkata, India. Out of 50 case of Acute Exacerbation of Chronic Obstructive Pulmonary disease, 21 patients were sputum culture positive and those were included in the study.

Variables included for the study were age, sex, smoking, signs and symptoms of the patient. The information regarding these variables was collected by using a pretested questionnaire.

Period of Study

Over a period of six months (Mar. 2012 to Aug. 2012)

Inclusion criteria for the case:

All clinically and spirometrically diagnosed Acute Exacerbation of Chronic Obstructive Pulmonary disease cases admitted in different tertiary care hospitals including OPD departments in Eastern India especially in Kolkata. Patients were diagnosed by the clinician concerned depending upon the presence of two of the following symptoms:

1. Increased cough
2. Increased purulence and/or volume of expectorations
3. Increased severity of dyspnoea.

Exclusion criteria for the case

- Bronchial Asthma/Lung Abscesses/Lung Cancer
- Subjects who were started Antibiotic Therapy 2-3 days before hospital admission
- Known case of Pulmonary Koch's
- Ischaemic Heart Disease.

Sample Collection

Sputum

Early morning samples were obtained from cases that were clinically diagnosed as acute exacerbation of chronic obstructive pulmonary disease. Patients were instructed to collect deep coughed sputum into a sterile wide mouth container with a screw cap.

The samples were brought to the Department of Microbiology of different tertiary care hospitals for analysis. Samples were labeled and numbered after their receipt in the laboratory and processed by conventional methods.

Sputum Culture

After collection and assessing the sputum, sample was sub cultured on following culture plates:

- 1) Blood agar - 5% sheep blood agar for isolation of hemolytic organisms.
- 2) Chocolate agar - For Haemophilus and Neisseria species.
- 3) MacConkey's agar - for isolation and differentiation of Gram negative bacilli

Identification of the Isolates

The primary isolation plates that are blood, chocolate and MacConkey's agar were first examined and a clear description of the colony growing on it was noted. A single well-separated colony was identified by Gram staining and biochemical tests.

Antibiogram

Antibiotic sensitivity tests of the isolates were performed on Mueller - Hinton agar plates by the disc diffusion method and also with the Minimum Inhibitory Concentration (MIC) in mcg/mL (E-strip) of different antibacterial agents against different bacteria. Sensitivity was performed using control strains of *Klebsiella pneumoniae* ATCC 700603, *Staphylococcus aureus* ATCC 25923, *E.coli* ATCC 25922, and *Pseudomonas* ATCC 27853.

Statistical Analysis

Candidate variables analysis was: age, sex, FEV1 as percent predicted, smoking habits, and bacteriological profile in sputum purulence and antibiotic sensitivity patterns. The co-morbidities were also assessed as per records.

RESULTS

Bacterial infections of AECOPD were analyzed. The individual bacterial isolates and

Age Distribution

The age group of the patient in the study, ranged from forty five to eighty five years. Out of twenty one (21) patients, the most common age groups were fifty five to sixty five and sixty five to seventy five years (33.33%). The next common age group was forty five to fifty five years (19.04%).

Sex Distribution

Out of twenty one (21) patients, clinically diagnosed as acute exacerbation of chronic obstructive pulmonary disease, sixteen (16)

(76.20%) were males and five (5)(23.80%) were females. The ratio between male and female is 3.2:1.

Co-Morbidities

Out of twenty one (21) patients, clinically diagnosed as acute exacerbation of Chronic obstructive pulmonary disease, they were associated with different co-morbidities like diabetes (9) (26%), coronary artery disease (8) (24%), hypertension (13) (38%) and depression (4) (12%).

Smoking Index

Out of twenty one (21) patients, eight (8) each were smoking and non-smoking patients and five (5) were ex-smokers. The percentages were 38.10% each and 23.80%. In smoking and ex-smoking groups all the patients were male

Spirometric Data

Out of twenty one (21) patients, there were ten (10) patients, whose COPD was detected with spirometer. According to spirometer protocol, there was not a single case of mild COPD, moderate and severe (4) each and 2 patients were of severe COPD in this study.

Bacteriological Profile

Out of twenty one (21) pathogenic bacteria isolated, fifteen (15) (71.42%) were Gram-negative bacteria and six (6) (28.58%) were Gram-positive bacteria (Table No.1 and Graph No.1). Out of twenty one (21) single pathogenic bacteria, *Klebsiella pneumoniae* was the commonest bacteria isolated, in seven (7) cases, followed by *Pseudomonas aeruginosa* in four (4) cases. Methicillin Resistant *Staphylococcus aureus* (MRSA) and *Staphylococcus aureus* isolated in three (3) and three (3) cases respectively. *Escherichia coli* and *Acinetobacter* spp., were isolated as two (2) and two (2) cases respectively. (Table No. 2 and Graph No.2)

Antibiotic Sensitivity Patterns of the Isolates

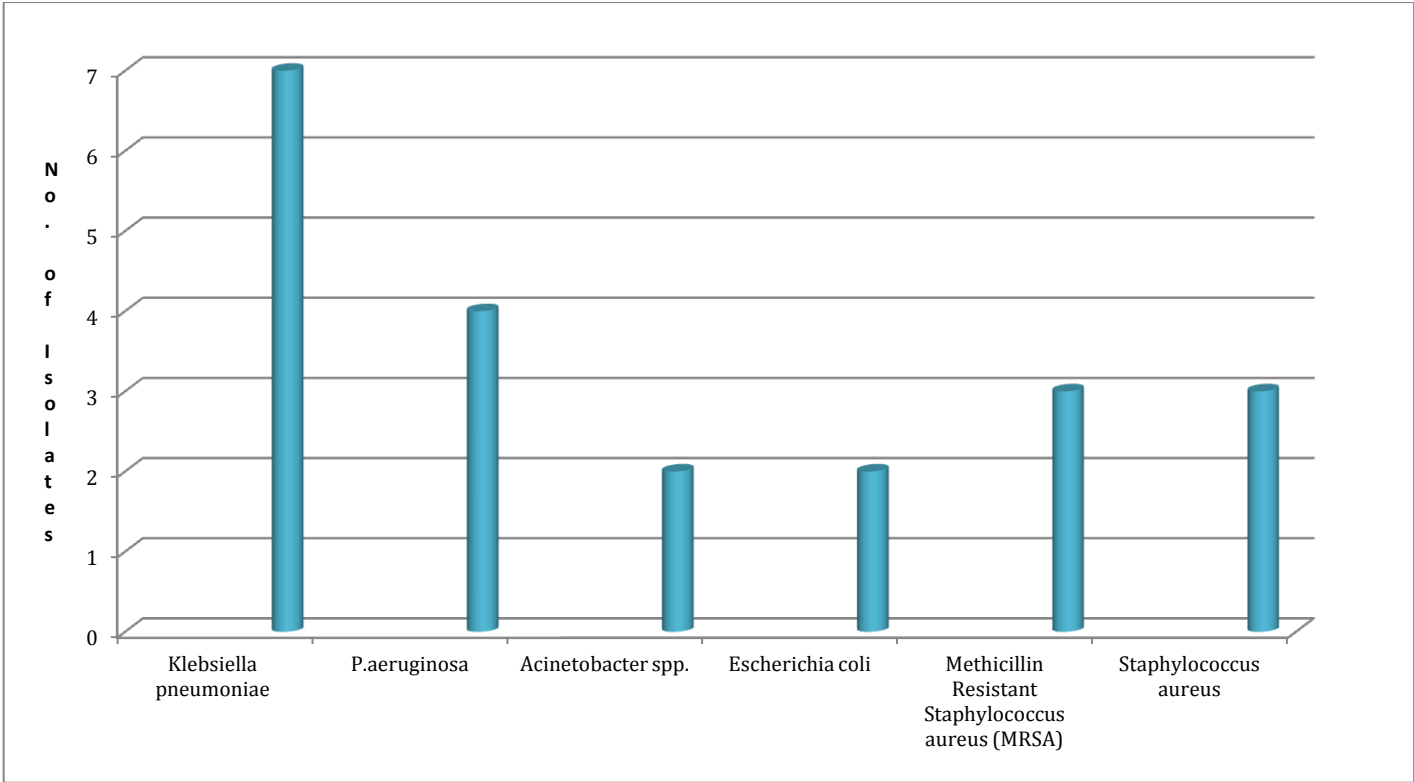
Klebsiella pneumoniae, which was the most common isolate, was sensitive to Amikacin, Meropenem, Imipenem and Cefoperazone-Sulbactam. *Staphylococcus aureus*, which was the prevalent Gram-positive isolate, were sensitive to Vancomycin, Piperacillin-Tazobactam, Azithromycin, Cefotaxime, Linezolid, Levofloxacin and Co-Trimoxazole. 50% of *Staphylococcus aureus* were Methicillin resistant (MRSA). *Pseudomonas aeruginosa* were mainly sensitive to Amikacin, Meropenem, Imipenem and Colistin. *Escherichia coli* were sensitive to Amikacin, Ciprofloxacin, Netilmicin, Ceftriaxone and Piperacillin-Tazobactam. (Table No.3, 4 and Graph No.3,4)

Table 1: Showing organism isolated from Sputum Culture

Sl No.	Name of the Organism	Number	Percentage
1.	<i>K. pneumoniae</i>	7	33.33%
2.	<i>P. aeruginosa</i>	4	19.05%
3.	<i>E. coli</i>	2	9.51%
4.	<i>Acinetobacter</i> spp.	2	9.51%
5.	<i>S. aureus</i>	3	14.30%
6.	MRSA	3	14.30%
Total		21	

Table 1 and Graph 1 describe the pattern of isolates. Out of 21, *Klebsiella pneumoniae* was the predominant organism isolated 33.33% (7/21), followed by *Pseudomonas aeruginosa* in 19.05% (4/21). Methicillin Resistant *Staphylococcus aureus* (MRSA) and *Staphylococcus aureus* isolated in 14.30% (3/21) respectively. *Escherichia coli* and *Acinetobacter* spp., were isolated as 9.51% (2/21) respectively.

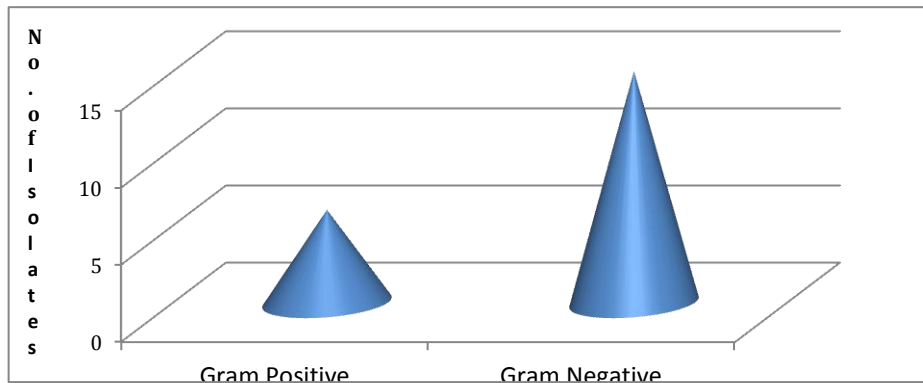
Table 2 shows the distribution of Gram positive organisms to be 28.58% (6/21) as against 71.42% (15/21) gram negative organisms.



Graph 1: Showing organisms in Sputum Culture

Table 2: Prevalence of Gram positive and Gram negative isolates in 21 positive sputum cultures

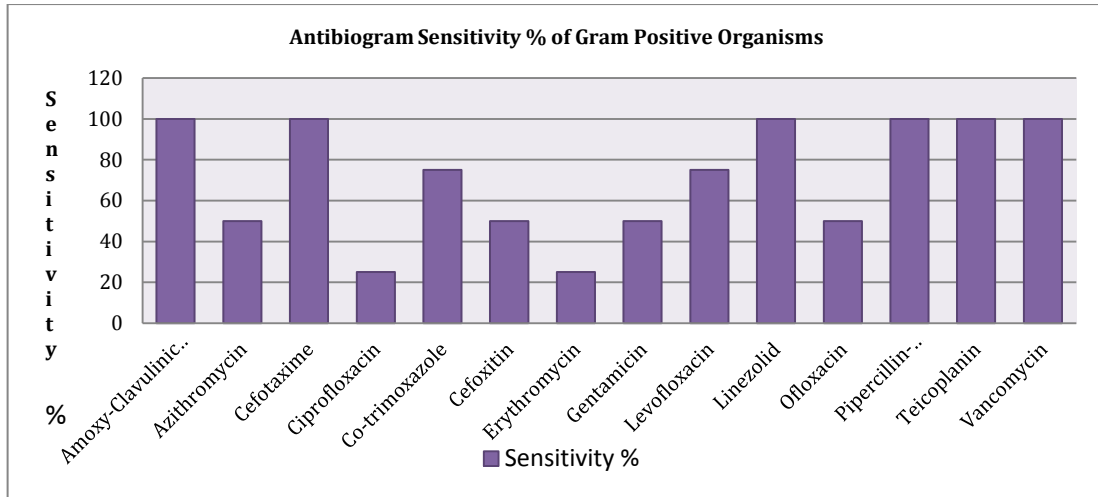
Organism	Number	Percentage
Gram Positive	6	28.58
Gram Negative	15	71.42



Graph 2: Prevalence of Gram positive and Gram negative isolates in 21 positive sputum cultures

Table 3: Antibigram (Sensitivity) of Gram (+) organisms

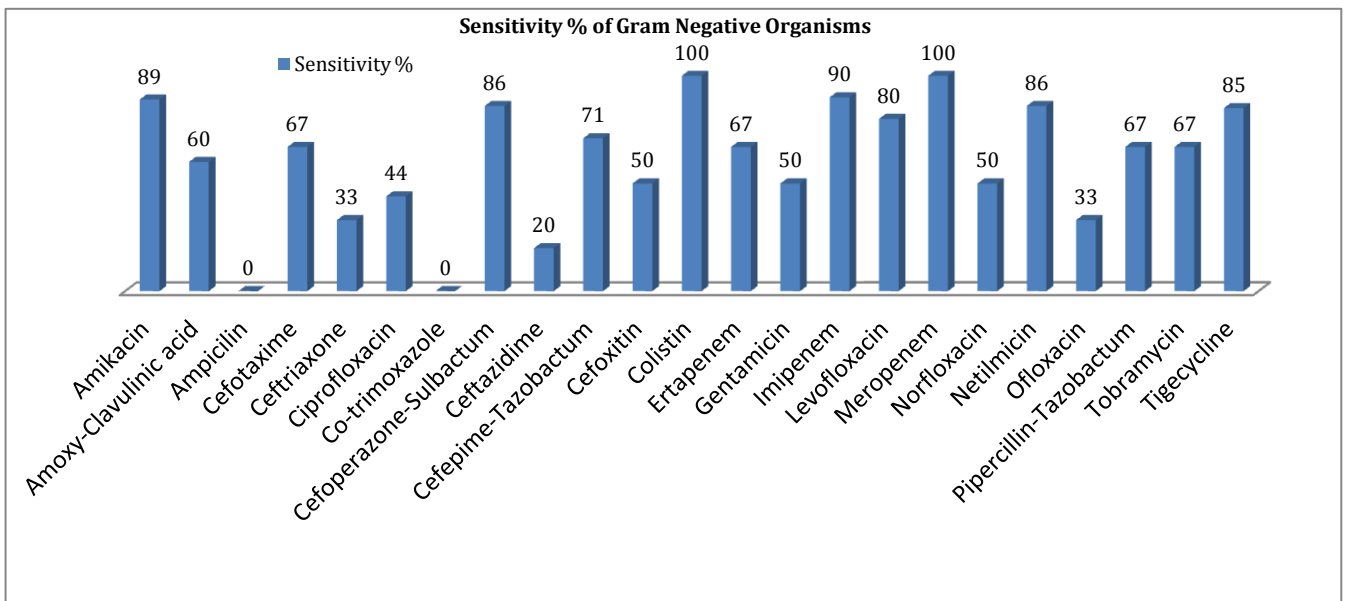
Sl No.	Antibiotics	Percentage
1.	Azithromycin	100%
2.	Amoxy-Clavulanic acid	50%
3.	Cefotaxime	100%
4.	Ciprofloxacin	25%
5.	Co-trimoxazole	75%
6.	Cefoxitin	50%
7.	Erythromycin	25%
8.	Gentamicin	50%
9.	Levofloxacin	75%
10.	Linezolid	100%
11.	Ofloxacin	50%
12.	Piperacillin-Tazobactam	100%
13.	Teicoplanin	100%
14.	Vancomycin	100%



Graph 3: Antibiogram (Sensitivity) of Gram Positive Organisms

Table 4: Antibiogram (Sensitivity) of Gram (-) organisms

Sl No.	Antibiotics	Percentage
1.	Amikacin	89%
2.	Amoxy-Clavulinic acid	60%
3.	Ampicilin	0%
4.	Cefotaxime	67%
5.	Ceftriaxone	33%
6.	Ciprofloxacin	44%
7.	Co-trimoxazole	0%
8.	Cefoperazone-Sulbactam	86%
9.	Ceftazidime	20%
10.	Cefepime-Tazobactam	71%
11.	Cefoxitin	50%
12.	Colistin	100%
13.	Ertapenem	67%
14.	Gentamicin	50%
15.	Imipenem	90%
16.	Levofloxacin	80%
17.	Meropenem	100%
18.	Norfloxacn	50%
19.	Netilmicin	86%
20.	Ofloxacin	33%
21.	Piperillin-Tazobactum	67%
22.	Tobramycin	67%
23.	Tigecycline	85%



Graph 4: Antibiogram (Sensitivity) of Gram Negative Organisms

DISCUSSION

AECOPD are a major cause of hospital admission and health care utilization. They have a major impact on the quality of life of patients with different conditions. AECOPD was more common in men with ratio of 3.2:1¹². Bacterial infection in AECOPD was seen more in the age group of 55-65 and 65-75 years¹³. *Klebsiella pneumoniae* was the commonest isolate followed by *Pseudomonas aeruginosa* and *Staphylococcus aureus*¹⁴. 40% COPD cases were bacterial culture positive. Effective drugs like Vancomycin, Piperacillin-Tazobactam, Azithromycin, Cefotaxime, Linezolid are available for treatment of Gram-positive isolates and Amikacin, Meropenem, Imipenem, Colistin, Cefoperazone-Sulbactam are available for treatment of Gram-negative isolates.

Health education is a must to highlight the dangers caused by smoking and environmental pollution¹⁵. To study the epidemiology, aetiology & complications due to bacteria in AECOPD, sputum culture is a good and simple tool.

There is a need to develop a correct treatment protocol to combat against AECOPD. Following antibiogram, antibiotic policy should be developed. It also helps in screening resistant pathogens and better drug for treatment, thereby helping to decrease the mortality and morbidity associated with co-morbidities. To conclude, in addition to the host genetic factors, smoking behaviour, accessibility to health care and presence of co-morbid conditions contribute to severity due to AECOPD.

Comparing with the other studies conducting in other parts of the country, there is a reflection of changing patterns of antibiotic sensitivity and bacteriological profile. The carbapenems, aminoglycoside, polymyxin, fluoroquinolone group of drugs are mostly sensitive to Gram-negative organisms. Cephalosporin and penicillin group of drugs are more effective against Gram-positive organisms than Gram-negatives. It has constantly observed that admissions to COPD increased on days with high pollution levels. [40] Other risk factors that are likely to be relevant in the development of COPD are occupation, low socioeconomic status, diet and possibly some environmental exposures in early life. Although this a short period of study, there should be retrospective analysis throughout the year to assess the epidemiological study of the bacterial microbiology in Kolkata, India.

ACKNOWLEDGMENT

We are most grateful to the Managing Director of Medica Superspecialty Hospital and Director of Clinical Research Centre, Jadavpur University for helping us to collect clinical data.

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