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ORIGINAL ARTICLE

Bacteriological Profile and their Antibiogram from Cases of Acute Exacerbations of Chronic Obstructive Pulmonary Disease: A Hospital Based Study

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ABSTRACT

Background and objectives: Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) are defined as presence of increased sputum volume, sputum purulence and dyspnoea. Bacteria are responsible for causing 30-50% of exacerbations. As only few studies are done in this field from India, the present study was undertaken to see the bacteriological profile and the resistant pattern of the isolates from cases diagnosed with this pathology.

Settings and Design: It was a prospective study carried out at Kasturba Hospital Manipal, Karnataka from June, 2006-Dec, 2006.

Methods: The present study comprised of 75 patients (53 treated as in-patients and 22 as out-patients). All the sputum samples were subjected to gram staining, bacterial culture and antibiotic sensitivity for bacterial isolates as per standard techniques.

Results: Growth of pathogens was obtained from 50.94% of sputum samples in case of in-patients and 68.18% in out-patients. Gram negative bacilli outnumbered the growth of other organisms. *Pseudomonas aeruginosa (25.92%)* was the predominant organism in hospitalized patients, whereas *Klebsiella pneumoniae (33.33%)* was the most common pathogen isolated from out-patients. *Haemophilus influenzae* was not isolated. Quinolones were found to be the most effective antibiotics against gram negative organisms.

Conclusions: The bacterial etiology of AECOPD is different in India from what has been shown in western studies. More studies involving large patient populations will provide better understanding of its bacterial etiology and thus proper management of disease.

Key words: COPD, Acute exacerbations, Bacterial etiology

Key messages:

1) Bacteria causing AECOPD are different in India as compare to western studies.
2) More is the severity of acute exacerbations, more is the chance of isolating *Pseudomonas aeruginosa* as the causative organism.
3) The number of resistant strains causing acute exacerbations are also increasing, so antimicrobial sensitivity pattern must be checked for the causative organism.

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Introduction

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and one of the principal causes of the death worldwide. [1] Exacerbations of COPD have considerable impact on health care system at both primary and tertiary care levels as they are the major reason for antibiotic use and admissions; additionally, exacerbations lead to indirect costs because of days lost from work.[2] COPD affects 30% of patients seen in chest clinics and constitutes 1-25% of hospital admissions all over India.[3] The disease is also associated with

working and social incapacity and has tendency to repeated exacerbations, both infective and non-infective. Cigarette smoking or inhalation of dust or fumes are important contributing factors. [4] The role of bacterialinfection in exacerbations of chronic bronchitis and the use of sputum cultures to reach an etiological diagnosis to guide clinical management are subjects of current debates.

The disease is defined by the clinical symptoms in which excessive mucus production leads to coughing up sputum on most days during at least 3 consecutive months for more than two successive years.[5] During episodes of acute exacerbations patient is having increased expectorations and usually associated with increased clinical symptoms, signs and functional disability.[6] Organisms most commonly associated with exacerbations are *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Moraxella catarrhalis*.[7] Because of chronic colonization, it is difficult to incriminate one of these organisms as a specific cause of an acute infection. But predominant growth of one organism and its correlation with gram staining can resolve this dispute.

Over 90% of patients with AECOPD are treated with antibiotics, [8] although the effectiveness of many is uncertain because of emergence of resistant strains of most common respiratory pathogens in past 15 years. The acute exacerbations can contribute to irreversible progression of disease.[9] Hence, timely institution of correct management is imperative for better prognosis of the disease.

This study was conducted to find out the bacteriological profile and their antibiotic sensitivity pattern in AECOPD as scanty reports are available from India.

Materials and Methods

It was a prospective study comprising 75 cases diagnosed as having AECOPD from June 2006-Dec 2006.

Inclusion Criteria:

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:

1. All cases who had evidence of pneumonia or bronchiectasis developed as a sequelae of other disease, clinically or on chest radiography (PA view)
2. Those patients who were already taking treatment in the hospital

Patients who were having severe breathlessness or wheezing or chest pain or altered sensorium or lowered arterial oxygen were admitted in hospital. History of smoking or immunization for *H.influenzae* or *S.pneumoniae* was also noted down for all patients.

Sputum samples (preferably two) were collected for all patients after rinsing the mouth twice with plain water. In few out-patients second sample could not be collected because of non-compliance of patients. Routine hematological investigations and chest radiography (PA view) were done on the day of presentation.

The sputum samples were subjected to direct gram staining and culture on two sheep blood agar (SBA), McConkey agar (MA) and chocolate agar (CA) plates. On one SBA streaking with staphylococci was done to facilitate growth of *H.influenzae*. Sheep blood agar plates were kept in 5-10% CO_2 incubator. All plates were incubated at 37°c for 24-48 hours. Gram stain reporting was done according to Bartlett's grading system[10] and culture isolates were identified according to standard techniques.[11] Antibiotic sensitivity for the pathogenic organisms isolated in culture was done by Kirby-Bauer method according to CLSI standards.[12]

Results

Seventy five cases were included in the prospective study. The maximum numbers of patients (76.74%) were above 55years of age. Sex-wise distribution showed 66 (88%) males as compare to 9 (12%) females. Fifty three cases (70.66%) needed hospital admission and 22 (29.33%) were outpatients. None of the patients had received immunization for *H.influenzae* or *S.pneumoniae* in the past. About 40% males were chronic smokers.

Growth of pathogenic organisms was obtained in 27/53 (50.94%) of hospitalized cases and 15/22 (68.18%) of outpatients. Gram negative bacilli outnumbered the growth of other organisms as shown in Table/Fig 1. Single organism was isolated in most of the samples 92.85% (39/42) but in 7.14% cases (3/42) growth of two organisms was

observed. *P.aeruginosa* was the predominant isolate (25.92%) amongst the hospitalized patients followed by *S.pneumoniae* and *Acinetobacter* spp (18.51% each), *Klebsiella spp.* and *M.catarrhalis* (14.80% each). In out-patient cases *K.pneumoniae* (33.33%) was responsible for causing most of the infections followed by *P.aeruginosa* (20%), *M.catarrhalis & Acinetobacter spp* (13.33% each) and *Streptococcus pyogenes* (11.11%). In one case growth of *E.coli* was obtained and in another single case *Enterobacter spp* was isolated. In 90% of cases (67 of 75 samples) gram staining findings were correlating with culture findings. It was observed that purulent or mucopurulent sputum gave better isolation of pathogens than mucoid or mucosalivary sputum. Antibiotic sensitivity of gram negative bacilli is shown in Table/fig 2. In 33.33% (2 out of 6) of *M.catarrhalis* strains, resistance was observed to macrolides and another 33.33% of isolated strains showed resistance to penicillin. *S.pneumoniae* isolates showed sensitivity to both penicillins and macrolides.

Table/Fig 1: Pathogens isolated from sputum cultures.

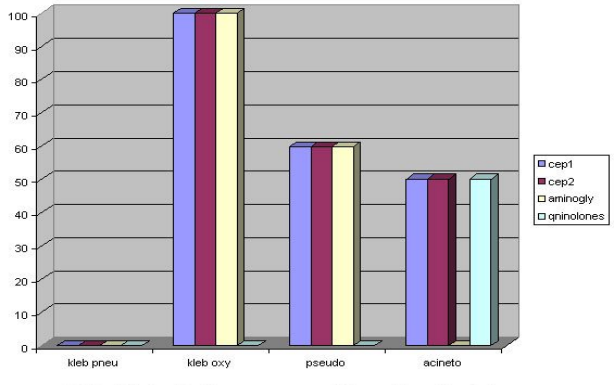
In Patients (n= 53)		Out Patients (n=22)	
Pathogen	No. (%)	Pathogen	No. (%)
Pseudomonas sps.	7(25.92)	*Klebsiella pneumoniae*	5(33.33)
Klebsiella spp	4(14.80)	*Pseudomonas spp*	3(20.00)
Moraxella catarrhalis	4 (14.8)	*Moraxella catarrhalis*	2(13.33)
Acinetobacter sps	5 (18.51)	Acinetobacter sps	2(13.33)
Streptococcus pneumoniae	5 (18.51)	*Streptococcus pyogenes*	1(7.14)
Streptococcus pyogenes	2 (7.40)	others	2(13.33)
Normal oropharyngeal Flora (NOF)	26(49.05)	NOF	7(31.81)

Discussion

Bacterial infections are generally considered to be the most common cause of COPD. It is estimated that more than 40% of all exacerbations are of bacterial origin.[13] Accordingly, antibiotics should be administered in inpatients and outpatients with AECOPD exacerbations and change in sputum characteristics suggestive of bacterial infection.[14] COPD exacerbations may be triggered by acquisition of new bacterial species or by an increase in the absolute number of same bacteria or their different strain that colonize the airways.

The maximum numbers of cases showing AECOPD were >55years of age in our study, which can be explained by the fact that chronic bronchitis has highest prevalence in fifth and sixth decade. [15] Predominance of male over female patients as shown in the study can be explained by the fact that in our country males are exposed more to outside environment because of their more mobility as compare to females. Moreover smoking habits are more pronounced in males that constitute one of the predisposing factors for the development of COPD. Smoking and air pollution are responsible for decrease in mucociliary clearance and innate immunity. [20] It leads to increased bacterial colonization that can give rise to increased airway inflammation and thus exacerbations.

Growth of pathogenic organisms was obtained in 56% (42/75) of sputum samples. Culture positivity depends on nature of sputum, transportation time and the number of organism present in the sample. Arora et al[16] have obtained growth in 72% cases, whereas Dalvi et a[6] obtained growth in 57% of samples that is corresponding with our study. It is estimated that 50-75% of infective exacerbation are bacterial in origin. Gram staining, though viewed as a matter of controversy, but has remained a time honored method for sputum samples. If the Gram staining shows >25 pus cells and <10 epithelial cells/Low power field, sample is considered adequate for culture. [17] In our study Gram staining findings were in correlation with the culture findings in 90% cases.



Table/Fig 2 - Resistant pattern of Gram Negative isolates

P.aeruginosa was isolated more in hospitalized patients (25.92%) as compared to outpatients (20%). *S.pneumoniae* isolates also showed same results. This shows that more is the severity of the disease; more is the chance of isolating *P.aeruginosa* and *S.pneumoniae* as the causative organisms. The association of *P.aeruginosa* with severe airflow obstruction has already been

documented. [18], [19] Presence of Gram negative bacilli colonizing the oropharynx increase with severity of underlying respiratory alteration. *H.influenzae* was not isolated in our study and other Indian studies, though it is a common pathogen in western countries. [7] This difference may be due to different environmental conditions and inadvertent use of antibiotics.

The resistogram obtained in our study showed that *Klebsiella oxytoca* strains were resistant (100%) to 1st and 2nd generation cephalosporins and aminoglycosides. As only two strains of *K.oxytoca* were obtained in this study, both from hospitalized patients, it is difficult to comment upon their resistance pattern. Resistance shown by them can be because of colonization by the hospital strains. Moreover the resistogram (chart 1) is clearly showing that about 60% of isolated *Pseudomonas aeruginosa* and 50% of *Acinetobacter spp*. were resistant to the commonly used first and second generation cephalosporins. Resistogram could not be done separately for in-patients and out-patients because of insignificant difference between two groups. Though response to quinolones was excellent for majority of pathogens, it cannot be considered as the first option for starting treatment, as its frequent usage can lead to emergence of the resistant strains.[7] Mechanisms like selective pressure on organism due to uncontrolled use of quinolones, decreased permeability and active efflux of antimicrobial agent are involved for emergence of resistant strains.[21]

To conclude, present study and few previous Indian studies have shown that bacterial flora responsible for AECOPD is different in our country from that of western countries and so is their sensitivity pattern. So, for the management of these cases, can we rely fully on either British or American Thoracic Society guidelines? To get the answer to this query, there is need for more studies involving large population for proper management of these cases in our settings.

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