Original Research Article

Study of risk factors and bacterial pathogens isolated during acute exacerbation of chronic obstructive pulmonary disease

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Abstract

Background: Acute exacerbation of COPD 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. In patients likely to benefit from antibiotic therapy, an understanding of the relationship between severity of COPD, host risk factors and microbiology is paramount to guide respiratory physicians to treat the patients. **Material and Methods:** This prospective, observational study was conducted in clinically diagnosed Acute Exacerbation of Chronic Obstructive Pulmonary disease patients. **Results:** A total of 100 patients, clinically diagnosed as cases of AECOPD, were studied. Most common age group was 56 to 65 years (28%), the next common age group was 66 to 75 years (25%). 79 out of 100 patients had previous hospital admissions. Majority of the patients were in the age group of 56 years to 62 years, most of them males, with positive smoking history the average years of smoking being 20 to 30 years. Only 15 patients gave alcoholism history, 3 of them had asthma and 9 were on steroids in the form of inhaler use. Large number of patients had lower socioeconomic status 100 sputum samples were subjected to culture and sensitivity. Out of which, 76 sputum samples yielded pathogenic bacteria and 24 samples yielded oral commensals. A total of 70 sputum samples yielded Mono- microbial growth and 6 had polymicrobial infections. Among 82 isolated pathogens *Klebsiella pneumoniae* was the commonest bacteria isolated in 27 (32.9%) cases, followed by *Pseudomonas spp.* isolated in 16 (19.5%) cases. *Streptococcus pneumoniae* was isolated in 2 (2.4%) cases. Other common organisms isolate were MRSA in 11 (13.4%) cases, *Acinetobacter spp.* in 8 (9.7%) cases. *Escherichia coli*, Candida were isolated as 8 (9.7%) and 5 (6%) cases respectively. **Conclusion:** Lower socioeconomic strata, Positive occupational history and history of repeated hospitalization WERE major risk factors noted during acute exacerbation of chronic obstructive pulmonary disease. Predominant organisms were Klebsiella pneumoniae, Pseudomonas species and MRSA.

Keywords: AECOPD, bacterial infection, smoking, *klebsiella*

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INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a spectrum of disorders that results in airflow obstruction. At one end of the spectrum is chronic bronchitis, which is characterized by airway inflammation, mucus hyper secretion and airway reactivity. At the other end of the spectrum is emphysema, characterized by alveolar destruction and small airway abnormalities.[1] Acute exacerbation of COPD 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 average patient with COPD experiences two episodes of AECOPD per year and 10%

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of these episodes require hospitalization. Bacterial infections are implicated in the majority of AECOPD episodes, because the patient with COPD has airways that are prone to infections, with impaired local defenses and frequent bacterial colonization.[3] As COPD progresses, exacerbations tend to become more frequent, the average being about more than three episodes per year.[4] Hence timely institution of correct management is imperative for better prognosis of the disease. In patients likely to benefit from antibiotic therapy, an understanding of the relationship between severity of COPD, host risk factors and microbiology is paramount to guide respiratory physicians to treat the patients. This study was taken up to know various risk factors associated with AECOPD and the bacteria predominantly causing the respiratory infections in AECOPD in our geographical area.

MATERIAL AND METHODS

This prospective, observational study was done on 100 patients admitted at KR hospital, Mysore during a period of Jan 2015 to Dec 2015. Institutional ethical committee approval was taken.

Inclusion criteria:

All clinically diagnosed Acute Exacerbation of Chronic Obstructive Pulmonary disease (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) patients admitted.

Exclusion criteria: Bronchial Asthma/Lung Abscesses/Lung Cancer. Patients who were recently started on Antibiotic Therapy. Known case of Pulmonary Tb.

Variables included for the study were age, sex, occupation, previous history of hospital admissions, antibiotic intake, alcoholic, smoking, socioeconomic status, asthma, steroid intake, COPD since many years. The information regarding these variables was collected by using a pretested questionnaire.

Sputum sample, spontaneous or induced: early morning specimen generated after a bout of cough was collected by patient and processed by conventional methods in Department of Microbiology. The macroscopic appearance of the sputum was observed and noted and a portion of the purulent or mucopurulent sputum was used for the preparation of a Gram-stained smear.

Sputum culture

A floccule of purulent material was selected and inoculated on to the various culture plates.

a. Bacterial culture Blood agar, Chocolate agar, Mac Conkey agar.
b. Fungal culture - Sabouraud dextrose agar

The presence of Gram-positive, yeast-like structures in the Gram stain smear was further inoculated onto Sabouraud dextrose agar (which was to be incubated for at least 3 days at 35-37 °C). Identification of Gram-positive yeast was performed using standard test. Cultures were inspected after incubation overnight but reincubation for an extra 24 hours was done when growth was less than expected from the microscopic findings or when only tiny colonies were present. Each colony was identified based on the preliminary tests.

a. Any Gram-positive cocci preliminary test like catalase, oxidase test was done.
b. Any Gram-negative bacilli, preliminary tests like catalase, oxidase and motility were done.

After preliminary identification of the organism a battery of tests were adopted to speciate them. Further biochemical tests were done like Oxidative-Fermentative test, Nitrate reduction test, MR test, VP test, Indole test, Triple Sugar Iron, Citrate test, Urease test, Sugar fermentation test, Amino acid utilization test. All the isolates were subjected to antibiotic susceptibility testing by Kirby - Bauer disc diffusion technique according to CLSI guidelines.[28] The cultures suggestive of Streptococcal growth were put for direct sensitivity on Chocolate agar. Antibiotic susceptibility testing was done by measuring zones of inhibition and correlated with the standard tables provided by CLSI to categorize into sensitive, moderately sensitive, resistant.[5] Multidrug resistant organism - For epidemiologic purposes, MDROs are defined as microorganisms, predominantly bacteria, that are resistant to ≥3 classes of antimicrobial agents. Certain MDROs describe resistance to only one agent (e.g., MRSA, VRE) these pathogens are frequently resistant to most available antimicrobial agents.[6] Results were collected and entered in Microsoft excel sheet. Statistical analysis was done using descriptive statistics.

RESULTS

A total of 100 patients, clinically diagnosed as cases of AECOPD, were studied.

The age group of the patient in the study, ranged from 45 to 85 years. Out of one hundred patients, the most common age group was 56 to 65 years (28%), the next common age group was 66 to 75 years (25%). 87% were males and 13% were females. The ratio between male and female is 6:1. 57 patients had COPD between 1- 10 years whereas only one patient had COPD for >30 years.

Table 1: Age and gender distribution

Age(in yrs.)	Number	Percent (%)
35 – 45	10	10
46 – 55	23	23
56 – 65	28	28
66- 75	25	25
76 -85	14	14

Gender		
Male	87	87
Female	13	13
Duration		
1-10 yrs.	57	57
11-20 yrs.	36	36
21-30 yrs.	5	5
>30 yrs.	1	1

79 out of 100 patients had previous hospital admissions. Majority of the patients were in the age group of 56 years to 62 years, most of them males, with positive smoking history the average years of smoking being 20 to 30 years. Only 15 patients gave alcoholism history, 3 of them had asthma and 9 were on steroids in the form of inhaler use. Large number of patients had lower socioeconomic status i.e., 75 patients and 25 patients belonged to middle class. 22 laborers(25.2%) working in factory or outdoors had AECOPD, 8 (9.1%) patients as cement worker and 4 (30%) females cooking indoor suffered from AECOPD infection.

Table 2: Risk factors associated with respiratory infections in AECOPD

Variables	Male (n=87)	Female (n=13)
Age (in years)	62.54 years	56 years
Occupational history positive	30 (34.48%)	4 (30.77%)
• Labourer	22 (25.2%)	
• Cement worker	8(9.1%)	
• Women cooking indoor with biomass		4 (30.77%)
Smoker	66 (75.86%)	2 (15.38%)
Smoke years	20- 30 yrs.	2- 5 yrs.
Previous history of hospitalization	71 (81.61%)	8 (61.54%)
Alcoholic	15 (17.24%)	0
Asthma	3 (3.45%)	1 (7.69%)
Steroid use as inhaler	9 (10.34%)	1 (7.69%)

One hundred sputum samples were subjected to culture and sensitivity. Out of which, 76 sputum samples yielded pathogenic bacteria and 24 samples yielded oral commensals. A total of 70 sputum samples yielded Mono- microbial growth and 6 had polymicrobial infections. All the growths were analyzed with Gram stain report and noted. Out of 76 sputum samples which yielded pathogenic organisms, a total of 82 nonrecurring isolates were obtained. Among these 82 isolates, 61 (74.39%) were Gram-negative bacteria, 16(19.5%) were Gram-positive cocci and 5(6%) were Gram positive yeasts. Among 82 isolated pathogens *Klebsiella pneumoniae* was the commonest bacteria isolated in 27 (32.9%) cases, followed by *Pseudomonas spp.* isolated in 16 (19.5%) cases. *Streptococcus pneumoniae* was isolated in 2 (2.4%) cases. Other common organisms isolate were MRSA in 11 (13.4%) cases, *Acinetobacter spp.* in 8 (9.7%) cases. *Escherichia coli*, Candida were isolated as 8 (9.7%) and 5 (6%) cases respectively.

Table 3: Isolates from Sputum Culture

Name of organism	Number	Percent
Klebsiella pneumonia	27	32.9%
Pseudomonas species	16	19.5%
MRSA	11	13.4%
E coli	8	9.7%
Acinetobacter species	8	9.7%
Candida albicans	5	6%
Staphylococcus aureus	3	3.6%
Streptococcus pneumonia	2	2.4%
Enterobacter species	1	1.2%
Serratia marcescens	1	1.2%

Imipenem group of drugs were most sensitive to Gram negative bacilli whereas Ampicillin (100%) and cephalosporins (100%) are most resistant. For Klebsiella maximum resistance was showed by Penicillins (100%) and Cephalosporins (55%) group of antibiotic, whereas the most sensitive were Aminoglycosides (3%) and Carbapenems (22%).

Table 4: Drug Resistance Pattern of Gram-Negative Isolates

Organisms	Amp	Ce	Ca	Ci	Cu	Ac	Cf	G	Co	I	PT
Klebsiella	27	19	17	13	17	27	16	1	18	6	-
(n=27)	100%	70%	62%	48%	62%	100%	59%	3%	66%	22%	
Pseudomonas	-	8	14	10	12	-	5	8	8	0	10
(n=16)		50%	87%	62%	75%	75%	31%	50%	50%	0	67%

E.coli	8	6	7	8	8	8	8	5	8	4	-
(n=8)	100%	75%	87%	100%	100%	100%	100%	62%	100%	50%	
Acinetobacter	-	8	7	6	6	-	3	2	5	3	7
(n=8)		100%	87%	75%	75%		(37%)	25%	62%	37%	87%
Enterobacter	1	0	1	0	0	1	1	1	1	1	-
(n=1)	100%	0	100%	0	0	100%	100%	100%	100%	100%	
Serratia	1	1	0	0	0	1	1	1	1	0	-
(n=1)	100%	100%	0	0	0	100%	100%	100%	100%	0	

*Amp- Ampicillin, Ac- Amoxiclav, Ce- Cefotaxime, Ca- Ceftazidime, Ci- Ceftriaxone, Cu- Cefuroxime, Cf- Ciprofloxacin, G- Gentamicin, Co- Cotrimoxazole, I- imipenem, PT- Piperacillin tazobactam

DISCUSSION

Respiratory infections in COPD resulting in exacerbation deteriorates pulmonary function and increases airway inflammation and is a major cause of morbidity, mortality and reduced health-related quality-of life in these patients. Early antibiotic treatment of these infections can shorten recovery time, improve lung function and reduce the risk of treatment failure. In the present study, maximum number of cases in the age group of 45 to 55 yrs., mean age being 62.5 years. Similar demographic findings was observed in a study done by Gerard R *et al.*[7] where in maximum number of cases were in the age group of >55yrs, and in a study done by Patel A *et al.*[8] maximum number of cases were seen in the age group of >58yrs. This could be due to more exposure to dust or fumes, more years of smoking or biomass combustion fumes in case of females. The present study showed that AECOPD was higher in males 87% as compared to females 13%. Also there are less women smokers than males in our country. Males are more exposed to occupational hazards like organic dust in the form of agriculture, mining, metallic fumes etc. Apart from this genetics play an important role.[9] Males are at more risk of acquiring lower respiratory tract infections than females, while asthma is more common in females increasing the morbidity and mortality in female COPD patients. While smoking is the major cause of chronic obstructive pulmonary disease (COPD), occupational exposures to vapors, gases, dusts, and fumes (VGDF) increase COPD risk. Construction workers are at increased risk of COPD as a result of broad and complex effects of many exposures acting independently or interactively.[10] In our study 30 (34%) out of 87 males had occupational exposure either working in cement factory or laborers at construction work. If occupational exposure with smoking history is present, it increases the risk of acquiring the disease by 20%. The exposure to dust, gas, fumes is directly proportional to severity of symptoms like cough and dyspnea. Construction workers exposed to inorganic dust have increased mortality due to COPD. Furthermore the effect of occupational exposure is generally more marked in women. Indoor air pollution has been shown to be a risk factor for COPD.[11] Active smoking is the main risk factor for COPD. The risk attributable to active smoking in COPD is thought to vary from 40% to 70% according to the country.[11] Active smoking damages the airway tract, increases the amount of inflammation and inflammatory mediators which in turn makes the lower airway more prone to infections. Furthermore the local immunity at the site is hampered through which organisms gain access and then commensals can also act as pathogens in these compensated airway cases. Studies like Müllerová H *et al.*[12], Movahed M *et al.*[13] suggest association between exacerbation frequency and respiratory infections in COPD which results in exacerbations. Most of the patients presented with repeated history of hospitalization for exacerbations. Exacerbations are an important outcome, not only because they pose a considerable economic burden but more importantly because repeated exacerbations of COPD lead to deteriorating health-related quality of life and, when associated with ventilatory failure, to premature death.[8] Exacerbations represent an increase in the inflammation that is present in the stable state, with increased numbers of inflammatory cells and cytokines.[13] Increased inflammatory mediators increases the risk of exacerbations. Also due the MDR strains the patients were again visiting hospitals for exacerbations thus resulting in a vicious cycle. Many studies from developed countries suggested that socioeconomic status (SES), measured by income and educational level is associated with lung function and COPD in terms of exacerbation, prevalence and mortality. This is due to lower education, a smaller number of people seeking help for exacerbations and less compliance in which the smokers subset was more. The study done by Jafar A *et al.* reported that COPD patients with the lowest socioeconomic level had a three-fold risk of re-hospitalizations compared to those with the highest. Low socioeconomic status has also been reported to be associated with greater mortality in COPD patients.[14] Other studies supporting the fact of lower socioeconomic strata are Yin P *et al.*[15] in which he mentioned possible mechanism explaining the adverse effects of low SES on COPD among never smokers might be poor dietary habits (low in antioxidants and fresh fruit), poor housing conditions , more occupational dust exposure and indoor air pollution from biomass combustion in low SES group.[15]

This study suggest a strong correlation between COPD exacerbations prevalent in lower socioeconomic strata ($p<0.001$). In the present study Gram negative bacteria have dominated over Gram positive bacteria which is similar to other studies like Vishwambhar V *et al.*[16], Feng Y *et al.*[17]. As we can observe from the above table the prevalence of Gram-positive cocci was more in earlier era but in recent times the prevalence of Gram-negative bacteria in exacerbations went on increasing. This was mainly due to vaccination in cases of COPD patients, mainly *H.influenza*, *Streptococcus pneumonia*, whooping cough.[12] Other reason for it could be due to increased exacerbations, frequent admissions to hospitals during which hospital acquired multi drug resistant strains might have been acquired. And lastly Gram-negative organisms were more common in severe cases of COPD. Also empirical treatment might have killed fragile bacteria like *H. influenza*, *Streptococcus pneumonia* and left with difficult to treat pathogens like Klebsiella and others as seen in studies done by Bashir *et al.*[18] Profile of organisms have been changing as the years have passed and recent times we are left with drug resistant bacteria. In our study 6% samples yielded candida as pure growth. The culture findings were correlating with sputum direct smear wherein pseudohyphae was seen as seen in other studies like Yu S *et al.*[19] As we have focused only on bacterial and fungal pathogens other organisms causing respiratory infections in COPD were not diagnosed like mycoplasma pneumonia, various respiratory viruses, atypical bacteria. Molecular diagnosis could have helped in identification of resistant gene which was again lacking in our study.

CONCLUSION

Lower socioeconomic strata, Positive occupational history and history of repeated hospitalization WERE major risk factors noted during acute exacerbation of chronic obstructive pulmonary disease. Predominant organisms were Klebsiella pneumoniae, Pseudomonas species and MRSA.

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