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A Study on Sputum Bacteriology and Antibiotic Sensitivity Pattern of Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease in a Tertiary Care Hospital

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ABSTRACT
Chronic obstructive pulmonary disease (COPD) is a multisystem condition that mostly affects the lungs. Acute exacerbation of COPD (AECOPD) contributes to the disease's overall severity and irreversible progression. Bacterial infections are the leading cause of AECOPD in India, accounting for more than 40% of all exacerbations. To assess prevalence of bacterial exacerbations of COPD and detect type of bacteria causing AECOPD with its antibiotic sensitivity pattern. This is a hospital based observational descriptive cross sectional study carried out from January 2017 to June 2018, Department of Respiratory Medicine, Medical College Hospital, Kolkata. Total 105 patients were included in this study. In our study smoking habit is not statistically significantly associated with severity of COPD. But it was strongly associated with COPD i.e., COPD is more common in smokers. It was observed that all cases of very severe COPD (100%) and most of the severe COPD (88.24%) developed in smokers and *Klebsiella pneunoniae* (38.46%), followed by *Staphylococcus aureus* (23.08%), *Streptococcus* species (15.39%), *Pseudomonas aeruginosa* (10.26%), *E. coli* (5.13%), *Acinetobacter* species (5.13%) and *Enterobacter* species (2.56%). Smoking habit was strongly and statistically significantly associated with COPD but statistically not significantly associated with severity of COPD and Most frequently isolated bacteria, Klebsiella pneumoniae was mostly sensitive to Piperacillin/tazobactum, Meropenem, Amikacin, Levofloxacin and Colistin.

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Key Words
COPD, exacerbation, bacteriology, antibiogram, obstructive

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INTRODUCTION

COPD (Chronic Obstructive Pulmonary Disease) is a multisystem disease that mostly affects the lungs.

According to the GOLD guideline, COPD is defined as a common, preventable and treatable disorder characterised by persistent respiratory symptoms and airflow limitation caused by airway and/or alveolar abnormalities caused by significant exposure to noxious particles or gases[1].

COPD is a prominent source of illness and death around the world[2]. It is currently the fourth largest cause of death in the world and will rise to third by 2020. COPD caused around three million deaths worldwide in 2012, accounting for 6% of all deaths[2].

This disease affects 4-10% of adult males in India and 3.5-6.5% of the population in Asia Pacific countries[3].

According to the Burden of Obstructive Lung Diseases (BOLD) project, 384 million COPD cases were reported in 2010, with a global prevalence of 11.7% (95% confidence interval (CI) 8.4-15.0%)[4]. With rising smoking rates in low-income countries and an ageing population in high-income countries, the incidence of COPD is expected to rise over the next 30 years, with over 4.5 million deaths from COPD and related disorders by 2030[5,6].

According to the Global Burden of Disease Study (GBDS), COPD is anticipated to ascend to the fifth place as the leading cause of disability adjusted life years (DALYs) loss by 2020. The greatest increase in tobacco-related mortality is expected in India, China and other Asian countries[7].

According to a recent estimate in INDIA, chronic respiratory disease accounts for 7% of deaths and 3% of DALYs lost, with COPD accounting for the majority of these losses[8].

COPD morbidity calculated in disability adjusted life years was 690 per 100 000 population in 2004, according to World Health Organisation country data. In a country with a population of 1.25 billion people, this is quite likely. The age-standardized death rate of 64.7 per 100,000 population accounts for 20% of global COPD mortality (556 000 cases out of 2 748 000 cases) in a given year[9].

MATERIALS AND METHODS

Type of study: Hospital based observational descriptive study.

Study design: Cross-sectional.

Study setting: Within the premises of Medical College Hospital, Kolkata.

Place of study: Department of Respiratory Medicine, Medical College Hospital, Kolkata.

Period of study: January 2017 to June 2018.

Study population: Patients with acute exacerbation of COPD admitted in Respiratory Medicine Department of Medical College Hospital, Kolkata.

Sample size: About 105 patients have been taken from among the admitted COPD patients.

Study technique: About 105 cases were selected from among admitted AECOPD patients after fulfilling inclusion and exclusion criteria. Data were collected using predesigned questionnaire after getting written informed consent and were analyzed statistically. Results obtained were compared with observations made elsewhere.

Inclusion criteria:

- Previously diagnosed patient of COPD on the basis of history of exposure to risk factors, clinical history and examination Supported by spirometric evidence of post bronchodilator FEV1/FVC $\leq$0.7 (GOLD criteria)
- Acute exacerbation of COPD according to the following criteria (Presence of any one of the following):
    - Increased severity of dyspnoea
    - Increased sputum volume
    - Increased sputum purulence
    - Increased cough
- Sputum sample contains <10 squamous epithelial cells/LPF and>25 neutrophils/LPF.

Exclusion criteria:

- Patients having concomitant bronchiectasis
- Patients having sputum positive for acid fast bacilli (AFB)
- Exacerbation due to pneumonia, pneumothorax, pleural effusion, cor-pulmonale, left ventricular failure and arrhythmia

RESULTS AND DISCUSSIONS

The present observational, descriptive, cross sectional, hospital based study was conducted in the Department of Respiratory Medicine, Medical college ,Kolkata in the period of January 2017 to June 2018. In our study, 105 patients of Acute Exacerbation of Chronic Obstructive Pulmonary Disease (AECOPD).

There were 105 AECOPD patients in our study. Range of age of the patients was 40 to 80 years, mean and median ages were 57.42 and 58.00 years, respectively. Among them 63 were males (60%)

Table 1: Association of smoking habit with severity of background COPD in male patients (n = 63)

	Severity of COPD				
Smoking habit	Mild	Moderate	Severe	Very severe	Total
Yes	10 (71.43)	19 (67.86)	15 (88.24)	4 (100.00)	48 (76.19)
No	4 (28.57)	9 (32.14)	2 (11.76)	--	15 (23.81)
Total	14 (100.00)	28 (100.00)	17 (100.00)	4 (100.00)	63 (100.00)

Table: Association of severity of background COPD with smoking index (n=25)

	Smoking index		
Severity of COPD	1-300	>301	Total
Mild	2 (25.00)	--	2 (8.00)
Moderate	6 (75.00)	7 (41.18)	13 (52.00)
Severe	--	7 (41.18)	7 (28.00)
Very severe	--	3 (17.65)	3 (12)
Total	8 (100.00)	17 (100.00)	25 (100.00)

Table 3: Association of mean CAT score with severity of background COPD (n=105).

		CAT score					
Severity of COPD	No. of COPD patients	Mean	SD	Minimum	Maximum	Median	p-value
Mild	28	14.43	3.3602	8	24	14.5	<0.0001
Moderate	50	19.82	5.6666	0	34	20	
Severe	21	29.71	3.408	22	35	30	
Very severe	6	33.50	2.51	30	36	33.50	

whereas 42 were females (40%). Ratio is 1.5:1.Majority of the study subjects were from 61-70 years age group. Patel *et al*.[10] conducted an observational prospective hospital based study at Vadodhara, Gujarat, India from June, 2011 to 2012. Out of total 50 patients, 41 were male and 9 were female having mean age of 60.18 years (Table 1).

In a hospital based study comprising of 81 AECOPD patient, 64 (79%) was males and 17 (21%) was female aged between 35 and 85 years[11].

In our study, mean age of the patients under study were 57.42 years which is higher than study conducted by Aleemullah *et al*.[12] and lower than study conducted by Patel AK et al. Majority of the present study subjects were male which is in concordance with all other studies cited above.

In the present study, we found that among 63 male patients 48 were smokers (76.19%), 15 were non-smoker (23.81%) but Among 42 female patients 4 were smokers (9.52%) and 38 were non-smoker (90.48%). Smoking habit is statistically significantly associated with COPD and also with COPD exacerbation (p>0.05). This correlation is consistent with the study conducted by Narayanagowda *et al*.[13] where there were Seventy two (72) male patients out of total 107. Out of seventy two, 45 (62.5%) were smokers and twenty seven (37.5%) were non-smokers. There are other studies which stated same correlation of smoking and COPD (Table 2)[14].

Among male cases 28.57% were primary literate, followed by secondary and higher secondary literate (20.63% each), 19.05% illiterate. Among females 47.62% were illiterate, followed by 23.81% primary literate (p<0.05) (Table 3).

Smoking and exposure to biomass fuels cause a reduction in mucociliary clearance and innate immunity. It promotes bacterial colonisation, which can lead to increased airway irritation and consequently exacerbations[15].

Pseudomonas aeruginosa was the most commonly isolated gramme negative bacterium, accounting for 26.7% of cases, followed by Klebsiella (20%). Streptococcus pneumonia (22.2%) and Streptococcus pyogenes (15.56%) were the most prevalent gramme positive species, followed by *Staphylococcus aureus*. 4.4% of the time[16].

About 12 patients (60%) had purulent sputum, 7 (30%) had mucopurulent sputum and 1 (5%) had mucoid sputum. There was no statistically significant difference between different physical properties of sputum in terms of isolated bacteria (p = 0.35). *Streptococcus pneumoniae* (43.3%) was the most commonly isolated bacterial pathogen, followed by MRSA (10%), *Haemophilus influenzae* (6.7%) and finally Acinetobacter spp. and *Moraxella catarrhalis* (3.3% each). The most dangerous to organisms were quinolones, followed by ceftriaxone[17].

In our study Gram negative bacteria were mainly sensitive to Piperacillin/tazobactum (78.05%), Meropenem (73.17%) and Amikacin (73.17%) Levofloxacin was equally effective for both Gram negative and Gram positive bacterias.

In agreement with our study Sharan *et al*.[18] in their study found that Vancomycin, linezolid, ceftrixone, azithromycin and clarithromycin were the most effective antibiotics against gramme positive cocci, whereas meropenem and pipercillin-tazobactum were the most effective against gramme negative bacilli. They also discovered that amikacin and Levofloxacin were effective against both gramme positive cocci and gramme negative bacilli in their investigation[18].

In the present study we found that gram positive cocci were mostly sensitive to Linezolid (88.89%), Vancomycin (83.33%), Ceftriaxone (83.33%), Cefuroxime (83.33%), Azithromycin (77.78%), Piperacillin+tazobactum (72.22%), Meropenem (72.22%). The study conducted by Patel *et al*.[10] Stated that Among macrolides, Azithromycin was the most effective drug against gram positive which agrees with our study. Another study discovered that Vancomycin and Linezolid were effective against all Gram-positive bacteria which agrees partially with our findings[12].

CONCLUSION

Total number of patients in the present study were 105. Mean age of the AECOPD patients was 57.42 years. Majority of the study population were males (60%). Majority of the patients were from 61-70 years age group (34.29%). Majority of the patients were from Islam religion (52.38%). Most of the patients were illiterate (30.48%). More number of AECOPD patients 55(52.38%) were resident of Rural area. Majority of the study population were found to belong to modified B G Prasad's Socio-economic class II (61.90%) i.e. upper middle class. Among study population 49.52% were smokers of which majority were male. Smoking habit was statistically significantly associated with sex ($p<0.05$). Most of the females (73.81%) were exposed to biomass fuel. Biomass fuel exposure was significantly associated with sex ($p<0.05$). Majority of exposed females (77.42%) were from rural area. This association was statistically significant ($p<0.05$). Most of the females (74.19%) were exposed to wood. Patients with severe and very severe background COPD were found to come from rural area which is statistically significant ($p<0.05$). No statistical significant association was found between background COPD and age group, religion and education level. Smoking habit was strongly and statistically significantly associated with COPD but statistically not significantly associated with severity of COPD. Smoking index (for bidi) is statistically significantly associated with severity of COPD ($p<0.05$). Dyspnoea grade (mMRC) is statistically significantly associated with severity of COPD. Severity of COPD is statistically significantly associated with number of hospitalization in previous year and vice versa. Most common co-morbidity associated with COPD was Hypertension. Majority of COPD patients admitted to our departmental indoor belonged to AECOPD without any respiratory failure (A). CAT score was statistically significantly associated with severity of COPD. About 21 Severity of background COPD was statistically significantly associated with severity of exacerbation ($p<0.0001$). Among isolated bacteria ($n = 59$) from sputum of 105 AECOPD patients, majority were gram negative bacteria (69.49%), followed by gram positive cocci (30.51%). Severity of both background COPD and AECOPD was statistically significantly associated with isolation of gram negative bacteria ($p<0.0001$). Bacteria grown in 56.19% cases from sputum samples of 105 AECOPD patients i.e. in 56.19% cases AECOPD was caused by bacterial infections. Most frequently isolated bacteria were Klebsiella pneumonia (28.81%). All bacteria were isolated from purulent and mucopurulent sputum. The gram staining reports of the sputum were 100% corroborating with sputum culture result. *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* were isolated from patients with worse lung function (Severe and very severe COPD), whereas maximum number of Streptococcus pneumoniae, H. influenzea and M. catarrhalis were isolated in sputum cultures of patients with mild to moderate COPD. Gram negative bacteria were mainly sensitive to Piperacillin/tazobactum (78.05%), Meropenem (73.17%) and Amikacin (73.17%) gram positive cocci were mainly sensitive to Linezolid (88.89%), Vancomycin (83.33%), Ceftriaxone (83.33%), Cefuroxime (83.33%), Azithromycin (77.78%), Piperacillin/tazobactum (72.22%) and Meropenem (72.22%). Overall most effective antibiotics in our study were piperacillin/tazobactum followed by Meropenem. Most frequently isolated bacteria, Klebsiella pneumoniae was mostly sensitive to Piperacillin/tazobactum, Meropenem, Amikacin, Levofloxacin and Colistin. 2nd most common isolate, Streptococcus pneumoniae was mostly sensitive to Piperacillin/tazobactum (85.71%), Meropenem (85.71%), Azithromycin (85.71%) and Linezolid (85.71%) followed by Ceftriaxone (78.57%), Cefuroxime (78.57%) and Levofloxacin (64.29%).

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