ORIGINAL ARTICLE

Clinical and Microbiological Profile of Patients with Acute Exacerbation of COPD

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ABSTRACT

Aim: The Objectives of our study were to study the clinical profile and microbiological etiology of AE-COPD.

Methods: It was a hospital-based cross-sectional study, conducted in a tertiary care center and included patients hospitalized with a principal diagnosis of AE-COPD. Diagnosis of COPD was based on the GOLD guidelines. Detailed history, physical examination, sputum microbiology and blood investigations were recorded for all patients. All statistical analyses were done using Epi info 7.2.

Results: Mean age of the patients was 66.9 years. Majority of the patients (66) were ex-smokers, 26 were current- and 8 were never-smokers. One-third of the patients were frequent exacerbators. Most common comorbidity was hypertension (25%) followed by diabetes (10%). Increased dyspnea was seen in all the patients, followed by increased quantity of sputum in 56. The most common clinical findings were use of accessory muscles of respiration in 92 patients, followed by crackles (84) and decreased breath sound intensity (62). Majority of the exacerbations (55%) were non-infectious, followed by 33% bacterial and 12% viral exacerbations. The most common isolated bacteria were Streptococcus pneumoniae (31%), Pseudomonas (27%) and Klebsiella (12%).

Conclusion: This study shows the common risk factors and clinical features presented by COPD patients hospitalized with severe exacerbation. Majority of the exacerbations were non-infectious, warranting further studies to determine the environmental factors. Although one-third of the exacerbations were bacterial, viruses were important etiological agents.

Keywords: AE-COPD, Etiology, Presentation, Pseudomonas, Viruses

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is the third most common cause of deaths and the seventh leading cause of disability-adjusted life-years (DALYs), globally.[1] In India also, prevalence of COPD is increasing. In 2016, COPD was the second most common cause of disease burden in India, contributing 8.7% of total mortality and 4.8% of total DALYs.[2, 3] Acute exacerbations of COPD (AE-COPD) are responsible for the majority of mortality as well as morbidity in a COPD patient. They are defined as an acute worsening of the respiratory symptoms resulting in an additional therapy.[4]AE-COPD are complex events that cause increased mucus production, airway inflammation and increased gas trapping; leading to increased breathlessness, increased sputum production and purulence. COPD exacerbations cause accelerated decline in lung function.[5] Although most of the exacerbations develop because of infections, others occur due to environmental causes. The most common organisms associated with the exacerbations are Haemophilus influenzae, Streptococcus pneumoniae and Moraxella catarrhalis. Around 40% of AE-COPD are associated with viral infections, rhinovirus being the most common of all.[6]

Although AE-COPD is a frequent reason of hospital visits, only a few studies have examined the etiologic factors in hospitalized patients with severe AE-COPD in our region. Also, there are only a few studies which have looked for viruses responsible for developing AE-COPD. This study is designed to study the clinical presentation, laboratory abnormalities, microbiological etiology and short-term outcomes in patients with COPD exacerbation requiring hospital admission. Knowing about the exacerbation causing bacteria and their antibiotic sensitivity is helpful to formulate the empirical antibiotic-strategies and

thereby decreasing the emergence of drug resistance. The primary objectives of this study are to study the clinical profile and microbiologic etiology of AE-COPD patients requiring hospital admission.

METHODS

The study was a hospital-based cross-sectional study conducted at the Department of Pulmonary Medicine and Department of Microbiology in a tertiary care hospital in North India, from July 2018 to June 2019. Approval of the Institutional Ethical Committee was taken.

Selection of cases

One hundred consecutive patients who attended Pulmonary Medicine OPD or Emergency Room and subsequently admitted in Pulmonary Medicine ward or Respiratory ICU with the principal diagnosis of AE-COPD were enrolled for the study after taking informed consent. The diagnosis of COPD was based on the GOLD guidelines.[7]

Patients hospitalized with a principal diagnosis of AE-COPD, age above 40 years and willing to take part in the study were included in the study. Patients with the previous diagnosis of bronchial asthma or neoplasia, immunosuppressed state and patient hospitalized within 1 month prior to the present admission were excluded from the study.

A detailed history from the patients was taken as per pre-designed proforma. Demographic and clinical data were collected including name, age, sex, address, level of education, socioeconomic status, smoking load (smoking index) and co-morbid medical conditions. The patient-reported history of prior exacerbations in preceding one year was recorded. Patients were categorized into the frequent exacerbator group including patients with two or more exacerbations during preceding 1 year and the infrequent exacerbator with <2 episodes of exacerbations during preceding 1 year.[8, 9]The patients were subjected to the detailed clinical examination, blood investigations, sputum microbiological examination and throat swab examination.

After collecting and assessing the quality of sputum, it was cultured on 5% sheep blood agar (for isolation of hemolytic organisms), chocolate agar (for Haemophilus species) and MacConkey's agar (for Gram-negative bacteria). The plates were then incubated for a period of 24 hours after which they were examined for bacterial growth. Bacterial growth was identified by colonial morphology and standard laboratory procedures. In case of no growth occurring on plates, a report of no organism grown on culture after 24 hours of incubation was given.

Throat swabs were collected from study subjects for presence of influenza A and B viruses by Reverse transcription polymerase chain reaction (RT-PCR), and those positive for influenza A viruses were further subtyped for A/H1N1pdm09, A/H3N2, and seasonal H1N1 using US Centers for Disease Control designed probes and primers.

The results were summarised in tables and percentages on MS Excel spreadsheet. Comparison of groups was done using t-test (numeric scale parameters) and Chi-square test (nominal parameters). Quantitative data was summarized as means ± Standard Deviation (SD). All the analyses were done using EPI Info version 7.2. A P-value of less than 0.05 was considered statistically significant.

RESULTS

The study included 100 patients of AE-COPD. The mean age of the patients was 66.96 years and 67 out of 100 were male patients. Of all patients, 33 were frequent exacerbators and 67 were infrequent exacerbators.

Table 1: Baseline characteristics, risk factors, comorbidities and symptomatology in the study group.

Characteristic	Cases
Age (years) (Mean±SD)	66.96±8.61
Sex (n=100)	
Male	67
Female	33
Smoking Status (n=100)	
Current Smokers	26
Former Smokers	66
Never Smokers	8
Smoking Index (Mean±SD)	
Male	480±307
Female	268±248
Risk Factors (N=100)	
Smoking	92
Indoor air pollution	81
History of TB	20
Smoking + History of TB	19
Indoor air pollution + History of TB	15
Co-morbidities (N=100)	
Hypertension	25
Diabetes Mellitus	10
Cardiac Illness	7
Symptoms (N=100)	
Dyspnea	100
Increased Volume of sputum	56
Increased Purulence of sputum	24
Orthopnea	42
Fever	46
Altered Sensorium	1
Inability to Complete Sentence while Walk	26
Upper Respiratory Symptoms	29

Table 2: Mean values of the blood investigations in the study group.

Investigation	Mean	SD
ABG		
pH	7.38	0.07
pO_2 (mmHg)	49.62	13.98
pCO_2 (mmHg)	50.09	15.03
HCO_3 (mmol/L)	26.74	7.30
Hemoglobin (g/dL)	16.59	2.95
TLC (thou/μL)	10.11	3.90
Platelet Counts (thou/ μL)	174.33	97.28
Blood Urea (mg/dL)	34.19	21.88
Serum Creatinine (mg/dL)	2.59	11.64
Serum Sodium (mmol/L)	136.11	6.81
Serum Potassium (mmol/L)	4.87	5.11
Serum Chloride (mmol/L)	96.04	11.59
Total Bilirubin (mg/dL)	2.57	13.51
Direct Bilirubin (mg/dL)	0.45	0.72
ALT (U/L)	86.53	229.93
AST (U/L)	100.50	289.87
ALP (U/L)	110.17	76.97
Total Proteins (g/dL)	6.60	0.67
Serum Albumin (g/dL)	3.40	0.47

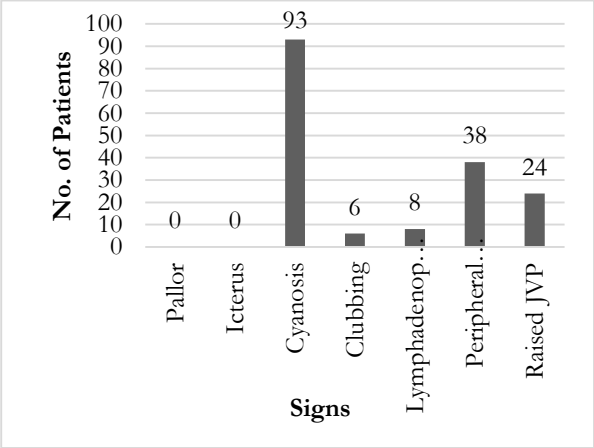

Fig. 1: General physical examination findings in the study group.

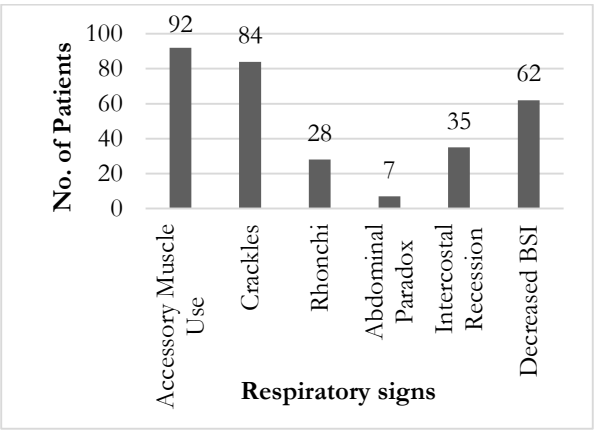

Fig 2: Respiratory examination findings in the study group.

The exposure to the tobacco smoke was reported by 92 patients with the mean smoking index of 480 in males and 268 in females. The exposure to indoor air pollution was present in 81 patients. The most common symptom was increased breathlessness, present in all study patients, followed by increased quantity of sputum in 56 patients. Other risk factors and symptoms are shown in Table 1.

On examination, 93 patients were cyanosed, and 38 patients had peripheral edema (Fig. 1). The most common findings in respiratory examination were use of accessory muscles of respiration in 92 patients, followed by crackles and decreased breath sound intensity (BSI) on auscultation in 84 and 62 patients respectively (Fig. 2). The mean values of the vitals were as follows: pulse rate 95.1 beats/min, respiratory rate 19.5 cycles/min, systolic BP 113.6 mmHg, diastolic BP 72.2 mmHg and oxygen saturation 66.3%. The blood investigations done in the study patients are shown in Table 2.

In this study, 55 patients had non-infectious exacerbations, 33 had bacterial and 12 patients had viral exacerbations. In bacterial exacerbations, most common isolated bacteria were Streptococcus pneumoniae in 10 patients, followed by Pseudomonas aeruginosa in 9 and Klebsiella pneumoniae in 4 patients (Fig. 3). Among viruses, 5 patients had H3N2 and 7 patients had H1N1 infections. In this study, non-invasive ventilation (NIV) was utilized by 33 patients, 24 got admitted to ICU and 17 were intubated. Total mortality in the study was 9 and readmission within 1 month was seen in 20 patients.

DISCUSSION

This hospital-based cross-sectional study describes the clinical profile, microbiological etiology and short-term outcomes of 100 patients of COPD, hospitalized with severe exacerbation of COPD to a tertiary care hospital. In our study, the mean age of the patients was 66.96 years, which is similar to the other studies done earlier.[10-12]In our study, male predominance was seen with 67% males compared to 33% female patients, which was similar to other studies conducted by Narayanagowda et al.[13] and Bashir et al.[14] Some other studies have shown up to 90% male preponderance in AE-COPD.[15, 16] It may be partly because smoking is more prevalent in males. This may also suggest poor access to healthcare by female COPD patients due to social taboos or financial constraints or due to self-negligence to COPD symptoms. In our study, 66% of patients were former smokers, 26% were current smokers and only 8% were never-smokers. In a study done by Gaude et al.[10] from 2008 to 2011, among patients of AE-COPD, 84.4% were current or former smokers, but in another study conducted by Narayanagowda et al,[13] there were 62.5% smokers. In our study, 81% of the patients were exposed to indoor air pollution.

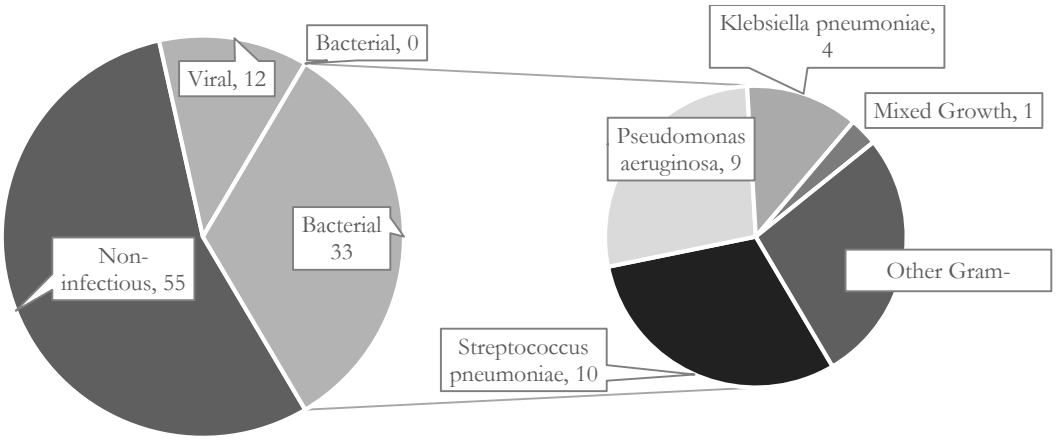

Fig 3. Etiological types of exacerbation in the study group.

The mean smoking index was significantly more in the males (480) than in the females (268) included in our study (P-value <0.01). The mean duration of COPD in our patients was 4.16 years. In our study, the most common comorbidity was hypertension (25%), followed by diabetes mellitus (10%) and cardiac illness (7%). Other studies have also reported hypertension to be the most common comorbidity in AE-COPD patients.[10, 14, 17, 18]All patients in our study had presented with the symptom of breathlessness as it is a cardinal symptom of COPD. Other symptoms were cough with increased sputum production, increased sputum purulence, fever etc. In the general-physical examination, our study documented cyanosis in 93% of the patients, followed by peripheral edema in 38% and raised JVP in 24% of the patients. Some patients also had lymphadenopathy (8%) and clubbing (6%). The mean BMI of the study patients was 20.55 kg/m^2 and 31% of the patients were underweight. The study by Gudagunti et al.[17] have found pedal edema in 18% patients, clubbing in 11% patients and mean BMI of 21.8 kg/m^2 in the COPD patients. The study by Pipliwal et al.[12] documented a mean BMI of 23.2 kg/m^2 in their patients. The majority of the exacerbations in the study patients were non-infectious (55%), followed by a bacterial exacerbation in 33% of the patients and viral exacerbation in 12% of the patients. But in our study, we tested only for influenza viruses thereby missing viral exacerbation caused by other viruses. A systemic review involving 19 studies have shown Rhino-/enteroviruses, Respiratory syncytial viruses and influenza viruses to be the most prevalent viruses with lower detection rates of parainfluenza and coronaviruses in AE-COPD.[19] Although our detection rate of viral exacerbations was close to that reported by Mohan et al,[20] i.e., 13.1%, other studies have shown higher detection rates of 19.7% by Koul et al,[18] 37% by McManus et al[21] and 56% by Rohde et al.[22]We might have missed the viral exacerbations caused by viruses other than influenza and have misclassified the same as non-infectious exacerbations, which is one of the limitations of the study. On subtyping, H3N2 was detected in 41.67% and H1N1 in 58.33% of the viral exacerbations in our patients.

We detected bacterial growth in 33% of the study patients, which was more than that reported by Mohan et al.[23] i.e., 21.6% in severe hospitalized AE-COPD patients. But some other studies have shown higher bacterial detection rates in the patients of AE-COPD. Narayanagowda et al.[13] have obtained bacterial growth in 41% of the patients, Gerard et al.[24]have detected bacterial growth in 42% of the patients and Chawla K et al.[25] have detected bacterial isolates in 50.94% of the hospitalized patients. It was observed that muco-purulent or purulent sputum gave better isolation of pathogens than the muco-salivary or mucoid sputum.

Among the culture-positive cases, the most common isolated bacteria were Streptococcus pneumoniae in 30.30%, followed by Pseudomonas aeruginosa in 27.27% and Klebsiella in 12.12% of the cases. In 27.27% of the culture-positive cases, growth of Gram-negative bacilli was obtained that could not be further classified, and mixed growth was obtained in 3.03% of the culture positive cases. Hence, in our study, Gram-negative bacilli outnumbered the growth of Gram-positive bacteria, which is in accordance with the other studies.[13, 15, 24, 25]Our findings were close to the findings obtained in a study done by Chawla K et al.[25]in which Pseudomonas aeruginosa was isolated in 25.92% and Klebsiella in 14.80% of the patients hospitalized with AE-COPD. Kulkarni et al.[15] also reported Pseudomonas aeruginosa in 26.7% of AE-COPD patients. As found in our study, Streptococcus pneumoniae was the single most common isolated bacteria in the studies conducted by Gerard et al.[24] and Mohan et al.[23]But most of the other studies have reported non-typeable Haemophilus influenzae, Moraxella catarrhalis, and Streptococcus pneumoniae as the predominant bac-

teria responsible for exacerbations in COPD patients.[26, 27]The use of over-the-counter oral antibiotics is very common in India. It is very likely that patients received antibiotics for some time before being brought to our hospital (being a tertiary care center) which could have eradicated the sensitive community acquired bacteria, thereby bringing down their contribution in our patients.

In our study, NIV was required by 33% of the patients, 24% got admitted to ICU and 17% were put on invasive mechanical ventilation (IMV). The figures were close to a study done by Agarwal et al.[28] which reported 22.8% of patients admitted to ICU and 17% put on IMV. A study done by Mohan et al.[20]reported a much higher number of patients (51.8%) requiring IMV.

CONCLUSION

This study shows the common risk factors, comorbidities and clinical features present in COPD patients, hospitalized with severe exacerbation in our hospital. Although one-third of the exacerbations had bacterial etiology, viruses were also important etiological agents and the routine use of influenza as well as pneumococcal vaccination should be strengthened in COPD patients. S. pneumoniae was the single most common isolated bacteria, but the most common group was formed by the Gram-negative bacilli. So, empirical antibiotic therapy should include coverage for both. Further studies are needed to determine the environmental factors causing AE-COPD as more than half exacerbations were non-infectious.

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