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Study the Pattern of Bacterial Infections to Formulate an Empirical Treatment for Patients Admitted with Acute Exacerbation of COPD

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ABSTRACT
The second most common cause of Non communicable disease (NCD) and related deaths in India. Age-specific prevalence of COPD increases rapidly after 30 years of onset. To study the pattern of bacterial infections to formulate an empirical treatment for patients admitted with acute exacerbation of COPD to our hospital. We had conducted a prospective observational study for a period of one year by recruiting 110 Patients of either gender, aged >18 years diagnosed and admitted for the management of acute exacerbation of COPD. Demographic detail, detailed past history and the drug history was noted. All the patients underwent X ray chest. Prevalence of gram negative organisms was statistically high compared to gram positive accounting for about 50.91% and 24.55% respectively. Among which the prevalence of Klebsiella was the highest with the prevalence of 32.14% of the gram negative organisms followed by Acinetobacter, Enterobacteriaceae and Moraxella species. Of all the gram positive cases, 48.15% were Streptococcus followed by 44.44% of Staphylococcus. Among the gram positive organisms streptococcus was highest. Prevalence of gram negative organisms was statistically high compared to gram positive, among which the prevalence of Klebsiella was the highest. Among the gram positive organisms streptococcus was highest.

INTRODUCTION

Chronic obstructive pulmonary disease-COPD is a progressive disease state characterised by limitations in airflow which is not fully reversible[1]. COPD reported to be the third leading cause of death worldwide. Patients will be presenting with features of progressive shortness of breath, wheezing, cough and expectoration. Exacerbations are acute and episodic worsening of the above respiratory symptoms[2]. COPD patients are known to be colonized with the potential respiratory pathogens and it is often difficult to identify the specific pathogen[3]. Bacteria are responsible for 60% of exacerbations followed by the viral infections accounting for about 30% of exacerbations but few PCR studies have shown that up to 40% of exacerbations in COPD are associated with viruses[3]. The most common bacteria implicated in COPD exacerbations are Streptococcus pneumoniae, Haemophilus influenzae and Moraxella catarrhal is. In addition, Mycoplasma pneumoniae or Chlamydia pneumoniae are found in 5-10% of exacerbations. Patients with AECOPD treated with antibiotics on empirical basis without sputum analysis so the effectiveness of treatment is uncertain due to emerging new strains and their resistant pattern[4]. Pulmonary rehabilitation therapy further improves exercise tolerance, dyspnea and hence the overall health status[5]. Nowadays most of the pathogens have been resistant to various conventional antimicrobial agents used in the treatment of COPD. Hence antibiotic regimen must be formulated at the institutional level.

MATERIALS AND METHODS

The cross-sectional study was conducted among all patients with Acute Exacerbation of Chronic Obstructive Pulmonary disease visiting at Departments of General Medicine , SDM Medical College, Dharwad. In association with Departments of Emergency Medicine and Pulmonology at SDM Medical College and Hospital, Dharwad. duration of study was September 2019-June2021

Inclusion Criteria: All admitted patients of >18 years of age diagnosed as Acute Exacerbation of COPD.

Exclusion Criteria:

- Patients having Bronchiectasis, Tuberculosis.
- Patients who are diagnosed with bronchogenic carcinoma.

Sample Size Calculation: Approximately 95 are the samples But we found110 cases of COPD exacerbation during our study period. Hence have recruited all the patients for better analysis.

Method of Sampling: Convenience sampling.

Data Collection: Data was collected from patients who satisfied the inclusion criteria, using a preformed questionnaire. Demographic details like name, age sex, address, date of admission, clinical data like complaints, personal history, past medical history, chest x-ray, examination findings and details of clinical diagnosis were noted. Blood investigation such as Haeamoglobin, TLC, GRBS, Blood urea and S.creatinine levels were noted.

Sample: Sputum-expectorated or induced.

Sample Collection: Sputum samples will be obtained from patients that are clinically diagnosed as acute exacerbation of chronic obstructive pulmonary disease. Patients will be instructed to collect sputum into a sterile wide mouth container with a screw cap. Deeply coughed sample and they we retold to brush their teeth and rinse their mouth with water, just before collecting the sample. Early morning sputum was collected under direct supervision and before any food intake. Samples taken to the laboratory within 1 hour of collection. Induced sputum-after patients inhale aerosolized droplets of 3% NACL for 10 minutes or until a strong cough reflex is induced. The samples will be transported to the department of microbiology SDM College and Hospital for analysis. Samples will belabeled and numbered after their receipt in the laboratory and processed by conventional methods.

Statistical Analysis: Cross-sectional study of all data will be entered in SPSS software and data will be analyzed using frequencies and percentage.

RESULTS AND DISCUSSIONS

After recruiting the demographic details and laboratory parameters, data was entered in Microsoft Excel and analyzed using suitable statistical tests and the analyzed data in SPSS software, IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. The results are tabulated and discussed as follows., Mean age of the recruited participants was 66.72±9.05 of which, 81.8% of them were aged >60 years and the rest 18.2% were ages less than 60 years. Out of 110 patients recruited,76(69.1%) were males and 34(30.9%) were females. Out of 110 patient srecruited, the majority of them were hypertensive with the prevalence of 39.1% of the overall population and 21 (19.1%) of them were Diabetes. 47(42.7%) of the study samples were chronic smokers. These patients had a significant correlation with COPD. 31.8%of the recruited study population were presented with hypoxia. Of the 110 recruited population, 32 (29.1%) of the patients were found to have total leucocyte count <11,000 and 78 (70.9%) patients with >11,000 cells/mm2

Majority of the recruited study population were found with increased CRP level with the incidence of 105 (95.5%). Majority of the recruited samples were found to have emphysematous changes in chest x ray. Whereas 72 patients with abnormal chest X-ray. Out of which, 51 (46.36%) of the overall population were presented with findings of emphysema and 21 (19.1%) were presented with pneumonia.

Table1: Frequency Distribution Of The Culture Positive Organisms

Organism	Total
Gram Negative	56(50.91%)
Gram Positive	27(24.55%)
Mixed Infection	4(3.64%)
Others	23(20.91%)

56 (50.91 %) of the recruited patients were found to be having gram negative infection followed by 27 (24.55%) with gram positive and 4 (3.64%) had mixed infection. Whereas rest 23 (20.91%) had infections other than these.

Table2: Distribution of Gram Negative Organism

Gramnegative organisms	56	50.91%
Klebsiellapneumoniae	18	32.14%
Acinetobacter	10	17.86%
Enterobacteriaceae	10	17.86%
Moraxella	10	17.86%
Pseudomonasaeruginosa	8	14.29%

Further analysis of the gram negative organism showed 50.91% of the isolate being positive for Klebsiellapneumoniae followed by Acinetobacter, entero-bacteriaceaeand moraxella. Pseudomonas was found among 14.29% of the isolates.

Table 3: Distribution of Gram Positive Organism

Grampositive organisms	27	24.55%
Streptococcus	13	48.15%
Staphylococcus	12	44.44%
Enterococcus	2	7.41%

On analyzing the number of gram positive isolates, 13/27 (48.15%) were positive for streptococcus followed by 12/27 (44.44%) for staphylococcus and the rest 7.41%were tested positive enterococcus

Table 4:Mixed Infection

Mixed organisms	4	3.64%
E.coli, klebsiellapneumoniae	1	25.00%
Pseudomonasaeruginosa, klebsiella Pneumoniae	2	50.00%
Staphylococcus, candida	1	25.00%

Out off our isolates that grew multiple organisms, two isolates had pseudomonas aeruginosa+klebsiella and E.coli+klebsiella. >50% of the samples of 23 did not show any growth whereas 30.43% and 17.39% had shown candida and oral commensals respectively. Out of 21 isolates obtained from the DM patients, 18 (85.7%) had grown the organisms and 3 (14.2%) had shown the growth other than gram positive and negative.

Of the isolates tested from 21diabetic patients, 18 (85.7%) of them had shown significant growth. Among these 77.7% grew gram negative whereas 22.2% withdraw positive.

Table 5: Distribution of Gram Negative Organisms Among T2DM

Gramnegative organisms	14	
Acinetobacter	5	35.7%
E-coli	4	28.5%
Pseudomonasaeruginosa	3	21.4%
Klebsiellapneumoniae	1	7.14%
Moraxella	1	7.14%

Overall 14 isolates obtained from the gram negative organisms. Of which 5 isolates showed the acinetobacter.

Table6: Distribution of Gram Positive Organisms Among T2DM

Grampositive organisms	4	
Staphylococcus	3	75.00%
Enterococcus	1	25.00%

Four isolates had grown gram positiveorganisms of which 3(75%) of the isolates were Staphylococcus and 1 (25%) was enterococcus. Three isolates from the DM patients showed other than gram positive and negative organisms. 2 (66.6%) were oral commensals and 1 (33.3%) was candida species.

Table7: Distribution of Gram Positive and Negative Organisms Among HTN

HTN	43	
Gram negative	28	65.12%
Gram positive	8	18.60%
Others	7	16.28%

In hypertension patients also the commonest organism grown was gram negative with the frequency of 65.12% (28) followed by 18.6% had gram positive. Whereas rest 16.28% grew other than gram positive and negative.

Table 8:Distribution of Gram Negative Organisms Among HTN

Gram negative organisms	28	
Klebsiella pneumoniae	9	32.14%
Enterobacteriaceae	5	17.86%
Moraxella	5	17.86%
Pseudomonas aeruginosa	5	17.86%
Acinetobacter	4	14.29%

Out of 43 gram negative organisms were 28, 9 were klebsiella, five each were Enterobacteriaceae, Moraxella and Pseudomonas aeruginosa. Whereas 4 gram negative isolates were found to be Acinetobacter. Out of 8gram positive isolates, 4(50%) of them were staphylococcus, 3 (37.5%) were streptococcus and the rest one isolate was Enterococcus. COPD has been one of the leading cause of mortality and morbidity both immediate and long term diseases. The episodes of exacerbation increase the burden of the disease and have been the major reason for hospitalizations and intensive care admissions. Most exacerbations are commonly

associated with infective triggers either viral or bacterial, although non-infective triggers such as air pollution and smoking are also important factors[1,6]. Hence the present study was conducted to analyze the distribution and association of demographic profile with the risk of AECOPD. And to analyze the microbiological factors and sensitivity pattern among the patients admitted with AECOPD. Mean age of the recruited participants in our study was 66.72±9.05 of which, 81.8% of them were aged >60 years. Similar to our study Priya N *et al* also presented the average age of their patients 66.5±8.5 years[7]. In our study, the prevalence of male patients was high with the prevalence of 76 (69.1%) the rest 34 (30.9%) samples being females. Similar to our findings, Sharma P *et al* also observed a 61:19 of Male: Female ratio in their study[8]. Prevalence of male patients in Priya N *et al* was also 79.8%[7]. This might be because of lack of immunity in elderly patients and the physiological changes with respect to local immune factors. Majority of males were found with substance abuse such as smoking cigarettes/beedi or chewing tobacco, which were the highest risk factors for acute exacerbation and also leading to secondary infections. In our study, the majority of the study samples were hypertensive with the prevalence of39.1% and 21(19.1%) are type 2 diabetes mellitus. Lee H *et al* and Mannino DM *et al* in their individual studies have reported HTN being the independent risk factor for COPD, with the commonest finding among their study samples[9,10]. Mannino *et al* also described that the patients with comorbidities were associated with a higher prevalence of hospitalisation and also higher mortality[10]. In our study, 47 (42.7%) of the study samples were found to be chronic smokers and these have a statistically significant association with COPD. The most important finding in the study by Priya *et al* was that male patients were chronic smokers. And the majority of female participants in their study had exposure to passive smoking either by biomass/ firewood exposure while cooking or occupational exposure[7]. 31.8% of the recruited study population in our study were presented with <88% of oxygen saturation and the rest with >88%. Of the 110 recruited population in our study, 32 (29.1%) were found to have the total leucocyte count <11,000 a78 (70.9%) patients with >11,000 cells/mm^2. Majority of the recruited study population in our study were found with increased CRP level with the incidence of 105 (95.5%), as CRP is one of the acute phase reactants. On analysing the radiological findings of our cases, we found that the majority of recruited patients were found to have COPD changes in chest x-ray. 38 of the having normal chest x-ray and remaining 21 of them had pneumonia. In our study the majority of patients, 56 (50.91%) of the recruited patients were found to be having gram negative infection followed by 27 (24.55%) with gram positive and 4(3.64%) had mixed infection. Out of 56 gram negative isolates grown, the majority of them were Klebsiella pneumonia followed by Acinetobacter, entero-bacteriaceae and moraxella Pseudomonas was found among 14.29% of the isolates. Streptococcus and staphylococcus were the commonest among the gram positive growth. Same as our findings, Sharma P *et al* also observed Gram Negative Bacteria(GNB) as the predominant etiological agent responsible for AECOPD in 35.7% patients[8]. But individually, Streptococcus pneumoniae was the commonest etiological agent in their study. Whereas in Sobhy KE *et al,* the commonest isolate found was Klebsiella and even in severe COPD[11]. Same as our findings, Raveendra KR *et al* also observed gram negative organisms as the commonest with higher prevalence of Klebsiella (20%)[12].

CONCLUSIONS

Based on the above observation we conclude that frequency of the AECOPD is higher among the patients aged >60 years. Though there was higher predominance of male patients, there is no significant difference found in the pattern of organism and sensitivity with respect to age or gender. COPD patients with a history of chronic smoking and the other comorbidities such as DM and HTN are more prone to develop acute exacerbation than the patients without comorbid conditions. Prevalence of gram negative organisms was statistically high compared to gram positive, among which the prevalence of Klebsiella was the highest. Among the gram positive organisms streptococcus was highest.

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