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Bacterial Pathogens and their Antibiogram in Acute Exacerbation of Chronic Obstructive Pulmonary Disease.

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ABSTRACT

Acute Exacerbations of Chronic Obstructive Disease (AECOPD), a common preventable and treatable condition, causes great impact on individual health and health care system and contribute to irreversible progression of disease. Knowledge of possible bacterial etiology and their antibiogram is essential for effective antibiotic treatment and reducing emergence of antibiotic resistance. In this cross-sectional study, sputum culture was done for 100 clinically diagnosed cases of AECOPD. The bacterial pathogens were identified, isolated and their antibiogram was determined. Sputum culture for bacterial pathogens was positive in 41 cases (41%). Gram negative isolates (87.8%) were more common than Gram positive isolates. (12.2%) *Pseudomonas aeruginosa* was the commonest isolate (46.34%). Most Gram-negative isolates were multi drug resistant. The most sensitive antibiotics were Amikacin (90%) and the Carbapenems (89.5%).17% of the patients developed Cor Pulmonale and 6% of the patients progressed to Respiratory failure. Amoxycillin-Clavulanate, one of the most commonly used empirical antibiotic to treat AECOPD was tested resistant by most of the isolates. The present study has shown that bacterial pathogens responsible for AECOPD is different in our country from that of western countries and so is their antibiotic sensitivity pattern. Hence sputum culture and sensitivity is advised in all cases of AECOPD.
Keywords: AECOPD, sputum, bacterial pathogens, antibiogram

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common preventable and treatable condition. It is characterized by a persistent restriction of ventilation that is frequently progressive and is associated with an elevated chronic inflammatory response in the lungs and airways in response to harmful particles or gases [1]. Chronic obstructive pulmonary disease (COPD) is the fourth most prevalent cause of mortality worldwide, accounting for approximately 5% of all global fatalities in 2021 with 3.5 million fatalities. Nearly 90% of fatalities from COPD in individuals under the age of 70 occur in low- and middle-income (LMIC) countries. In terms of disability-adjusted life years, COPD is the ninth most prevalent cause of ill health worldwide, as per the World Health Organization. The United Nations 2030 Agenda for Sustainable Development and the WHO Global Action Plan for the Prevention and Control of Non-communicable Diseases (NCDs) both encompass COPD.

An acute episode of COPD exacerbation is characterized by a deterioration of the patient's respiratory symptoms that exceeds the typical daily fluctuations and requires a medication adjustment [1].

The rate at which exacerbations occur varies greatly between patients. Acute exacerbations form the major component of economic burden of COPD and leads to indirect costs because of days lost from work [2]. It causes great impact on individual health and health care system and contribute to irreversible progression of disease [3]. Therefore, timely institution of correct management is imperative for better prognosis of disease.

Up to three-fourths of Acute Exacerbation of COPD (AECOPD) episodes are caused by an infection. Isolation of pathogens in lower respiratory tract secretions [4] provides evidence of a bacterial infection as the inciting event for AECOPD. The number of bacterial isolates in acute exacerbations of COPD can vary based on geographic location, the prevalence of bacteria in the community and hospital setting in a given area, and the use of antibiotics both in the hospital and in the community [5].

The usefulness of empirical antibiotics in treating a significant number of patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease is questionable due to the rise of resistant strains.

To effectively treat bacteria and prevent the evolution of antibiotic resistance, it is crucial to understand their potential etiology and pattern of antibiotic sensitivity [6, 7].

Thus, the goal of the current study is to determine which bacterial pathogens are responsible for acute exacerbations of chronic obstructive pulmonary disease in our environments, as well as to investigate the pattern of antibiotic susceptibility of these pathogens.

MATERIALS AND METHODS

For nine months, from January to September, 100 patients with clinically diagnosed in-patient cases of AECOPD from the departments of General medicine and Pulmonary medicine participated in this prospective cross-sectional study, which was carried out in the department of Microbiology at Government Medical College in Kottayam, Kerala. The Institutional Ethics Committee approved the study procedure, and informed consent was obtained. Using the formula 4PQ/d2, the sample size was determined. A total of 100 samples were gathered, with an initial estimate of 81 patients.

Inclusion criteria

Sputum samples from patients with any two of the following symptoms who have been clinically diagnosed with chronic obstructive pulmonary disease.

- Increase in cough
- Increase in purulence and / or volume of expectoration
- Increase in severity of dyspnoea
- Fever and leucocytosis

Exclusion criteria

- Patients with Pulmonary Tuberculosis

Data collection

One hundred instances in all were examined. Prior to sample collection, the patient's information was put into the proforma and consent was obtained. Co-morbidities, the history of hospitalization, the frequency of exacerbations, the history of the current illness, and the use of antibiotics during the previous four weeks were recorded. Additionally gathered were past smoking history, work history, and any history of indoor air pollution exposure.

Sample collection

The patient was instructed to rinse their mouth twice with plain water before collecting deeply expectorated sputum samples (ideally 2 per patient) in a sterile container. This should be done preferably on the day of arrival, prior to getting antibiotics in this hospital. The containers containing the samples were appropriately labeled and then brought to the lab.

Microscopic examination of sputum

Microscopic analysis was used to determine the sputum quality. The region of maximum purulence was studied by analyzing a Gram-stained smear . Sputum was microscopically evaluated using Bartlett's grading system.

A sputum sample was deemed unfit if its final score was zero or below. We eliminated any specimens that were not appropriate and gathered a new one. To further rule out pulmonary tuberculosis, all sputum samples were acid fast stained using Ziehl Neelsen's staining. Sputum samples that met Bartlett's criteria were then subjected to further processing.

Sample processing

Sheep Blood agar, Chocolate agar, Mac Conkey agar, and Tryptic protein digest agar supplemented with blood were inoculated directly with quality certified samples. Afterwards, Dithiothreitol was used to homogenize each sample. To the sputum, we added 0.1% Dithiothreitol in an equivalent amount, mixed well, and then incubated it at 37 ºC for 15 minutes [8]. Sheep Blood, Chocolate, Mac Conkey, and Tryptic protein digest agars were subsequently inoculated with homogenized materials. A temperature of 37º C and 5% carbon dioxide were used to incubate the plates. Following 48 hours of incubation, the plates were analyzed using established procedures for pathogen identification, following an overnight incubation period [9].

Identification of the Bacterial Pathogen

The cultures were analyzed after 18 to 24 hours and after 48 hours. The identification of bacterial pathogens was conducted using staining, cultural, and biochemical features using standard laboratory protocols [9-11].

Antibiotic Sensitivity Testing

Antibiotic sensitivity testing of bacterial isolates were conducted using Kirby Bauer and Stokes disc diffusion technique, VITEK-2 system was also used. The antibiotic discs were chosen based on the organism isolated following CLSI recommendations. [12].

Detection of Resistance

- Following accepted standards, ESBL, Amp C Beta Lactamases and Carbapenemases were identified [12].

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Statistical analysis

The data was entered into the Microsoft Office Excel and analysis conducted using Statistical Package for Social Sciences (SPSS) version 22 and the findings were assembled in tabular and graphical representation using Microsoft Word and Microsoft Excel.

RESULTS

The following results were obtained after 100 sputum samples from patients experiencing an acute exacerbation of Chronic Obstructive Pulmonary Disease were collected and processed in accordance with the inclusion and exclusion criteria:

Table 1: Distribution of study sample based on age group.

Age In Years	Number Of Cases	Percentage
41- 50	08	08%
51-60	27	27%
61-70	40	40%
71-80	21	21%
81-90	04	04%
Total	100	100%

Figure 1: Distribution of study sample based on gender.

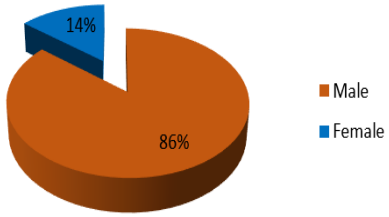

Table 2: Distribution of study sample based on clinical presentation.

Symptom	Number Of Cases	Percentage
Increased breathlessness	100	100%
Increased sputum production	67	67%
Increased cough	60	60%
Fever	22	22%
Total	100	100%

Table 3: Distribution of study sample based on frequency of exacerbations.

Frequency Of Exacerbation	Number Of Cases	Percentage
1-2/year	38	38%
2-3/year	53	53%
>3/year	09	09%
Total	100	100%

Figure 2: Common Co-morbidities associated with AECOPD in the study sample.

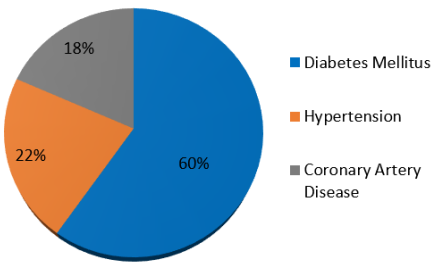

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Table 4: Association of Exposure to particles as a risk factor in AECOPD.

Type Of Exposure	Number Of Cases	Percentage
Active smoking	69	69%
Passive smoking	06	06%
Occupational exposure	06	06%
Active smoking &Occupational exposure	14	14%
Passive smoking and occupational exposure	05	05%
Total	100	100%

Table 5: Distribution of study sample based on treatment history previous one month.

Treatment Received In	Number Of Cases	Percentage
Out -Patient Department	35	35%
In-Patient Department	44	44%
No Treatment	21	21%
Total	100	100%

Table 6: Distribution of study sample based on Macroscopy of sputum sample.

Macroscopy	Number Of Cases	Percentage
Mucoid	73	73%
Mucopurrulent	25	25%
Purrulent	02	02%
Total	100	100%

Table 7: Distribution of study sample based on culture result for bacterial pathogen.

Culture Result	Number Of Cases	Percentage
Culture negative	59	59%
Culture positive	41	41%
Total	100	100%

Table 8: Culture positivity based on homogenization with Dithiothreitol.

Mode Of Processing	Number Of Culture Positives	Percentage
Before homogenization	25	60.9%
After homogenization	16	39.1%
Total	41	100%

Figure 2: Nature of isolates.

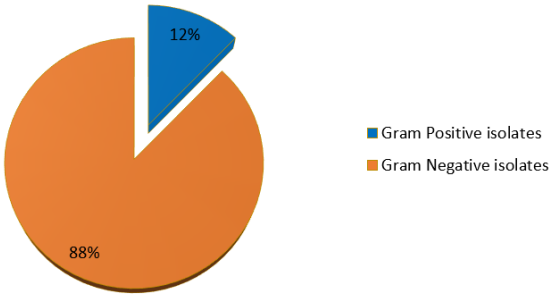

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Table 9: Distribution of study sample based on Bacterial profile of AECOPD.

Isolate	Number Of Isolate	Percentage
Pseudomonas aeruginosa	19	46.34%
Klebsiella pneumoniae	09	21.95%
Streptococcus pneumoniae	05	12.20%
Acinetobacter baumanii	04	09.76%
Escherichia coli	03	07.31%
Burkholderia cepacia complex	01	02.44%
Total	41	100%

Table 10: Antibiotic sensitivity pattern of *Streptococcus pneumoniae.*

Antibiotic	Number Of Sensitive Strains	Percentage
Penicillin	05	100%
Ampicillin	05	100%
Erythromycin	05	100%
First generation Cephalosporin	05	100%
Vancomycin	05	100%
Trimethoprim-sulfamethoxazole	05	100%
Third generation cephalosporin	05	100%
Amoxycillin-clavulanate	05	100%
Fourth generation Cephalosporin	05	100%
Meropenem	05	100%

Table 11: Antibiotic Sensitivity pattern of Gram-Negative Isolates.

Antibiotic	*P. aeruginosa*	*Klebsiella pneumoniae*	*Acinetobacter baumanii*	*E. coli*	*Burkholderia cepacia complex*
Ampicillin	NT	0	NT	0	NT
Gentamicin	06 (31.6%)	06 (66.7%)	01 (25%)	02 (66.7%)	NT
First generation cephalosporin	NT	03 (33.3%)	NT	0	NT
Amikacin	15 (78.9%)	09 (100%)	01 (25%)	03 (100%)	NT
Third generation Cephalosporin	17 (89.5%)	04 (44.4%)	0	01 (33.3%)	01 (100%)
Trimethoprim-sulfamethoxazole	NT	07 (77.8%)	02 (50%)	02 (66.7%)	01 (100%)
Ciprofloxacin	15 (78.9%)	05 (55.6%)	01 (25%)	03 (100%)	01 (100%)
Amoxycillin-Clavulanate	NT	04 (44.4%)	NT	01 (33.3%)	NT
Piperacillin-Tazobactam	18 (94.7%)	06 (66.7%)	01 (25%)	03 (100%)	NT
Meropenem	17 (89.5%)	08 (88.9%)	03 (75%)	02 (66.7%)	01 (100%)
Imipenem	18 (94.7%)	09 (100%)	03 (75%)	02 (66.7%)	NT
Colistin	19 (100%)	NT	04 (100%)	NT	NT
Fourth generation cephalosporin	18 (94.7%)	07 (77.8%)	02 (50%)	03 (100%)	NT

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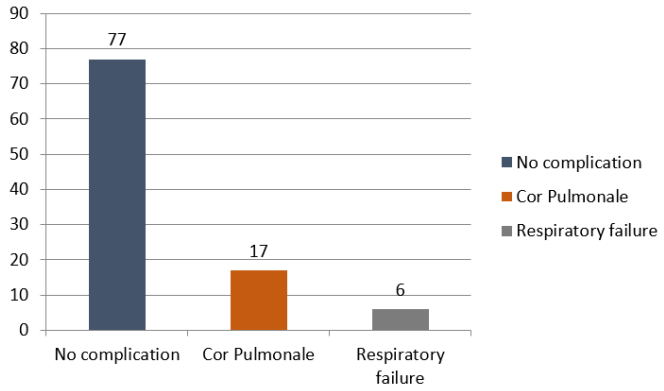
Table 12: Nature of resistance enzymes in Multi Drug Resistant Isolates.

ENZYME	*E. coli*	*Klebsiella pneumoniae*	*Pseudomonas aeruginosa*
Beta Lactamases	01 (50%)	03 (60%)	NT
Carbapenemases	01(50%)	01 (100%)	01(50%)

Figure 3: Incidence of complications.



DISCUSSION

The study was performed to examine bacterial pathogens and their antibiogram in acute exacerbations of Chronic Obstructive Pulmonary Disease at Government Medical College, Kottayam, for a duration of 9 months. One hundred cases were analyzed, yielding six isolates from forty-one culture-positive samples.

The study encompassed participants aged 42 to 88 years, revealing that Acute Exacerbation of Chronic Obstructive Pulmonary Disease was most frequent in the 61-70 age group (40%), followed by the 51-60 age group (27%) [13]. According to several investigations, including the current one, the incidence of AECOPD was somewhat typical after 40 years. The likely explanation might be manifestation of declining host defenses at the bronchial mucosal level in individuals with severe lung disease [14, 15]. These patients had severe lung disease due to the normal decline in lung function associated with aging, exacerbated by cumulative damage from smoking and other comorbid disorders [15]. In the current study, males constituted 86% while females accounted for 14% of the participants. The study's finding of a male predominance over female patients can be attributed to the greater mobility of males in our nation, resulting in increased exposure to the external world. Furthermore, smoking behaviors are more prevalent in males, which is a contributing factor to the development of COPD [13].

Examining the clinical presentation pattern, the current study found that among the patients with AECOPD getting admission in this hospital, the most often occurring symptom was increased breathlessness (100%) which was linked with either increased sputum generation (67%) or increased cough (60%). Fever was present only in 22% of cases. Furthermore, showing a low frequency of fever among patients with AECOPD (16.7%), is the research by Ko et al [16]. The study analyzed the frequency of exacerbations among the samples, revealing that 53% experienced 2-3 episodes annually necessitating treatment, 38% had 1-2 episodes per year, and 9% encountered more than 3 exacerbations annually. However, as noted by Seemungal et al., depending on patients' recollection of exacerbations may not be as precise as active surveillance [17]. The most often occurring co morbidities linked to AECOPD in the research sample were also investigated; 52% of individuals had diabetes mellitus, Hypertension was present in 19% and coronary artery disease in 16% of cases. This study examined the statistically negligible link between diabetes mellitus and cultural positivism. Baker et al. note that it is unknown if hyperglycemia directly causes bad outcomes from COPD exacerbations or serves as a marker for additional negative prognostic variables such treatment variation, comorbidities or degree of acute illness (18). Examining the treatment history of the study sample over the past one month prior to the present hospital admission, it was found that 79% of the patients had received prior treatment with antibiotics elsewhere, of which 44% had received In-patient treatment with Intravenous antibiotics whilst 35% received treatment on Out-

patient basis. Most of the instances lacked the specifics of the former antibiotics consumed. Since this hospital environment is a tertiary care, referral facility, the larger percentage of previously treated cases makes sense and consequently it was unable to eliminate the previously treated cases as done in some research. But in the current investigation, the samples were gathered on the day of admission prior to the starting antibiotics in the institution.

Five percent of the patients were at risk to both occupational exposure and passive smoking; sixty-nine percent of the patients were active smokers or ex-smoking, six percent was exposed to passive smoking, fourteen percent had both occupational exposure and active smoking.

Of the 100 samples examined, 12.2% were gram positive isolates and 87.8% were Gram negative isolates; 41% of the samples were culture positive. This is in line with research by Rakesh et al [14] in India with a culture positivity of 42% and by Cuklc et al. in Bosnia with a culture positivity of 41%. Nature of sputum, timing of collecting, past antibiotic usage all determine culture positivity. Consequently, the fact that 79% of the patients had past treatment would have affected the outcome of the cultural analysis.

As in the present study, Chawla et al [13], Viswambhar et al [5], Shahnawaz et al [20], Surinder et al [21] likewise reported Pseudomonas aeruginosa as the most often occurring bacterial pathogen in AECOPD. Higher incidence of Pseudomonas aeruginosa in chronic lung diseases has been documented in various investigations. In spite of utilizing Tryptic Protein digest agar for selective isolation, the present investigation revealed no isolates of Haemophilus influenzae. It may have happened because of seasonal variations or past antibiotic usage [14, 19, 20]. Most Western research show that it is a prevalent pathogen. This is in line with practically all of the Indian investigations, though, which suggests that bacterial flora causing AECOPD is unique in our nation compared to others.

Furthermore, investigated in great depth were the isolates' antibiotic sensitivity patterns. A number of studies in literature indicate gradual increase in the emergence of antibiotic resistant microorganisms in COPD. Most of the isolates acquired in the current work were resistant to many drugs. This is in accordance from the worldwide estimates of antibiotic resistance in microorganisms. In this institution, the two often used empirical antibiotics for the treatment of AECOPD were Azithromycin and Amoxycillin-clavulanate. In the current work, however, Amoxycillin-Clavulanate have shown a significant rate of resistance. In this investigation, most of the first line antibiotics proved resistant. The Carbapenems and Amikacin were the most delicate antibiotics. This is in accordance with Raakhee et al.'s research [22].

Six percent of participants in the present research suffered Type II respiratory failure and seventeen percent developed Cor Pulmonale. In 77%, there were no complications, where clinical improvement was seen following appropriate antibiotic therapy.

Limitations of the Study

The study period was for 9 months; hence it was impossible to investigate the month wise distribution of the COPD aggravation throughout a year. In the current work, microbiological sampling made use of spontaneously expectorated sputum. Therefore, in a few dyspnoeic and unwell patients,collection of sputum on the day of arrival, prior to starting antibiotic at this hospital proved challenging. By collecting the sample bronchoscopically, might help to raise the accuracy. Furthermore, the role of Atypical bacteria could not be studied.

CONCLUSION

More common in men, smokers, and older age groups, Chronic Obstructive Pulmonary Disease is a main cause of illness and death worldwide. Simple tool for investigating the etiology and sensitivity pattern of bacteria in Acute Exacerbation of COPD is sputum culture.

In this investigation, Gram negative microbes were the most often occurring organism aggravating COPD. Pseudomonas aeruginosa was the most common isolate among Gram negative organisms isolated, followed by Klebsiella pneumoniae. In this work, homogenization of a sputum sample enhanced culture sensitivity. Therefore, homogenisation of the sputum samples before culture can help to enhance the outcomes of the culture.

For the treatment of AECOPD in this institution, Amoxycillin-clavulanate was the most often emprically administered antibiotic. In the present work, however, Amoxycillin-Clavulanate revealed a significant incidence of resistance among the susceptible isolates Also it is ineffective against *Pseudomonas aeruginosa* which was the most common isolate in this study. This emphasizes that the clinician should be aware of the emerging resistance to a widely used antibiotic and the need to send sputum for culture and sensitivity before empirical antibiotic treatment.

In conclusion, current research and few previous Indian investigations have revealed that bacterial infections causing AECOPD differ in our nation from those of western nations and thus also is their antibiotic sensitivity pattern. Sputum culture and sensitivity are therefore indicated in all patients of AECOPD.

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