

Original Research Article

Study of microbial pattern and antibiotic sensitivity pattern in hospitalised acute exacerbation of COPD patients

Raveendra K. R., Devapriya Rejeev*, Nandan Kodur

Department of Medicine, Bangalore Medical College and Research Institute, Bangalore, Karnataka, India

Received: 10 July 2019

Accepted: 03 August 2019

***Correspondence:**

Dr. Devapriya Rejeev,

E-mail: priya.snid@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Most of the acute exacerbations of COPD are preventable and curable. More than 50% of them are infectious in nature and strain of the pathogen causing them is quite variable from place to place and often determines the severity of exacerbation. Antibiotic resistance has created a bigger challenge for the treating physicians to have a better treatment outcome. Our objective was to study the bacterial profile and antibiotic sensitivity pattern in all acute exacerbation of hospitalized COPD patients.

Methods: All patients admitted for COPD exacerbation were evaluated for their sputum culture and sensitivity and followed up.

Results: Totally 148 patients were included in the study and organisms were isolated 72 patients. Important organisms isolated were Klebsiella (20), Pseudomonas (16), Streptococci (8), Staphylococcus aureus (8), MTB (4) etc. Many MDR strains were noted. Resistance to newer antibiotics were also noted. 64 patients out of 148 required a change in antibiotic (40 in culture positive group, 24 in culture negative group) and there were 12 deaths noted in study. Mortality and morbidity were more in culture negative group and in those who had MDR strains.

Conclusions: Gradual shift to gram negative bacilli was observed in infective exacerbation of COPD. Multiple resistant strains were noted and often responsible for poor recovery. Early diagnosis and proper antibiotic selection is the key for a good treatment outcome.

Keywords: Antibiotic resistance, COPD, Infective exacerbation, MDR strains

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common respiratory disease which is characterized by chronic progressive inflammation of the airways and the lung parenchyma.¹ In 2010 WHO declared COPD as the third cause of death globally.² The incidence and prevalence is fast increasing globally and more deaths occurred in India and other low and middle income countries.³ Acute exacerbation is a major event and is often triggered by infections (viral, bacterial) and often non infective agents like air pollution.⁴ Each exacerbation can worsen the lung function and quality of life in COPD

patients.⁵ 30% of the patients having acute exacerbation of COPD have co-morbid infections like bacteria and viruses and often require ICU support.⁶ Cigarette smoking and bacterial colonization modify the airways into a pro inflammatory state and induce hyper reactivity state, often as acute exacerbation. Patients with reduced lung function (FEV1<50%) have six fold higher risk of exacerbation by *H. influenzae* and *P. aeruginosa*.⁷ Age of the patient, presence of co-morbid conditions, strain of the bacterial pathogen, emergence of multi drug resistant pathogens contribute to the severity of exacerbation and treatment outcome. Hence the present study was planned to evaluate the patients admitted with acute exacerbation

of COPD for microbial pattern and their sensitivity pattern to antibiotics.

Aims of the study

- To study the microbial (bacterial) profile in patients admitted for acute exacerbation of COPD.
- To study the microbial sensitivity pattern to different antibiotics.

METHODS

This study was designed as a cross sectional study conducted at Victoria hospital, a tertiary care centre attached to Bangalore Medical College and Research Institute from June 2017 to May 2018 for a period of one year. A total of 168 patients were hospitalised for acute exacerbation of COPD admitted under medicine department were screened and 148 patients were enrolled in the study. All the patients were evaluated with spirometry, sputum examination (gram staining, culture sensitivity and AFB staining), radiological tests (chest X-ray, CT Chest) and other protocol investigations.

All patients were treated with empirical antibiotics in the beginning and later switched over to the appropriate antibiotics according to the culture and sensitivity report. Symptomatic and supportive care was given including bronchodilator therapy and nebulisation. Co- morbid medical conditions were treated appropriately and patients requiring ventilator support were shifted and treated in the medical ICU. Patients were monitored throughout for vitals, investigations and treatment outcome.

RESULTS

A total of 148 patients (males 124, females 24) were included in the study. Majority of the patients belonged to the age group of 50 -70 years (83.78%). Cough (94.59%), Breathlessness (97.2%), Fever (89.18%), chest discomfort (59.45%) were the most common symptoms. Most of the patients have COPD more than 10 years and on regular treatment with regular follow up with their consultants (59.45%). History of smoking was observed in 75% of male COPD patients ,out of which 67.77% are current smokers. No female patients were current smokers but 50% of them are passive smokers and history of exposure to biomass fuel was noted in 25% of the patients .Important co-morbid conditions were diabetes (18.91%), hypertension (21.62%), IHD (8.1%), old PTB (2.7%), Anemia (10.81%), HIV (1.3%). Of the 148 patients 59.45% of the patients were regular users of inhalers and 50% of them were subjected to spirometry at least once in the last one year. 28.37% of the patients have been hospitalized repeatedly more than three times in last one year for the same acute exacerbations. 43.24% of the patients have been exposed to different antibiotics more than three times in a year and 16.21% of the

patients have history of antibiotic abuse (self-antibiotic use >3 times a year).

Organisms were isolated through sputum culture in 72 patients (48.64%) and common organisms were *Klebsiella*(20), *Pseudomonas*(16), *Streptococcus pneumoniae*(8), *Staphylococcus aureus*(8) other streptococcus group (4), *Acinetobacter*(4), MTB(4), *E. coli*(2) and others in 6 patients. All patients were started with antibiotics, empirically, Ceftriaxone(60), Cefotaxime+Sulbactam(12), Augmentin(10), Ciprofloxacin(14), Piperacillin(24), Meropenam(6), Ciprofloxacin+ Gentamycin 10), Azithromycin+ Cefotaxime(12).

There were 64 out of the 148 patients required a change of antibiotic after culture sensitivity report. Metronidazole was used in some patients with suspected anaerobic infection. Finally, one antibiotic was used in 60 patients, 2 in 52 patients and 3 in 28 patients and more than three in 8 patients. 40 patients required a change in antibiotic in the culture positive group (72) and 24 patients among the culture negative group (68). Culture sensitivity could not be done in 8 patients. Sputum for AFB positive patients were later started later on ATT under RNTCP. Twelve patients (8 from culture negative groups) required ICU support. Average duration of stay was 7 to 14 days and prolonged hospitalization was noted among the patients with co-morbid conditions, culture negative group and in elderly population.

There were 12 death noted in this study and cause of death were acute respiratory failure with sepsis (6) Diabetic Keto Acidosis (2), MODS (2), Acute Myocardial Infarction (1) and Acute Renal Failure (1). Four deaths were noted in culture positive groups and 8 deaths in culture negative group.

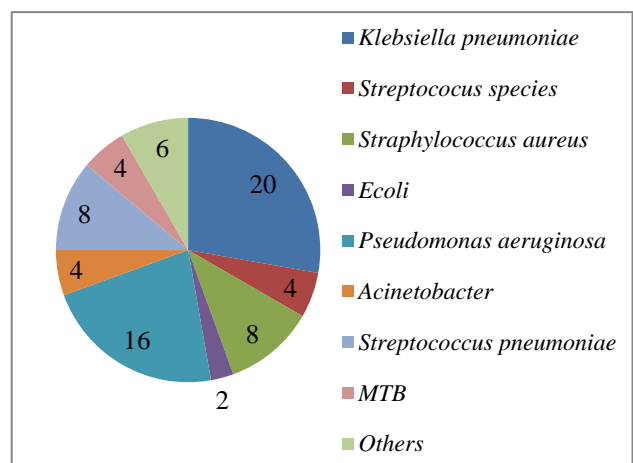


Figure 1: Results of sputum cultures in patients with Acute exacerbation of COPD.

Resistance in *Klebsiella species* was seen in 66.66% for Gentamycin, 50 % for Amikacin, 83.33% for Augmentin and Ciprofloxacin, 82.05% for Ceftriaxone, 44.44% for

Piperacillin, 41.66% for Netilmicin. Resistance in Pseudomonas was observed 88.88% for Ceftriaxone, 72.22% for Ciprofloxacin, 55.55% for Amikacin and Meropenam, 50% in Piperacillin and Netilmicin.

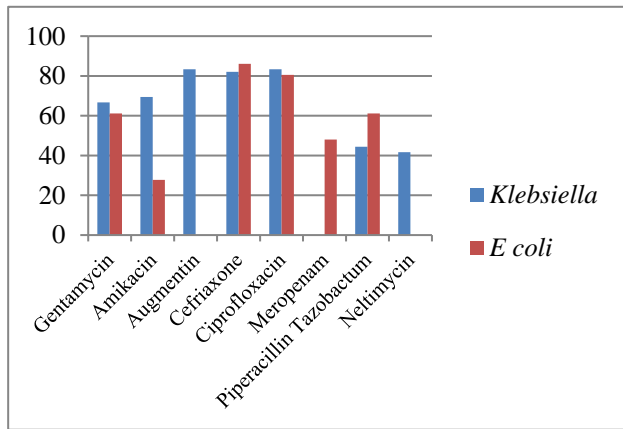


Figure 2: Resistance profile of *Klebsiella pneumoniae* and *E. coli*.

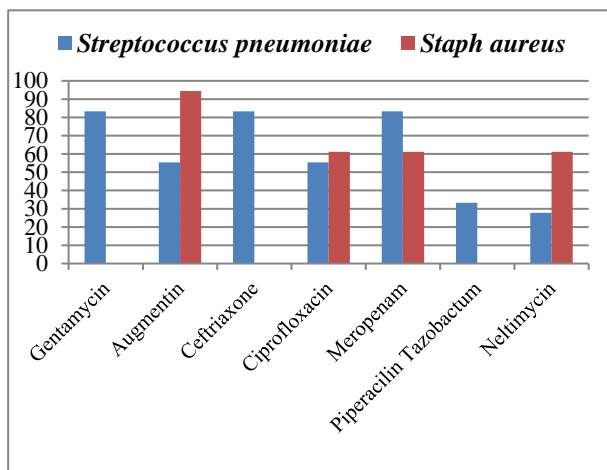


Figure 3: Resistance profile of *Streptococcus pneumoniae* and *Staphylococcus aureus*.

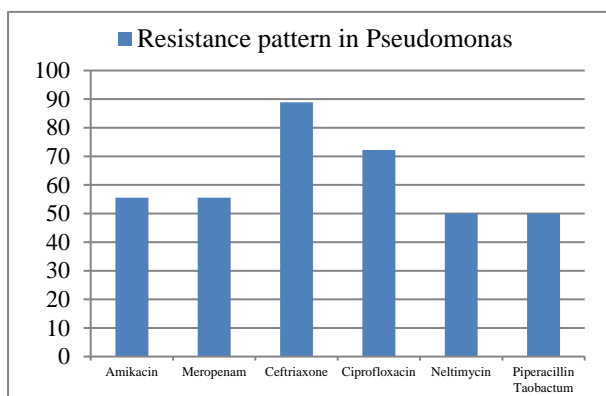


Figure 4: Resistance pattern in *Pseudomonas*.

Resistance in Streptococcus pneumoniae noted in 83.33% for Gentamycin, Meropenam, Ceftriaxone and 55.55%

Augmentin, Piperacillin and Ciprofloxacin. Resistance to Staphylococcus aureus was observed in 94.44% for Augmentin, 61.11% for Ciprofloxacin, Meropenam and Netilmicin. Resistance to E. coli was observed in 61.11% for Gentamycin and Piperacillin, 80.55% for Ciprofloxacin and Meropenam, 86.11% for Ceftriaxone and 27% for Amikacin.

DISCUSSION

Acute exacerbation of COPD is a change in the patient's dyspnoea, cough and sputum production that is beyond the day to day variations, requiring a change in the regular medication.⁸ The prevalence of the viral infections causing exacerbations was 39.3% according to the meta-analysis of 17 studies and hence the use of antibiotics in all COPD exacerbations is controversial.^{9,10} There were 68 patients in the culture negative group, mostly of viral etiology.

According to the western studies, the common organisms isolated from the Acute exacerbation of COPD patients include *H. influenzae* (20-30%), *Streptococcus pneumoniae* (10-15%), *Moraxella catarrhalis* (10%), *Pseudomonas aeruginosa* (10%).¹¹ A different microbiome was noted in the Chinese study where the common organisms were *Klebsiella pneumoniae* (16.94%), *Pseudomonas* (16.94%), *Acinetobacter* (11.29%), *Streptococcus pneumoniae* (8.87%) and *Staphylococcus aureus* (7.26%).¹² A study from Kolkata, India has demonstrated following organisms isolated - *Klebsiella pneumoniae* (38.46%), *Staphylococcus aureus* (23.08%), *Pseudomonas aeruginosa* (10.26%), *E. coli* (5.13%) etc.¹³ Our study also is in par with the Asian studies demonstrating *Klebsiella* as the commonest organism followed by *Pseudomonas*, *Streptococcus pneumoniae*, *Staphylococcus aureus* etc.

COPD patients are often exposed to different antibiotics for routine LRTI (Lower Respiratory Tract Infections) and pneumonia. Emergence of MDR (Multi Drug Resistance) strains is very common and our study 3 antibiotics were used in 28 patients and more than three antibiotics in 8 patients. *Streptococcus pneumoniae* was then the commonest organism isolated as a cause of CAP in COPD patients and was isolated in 11.11% of the patients in our study.¹⁴

For better treatment outcome a proper stratification of the bacteriological profile and treatment is required but empirical selection of antibiotics is often based on the past experience, availability of antibiotics in the hospital (government set up), cost and last but not the least - the best guess method.¹⁵ There is a wide variation of using antibiotics as "there are no governing laws towards their rational use". Resistance was seen to many antibiotics, even for the higher antibiotics and hence MDR strains were commonly encountered.¹⁶ Unfortunately, Piperacillin and Tazobactam, meropenam and third generation Cephalosporin are often used as empirical antibiotics, due

to this there is a fast growth of Carbapenem resistance organism referred as MDR strains and finally may end up as a pan drug resistant gram negative organism. Hence, the infection disease society of the America has warned of antibiotic crises across the globe.¹⁷

Culture driven antibiotic therapy has a better treatment outcome and more deaths occurred in culture negative group in the present study. mortality was noted in 8.1% of the patients in this study and Merino - Sanchez and colleagues have demonstrated a mortality of 12.5% patients.¹⁸ Late medical attention, advanced age, co-morbid conditions, previous antibiotic usage, all contributed to the mortality. Patients presented with multidrug resistant organisms carried poor prognosis in the form of prolonged stay, ICU admissions, multi organ dysfunction and deaths.

CONCLUSION

Acute exacerbation of COPD alters the lung function and increases the morbidity and mortality. Chronic colonization increases the risk for exacerbation and hence it should be dealt with greater care in COPD patients. Since viral exacerbations are also common and pathogen directed antibiotic therapy is the order of the day, misuse of empirical antibiotics should be avoided. Antibiotic prescriptions should be based on the local bacterial sensitivity pattern and prescribed in patients with history of production of purulent sputum and is worth following the guidelines or protocol. It is high time to have a policy for antibiotics usage at different levels- district, state and country to prevent the emergence of MDR strains. Banning across the counter sale of antibiotics is a recommended strategy to tackle the drug resistance menace.

ACKNOWLEDGEMENTS

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

- Seeger W, Adir Y, Barberà JA, Champion H, Coghlan JG, Cottin V, et al. Pulmonary hypertension in chronic lung diseases. *J Am Col Cardiol*. 2013 Dec 24;62(25 Supplement):D109-16.
- Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *The Lancet*. 2012 Dec 15;380(9859):2095-128.
- Noncommunicable Diseases in the South-East Asia Region [Internet]. South-East Asia Regional Office. 2019 [cited 22 September 2019]. Available at: http://www.searo.who.int/entity/noncommunicable_diseases/documents/9789290224136/en/.
- Chhabra SK, Dash DJ, Acute exacerbation of chronic obstructive pulmonary disease causes and impacts: *Ind J Chest Dis Allied Sci*. 2014 Jun;56(2):93-104.
- Rubinsztajn R, Przybyłowski T, Maskey-Warzęchowska M, Karwat K, Chazan R. Exacerbations of chronic obstructive pulmonary disease and quality of life of patients. In *Pathophysiology of Respiration*; Springer, Cham; 2015:69-74.
- Papi A, Bellettato CM, Braccioni F, Romagnoli M, Casolari P, Caramori G, et al. Infections and airway inflammation in chronic obstructive pulmonary disease severe exacerbations. *Am J Res Crit Care Med*. 2006 May 15;173(10):1114-21.
- Miravittles M, Espinosa C, Fernández-Laso E, Martos JA, Maldonado JA, Gallego M. Relationship between bacterial flora in sputum and functional impairment in patients with acute exacerbations of COPD. *Chest*. 1999 Jul 1;116(1):40-6.
- Rodriguez-Roisin R. Toward a consensus definition for COPD exacerbations. *Chest*. 2000 May 1;117(5):398S-401S.
- Wu X, Chen D, Gu X, Su X, Song Y, Shi Y. Prevalence and risk of viral infection in patients with acute exacerbation of chronic obstructive pulmonary disease: a meta-analysis. *Mol Bio Reports*. 2014 Jul 1;41(7):4743-51.
- Ram SFS, Rodriguez-Rohin R, Grandos NA, Gracia AJ, Barnes N. Antibiotics for exacerbations of chronic obstructive pulmonary disease. *Thorax*. 2002;57:847-52.
- Rangelov K, Sethi S. Role of Infections. *Clin Ches Med*. 2014 Mar;35(1):87-100.
- Ma X, Cui J, Wang J, Chang Y, Fang Q, Bai C, et al. Multicentre investigation of pathogenic bacteria and antibiotic resistance genes in Chinese patients with acute exacerbation of chronic obstructive pulmonary disease. *J Intern Med Res*. 2015 Oct;43(5):699-710.
- Sharan H, Aerobic Bacteriological Study of Acute Exacerbation of Chronic Obstructive Pulmonary Disease. *J Clin Diagn Res JCDR*. 2015 Aug;9(8):DC10-2.
- Desai H, Richter S, Doern G, Heilmann K, Dohrn C, Johnson A, et al. Antibiotic resistance in sputum isolates of *Streptococcus pneumoniae* in chronic obstructive pulmonary disease is related to antibiotic exposure. *COPD: J COPD*. 2010 Sep 1;7(5):337-44.
- Goshal AG, Dhar R, Kundu S. Treatment of acute exacerbation of COPD. *J Assoc Physicians India*. 2012 Feb;60 Suppl:38-43.
- Phillips I in Prudent Use of Antibiotics: Are Our Expectations Justified? in *Clin Infect Dis*. 2001;33 (Supplement 3):S130-S132.
- Multi-resistance hospital bacteria linked to India and Pakistan health production report 2009;3:26:3. Available at:

https://www.researchgate.net/publication/51201467_Country-to-Country_Transfer_of_Patients_and_the_Risk_of_Multi-Resistant_Bacterial_Infection.

18. Merino-Sanchez M, Alfageme-Michavila I, Reyes-Nunez N, Lima-Alvarez J. Prognosis in patients with pneumonia and chronic obstructive pulmonary

disease. *Archivos de Bronconeumología (English Edition)*. 2005 Nov 1;41(11):607-11.

Cite this article as: Raveendra KR, Devapriya R, Kodur N. Study of Microbial pattern and antibiotic sensitivity pattern in hospitalised acute exacerbation of COPD patients. *Int J Adv Med* 2019;6:1652-6.