Bacteriological Profile in Sputum and their Antibiogram among the Patients of Acute Exacerbation of COPD

Gauri Kulkarni¹, Deependra Chaudhary², Anup Bhoyar^{3*}, Sushma Dugad⁴ and Abhijit Telkhade³

¹Associate Professor, Department of Respiratory Medicine, Dr. Vasantrao Pawar Medical College Hospital & Research Centre, Nashik - 422003, Maharashtra, India; gaurisuhas@yahoo.com

²Assistant Professor, Department of Respiratory Medicine, Dr. Vasantrao Pawar Medical College Hospital & Research Centre, Nashik - 422003, Maharashtra, India;

³PG Resident, Department of Respiratory Medicine, Dr. Vasantrao Pawar Medical College Hospital & Research Centre, Nashik - 422003, Maharashtra, India; dranupbhoyar11@gmail.com

⁴Associate Professor, Department of Respiratory Medicine, Dr. Vasantrao Pawar Medical College Hospital & Research Centre, Nashik - 422003, Maharashtra, India.

Abstract

Background and Objectives: Chronic Obstructive Pulmonary Disease (COPD) is an important cause of disability and death globally and scenario has been infact worsened. Acute exacerbation of COPD (AECOPD) is associated with airway inflammation resulting in increased air trapping, further obstruction of airways and deterioration of gas diffusion. Objectives: The objective of this study is to find out the bacteriological profile and their antibiogram in AECOPD and to study the clinical presentation of AECOPD patients. Materials and Methods: This is a cross sectional study comprising of 45 patients diagnosed with AECOPD. Before starting on antibiotics all patients sputum was sent for culture and sensitivity. All patients were instructed to collect early morning, deep coughed sputum into a sterile sputum container (preferably two). Results: The present study reveals that total 45 cases, 89% were males and 11% were females. The most common organisms isolated were gram negative bacilli (71%) and gram positive bacilli (29%). Pseudomonas aueroginosa was the commonest bacteria isolated (26.7%) followed by streptococcus pneumonia (22.2%), Klebsiella pneumoniae (20%). The drug sensitivity testing revealed that Ciprofloxacin with amikacin is the best empirical antibiotic followed by Cephalosporin with amikacin. Conclusion: AECOPD is more common in adult males above the age of fifty five years secondary to smoking practices. As an empirical therapy in AECOPD patients the best choice of antibiotic therapy would be Ciprofloxacin with amikacin. Other best monotherapy antibiotic would be piperacillin with tazobactam or cefoperazone with sulbactum

Keywords: AECOPD-Acute exacerbation of copd

1. Introduction

Chronic Obstructive Pulmonary Disease (COPD) is common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway or alveolar abnormalities usually caused by significant exposure to noxious particle and gases¹. ATS/ERS guidelines define Acute Exacerbation of Chronic Obstructive Pulmonary Disease (AECOPD) as an event characterized by an increase in patients daily symptoms of dyspnea, cough, and/or sputum beyond normal day-to-day variability

and severe enough to require a change in management^{2,3}. The severity of Acute exacerbation of chronic obstructive lung disorder patients without respiratory failure are classified according to Winnipeg criteria⁴. Chronic Obstructive Pulmonary Disease (COPD) is an important cause of disability and among top five causes of death globally. Exacerbations of COPD has major impact on economy and health care system. According to Indian statistics COPD affects 30% of patients attending outpatient department and contributes to 1-2.5 % of indoor patients⁵AECOPD causes 24% hospital mortality in ICU patients and it increases to 30% if patient >65

years⁶. In COPD, acute exacerbation is a common problem during its natural course. COPD patients get exacerbation usually secondary to bacterial infection. The cultures and sensitivity of sputum plays an important role to find out an etiology, which is helpful to guide the antibiotic treatment. The pathogens causing AECOPD are respiratory viruses, atypical bacteria, streptococcus pneumonia, haemophilus influenza, pseudomonas aeruginosa, klebsiella pneumonia⁷⁻¹⁰. Sputum culture is good tool to find causative organism responsible for AECOPD. Over 90% of patients of AECOPD who are under treatment with antibiotics, the response will change depending on drug resistant pattern of organisms. Antibiogram helps in correct treatment protocol during management of AECOPD¹¹⁻¹⁵. It is necessary for finding out the resistant pathogens so treatment can be planned according to organisms, which may decrease the mortality and morbidity. Hence present study is undertaken to find out the bacteriological profile and their antibiogram in AECOPD and to study clinical presentation of acute exacerbation of COPD patients, which may be helpful to determine the cost of COPD treatment.

2. Aims and Objectives

- To study the various bacterial pathogens isolated in aetiology of AECOPD.
- To study antibiotic sensitivity and resistance pattern to antibiotics in these bacteria.
- To study clinical profile of acute exacerbation of COPD patients.

3. Materials and Methods

This is a cross sectional study comprising of 45 patients diagnosed with AECOPD from Dr. Vasantrao Pawar Medical College, Adgaon, Nashik. The study was carried out from August 2014 to December 2014. The study was done on indoor patients with acute exacerbation of COPD. The patients who were diagnosed COPD according to GOLD criteria were included in the study.

The following information was collected regarding age, sex, smoking, dyspnea, cough with expectoration, leucocytosis, ESR, chest X ray, fever. Diagnosed cases of pulmonary tuberculosis, pneumonia, suppurative lung diseases, patients on antibiotics before selection, patients of ischemic heart disease, and patients of AECOPD not yielding organisms on culture were excluded. Before starting on antibiotics all patients' sputum was sent for culture and sensitivity. All patients were instructed to collect early morning, deep coughed sputum into a sterile sputum container (preferably two), thick, mucoid,

purulent sputum was consider valid by microbiology department. Patients were asked to rinse the mouth with tap water. Samples were sending to laboratory after being labeled and numbered. All sputum samples were processed by conventional media like blood agar, maconkey agar, chocolate agar. Organisms were isolated using standard protocol process by microbiology department. Culture sensitivity was done by diffusion method. Routine hematological investigations, ESR and chest radiography were done on the day of presentation. According to the growth on culture, the sensitivity testing was done with following antibiotics ciprofloxacin, levofloxacin, ceftriaxone, cefotaxime ceftazidime, cefepime, amoxicillin with clavulanic acid, piperacillin with tazobactam, cefoperazone with sulbactam, gentamicin, amikacin, erythromycin, azithromycin, amoxicillin, penicillin, etc. The analysis was done using Statistical Package for Social Sciences (SPSS) version 17.

4. Results

A total of 45 cases of AECOPD admitted in pulmonary medicine ward at tertiary care hospital were included in our study.

In the present study, 51 to 60 years (44.4%) was the most common age group followed 61 to 70 years (26.6%) and 41 to 50 years (15.6%). Out of 45 cases 40 cases were males and 5 cases were females. Most of the male cases were smokers.

In the present study, Cough, Purulent expectoration, Dyspnoea and Fever was present in 75.56%, 77.78%, 71.11% and 22.22% of study population. In the present study, Cough, Purulent expectoration, Dyspnoea and Fever was present in 75.56%, 77.78%, 71.11% and 22.22% of study population.

In our study, along with clinical features we observed raised ESR and TLC

The frequently identified organisms were gram negative 71% only 29% were gram positive. The pseudomonas aeruginosa was the frequently identified gram negative organisms isolated in 26.7% of cases followed by Klebsiella (20%).

The most common gram positive organisms were Streptococcus pneumonia in (22.2%) and Streptococcus pyogenes (15.56%) % of cases followed by Staphylococcus aureus 4.4% of cases.

In the present study, Amoxycillin(60%) was the most common 1st antibiotic used amongst study population followed Ceftriaxone (26.67%) and Cefotaxime (8.89%).

The present study shows pseudomonas was the frequently identified Gram negative organism and was found to be sensitive to Amikacin, Cefoperazone-

sulbactum, Pipzo (piperacillin-tazobactum), Cefotaxime, Cefepime, Gentamicin, Levofloxacin, Amoxyclav (amoxicillin-clavulanic acid), Ciprofloxacin. In the present study, E coli was the second frequently identified Gram negative organism and was sensitive to Levofloxacin, Ciprofloxacin, Pipzo (piperacillin-tazobactum), Cefoperazone-Sulbactum, Amikacin, and was resistant to ampicillin and amoxiclav (amoxicillin-clavulanic acid). In the present study, Strepto pneumonia was the frequently identified Gram positive organism and was sensitive to 1st generation cephalosporin, 2nd generation cephalosporin, 3rd generation cephalosporin and fluoroquinolones. Streptopyogenes was the second frequently identified Gram positive organism and was sensitive to Cefotaxime, Ceftriaxone, Ceftazidime, Cefepime, Levofloxacin, Ciprofloxacin, Pipzo (piperacillin-tazobactum), Cef-Sulbac.

Table 1. Sensitivity pattern of pseudomonas areuginosa bacteria

Antibiotics	Sensitivity(%)	Resistant(%)	Total
Cefotaxime	10(83.33%)	2(16.77%)	12
Ceftriaxone	9(75%)	3(25%)	12
Ceftazidime	4(44%)	5(66%)	9
Cefepime	6(85%)	1(15%)	7
Levofloxacin	7(63%)	5(37%)	11
Ciprofloxacin	3(25%)	9(75%)	12
Amoxyclav(amoxicil-	4(40%)	6(60%)	10
lin-clavulanic acid)			
Pipzo(piperacillin-ta-	8(80%)	2(20%)	10
zobactum)			
Cefoperazone-Sulbac-	6(85%)	1(15%)	7
tum			
Gentamicin	7(58%)	5(42%)	12
Amikacin	9(90%)	1(10%)	10
Azithromycin	0(0)	1(100%)	1
Penicillin	0(0)	5(100%)	5
Erythromycin	0(0)	4(100%)	4
Amoxycillin	1(0)	7(100%)	7

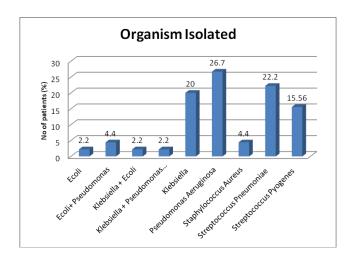
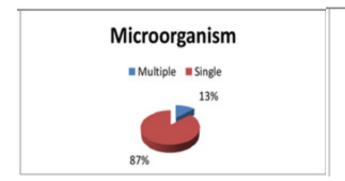


Figure 1. Microorganisms isolated in sputum of study participants.

5. Discussion

Chronic obstructive pulmonary disease accounts for major cause of morbidity and mortality in adults globally. In next two to three decades this scenario is unlikely to improve, in fact it has been predicted to worsen. The World Health Organization predicts that by 2020, COPD will be the third leading cause of death (currently fourth) and fifth leading cause of disability (currently twelfth) worldwide^{16,17}. According to Anthonisen (Winnipeg) criteria¹⁸ an acute exacerbation of COPD (AECOPD) is defined as a sudden worsening of COPD symptoms (shortness of breath, quantity and color of phlegm) that typically lasts for several days.

We observed raised ESR and TLC in our study. ESR&TLC is cost effective test and may be the good alternative to newer and more expensive tests like C-reactive protein and procalcitonin for diagnosis of AECOPD due to bacterial infection^{19,20}. Bacterial infection, viral infection or environmental pollutants may be the cause for triggering AECOPD. During



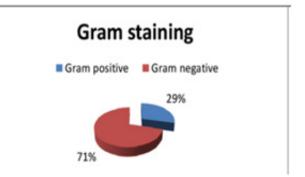


Figure 2 and 3. Status and Staining pattern of microorganism isolated in sputum of study participants.

exacerbation there is increased airway inflammation, increased hyperinflation, decreased expiratory air flow and ventilation perfusion mismatch.

Over the years, bacterial flora during acute exacerbations has changed from usual organisms to Enterobacteriaceae family organisms and Pseudomonas species with increased severity of disease21. These organisms further worsen the situation by virtue of their multidrug resistant and thus limit the therapeutic option. The antibiotic therapy always remains empiric, which is frequently an avoidable.

In the present study, 51 to 60 years (44.4%) was the most common age group. The more male predominance may be due to reason that males are more in habit of smoking which makes them more prone to development of COPD. In the present study, Cough, Purulent expectoration, Dyspnoea and Fever was present in 75.56%, 77.78%, 71.11% and 22.22% of study population.

In the present study, single and multiple organisms were isolated in 86.67% and 13.33% of study population. This findings are similar with the study conducted by Saxena et al²². Similar findings were observed by Narayanagowda DS et al²³. In the present study, Gram positive and Gram negative organism was isolated in 28.89% and 71.11% of study population. Aeruginosa (26.7%) was the most common organism isolated followed by Streptococcus Pneumoniae (22.2%) and Klebsiella (20%) and Streptococcus Pneumoniae (15.56%). Similar findings were observed in study conducted by Sethi Sanjay et al⁷ and R.I.M. El Korashy et al²⁴.

The present study shows pseudomonas was the most common Gram negative isolate and was found to be sensitive to Amikacin, Cefoperazone-Sulbactum, Pipzo(piperacillin-tazobactum), Cefotaxime, Cefepime Gentamicin, Levofloxacin, Amoxyclav, Ciprofloxacin. Similar findings were observed by Narayanagowda DS et al²³. In the present study, Klebsiella which was the second most common Gram negative isolate and was tested to be sensitiveto Cefperazone-Sulbactum, Pipzo (piperacillintazobactum) Amikacin, Ceftriaxone, Ceftazidime, Cefepime, Levofloxacin, Gentamicin, Ciprofloxacin, Amoxyclav. These findings are same as observed in the study carried out by Saxena et al²².

In the present study, E coli which was the second frequently identified Gram negative organism and was sensitive to Levofloxacin, Ciprofloxacin, Pipzo (piperacillin-tazobactum), Cef-Sulbac, Amikacin, and was resistant to ampicillin and amoxiclave. These findings are similar with the study conducted by Saxena et al²². They were resistant to ampicillin and amoxiclave. In the present study, Strepto pneumonia was frequently identified Gram positive organism and was sensitive to Cefotaxime, Ceftriaxone, Ceftazidime, Cefepime, Levofloxacin, Ciprofloxacin, Gentamicin, Pipzo (piperacillintazobactum), Cefperazone-Sulbactum. Similarly in the study conducted by Narayanagowda DS et al²³ and Saxena et al²². In the present study, Streptopyogenes was second frequently identified Gram positive organism and was sensitive to Cefotaxime, Ceftriaxone, Ceftazidime, Ciprofloxacin, Levofloxacin, Cefepime, Pipzo (piperacillin-tazobactum), Ceperazonef-Sulbactum.

In our study after isolating and individual drug Aeruginosa, sensitivity testing of Pseudomonas Streptococcus Pneumoniae and Klebsiella. Patients with mild exacerbations are given symptomatic treatment and antibiotics are prescribed if symptoms worsened. Due to incidence of β-lactamase production leading to antibiotic resistance amoxicillin is not the drug of choice. Earlier the standard treatment for AECOPD was aminopenicillin either ampicillin or amoxicillin. Their use is limited due to development of resistance among respiratory pathogens. Now a days aminopenicillins with beta lactamase inhibitor is a better choice. Cephalosporinshave demonstrated better clinical efficacy and tolerability than standard aminopenicillins. As levofloxacin is reserved drug so to cover both gram positive and gram negative bacterias in our institute we can start empirical cephalosporins plus amikacin or ciprofloxacin plus amikacin. Very severe exacerbations of COPD are treated with the newer antibiotics which are more effective like pipericillin plus tazobactam and cefoperazone plus sulbactam. They should be used cautiously to prevent the emergence of resistance.

6. Conclusion

Sputum culture is a very simple and useful investigation for diagnosis of aetiology & complications due to bacteria in AECOPD. If done well, it can replace the costlier diagnostic methods like immunodiffusion. Antibiogram helps in the correct treatment protocol during management of AECOPD. It is necessary for finding out resistant pathogens so treatment can be planned according to organisms, which may decrease the mortality and morbidity. Cephalosporins and Quinolones like, levofloxacin ciprofloxacin with amikacin have a broad spectrum of activity against gram positive and gram negative organisms responsible for AECOPD. AECOPD is commonly observed in adult males above 50 years of age secondary to smoking practices. Identifying early clinical features of AECOPD is essential to start early treatment. At our hospital set up cephalosporin with amikacin or Ciprofloxacin with amikacin can be started as empirical

therapy in AECOPD patients. Other best antibiotic would be pipericillin-tazobactam or cefperazone-sulbactum reserved for severe AECOPD patients and can be started as mono antibiotic.

7. References

- 1. Gold intiative for chronic obstructive lung disease. Available from: www.goldcopd.org
- 2. Wedzicha AA, Hurst JR, Calverley PMA, Albert RK, Anzueto A. Management of COPD exacerbations: A European respiratory society/American thoracic society guideline. Eur Respir J. 2017; 49:1600791. https://doi. org/10.1183/13993003.00791-2016 PMid:28298398
- 3. Rodriguez- Roisin R. Toward consensus definition for COPD exacerbations. Chest. 2000; 117:398-401. https:// doi.org/10.1378/chest.117.5_suppl_2.398S
- 4. Macintyre N, Huang YC. Acute exacerbation and respiratory failure in COPD. Proc am thoracsoc. 2008; 5:530-5. https:// doi.org/10.1513/pats.200707-088ET PMid:18453367 PM-Cid:PMC2645331
- 5. Arora N., Daga MK, et al. Microbial pattern of acute infective exacerbation of chronic obstructive airway disease in a hospital based study. Indian Chest Dis Allied Sci. 2001; 43:157-62.
- 6. Seneff et al. Hospital and 1 year survival of patients admitted to ICU with AECOPD. JAMA. 1995; 274:1852-7. https:// doi.org/10.1001/jama.274.23.1852 https://doi.org/10.1001/ jama.1995.03530230038027 PMid:7500534
- 7. Sanjay S. Infectious etiology of acute exacerbations of chronic bronchitis. Chest. 2000; 117(May 5):375S-85S.
- 8. Nestor S, Torres A, et al. Bronchial microbial patterns in severe exacerbations of Chronic Obstructive Pulmonary Disease (COPD) requiring mechanical ventilation. AMJ Resp Crit Care Med. 1998; 157:1498-505. https://doi. org/10.1164/ajrccm.157.5.9711044 PMid:9603129
- 9. Sanjay S, Murphy TF. Bacterial infection in chronic obstructive pulmonary disease in 2000: A State-of-the-Art Review. Clinical Microbiology Reviews. 2001; 14(2):336-63. https:// doi.org/10.1128/CMR.14.2.336-363.2001 PMid:11292642 PMCid:PMC88978
- 10. Beasleyet V. Lung microbiology and exacerbations in COPD. Int J Chron Obstruct Pulmon Dis. 2012; 7:555-69. DOI: 10.2147/COPD.S28286 https://doi.org/10.2147/ COPD.S28286
- 11. Michael SN. Antibiotic therapy of exacerbations of chronic bronchitis. Seminars in Resp Inf. 2000; 15(1):59-70. https:// doi.org/10.1053/srin.2000.0150059
- 12. Miravitlles M, Mayordomo C, Arte's M, Sanchez-Agudo L, Nicolau F, Segu JL and on Behalf of the EOLO Group. Treatment of chronic obstructive pulmonary disease and its ex-

- acerbations in general practice. Respir Med 1999; 93: 173-9. https://doi.org/10.1016/S0954-6111(99)90004-5
- 13. Adams SG, Melo J, Luther M, Anzueto A. Antibiotics are associated with lower relapse rates in outpatients with acute exacerbations of COPD. Chest. 2000; 117:1345-52. https:// doi.org/10.1378/chest.117.5.1345 PMid:10807821
- 14. Vogel F. A guide to the treatment of lower respiratorytract infections. Drugs. 1995; 50(1):62-72. https://doi. org/10.2165/00003495-199550010-00006 PMid:7588090
- 15. Chawla K, et al. Bacteriological profile and their antibiogram from cases of acute exacerbations of chronicobstructive pulmonary disease: A hospital based study. JCDR. 2008; 2(1):612-6.
- 16. Manino DM, Homa DM, Akinbami LJ, Ford ES, Redd SC. Chronic obstructive pulmonary disease surveillance: United States, 1971-2000. MMWR Surveill Summ. 2002; 51:1-16.
- 17. Chen JC, Manino DM. Worldwide epidemiology of chronic obstructive pulmonary disease. Curr Opin Pulm Med. 1999; https://doi.org/10.1097/00063198-199903000-00003
- 18. Anthonisen NR, Manfreda J, Warren CP, et al. Antibiotic therapy in exacerbations of chronic obstructive pulmonary disease. Ann Intern Med. 1987; 106:196-204. https://doi. org/10.7326/0003-4819-106-2-196 PMid:3492164
- 19. Bochen K, Krasowska A, Milaniuk S, Kulczyńska M, Prystupa A, Dzida G. Erythrocyte sedimentation rate- an old marker with new applications. JPCCR. 2011; 5(2):50-5.
- 20. Shaw JG, Vaughan A, Dent AG, O'Hare PE, Goh F, Bowman RV, et al. Biomarkers of progression of Chronic Obstructive Pulmonary Disease (COPD). J Thorac Dis. 2014 Nov; 6(11):1532-47. DOI: 10.3978/ j.issn.2072-1439.2014.11.33.
- 21. Eller J, Ede S, Schaberg T, Neiderman MS, Mauch H, Lode HO. Infective exacerbations of chronic bronchitis relation between bacteriological etiology and lung function. Chest. 1998; 113(6):1542-8. https://doi.org/10.1378/ chest.113.6.1542 PMid:9631791
- 22. Saxena S, Ramnani VK, Nema S, Tripathi K, Dave L, Srivastava N. Bacteriological profile in acute exacerbation of Chronic Obstructive Lung Disease (AECOPD). Ann Int Med Den Res. 2016; 2(5):MB01- MB06. https://doi. org/10.21276/aimdr.2016.2.5.MB1
- 23. Narayanagowda DS, Golia S, Jaiswal J, Manasa SS. A bacteriological study of acute exacerbation of chronic obstructive pulmonary disease over a period of one year. Int J Res Med Sci. 2015; 3:3141-6. https://doi.org/10.18203/2320-6012. ijrms20151152
- 24. El Korashy RIM, El-Sherif RH. Gram negative organisms as a cause of acute exacerbation of COPD. Egyptian Journal of Chest Diseases and Tuberculosis. 2014; 63:345-9. https:// doi.org/10.1016/j.ejcdt.2013.12.013