

An Observational Assessment of Bacterio-Etiologic in the Course of Disease and Their Drug Sensitivity Pattern of Sputum in Acute Exacerbation of Chronic Obstructive Pulmonary Disease (COPD)

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Received: 01-02-2023 / Revised: 26-02-2023 / Accepted: 17-03-2023

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Conflict of interest: Nil

Abstract

Aim: The study was carried out to find out the bacterial etiology in the course of disease and their drug sensitivity pattern.

Methods: All hospitalized patients diagnosed with AECOPD admitted in the Department of general medicine, BMIMS, Pawapuri, Nalanda, Bihar, India for the period of one year were evaluated. The individual bacterial isolates and their sensitive pattern to various antibiotics were also recorded in all 100 patients. The study was carried out and COPD was diagnosed according to the Global Initiative for Obstructive Lung Disease (GOLD) guidelines.

Results: Out of 100 patients, clinically diagnosed as AECOPD, 80% were males and 20% were females. 38% patients were in the age group 56-65 years followed by 66-75 (24%) age group. Out of a total 100 cases, forty-four (44%) were positive for pathogenic bacteria and fifty-six (56%) were non-pathogenic. Out of forty-five pathogenic bacteria, *K. pneumoniae* was the commonest (35.55%) followed by *P. aeruginosa* (22.22%), *S. aureus* (15.55%), *S. pneumoniae* (11.11%), *S. pyogenes* (6.66%). Among antibiotics, Amikacin was found highest sensitive followed by Azithromycin (68.68%), Amoxycillin Clavulanic acid (66.66%), Ciprofloxacin (62.22%) and Gentamycin (55.55%). However, Levofloxacin and Co-trimoxazole were found to be highly resistant 68.88% and 62.22% respectively among the drugs used in culture and sensitivity of 45 isolated pathogenic bacteria.

Conclusion: Repeated exacerbation and hospital admission leads to a major impact on the quality of life of patients with COPD. Antibigram helps in screening resistant pathogens and prescribing right treatment protocol.

Keywords: AECOPD, Bacteria, antibiogram.

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Introduction

Chronic obstructive pulmonary disease (COPD) is one of the most prevalent diseases in the world. Furthermore, the number of individuals affected has grown since the 1980s and this increase is expected to continue during the next 20

years. [1] COPD is characterized by intermittent acute exacerbations associated with worsening symptoms and lung function. These acute exacerbations contribute considerably to mortality and diminished quality of life. [2]

COPD is a heterogeneous disease defined by a chronic inflammation of the bronchial tree, bronchial hyper reactivity, mucus hyper secretion, irreversible degeneration of lung tissue and poorly reversible airway obstruction. Tobacco is the most important risk factor for development of COPD complemented by other environmental factors. [3] The disease is characterized by acute frequent exacerbations, which contribute to an accelerated decline of the lung function. [4] The exacerbations are characterized by acute increase of dyspnoea, cough and appearance of purulent sputum. It is well established that the frequency of exacerbations increases with reduction of forced expiratory volume in 1 s (FEV1). [5] The exacerbations exert a negative influence on the quality of life of patients with COPD² and often lead to hospitalization, higher rates of morbidity and mortality. [6,7] COPD exacerbation is a strong marker of death, the 5-year mortality being up to 50%. [8] Most exacerbations are caused by infections in the bronchial tree with bacteria and/or virus. Several studies have shown that bacteria are implicated in 50-70% of the exacerbations and that *Streptococcus pneumoniae* (*S. pneumoniae*), *Haemophilus influenza* (*H. influenzae*), *Moraxella catarrhalis* (*M. catarrhalis*) and *Pseudomonas aeruginosa* (*P. aeruginosa*) are the most frequently isolated bacteria. [9-12]

Several potential contributions of bacterial infection to the etiology, pathogenesis and clinical course of COPD can be identified. Three classes of pathogens have been implicated as causing AECOPD by infecting the lower respiratory tract: respiratory viruses, atypical bacteria, and aerobic Gram-positive and Gram-negative bacteria. The relative contributions of these three different classes of pathogens may change depending on the severity of the underlying obstructive airway disease. Such changes may also happen within a class, especially for bacterial pathogens.

[13] In last decade with the increasing use of fiber optic bronchoscopy, newer sampling methods like trachea bronchial aspirated sample (TBAS), Broncho alveolar lavage fluid (BALF), and protected specimen brushing (PSB) have emerged. [14] This has renewed interest in the area of bacteria and COPD, and this should lead to a precise delineation of the contribution of bacterial infection to the disease. [15]

In COPD, acute exacerbation is the common problem during natural course. The study was carried out to find out the bacterial etiology in the course of disease and their drug sensitivity pattern.

Materials and Methods

All hospitalized patients diagnosed with AECOPD admitted in the Department of general medicine, BMIMS, Pawapuri, Nalanda, Bihar, India for the period of one year were evaluated. The individual bacterial isolates and their sensitive pattern to various antibiotics were also recorded in all 100 patients. The study was carried out COPD was diagnosed according to the Global Initiative for Obstructive Lung Disease (GOLD) guidelines.

AECOPD was assumed when a patient presented with at least two of the three following symptoms: (a) worsening dyspnea, (b) increased cough, and (c) increased sputum production. Written informed consent was obtained from all the study participants. This study was approved by the institutional ethics committee. Patients were excluded for the study if (1) they had an outpatient status; (2) received antibiotic within last 48 hours of hospital admission; (3) Evidence of bronchiectasis, pneumonia or asthma; (4) other known chronic respiratory disorder; (5) active malignancy; (6) immunosuppression; (7) Absence of adequate sputum sample; and 8) Patient on mechanical ventilation. Patients were included only once in study even if they

hospitalized frequently during study period.

Variables included in the study were age, gender, smoking history or exposure to indoor smoke, signs at presentation and nature of sputum. After giving an informed consent, all patients were subjected to detailed history and both general and systemic examination. After clinical examination all patients underwent a chest radiography, complete blood counts, differential blood count, oxygen saturation by pulse oximetry. Early morning deep

coughed sputum sample was collected from all participants according to standard guideline. Within 24 hours of admission, patients were asked to collect sputum into a universal sterile wide mouthed container with a screw cap. Sputum samples were examined for physical appearance, gram stain, acid fast bacilli smear, culture for bacterial organism and drug sensitivity testing. All data was entered and analyzed by SPSS software program. Categorical variables will be reported as percentage.

Results

Table 1: Age and Sex distribution

Age	Male	Female	Percentage
18 – 35	0	0	0
36 – 45	8	0	8
46 – 55	12	4	16
56 – 65	30	8	38
66 – 75	20	4	24
76 – 85	10	4	14
Total	80	20	100

Out of 100 patients, clinically diagnosed as AECOPD, 80% were males and 20% were females. 38% patients were in the age group 56-65 years followed by 66-75 (24%) age group.

Table 2: Bacteriological profile and Type of bacteria isolated in AECOPD

Bacteriological profile	N%
Pathogenic	45 (45)
Non- Pathogenic	55 (55)
Type of bacteria	
Gram positive	35%
Gram negative	65%

Out of a total 100 cases, forty-five (45%) were positive for pathogenic bacteria and fifty-five (56%) were non-pathogenic. Among total 45 pathogenic microbial, 65% were Gram-negative bacteria and 35% were Gram-positive bacteria.

Table 3: Strains Isolated from Sputum Samples

Name of the organism	Number	Percentage
K. pneumoniae	16	35.55
P. aeruginosa	10	22.22
S. aureus	7	15.55
S. pneumoniae	5	11.11
S. pyogenes	3	6.66
E. coli	3	6.66
MRSA	1	2.22

Out of forty-five pathogenic bacteria, *K. pneumoniae* was the commonest (35.55%) followed by *P. aeruginosa* (22.22%), *S. aureus* (15.55%), *S. pneumoniae* (11.11%), *S. pyogenes* (6.66%).

Table 4: Antimicrobial Susceptibility pattern of isolated bacteria

Antibiotics	Number	Percentage
Amikacin	34	75.55
Amoxy Clavulanic acid	30	66.66
Cefuroxime	18	40
Ceftriaxone	19	42.22
Ciprofloxacin	28	62.22
Co-trimoxazole	16	35.55
Gentamicin	25	55.55
Azithromycin	31	68.88
Levofloxacin	13	28.88

Among antibiotics, Amikacin was found highest sensitive followed by Azithromycin (68.68%), Amoxy Clavulanic acid (66.66%), Ciprofloxacin (62.22%) and Gentamycin (55.55%).

Table 5: Resistant pattern among Bacterial isolates

Antibiotics	Number	Percentage
Amikacin	10	22.22
Amoxy Clavulanic acid	14	31.11
Cefuroxime	25	55.55
Ceftriaxone	24	53.33
Ciprofloxacin	16	35.55
Co-trimoxazole	28	62.22
Gentamicin	19	42.22
Azithromycin	13	28.88
Levofloxacin	31	68.88

However, Levofloxacin and Co-trimoxazole were found to be highly resistant 68.88% and 62.22% respectively among the drugs used in culture and sensitivity of 45 isolated pathogenic bacteria.

Discussion

Chronic Obstructive Pulmonary Disease (COPD) is a major health problem all over the world. It is highly prevalent, undertreated and under perceived disease. The number of individuals affected has grown since 1980 & this increase is expected to continue during next decades. [16] COPD is characterized by intermittent acute exacerbation associated with worsening of symptoms and lung function. Acute exacerbations reduce quality of life,

speed disease progression. Bacterial infections in patients of COPD are still continued as a health problem especially in developing countries with high morbidity and mortality often due to respiratory failure. COPD related death is probably underestimated because of the difficulties associated with identifying the precise cause of death. [17] Sputum culture is a good and simple tool to study the aetiology & complications due to bacteria in AECOPD. If done well, it can replace the costlier diagnostic methods like Immunodiffusion. Antibigram helps in the correct treatment protocol during management of acute exacerbation of COPD. [18]

It was observed that AECOPD was prevalent in 35-85 years age group. However, among them, 56-65 years age constituted 38%. This is because it was more commonly seen in patients with advanced lung disease as an expression of deterioration in host defense at the bronchial mucosal level. [19] It is well known that the frequency of infection resulting in acute exacerbation of COPD by various microorganisms varies from one geographical area to another. Out of 100 sputum sample, pathogenic bacteria were found in 45% of patients with AECOPD. This could be due to declining lung function. [20] The prevalence of Gram negative isolates was 65%, as compared to 35% of gram positive. The Gram negative organisms were more common in the patients with the most severe lung dysfunction, where the Gram positive bacteria predominated in the exacerbations of the patients with the mildest degree of lung function abnormalities. [21]

K. pneumoniae was the commonest (35.55%) followed by *P. aeruginosa* (22.22%), *S. aureus* (15.55%), *S. pneumoniae* (11.11%), *S. pyogenes* (6.66%). Kuwal A conducted a study on Indian patients involving different hospitals all over india and at the end point, pathogenic bacteria were isolated in 47.22% cases, where *Pseudomonas aeruginosa* was the commonest bacteria (38.23%) followed by *Klebsiella pneumonia* (29.41%), *Staphylococcus aureus* (23.93%). [22] Majority of isolated bacteria were Gram-negative bacilli viz. *Pseudomonas* and *Klebsiella* species. The prevalence of lower airway bacterial colonization in outpatients with stable COPD is high and is mainly due to Gram-negative bacilli like *Pseudomonas* spp. The greater rate of isolation of pathogenic bacteria in exacerbated COPD than in stable COPD in different studies, supports the pathogenic role of bacteria in a proportion of AECOPD. [23]

Based on the sensitivity pattern, the highest sensitive antibiotic was Amikacin followed by Azithromycin (68.68%), Amoxycillin Clavulanic acid (66.66%), Ciprofloxacin (62.22%) and Gentamycin (55.55%). Although virus infection is undoubtedly the cause of AECOPD in many cases, antibiotic treatment is mandatory in most affected patients since it is associated with reduced short-term mortality, fewer treatment failures, reduction of sputum purulence and a faster recovery of lung function. [24,25] Therefore, antibiotics are an essential part of the worldwide treatment guidelines for AECOPD. Because of diagnostic delay, due to the fact that results of sputum culture are first available 2-3 days after the sputum sample is collected, the initial antibiotic treatment will always be empirical. Therefore, when treating patients admitted to a hospital with COPD exacerbation, the most important question is not if the patient should be treated with antibiotics, but which antibiotic to choose. [26]

Conclusion

AECOPD represents a major health burden which is both economic and social because of the propensity of readmissions that resulting transient or permanent deterioration in quality of life. Good laboratory facilities for proper culture and sensitivity of sputum, guide physicians to choose appropriate antibiotic minimizing AECOPD as well as sharp eye on changing pattern of the isolates.

References

1. Global Initiative for Chronic Obstructive Lung Diseases. 2001. Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease: NHL/WHO workshop report, NIH publication No. 2701. Bethesda: US Department of Health and Human Services.

2. Seemungal TA, Donaldson GC, Paul EA, Bestall JC, Jeffries DJ, Wedzicha JA. Effect of exacerbation on quality of life in patients with chronic obstructive pulmonary disease. *American journal of respiratory and critical care medicine*. 1998 May 1;157(5):1418-22.
3. Mannino DM, Watt G, Hole D, Gillis C, Hart C, McConnachie A, Smith GD, Upton M, Hawthorne V, Sin DD, Man SF. The natural history of chronic obstructive pulmonary disease. *European Respiratory Journal*. 2006 Mar 1;27(3):627-43.
4. Donaldson GC, Seemungal TA, Bhowmik A, Wedzicha J. Relationship between exacerbation frequency and lung function decline in chronic obstructive pulmonary disease. *Thorax*. 2002 Oct 1;57(10):847-52.
5. Groenewegen KH, Wouters EF. Bacterial infections in patients requiring admission for an acute exacerbation of COPD; a 1-year prospective study. *Respiratory medicine*. 2003 Jul 1;97(7):770-7.
6. Miravittles M. Health status and costs of exacerbations of chronic bronchitis and COPD: how to improve antibiotic treatment. *Expert Review of Pharmacoeconomics & Outcomes Research*. 2005 Aug 1;5(4):423-35.
7. Burrows B, Earle RH. Course and prognosis of chronic obstructive lung disease: a prospective study of 200 patients. *New England Journal of Medicine*. 1969 Feb 20;280(8):397-404.
8. Rivera-Fernández R, Navarrete-Navarro P, Fernández-Mondejar E, Rodríguez-Elvira M, Guerrero-López F, Vázquez-Mata G, Project for the Epidemiological Analysis of Critical Care Patients (PAEEC) Group. Six-year mortality and quality of life in critically ill patients with chronic obstructive pulmonary disease. *Critical care medicine*. 2006 Sep 1;34(9):2317-24.
9. Sethi S, Evans N, Grant BJ, Murphy TF. New strains of bacteria and exacerbations of chronic obstructive pulmonary disease. *New England Journal of Medicine*. 2002 Aug 15;347(7):465-71.
10. Ko FW, Ng TK, Li TS, Fok JP, Chan MC, Wu AK, Hui DS. Sputum bacteriology in patients with acute exacerbations of COPD in Hong Kong. *Respiratory medicine*. 2005 Apr 1;99(4):454-60.
11. Soler N, Torres A, Ewig S, Gonzalez J, Celis R, El-Ebiary M, Hernandez C, Rodriguez-Roisin R. Bronchial microbial patterns in severe exacerbations of chronic obstructive pulmonary disease (COPD) requiring mechanical ventilation. *American journal of respiratory and critical care medicine*. 1998 May 1;157(5):1498-505.
12. 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.
13. Sethi, Sanjay. Infectious Etiology of Acute Exacerbations of Chronic Bronchitis. *CHEST*; 2000 May; 117(5): 380-385.
14. Soler Nestor, Antoni Torres, Santiago Ewig, Julia Gonzalez, Rosa Celis, Mustafa El-Ebiary; "Bronchial Microbial Patterns in severe Exacerbations of Chronic Obstructive Pulmonary Disease (COPD) Requiring Mechanical Ventilation. *A.M.J. Resp. Crit Care Med*; 1997 Nov 11;157(5): 1498- 1505.
15. Sethi Sanjay, Timothy F. Murphy. 2001 "Bacterial Infection in Chronic Obstructive Pulmonary Disease in 2000: a State-of-the-Art Review; *Clinical Microbiology Reviews*; 2000 Dec 18; 14(2): 336-363.
16. Anthony Seaton, Douglas Seaton, A. Gordon Leitch Chronic Bronchitis and

- Emphysema. Chronic obstructive pulmonary diseases 'Crofton and Douglas's Respiratory Disease 5thEd. Wiley-Blackwell. 2008.
17. Catia Saraiva, Djamila Neves, Tiago Abreu, Fatima Rodrigues. Mortality in COPD: role of comorbidities. *European Respiratory Journal*; 2014 23 December; 44 (58): 603.
 18. S R Kamat, A P Mehta, V B Doshi, S Walimbe, V V Jayakar V; A Comparative Study of various Antibacterial Drugs in Lower Respiratory Tract Infections and Pneumonias in Adults; *JAPI*; 1983 Apr; 31(4):209-215.
 19. Eller J, Ede A, Schaberg T, Niederman MS, Mauch H, Lode H. Infective exacerbations of chronic bronchitis: relation between bacteriologic etiology and lung function. *Chest*. 1998 Jun 1;113(6):1542-8.
 20. N Roche, B Kouassi, A Rabbat, A Mounedji, C Lorut, G Huchon; Yield of sputum microbiological examination in patients hospitalized for exacerbations of COPD with purulent sputum; *respiration*; 2006 Dec; 74(1): 19-25.
 21. Niederman Michael S. "antibiotic Therapy of Exacerbations of Chronic Bronchitis." *Seminars in Resp. Inf*; 2000 Mar 01; 15(1):59-70.
 22. Kuwal A, Joshi V, Dutt N, Singh S, Purohit G; A Prospective Study of Bacteriological Etiology in Hospitalized Acute Exacerbation of COPD Patients: Relationship with Lung Function and Respiratory Failure; *Turk Thorac J*; 2018 Jan; 19 (1):19-27.
 23. M R Bari, M M Hiron, S M Zaman, M M Rahman, K C Ganguly; Microbes responsible for acute exacerbation of COPD; *Mymensingh Med J*; 2010 Oct; 19(4):576-85.
 24. Ram FS, Rodriguez-Roisin R, Granados-Navarrete A, Garcia-Aymerich J, Barnes NC. Antibiotics for exacerbations of chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews*. 2006(2).
 25. Brand RA. Local Chemotherapy with Primary Closure of Septic Wounds by Means of Drainage and Irrigation Cannulae: MN Smith-Petersen MD (1886–1953), Carroll B. Larson MD, Williams Cochran MD The 12th President of the AAOS 1943 (MNS-P). *Clinical Orthopaedics and Related Research*. 2008 Jan; 466:104-12.
 26. Onyinye A. U., C, U.C. H., & A, O. J. Sexual Assault; Our experience at One Stop Shop for Women and Girls, National Obstetric Fistula Centre, Abakaliki, Ebonyi State. Southeast Nigeria: A retrospective study. *Journal of Medical Research and Health Sciences*, 2022; 5(7): 2118–2124.