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Sputum Bacteriology in Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease

Mahmoud Ahmed Arafa[1, 2]

[1] Department of Chest Disease, Faculty of Medicine, Al-Azhar University, Egypt

[2] Pulmonary Consultant, Buraidah Central Hospital, Alqasim, Saudi Arabia

Corresponding author: Mahmoud Ahmed Arafa, **Mobile:** 00966561429453, **E-Mail:** mahmoudarfa1977@gmail.com

Abstract

Background: Acute exacerbation is a common problem in the usual course of chronic obstructive pulmonary disease (COPD). Infections play a chief role in Acute Exacerbation of Chronic Obstructive Lung Disease (AECOPD) that leads to significant morbidity and mortality.

Objective: To assess the bacteriology in COPD exacerbations of hospitalized patients and correlate with clinical and laboratory data of the patients.

Patients and Method: a prospective study was conducted to correlate clinical, laboratory data with sputum culture results of 52 patients, admitted to the Pulmonology Department of Buraidah Central Hospital (BCH) with an AECOPD from 1st January 2018 till 31 August 2018. All collected sputum samples were subjected to standard microbiological procedures.

Results: Growth of pathogenic organisms was seen in 37 (71%) of the 52 sputum samples tested. Gram-positive organisms were found in the majority 20 (54 %). Gram negative microbes accounted for 17 (46%). Streptococcus pneumoniae (24.3 %) was found to be the most common bacterial agent responsible for COPD exacerbations, followed by Klebsiella pneumonia 7 (18.9 %), Haemophilus influenzae (H influenzae) and Staphylococcus aureus; each was 5 (13.5%), Streptococcus pyogenes (Streptococcus pyogenes) 4 (10.8%), Moraxella catarrhalis (M catarrhalis), Pseudomonas aeruginosa, and Methicillin-resistant Staphylococcus aureus (MRSA) each was 2 (5.4%)

Conclusion: Sputum culture is considered a simple and good diagnostic modality to identify bacteria in AECOPD. Antibiogram would assist in developing a local antibiotic strategy and reducing the appearance of resistance stains.

Keywords: Antibiogram, Bacteria, Sputum, Culture.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common treatable and preventable disease characterized by limitation of the airflow, which is progressive and persistent and caused by alveolar and/or airway inflammation, caused by prolonged exposure to noxious gases or particles and affected by host factors such as lung development abnormality [(1)].

COPD is a range of airway diseases that includes chronic bronchitis on one side and emphysema on the other side. Actually, the majority of patients have both [(2)]. COPD remains a major reason of morbidity and mortality and this varies across countries. In the United States of America alone, around twenty-four million persons agonize from COPD and has become the 3rd principal cause of death [(3)]. Usual history of COPD is interrupted by exacerbations, which is persistent worsening of the condition of the patient from the stable condition and outside ordinary daily variation, it is acute in onset and needs change in ordinary medications [(1)].

Recurrent attacks of exacerbations lead to rapid reduction of lung function, decreased physical activity, poorer quality of life, and increased mortality [(4,5)]. To decide if the patient needs antibiotic or not and to assess the severity of exacerbation attack, Winnipeg criteria are used, which are based on new events, which include increased shortness of breath, increase amount of sputum and purulence of sputum. Antibiotics are indicated if there are at least 2 or more of symptoms [(6)]. Exacerbations are classified into mild, moderate and severe. Mild (need only short acting bronchodilator), moderate (treated with short acting bronchodilator, antibiotic and or corticosteroid) and severe (necessitate hospitalization or visit to the emergency department), respiratory failure may present [(1)]. Infection and air pollution are common causes of COPD exacerbations, in one-third of patients the cause remains idiopathic [(7)].

Three classes of pathogens included in AECOPD are: viruses, atypical bacteria, typical bacteria (aerobic gram positive and gram-negative). Bacterial infection is responsible for about 50% of COPD acute exacerbations [(8)], most common organisms are S. pneumoniae, H. influenzae which are common in mild and moderate cases, while M. catarrhalis, and P. aeruginosa are more prevalent in advanced cases [(9)].

The current study was carried out in order to assess sputum bacteriology in AECOPD of the patients admitted at the Chest Department of Buraidah Central Hospital (BCH). Also, the patients' clinical and laboratory data were compared with culture results to determine whether these parameters can provide a clue of bacterial infection before the availability of culture results.

PATIENTS AND METHOD

The current study was conducted at Chest Department in Buraidah Central Hospital, Alqasim Area from 1st of January 2018 to 31st of August 2018. It was a prospective observational study.

Inclusion criteria: Patients diagnosed as COPD according to GOLD guidelines 2017, and admitted with AECOPD.

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Exclusion criteria: Patients received antibiotic therapy in the last 48 hours, presence of bronchiectasis and/or pneumonia, severely immunocompromised patients, patients managed as outpatient case, and patients in need for mechanical ventilation.

Detailed history and physical examination, chest radiography, laboratory, and microbiological investigations were done on the same day of admission.

Microbiological assessment of sputum sample:

Spontaneously expectorated sputum samples were taken from all patients under the study. Direct smear was done for all samples to qualify them regarding pus cells and epithelial cells. Only samples with <10 epithelial cells and >25 pus cells per high power field were acceptable for further processing. Good quality samples were cultured on blood, MacConkey and chocolate agar and incubated at 37° C for 24-48 hours. Growth on plates was considered significant if achieved (10)6 colony-forming unit (cfu)/ml, with the exception of S. pneumoniae, which was assessed sufficient with (10)5 cfu/ml. Isolated organisms were identified through standard laboratory methods [(10)].

Lung function:

Lung function parameters were obtained from patient files through the hospital information system, all patients had diagnosed before as COPD by spirometry, a post-bronchodilator forced expiratory volume in one second/forced vital capacity (FEV1/FVC) ratio of <0.70, and categorized according to airflow limitation into 4 stages according to FEV1.

Mild: FEV1 ≥80% predicted, moderate: 50% ≤ FEV1 <80% predicted, severe: 30% ≤ FEV1 <50% predicted, very severe: FEV1 <30% predicted.

Ethical consent:

An approval of the study was obtained from Buraidah Central Hospital, Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of sharing in the study. This work was carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

All data were collected, tabulated and statistically analyzed using SPSS 22.0 for windows (SPSS Inc., Chicago, IL, USA 2011). Quantitative data were expressed as mean ± SD and median (range), and qualitative data were expressed as frequency (percentage). Mann Whitney U test was used to compare between non-normally distributed variables of two groups. Categorical variables were compared using Chi-square test or Fisher Exact test when appropriate. All tests were two sided. P value < 0.05 was considered significant.

RESULTS

This study included 52 patients already diagnosed as COPD and presented with acute exacerbation, admitted to the pulmonary unit, with 49 males and 3 females. Age ranged from 45 years to 84 years and 9 patients were smokers. In regard to bacteriology, positive culture results were seen in 37 patients. There was statistically significant relation between positive culture and each of sex and smoking habit (Table 1).

Table (1): Demographic data of the study group and relation with culture results

Variables	Total patients No. 52		Positive culture group(No. 37)		Negative culture group No. 15		p-value
	No.	%	No.	%	No.	%	
Age per							
40 to 50	1	1.9	1	2.7	0	0	
51 to 60	15	28.8	11	29.7	4	26.7	
61 to 70	23	44.2	16	43.2	7	46.7	0.965
71 to 80	9	17.3	6	16.2	3	20.0	
>80	4	7.7	3	8.1	1	6.7	
Sex		.	.	.	.	.	
Female	3	5.8	0	0.0	3	100.0	0.021*
Male	49	94.2	37	75.5	12	24.5	
Smoking habit							
Ex -smoker	33	63.5	29	87.9	4	12.1	<0.0001*
Non smoker	9	17.3	0	0	9	100.0	
Smoker	10	19.2.	8	80.0	2	20.0.	

*: Significant P

Regarding pulmonary function and according to GOLD guidelines 2017, 6 patients (11.53%) were found to be mild, 28 patients (53.84%) were moderate and 18 patients (34.6%) were severe. There was relation between degree of severity of COPD and isolated organisms, Streptococcus pneumoniae (S. pneumoniae), Haemophilus influenzae (H influenzae), Streptococcus pyogenes (S pyogenes) were the predominant isolates in mild cases, while in severe COPD, Klebsiella pneumonia (K. pneumonia), H influenzae, and Staphylococcus aureus (Staph. aureus) organisms were more common (Table 2).

Table (2): FEV1 of the study group and relation with culture results

Types of microorganism		FEV1 grade			Total
		Mild No. **3**	Moderate No. **20**	Severe No. **14**	
S. pneumoniae	No.	1	6	2	9
	%	33.3%	30.0%	14.3%	24.3%
E COLI	No.	0	1	0	1
	%	0.0%	5.0%	0.0%	2.7%
H influenzae	No.	1	1	3	5
	%	33.3%	5.0%	21.4%	13.5%
Klebsiella	No.	0	2	5	7
	%	0.0%	10.0%	35.7%	18.9%
M. catarrhalis	No.	0	0	2	2
	%	0.0%	0.0%	14.3%	5.4%
MRSA	No.	0	1	1	2
	%	0.0%	5.0%	7.1%	5.4%
Pseudomonas aeruginosa	No.	0	1	1	2
	%	0.0%	5.0%	7.1%	5.4%
Staphylococcus aureus	No.	0	5	0	5
	%	0.0%	25.0%	0.0%	13.5%
Streptococcus pyogenes	No.	1	3	0	4
	%	33.3%	15.0%	0.0%	10.8%
P		0.26			

The study showed statistically significant relation between positive culture results and sputum character, among positive culture, 56.8% had purulent sputum and 43.2% of cases had mucopurulent sputum table (3).

Table (3): Relation between sputum character and culture results

Variables	Sputum culture				p-value
	Positive culture group (n.37)		Negative culture group (n.15)		
	No.	%	No.	%	
Mucoid	0	0.0	4	26.7	0.004*
Mucopurulent	16	43.2	7	46.6	
Purulent	21	56.8	4	26.7	

*: Significant P

Growth of pathogenic organisms was seen in 37 of the 52 sputum samples tested. Gram-positive organisms were found in 20 samples and Gram negative microbes in 17 samples (Table 4)

Table (4): Incidence of microorganisms in positive culture group (n=37)

Variables	No.	%
Gram positive	**20**	**54**
• Sterpt. pneumoniae	9	24.3
• Staph, aureus	5	13.5
• Sterpt, pyogen	4	10.8
• MRSA	2	5.4
Gram negative	**17**	**46**
• Klebsiella	7	18.9
• H influenzae	5	13.5
• M. catarrhal	2	5.4
• Pseudomonas aeruginosa	2	5.4
• E coli	1	2.7

Among the study group, fourteen patients did not respond to conservative treatment and were referred to ICU, 9 patients needed respiratory support by noninvasive ventilation (NIV), while 5 patients were intubated and mechanically ventilated, all ventilated patients had positive culture results but it was statistically significant in patients received NIV (Table 5).

Table (5): Patients' ventilation in relation to culture results

		Total patients (No. 52)		Positive culture group No. 37		Negative culture group No. 15		p-value
		No.	%	No.	%	No.	%	
Noninvasive ventilation	No	43	82.7	28	65.1	15	34.9	0.046*
	Yes	9	17.3	9	100	0	0	
Invasive ventilation	No	47	90.4	32	68.1	15	31.9	0.305
	Yes	5	9.6	5	100	0	0	

As regard outcome, patients with positive culture had prolonged hospital stay and this was statistically significant, also all expired patients had positive culture but this was statistically insignificant (Table 6).

Table (6): Patients' outcome in relation to culture results

	Total patients No. **52**		Positive culture group No. **37**		Negative culture group No. **15**		p-value
	No.	%	No.	%	No.	%	
Hospital stays mean± SD median (range)	6.17±1.96 6 (3-9)		6.97±1.65 7 (3-9)		4.2±1.08 4 (3-7)		<0.0001*
Outcome	.	.	.	.	.	.	
Died	3	5.8	3	100.0	0	0.0	0.548
Discharge	49	94.2	34	69.4	15	30.6	

Table (7) illustrates the sensitivity of isolated organisms to antibiotics, S. pneumoniae was sensitive to amoxicillin-clavulanic, azithromycin, levofloxacin and moxifloxacin, while MRSA was sensitive to vancomycin, linezolid and most of gram-negative organisms were sensitive to cefepime, ceftazidime, and respiratory quinolones.

Table (7): Antibiotic sensitivity of different organisms

Types of antibiotics		Organisms								
		1	2	3	4	5	6	7	8	9
Amox_clavulinic	N	7	0	1	1	2	0	0	4	1
	%	77.8%	0.0%	20.0%	14.3%	100%	0.0%	0.0%	80.0%	25.0%
Azithromycin	N	9	0	0	2	0	0	0	4	3
	%	100%	0.0%	0.0%	28.6%	0.0%	0.0%	0.0%	80.0%	75.0%
Doxycycline	N	7	0	0	0	0	0	0	4	3
	%	77.8%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	80.0%	75.0%
Ceftriaxone	N	8	1	2	1	2	0	0	3	3
	%	88.9%	100%	40.0%	14.3%	100%	0.0%	0.0%	60.0%	75.0%
Cefepime	N	7	1	4	7	2	1	2	4	4
	%	77.8%	100%	80.0%	100%	100%	50.0%	100%	80.0%	100%
Ceftazidime	N	7	1	4	6	2	0	2	3	2
	%	77.8%	100%	80.0%	85.7%	100%	0.0%	100%	60.0%	50.0%
Piperacillin tazobactam	N	9	1	3	7	2	2	2	4	4
	%	100%	100%	60.0%	100%	100%	100%	100%	80.0%	100%
Ciprofloxacin	N	5	1	4	6	2	1	2	3	2
	%	55.6%	100%	80.0%	85.7%	100%	50.0%	100%	60.0%	50.0%
Levofloxacin	N	9	1	5	7	2	0	2	5	4
	%	100%	100%	100%	100%	100%	0.0%	100%	100%	100%
Moxifloxacin	N	9	1	5	7	2	0	2	5	3
	%	100%	100%	100. %	100%	100%	0.0%	100%	100%	75.0%
Vancomycin	N	9	0	0	1	0	2	0	5	4
	%	100%	0.0%	0.0%	14.3%	0.0%	100%	0.0%	100%	100%
Linezolid	N	0	0	0	0	0	2	0	0	0
	%	……	0.0%	0.0%	0.0%	0.0%	100%	0.0%	0.0%	0.0%
Meropenem	N	9	1	5	7	2	2	2	5	4
	%	100%	100%	100. %	100%	100%	100%	100%	100%	100%
Amikacin	N	0	1	3	4	2	1	2	4	0
	%	0.0%	100%	60.0%	57.1%	100%	50.0%	100%	80.0%	0.0%
Total number organism		9	1	5	7	2	2	2	5	4

1- S. pneumoniae . 2- E coli . 3- H influenzae 4- K. pneumonia, 5- M. catarrhalis 6- MRSA .7- Pseudomonas aeruginosa 8- Staph aureus 9- S. pyogenes

DISCUSSION

COPD is a principal reason of morbidity and mortality both direct and long term. Exacerbations increase the load of the disease and consider a chief cause of health care consumption including hospitalizations and admission to intensive care. Exacerbation may be infective or non-infective, infective causes may be viral or bacterial which may be either typical or atypical, while non-infective causes like air pollution play important role in exacerbation firing [(1)].

This study involved 52 patients, 49 (94.2%) males and 3 (5.7%) females, diagnosed as COPD with acute exacerbation. Predominance of male over female patients as shown in the study can be clarified by the fact that smoking habits, which constitute the main predisposing factors for the development of COPD are more obvious in males, and this is reliable with **Chawla *et al.*** [(11)] and **Diamantea *et al.*** [(12)] and the study of **Kojima *et al.*** [(13)], which state that prevalence of COPD are more among men than in women. As regard age the study group ranged from 45 years to 84 years, the age group from 61 to 70 years represented 44%, because chronic bronchitis has maximum prevalence in the same age group [(14)].

The current study showed that bacterial pathogens were isolated from sputum in 37 patients (71.2%). **Iyer *et al.*** [(15)] determined that bacterial pathogens can be isolated from sputum in 45% of patients presented with AECOPD. **Erkan *et al.*** [(16)] detected bacterial pathogens in 55% of patients presented with exacerbation of COPD. **Patel *et al.*** [(17)] concluded that sputum culture was positive in 82% of patients with AECOPD, which was higher as compared to other studies [(18)]. This difference can be explained by the fact that culture results depend on previous use of antibiotic, nature of sputum and time of collection sputum [(19)].

The current study revealed that Gram-positive organisms were found in 20 (54 %) of isolates, while Gram negative microbes accounted for 17(46%), also **ElFeky *et al.*** [(20)] conducted that Gram positive bacteria represented 80% of isolates, while Gram-negative bacteria represented the remaining 20%. However other studies reported the predominance of Gram-negative bacteria [(21, 22)].

S. pneumoniae was the most common isolated organism (24.3%). This finding is in concordance with study results of **Sethi** [(23)] and on the same line **Patel *et al.*** [(17)] who described similar results in 2015.

K. pneumonia was isolated in 7 patients (18.9 %), H. influnzae and Staph. aureus each in 5 patients (13.5%), S. pyogenes was in 4 patients (10.8%), M catarrhalis, Pseudomonas aeruginosa, Methicillin-resistant Staphylococcus aureus (MRSA) each was in 2 patients (5.4%), others [(24, 25)] have concerned P. aeruginosa and Klebsiella species as the most common organisms causing exacerbation of chronic bronchitis.

Antibiogram revealed that gram positive organisms e.g., S. pneumoniae, staph aureus, S. pyogenes were sensitive to amoxicillin clavulanic acid, macrolides, cephalosporins, respiratory quinolones and meropenem. MRSA was sensitive to vancomycin, linezolid, piperacillin tazobactam and meropenem and resistant to amoxicillin clavulanic acid, macrolides.

As regard gram negative bacteria Klebsiella, M catarrhalis, H. influnzae, Pseudomonas aeruginosa and E coli were sensitive to meropenem, ceftazidime, cefepime, respiratory quinolones and mostly resistant to amoxicillin clavulanic acid, macrolides. In the current study no multidrug-resistant (MDR), extensively drug-resistant (XDR) and pandrug-resistant (PDR) were found, similar data reported by **Madhavi *et al.*** [(22)]. **ElKorashy and El-Sherif** [(26)] exposed that the gram-negative organisms were sensitive to carbapenems, aminoglycosides. MDR were found in 28.6% of the gram-negative organisms and 7.4% of the whole cases of AECOPD.

Sharan *et al.* [(27)] revealed that piperacillin tazobactam, carbapenem, aminoglycosides, moxifloxacin were effective against gram negative bacilli, and about 50% of isolated acinetobacter and 60% of Pseudomonas aeruginosa pathogens were resistant to first and second generation cephalosporins. Low resistance pattern in the present study can be explained by lesser use of higher antibiotics in most of the patients as they were not affordable to them.

Patel *et al.* [(17)] found that antipseudomonal penicillin (piperacillin-tazobactam) was the most effective antibiotic against isolated organisms while respiratory quinolones were less effective.

All ventilated patients had positive culture but it was statistically significant in patients received NIV. As regard outcome, patients with positive culture had prolonged hospital stay, which was statistically significant. Also all expired patients had positive culture but statistically insignificant. These findings are in line with meta-analysis done on role of antibiotic treatment in AECOPD, which reported that patients with severe exacerbations are more probable to benefit from treatment with antibiotics [(28)]. **Adams *et al.*** [(29)] also found lower relapse rates in patients treated with antibiotic during AECOP. On the other hand some studies found antibiotic treatment was of no benefit in AECOPD [(30, 31)].

Limitations of the current study need further discussion:

The current study has not involved data on atypical organisms like Mycoplasma and Chlamydia in COPD exacerbations, this point has been evaluated in some studies, in mild-to moderate AECOPD treated as outpatient, incidence of Chlamydia pneumoniae was 4% [(32)]. Another study of patients on mechanical ventilation with AE COPD, Chlamydia. Pneumoniae was 18% [(33)]. Also, the role of viral infection in AECOPD was not evaluated. So, the role of viral infections and atypical organisms like Chlamydia and

Mycoplasma in the pathogenesis of COPD exacerbations needs further study.

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