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ORIGINAL ARTICLE

Study of plasma C - Reactive Protein Level in Bacteriological Sputum Culture Positive & Culture Negative Patients of COPD with Exacerbation

Abdullah Al Mujahid[1] Md. Ali Hossain[2] Md.Abu Raihan[3] Md. Khairul Anam[4] Md. Habib Uddin Ahmad[5] Samprity Islam[6] S.M.Abdur Razzaque[7] Nihar Ranjan Saha[5]

Abstract

Objective: *To determine whether levels of Plasma C-reactive protein (CRP) could be a useful biomarker in addition to bacteriological sputum culture for early decision of antibiotic treatment in COPD patients with exacerbation*

Material and Methods: *This cross sectional observational study was done in the Department of Respiratory Medicine, NIDCH, Mohakhali, Dhaka during July, 2015 to June, 2016. A total of 100 patients with COPD exacerbations admitted in NIDCH were included in this study. C-reactive protein (CRP) and sputum culture were done in all of the patients. Patients having sputum culture positive and culture negative were considered as group I and group II respectively. Age 40 or over, both sexes, acute exacerbation of COPD according to the GOLD guideline, criteria for hospital admission according to the GOLD guideline, former or current smoker with a minimum smoking history of 20 pack years and/or exposure to biomass fuel were enrolled.*

Results: *Fourty two (42.0%) patients had sputum culture positive and 58(58.0%) patients had culture negative. Majority (40.5%) patients age belong to 50-59 years in group I. Male were predominant 40(95.2%) and 48(82.8%) in both group I and group II. 22(52.4%) patients had raised plasma CRP level >10(mg/dl) in culture positive group and that was only 3(5.2%) in culture negative group. In addition, more than 90% culture positive patients had CRP level >5 (mg/dl) as a whole whereas it was only 19% in culture negative group. ROC curve for prediction of sputum culture positive according to CRP level with a cutoff value 5.0mg/dl having area under curve (AUC) 0.893, with 76.2% sensitivity and 86.2% specificity for prediction of culture positive result.*

Conclusion: *Elevated C-reactive protein (CRP) could be a useful biomarker in addition to bacteriological sputum culture for early decision of antibiotic treatment in COPD patients with exacerbation*

Key words: *AECOPD, sputum culture, C-reactive protein.*

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1. Junior consultant (Respiratory Medicine), 250 Bedded TB Hospital, Shyamoli, Dhaka, Bangladesh.
2. Professor of Respiratory Medicine & Former Director National Institute of Diseases of the Chest & Hospital(NIDCH), Mohakhali, Dhaka, Bangladesh.
3. Deputy Director & Project Director & Associate Professor (Respiratory Medicine), 250 Bedded TB Hospital, Shyamoli, Dhaka, Bangladesh.
4. Associate Professor of Respiratory Medicine, Shaheed Suhrawardi Medical College, Sher E Bangla Nagar, Dhaka, Bangladesh.
5. Associate Professor of Respiratory Medicine,National Institute of Diseases of the Chest & Hospital, Mohakhali, Dhaka, Bangladesh.
6. Medical Officer, Department of Internal Medicine, BSMMU, Dhaka, Bangladesh.
7. Associate Professor of Respiratory Medicine, Shaheed Tajuddin Ahmad Medical College, Gazipur, Bangladesh.

Correspondence to: Dr.Abdullah Al Mujahid, Junior consultant (Respiratory Medicine), 250 Bedded TB Hospital, Shyamoli, Dhaka, Bangladesh. Mobile: 01712 268285, E-mail: dr.mujahid37@gmail.com.

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Introduction:

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality throughout the world. It is the fourth leading cause of death worldwide. [1] A clinical diagnosis of COPD should be considered in any patient who has dyspnea, chronic cough or sputum production, and/or a history of exposure to risk factors for the disease.[2]

COPD may be punctuated by periods of acute worsening of respiratory symptoms, called exacerbations.[3] Exacerbations can be precipitated, among other causes, by bacterial and viral infections, and by common pollutants, such as tobacco and air pollution. But in up to 30% of cases, an etiological diagnosis cannot be achieved.[4] In addition to this, 25-50% of COPD patients are colonized with potential respiratory pathogens, especially Haemophilus influenza, Streptococcus pneumonia and Moraxella catarrhalis.[4] In fact, in some COPD patients it is possible to isolate potential pathogenic bacteria in sputum, not only during an exacerbation but also during at stable state, so the presence of pathogenic bacteria does not prove its direct implication in the episode.

For these reasons, new strategies for the management of COPD patients are required, not only for identifying the origin of the exacerbation episodes, but also to assess individual risk for each patient. Culture of sputum is time consuming and frequently do not give reliable result. Even though the presence of mucopurulent sputum expectoration is associated with isolation of pathogenic bacteria, it is difficult, or even impossible, to differentiate colonization from infection. Color of sputum reported by patients is not always reliable and inspection of sputum is not always possible. Thus, a negative result or a normal flora does not exclude the presence of a microorganism responsible for the exacerbation. The criteria published by Anthonisen et al and the presence of other clinical symptoms are likelihood criteria for infective exacerbation. But they are subjective and prone to interobserver variation. In contrast, the measurement of biological markers offers objective data, although it has to be considered in combination with the clinical criteria.[5]

Several serum biomarkers such as C-reactive protein (CRP) and procalcitonin (PCT) are now available. Procalcitonin test is expensive. In some recent trials, it has been found that plasma CRP is significantly high in sputum positive bacterial exacerbation of COPD and can guide for antibiotic therapy and can reduce overall treatment cost & also contributes to the spread of resistant microorganisms.[8]

Materials & Methods:

This cross sectional observational study was carried out - Consecutive 100 patients of both sexes with the age of 40 years or above admitted to Inpatient Department of NIDCH, Mohakhali, Dhaka during July 2015-June 2016 due to acute exacerbation of COPD. Criteria for the diagnosis of COPD, acute exacerbation of COPD and hospital admission were based on GOLD guideline.[9] CBC , ECG, Chest X-Ray P/A View , Spirometry, ABG, Sputum for AFB, Plasma CRP level & Sputum for culture were done for all patients . Total 42 patients having positive sputum culture for bacterial organisms were considered as group I and 58patients having negative sputum culture were considered as group II. Recent antibiotic treatment, pneumonia, bronchiectasis, malignancy, pneumothorax, Tuberculosis & IHD were excluded from the study.

Results:

Total 100 COPD patients with acute exacerbations were included in the study and among them 42(42.0%) patients were found to have positive sputum culture for bacteriological organisms (Group I). On the other hand, 58 (58.0%) patients were found to have negative sputum culture for bacteriological organisms (Group II). (Figure-1)

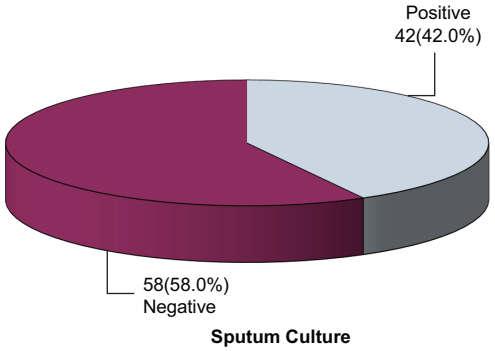

Fig.-1: *Pie chart showing distribution of the study population by Sputum culture*

It was observed, in the demographic variables, that majority (40.5%) patients belonged to 50-59 years age group in group I. On the other hand, majority (34.5 %) patients belonged to 60-69 years age group in group II. Majority patients were male in both group I and group II (95.2% & 82.8% respectively).Regarding occupation, farmers predominated in both the groups (50.0%& 27.6% respectively). More than three forth (78.6%) patients were current smoker in group I and 37(63.8%) in group II. Based on age, sex, occupational status and smoking habit, there was no statistically significant difference ($p<0.5$) between the two groups. (Table- I)

It was observed that, almost three fourth (71.4%) patients expectorated 15-30 ml sputum per day in group I who were positive for bacteriological organism in sputum culture and only 8(13.8%) patients expectorated this volume in group II who were negative for bacteriological organism in sputum culture. In addition 12(28.6%) patients expectorated >30ml/day in group I where as none in group II. The difference was statistically significant ($p<0.05$) between two groups. (Table-II)

It was found in this study that, almost three fourth (71.4%) patients had mucopurulent sputum in group I and 54(93.1%) had mucoid sputum in group II. Purulent sputum was found in 11(26.2%)patients in group I and none in group II. Number of patients having mucopurulent and purulent sputum were significantly higher in group I and the difference was statistically significant ($p<0.05$) between the groups.(Table-III)

It was observed that 4(9.5%) patients in culture positive & 39(67.2%) patients in culture negative group belonged to 0.5-5 (mg/dl) CRP level and more than half (52.4%) patients belonged to >10 (mg/dl) CRP level in culture positive patients and only 3(5.2%) patients in culture negative group belonged to this range of CRP. More than 90% culture positive patients had CRP level >5 (mg/dl) as a whole, in comparison to only 19% in culture negative group. (Table-V)

Table-I

Distribution of the study population by demographic variable (n=100)

	Group-I (n=42)		Group-II (n=58)		P value
	N	%	N	%	
Age group (years)					
40-49	5	11.9	7	12.1	
50-59	17	40.5	19	32.8	
60-69	10	23.8	20	34.5	0.843^{ns}
70-80	9	21.4	11	19	
>80	5	11.9	7	12.1	
Sex					
Male	40	95.2	48	82.8	0.058^{ns}
Female	2	4.8	10	17.2	
Occupational status					
Farmer	21	50	16	27.6	
Service holder	3	7.1	9	15.5	
Businessman	3	7.1	6	10.3	0.188^{ns}
Laborer	7	16.7	7	12.1	
House wife	3	7.1	8	13.8	
Rickshaw-puller	5	11.9	12	20.7	
Smoking Status					
Smoker	33	78.6	37	63.8	
Ex-smoker	5	11.9	10	17.2	0.263^{ns}
Non-smoker	4	9.5	11	19.0	

s=significant, ns= not significant, p value reached from chi square test

Table-II

Presentation of the study population by sputum production (n=100)

Sputum Production (ml/day)	Group-I (n=42)		Group-II (n=58)		P value
	N	%	N	%	
<15	0	0	50	86.2	
15-30	30	71.4	8	13.8	0.001[s]
>30	12	28.6	0	0	

s=significant ,p value reached from chi square test

Table-III

Presentation of the study population by sputum Character (n=100)

Sputum Character	Group-I (n=42)		Group-II (n=58)		P value
	N	%	N	%	
Mucoid	1	2.4	54	93.1	
Mucopurulent	30	71.4	4	6.9	0.001[s]
Purulent	11	26.2	0	0	

s=significant , p value reached from chi square test

Table-V

Association between plasma CRP level with sputum culture of the population (n=100)

Plasma CRP status (mg/dl) Positive(n=42)	Plasma CRP on the basis of sputum culture Negative(n=58)			
	n	%	n	%
0.5-5.0	4	9.5	39	67.2
5.1-10.0	16	38.1	8	13.8
>10 22	52.4	3	5.2	
Mean±SD	6.7	±5.7	5.1	±4.8
Reange (min, max)	0.5	,44.6	0.5	,29.9

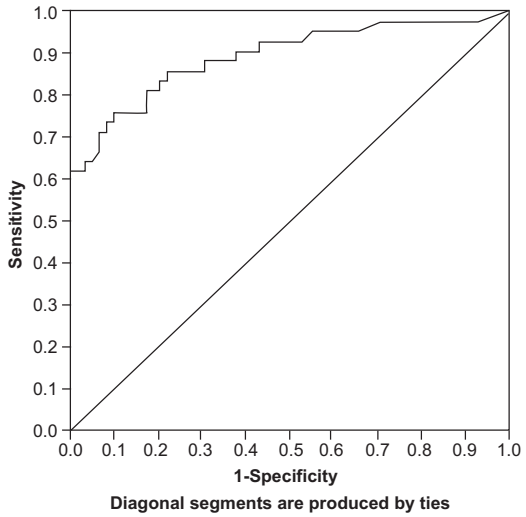

Fig.-4*: Receiver-operator characteristic curves of plasma CRP by culture positive population*

A receiver-operator characteristic (ROC) curve was formulated to find out the ideal cutoff point of Plasma CRP for distinguishing patients of AECOPD with positive sputum culture from AECOPD patients with negative sputum culture. The area under the curve (AUC) for prediction of Plasma CRP was 0.893, which gave a cut off value 5.0 mg/dl with 76.2% sensitivity and 86.2% specificity for prediction of culture positivity. (Figure- 4)

Discussion

In this present study, it was observed that 42 cases were sputum culture positive and 58 cases were culture negative. Bari and colleagues found the similar result.[10]

Sputum purulence may be a marker of bacterial infection during an exacerbation of COPD.

Stoller and colleagues showed that sputum purulence is an important indicator of bacterial infection in patients with an exacerbation of COPD.[11] In this study it was observed that almost three forth (71.4%) patients expectorated 15-30 (ml/day) in group I and 8(13.8%) in group II. There was also 12(28.6%) patients expectorate >30 (ml/day) in group I whereas none in group II. The difference was statistically significant ($p<0.05$) between two group.

It was observed that almost three fourth (71.4%) patients had mucopurulent sputum in group I and 93.1% had mucoid sputum in group II. Purulent sputum was found 26.2% in group I and not found in group II. Mucopurulent and Purulent sputum were significantly higher in group I. Weis and Almdal reported in 2006 that mucopurulent expectoration had higher levels of CRP than patients with mucoid expectoration.[12] Bircan and colleagues also reported similar findings.[13]

It was observed that 4(9.5%) patients in culture positive & 39(67.2%) patients in culture negative group belonged to 0.5-5 (mg/dl) CRP level and. More than half (52.4%) patients belonged to >10 (mg/dl) CRP level in culture positive patients and only 3(5.2%) patients in culture negative group belonged to this range of CRP. More than 90% culture positive patients had CRP level >5 (mg/dl) as a whole, in comparison to only 19% in culture negative group. A study by Stolz and colleagues demonstrated at the time of acute exacerbation, the mean CRP level in patients whose sputum was sterile on culture was 4.5+1.9 mg/dl while in patients whose sputum yielded any of the organisms, it was 7.9+1.6 mg/L which is significantly higher ($p<0.05$).[16] The above findings was concordant with the previous study done by Arora and colleagues in which, they found that CRP level was elevated (>10mg/dl) in all COPD patients where recognized bacterial pathogens were isolated in 62.0% patients.[15]

Chunhong et al reported that high median CRP levels were observed in AECOPD with bacterial aetiology compared with nonbacterial AECOPD.[17] The ideal cutoff point for distinguishing patients with bacterial AECOPD from those with nonbacterial AECOPD was 3.9 mg/dl with sensitivity 78.18%; specificity 84.61%; AUC, 0.832. Purulent sputum had a significantly higher CRP level than mucoid sputum, but with an AUC of only 0.617 (95% confidence interval, 0.49-0.74) to diagnose bacterial AECOPD. The cutoff value differs with the current study, which may be due to genetic causes, geographical variations, racial and ethnic differences with our population.

Conclusion

It can be concluded that the elevated Plasma C-reactive protein (CRP) could be a useful biomarker in addition to bacteriological sputum culture for early decision of antibiotic treatment in COPD patients with acute exacerbation as it is an early maker of the exacerbation.

This study did not search for viral etiology of AECOPD though it is one of the important causes of AECOPD & also raise serum CRP level. Detection of virus in sputum is expensive & often not available in our setting. The study was also missing the mixed infectious etiology (ie, viral with bacterial cause in a same individual) due to resource limitation & unavailable tools.

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