E-ISSN: 2706-9575
P-ISSN: 2706-9567
IJARM 2021; 3(2): 577-579
Received: 19-10-2021
Accepted: 25-12-2021

Dr. Madhu S
Associate Professor, Department of General Medicine, Basaveshwara Medical College and Hospital, Chitradurga, Karnataka, India

Dr. Vrushabhveer CP
Senior Resident, Department of General Medicine, Basaveshwara Medical College and Hospital, Chitradurga, Karnataka, India

Dr. Sharvani R Setty
Associate Professor, Department of Pathology, Basaveshwara Medical College and Hospital, Chitradurga, Karnataka, India

Dr. Vagesh Kumar SR
Professor and Head of Department, Department of General Medicine, Basaveshwara Medical College and Hospital, Chitradurga, Karnataka, India

Corresponding Author:
Dr. Vrushabhveer CP
Senior Resident, Department of General Medicine, Basaveshwara Medical College and Hospital, Chitradurga, Karnataka, India

CRP levels in acute bacterial exacerbation of COPD: Its focus on microbial etiology

Dr. Madhu S, Dr. Vrushabhveer CP, Dr. Sharvani R Setty and Dr. Vagesh Kumar SR

DOI: https://doi.org/10.22271/27069567.2021.v3.i2i.307

Abstract
Objective: Chronic obstructive pulmonary disease (COPD)- exacerbation have a significant mortality impact. Exacerbations are severe and frequent as the severity of copd increases. Predicting a bacterial cause of an exacerbation of COPD is difficult. C-reactive protein (CRP) levels increase during exacerbations but the relationship with etiology is not established. We aimed to explore the relationship between levels of CRP and various microorganisms responsible for infective exacerbation.
Methods: In this study, patient serum was obtained and C-reactive protein (CRP) levels were measured using an automated latex-enhanced turbidimetric assay. Sputum samples were obtained and evaluated microscopically. Episodes of exacerbations meeting Anthonisen's criteria type I–II were evaluated, analyzing the etiology and inflammatory response as measured by CRP in blood. The relationship between CRP and the bacterial colonies in sputum/blood in 92 patients with an exacerbation of COPD was assessed. Results categorized according to the etiology of sepsis (gram negative or gram positive) were also compared.
Results: A total of 92 patients were examined, Full microbiology analysis was available in 90 samples. Klebsiella pneumonia (27) and staphylococcus arues (14) were the most common gram negative and gram positive organism isolated respectively. Median CRP levels were 46.56(IQR – 15.38 – 95.08). Univariate and multivariate logistic regression analysis showed that High CRP levels were associated with male gender, elderly population, longer disease duration and prolonged hospital stay, and these factors were found to be statistically significant.
Conclusion: CRP levels were higher in gram positive infections when compared to gram negative infections. High CRP levels can be used as biomarker for prediction bacterial exacerbation.

Keywords: COPD exacerbation, CRP, microbial etiology

Introduction
Chronic obstructive pulmonary disease (COPD) has a high rate of morbidity and mortality worldwide [1]. Exacerbations are thought to be caused by complex interactions between the host, respiratory viruses, airway bacteria and environmental pollution. Recent studies have shown that bacteria play an important role in the exacerbation of COPD, and up to 50% of exacerbations are caused by bacterial infections.
C-reactive protein (CRP) levels are useful in evaluating COPD exacerbation [2, 3]. High serum levels of CRP are found in purulent bronchitis and COPD exacerbation with potential pathogenic microorganisms (PPMs) in the sputum.
CRP levels when compared to baseline levels are significantly higher during acute exacerbations of COPD compared, especially if a bacterial origin is likely [4]. A previous study has shown that patients with an acute exacerbations of COPD admitted to hospital with a CRP level of ≥ 50 mg·L^{-1} showed a trend to benefit more from antibiotics than patients with low CRP values [5].

Methods
Patients
Ninety three patients with acute exacerbations of COPD (AECOPD) were recruited from south Indian hospital. COPD was defined as forced expiratory volume in 1 second (FEV1) of < 80% predicted for age and height, and a ratio of FEV1-to-forced-vital-capacity of <70%. Exacerbation was considered if the patient had a background COPD with a combination of worsening respiratory symptoms including shortness of breath, a change in volume and color of sputum, cough, wheeze or systemic symptoms.

Inclusion criteria

- Age >18 years of age
- Patient with bacterial exacerbation of COPD. Bacterial exacerbation was defined by van der Valk *et al*. as follows:

1. The abundance of >= 1 PPMs in excess (>= log) of the normal microbiological flora in sputum
2. PPMs reaching a level of absolute growth of $>10^6$ colony-forming units per milliliter, except for Streptococcus Pneumoniae, for which a level of growth of $>10^5$ colony-forming units per milliliter was sufficient

Exclusion criteria

- History of asthma
- Bronchiectasis, tuberculosis, malignancies
- Any other inflammatory diseases arthritis, connective tissue disorders or inflammatory bowel disease.
- Infiltrates on chest x-ray examination were diagnosed as having pneumonia and Patients with pneumonia were also excluded.

Sputum sample

Sputum was examined by Gram stain microscopy according to local protocols and reported semi-quantitatively. Sputum was cultured on sheep blood agar and chocolate agar plates according to local protocols. The plates were then incubated for 18 hours in 5% CO2 at 37°C with, and bacterial colonies were counted and sub cultured for identification using standard morphological and biochemical assessments. Bacterial agents were classified as PPMs or non-PPMs as described by Cabello *et al*.

CRP Assay

Blood samples were obtained and CRP levels measured using an automated latex-enhanced turbidimetric assay (Beckman Image 800, Beckman Coulter Inc, Fullerton, CA) with an analyzer according to the manufacturer's instructions.

Statistical analysis

The data were analyzed using SPSS 11.5 software (SPSS Inc, Chicago, IL). Categorical variables were compared using the univariate analysis, and continuous variables using the Student's t test or the Mann-Whitney's U test.

Results

Of the 93 hospitalized patients with COPD, 90 were selected for evaluation. The remaining 3 patients were excluded because of the absence of CRP measurements on the day of admission and sputum culture contamination. Baseline characteristics of patients with acute exacerbations of chronic obstructive pulmonary disease (COPD) in table 1. Among all identifiable pathogens Klebsiella pneumonia and staphylococcus species were most common isolated gram negative and gram positive organism respectively (table 2). Median CRP levels for gram positive and gram negative organism were 62.84mg/dl and 40.86mg/dl respectively. There was statistically significant differences in median CRP levels for gram positive and gram negative pathogens, with median CRP levels higher in gram positive pathogens and p value was <0.5. Patient with high CRP level were noted in older age group (age >65 years), duration of COPD more than 5 years, male gender, Univariate and multivariate logistic regression analysis was applied and showed it to be statically significant. Patient with high CRP levels had longer duration of stay in the hospital when compared to patient with low CRP levels and statically significant.

Discussion

In this study, our results suggest that High CRP level is a good potential biomarker for the diagnosis of bacterial infections- caused by gram positive organism, especially in patients with AECOPD. Klebsiella pneumonia, the most common causative agent in our geographic area, played a major role in 30% of exacerbations, whereas staphylococcus species occurred in 15.5% of exacerbations in our study, which was different from other studies. This discrepancy may be because of distinct antibiotic pressure in different geographic areas and the exclusion of patients with pneumonia. There was significant difference in the CRP values among the different pathogens in patients with AECOPD was observed in these studies. Gram positive pathogens had high CRP levels when compared to gram negative organisms. And patient with high CRP levels at presentation had long duration of hospital stay when compared with the rest.

Conclusion

CRP levels were higher in gram positive infections when compared to gram negative infections. High CRP levels can be used as biomarker for prediction of bacterial exacerbation and prolonged hospital stay.

Table 1: Baseline characteristics of patients with acute exacerbations of chronic obstructive pulmonary disease with comparison CRP levels

Parameters	N (%)	CRP		Univariate analysis P value
		High	Low	
Age group				
<65 years	39	25	14	0.007
>65 years	53	44	9	
Gender				
Male	65 ()	53	12	0.032
Female	27 ()	16	11	
Duration of COPD				
<5 years	40	32	8	0.006
>5 years	52	37	15	
Diabetes mellitus				
Yes	25	19	6	0.431
No	67	17	50	
Hypertension				
Yes	28	21	7	0.381
No	64	48	16	

Smoking				
Yes	47	36	11	0.165
No	45	33	12	
Cough with expectoration				
Yes	80	60	20	0.678
No	12	9	3	
Fever				
Yes	34	28	6	0.229
NO	58	41	17	
High TLC count				
Yes	53	41	12	0.137
No	39	28	11	
Gram Stain				
Positive	22	20	2	0.046
Negative	69	49	20	
Duration of Hospital stay				
>7 days	28	17	11	0.008
<7 days	64	52	12	

Table 2: Serum C-reactive protein values in patients with bacterial acute exacerbations of chronic obstructive pulmonary disease according to the causative pathogen

Pathogen	No. case	Median CRP(mg/dl)
Klebsiella pneumoniae	27	40
Pseudomonas aeruginosa	10	43.75
Acinetobacter species	10	26.6
Staphylococcus areus	14	94.38
E.coli	8	35.18
Enterobacter species	5	56
Non fermenting GNB	5	53.26
Moraxella species	5	41

Table 3: Shows the Variables N (%) CRP N (%) Unadjusted OR (95%C.I) P value Adjusted OR (95% CI) P value

Variables	N (%)	CRP N (%)		Unadjusted OR (95%C.I)	P value	Adjusted OR (95% CI)	P value
		High	Low				
Age							
>65 years	53	44	9	4.57 (1.33-15.68)	0.016	4.57 (1.33-15.68)	0.016
<65 years	39	25	14				
Duration of COPD							
<5 years	40	32	8				
>5 years	52	37	15	4.34 (1.34-13.19)	0.014	3.51 (1.08-11.36)	0.035
Gender							
Male	65	53	12	3.5 (1.08-11.36)	0.035	3.51(1.08-17.9	0.017
Female	27	16	11				
Duration of hospital stay							
<7 days	28	17	11			-	-
>7 days	64	52	12	4.88 (1.33-17.9)	0.017	4.21 (1.34-13.19)	0.014

References

1. Wedzicha JA, Seemungal TA. COPD exacerbations: defining their cause and prevention. Lancet. 2007;370:786-796.
2. Hurst JR, Donaldson GC, Perera WR, *et al*. Use of plasma biomarkers at exacerbation of chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2006;174:867-874.
3. Minnaard MC, van de Pol AC, de Groot JAH, *et al*. The added diagnostic value of five different C-reactive protein point-of-care test devices in detecting pneumonia in primary care: a nested case-control study. Scand J Clin Lab Invest. 2015;75:291-295.
4. Bafadhel M, McKenna S, Terry S, *et al*. Acute exacerbations of chronic obstructive pulmonary disease: identification of biologic clusters and their biomarkers. Am J Respir Crit Care Med. 2011;184:662-671.
5. Daniels JM, Snijders D, De Graaff CS, *et al*. Antibiotics in addition to systemic corticosteroids for acute exacerbations of chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2010;181:150-157.