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Role of CRP in Acute Exacerbation of Chronic Obstructive Pulmonary Disease

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ABSTRACT

Chronic obstructive pulmonary disease (COPD), a common respiratory disorder has high morbidity and mortality. The frequency and severity of disease exacerbation are the most important factors in determining the overall prognosis of COPD. 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. Serum C-reactive protein (CRP), a sensitive biomarker for systemic inflammation and tissue damage, is a good indicator of lower respiratory tract bacterial infections. This study was conducted to evaluate role of CRP in acute exacerbation of COPD (AECOPD), and whether it can guide the clinician to start prescribing appropriate antibiotics rationally and avoid their indiscriminate use. A total of 65 patients were included in this study over a period of 18 months conducted and studied using standard statistical methods. 78.46% patients had raised CRP levels (>6mg/dL). 56.9% of patients had bacterial aetiology for AECOPD, of which more than 50% had positive sputum bacterial culture. Normal CRP was seen in 8.1% patients with bacterial exacerbations against 39.3% patients with nonbacterial exacerbation which was statistically significant (p value 0.006). The mean CRP levels too were significantly higher in bacterial exacerbations group (p value 0.0011). The sensitivity of CRP (> 6 mg/dl) to detect bacterial AECOPD is 91.8% and specificity is 39.2%. CRP may be used as an initial investigation in deciding use of appropriate antibiotics in acute exacerbation of COPD.

Keywords: Acute exacerbation of chronic obstructive pulmonary disease, C-reactive protein

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INTRODUCTION

COPD (Chronic Obstructive Pulmonary Disease) is defined as a disease state characterized by persistent respiratory symptoms and airflow limitation that is not fully reversible[1]. COPD is currently the fourth leading cause of death in the world[2]. COPD represents an important public health challenge that is both preventable and treatable. Many people suffer from this disease for years and die prematurely from it, or its complications. Globally, the COPD burden is projected to increase in coming decades because of continued exposure to COPD risk factors and ageing of the population[3].

CRP is most widely used biomarker when investigating and monitoring respiratory infections. Multiple studies have found that CRP levels rise consistently during an acute COPD exacerbation. Few studies have indicated that it is the most effective marker for determining the bacterial etiology due to significant rise of CRP in bacterial infection[4,5].

The guidelines of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) recommend the use of antibiotics in moderately or severely ill patients with acute exacerbations of COPD who have increased cough and sputum purulence[6]. Recommendations for antibiotic prescribing in primary care practice are generally based on clinical features alone (e.g., the Anthonisen criteria[7], which include increased dyspnea, increased sputum volume, and increased sputum purulence), but these features are subjective and insufficiently accurate in predicting which patients can be treated safely without antibiotics[8]. Thus, if CRP can guide that the cause of exacerbation in COPD is bacterial, then it would help to reduce the rate of antibiotic prescriptions for acute exacerbation of COPD.

MATERIALS AND METHOD

This is a cross sectional study carried out in Dhiraj hospital, Pipariya, over a period of one and a half year from the date of approval from the ethics committee. SVIEC/ON/MEDI/BNPG19/D20020

Inclusión criteria

- Age >18 years
- Any know COPD patients (PFT proven) presenting with exacerbation
- Criteria for diagnosing exacerbations of COPD – Patients presenting with any of the following symptoms
    - Increased dyspnea
    - Increased sputum volume
    - Increased sputum purulence
- Patients with acute exacerbation of COPD in whom antibiotic has not been started approval from the institutional ethics committee. It was an observational cross-

sectional study.

Exclusion criteria

- Any person who is not willing to participate in the study
- Age < 18 years
- Pregnant Females
- Patient with active infection
- Patient with history of surgery/ trauma in past 3 months
- Patient who is known case of asthma
- Patient with active tuberculosis
- Patient with active chronic inflammatory condition (eg rheumatoid arthritis, systemic lupus erythematosus)
- Patient who is currently taking steroids
- Patient who has taken oral antibiotics in previous four weeks
- Patient having any malignancy
- Patient with bronchiectasis of any etiology other than COPD
- Patient with any chronic kidney disease or chronic liver disease

RESULTS AND DISCUSSION

Natural history of COPD is characterized by gradually progressive impairment in lung function, which is interrupted with exacerbations of varying severity. Exacerbations are associated with significant decrease in quality of life, increased health care resource utilization, morbidity and mortality. Several factors responsible for AECOPD are respiratory tract infections, air pollution, allergen exposure, and interruption of medications. Respiratory tract infections are the most common cause of AECOPD. Bacterial infection account for more than half of these acute episodes, while viruses cause around one fourth episodes. CRP is an acute phase reactant and is a reliable marker of inflammation. It is quantifiable and can be measured within minutes. Present study was undertaken to know if CRP levels can be used to identify bacterial exacerbation to help differentiate between bacterial and non-bacterial cause of exacerbation and to identify if the CRP level correlated with the specific bacterial organism ; so as to use CRP as a marker to guide treatment in AECOPD.

In present study, maximum number of patient were in the age group ≥ 60 years. The mean age of study group was 60.7±11.3 years. This is comparable to the study by Miguel Gallego[9], to know the role of CRP in acute exacerbation of COPD, in which mean age of study group was 65.9±8.2 years. While in study conducted by D. Dev et al[10], to study value of CRP in acute exacerbation of COPD, mean age of study group was slightly on higher side; 71± 8 years. This shows that most of the patients present in late adulthood favouring slow

progression of COPD which develops over years. In present study, 86.% were males and 13.8% were female, showing a male predominance with male : female ration of 6.2:1. Similar male predominance was seen in study by Reshu Agrawal et al[11] and Prakhar Sharma et al[12]. As the most common cause of COPD is smoking and addiction of smoking is more common in males than females, this predominance may be explained. It was observed that most of the patients were in Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage 2 and 4 in the present study (Table 1), while in the study by Miguel Gallego[9] most of the patients were in GOLD 4 and in study by Christopher C. Buttler[13] most of patients were in GOLD stage 2 and 3. This suggest that patient of any GOLD stage can present with exacerbation events.

Table 1: Baseline distribution of GOLD Stage

Gold stage	No. of patient (n)	Percentage (%)
Stage 1	12	18.46
Stage2	20	30.77
Stage 3	13	20.00
Stage 4	20	30.77
Total	65	100.00

Several studies have shown CRP level is increased in acute exacerbation of COPD. In present study, raised CRP (>6mg/dl) was found in 78% of patients at the time of presentation to hospital (Table 2). Also, study by D. Dev et al[10] concluded 84% patients in AECOPD had an elevated CRP at the time of admission to hospital. In study by Ahmet Bircan et al[14], raised CRP was found in AECOPD (COPD patient with acute exacerbation) and PCOPD (COPD patients with pneumonia on chest x ray). As previous studies have suggested CRP to be a marker of AECOPD, similar observation was made in the present study.

Table 2: Correlation of CRP with acute exacerbation of COPD

CRP	No. of patients (n)	Percentage (%)
NORMAL(<6.0 mg/dl)	14	21.54
ABNORMAL(>=6.0 mg/dl)	51	78.46
TOTAL	65	100

In present study, mean CRP (23.93 mg/dl) in patients in whom sputum culture and/or microscopy was positive for bacterial infection was significantly higher than mean CRP (8.2 mg/dl) in patients in whom microbiology studies were negative for bacteria (Table 3). This finding was consistent with the study by Miguel Gallego[9], who also found median CRP in patients with positive culture for bacteria to be on higher side than in patients positive for viruses and patients negative for any microorganism; and also to the study by Ahmet Bircan et al[14], who observed raised CRP in PCOPD compared to AECOPD. In this study, CRP was raised in both the groups, but CRP was significantly higher in patients having bacterial infection as the cause for acute exacerbation.

This observation was similar to the observation in the study by Weis and Almdal et al[15] that high CRP levels may be a marker of significant bacterial infection and thus, may be used in deciding whether or not to start antibiotic treatment. Another study by Cristopher C. Butler et al[13], showed CRP-guided prescription of antibiotics for exacerbations of COPD in primary care clinics resulted in a lower percentage of patients who reported antibiotic use and who received antibiotic prescriptions from clinicians, with no evidence of harm[13]

Table 3: Mean CRP in Bacterial cause and other cause for AECOPD

Cause of Exacerbation	CRP (Mean)	Standard deviation	P value
Bacterial cause (n=37)	23.93	22.14	0.0011
Other Cause (n=28)	8.20	11.38	

Out of 65 number of patients presenting with COPD exacerbation, 56.8% of patients had bacterial cause proven by sputum culture and/or sputum microscopy (Table 4). This finding of the present study can be correlated with the literature stating approximately 50% of COPD exacerbation are associated with bacterial infection as the etiology for exacerbation. Similar frequency of bacterial isolation has been seen in several Indian and foreign studies. In study by Prakhar Sharma et al[12], who studied sputum bacteriology and antibiotic sensitivity pattern in COPD exacerbation in India, found sputum culture positive in 48.7% of patients and in study by Miguel Gallego et al[9], 64.3% of patients; and also in study by Dev et al[10], 58% of patient in acute exacerbation had positive sputum culture for bacteria. From Table 5, it is observed that out of 37 patients with bacterial exacerbation, 91.8% had raised CRP (>6 mg/dl) and out of 28 patients in whom bacterial cause of exacerbation was not found 60.7% had abnormal CRP. While, out of 37 patients with bacterial exacerbation, 8.1% patient had normal CRP levels; and out of 28 patients in whom bacterial cause of exacerbation was not found 39.3% patients had normal CRP levels. This finding is statistically significant (p = 0.006).

Table 4: Frequency of patients with acute exacerbation of COPD due to bacterial infection (Bacterial AECOPD)

Sputum Positive (Bacterial AECOPD)	No. of patients (n)	Percentage (%)
Culture positive	19	29.2
Gram stain positive, culture negative	18	27.6
Total	37	56.8

Table 5: Correlation of CRP in patients with Bacterial AECOPD versus Other cause for AECOPD

CRP	Bacterial AECOPD n (%)	Other Cause n (%)	P value
Abnormal	34 (91.89 %)	17 (60.71%)	0.006
Normal	3 (8.11 %)	11(39.29%)	
Total	37	28	

The sensitivity of CRP (> 6 mg/dl) to detect bacterial AECOPD is 91.8% and specificity is 39.2 %(Table 6).

Table 6: Sensitivity and specificity of CRP

Sensitivity	91.89%
Specificity	39.29%
Positive Likelihood Ratio	1.51
Negative Likelihood Ratio	0.21
Disease prevalence	56.92%
Positive Predictive Value	66.67%
Negative Predictive Value	78.57%

Also, in our study, we observed and derived few interesting observations like abnormally high CRP levels were present in patients with higher pack years history. Also, at higher GOLD stage, CRP levels were abnormally high. However, these findings are not statistically significant. These findings although insignificant, they may provide insight for planning further studies in this area.

CONCLUSION

This study demonstrates high prevalence of bacterial infection as the cause of acute exacerbations in Chronic Obstructive Pulmonary Disease, (in about half of the patients). CRP is raised in exacerbations of Chronic Obstructive Pulmonary Disease; and has significantly higher values in exacerbation due to bacterial infection than other causes. Bacteria isolated in our study were Haemophilus influenzae, Streptococcus pneumoniae, Pseudomonas aeruginosa, Moraxella catarrhalis, Klebsiella pneumoniae and Escherichia coli. From this study it may be concluded that raised CRP level is an indicator of bacterial infection and may be used for deciding use of antibiotics in acute exacerbation of COPD.

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Abbreviations

1. COPD- Chronic Obstructive Pulmonary Disease
2. CRP-C reactive Protein
3. AECOPD- Acute Exacerbation of COPD
4. PCOPD-Pneumonia on Chest X-ray in AECOPD
5. GOLD-Global Initiative for Obstructive Lung Disease

Declarations

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REFERENCES:

1. Edwin K. Silverman, James D. Crapo, Barry J. Make; Chronic Obstructive Pulmonary Disease. Harrison's Principle of Internal Medicine 20th Edition; Volume (2), section 286.
2. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010:a systematic analysis for the Global Burden of Disease Study 2010.Lancet 2012;380(9859):2095-128.
3. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Mede 2006;3(11): e442.
4. Bafadhel M, McKenna S,Terry S, et al. Acute exacerbation of COPD: identification of biological clusters and their biomarkers. Am J Respir Crit Care Med 20111;186:662-71.
5. Chuynhong Peng, Tian Chan, et al. C - reactive protein Levels Predict Bacterial Exacerbation in patients with Chronic Obstructive Pulmonary Disease; The American Journal of Medical Sciences, 345, 3(2013).
6. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease: 2021 Report. www.goldcopd.org (Accessed on September 30, 2021).
7. Anthonisen NR, Manfreda J, Warren Cp, Hershfield Es, Harding GK, Nelson NA. Antibiotic therapy in exacerbations of chronic obstructive pulmonary disease. Ann Intern Med 1987:106:196-204.
8. Miravitles M, Morgas A, Hernandez S, Bayona C, Llor C. Is it possible to identify exacerbations of mild to moderate COPD that do not require antibiotic treatment? Chest 2013;144:1571-7.
9. Gallego M, Pomares X, Capilla S, Marcos MA, Suárez D, Monsó E, Montón C. C-reactive protein in outpatients with acute exacerbation of COPD: its relationship with microbial etiology and severity. International J Chronic Obstructive Pulmonary Disease. 2016; 11:2633.
10. Dev D, Wallace E, Sankaran R, Cunniffe J, Govan JR, Wathen CG, Emmanuel FX. Value of C-reactive protein measurements in exacerbations of chronic obstructive pulmonary disease. Respiratory medicine. 1998 Apr 1; 92(4):664-7.
11. Agarwal R, Zaheer MS, Ahmad Z, Akhtar J. The relationship between C-reactive protein and prognostic factors in chronic obstructive pulmonary disease. Multidisciplinary respiratory medicine. 2013 Dec; 8(1):1-5.
12. Sharma P, Narula S, Sharma K, Kumar N, Lohchab K, Kumar N. Sputum

bacteriology and antibiotic sensitivity pattern in COPD exacerbation in India. Egyptian Journal of Chest Diseases and Tuberculosis. 2017 Oct 1; 66(4):593-7.

13. Butler CC, Gillespie D, White P, Bates J, Lowe R, Thomas-Jones E, Wootton M, Hood K, Phillips R, Melbye H, Llor C. C-reactive protein testing to guide antibiotic prescribing for COPD exacerbations. New England Journal of Medicine. 2019 Jul 11;381(2):111-2
14. Bircan A, Gokirmak M, Kilic O, Ozturk O, Akkaya A. C-reactive protein levels in patients with chronic obstructive pulmonary disease: role of infection. Medical Principles and Practice. 2008;17(3):202-8.
15. Weis N, Almdal T. C-reactive protein can it be used as a marker of infection in patients with exacerbation of chronic obstructive pulmonary disease? European Journal of Internal Medicine. 2006 Mar 1; 17(2):88-91.