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C - reactive protein as A Marker of Status of Chronic Obstructive Pulmonary Disease (COPD): A Prospective Study from PGIMS, Rohtak

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Original Research Article

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Abstract: In spite of the relation between systemic inflammation and CRP in COPD, only a few studies have assessed the role of CRP in measuring the level of systemic inflammation in COPD to assess the status of disease. The present study was planned to correlate the levels of C-reactive protein as a marker of status of COPD. A total of 100 known patients of COPD, diagnosed on the basis of GOLD guidelines, presenting with moderate acute exacerbation were taken in the study. All of these patients were evaluated at the time of admission, discharge from the ward and at follow-up at six week and levels of CRP were correlated with disease duration, spirometric lung function FEV_1, arterial oxygen tension and total leucocyte count to evaluate it as a marker of status of COPD. It correlated significantly positively with TLC and negatively with FEV_1 and SpO_2. CRP at discharge and follow-up showed significant negative correlation with disease duration. However, it did not correlate with age, duration of smoking and pack years. As CRP elevation was also found in the cases where infective exacerbation could not be demonstrated, so it may be a marker for non-infective exacerbation also. CRP is an important biomarker in COPD to evaluate the status of disease. It is a useful and early marker of the exacerbation and is also beneficial in assessing efficacy of treatment. Thus, CRP estimation should be a routine investigation in COPD patients to know the baseline level, indication of exacerbation and response to therapy in each patient.
Keywords: C-reactive protein, COPD, marker, spirometry

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality throughout the world [1]. According to the Global Burden of Disease Study, it results in 1.68 years of living with disability (YLD) per 1,000 population, representing 1.8% of all YLDs, with a greater burden in men than in women (1.93% vs. 1.42%)[2]. Considering the global trends of the present day, increases in the prevalence and mortality of the disease have been predicted in the coming decades.

CRP has been found to be elevated in stable COPD patients as a marker of persistent low-grade systemic inflammation [3]. It seems to increase with increasing severity of COPD [4]. CRP elevation has been found in patients with proven infection and also in those where infection was not proven. Thus, it is possible that while it is a marker for COPD exacerbation, it is not necessarily a marker of bacterial infection [5,6].

In spite of the relation between systemic inflammation and CRP in COPD, only a few studies have assessed the role of CRP in measuring the level of systemic inflammation in COPD to assess the status of disease. The present study was planned to correlate the levels of C-reactive protein with disease duration, spirometric lung function FEV_1, arterial oxygen tension and total leucocyte count in patients of chronic obstructive pulmonary disease presenting with acute exacerbation, discharge and follow up after 6 weeks to evaluate it as a marker of status of COPD.

MATERIALS & METHODS

The study was conducted in Department of Tuberculosis and Respiratory Medicine in collaboration with Department of Biochemistry, Pt. Bhagwat Dayal Sharma Post Graduate Institute of Medical Sciences, Rohtak. A total of 100 known patients of COPD, diagnosed on the basis of GOLD guidelines, presenting with moderate acute exacerbation were taken in the study. Patients with disease duration less than six months, with recent use of oral steroids, history of respiratory disease other than COPD, or having any comorbid condition / inflammatory disease were excluded from the study. All of these patients were evaluated at the time of admission, discharge from the ward and at follow-up at six week and levels of CRP were correlated with disease duration, spirometric lung function FEV_1, arterial oxygen tension and total leucocyte count to evaluate it as a marker of status of COPD.

After detailed history, clinical examination, and routine investigations each case was subjected to spirometry, blood gas analysis and CRP estimation by quantitative turbidimetric test. All the proforma were manually checked and edited for completeness and consistency and were then coded for computer entry. After compilation of collected data, analysis was done using Statistical Package for Social Sciences (SPSS), version 20 (IBM, Chicago, USA). The results were expressed using appropriate statistical methods.

RESULTS

The mean age of the patients was 59.38±11.70 years. Majority of the patients (80%) were between 45-74 years of age. All patients had airflow limitation that was not fully reversible (postbronchodilator FEV_1 < 80% of the predicted value in combination with FEV_1/FVC ratio < 70%). Mean duration of admission was 8.76±4.62 days. Most of the patients were chronic smokers (56%). 27 (27%) of the patients were ex-smokers and 17 (17%) were non-smokers. The mean duration of admission was 8.76±4.62 days ranging from 3 to 35 days.

The correlation between CRP at admission and COPD parameters like age, duration of illness, duration of smoking, pack-years, FEV_1, FEV_1 % predicted, TLC and SpO_2 at the time of admission. CRP at admission showed statistically significant negative correlation with FEV_1, FEV_1 % Predicted and SpO_2. CRP at admission showed statistically significant positive correlation with Total leukocyte count. No significant correlation was evident between CRP level at admission and age, duration of illness, duration of smoking and pack-years of smoking. (Table 1)

Table-1: Correlation of CRP with Age, Duration of Illness & Smoking, Pack-years, FEV_1, FEV_1 % Predicted, TLC AND SpO_2 at Admission

Variables	CRP at Admission	
	Pearsons' coefficient (r)	p-value (p)
Age	-0.013	0.901
Duration of Illness	0.032	0.751
Duration of smoking	0.047	0.644
Pack-years	-0.023	0.819
FEV_1	-0.442**	0.000
FEV_1 % Predicted	-0.410**	0.000
TLC	0.560**	0.000
SpO_2	-0.237*	0.018
**Significant at the 0.01 level, *significant at the 0.05 level		

The correlation between CRP at discharge and COPD parameters like age, duration of illness, duration of smoking, pack-years, FEV_1, FEV_1 % predicted, TLC and SpO_2 at the time of discharge from the ward. CRP at discharge showed statistically significant negative correlation with FEV_1, FEV_1 % predicted. CRP at discharge showed statistically significant positive correlation with Total leukocyte count and duration of illness. No statistically significant correlation was evident between CRP value at discharge and age, duration of smoking, pack-years of smoking and SpO_2. (Table 2)

Table-2: Correlation of CRP with Age, Duration of Illness & Smoking, Pack-years, FEV_1, FEV_1 % Predicted, TLC AND SpO_2 at Discharge

Variables	CRP at Discharge	
	Pearsons' coefficient (r)	p-value (p)
Age	-0.081	0.420
Duration of Illness	0.212*	0.034
Duration of smoking	-0.024	0.816
Pack-years	-0.131	0.195
FEV_1	-0.297**	0.003
FEV_1 % Predicted	-0.261**	0.009
TLC	0.328**	0.001
SpO_2	-0.091	0.370
**Significant at the 0.01 level, *significant at the 0.05 level		

The correlation between CRP at follow-up and COPD parameters like age, duration of illness, duration of smoking, pack-years, FEV_1, FEV_1 % predicted TLC and SpO_2 at the time of follow-up at six weeks. CRP showed statistically significant negative correlation with FEV_1 and SpO_2 at follow-up. It showed statistically significant positive correlation with Total leukocyte count and duration of illness. No statistically significant correlation was evident between CRP value at follow-up and age, duration of smoking, pack-years of smoking and FEV_1 % predicted. (Table 3)

Table-3: Correlation of CRP with Age, Duration of Illness & Smoking, Pack-years, FEV_1, FEV_1 % Predicted, TLC and SpO_2 at Follow-up

Variables	CRP at Follow-up	
	Pearsons' coefficient (r)	p-value (p)
Age	0.073	0.472
Duration of Illness	0.207*	0.039
Duration of smoking	-0.002	0.988
Pack-years	-0.085	0.402
FEV_1	-0.287**	0.004
FEV_1 % Predicted	-0.195	0.051
TLC	0.364**	0.000
SpO_2	-0.315**	0.001
**Significant at the 0.01 level, *significant at the 0.05 level		

DISCUSSION

CRP is an acute-phase protein produced by the liver in response to IL-6 stimulation. CRP is raised in most conditions associated with infection, inflammation, or tissue damage, for which it is a sensitive marker[7]. Evidence suggests that CRP may also be implicated in the pathophysiology of COPD: many deaths at exacerbation are due to cardiovascular disease and an elevated CRP concentration is associated with increased cardiovascular morbidity[8]. CRP and IL-6 could therefore provide a link between airway inflammation, systemic inflammation, and cardiovascular disease in COPD[9].

It is now widely accepted that COPD is associated with increased systemic inflammation compared with control subjects, and that there is further up-regulation of systemic inflammation at the time of exacerbation[10]. Markers reported to be higher in blood during exacerbation compared with the baseline state include CRP, IL-8, tumor necrosis factor-alpha, leptin, endothelin-1, eosinophil cationic protein, myeloperoxidase, fibrinogen, IL-6, alpha-1-antitrypsin, and leukotriene E4[11]. However, no studies have specifically reported the use of such assessment in the confirmation of exacerbation. Also, serum IL-6 and CRP concentrations at exacerbation are correlated with selected markers of airway inflammation, and are higher in the presence of a bacterial pathogen. This suggests that assay of systemic inflammatory markers may to some extent reflect inflammatory load in the airway, although the precise source of systemic inflammation remains to be confirmed[12].

Among all the 100 patients, the mean age was 59.38±11.70 years ranging from 35 to 84 years. Maximum numbers of patients (80%) were between 45-74 years of age. Mean age was similar to previous studies[13]. Bircan *et al*. detected that the CRP levels were positively correlated with leukocyte count both in the AECOPD group (r = 0.575, p =0.0001) and in the entire study population (r = 0.536, p =0.0001)[14].

We observed that CRP at admission showed statistically significant negative correlation with FEV_1, FEV_1 % Predicted and SpO_2. CRP at admission showed statistically significant positive correlation with Total leukocyte count. No significant correlation was evident between CRP level at admission and age, duration of illness, duration of smoking and pack-years of smoking. Dev et al found that both peak CRP level and fall in CRP correlated positively with the corresponding TLC count ($r=0.44$, $p<0.01$)[6].

Bircan *et al***.** found that CRP levels were negatively correlated with partial pressure of arterial oxygen, FEV_1 and FEV_1 % in the overall study population ($r = 0.317$, $p = 0.0001$; $r = 0.203$, $p = 0.0001$; $r = 0.410$, $p = 0.0001$, respectively). However, no correlation was found when the population was restricted to the AECOPD group[14].

CONCLUSION

CRP is an important biomarker in COPD to evaluate the status of disease. It is a useful and early marker of the exacerbation and is also beneficial in assessing efficacy of treatment. It correlated significantly positively with TLC and negatively with FEV_1 and SpO_2. CRP at discharge and follow-up showed significant negative correlation with disease duration. However, it did not correlate with age, duration of smoking and pack years. As CRP elevation was also found in the cases where infective exacerbation could not be demonstrated, so it may be a marker for non-infective exacerbation also. Thus, CRP estimation should be a routine investigation in COPD patients to know the baseline level, indication of exacerbation and response to therapy in each patient.

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