



Original Research Article

A study of factors associated with raised C reactive protein levels in patients with chronic obstructive pulmonary disease

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ABSTRACT

Background: C-reactive protein (CRP) is used to predict the prognosis of patients with COPD. It has been observed that the degree of obstruction in the airflow is related with the levels of CRP.

Objective: To study factors associated with raised C reactive protein (CRP) levels in patients with chronic obstructive pulmonary disease

Materials and Methods: The present study was Hospital based cross-sectional study among 47 subjects with stable chronic obstructive pulmonary disease (COPD). Detailed history, thorough clinical examination was carried out. Body mass index (BMI), Six minute walk distance test (6MWD) was performed, forced expiratory volume in 1 second (FEV₁ % Pred), arterial oxygen tension (PaO₂) and smoking status (no. of pack years) was assessed for subjects

Results: The prevalence of raised CRP was significantly more in those with 6MWD with <450 meters compared to those with 6MWD of >450 meters. The prevalence of raised CRP was significantly more in those with FEV₁ % Predicted <30–50 compared to those with FEV₁ % Predicted 51–100. The proportion raised CRP was significantly more in those having PaO₂ (mmHg) <60–70 compared to those with PaO₂ (mmHg) 71–100. Underwent had raised CRP compared to only normal weight cases. Prevalence of raised CRP was 87.5% among those who smoked more than five pack years of cigarette compared to only 50% but this association was not found to be statistically significant (p>0.05)

Conclusion: Serum CRP levels were significantly associated with 6MWD test, BMI, FEV₁ % Predicted and PaO₂ in patients with stable COPD. But it was not associated with smoking.

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1. Introduction

Global Initiative on Obstructive Lung Disease (GOLD) recognized chronic obstructive pulmonary disease (COPD) as a chronic disease and also as inflammatory disease. It is preventable disease. It is also treatable. It has extra-pulmonary effects and they are correlated with the severity of the disease. There is irreversible and progressive limitation of the airflow. The lungs in COPD react to gases

and particles abnormally.¹

There is limitation to the air flow during expiration which happens to be progressive and takes years to do so.² COPD is an important public health problem from the point of view that its prevalence is increasing and at the same time the mortality due to COPD is increasing.³

Studies have pointed out that an inflammatory response which is not normal takes place outside lungs in patients with COPD. It also leads to other manifestations like loss of weight, dysfunction of the skeletal muscles. COPD patients are prone to develop cardiovascular diseases, depression as

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well as osteoporosis.^{4,5}

C-reactive protein (CRP) is one marker of inflammation which is evaluated in the patients with COPD. It is mainly synthesized in the liver as a result of inflammation in the body or any cases of damage to the tissue.⁶ CRP raised levels are an indicator of overall inflammation in a person. In COPD also it increases even when the patient is stable.^{7,8}

C-reactive protein (CRP) is used to predict the prognosis of patients with COPD. It has been observed that the degree of obstruction in the airflow is related with the levels of CRP.⁹

Few studies are there that study the factors associated with raised CRP or which factors act as aggravating factors for raised CRP in patients with stable COPD. Hence present study was undertaken with an aim to study factors associated with raised C reactive protein levels in patients with chronic obstructive pulmonary disease

2. Materials and Methods

2.1. Study design

Hospital based cross sectional study.

2.2. Study period

From July 2009 to October 2010.

2.3. Settings

Department of Pulmonary Medicine, GSVM Medical College, Kanpur, Uttar Pradesh.

2.4. Sample size

We were able to include 47 participants eligible as per the inclusion and exclusion criteria.

2.5. Ethical considerations

Institute Ethics Committee approval was obtained. Informed consent was taken. All patients were given treatment as per standard guidelines.

2.6. Inclusion criteria

1. Known cases of stable COPD as per standard guidelines admitted in the Pulmonary Medicine wards or out-patient department subjects
2. Post bronchodilator FEV₁/FVC ratio of <0.7 after 400 micrograms of inhaled salbutamol

2.7. Exclusion criteria

1. Unstable COPD patients.
2. Not willing to participate in the present study.
3. Eligible patients but with severe comorbidities.

The participants were explained the nature of the study and if they were found eligible and willing, informed consent was taken. As per pre tested, pre designed and semi structured study questionnaire developed for the present study, detailed history was taken and recorded. Thorough clinical examination was carried out. For body mass index, height and weight were measured and recorded as per the standard guidelines. Body mass index less than 18.5 kg/m² were taken as underweight, 18.5 to 24.9 kg/m² as normal weight and more than 25 kg/m² as overweight. Six minute walk test was performed. Forced expiratory volume in 1 second (FEV₁% Pred), arterial oxygen tension (PaO₂) and smoking status (no. of pack years) was assessed for subjects

2.8. Statistical analysis

The data was entered in Microsoft Excel worksheet and analyzed using proportions. Chi square test was applied and two tailed p value was calculated. P value less than 0.05 was taken as statistically significant.

3. Results

The prevalence of raised CRP was 94.3% in those with 6MWD with < 450 meters compared to only 16.7% in those with 6MWD of >450 meters. This association was found to be statistically significant (p<0.05). (Table 1)

The prevalence of raised CRP was 87.5% in those with FEV₁% Pred <30 – 50 compared to only 46.7% in those with FEV₁% Pred 51-100 and this association was found to be statistically significant. (Table 2)

The proportion raised CRP was 92.6% with those having PaO₂ (mmHg) <60-70 which was found to be significantly higher compared to 50% among those with PaO₂ (mmHg) 71-100 (p<0.05) (Table 3)

It was observed that 87.1% of underwent had raised CRP compared to only 50% from normal weight category as per body mass index and this association was found to be statistically significant. (Table 4)

Out of 47 subjects included in the present study, 20 had history of smoking. Among them it was observed that the prevalence of raised CRP was 87.5% among those who smoked more than five pack years of cigarette compared to only 50% but this association was not found to be statistically significant (p>0.05) (Table 5).

4. Discussion

The prevalence of raised CRP was 87.5% in those with FEV₁% Pred <30 – 50 compared to only 46.7% in those with FEV₁% Pred 51-100 and this association was found to be statistically significant. The proportion raised CRP was 92.6% with those having PaO₂ (mmHg) <60-70 which was found to be significantly higher compared to 50% among those with PaO₂ (mmHg) 71-100 (p<0.05) Out of 47 subjects included in the present study, 20 had history of

Table 1: Association between Serum CRP levels with six minute walk distance (6MWD)

CRP level (mg/dl)	6MWD (meters) 451-600	6MWD (meters) <450	Chi square	P value
<0.6 – 1.2	10 (83.3%)	2 (5.7%)	24.38	<0.0001
1.3 - >2.4	2 (16.7%)	33 (94.3%)		
Total	12 (25.5%)	35 (74.5%)		

Table 2: Association between Serum CRP levels with forced expiratory volume in 1 second (FEV₁% Pred)

CRP level (mg/dl)	FEV ₁ % Pred 51-100	FEV ₁ % Pred <30 – 50	Chi square	P value
<0.6 – 1.2	8 (53.3%)	4 (12.5%)	6.937	0.008
1.3 - >2.4	7 (46.7%)	28 (87.5%)		
Total	15	32		

Table 3: Association between Serum CRP levels with arterial oxygen tension (PaO₂)

CRP level (mg/dl)	PaO ₂ (mmHg) 71-100	PaO ₂ (mmHg) <60-70	Chi square	P value
<0.6 – 1.2	10 (50%)	2 (7.4%)	8.837	0.002
1.3 - >2.4	10 (50%)	25 (92.6%)		
Total	20 (42.6%)	27 (57.4%)		

Table 4: Association between Serum CRP levels with body mass index (BMI)

CRP level (mg/dl)	BMI (Kg/m ²) 18.5-24.9	BMI (Kg/m ²) < 18.5	Chi square	P value
<0.6 – 1.2	8 (50%)	4 (12.9%)	5.812	0.015
1.3 - >2.4	8 (50%)	27 (87.1%)		
Total	16 (34.1%)	31 (65.9%)		

Table 5: Association between Serum CRP levels with smoking status (no. of pack years) (N=20)

CRP level (mg/dl)	< 5 pack years	> 5 pack years	Chi square	P value
<0.6 – 1.2	2 (50%)	2 (12.5%)	0.957	0.327
1.3 - >2.4	2 (50%)	14 (87.5%)		
Total	4 (20%)	16 (80%)		

smoking. Among them it was observed that the prevalence of raised CRP was 87.5% among those who smoked more than five pack years of cigarette compared to only 50% but this association was not found to be statistically significant ($p > 0.05$)

Lapperre TS et al¹⁰ observed that levels of CRP can be used to predict the occurrence of COPD in people. This prediction was found to be irrespective of results of the lung function in cases.

Inga Sif Ólafsdóttir et al¹¹ found from their study that in cases with reduced lung function test results, the CRP levels were increased. This negative association was more marked in males compared to females. They also reported that there was a significant association between raised CRP and FEV₁ for males but not for females. Mannino DM et al¹² also reported that after controlling for smoking that there is association between raised CRP levels and reduced FEV₁. Shaaban et al¹³ analyzed 531 subjects and found that as FEV₁ decreased, the CRP increased significantly. Man SFP et al¹⁴ also noted that as the CRP increased, the FEV₁ decreased and concluded that CRP can be a useful tool for screening high risk patients.

In the present study The prevalence of raised CRP was 94.3% in those with 6MWD with < 450 meters compared to only 16.7% in those with 6MWD of >450 meters. This association was found to be statistically significant ($p < 0.05$). Koechlin C et al¹⁵ observed that as the endurance time increased the CRP levels decreased. Broekhuizen R et al¹⁶ noted that those patients who demonstrated poor capacity to exercise, the CRP in such cases was high. Pinto-Plata VM et al¹⁷ evaluated 88 cases of COPD and compared them with 71 controls and they observed that more the distance covered in 6MWD, less the CRP reading was controlling for age, sex and smoking. The pathogenesis behind this poor 6MWD is that the COPD results as a result of dysfunction of the skeletal muscles. COPD patients are prone to loose muscle and hence they are unable to pass the 6MWD test.¹⁸

It was observed in the present study that 87.1% of underwent had raised CRP compared to only 50% from normal weight category as per body mass index and this association was found to be statistically significant. No one patient in the present study was obese. Breyer MK et al¹⁹ noted that the risk of raised CRP was 3.3 times more in obese cases compared to normal weight cases.

At the same time, they also noted that underweight cases were two times less likely to have raised CRP compared to the normal weight cases. But in the present study, we found that prevalence of raised CRP was much more and significant among the underweight cases compared to the normal weight cases. Schols AM et al²⁰ found that those patients having low fat free mass along with the high resting energy expenditure, the CRP levels were high.

Based on the results from different studies, it is recommended that the investigation of serum CRP should be carried out to detect the cardiovascular diseases. CRP can also be used as an important tool for prevention of these diseases.²¹ If the patient is having COPD along with cardiovascular disease, the risk of death is more in such cases.²² Acute attacks in patients with COPD can be predicted based on CRP levels.²³ CRP can also be used to predict the number of hospital admissions as well as death rate in COPD cases.²⁴ CRP is also a marker of poor capacity to exercise. Thus CRP should be routinely done as a screening tool.

5. Conclusion

Serum CRP levels were significantly associated with six minute walk distance test, body mass index, forced expiratory volume and arterial oxygen tension in patients with stable COPD. But it was not associated with smoking.

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No financial support was received for the work within this manuscript.

7. Conflicts of Interest

No conflicts of interest.

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