ORIGINAL REPORT

Association between Serum C- reactive Protein Levels and Other Important Predictive Markers of Outcome in COPD

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Abstract- C-reactive protein (CRP) is an acute-phase protein synthesized predominantly by the hepatocytes in response to tissue damage or inflammation. Levels of acute-phase proteins rise rapidly, during infection and after injury. We take up the study to correlate serum CRP levels with other important predictive markers of outcome in COPD. Patient with stable COPD (no exacerbation in the last two months) were taken up for the study. Parameters taken to correlate were age, grade of dyspnea, FEV1. It was found the CRP is negatively correlated with FEV1 and grade of dyspnea but not correlated with age.

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Keywords: Pulmonary disease, chronic obstructive; C-reactive protein; Forced expiratory volume

Introduction

Elevated CRP has been known for some time to be a predictor of adverse events in cardiovascular disease and is increasingly used as a surrogate marker of systemic inflammation in diverse conditions. The association of elevated CRP with poor lung function indices was first observed a few years ago in population surveys (1).

Non-hepatic production of CRP by monocytes and lymphocytes has been demonstrated and it is possible that some CRP is made locally in the inflamed lung. It is widely accepted that CRP levels relate to the presence of airflow obstruction. It is widely accepted that CRP levels relate to the presence of airflow obstruction (2). This study aims to correlate how CRP is related to prognostic factors of COPD.

Patients and Methods

The study was carried out in the department of Tuberculosis and Chest Diseases, Jawaherlal Nehru Medical College, Aligarh Muslim University, Aligarh (U.P) India, between June 2006 and March 2007. The Ethical Committee of the Hospital (IEC) approved the study and all participants gave written informed consent.

Patients with all levels of airflow severity were included if-

i) Smoker >20 packs years per day.

ii) Post bronchodilator increase in FEV1 <12%.

iii) Patients were clinically stable (no exacerbation for 2 months) at the time of Evaluation.

Exclusion criteria-

i) They had a history of asthma and/or their FEV_1 increased more than 12% or 200 mL after bronchodilation.

ii) Bronchiectasis, tuberculosis or other confounding inflammatory diseases such as malignancy, arthritis, connective tissue disorders or inflammatory bowel disease.

The following variables, which are known to predict outcome in COPD, were evaluated:

Age, dyspnea, degree of airflow obstruction, *via* FEV_1.

FEV_1 and Post Bronchodilator FEV_1 were measured by using Morgan portable spirometer.

Level of dyspnea was graded according to New York Heart and Lung Classification.

Blood samples for CRP measurement were taken after 4 h of fasting, at the same time of the day (08:00 h).

Statistical analysis was done Pearson's correlations with CRP and Spearman's Correlation.

Results

The study was conducted in the department of Tuberculosis and Chest diseases, Jawaherlal Nehru

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Medical College, Aligarh Muslim University Aligarh U.P India between July 2006 till January 2007. 50 patients with COPD (GOLD Guidelines) were enrolled for the study. The mean ± SD age of the patients were 55.86±6.6, Mean ± SD CRP levels were 15.97 ± 8.5, mean ± SD FEV_1 was 0.37 ± 0.13. Significant correlation of CRP with Age (Significant association between age and serum CRP values) was noticed. There was significant correlation between age of the patients and serum C-Reactive Proteins values Pearson's correlations (-0.177; *P*=0.220). Co-Relation of CRP with FEV1 (% predicted) (strong co-relation between serum CRP and FEV1) CRP is negatively associated with FEV_1 values, Values of CRP increases inversely with FEV_1, Pearson's correlations (-0.736, *P*<0.001).

Co-Relation of CRP with dyspnea (strong co-relation between serum CRP and dyspnea) CRP is negatively associated with dyspnea, values of CRP increases inversely with increase in level of dyspnea, Spearman's Correlation (.734, *P*<0.001)

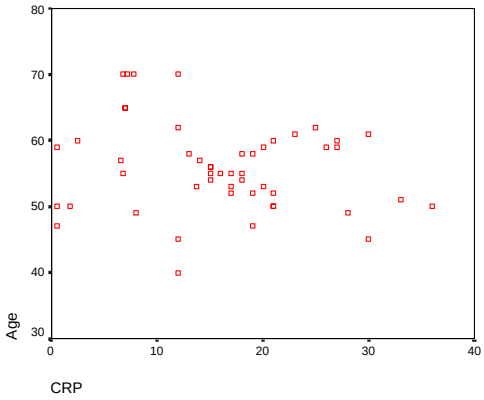

Figure 1. Co-Relation of CRP with Age (Significant association between age and serum CRP values) There was significant correlation between age of the patients and serum C-Reactive Proteins values Pearson's correlations (-0.177; *P*=0.220).

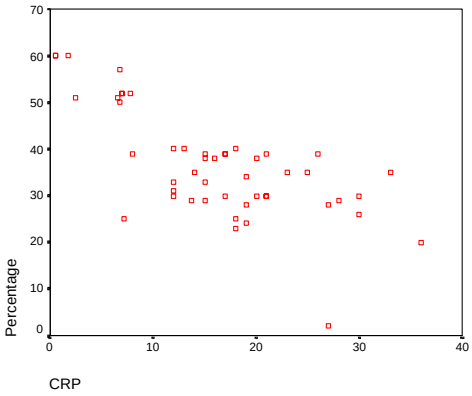

Figure 2. Correlation of CRP with FEV1 (% predicted) (strong co-relation between serum CRP and FEV1) CRP is negatively associated with FEV_1 values, Values of CRP increases inversely with FEV_1, Pearson's correlations (-.736, *P*<0.001)

Table 1. Characteristics of chronic obstructive pulmonary disease patients

Serial Number	Parameters	Subject	Values
1.	Age	50	55.86 ± 6.6
2.	Mean CRP	50	15.97 ± 8.5
3.	FEV_1	50	0.37 ± 0.13

Pearson's correlations with CRP

	Variables	CRP	p
1.	Age	-0.177	0.220
2.	FEV1	-0.736	<0.001

Spearman's Correlation

1.	Dyspnea	0.734	<0.001

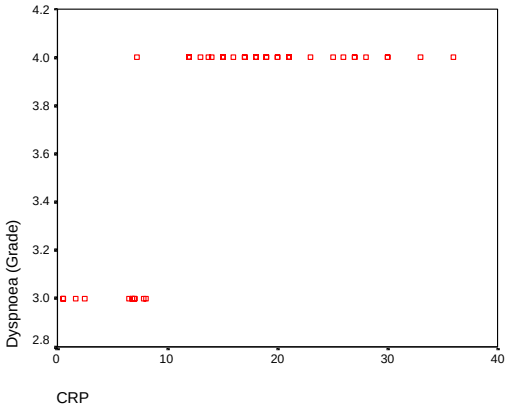

Figure 3. Correlation of CRP with dyspnea (strong co-relation between serum CRP and dyspnea) CRP is negatively associated with dyspnea, Values of CRP increases inversely with increase in level of dyspnea, Spearman's Correlation (0.734, *P*<0.001)

Discussion

The present study support the presence of "extra-pulmonary or systemic" consequences of COPD that can be detected clinically (3) and that could also be measured by the determination and level of increased systemic inflammatory markers (4). CRP is one of these markers. It is an acute-phase protein synthesised predominantly by the hepatocytes in response to tissue damage or inflammation reflecting the total systemic burden of inflammation of individuals. Gan and co-workers (4, 5) were the first to note the importance of high CRP levels in COPD patients. They showed that CRP is elevated in patients who actively smoked, had

reduced lung function (5) or stable COPD (4). They also demonstrated that in patients with COPD, CRP levels predicted cardiovascular mortality and decreased with treatment with inhaled fluticasone (6). Other researchers have shown that: patients with COPD have higher levels of CRP, independent of cardiovascular risk factors; CRP predicts mortality in patients with chronic respiratory failure (7); and CRP levels decrease with exercise (8) and pharmacological therapy with statins (9). Recently, Broekhuizen *et al.* (10) found that high-sensitivity CRP was a marker of impaired energy metabolism, functional capacity and distress in 102 severe COPD patients.

As elevated CRP was found in stable asthma and ex-smokers with COPD, it seems unavoidable to conclude that diseased lung tissue itself must provide the sustained and unrelenting "danger" signal that drives CRP synthesis. This could be because damaged lung tissue might generate endogenous TLR ligands, such as fibronectin, or heat shock proteins, triggering direct inflammation. This could be further amplified by persistent somatic mutations in regulatory genes, such as epidermal growth factor receptor, *ras* oncogene and phosphatase and tensin homologue deleted on chromosome 10 that abound in smoke-exposed epithelium (11), and by transcriptional dysregulation secondary to loss of histone deacetylases (12), especially in more severe disease. In conclusion, CRP is strongly (Negative) associated with FEV_1 and grade of dyspnoea. Patient with increased level of CRP should be managed aggressively before they land up in acute exacerbation.

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