International Journal of Research in Medical Sciences
Mandal P et al. Int J Res Med Sci. 2018 Sep;6(9):3147-3151
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20183660

Original Research Article

Correlation of BMI and serum albumin with c-reactive protein in male patients with stable chronic obstructive pulmonary disease

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Received: 11 July 2018
Accepted: 07 August 2018

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ABSTRACT

Background: There is growing consensus that chronic obstructive pulmonary disease (COPD), a chronic inflammatory disease of the airways and lung parenchyma is associated with low grade systemic inflammation even in stable COPD, which increases during acute exacerbation. It is still debated whether the inflammation is a spill-over from the lung or the lung bears the share of systemic inflammation in COPD. There is systemic manifestation in COPD which is responsible for its severity in individual cases, but it is not clearly known whether the systemic inflammation give rise to systemic manifestations.
Methods: In this background we measured serum C-reactive protein (CRP) level in 53 stable COPD patients and 32 age/sex matched control without known ischemic heart disease (IHD)/ diabetes mellitus (DM)/ peripheral arterial disease and normal chest X-ray and tried to find out any correlation of serum CRP level (marker of systemic inflammation) with BMI and serum albumin (marker of nutritional abnormality).
Results: The study found that serum CRP level was significantly higher in stable COPD patient in comparison to healthy control. (6.226±3.9 vs 1.31±0.53).
Though serum CRP level did not significantly increase with increasing severity of the disease, but serum CRP level was significantly increased in COPD patients with low BMI and low serum albumin (9.10±3.14 vs 4.01±2.90 p value <0.001 and 8.51±3.5 vs 3.59±2.5 with p value <0.001 respectively for BMI and serum albumin).
Conclusions: So, the study concluded that stable COPD is associated with increased systemic inflammatory markers than normal control, correlates significantly with nutritional parameters in COPD like BMI and serum albumin level and may be an indicator of malnutrition regardless of lung function impairment.

Keywords: BMI, COPD, CRP, Systemic inflammation

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a leading cause of morbidity and mortality in developing and developed countries.

Global Initiative for Chronic Obstructive Lung Disease (GOLD) has estimated that, COPD is going to be the third leading cause of death in the world by the year of 2020.[1]

COPD is a multi-component disease, not restricted to lung only, having systemic complications like unexplained weight loss, skeletal muscle weakness, nutritional abnormalities like decrease in haemoglobin and serum albumin, cardiovascular complications and cancer which is related to severity in individual cases and may be responsible for morbidity and mortality due to COPD.[2] Various studies have shown that the most common cause of death in mild to moderate COPD is cardiovascular disease, not the respiratory insufficiency. So, early diagnosis of the disease and its complication is important for effective COPD management. In COPD, there is chronic airway limitation which results from abnormal inflammatory response to various noxious particles and gases specially cigarette smoking. This inflammation is not restricted to lung only. It has been shown that in COPD, there is chronic systemic inflammation even in stable COPD and milder disease.[3] The origin of this systemic inflammation in COPD is still not definitely known and it is unclear whether the inflammation is a "spill-over" from the lung or the lung bears share of systemic inflammation.[4] Whatever may be the mechanism, increased markers of systemic inflammation are seen in stable COPD, the level of which increases with increasing severity of the disease, presence of systemic co-morbidities and particularly during acute exacerbations.[5]

One of the inflammatory markers which is extensively evaluated in COPD patients is C-reactive protein (CRP). It is an acute phase reactant, appears early in the course of COPD, can be easily measured and gives useful information. In stable COPD, plasma concentration of CRP is increased, and it is related to mortality in mild to moderate but not in severe disease stage.[6] The level of CRP is also related to health status and exercise capacity and seems to be significant predictor of BMI.[7] Elevated level of CRP is also observed in patients with stable coronary artery disease, peripheral arterial disease and diabetes compared to normal control.[8]

The relationship between systemic inflammation and extra pulmonary complication remains elusive. Still there is debate whether systemic inflammation is responsible for metabolic abnormalities in COPD patients or altered metabolic profile gives rise to an inflammatory response. The systemic inflammation itself may account for this extra pulmonary complication in COPD but so far, the evidence is circumstantial and the exact mechanism responsible for the association have not yet been totally understood.

In present study, we tried to fill up this lacuna. Authors measured serum CRP level and nutritional parameters like BMI and serum albumin in stable COPD patients to see (a) whether there is any significant difference in plasma CRP level in diagnosed cases of COPD patients without ischemic heart disease/ diabetes mellitus/chronic liver disease in comparison to age and sex matched healthy control. (b) the correlation of serum CRP level with severity of disease (as per GOLD guideline), (c) any correlation between the CRP level (marker of systemic inflammation) and nutritional abnormalities (serum albumin and BMI).

METHODS

The prospective, observational, controlled study was performed from September 2010 to August 2011 in a tertiary care hospital in Kolkata.

Inclusion criteria

Fifty-three diagnosed cases of stable COPD attending the chest OPD of NRS Medical College, Kolkata were included in the study.

Exclusion criteria

- COPD patient with acute exacerbation,
- Clinical and electrocardiographical evidence of ischemic heart disease,
- Overt heart failure from any cause,
- Presence of diabetes mellitus or chronic liver/kidney disease,
- Patients with cardiomegaly/parenchymal infiltrate /pleural disease in Chest X ray.

All cases were male. Diagnosis of COPD was made clinically and confirmed by office spirometry as per GOLD guideline (i.e. post bronchodilator FEV1/FVC <70%).

A questionnaire was filled out containing demographic characteristics, smoking status, h/o exacerbation in last three months and presenting complaints. Clinical examination was done including measurement of height in cm and weight in kg for BMI calculation. As per WHO classification patients with BMI <18.5 is regarded as underweight, between 18.5-25 normal and >25 BMI is taken as overweight/obese.

Spirometry was done in each case to confirm clinical diagnosis of COPD, to rule out asthma by bronchodilator reversibility testing and to define the severity of disease by measuring FEV1 as per GOLD guideline.

Chest X ray (PA view), ECG, serum creatinine, SGPT and fasting blood sugar was done in relevant cases to exclude cases as per exclusion criteria.

Thereafter a group of healthy subjects with normal spirometry and matched COPD patients in terms of age, sex and h/o smoking status were selected as control.

After resting for 10 minutes, 5ml of blood sample was taken from each patient and control for measurement of CRP and serum albumin. CRP was measured by Particle Enhanced Turbidimetric Immunoassay Technique

(PETIA). Results were analysed and statistically correlated.

RESULTS

In this prospective, observational, controlled study 53 stable COPD patients without documented ischemic heart disease, diabetes mellitus, chronic liver/kidney disease, radiological evidence of parenchymal infiltrate, pleural disease or cardiomegaly were evaluated, and 32 healthy subjects were taken as control. All cases were male. The two groups were matched in terms of age (40-65 years) and cigarette smoking.

Table 1: Mean CRP level in different study population of stable COPD and normal control.

Study population	No. of cases (n)	Mean CRP level mg/ml	p-value
Stable COPD	53	6.226±0.93	<0.001
Normal control	32	1.31±0.53	
Stable COPD patients with			
Moderate airway obstruction	18	5.09±2.50	>0.50
Severe airway obstruction	35	5.89±2.57	

Regarding severity of disease according to GOLD guidelines 40% (18 cases) had moderate COPD (FEV1>50%) and 60% (35 cases) had severe COPD (FEV1<50%). There was no case of mild COPD. No patient had any exacerbation in last three months. Ninety-four COPD patients were smoker and 60% of patients were using inhaled corticosteroid (ICS).

Mean serum CRP level was significantly higher in stable COPD patients than in healthy control. (6.226±3.9 vs 1.31±0.53) p value <0.001 (Table 1). Among the COPD cases, serum CRP level was positive in 35 cases with mean CRP level 8.55±2.71 and 18 cases showed negative CRP value (1.69±0.24).

When authors compared serum CRP level with severity of COPD, serum CRP level was higher in severe COPD in comparison to moderate COPD, but difference was not statistically significant (5.09±2.50 vs 5.89±2.57, p value >0.50).

Authors also correlated serum CRP level with BMI and serum albumin in COPD patients independently. Serum CRP level was significantly higher in COPD patients with BMI<18.5 than those with normal to high BMI (9.10±3.14 vs 4.01±2.90, p value <0.001). Stable COPD patients with serum albumin <3.5mg/dl also showed significantly higher serum CRP level in comparison to patients with serum albumin >3.5mg/dl (Table 2).

Table 2: Independent co relation of BMI and Serum albumin with mean plasma CRP level in stable COPD patients.

Study population	No. of cases (n)	Mean CRP level mg/ml	p-value
Stable COPD patients with			
BMI>= 18.5	30	4.01±2.90	<0.001
BMI<= 18.5	23	9.10±3.14	
Stable COPD patients with			
Serum albumin >= 3.5mg/dl	25	3.59±2.50	<0.001
Serum albumin <= 3.5mg/dl	28	8.51±3.50	

DISCUSSION

The present study was performed on stable COPD patients (n=53) and healthy control to determine the value of CRP as a biomarker of systemic inflammation. Assessment was done to see the correlation between serum CRP level in stable COPD and BMI and serum albumin and also with severity of COPD. Mean serum CRP level was found to be significantly higher in stable COPD patients than in control subjects.

Gan et al, were the first to establish the importance of high CRP level in COPD patients. They showed elevated CRP level in stable COPD which also predicted cardiovascular mortality.[9]

Yende et al, reported a higher level of serum CRP in cases with an obstructive pattern in the spirometry (3.5mg/L) in comparison to healthy control (2.5mg/L) p value <0.0001.[6]

In a study conducted by Broekhuizen et al, stable COPD patient had increased level of inflammatory marker like CRP (p=0.03).[7]

In another study by Plata P et al, there is a significant higher level of CRP in COPD patient (50.03±1.51mg/L) as compared to smoking (2.62±1.04mg/L) and nonsmoking control group (2.24±1.04 mg/L) p <0.0001.[10]

Inverse association had been reported between circulating CRP level and FEV1.[5] In present study regarding severity of disease based on GOLD criteria, the mean CRP level was increased in severe cases, but the correlation was not statistically significant. Dentener et al, also found no correlation between serum CRP and lung function in stable COPD patients.[11] Plata P et al, showed that there was no significant difference between the severity of disease and CRP level.[10] But in a study by De Toress et al, serum CRP level was significantly increased by severity of disease.[12] Therefore although it is expected

that serum CRP level should increase with severity of disease, more study are required in these cases.

COPD is a multi-component disease having pulmonary and systemic manifestations. But unfortunately, patho-biology of these systemic manifestations cannot be fully explained by lung function abnormality, lung hyperinflation, oxidative stress due to smoking and degree of hypoxemia. Extensive research all over the world in last decade has shown that COPD is associated with systemic inflammation which has been postulated to be a missing link between Pulmonary and extra-pulmonary manifestation in COPD. The mechanism of systemic inflammation is not yet clear but spilling over of reactive oxygen species and cytokines from lung parenchyma into the systemic circulation or peripheral liberaton of pro-inflammatory cytokines by inflammatory and/or structural cell have been postulated. Whatever may be the cause, liberated pro-inflammatory mediators amplify their effects through their action on organs like bone marrow, liver and skeletal muscle.[3] One of the major systemic manifestation in COPD patients is loss of muscle mass leading to cachexia and quadriceps weakness.

As high sensitivity CRP was found to be a marker of impaired energy metabolism and COPD patients were shown to have cachexia and loss of muscle mass leading to low BMI.[7]

Authors compared serum CRP level in stable COPD patient with a low BMI/serum albumin level to those with a normal to high BMI/serum albumin and found a significantly higher plasma CRP level in stable COPD patients with low (<18.5) BMI/serum albumin (<3.5mg/dl).

A study by Karadag F et al, also confirmed that measurable CRP level was higher in stable COPD patients and CRP level was significantly higher in COPD patients with low BMI and he concluded that CRP may be considered as an indicator of malnutrition in COPD patients.[13] This finding was further confirmed by an earlier study in which Schol AM et al, observed high CRP level in a special subset of 16 COPD patients with high energy expenditure and low fat-free mass index.[14] On the other hand, a recent study by De Toress, serum CRP level correlated directly with BMI.[12] However, since our study was done on a limited number of patients, this conclusion should be confirmed by further studies.

The present study observes that serum CRP level is higher in stable COPD patients without acute exacerbation, in comparison to normal control which is statistically significant. However, the correlation between grading of severity according to FEV1 value compared to raised serum CRP level did not reach statistical significance. On the other hand, the raised serum CRP level had a significant and independent correlation with low serum albumin and low BMI in stable COPD patients irrespective of FEV1 grading.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Mandal P, Sit N, Agarwala A, Ghoshal AG, Bandyopadhyay D. Correlation of BMI and serum albumin with c-reactive protein in male patients with stable chronic obstructive pulmonary disease. Int J Res Med Sci 2018;6:3147-51.