Association of CRP and Fibrinogen in Patient with COPD – an Observation Study

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ABSTRACT

Introduction: Chronic obstructive pulmonary disease (COPD) is a multicomponent disease characterized by obstruction of airflow which is not completely reversible due to aberrant inflammatory reaction to aero toxins, smoke of cigarette, and fumes of biomass. Present study aimed to establish a relation between routinely used and cost effective markers and COPD.

Material and Methods: A total of 50 COPD (chronic obstructive pulmonary disease) patients diagnosed based on spirometry and post bronchodilator FEV1/FVC <0.7 were selected as cases for the study and equal no of controls were selected with no history of SOB, use of bronchodilators and spirometry with post bronchodilator FEV1/FVC > 0.7.

Results: The mean age of study population was 52.58 ± 11.25 in case group and 52.54 ± 11.07 in controls p (>0.05). Case group comprised of 90% males and 10% females compared to 86% males and 14% females in controls (p>0.05).Mean BMI in cases was 20.96 ± 2.32 which was significantly lower than controls 22.1 ± 2.69, Mean CRP in cases was 4.65 ± 3.5 which was significantly higher than controls 0.44 ± .29 (p <0.05). Mean Fibrinogen in cases was 485.5 ± 187.7 which was significantly higher than controls 292 ± 73.7 (p <0.05). There was a significant and negative correlation observed between BMI and severity of COPD (r = -0.656, p <0.05) where as significant and positive correlation was observed between severity of COPD and Fibrinogen (r = 0.687, p <0.05) and between severity of COPD and CRP (r = 0.351, p <0.05).

Conclusion: Plasma fibrinogen and serum CRP are reliable inflammatory markers with positive correlation to severity of COPD. Ease of availability of both these cost effective markers in COPD helps in early intensification of therapy. It is concluded that use of biomarkers to establish systemic inflammation in COPD helps in both reflecting disease severity and assessing prognosis in patients.

Keywords: C – Reactive Protein, Fibrinogen, Chronic Obstructive Pulmonary Disease, Smoking, Pulmonary function Test, Systemic Inflammatory Markers, Biomarkers

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is progressive life threatening disease of lung. It is estimated that by the year 2020 COPD would be the most common cause of death. It is well known that smoking of cigarette plays a very important role in the Pathogenesis of COPD, but the steps involved in its pathogenesis are still unclear.[1] Majority of patients with COPD usually develop emphysema of lung with its typical pattern involving destruction of alveolar and abnormal repair apart from inflammation of small airway which is persistent even years after cessation of smoking.[2-3]

Chronic obstructive pulmonary disease (COPD) is a multicomponent disease characterized by obstruction of airflow which is not completely reversible due to aberrant inflammatory reaction to aero toxins, smoke of cigarette, and fumes of biomass.[4] The obstruction of airflow can be a result of either disease of airways or destruction of alveolar (emphysema) and it is associated with loss of lean body mass, hypersecretion of mucus, and an increased risk of comorbidities. The progression and severity of disease can be assessed with the help of ratio of FEV_1 (forced expiratory volume)/ FVC. Lot of emphasis is laid on Biomarkers which could become relevant for early detection of disease, risk stratification of subjects and clinical trials endpoints.[4-7]

Association of systemic inflammatory biomarkers with COPD has been studied by various authors. Present study aims to establish a relation between routinely used and cost effective markers and COPD.

MATERIAL AND METHODS

A total of 50 COPD (chronic obstructive pulmonary disease) patients diagnosed at our medical college and based on the spirometry and post bronchodilator FEV1/FVC <0.7 were selected as cases for the study and equal no of controls were selected with no history of SOB, use of bronchodilators and spirometry with post bronchodilator FEV1/FVC > 0.7. Patients with COPD were further classified based on severity based on GOLD guidelines as mild, moderate and severe obstruction. Both males and female between age group 30 – 70 years were enrolled for the study and Patients with airway disease other than COPD were excluded.

Inclusion Criteria

1. Males and female between age group 30 – 70 yrs
2. COPD patients diagnosed based on spirometry and post bronchodilator FEV1/FVC <0.7 were selected as cases for the study.
3. Patients were clinically stable (no exacerbation for 2 months) at the time of evaluation.

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Exclusion criteria

1. Age less than 29years and more than 71years
2. Patients with airway disease other than COPD
3. History of asthma
4. History of collagen vascular/autoimmune diseases,
5. History of malignancy,
6. History of pulmonary embolism,
7. History of renal insufficiency,
8. History of cirrhosis and other serious liver diseases

The BMI was then calculated by dividing the weight in kilograms by height in meter square. Serum CRP and plasma Fibrinogen was estimated in both groups.

STATISTICAL ANALYSIS

The data obtained was analyzed using SPSS v 17. Chi square test was used for comparison and to calculate p Value.

RESULTS

Table 1 depicted below shows the mean age of study population was 52.58 ± 11.25 in case group and 52.54 ± 11.07 in controls p (>0.05). Case group comprised of 90% males and 10% females compared to 86% males and 14% females in controls (p>0.05). Table 2 depicted below shows that in patients with COPD 42% (n=21) had history of HTN and 32% (n=16) had history of diabetes compared to 34% HTN patients and 46% diabetic patients in control group p (>0.05).

Mean BMI in cases was 20.96 ± 2.32 which was significantly lower than controls 22.1 ± 2.69, Mean CRP in cases was 4.65 ± 3.5 which was significantly higher than controls 0.44 ± .29 (p <0.05) and graphical analysis is shown in Figure 1. Mean Fibrinogen in cases was 485.5 ± 187.7 which was significantly higher than controls 292 ± 73.7 (p <0.05). It is shown in figure 2. There was a significant and negative correlation observed between BMI and severity of COPD (r = -0.656, p <0.05) where as significant and positive correlation was observed between severity of COPD and Fibrinogen (r = 0.687, p <0.05) and between severity of COPD and CRP (r = 0.351, p <0.05).

Patients were divided into nonsmokers and Smokers, smokers were further classified as ex-smokers and current smokers. It was observed that smokers contributed 90% of COPD cases compared to 62% on non-Controls there was a significant and positive correlation observed between smoking and fibrinogen (r = 0.44, p <0.05). There was a significant and positive correlation between smoking and severity of COPD (r = 0.471, p <0.05) which is shown in table 2 also.

DISCUSSION

COPD is a chronic obstructive lung disease; it is diagnosed based on Pulmonary Function test (PFT), Symptoms and History of previous episodes of Exacerbation. GOLD (Global Initiative for Chronic Obstructive Lung Disease) guidelines have been formulated based on the above criteria Based on airflow limitation GOLD system classification is as Follows In patients with FEV1/FVC <0.70:

- GOLD 1 –if FEV1≥ 80% predicted, it is considered as mild

	COPD	Controls	
	Mean ±SD	Mean ± SD	p value
Age	52.58 ± 11.25	52.54 ± 11.08	.986
BMI	20.96 ± 2.32	22.10 ± 2.70	.026
CRP	4.66 ± 3.50	0.44 ± .29	<0.001
Fibrinogen	485.56 ± 187.78	292.22 ± 73.71	<0.001

Table-1: Descriptive

	COPD	Controls	
	Mean ±SD	Mean ± SD	p value
Gender			
Males	45 (90%)	43 (86%)	0.538
Females	5 (10%)	7 (14%)	
DM	16 (32%)	23 (46%)	0.151
HTN	21 (42%)	17 (34%)	0.410
Non Smoker	5 (10%)	19 (38%)	0.002
Ex-smoker	22 (44%)	10 (20%)	
Current smoker	23 (46%)	21 (42%)	

Table-2: descriptive

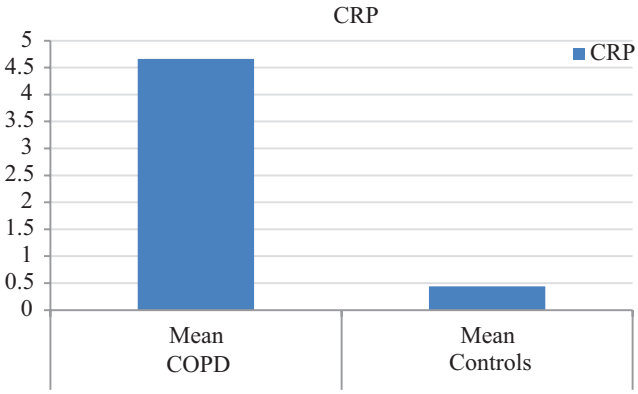

Figure-1: CRP

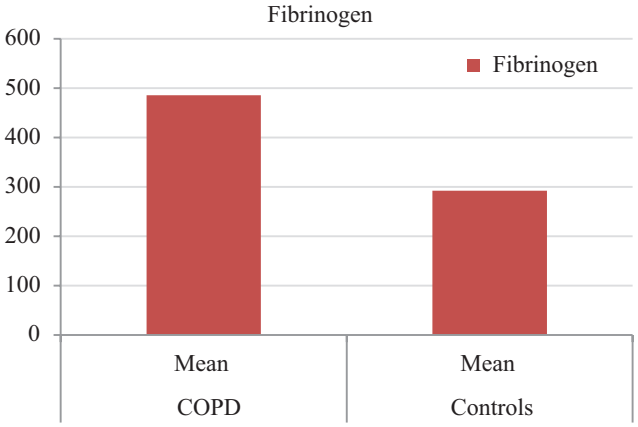

Figure-2: Fibrinogen

- GOLD 2 – if 50% ≤ FEV1 < 80% predicted, it is considered as predicted moderate
- GOLD 3 – if 30% ≤ FEV1 < 50% predicted it is considered as severe
- GOLD 4 – if FEV1 <30% predicted. it is considered as very severe

Apart from airflow limitations Gold Guidelines have used various other parameter for the assessment of COPD like

active symptoms (using MRC and CAT scale) previous exacerbations history.[9]

- Group A: nil or one episode of exacerbation per year or not hospitalisation andmMRC symptoms scoring is 0-1 or CAT scoring is less than 10 - Low Risk.
- Group B: nil or one episode of exacerbation per year or not hospitalisation and mMRC symptoms scoring is more than 2 or CAT scoring is more than 10 - Low Risk.
- Group C: More than two episodes of exacerbation per year or requiring hospitalisation one or more times and mMRC symptoms scoring is 0-1 or CAT scoring is less than 10 - High risk.
- Group D: More than two episodes of exacerbation per year or requiring hospitalisation one or more times and mMRC symptoms scoring is morethan 2 or CAT scoring is more than 10 - High risk.

Various biomarkers in COPD have been centered on proteins and on other molecules, such as in BAL, sputum, blood, urine. Profiling of various blood biomarkers have been identified that may help in distinguishing with people suffering from COPD versus control subjects, such as SP-D (surfactant protein-D), CC-16 (lung-derived Clara cell protein-16), and CCL-18, extracellular matrix. However the availability of above markers for routine diagnostics is difficult.

In the Present study serum fibrinogen was observed to be increased in patients with COPD and there was a positive correlation observed between fibrinogen and COPD. Fibrinogen is an acute phase soluble plasma glycoprotein. Fibrinogen is synthesized in the liver and it is converted into fibrin during coagulation cascadein presence of thrombin. During acute phase stimulation in response to increased production of IL-6 there is increased production of fibrinogen levels that can increase upto threefold.[7-8] IL-6 has been an established inflammatory marker for COPD.

It has also shown by various studies that increasing levels of serum CRP levels is associated with inflammation in atherosclerosis and also increasing the risk of Myocardial infarction and CHD (coronary heart disease). Large evidence suggests that even in stable COPD if there is an increased level of serum CRP levels it is associated with inflammation in lung. Hence serum CRP can be used as a marker in COPD patients with ongoing lung inflammation.

Gan et al(2004)had collected the data of five cross-sectional studies and have done the estimation of mean average increase of CRP in stable COPD. It was also concluded that Increased CRP was associated with all-cause mortality predominantly in patients with COPD (mild to moderate), Decline in FEV1, and in patients with diminished lung function.[10]

Randeep Guleria et.al (2011)has done a study on 93 patients of COPD with acute exacerbation who were on invasive mechanical ventilation were evaluated and these patients were investigated for CRP and Prealbumin levels.it was shown that patient who died had higher CRP and patients with low CRP and high prealbumin.[11] Dahl et.al. 2011 have also shown that elevated levels of CRP plays an important role in relation to outcome of patients in COPD andfurther subsequent hospital admission.[12]

Fisun et.al. 2008 study confirms that CRP levels can be used as a biomarker for low-grade systemic inflammation. Apart from this, it was also seen that CRP was significantly higher in COPD patients with a low BMI.[13]

CONCLUSION

Plasma fibrinogen and serum CRP are reliable inflammatory markers with positive correlation to severity of COPD. Ease of availability of both these cost effective markers in COPD helps in early intensification of therapy. It is concluded that use of biomarkers to establish systemic inflammation in COPD helps in both reflecting disease severity and assessing prognosis in patients.

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