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Evaluating serum C-reactive protein level in patients with chronic obstructive pulmonary disease – A cross-sectional study

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Abstract

Patients with the chronic obstructive pulmonary disease have ongoing systemic inflammation, which can be assessed by measuring serum C- reactive protein.

Objective: To explore whether CRP could be used as an independent predictor of disease outcome in COPD.

Methods: A cross-sectional study was conducted among 50 COPD patients attending Respiratory Medicine outpatient services in the Regional Institute of Medical Sciences (RIMS), Imphal from January 2015 to September 2016. Patients aged 18-67 were included in the study after obtaining Ethical approval from the Research Ethics Board, RIMS, Imphal. Computerized Spirometer Helios 401 was the instrument used to measure lung volumes and capacities. BeneSphera^{TM} CRP Latex Slide test kit was used to estimate serum c-reactive protein.

Results and observation: The present study was conducted on fifty COPD patients in which serum CRP level showed positive correlation with COPD (p=0.002) but serum CRP level with spirometric parameters showed significant negative correlation;FEV_1 (r=-0.451, p=0.001), FEV_1/FVC (r=-0.617, p<0.001) and PEFR (r=-0.398, p=0.004).

Conclusion: In our study, we found an association between serum CRP level and severity of COPD and Plasma CRP may be used as a marker of prognosis in COPD as the small increase is associated with poorer prognosis in COPD.

Keywords: *CRP; Chronic obstructive pulmonary disease (COPD); Imphal.*

INTRODUCTION

Obstructive airways disease is a group of condition distinguished by increased resistance and obstruction in the air passages, especially during expiration. The term OAD includes bronchial asthma; chronic obstructive pulmonary disease, consisting of chronic bronchitis and emphysema; bronchiectasis; cystic fibrosis and bronchiolitis.[1]

COP is a disease state characterized by airflow limitation that is not fully reversible. The airflow obstruction is usually both progressive and associated with an abnormal inflammatory response of

the lungs to noxious particles and gas. There are around 50 million patients with COPD in India and COPD is the second leading cause of death in India. Estimate suggests that COPD will rise from the sixth to the third most common cause of death worldwide by 2020.[2]

Diagnosis of OAD is based on the patient`s history, signs, and symptoms, and on the results of spirometry and other pulmonary function tests. Spirometry assesses the obstruction of expiratory airflow, which is the characteristic functional defect in OAD. Spirometry is the most effective way of determining the severity of obstructive airway diseases.[3]

C-reactive protein was first isolated in 1930 from the plasma of patients with pneumococcal pneumonia, CRP was so named because it binds to the C-polysaccharide of the pneumococcus. Modern molecular studies have determined that CRP is a member of the pentraxin family of proteins. It comprises five protomers, each of 206 amino acids, molecular weight 23 kDa, arranged in cyclic symmetry. With the participation of Ca^2 ions, it binds various proteins and phospholipids, particularly phosphocholine. It opsonizes particles and also activates complement via the classical pathway, but its actual biological function is unknown.[4]

In lungs, CRP has protective function by acting against bacteria and apoptotic cells. Activated epithelial cells, alveolar macrophages and other inflammatory cells in COPD releases IL-6 into the circulation. CRP is primarily produced by hepatocytes in response to IL-6 stimulation.[5] This stimulates an acute-phase response and increases the level of plasma CRP. C-reactive protein appears in blood in the acute stages of various inflammatory disorders but is undetectable in the blood of healthy persons.[6]

Worldwide studies show that it has variable roles in COPD, some showing correlation with spirometric lung function while others show no significant relation. We would therefore like to explore its role in our study population and also try to explore whether it could become an independent predictor of disease outcome in COPD.

METHODS

Study design: A Cross-sectional study was conducted among 50 COPD patients attending Respiratory Medicine outpatient services in Regional Institute of Medical Sciences (RIMS), Imphal from January 2015 to September 2016. Patients aged 18-67 were included in the study after obtaining Ethical approval from the Research Ethics Board, RIMS, Imphal. The participants were recruited by Purposive sampling. Diagnosed COPD patients sent from Respiratory Medicine OPD, RIMS, Imphal were included in this study.

The patients with chronic disorders like hypertension, diabetes mellitus, cardiovascular diseases, bleeding disorders, inflammatory disorders, infection, malignancy and patients who had recent surgery were excluded from the study.

Computerized Spirometer Helios 401 of the Recorders and Medicare System, Chandigarh, India was the instrument used to measure lung volumes and capacities. The Helios software contains set of prediction equations for computation of predicted parameter values.

The procedure was explained to the patient followed by a demonstration. The patient was asked to “take as deep a breath as possible” and then “blast as fast and hard as you can” and “keep blowing until I ask you to stop” preferably at least 3 seconds followed by a rapid inhalation (inspiration). A tight seal was ensured around the mouthpiece. During the test, soft nose clip was used to prevent air escaping through the nose. Coaching was active and vigorous; instructions were repeated as necessary. Three consecutive maneuvers were performed with a rest of 5 to 10 minutes between two maneuvers.

The best result among the three tests was recorded in the proforma. The results were compared

with the predicted values for the same age, sex, height, and weight. Patients were classified on the basis of GOLD Classification of COPD (2006)[7]

The study variables which include Forced Vital Capacity (FVC), Forced Expiratory Volume in one second (FEV_1), FEV_1/FVC ratio, Forced Expiratory Flow during 25-75% of expiratory flow ($FEF_{25-75\%}$), and Peak Expiratory Flow Rate (PEFR), were recorded by Helios Computerized Spirometer Model No. 401, in a sitting position. Spirometric values are better when done in standing position but sitting posture is usually preferred because of the risk of fall due to cough syncope when done in standing.

BeneSphera™ CRP Latex Slide test kit of Avantor Performance Materials India Ltd, Dehradun, Uttarakhand, was used to estimate serum c-reactive protein in human. The test was expected to be positive with serum CRP levels between 0.6 and 100mg/dl.

Statistical analysis:

The collected data were entered and analyzed using IBM SPSS Statistics V21.0 (IBM Corporation, US). Summarizations of data for frequency distribution for variables of interest were carried out by using descriptive statistics such as mean, standard deviation and percentages. Chi-square test was employed to test the association between asthma with variables of interest. A p-value of <0.05 was considered to be statistically significant.

RESULTS AND OBSERVATION

A total of 50 patients with chronic obstructive pulmonary disease were included in the study. Of which Maximum percentage (92%) of patients belong to the age group (38-67 years) while minimum percentage (8%) of the patients belong to age group (18-37 years). About two third of the Obstructive Airway Disease patients were male. Out of 50, 32% patients were non-smoker, 38% were smoker, and 30% were ex smokers and smoking pack years was less than 100 in 38 % and more than 100 in 62 % in the study population.

Socio-demographic characteristics like age, sex, smoking history were recorded. Thorough physical examination, degree of airflow obstruction and serum C-reactive protein were recorded after obtaining Prior written informed consent from from all the participants.

Patients were classified on the basis of GOLD Classification of COPD.

We found that 22% of COPD patients were in moderate category (FEV_1/FVC < 0.70 and FEV_1=0.50-0.80), 18% of patients were in severe category (FEV_1/FVC < 0.70, and FEV_1=0.30-0.50), and 14% of patients were classified as very severe (FEV_1/FVC < 0.70, and FEV_1 < 0.30). Only 6% of the patients had mild airflow limitation while 40% of COPD patients had no airflow limitation during spirometry.

Spirometric parameters	Minimum Value(% pred)	Maximum Value(% pred)	Mean(% pred)	Standard Deviation
FVC	36.00	158.00	83.96	30.98
FEV_1	9.00	155.00	61.16	32.63
FEV_1/FVC	11.00	111.00	71.06	20.25
$FEF_{25-75\%}$	6.00	138.00	34.20	27.53
PEFR	6.00	87.00	34.70	19.70

Table 1. *Mean±SD of FVC, FEV_1 , FEV_1 /FVC, $FEF_{25-75\%}$, and PEFR in COPD patients (n=50)*

Table 1 shows the lung function test values of COPD patients as measured by spirometer. FVC

values were within normal limit. But the mean values of FEV_1, $FEF_{25-75\%,}$ and PEFR were lower. The results suggest that in the COPD patients larger and smaller airways both were involved.

Severity of COPD	CRP			Total	p-value*
	LESS THAN 6mg/L	6mg/L	12 mg/L		
Normal	19	1	0	20	0.002
Mild	1	2	0	3	
Moderate	5	3	3	11	
Severe	4	3	2	9	
Very severe	1	2	4	7	
Total	30	11	9	50	

Table 2. *Association of the serum CRP level with the severity of COPD* *Chi-Square Test

Above table shows association between serum CRP level and severity of COPD. Total 9(18%) COPD patients had serum CRP level 12mg/L, in which 3(6%) patients belong to moderate category, 2(4%) patients belong to severe category, and 4(8%) patients belong to very severe category. And 11(22%) COPD patients had serum CRP level 6mg/L, it included; 1(2%) patient with normal spirometry, 2(4%) patients were in mild category, 3(6%) patients were in each moderate and severe category, and 2(4%) patients were in very severe category (p=0.002).

Variables	**Correlation coefficient(r)***	**p-value**
FEV_1	-0.451	0.001
FEV_1/FVC	-0.617	<0.001
PEFR	-0.398	0.004

Table 3. *Correlation of different parameters of spirometry and age with serum CRP level in COPD patients (n=50)*
*Pearson`s bivariate correlation coefficient

Table 3 shows that age, FEV_1, FEV_1/FVC and PEFR were negatively correlated with serum C-reactive protein

DISCUSSION

COPD is the second leading cause of death in India and the disability from this disease is substantial and is expected to rise in India and worldwide. There are several evidence pointing towards smoking being a risk factor COPD and for increased clinical symptoms and poorer lung function in COPD patients. Hence all possible efforts should be taken to make people quit smoking, by adopting more awareness and control programmes. But smoking cessation is challenging so education advice, behavioural intervention along with drug therapy like nicotine replacement therapy with gums, patch or inhaler can be tried for better results.

The treatments available today have minimum impact on the disease progression, so early diagnosis and treatment is necessary. Measures such as screening with spirometric tests in high risk individuals especially the smokers in age group of 40-55 should be considered to reduce the mortality and morbidity due to COPD. In this study we were trying to find whether CRP levels can be used as a valid tool and an independent predictor of disease outcome in COPD, so that it could be used to evaluate the clinical, prognostic and therapeutic outcomes.

The present study was conducted on fifty COPD patients in which serum CRP level showed positive correlation with COPD (p=0.002) but serum CRP level with spirometric parameters showed significant negative correlation;FEV_1 (r=-0.451, p=0.001), FEV_1/FVC (r=-0.617, p=0.000) and PEFR (r=-0.398, p=0.004).

There are evidences supporting our study from previous research work conducted by Moreton RE and Kennedy CR reported that CRP concentration in patients (age range 0.03-16.1 years, median: 6.7 years) with cystic fibrosis ranged from 0.01-304 mg/L while in healthy children ranged from 0.01-2.8 mg/L and correlation between CRP and FVC% predicted was significant (r=-0.781; p<001).[8]

Gan and colleagues aggregated data from five cross-sectional studies and estimated an average mean increase in serum CRP of 1.85 mg/L in individuals with stable COPD[9]. There were similar results in the study conducted by Fares M et al[11]. They showed that CRP level >1.1mg/L in infants with bronchiolitis. Hsieh MH et al[12] found good correlation between serum hs-CRP and HRCT scores in the patients with stable non-cystic fibrosis bronchiectasis.

Similar results were shown in the study conducted by Tores et al[13] and Seemungal et al[14] the mean CRP level between control group and COPD group were compared and was different by greater than 3.3 mg/L, which was found to be significant (P<0.001)

CONCLUSION

In this study we were trying to find whether CRP proteins levels can be used as a valid tool in COPD patients, so that it could be used to evaluate the clinical, prognostic and therapeutic outcomes. In our study we found association between serum CRP level and severity of COPD and Plasma CRP may be used as a marker of prognosis in COPD as small increase is associated with poorer prognosis in COPD.

LIMITATIONS

The serum CRP has been used for evaluation of COPD and other inflammatory conditions but several factors might affect serum levels of CRP. CRP may be elevated in obese individuals and also in people who have the habit of smoking. Ageing is also another confounding factor. Further longitudinal studies are necessary to evaluate whether CRP could be used an independent predictor of disease outcome.

Ethical clearance- Ethical approval was obtained from the Research Ethics Board, RIMS, Imphal before the beginning of the study.

Source of funding- Self

Conflict of Interest – Nil

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