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A STUDY ON SERUM CRP AND ITS CORRELATION WITH DISEASE SEVERITY IN STABLE COPD

Respiratory Medicine

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ABSTRACT

BACKGROUND: Cardiovascular disease is one of the major causes of mortality in COPD patients. Raised CRP level has strong association with cardiovascular events. Objective of the study was to find out relationship of serum CRP with clinical and physiological parameters in COPD patients. **METHODS:** This study was carried out on COPD patients attending outpatient department of Respiratory Medicine, IRD, SMS Medical College, Jaipur during July 2018–June 2019. 40 stable COPD patients and 40 healthy controls were enrolled. Serum CRP levels, ABG analysis, BMI, spirometry and BODE index were assessed. **RESULTS:** Serum CRP levels increased with increasing severity of disease. **CONCLUSION:** COPD patients should be screened regularly with serum CRP to determine risk of cardiovascular consequences so that adequate decision of interventional strategies can be taken out to prolong survival.

KEYWORDS

COPD, CRP, cardiovascular

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is one of the most prevalent diseases, expected to move to the 3rd leading cause of mortality in 2020(1). Nevertheless, the pathological mechanisms and clinical manifestations of COPD are not restricted only to pulmonary inflammation and airway remodeling(2). In contrast, over the last decade, the recognition of COPD as a systemic disease has developed. Cardiovascular disease is a major cause of mortality in COPD, particularly in patients with mild to moderate severity. The discovery of novel biomarkers helps identify cardiovascular risk in patients with COPD. Serum CRP is one such biomarker which is an acute phase protein synthesized in liver in response to number of stimuli involving tissue damage. It is a marker of inflammation that has been associated with an increased risk of incident myocardial infarction, stroke, unstable angina, and sudden coronary death because of its proatherogenic property. CRP levels of 1, 1–3 and 3 mg/l are associated with lower, moderate and higher cardiovascular risks, respectively. In COPD patients, CRP levels are reported to be associated with increased cardiovascular morbidity.

In most of the studies, CRP was shown to be negatively correlated with forced expiratory volume in 1 second (FEV1)(3) and grade of dyspnea, but was not correlated with age in stable COPD patients. On the other hand, another study demonstrated that CRP had a weak correlation with COPD severity in elderly stable patients(4)

Given the conflicting results of prior studies, we aimed to investigate an association between CRP levels with clinical and physiological parameters in COPD patients apart from assessing the prevalence of CRP levels in stable COPD patients.

Materials and Methods

The present study consisted of 40 consecutive stable COPD patients and 40 healthy controls of either sex, aged between 40 to 80 years who attended the out-patient department of the Respiratory Medicine, IRD, SMS Medical College, Jaipur from July 2018 to June 2019. Both COPD patients and healthy controls for this study were randomly selected.

Patients were excluded based on following criteria- Chronic kidney disease, Acute exacerbation of COPD, Diabetes mellitus, Ischemic heart disease, Heart failure, other Respiratory diseases such as asthma, tuberculosis, lung infections, lung malignancy, pulmonary embolism. The control group consisted of apparently healthy volunteers with normal spirometry. Approval of the Institutional Ethical Committee was taken.

Patients were examined clinically and radiologically to establish the diagnosis of COPD, as per GOLD guidelines. Routine blood investigations, serum protein, serum albumin and urine microscopy, was done in all the participants. Chest X-ray, spirometry, electrocardiogram, 6-minute walk test were done. Body mass index (BMI) was calculated by measuring weight and height. Exercise capacity was assessed by 6-minute walk distance (6MWD) test according to American Thoracic Society (ATS) guidelines(5). Dyspnea was assessed based on modified British Medical Research Council (mMRC) dyspnea scale(6). The multi-dimensional BODE (body-mass index, airflow obstruction, dyspnea and exercise) index was calculated from BMI, forced expiratory volume in one second (FEV1%), mMRC dyspnea scale, and 6MWD.

Measurement of serum CRP levels

Venous Blood samples (5ml) were collected from all patients and healthy controls and centrifuge to analyze levels of C- reactive protein in serum. The obtained serum was kept at -80°C until the time of the analysis. CRP level was assessed in serum by Elisa method according to manufacturer protocol.

STATISTICALANALYSIS

Correlation of different parameters used to assess clinical severity of COPD with Serum CRP was carried out using spearman's correlation analysis on Statistical Package for the Social Sciences (SPSS) version 16.0 software. One-way analysis of variance (ANOVA) was used to compare mean values of >2 sub-groups.

RESULTS

Out of 40 cases, 35 were male. Majority of cases (26) were over 50 years of age contributing to 65% in case group. Out of 40 controls, 36 were male. The difference in mean age between cases and controls was statistically significant (p=<0.001).

Our study showed mean value of serum CRP levels significantly higher in case group as compared to control group(7.224±3.161 Vs 1.357±0.5951, P<0.0001).

Abnormal CRP levels seen more in case group- 95% which was statistically significant.

Data of various other parameters are presented in Table 1.

Table 1: Comparison of cases with COPD and controls

Parameters	Control group (Mean±SD)	Cases group (Mean±SD)	P-value
Mean Age(yrs)	55.58±8.00	62.12±5.753	<0.0001
Male (%)	35(75%)	36(90%)	1.000
BMI (kg/m2)	23.88±2.209	21.40±2.037	<0.0001
PaO2	93.05±5.188	74.90±10.04	<0.0001
SPO2	96.98±1.187	94.90±2.881	<0.0001
6MWD (meter)	533.9±36.92	478.3±86.98	0.0004
BODE index	0.4750±0.5057	2.900±1.985	<0.0001
FEV1%	89.40±7.500	53.88±19.46	<0.0001
FEV1/FVC	95.63±7.977	48.83±5.275	<0.0001
Serum CRP levels	7.224±3.161	1.357±0.5951	<0.0001

The comparison of mean value of PaO2, SPO2, 6MWD (meter), BODE index, FEV1% predicted & FEV1/FVC ratio, Serum CRP levels in both groups were statistically significant (P<0.0001, P<0.0001, P<0.0001, P =0.0004, P<0.0001, P <0.0001 & P<0.0001 respectively).

Abnormal serum CRP levels(>3 mg/l) was present in all cases. Table 2.

Table 2: Serum CRP levels (>3 mg/l) with Severity of COPD

Severity of COPD	S.CRP(>3 mg/l)	Percentage (%)	(Mean±SD)
Mild(n=12)	10	83.33	5.495±1.929
Moderate(n=7)	7	100	7.155±2.490
Severe(n=14)	14	100	9.06±3.007
Very Severe(n=7)	7	100	9.14±3.323
Total (n=40)	38	95	7.45±3.07

There was a negative correlation (r=-0.7313) between FEV1% and CRP levels among cases. The mean CRP values on one-way analysis of variance (ANOVA) among the three groups were statistically significant (p<0.0001).

There was positive correlation between BODE index and CRP levels (r=0.8091) among the cases and the difference in mean CRP values among three group were statistically significant (p=0.0008).

There was a negative correlation between PaO2 and CRP levels (r=-0.2872) among the cases. The difference in mean CRP values were statistically significant (p<0.0001).

There was a positive correlation between mMRC grading and CRP levels (r=0.5402) among the cases. The difference in mean CRP values among 4 groups of cases with mMRC grade were statistically significant (p=0.0004).

There was a negative correlation (r=-0.701) between 6MWD and CRP values. The difference in mean CRP values among cases with 6MWD >500m, 401-500 m, 301-400 m and 201-300 m were statistically significant (p=0.0007). Table 3

Table 3: Association of serum CRP with FEV1, BODE index, PaO2, mMRC grade and 6MWD

Subgroups		Serum CRP (mg/l)			P-value (ANOVA test)	Spearman correlation (r)	P-value
		<3 mg/l (N=2)	>3 mg/l (N=38)	Mean±SD			
FEV1%	50-80%	2	17	5.675±2.305	<0.0001	-0.7313	0.0094
	30-50%	0	14	8.670±3.237			
	<30%	0	7	8.536±3.440			
BODE index	0-3	2	23	6.346±2.778	0.0008	0.8091	0.0472
	4-6	0	14	8.341±3.140			
	7-10	0	1	13.53			
PaO2	>80	2	12	5.456±2.391	<0.0001	-0.2872	<0.0001
	71-80	0	11	5.204±1.745			
	61-70	0	14	10.47±1.903			
	51-60	0	1	8.62			
mMRC	Grade I	2	2	3.410±0.7863	0.0004	0.5402	0.0024
	Grade II	0	21	6.687±2.743			
	Grade III	0	13	8.585±2.928			
	Grade IV	0	2	11.65±2.666			
6MWD test	>500	2	17	5.675±2.305	0.0007	-0.7001	0.0237
	401-500	0	14	8.670±3.237			
	301-400	0	5	8.814±3.827			
	201-300	0	2	9.415±3.203			

DISCUSSION

COPD is a multicomponent disease in which structural and functional changes are seen in lungs and extra-pulmonary organs. Therefore, systemic involvement in patients with COPD should certainly be considered.

Our study showed that the mean levels of CRP is increased significantly in cases than controls which was similar to studies by de Torres JP et al(7),Gan WQ et al(8)

In our study prevalence of abnormal serum CRP(>3 mg/l) was 95% which was quite higher to study by Denise Rossato silva et al(9).

COPD cases showing prevalence of abnormal serum CRP in our study were from moderate, severe and very severe COPD(100%) cases, similar to study by Denise Rossato silva et al(9).

There was a negative correlation between FEV1%(r=-0.7313), PaO2 (r=-0.2872) & 6MWD (r=-0.701) and CRP levels among cases and there was a positive correlation between BODE Index(r=0.8091), mMRC grading(r=0.5402) and CRP levels. We compared our study of serum CRP with disease severity with following studies- Pinto-Plata et al(10) reported that 6MWD, age and BMI significantly predicted CRP levels in cases with COPD; the most important clinically relevant predictor was 6 MWD, which decreased with increasing CRP.

De Torres et al(7)found that CRP levels are elevated in clinically stable COPD cases and that CRP levels correlate best with arterial oxygen tension and 6 MWD and also no differences in CRP levels between those with cardiovascular risk factors or disease and those without them.

CONCLUSION

COPD patients should be screened regularly with serum CRP levels to determine the risk of/and progression of cardiovascular morbidity and mortality so that adequate decision of interventional strategies can be taken out to prolong the survival in COPD patients.

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CONFLICTS OF INTEREST

There are no conflicts of interest.

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