Research Article

Comparison of serum CRP levels in healthy controls and different stages of COPD

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) is the leading cause of morbidity and mortality in developing and developed countries.

Objective: To compare the serum C-reactive protein (CRP) levels in healthy controls and patients with COPD.

Materials and Methods: Serum CRP levels were evaluated in 100 healthy controls and 100 patients with COPD. Serum CRP levels were estimated and Pulmonary function tests were done in controls and patients with COPD. Results were drawn and analyzed using appropriate statistical tests.

Result: In this study, values of CRP in patients with COPD and healthy control subjects were estimated and compared. When these values of mean serum CRP levels in control subjects were compared with those of total patients with COPD using unpaired *t*-test, it showed statistically highly significant difference with $P < 0.001$. A highly significant difference between mean CRP levels in stages III and IV was observed. Highly significant difference between mean CRP levels in healthy controls and patients of all stages with COPD individually was observed. Correlation test was applied, and Pearson's correlation coefficient was calculated between serum CRP levels and predicted FEV_1% (forced expiratory volume in 1 s expressed as percentage) showing a negative correlation with a value of –0.564 (between 0 and –1).

Conclusion: There was a significant difference in the mean serum CRP levels between patients with COPD and healthy control subjects, as the mean serum CRP level was higher in patients with COPD and the difference was statistically highly significant. There was increase in CRP level with the increase in severity of the disease in different stages ($P < 0.001$). There was a significant difference between the severity of dyspnea (FEV_1% predicted) and the level of CRP ($P = 0.001$).

KEY WORDS: Serum C-reactive protein, chronic obstructive pulmonary disease, predicted forced expiratory volume 1

Introduction

According to the WHO, chronic obstructive pulmonary disease (COPD) is a lung disease characterized by the chronic obstruction of lung airflow that interferes with the normal breathing and is not fully reversible.[1] COPD is a leading cause of morbidity and increasing mortality in developing and developed countries.[2]

C-reactive protein (CRP) is extensively evaluated in clinical situations. Its levels are increased in the presence of localized bacterial and viral infections and in chronic inflammatory conditions.[3]

There is a significant difference in the mean serum CRP levels between patients with COPD and healthy subjects, as serum CRP concentration was higher in patients with COPD.[4] CRP levels are raised in patients with moderate to severe COPD.[5] There is an excellent correlation of circulating CRP concentrations with the severity, extent, and progression of many different pathologies, and the prognostic significance of these associations are consistent with serum CRP levels not only just being a marker of disease but also contributing

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to pathogenesis.[6] It is known as a predictive factor for the course of COPD.[4]

This study was an attempt to estimate serum CRP levels in patients with COPD and compared those with the serum CRP levels in controls and in different stages of COPD.

Materials and Methods

This study was carried out in the Department of Physiology, in collaboration with Department of Biochemistry between September 2009 to November 2011 at Government Medical College, Aurangabad, Maharashtra, India. The study protocol was approved by the Institutional Ethical Committee. Before enrollment in the study, informed written consent was obtained from each subject.

All the subjects aged between 20 and 70 years were selected from the outpatient department and from the admitted patients of the institution and divided in two groups, each of 100 subjects. Group one consisted of normal individuals without signs and symptoms of COPD, who were taken as control. Group two consisted of patients with COPD. Venous blood samples from the subjects were collected in a plane bulb, and the serum separated after clotting was tested for CRP levels. "CRP-ultra sensitive" kit from "SPINREACT" company was used for the purpose.

Pulmonary function test machine in the Department of Physiology to determine pulmonary function tests (PFTs) and semi-auto analyzer in the Department of Biochemistry to evaluate serum CRP levels were used. PFT was done to rule out COPD in control subjects and for confirming the diagnosis in patients with COPD.

On the basis of PFT, patients with COPD were classified into four stages using standards mentioned in global initiative for chronic obstructive lung disease (GOLD) criteria.[7]

Two consecutive sputum samples were tested before PFTs to rule out tuberculosis.

All the calculations and statistics were done using Microsoft Excel 2007, and all the statistics were compared by using "Graph Pad Prism 5 software," version 5.01. A *P* value of less than 0.05 ($P < 0.05$) was considered to be statistically significant. A *P* value of less than 0.01 ($P < 0.01$) was considered to be statistically highly significant.

For each parameter, the mean value and standard deviation were calculated. Postbronchodilator FEV_1, forced vital capacity (FVC), FEV_1/FVC, and predicted FEV_1% were calculated for staging of patients with COPD. CRP levels in control and all four stages of COPD were compared using one-way analysis of variance (ANOVA) test.

Result

In this study, values of CRP in patients with COPD and healthy control subjects were estimated and compared.

The observations and results of the study were tabulated. The demographic data (age, height, weight, and body mass index) of all the subjects in each study group were obtained [Table 1]. When the values of mean serum CRP levels in control subjects were compared with those of total patients with COPD using "unpaired *t*-test," it showed statistically highly significant difference with $P < 0.001$ [Table 2]. The mean serum CRP values in control and in different stages of COPD patients are shown in Table 3. Comparison between mean serum CRP levels in different stages of COPD is shown in Table 4.

Table 1: The demographic data of the two study groups

Parameter (mean ± SD)	Control	COPD patients
Age (years)	51.86 ± 10.83	56.67 ± 10.99
Weight (kg)	59.58 ± 9.63	55.58 ± 11.95
Height (m)	1.62 ± 0.07	1.58 ± 0.07
BMI	22.8 ± 3.98	22.90 ± 4.33

SD, Standard deviation.

Table 2: Mean serum CRP levels in control and total COPD patients

Parameter	Control	COPD patients	*P*
Serum CRP (mg/L) (mean ± SD)	0.8872 ± 0.47	3.8536 ± 1.5	<0.001

There was no significant difference between mean CRP levels in stages I and II and that of between stages II and III. A highly significant difference between mean CRP levels in stages III and IV was observed. A highly significant difference between mean CRP levels in control and all stages of COPD individually was observed.

A highly significant difference was observed between the mean CRP levels when each stage was compared with other remaining stages, except between stages I and II and stages II andIII as mentioned earlier.

Correlation test was applied, and Pearson's correlation coefficient was calculated between serum CRP levels and predicted FEV_1% showing negative correlation with a value of –0.564 (between 0 and –1) [Table 5, Figure 1].

Discussion

In this study, it was observed that serum CRP levels in control group were 0.8872 ± 0.47 mg/L. The mean serum CRP levels in patients with COPD was 3.8536 ± 1.5 mg/L. This study showed that there was a significant difference in mean serum CRP level between patients with COPD and healthy subjects, as the mean serum CRP levels were higher in patients with COPD and the difference was statistically highly significant [Table 2].

Similar findings were noted in the studies done by Halvani et al.,[4] who in their study noted that CRP level in COPD was 52.49 ng/mL in comparison with control 28.51 ng/mL ($P = 0.01$). Moreover, Pinto-Plata et al.[5] in their study showed that serum CRP levels were significantly higher in patients with COPD [5.03 (1.51) mg/L] than in controls (adjusted odds ratio 9.51; 95% confidence interval: 2.97 to 30.45).

Table 3: Mean serum CRP levels in control and different stages of COPD patients

Parameter	Control	Stages of COPD			
		Stage I	Stage II	Stage III	Stage IV
Serum CRP (mg/L) (mean ± SD)	0.8872 ± 0.47	2.735 ± 0.78	3.0855 ± 0.86	3.6558 ± 1.03	5.1361 ± 1.75

Table 4: Multiple comparisons between different groups and mean CRP levels

S.no.	Comparison	*P*	Significance
1	C–S (I)	<0.001	HS
2	C–S (II)	<0.001	HS
3	C–S (III)	<0.001	HS
4	C–S (IV)	<0.001	HS
5	S (I)–S (II)	>0.001	NS
6	S (I)–S (III)	<0.001	HS
7	S (I)–S (IV)	<0.001	HS
8	S (II)–S (III)	>0.001	NS
9	S (II)–S (IV)	<0.001	HS
10	S (III)–S (IV)	<0.001	HS

C, control; S, stage; NS, not significant; HS, highly significant.

Table 5: Correlation of serum CRP levels and predicted FEV_1% in COPD patients

Serum CRP levels (mg/L)	Predicted FEV_1%	Correlation coefficient
3.85 ± 1.5	45.34 ± 19.23	-0.564

Dahl et al.[8] in their study showed that baseline serum levels of CRP were higher in individuals who subsequently had a COPD outcome than in those who did not.

Correlation test was applied and Pearson's correlation coefficient was calculated between serum CRP levels and predicted FEV_1% showing negative correlation with a value of –0.564 (between 0 and –1). This shows that, as the severity of disease increases, serum CRP levels increases significantly [Table 5, Figure 1].

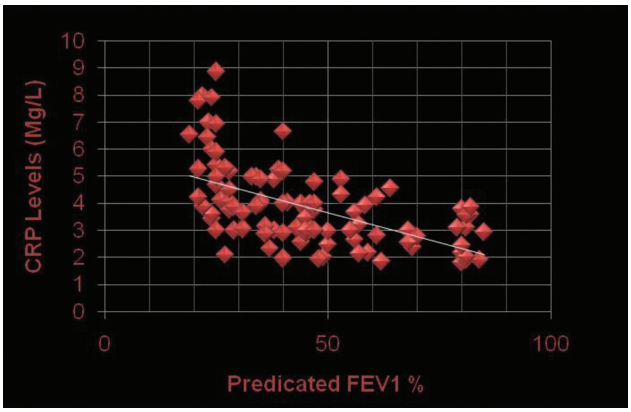

Figure 1: Scattered diagram showing negative correlation between serum CRP levels and predicted FEV_1%.

Our findings are in agreement with the study done by Wu et al.,[9] who reported that FEV_1 changes in COPD patients and serum CRP concentration was negatively correlated (r = –0.610 and P < 0. 001). Our finding also matches with those of study done by Amer et al.,[10] who showed that there was a positive significant correlation between the levels of serum CRP and stages of COPD according to FEV_1 and those of Broekhuizen et al.,[11] who showed that CRP was moderately inversely correlated with postbronchodilator FEV_1 (r= –0.22, P = 0.026).

In this study, there was increase in CRP levels with the increase in severity of the disease in different stages (P< 0.001) [Table 3]. Similar findings were noted in the studies done by Samy et al.,[12] who reported that serum CRP level was increased in COPD stages II, III, and IV, and this increase was significant when compared with controls, while, in stage I, there was no significant increase in CRP compared with controls. Moreover, de Torres et al.[13] showed that serum CRP level was significantly increased with increasing severity of the disease.

In our study, there was a significant difference between the severity of dyspnea (FEV_1% predicted) and the level of CRP (P = 0.001). As the severity of dyspnea increased by progression of COPD, we assume that there is a direct relationship between the severity of dyspnoea and increased serum CRP level. Similar finding was shown in study done by Shaaban et al.[14] who showed that FEV_1 as a percentage of predicted values was negatively associated with serum CRP concentration (P = 0.002). Moreover, similar findings were found in study done by Aksu et al.[15] (r = –0.318, P < 0.002).

Conclusion

This study suggests that CRP is a good candidate as a predictor for rapid decline of FEV_1 in COPD, although a larger size study with longer-term observation is needed to confirm this result, as biomarkers represent attractive options but are far from implementation in COPD. It is likely that, in the future, biomarkers shall be required to aid in determining those patients who will benefit from a given drug therapy to improve risk and/or cost benefit, especially, because it is becoming more widely considered in COPD. Because CRP is a systemic inflammatory marker and systemic inflammation is one of the major factors in development of extrapulmonary complications, we hope this marker can be applied for follow-up of patients, evaluation of treatment methods, and their efficacy.

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