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ORIGINAL ARTICLE

To determine the serum CRP level in patients with COPD and its correlation with disease severity

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ABSTRACT:

Aim: To determine the serum CRP level in patients with COPD and its correlation with disease severity. **Methods:** The Department of Pulmonary Medicine did a prospective research. The control group consisted of 60 COPD patients and 60 asymptomatic persons. Spirometry tests were performed on COPD patients, and the severity of the disease was assessed using the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria. The key inclusion criteria for COPD patients were symptoms or a history of COPD, as well as FEV1/FVC less than 70% after using a bronchodilator. **Results:** In the COPD group, 48.33% noted cigarette smoking during the study, 15% reported cigarette smoking in the past, and 36.67% mentioned a history of baking. In the control group, 10 subjects (16.67%) noted cigarette smoking during the study; 3 subjects (5%) mentioned cigarette smoking in the past, and 7 subjects (11.67%) reported a history of baking. The correlation between serum hsCRP and age, FEV1, PaO_2, and FEV1/FVC was studied in patients with COPD, where the Pearson correlation coefficients between hsCRP and the above-mentioned variables equaled 0.19, 0.09, -0.34, and -0.06, respectively ($P<0.05$ in the correlation between hsCRP and FEV1, and $P>0.2$ in other cases). Regarding smoking and its relationship with the severity of COPD, 29 patients reported as current smokers, where nine subjects had moderate COPD, 17 subjects had severe COPD, and 1 subject had very severe COPD. In this category, there was a significant relationship between the severity of COPD and current smoking ($P=0.035$). Furthermore, 9 subjects reported as past smokers. In this group, there was a significant correlation between the severity of COPD and a history of smoking ($P<0.001$). Moreover, from among patients with COPD, 22 patients noted a history of baking. In this group, there was no significant correlation between the severity of COPD and a history of baking ($P=0.33$). **Conclusion:** The current study found that plasma CRP is not only helpful in assessing inflammation in COPD, but also beneficial as a marker in monitoring inflammation throughout COPD therapy. CRP is reduced with inhaled corticosteroid therapy. Furthermore, in patients with COPD, screening of vitamin B12 and folic acid insufficiency is recommended, as is examination of blood IL-6 levels in patients with COPD exacerbation.

Keywords: COPD, serum CRP

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a form of lung illness that is characterised by airflow limitation and substantial long-term breathing issues. [1] The major hallmark of COPD is a sustained reduction in expiratory pressure flow. Inflammation has been linked to the pathophysiology of COPD, according to research. Furthermore, it has been demonstrated that in the latter stages of COPD, long after smoking cessation, the inflammation caused by smoking in the early stages of the illness continues. [1] According to studies, the relationship between decreasing pulmonary function and the intensity of smoking shows an increase in COPD as patient age increases, demonstrating a clear link between smoking and COPD. [2]

Indoor exposure to biomass smoke, such as wood, fertiliser, residual products, and charcoal, on the other hand, can cause acute respiratory difficulties in children as well as COPD and lung cancer in women, accounting for about 2.7 percent of all disability-adjusted life years (DALYs) globally. [3] Rather of evaluating breathlessness with lung function, the Global Initiative for Chronic Obstructive Lung Disease guideline proposes numerous symptomatic measures. [1] The COPD assessment test (CAT) is one of numerous questionnaires used in everyday practise to measure health-related quality of life. [4–6] It is a simple measurement using an eight-item questionnaire designed to evaluate the impact of COPD symptoms on the patient's health status with scores ranging from 0 to 40. 4 In clinically stable COPD patients, the CAT is also closely related to the St George's Respiratory Questionnaire.[7,8]

C-reactive protein (CRP) is a typical systemic biomarker that reflects an individual's complete systemic burden of inflammation. [9] Serum CRP is high in adults with stable COPD, and it is associated with disease severity and poor health outcomes in patients with mild-to-moderate COPD. [10] Increased levels of CRP and other systemic biomarkers were linked to an increased risk of COPD exacerbations in the Copenhagen City Heart Study and Copenhagen General Population Study. [11] The CAT score is also linked to patients who are at high risk of exacerbation and fluctuates dramatically during and after

exacerbations. [6,12] Furthermore, a higher CAT score during an exacerbation suggests the severity of the exacerbation. [6] In terms of the association between CAT score and CRP, the change in CAT score from baseline to the commencement of exacerbation was positively linked with the change in serum CRP. [6,13]

MATERIALS AND METHODS

After receiving clearance from the protocol review committee and the institutional ethics committee, a prospective research was undertaken at the Department of Pulmonary Medicine. The control group consisted of 60 COPD patients and 60 asymptomatic persons. Spirometry tests were performed on COPD patients, and the severity of the disease was assessed using the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria.

The key inclusion criteria for COPD patients were symptoms or a history of COPD, as well as FEV1/FVC less than 70% after using a bronchodilator. Exclusion criteria for COPD patients included hemoptysis, pneumothorax, acute coronary illness, recent MI, pulmonary embolism, vascular aneurysm, recent surgery, acute infection, history of malignancy, or any inflammatory cause other than COPD.

METHODOLOGY

All participants in the control and COPD groups were visited, evaluated, and their histories were obtained. The data was entered into a specific form. Age, gender, smoking history, baking history, medical history of the patient, and vital signs were all documented for all subjects. The COPD group had their tests (including CBC and biochemistry) reviewed, and if they met any of the exclusion criteria, they were eliminated. Patients in the control group were chosen based on examination and history, and if they had a history of previous illnesses, they were excluded based on the exclusion criteria. Individuals in both groups had blood drawn, and the patients' serum samples were centrifuged. Three samples were isolated for each subject to test hsCRP, and one sample was separated as a backup. The samples were kept at -20°C until they were used. HsCRP was tested in 50 COPD patients and 45 healthy controls. Because of the sensitivity of the hsCRP measurement, it was tested three times for each sample, and the mean was deemed the averaged hsCRP values. The immunoturbidometry test (Roche Diagnostics, Mannheim, Germany) and an auto analyzer (Lysis, Milan, Italy) were used to assess serum hs-CRP, with a normal result defined as 5000 ng/L.

STATISTICAL ANALYSIS

SPSS 24.0 software was used for statistical analysis (SPSS Inc., Chicago, IL, USA). Descriptive statistics were presented as percentages (for categorical variables) and means (standard deviations) (for continuous variables). To compare the values between groups, we utilised the t-test, with P0.05 chosen as the level of statistical significance.

RESULTS

This research had 120 participants (60 patients with COPD and 60 individuals as controls). The COPD group consisted of 40 males (66.67%) and 20 women (33.33%), whereas the control group consisted of 35 men (58.33%) and 25 women (41.67 percent). As a result, the COPD and control groups were gender matched. There was no statistically significant difference between the two groups. The COPD group had a mean age of 67.2±558 years while the control group had a mean age of 66.25±3.55 years. As a result, the COPD and control groups were age-matched.

In the COPD group, 29 participants (48.33 percent) reported smoking during the trial, 9 subjects (15 percent) reported smoking in the past, and 22 subjects (36.67 percent) reported baking. In the control group, 10 participants (16.67%) reported cigarette smoking during the trial, 3 subjects (5%) reported cigarette smoking in the past, and 7 subjects (11.67%) had a history of baking. hsCRP was evaluated in 60 COPD patients and 60 control persons in this research. The mean hsCRP in the COPD group was 7532±456 ng/mL and 4327±411 ng/mL in the control group. A significant difference ($p<0.001$) was detected in the comparative examination of the two groups utilising the t-test.

Spirometry and blood gas measurements were performed on the COPD group, followed by measurements of FEV1, FEV1 percent, FVC, and FEV1/FVC parameters. The severity of the condition was assessed using the GOLD criteria, with 18 participants (30%) scoring GOLD II, 30 subjects (50%) scoring GOLD III, and 12 subjects (20%) scoring GOLD IV. I identified no cases of GOLD among the subjects since the patients were hospitalised. The mean FEV1 was 1.27 L/s, the mean FVC was 2.14, and the mean FEV1/FVC was 60%. The correlation between serum hsCRP and age, FEV1, PaO_2, and FEV1/FVC was studied in patients with COPD, where the Pearson correlation coefficients between hsCRP and the above-mentioned variables equaled 0.19, 0.09, -0.34, and -0.06, respectively ($P<0.05$ in the correlation between hsCRP and FEV1, and $P>0.2$ in other cases).

Regarding smoking and its relationship with the severity of COPD, 29 patients reported as current smokers, where nine subjects had moderate COPD, 17 subjects had severe COPD, and 1 subject had very severe COPD. In this category, there was a significant relationship between the severity of COPD and current smoking ($P=0.035$). Furthermore, 9 subjects reported as past smokers. In this group, there was a significant correlation between the severity of COPD and a history of smoking ($P<0.001$). Moreover, from among patients with

COPD, 22 patients noted a history of baking. In this group, there was no significant correlation between the severity of COPD and a history of baking (P=0.33). The correlation between hsCRP in patients with COPD was r=0.028, and the correlation between hsCRP in the control group was r=0.001. The correlation between the severity of COPD and hsCRP equaled r=0.34 (P=0.03). Therefore, there is a significant correlation between the severity of COPD and hsCRP. There is also a significant correlation between hsCRP and the severity of COPD.

Table 1: Demographic characteristics and studied variables among COPD patients and asymptomatic individuals (control group)

Parameter	Control		COPD		P -value
Gender	**Number**	**%**	**Number**	**%**	
Male	35	58.33	40	66.67	
Female	25	41.67	20	33.33	
Age in years					
Below 30	12	20	10	16.67	
30-50	40	66.67	45	75	0.52
Above 50	8	13.33	5	8.33	
Mean Age	66.25±3.55		67.25±58		
Smoking(Now)	10	16.67	29	48.33	
Smoking(past)	3	5	9	15	
Backing	7	11.67	22	36.67	
Lung Function					
FEV1/L	-		1.27		
FVC/L	-		2.14		
FEV1/FVC	-		60%		
hcCRP (mmol/L)	4327±411		7532±456	0.001	

*P<0.05; statistically significant

Table 2: Smoking and its relationship with severity of COPD

	COPD severity			
	Moderate No. (%)	**Severe No. (%)**	**Very severe No. (%)**	**P-value**
Smoking(Now)	11 (37.93)	17(58.62)	1 (3.45)	0.033
Smoking(past)	-	2(22.22)	7 (77.78)	<0.001*
Baking	8(36.36)	12 (45.54)	2 (9.09)	0.31

P<0.05; statistically significant

DISCUSSION

Serum hsCRP levels were assessed in COPD patients and control participants in this study, and the relationship between partial pressure of oxygen (PaO2), FEV1, and age was investigated using the aforementioned blood factor. Serum CRP (SCRP) is a risk factor for cardiovascular and thromboembolic disease[14], and in patients with COPD, pulmonary inflammation appears to lead to systemic inflammation, as inhaled corticosteroids have been related with a reduction in SCRP and other indicators of systemic inflammation. [15] SCRP levels greater than 3 mg/L have been linked to a ten-year increase in death in these individuals. [16] In this study, the hsCRP level was measured for the control and COPD groups. CRP increases the risk of thrombotic events and cardiovascular mortality. In the lungs, CRP has a protective function against bacteria and apoptotic cells in the form of an intrinsic immune system. At first, CRP is produced by hepatocytes in the liver in response to IL-6, and then enters the lungs through the plasma. The inflammation in COPD activates epithelial cells and increases alveolar macrophages and other inflammatory cells which are responsible for the release of IL-6. This in turn leads to an acute phase response and an increase in plasma CRP. Moreover, IL-6 regulates two other acute phase reactors, namely fibrinogen and al-anti trypsin, both of which affect the pathogenesis of COPD.16. In further support of IL-6 in the development of COPD, studies have revealed that IL-6 increases the number of CD8 and CD4 cells, macrophages, B cells, and pul- monary neutrophils, which are matched with changes seen in the pathology of COPD. On the other hand, an increase in IL-6 leads to airspace enlargement in emphysema, peribronchial accumulations, monocel- lular cells, increased wall thickness of airways, sub- epithelial fibrosis, and increased airway response. In animals, a contact with ozone decreases IL-6 and, consequently, reduces pulmonary injury. Therefore, plasma CRP is associated with IL-6-dependent processes in airways, leading to the progress of COPD and severe clinical problems.[16,17]

In this study, to eliminate the role of infection in increasing CRP, all patients with abnormal CXR

(indicating pneumonia) who were febrile or had leukocytosis were excluded. In this study, consistent with the study by Tores *et al*. (2006), in Spain, and Seemungal *et al*. (2007), the mean hsCRP level between con- trol group and COPD group was different by greater than 3.3 mg/L, which was significant (P<0.001).[18,19] A significant negative correlation between hsCRP and FEV1% was found in this research study (r=0.28, P=0.4). A similar correlation was also reported between FEV1% and hsCRP by Fimognari *et al*. (2007) (r=0.37, P=0.01), which is also consistent with the re- sults from a study by Seemungal *et al*. (2009).[18,20]

CONCLUSION

The current study found that plasma CRP is not only helpful in assessing inflammation in COPD, but also beneficial as a marker in monitoring inflammation throughout COPD therapy. CRP is reduced with inhaled corticosteroid therapy. Furthermore, in patients with COPD, screening of vitamin B12 and folic acid insufficiency is recommended, as is examination of blood IL-6 levels in patients with COPD exacerbation. Furthermore, in COPD patients, dietary status, BMI, and serum albumin must be evaluated, as well as their relationship to disease prognosis.

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