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Research Article

Relationship between C-Reactive Protein and Stages of Chronic Obstructive Pulmonary Disease; A Cross-Sectional Study

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is an inflammatory lung disease that obstructs airflow. Here, we evaluate the relationship between C-reactive protein (CRP) levels and the stages of COPD.

Methods: A cross-sectional study involving 60 patients diagnosed with COPD aged between 35 to 70 years was performed, and the relationship between CRP and stages of COPD was noted. Data was tabulated and analyzed using Analysis of Variance (ANOVA), and a p-value of <0.05 was considered significant.

Results: Fifty percent of the study participants were aged between 51 to 60 years, with a mean of 55.85 ± 7.64 years. According to the Global Initiative for Lung Disease (GOLD) criteria, 50 percent of the study participants were diagnosed with Stage II COPD and 35% with Stage III COPD. The mean forced expiratory volume in one second (FEV1) was 84 ±2.39 percent in stage I COPD and 28.20 ±1.48 percent in stage IV. The mean CRP levels recorded were 3.91 ±1.26 mg/dL in stage I COPD (p<0.05), 5.79 ±1.23 mg/dL in stage II (p<0.05), 9.01 ±0.96 mg/dL in stage III (p<0.05) and 11.98 ±0.73 stage IV (p<0.05). Statistically significant incremental mean CRP level was noted with progressive stages of COPD.

Conclusions: COPD is a systemic inflammatory disease in which CRP levels significantly increase with the progression of the disease. This warrants serial measurement of CRP in patients with COPD to monitor the progression of the disease. In addition, the measurement of CRP should also be considered in stable COPD patients to document the baseline for follow-up.

Key Words: *C-reactive protein, COPD, Chronic obstructive pulmonary disease, Forced expiratory volume, GOLD Criteria, hs-CRP, Obstructive airway disease*

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INTRODUCTION

According to the Global Initiative for Lung Disease (GOLD), chronic obstructive pulmonary disease (COPD) is defined as "a disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lungs to noxious particles and gases" [1]. Several studies in recent years provide overwhelming evidence of COPD being a systemic condition characterized by an abnormal inflammatory response beyond the lungs. These manifestations include weight loss, skeletal muscle dysfunction, increased risk of cardiovascular disease, osteoporosis, and depression [2]. Here, we study the relationship between CRP levels and disease severity.

METHODS

A cross-sectional study was undertaken at Kempegowda Institute of Medical Sciences Hospital and Research Centre, Bengaluru, India. The duration of the study was 18 months spanning from September 2020 to March 2022. The Kempegowda Institute of Medical Sciences Institutional Review Board Ethical Committee clearance and Informed consent from the study participants were obtained. All methods were carried out following relevant guidelines and regulations. Patients diagnosed with COPD who attended the clinic and those admitted to the hospital were considered for the study. Sixty patients aged 35-70 years with spirometry-confirmed COPD ($FEV_1/FVC < 0.7$ post-bronchodilator)

who consented to participate in the study were included. Patients with other clinically detectable pulmonary disorders, obstructive sleep apnea, inflammatory arthritis, inflammatory bowel disease, and connective tissue disorders were excluded from the study. Data was tabulated and analyzed using SPSS version 25.0 (IBM Corp. Chicago, IL, USA). A comparison of the mean CRP values with the stages of COPD was performed using the Analysis of Variance (ANOVA) test, and a p-value of <0.05 was considered significant.

RESULTS

Fifty percent of the study participants were 51-60 years (Figure 1). The mean age of the study participants was found to be 55.85 ±7.64 years (Table 1).According to the GOLD Criteria, 50 percent of the study participants had stage II COPD, and 35 percent had stage III COPD (Table 2). The mean FEV_1 was found to be 84.0 ±2.39 percent in stage I COPD, 64.94±6.89 percent in stage II, 42.21±4.19 percent in stage III, and 28.20 ±1.48 percent in stage IV (Table 2).

As observed in this study, the mean CRP level rises with the progression in the stage of COPD (Figure 2). In addition, a statistically significant association ($p<0.05$) was found between CRP levels and the stages of COPD.The mean CRP levels were 3.91 ±1.26 mg/dL in stage I COPD ($p<0.05$), 5.79 ±1.23 mg/dL in stage II ($p<0.05$), 9.01 ±0.96mg/dL in stage III ($p<0.05$) and 11.98 ±0.73 stage IV ($p<0.05$)(Table 3).

DISCUSSION

COPD is characterized by the limitation of expiratory airflow, which is slowly progressive over the years [3] and primarily affects the respiratory system, among others. Studies have shown that the airway and systemic inflammatory markers increase over time, with higher levels corresponding to a faster decline in lung function [4]. Joppa et al. found that rising levels of pulmonary artery pressure in COPD patients were associated with an increase in inflammatory proteins such as C-reactive protein (CRP) and tumor necrosis factor-α (TNF- α) [5]. This highlights the possible role of systemic inflammation in the pathogenesis of pulmonary hypertension in COPD patients. It is also observed that the serum levels of lactate dehydrogenase isoenzyme-3 (LDH-3) are raised in patients with COPD and positively correlate with the rise in high sensitive C-reactive protein (hs-CRP) [6]. In addition, data in patients with COPD found that reduced quadriceps muscle strength was associated with systemic levels of CRP and IL-6 [7,8].

CRP is an established inflammatory marker that is elevated in patients with COPD. CRP is an acute-phase protein synthesized predominantly by the hepatocytes in response to tissue damage or inflammation. It has been found that the CRP levels relate to airflow obstruction and were lower in COPD patients treated with inhaled corticosteroid (ICS) [9]. Our study evaluates the levels of CRP in patients with COPD and the relationship between the mean levels of CRP and stages of COPD. Also, recent data has shown that CRP significantly predicts future exacerbation and hospital admission for COPD patients [10].

In the present study, we observed that 50 percent of the participants belonged to the age group 51-60 years with a mean age of 55.85 ±7.64 years, similar to a study by Agarwalet al. [11]. Agarwal et al. also stated that CRP and $FEV_1$are important clinical variables that help predict the outcome. The mean FEV_1in the present study was 28.20 ±1.48 percent in stage IV COPD, comparable to a study in the same context. This study also suggested that treating severe COPD should include nutritional rehabilitation [12].

In this study, we observe that the CRP levels are significantly associated ($p<0.05$) with the severity of the disease. In addition, a serial increase in CRP levels was noted with disease progression. Hence, routine monitoring of CRP levels beginning early in the disease process can help keep track of the progression of COPD. Therefore, we recommend performing a baseline CRP level during COPD diagnosis to monitor disease progression.

Limitations of the study

The authors understand that CRP is a nonspecific inflammatory marker, and its levels are variable and affected by various physiological and pathological processes. In the present study, efforts were made to reduce such confounding processes through a detailed history and physical examination. Further studies need to be conducted to strengthen the association between CRP and the progression of COPD. However, it is essential to note that the estimation of CRP is inexpensive and readily available in most laboratories, including the ones in limited-resource regions. This will prove beneficial as a cost-effective method to keep track of the disease worldwide, especially in resource-poor areaswhere the burden of COPD is on the rise.

CONCLUSION

COPD is a systemic inflammatory disease in which CRP levels significantly increase with the progression of the disease. This warrants serial measurement of CRP in patients with COPD to estimate the progression of the disease. Measurement of CRP should also be considered in stable COPD patients to document the baseline to monitor the progression of the disease.

Abbreviations
6MWD: Six-minute walk distance
ANOVA: Analysis of Variance
COPD: Chronic obstructive pulmonary disease
CRP: C-reactive protein
FEV_1: Forced expiratory volume in one second
FVC: Forced vital capacity
GOLD: Global Initiative for Lung Disease
ICS: Inhaled corticosteroid
IL-6: Interleukin 6
LDH: Lactate dehydrogenase
TNF- α: Tumor necrosis factor-α

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Conflict of Interest
The authors have no relevant conflicts of interest to declare.

Ethics Approval and Consent to participate
The Kempegowda Institute of Medical Sciences Institutional Review Board Ethical Committee clearance and Informed consent from the study participants were obtained. All methods were carried out following relevant guidelines and regulations. All experimental protocols were approved by the Kempegowda Institute of Medical Sciences Ethics Committee.

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TABLES

Table 1: Age distribution of the study participants

Age group	Number of Patients	Percentage
41-50 years	18	30
51-60 years	30	50
61-70 years	10	17
71-80 years	2	3
Mean ± Standard deviation	55.85 ± 7.64	

Table 2: Distribution of the study participants according to theirCOPD stages:

Stages of COPD	Number of Patients	Percentage	FEV1%	
			Mean	Standard Deviation
I	6	10	84.00	2.39
II	30	50	64.94	6.89
III	21	35	42.21	4.19
IV	3	5	28.20	1.48

Table 3: Stages of COPD with mean CRP levels of the study participants:

Stages of COPD	Mean CRP Levels	P value
I	3.91±1.26	**<0.05**
II	5.79±1.23	**<0.05**
III	9.01±0.96	**<0.05**
IV	11.98±0.73	**<0.05**

FIGURES

Figure 1: Distribution of the study participants according to their age group

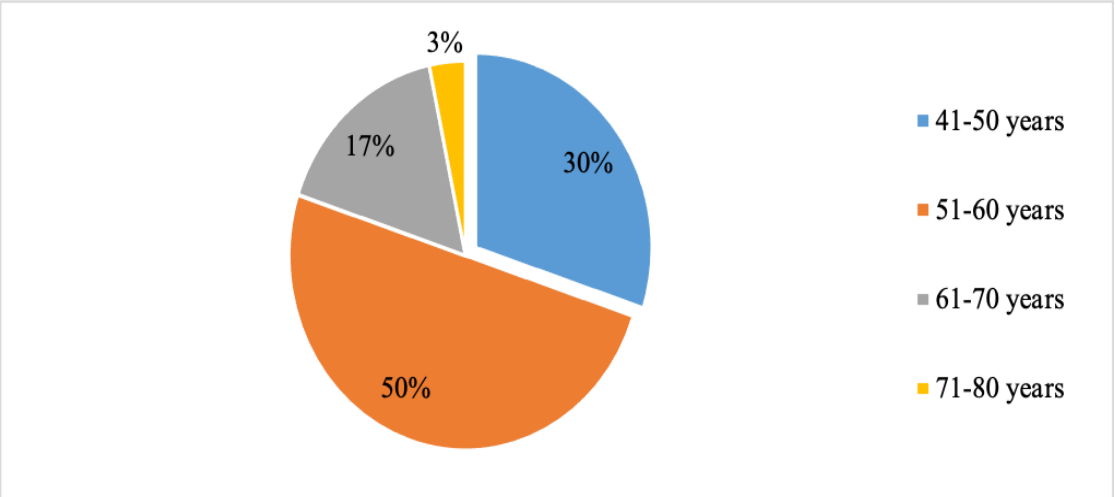

Figure 2: Stages of COPD (x-axis) with mean CRP levels (mg/dL) (y-axis)