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Original Article

Relationship of C-Reactive Protein Level with Stages of Chronic Obstructive Pulmonary Disease

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Abstract

Introduction: Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality throughout the world. C-reactive protein (CRP) is found in blood plasma, which rises in response to inflammation.

Aim: This study aims to study the level of CRP in COPD patients.

Materials and Methods: In this study, 50 patients diagnosed with COPD were included he study. Patients detailed history, physical examination, and spirometry were classified as per Global Initiative for Chronic Obstructive Lung Disease (GOLD) staging which were collected. Three milliliters of blood were drawn for CRP testing by the turbidometry method.

Results: Of the 50 patients, 11 (20%) were in GOLD Stage I on presentation, 21 (42%) were in GOLD Stage II, 14 (28%) in GOLD Stage III, and 5 (10%) in GOLD Stage IV. Serum CRP level was positive in 36 cases with mean CRP level 9.54 ± 2.13, and 14 cases showed negative CRP value (2.19 ± 1.54). The mean of CRP level for Stage 1 COPD was 3.2 ± 2.1, Stage 2 was 4.1 ± 2.4, Stage 3 was 9.9 ± 3.5, and Stage 4 was 12.4 ± 3.8, the difference was statistically significant ($P < 0.05$).

Conclusion: The levels of inflammatory marker, serum CRP are significantly elevated in patients with COPD.

Key words: Chronic obstructive pulmonary disease, C-reactive protein, Systemic inflammation

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major cause of chronic morbidity and mortality throughout the world and it is the fourth leading cause of death.[1] It is the only major worldwide disorder in which morbidity and mortality are increasing, and further increases are expected in the coming decades.[2] The airflow obstruction in COPD is also an important contributor to other common causes of morbidity and mortality, including ischemic heart disease, arrhythmias, and strokes.[3]

The chronic inflammation in COPD orchestrated by multiple inflammatory cells and mediators in the airways and the lung tissue is induced by inhalation of noxious gasses and particulate matter.[4] Systemic inflammation and oxidative stress are the most important features of COPD.[5] Although the origin of systemic inflammation present in COPD remains poorly understood and correlations in the regulation of inflammation in the pulmonary and systemic compartments are not well documented, yet, it is established that some inflammatory markers have risen in the systemic circulation of the blood-based biomarkers, C-reactive protein (CRP) has shown the greatest promise.[5-7]

The use of CRP as a marker is on increase. Whenever there is damage to the tissue or inflammatory process, the hepatocytes synthesize a protein which is an acute-phase reactant, and this is the CRP. Studies have shown that serum CRP levels are usually elevated during acute exacerbations of COPD.[8] The overall course of COPD can be predicted by the use of serum CRPs. The CRP has been found to be related to the degree of obstruction of the airflow.[9]

Aim

This study aims to study the level of CRP in COPD patients.

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MATERIALS AND METHODS

This observational study was conducted in the Department of General Medicine at Government Headquarters Hospital, Ramanathapuram, in COPD patients. Male and female patients who were diagnosed with COPD after detailed history, physical examination, and spirometry were classified as per Global Initiative for Chronic Obstructive Lung Disease (GOLD) staging. Patients with a history of pulmonary tuberculosis, diabetes mellitus, systemic hypertension, cardiovascular diseases, bronchiectasis, interstitial lung disease, malignancies, obstructive sleep apnea, and asthma overlap were excluded from the study.

Diagnosis of COPD was made clinically and confirmed by office spirometry as per GOLD guideline (i.e., post-bronchodilator forced expiratory volume (FEV)1/forced vital capacity <70%). Spirometry was done in each case to confirm the clinical diagnosis of COPD, to rule out asthma by bronchodilator reversibility testing, and to define the severity of the disease by measuring FEV1 as per the GOLD guideline. Three milliliters of blood were drawn for CRP testing by the turbidometry method.

Data were collected using a pro forma with a structured questionnaire, after obtaining informed consent.

RESULTS

In this study, 50 patients with COPD were included in the study. The mean age of the COPD patients was 59.26 ± 12.46 years. About 82% of patients are male and 18% of patients are female [Figure 1]. The mean BMI of the patients was 22.28 ± 3.51 kg m^{-2}. The mean CRP level of the patients was 9.28 ± 2.54 mg/dl.

Of the 50 patients, 11 (20%) were in GOLD Stage I on presentation, 21 (42%) were in GOLD Stage II, 14 (28%) in GOLD Stage III, and 5 (10%) in GOLD Stage IV [Figure 2].

All the male patients were categorized as per their smoking status such as non-smokers (10%), current smokers (19%), and reformed smokers (71%). Reformed smokers are the ones who have stopped smoking for at least 2 years [Figure 3].

Among the COPD cases, serum CRP level was positive in 36 cases with mean CRP level 9.54 ± 2.13, and 14 cases showed negative CRP value (2.19 ± 1.54) [Figure 4].

The mean of CRP level for Stage 1 COPD was 3.2 ± 2.1, Stage 2 was 4.1 ± 2.4, Stage 3 was 9.9 ± 3.5, and Stage 4 was 12.4 ± 3.8, the difference was statistically significant ($P < 0.05$) [Figure 5].

DISCUSSION

Patients with COPD often have extrapulmonary organ involvement related to oxidative stress and systemic inflammation.[10,11] In the early stages of the disease, the inflammatory process, initiated mainly by components of cigarette smoke, may be self-limiting and reversible. With time, pulmonary inflammation becomes persistent and extrapulmonary manifestations become evident. The mechanism of the systemic inflammation is not yet clear, but spilling over of reactive oxygen species and cytokines from airways into the systemic circulation or peripheral liberation of pro-inflammatory cytokines by inflammatory and/or structural cells have been postulated.[12,13] Liberated pro-inflammatory mediators amplify their effect through their action on organs such as bone marrow and liver. These organs

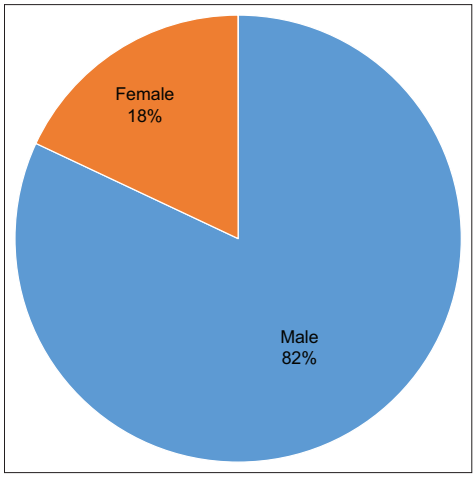

Figure 1: Gender distribution

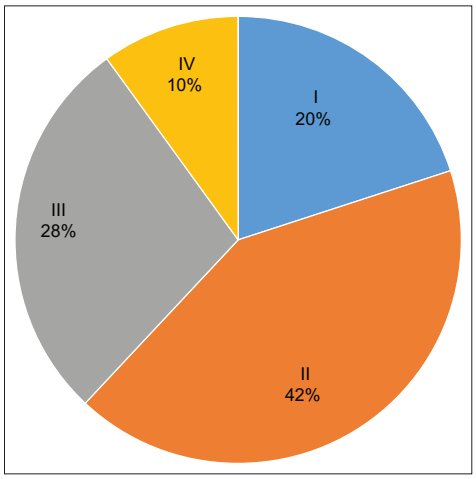

Figure 2: Gold stages of chronic obstructive pulmonary disease

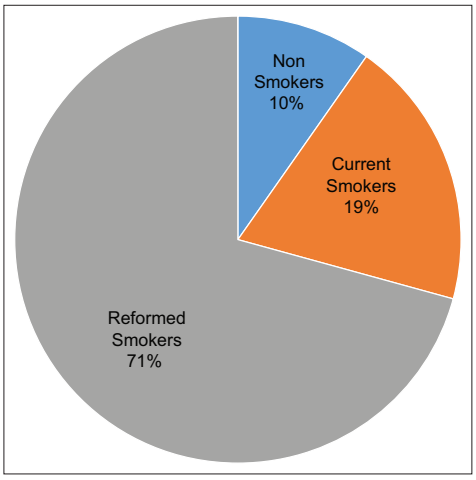

Figure 3: Type of smokers

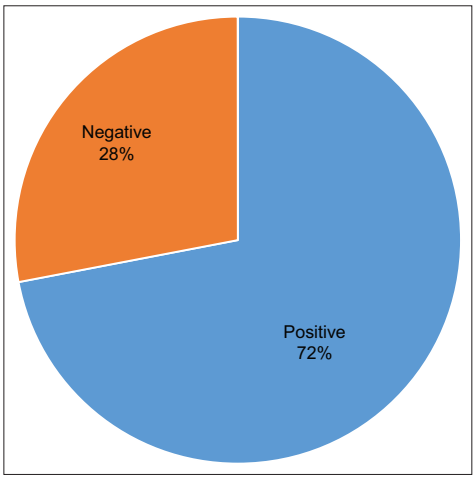

Figure 4: C-reactive protein level distribution

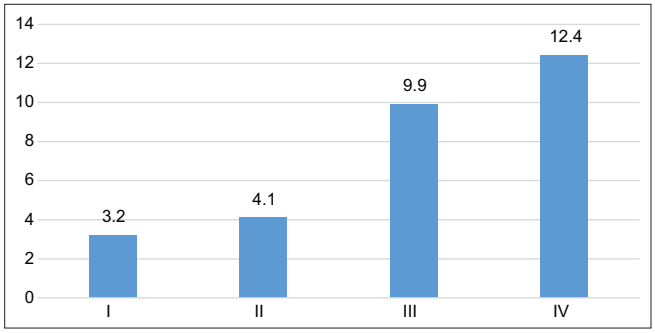

Figure 5: Association between stages of chronic obstructive pulmonary disease with C-reactive protein

produce more white blood cells, platelets, CRP, and fibrinogen when stimulated.[14] These processes usually interact, and more than 1 pathway may be operational at 1 time.

Gan *et al.* were the first to establish the importance of high CRP levels in COPD patients. They showed elevated CRP levels in stable COPD which also predicted cardiovascular mortality.[5]

Yende *et al.* reported a higher level of serum CRP in cases with an obstructive pattern in the spirometry (3.5 mg/L) in comparison to healthy control (2.5 mg/L), $P < 0.0001$.[14]

In a study conducted by Broekhuizen *et al.*, stable COPD patients had increased levels of inflammatory marker like CRP ($P = 0.03$).[15]

In another study by Pinto-Plata *et al.*, there is a significantly higher level of CRP in COPD patients (50.03 ± 1.51 mg/L) as compared to smoking (2.62 ± 1.04 mg/L) and non-smoking control group (2.24 ± 1.04 mg/L), $P < 0.001$.[16]

In the present study regarding the severity of disease based on GOLD criteria, the mean CRP level was increased in severe cases. Dentener *et al.* also found no correlation between serum CRP and lung function in stable COPD patients.[17] Pinto-Plata *et al.* showed that there was no significant difference between the severity of disease and CRP level.[16] However, in a study by De Torres *et al.*, serum CRP level was significantly increased by the severity of the disease.[18]

CONCLUSION

The circulation levels of the inflammatory marker serum CRP are much higher in patients with COPD, which supports the notion that COPD is partly an inflammatory illness with significant systemic inflammation. This implies follow-up of COPD patients to check CRP levels and the subsequent contribution for the development of complications.

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