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Original Research Article

ASSOCIATION OF SYSTEMIC INFLAMMATION (C-REACTIVE PROTEIN) WITH FUNCTIONAL CAPACITY AND DISEASE SEVERITY IN STABLE CHRONIC OBSTRUCTIVE PULMONARY DISEASE: A CROSS-SECTIONAL STUDY

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is a progressive respiratory disorder characterized by persistent airflow limitation and chronic systemic inflammation. C-reactive protein (CRP) is an important biomarker of systemic inflammation and may reflect disease severity and functional impairment in patients with stable COPD. **Objective:** To assess serum C-reactive protein (CRP) levels and evaluate their association with functional capacity and disease severity in patients with stable chronic obstructive pulmonary disease.

Materials and Methods: A hospital-based cross-sectional observational study was conducted among 105 clinically stable COPD patients attending the Department of Respiratory Medicine, Heritage Institute of Medical Sciences, Varanasi. Demographic characteristics, smoking history, body mass index (BMI), spirometric parameters, six-minute walk test (6MWT), and serum CRP levels were recorded. Pulmonary function was assessed using post-bronchodilator spirometry according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines. Functional capacity was evaluated using the 6MWT (BODE Index). Data were analysed using IBM SPSS, and a p-value <0.05 was considered statistically significant.

Results: Among the 105 participants, 34.3% belonged to the 70–79 years age group, 56.2% were underweight, and 52.4% were former smokers. Based on spirometry, 49.5% of patients had moderate airflow limitation, 48.6% had severe airflow limitation, and 1.9% had very severe airflow limitation. The mean serum CRP level was 13.74 ± 4.40 mg/L. The mean FEV_1/FVC ratio, FEV_1 (% predicted), and 6MWT BODE Index score were 53.23 ± 5.52%, 49.83 ± 11.14%, and 1.46 ± 0.87, respectively. Current smokers had significantly poorer pulmonary function and functional capacity than former and never smokers, with significant differences in FEV_1/FVC ratio ($p = 0.007$), FEV_1 (% predicted) ($p < 0.001$), and 6MWT BODE Index score ($p = 0.005$).

Conclusion: Stable COPD was characterized by elevated serum CRP levels, moderate-to-severe airflow limitation, and reduced functional capacity. Current smoking was associated with significantly poorer pulmonary function and exercise capacity. Comprehensive assessment incorporating spirometry, functional capacity, smoking history, and inflammatory biomarkers may improve disease evaluation and management. Further prospective studies are required to clarify the relationship between systemic inflammation and disease severity in stable COPD.

Keywords: Chronic obstructive pulmonary disease; C-reactive protein; Systemic inflammation; Spirometry; Functional capacity; Six-minute walk test; Smoking, Bode index (Body mass index, Airflow Obstruction, Dyspnea, and Exercise capacity Index), ANOVA (Analysis of Variance), SPSS (Statistical Package for the Social Sciences).

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common, preventable, and treatable respiratory disease characterized by persistent respiratory symptoms and progressive airflow limitation caused by abnormalities of the airways and alveoli following exposure to noxious particles or gases. COPD remains a major global public health challenge because of its increasing prevalence, high morbidity, mortality, and socioeconomic burden. According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2024 report, COPD is among the leading causes of death worldwide and is expected to become an even greater contributor to disability and healthcare utilization in the coming decades.[1] In India, COPD contributes substantially to respiratory morbidity owing to widespread tobacco smoking, biomass fuel exposure, environmental pollution, occupational hazards, and delayed diagnosis.[2]

Traditionally, COPD was considered a disease limited to the lungs; however, growing evidence indicates that it is a multisystem inflammatory disorder with important extrapulmonary manifestations. Persistent systemic inflammation plays a central role in the pathogenesis and progression of COPD and contributes to skeletal muscle dysfunction, weight loss, cardiovascular disease, osteoporosis, metabolic abnormalities, and reduced exercise capacity.[3,4] This chronic inflammatory response is mediated by inflammatory cytokines including interleukin-6 (IL-6), tumour necrosis factor-alpha (TNF-α), and interleukin-1β, which stimulate hepatic production of acute-phase proteins such as C-reactive protein (CRP).[4,5]

C-reactive protein is one of the most widely studied biomarkers of systemic inflammation because it is inexpensive, readily available, and reproducible. Elevated serum CRP levels have been reported in patients with stable COPD compared with healthy individuals and have been associated with worsening airflow limitation, frequent exacerbations, impaired quality of life, reduced exercise tolerance, and increased mortality.[6,7] Gan et al. demonstrated in a systematic review and meta-analysis that circulating CRP concentrations are significantly higher in patients with COPD than in healthy controls, suggesting that systemic inflammation persists even during clinically stable disease.[6] Similarly, de Torres et al. reported that elevated CRP was associated with clinically important outcomes among patients with stable COPD.[7]

Assessment of COPD severity has traditionally relied on spirometric measurements, particularly the forced expiratory volume in one second (FEV_1) and the FEV_1/forced vital capacity (FVC) ratio. Spirometry remains the gold standard for confirming airflow limitation and is an important component of COPD assessment according to the GOLD guidelines.[1,8] Nevertheless, spirometric indices alone do not adequately reflect symptom burden, exercise intolerance, or the systemic manifestations of COPD. Patients with similar FEV_1 values may exhibit considerable differences in dyspnoea, physical performance, nutritional status, and quality of life.[8]

Functional capacity has therefore become an important component of comprehensive COPD assessment. The six-minute walk test (6MWT) is a simple, validated, and widely accepted measure of exercise tolerance that provides useful information regarding functional status in patients with chronic respiratory disease.[9] The BODE Index, which integrates body mass index (BMI), airflow obstruction, dyspnoea, and exercise capacity, provides a multidimensional assessment of disease severity and predicts survival more accurately than spirometric measurements alone.[10] Consequently, combining inflammatory biomarkers with pulmonary function testing and functional assessment may provide a more comprehensive evaluation of disease severity.

Body mass index also plays an important role in COPD prognosis. Weight loss and low BMI are common in advanced COPD and may result from increased resting energy expenditure, systemic inflammation, reduced dietary intake, and skeletal muscle wasting. Malnutrition adversely affects respiratory muscle strength, exercise performance, and overall survival.[11] Therefore, nutritional assessment together with pulmonary function testing and inflammatory biomarkers may improve clinical evaluation of COPD patients.

Smoking remains the most important modifiable risk factor for COPD. Continued tobacco exposure promotes chronic airway inflammation, oxidative stress, mucus hypersecretion, and destruction of alveolar architecture, leading to accelerated decline in lung function and worsening systemic inflammation. Smoking cessation is the most important intervention for reducing the harmful effects of continued tobacco exposure and slowing lung-function decline.[1,12] Evaluating pulmonary function and functional capacity according to smoking status may therefore provide additional insights into disease severity among patients with stable COPD.

Although several international studies have evaluated systemic inflammation in COPD, data from the Indian population remain limited, particularly regarding the combined assessment of serum CRP, pulmonary function, and functional capacity in clinically stable patients. Understanding these relationships may facilitate earlier identification of patients at greater risk of disease progression and support individualized management strategies.

Therefore, the present study was undertaken to evaluate serum C-reactive protein levels and their relationship with pulmonary function, functional capacity, and disease severity among patients with stable chronic obstructive pulmonary disease attending a tertiary care hospital.

MATERIALS AND METHODS

Study Design and Setting

This hospital-based **cross-sectional observational study** was conducted in the Department of Respiratory Medicine, Heritage Institute of Medical Sciences, Varanasi, over a period of **18 months (August 2024 to January 2026)** after obtaining approval from the Institutional Ethics Committee.

Study Population

A total of **105 clinically stable COPD patients** attending the Respiratory Medicine Outpatient Department were enrolled consecutively after obtaining written informed consent. COPD was diagnosed according to the **Global Initiative for Chronic Obstructive Lung Disease (GOLD)** criteria using post-bronchodilator spirometry.

Inclusion Criteria

Patients were included if they:

- Were 40 years of age or older.
- Had a confirmed diagnosis of COPD with post-bronchodilator FEV_1/FVC <0.70 according to the GOLD guidelines.
- Were clinically stable, with no exacerbation during the preceding four weeks.
- Provided written informed consent.

Exclusion Criteria

Patients were excluded if they had:

- Acute exacerbation of COPD within the previous four weeks.
- Active tuberculosis, uncontrolled cardiac disease, malignancy, or other significant comorbidities affecting systemic inflammation or exercise tolerance.
- Physical or neurological limitations preventing spirometry or the six-minute walk test.
- Unwillingness or inability to provide informed consent.

Sample Size

The sample size was calculated assuming a **95% confidence level**, **80% statistical power**, COPD prevalence of **7.4%**, and an allowable error of **5%**, yielding a minimum required sample size of **105 participants**. Accordingly, **105 patients** were included in the study.

Data Collection

All enrolled participants underwent a detailed clinical evaluation using a structured proforma. Demographic characteristics, smoking history, exacerbation history, and comorbidities were recorded. Anthropometric measurements were obtained for calculation of body mass index (BMI). All participants underwent chest radiography, pulmonary function testing, six-minute walk testing, and laboratory estimation of serum C-reactive protein (CRP).

Pulmonary Function Testing

Pulmonary function tests were performed using an **RMS Helios 702 spirometer**. Pre- and post-bronchodilator spirometry was carried out, and patients with a **post-bronchodilator FEV_1/FVC ratio <0.70** were included. COPD severity was graded according to the latest **GOLD** classification based on **FEV_1 (% predicted)**.

Assessment of Functional Capacity

Functional capacity was assessed using the **Six-Minute Walk Test (6MWT)** under supervision, with continuous monitoring of oxygen saturation, pulse rate, and patient symptoms throughout the procedure.

Estimation of Serum C-Reactive Protein

Venous blood samples were collected under aseptic precautions, and serum **C-reactive protein (CRP)** levels were measured as part of the biochemical evaluation.

Ethical Considerations

The study protocol was approved by the **Institutional Ethics Committee, Heritage Institute of Medical Sciences, Varanasi** (Approval No. **HIMS/IEC/194/2024**, dated **30 August 2024**). Written informed consent was obtained from all participants before enrolment.

Statistical Analysis

Data were analysed using **IBM SPSS**. Continuous variables were expressed as **mean ± standard deviation (SD)** or median with interquartile range, while categorical variables were presented as frequencies and percentages. Correlation between study variables was planned using **Pearson's or Spearman's correlation coefficient**, as appropriate, and **multivariable regression analysis** was planned to identify independent predictors of morbidity. A **p-value <0.05** was considered statistically significant.

RESULTS

A total of 105 patients with stable chronic obstructive pulmonary disease (COPD) were enrolled in this cross-sectional study. Most participants were aged 70–79 years (34.3%), followed by 60–69 years (29.5%). More than half of the patients (56.2%) were underweight (BMI <18.5 kg/m^2), while 52.4% were former smokers.

Pulmonary function assessment revealed that 49.5% of patients had moderate airflow limitation, 48.6% had severe airflow limitation, and 1.9% had very severe airflow limitation, whereas no patient had mild disease. Most participants (48.6%) had an FVC of 70–89% predicted. [Tables 1 and 2]

The mean serum C-reactive protein (CRP) level was 13.74 ± 4.40 mg/L (95% CI: 12.88–14.59 mg/L), with a median value of 12.8 mg/L and no statistically significant difference in the one-sample t-test ($p = 0.539$). The mean FEV_1/FVC ratio, FEV_1 (% predicted), and 6-minute walk test (6MWT) BODE Index score were 53.23 ± 5.52%, 49.83 ± 11.14%, and 1.46 ± 0.87, respectively. Repeated-measures ANOVA demonstrated a statistically significant difference among these clinical parameters ($p < 0.001$). [Tables 3 and 4]

Comparison according to smoking history showed that current smokers had the lowest mean FEV_1/FVC ratio (48.82 ± 3.25%), FEV_1 (% predicted) (40.55 ± 6.38%), and the highest 6MWT BODE Index score (1.91 ± 0.54) compared with former and never smokers. The differences in FEV_1/FVC ratio ($p = 0.007$), FEV_1 (% predicted) ($p < 0.001$), and 6MWT BODE Index score ($p = 0.005$) across smoking categories were statistically significant, indicating poorer pulmonary function and functional capacity among current smokers. [Table 5] Overall, the findings demonstrated moderate-to-severe airflow limitation, elevated systemic inflammation, impaired functional capacity, and a significant adverse effect of smoking history on disease severity in patients with stable COPD. [Table 6]

Table 1: Baseline demographic and clinical characteristics of stable COPD patients (n = 105)

Variable	Category	n (%)
Age (years)	40–49	20 (19.0)
	50–59	18 (17.1)
	60–69	31 (29.5)
	70–79	36 (34.3)
BMI (kg/m²)	Underweight (<18.5)	59 (56.2)
	Normal (18.5–24.9)	46 (43.8)
	Overweight (≥25)	0 (0.0)
Smoking history	Never smoker	39 (37.1)
	Former smoker	55 (52.4)
	Current smoker	11 (10.5)

Table 2: Pulmonary function characteristics of stable COPD patients (n = 105)

Variable	Category	n (%)
FEV_1 (% predicted)	Mild (≥80%)	0 (0.0)
	Moderate (50–79%)	52 (49.5)
	Severe (30–49%)	51 (48.6)
	Very severe (<30%)	2 (1.9)
FVC (% predicted)	<50%	0 (0.0)
	50–69%	27 (25.7)
	70–89%	51 (48.6)
	≥90%	27 (25.7)

Table 3: Clinical characteristics of stable COPD patients (n = 105)

Variable	Mean ± SD	Median	Range	95% CI	p-value
BMI (kg/m²)	**18.03 ± 1.22**	18.0	16–21	17.80–18.27	0.823*
CRP (mg/L)	**13.74 ± 4.40**	12.8	5.6–24.1	12.88–14.59	0.539*

Table 4: Pulmonary function and functional capacity among stable COPD patients (n = 105)

Variable	Mean ± SD	Median	Range	95% CI
FEV_1/FVC (%)	53.23 ± 5.52	54	42–64	52.16–54.29
FEV_1 (% predicted)	49.83 ± 11.14	49	28–74	47.67–51.98
6MWT (BODE Index points)	1.46 ± 0.87	1	0–3	1.29–1.62

Table 5: Pulmonary function and functional capacity according to smoking history

Variable	Never smoker (n = 39)	Former smoker (n = 55)	Current smoker (n = 11)	p-value
FEV_1/FVC (%)	54.43 ± 4.47	53.25 ± 6.13	48.82 ± 3.25	**0.007**
FEV_1 (% predicted)	52.51 ± 9.67	49.78 ± 11.95	40.55 ± 6.38	**<0.001**
6MWT (BODE Index points)	1.41 ± 0.79	1.40 ± 0.95	1.91 ± 0.54	**0.005**

Table 6: Summary of disease severity indicators in stable COPD

Domain	Variable	Key finding
Airflow limitation	FEV_1 (% predicted)	Most patients had moderate to severe airflow obstruction (98.1%).
Nutritional status	BMI	More than half of the patients (56.2%) were underweight.
Systemic inflammation	CRP	Mean CRP level was 13.74 ± 4.40 mg/L, indicating systemic inflammation.
Functional capacity	6MWT (BODE Index points)	Mean score was 1.46 ± 0.87, suggesting reduced exercise capacity.

Smoking effect	Pulmonary function	Current smokers had significantly lower FEV_1/FVC and FEV_1 values and poorer functional capacity than never and former smokers ($p < 0.05$).

DISCUSSION

The present study evaluated the association of systemic inflammation, assessed by serum C-reactive protein (CRP), with functional capacity and disease severity in patients with stable chronic obstructive pulmonary disease (COPD). The majority of patients belonged to the 70–79 years age group, with more than half being underweight and former smokers. These findings are consistent with previous studies demonstrating that COPD predominantly affects older individuals because of cumulative exposure to tobacco smoke and age-related decline in lung function. Low body mass index (BMI) observed in the present study reflects nutritional depletion and muscle wasting, which are well-recognized systemic manifestations of COPD. Similar observations have been reported in the literature describing age, smoking exposure, systemic effects, and nutritional status as important factors associated with COPD severity.[3,11]

Pulmonary function assessment revealed that almost all patients had moderate-to-severe airflow limitation, with no patients classified as having mild disease. This distribution is comparable with hospital-based studies where patients usually present in more advanced stages because of delayed diagnosis and persistent exposure to risk factors. Spirometry remains central to the diagnosis and assessment of airflow limitation in COPD, as emphasized by the GOLD guidelines and ATS/ERS recommendations.[1,8]

The mean serum CRP concentration in the present study was 13.74 ± 4.40 mg/L, indicating persistent systemic inflammation despite clinical stability. Elevated CRP levels have been consistently reported in stable COPD and are associated with increased inflammatory burden and adverse clinical outcomes. Gan et al. demonstrated significantly higher CRP concentrations in patients with COPD compared with healthy controls, suggesting that systemic inflammation persists even during clinically stable disease.[6] Similarly, de Torres et al. reported that CRP levels were associated with clinically important predictive outcomes in stable COPD.[7] Therefore, the present findings further support the potential role of CRP as a useful biomarker of systemic inflammation in COPD.[6,7]

The present study also demonstrated impaired pulmonary function and reduced functional capacity, with mean FEV_1/FVC and FEV_1 (% predicted) values indicating moderate-to-severe airflow obstruction. The mean BODE Index score suggested reduced exercise tolerance among the study participants. Significant differences observed between pulmonary function indices and functional capacity emphasize the importance of multidimensional assessment of COPD. Similar findings have been reported by Celli et al., who demonstrated that the BODE Index, incorporating BMI, airflow obstruction, dyspnoea, and exercise capacity, provides a more comprehensive assessment and has greater prognostic value than FEV_1 alone.[10] The six-minute walk test is also an established measure of functional exercise capacity in patients with chronic respiratory disease.[9]

Smoking history significantly influenced pulmonary function and functional capacity in the present study. Current smokers had significantly lower FEV_1/FVC ratios and FEV_1 (% predicted) values together with poorer functional capacity than former and never smokers. These findings are consistent with the established adverse effects of continued cigarette smoking on lung function and disease progression. Continued smoking contributes to persistent airway inflammation, oxidative stress, and progressive structural damage within the lungs.[1] Smoking cessation has been shown to reduce the rate of lung-function decline in patients with mild-to-moderate COPD.[12]

Although the present study demonstrated elevated CRP levels together with impaired pulmonary function and reduced functional capacity, the thesis did not include a direct correlation or regression analysis between CRP and disease severity parameters. Therefore, while these findings suggest that systemic inflammation coexists with pulmonary impairment, a direct statistical association cannot be established from the available data. Future longitudinal studies with larger sample sizes and multivariable analyses are recommended to clarify the relationship between systemic inflammation and disease severity in stable COPD.

Overall, the findings of the present study indicate that stable COPD is characterized by persistent systemic inflammation, moderate-to-severe airflow limitation, reduced functional capacity, and the adverse effects of smoking on disease severity. Comprehensive assessment including pulmonary function testing, evaluation of exercise capacity, smoking status, nutritional assessment, and inflammatory biomarkers such as CRP may help in identifying high-risk patients and optimizing individualized management strategies.[1,6,9-12]

CONCLUSION

Patients with stable COPD exhibited moderate-to-severe airflow limitation, elevated serum CRP levels, and reduced functional capacity. Current smokers had significantly poorer pulmonary function and exercise capacity than former and never smokers. These findings indicate that systemic inflammation, impaired lung function, and smoking contribute to disease severity in stable COPD. Comprehensive assessment using spirometry, functional capacity, smoking status, nutritional assessment, and inflammatory biomarkers may aid

in better disease evaluation and management. Further large-scale prospective studies are needed to clarify the relationship between CRP and disease severity.

REFERENCES

1. Global Initiative for Chronic Obstructive Lung Disease. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease: 2024 Report. GOLD; 2024.
2. Salvi S, Agrawal A. India needs a national COPD prevention and control programme. J Assoc Physicians India. 2012;60(Suppl):5–7.
3. Agustí A. Systemic effects of chronic obstructive pulmonary disease. Proc Am Thorac Soc. 2005;2(4):367–370.
4. Barnes PJ. Inflammatory mechanisms in patients with chronic obstructive pulmonary disease. J Allergy Clin Immunol. 2016;138(1):16–27.
5. Sin DD, Man SFP. Why are patients with chronic obstructive pulmonary disease at increased risk of cardiovascular diseases? The potential role of systemic inflammation. Circulation. 2003;107(11):1514–1519.
6. Gan WQ, Man SFP, Senthilselvan A, Sin DD. Association between chronic obstructive pulmonary disease and systemic inflammation: a systematic review and meta-analysis. Thorax. 2004;59(7):574–580.
7. de Torres JP, Cordoba-Lanus E, López-Aguilar C, et al. C-reactive protein levels and clinically important predictive outcomes in stable COPD. Eur Respir J. 2006;27(5):902–907.
8. Celli BR, MacNee W; ATS/ERS Task Force. Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. Eur Respir J. 2004;23(6):932–946.
9. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med. 2002;166(1):111–117.
10. Celli BR, Cote CG, Marin JM, et al. The body-mass index, airflow obstruction, dyspnoea, and exercise capacity index in chronic obstructive pulmonary disease. N Engl J Med. 2004;350(10):1005–1012.
11. Schols AM, Broekhuizen R, Weling-Scheepers CA, Wouters EF. Body composition and mortality in chronic obstructive pulmonary disease. Am J Clin Nutr. 2005;82(1):53–59.
12. Scanlon PD, Connett JE, Waller LA, et al. Smoking cessation and lung function in mild-to-moderate chronic obstructive pulmonary disease: the Lung Health Study. Am J Respir Crit Care Med. 2000;161(2):381–390.