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Association Of Highly Sensitive CRP And COPD Assessment Test (CAT) Scores With Clinical Outcomes In Stable COPD Patients

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Abstract:
Introduction: *Chronic obstructive pulmonary disease (COPD) is a progressive inflammatory lung disorder associated with systemic inflammation, exacerbation, and increased morbidity. In addition to pulmonary dysfunction, COPD is influenced by systemic factors, including comorbidities such as cardiovascular disease, diabetes mellitus, and hypertension. Hs-CRP is a marker of systemic inflammation linked to COPD activity and prognosis, whereas the COPD assessment test (CAT) score quantifies symptom burden and its impact on daily life and health status.*
Aim: To study the association between hs-CRP levels and CAT scores and clinical outcomes in patients with stable COPD.
Materials and Methods: *This prospective observational study included 70 patients with stable COPD aged ≥30 years at SRM Hospital over six months. Demographic data, smoking history, pulmonary function test results, hs-CRP levels, and CAT scores were obtained. Statistical analyses included Pearson and Spearman correlation coefficients, chi-square tests, and logistic regression to assess the association between hs-CRP levels, CAT scores, and clinical outcomes.*
Results: *The mean age of the patients was 55.8 ± 8.6 years, with male predominance (81.4%). A significant positive correlation was observed between hs-CRP levels and CAT scores ($r = 0.448$, $p < 0.0001$). Most patients were of normal weight (41.4%) or overweight (40%), and 40% were smokers. Diabetes mellitus and hypertension were present in 34.3% and 27.1% of the patients, respectively. A significant moderate positive correlation was found between the hs-CRP levels and CAT scores ($r = 0.448$, $p < 0.0001$). Patients with very high CAT impact scores had the highest hs-CRP levels (9.10 ± 2.24 mg/L), whereas those with low impact scores had the lowest (5.69 ± 0.85 mg/L). Exacerbation frequency over six months showed a strong positive correlation with hs-CRP levels (Spearman's rho = 0.847, $p < 0.0001$). Logistic regression analysis identified hs-CRP as a significant predictor of clinical outcomes (OR = 75.147, $p = 0.004$), whereas CAT scores were not ($p = 0.568$).*
Conclusion: Elevated hs-CRP levels correlate with increased exacerbation frequency, suggesting its potential as a prognostic biomarker in stable COPD. Although CAT scores reflect the symptom burden, they may not independently predict clinical outcomes. Including hs-CRP in COPD assessment may enhance risk stratification and guide personalised management strategies
Keywords: *Biomarker, chronic obstructive pulmonary disease, COPD Assessment Test, exacerbation, high-sensitivity C-reactive protein.*

1. INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major global cause of morbidity and mortality, contributing significantly to annual deaths and disability-adjusted life years (DALYs), which reflect overall disease burden [1]. The World Health Organization (WHO) reported that COPD was responsible for about 3.5 million deaths in 2021, accounting for nearly 5% of all global deaths [2]. An epidemiological survey from China found a COPD prevalence of 13.6% among individuals aged 40 years and above [3]. Established risk factors include cigarette smoking, household biomass fuel use, and occupational exposures [4]. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) notes that smokers experience greater respiratory impairment, faster decline in forced expiratory volume in one second (FEV1), and higher mortality compared with nonsmokers. Passive smoke exposure, marijuana smoke, and indoor air pollution are additional contributors. In low- and middle-income countries, 60–70% of cases are attributed to burning wood, crop residues, animal dung, and other biomass fuels [3].

Inflammation is a key pathological feature of COPD and persists even in patients who are clinically stable [2]. Acute exacerbations of COPD (AECOPD) are characterised by heightened systemic and airway inflammation, which contribute to worsening symptoms, including increased sputum volume, changes in sputum purulence, and aggravation of dyspnoea. GOLD guidelines have reported that AECOPD is one of the leading causes of hospitalisation and mortality. In India, a 12% mortality rate has been reported among the hospitalised patients [3].

COPD is associated with comorbidities such as cardiovascular disorders, metabolic disturbances, and musculoskeletal impairment; therefore, identification of the high-risk patients early using relevant tools and biomarkers is important to reduce the mortality rates [5]. Spirometry is the gold standard for diagnosing COPD, but it does not fully assess its complete impact on patients' daily lives. C-reactive protein (CRP) is a diagnostic marker in chronic kidney disease, cardiovascular diseases, cancer, autoimmune diseases, and COVID-19; further, it is also used for guiding the therapy [6]. Recent studies show that CRP levels are nearly 50% higher in individuals with COPD compared to healthy populations. Elevated levels of high-sensitivity C-reactive protein (hs-CRP) have been linked to reduced lung function, a higher frequency of exacerbations, and an increased risk of adverse clinical outcomes in patients with COPD. The COPD Assessment Test (CAT) is an eight-item questionnaire that evaluates the impact of COPD on health status, with scores ranging from 0 to 40 [7]. It covers symptoms such as cough, sputum production, dyspnoea, and their effect on quality of life. Studies have shown that the CAT is sensitive to changes during exacerbations and is a useful tool for routine monitoring of disease severity [8].

. Both hs-CRP and CAT scores have independent predictive value, and their combined use may offer a more comprehensive risk assessment. hs-CRP reflects systemic inflammation in stable COPD, while the CAT measures the impact of symptoms on quality of life [6,7]. Together, these markers improve estimation of disease risk and guide management decisions. Previous studies reported that plasma CRP levels predicted hospital readmissions more effectively than sputum biomarkers, and that adding CAT scores and age further increased predictive accuracy [8]. These findings support hs-CRP as a marker of disease progression and exacerbation risk. Accordingly, the present study aimed to evaluate the association between CAT scores, hs-CRP, and clinical outcomes in stable COPD.

Objectives

To assess the combined predictive value of CAT scores and hs-CRP levels for clinical outcomes, and to evaluate the association of CAT scores and clinical outcomes in COPD patients.

MATERIALS AND METHODS

This prospective observational study was conducted on 70 patients with stable COPD at SRM Hospital for a period of six months.

Inclusion criteria

Patients aged 30–80 years with a confirmed COPD diagnosis were included if they were clinically stable for at least four weeks, had available PFT results, hs-CRP levels, and CAT scores, and were on stable therapy with controlled comorbidities for at least three months.

Exclusion criteria

Patients with asthma, lung cancer, other active malignancies, recent severe COPD exacerbations, or respiratory infections were excluded. Additional exclusions included systemic inflammatory disorders, cardiovascular events within the past six months, active infections (e.g., tuberculosis, hepatitis), severe cognitive or psychiatric illness, pregnancy or lactation, participation in other interventional studies, and incomplete medical records.

Sample size: The sample size was calculated using the following formula: $n = (Z_{\alpha/2} + Z_{1-\beta})^2 / [1/2 \log((1+\lambda)/(1-\lambda))]^2 + 3$, where $\lambda = 0.33$, $Z_{\alpha/2} = 1.96$, and $Z_{1-\beta} = 0.84$. Thus, providing $n = 69.67$, which was rounded off to 70.

METHODS

Baseline demographic and clinical information was recorded for all patients, including gender, age, smoking status, body mass index (BMI) and comorbid conditions such as HTN, diabetes mellitus (DM), and pulmonary function test results. Disease burden was assessed using the CAT, a validated eight-item questionnaire scored from 0 to 40, with higher scores reflecting a greater impact of COPD on health status. Venous blood samples were collected at baseline to measure the hs-CRP levels. Assays were performed in the hospital's central laboratory using a standardised immunoturbidimetric method. Patients were followed up for six months after enrolment, and the number of COPD exacerbations was

recorded.

STATISTICAL ANALYSIS

Data were analysed using SPSS (v25). Categorical variables were expressed as frequencies and percentages, and continuous variables as means ± SD. Associations were evaluated using Pearson's or Spearman's correlation, and group differences were evaluated using one-way ANOVA. Binary logistic regression was used to assess the predictors of clinical outcomes, and chi-square tests were used for categorical comparisons. Statistical significance was set at $p < 0.05$.

Ethical committee approval and informed consent

The study was designed in accordance with the principles of the Helsinki Declaration and approved by the Institutional Ethics Committee, and all participants provided written informed consent before enrolment.

RESULTS

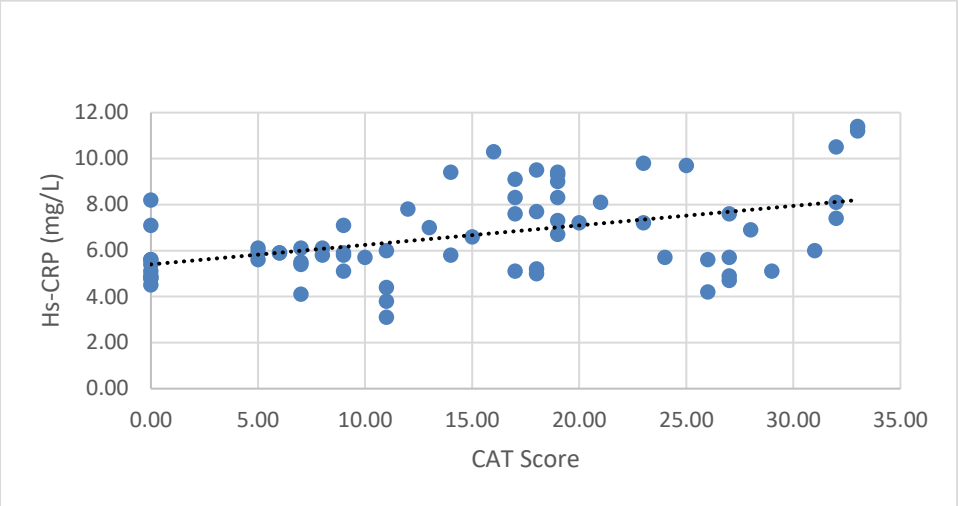
The majority were aged 51–60 years (50%), followed by those >61 years (32.9%), and males were predominant (81.4%) compared to females (18.6%). With respect to BMI, nearly equal proportions were of normal weight (41.4%) and overweight (40%), whereas 18.6% were obese. A smoking history was present in 40% of patients, while DM (34.3%) was slightly more common than HTN (27.1%). Regarding CAT scores, most patients had either low (37.1%) or medium impact (35.7%), whereas fewer reported high (18.6%) or very high impact (8.6%). In terms of exacerbations within six months, nearly half had no episodes (47.1%), while 25.7% experienced two, 14.3% had three, and 12.9% had one exacerbation [Table/Fig-1].

Categories		**Count** (%)
Age group (years)	< 50	12 (17.1%)
	51-60	35 (50%)
	> 61	23 (32.9%)
Gender	Female	13 (18.6%)
	Male	57 (81.4%)
BMI	Normal weight	29 (41.4%)
	Overweight	28 (40%)
	Obese	13 (18.6%)
Smokers		28 (40%)
DM		24 (34.3%)
HTN		19 (27.1%)
Impact based on CAT Score	Low	26 (37.1%)
	Medium	25 (35.7%)
	High	13 (18.6%)
	Very high	6 (8.6%)
Exacerbation Rate (6 months)	0	33 (47.1%)
	1	9 (12.9%)
	2	18 (25.7%)
	3	10 (14.3%)

Footnotes: Body Mass Index (BMI), Diabetes Mellitus (DM), Hypertension (HTN), COPD Assessment Test (CAT). Data are presented as frequency and percentage.

[Table/Fig-1]: Baseline characteristics

The relationship between CAT scores and hs-CRP levels was significant and moderately positive ($r = 0.448$, $p < 0.0001$) [Table/Fig-2].



Footnotes: High-sensitivity C-reactive protein (hs-CRP), COPD Assessment Test (CAT)

[Table/Fig-2]: Pearson correlation between CAT score and hs-CRP levels

Patients with a very high-impact CAT score had the highest hs-CRP levels (9.10 ± 2.24 mg/L), followed by those with a medium-impact score (7.16 ± 1.96 mg/L) and those with a high-impact score (6.55 ± 1.84 mg/L). Patients with a low-impact CAT score had the lowest hs-CRP levels (5.69 ± 0.85 mg/L). The difference across the groups was significant ($p < 0.0001$) [Table/Fig-3].

Impact based on the CAT score	Mean hs-CRP (mg/L)	p-value
Low	5.69 ± 0.85	< 0.0001
Medium	7.16 ± 1.96	
High	6.55 ± 1.84	
Very high	9.10 ± 2.24	

Footnotes: High-sensitivity C-reactive protein (hs-CRP), COPD Assessment Test (CAT). Data are presented as the mean ± standard deviation (SD). Comparisons across groups were performed using one-way ANOVA. Statistical significance was set at $p < 0.05$.

[Table/Fig-3]: Hs-CRP levels across CAT score categories

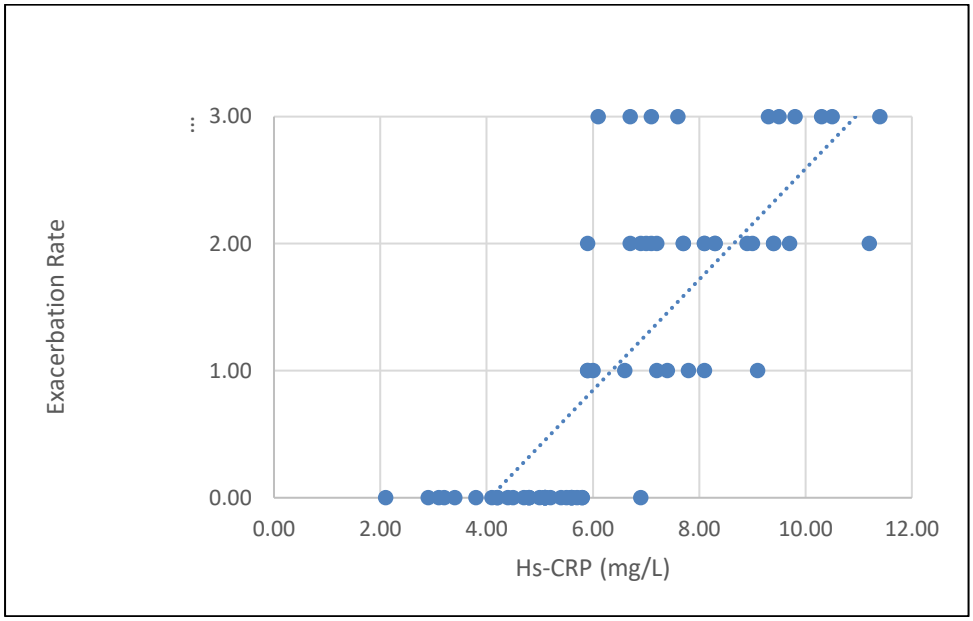
Patients with a very high-impact CAT score had significantly higher hs-CRP levels than those with a low-impact score (-3.41, $p < 0.0001$) and a high-impact score (-2.55, $p = 0.014$). Similarly, the hs-CRP levels in the medium-impact group were higher than those in the low-impact group (-1.46, $p = 0.013$). However, the differences between the other groups, including medium vs. high impact ($p = 1.00$) and medium vs. very high impact ($p = 0.066$), were not significant [Table/Fig-4].

Impact based on the CAT score		Mean difference	p-value
Low	Medium	-1.46369	0.013
	High	-0.86154	0.753
	Very high	-3.40769	< 0.0001
Medium	High	0.60215	1.00
	Very high	-1.94400	0.066
High	Very high	-2.54615	0.014

Footnotes: COPD Assessment Test (CAT). Data are presented as the mean difference. Comparisons were performed using one-way ANOVA (Tukey's test). Statistical significance was set at $p < 0.05$.

[Table/Fig-4]: Pairwise comparison of hs-CRP levels across CAT score categories

Over six months, there was a significant positive connection between the exacerbation rate and hs-CRP levels (Spearman's rho = 0.847, $p < 0.0001$) [Table/Fig-5].



Footnotes: High-sensitivity C-reactive protein (hs-CRP)

[Table/Fig-5]: Spearman's rho correlation between exacerbation rate (6 months) and hs-CRP levels

Binary logistic regression revealed that hs-CRP was a significant predictor of outcome (B = 4.319, p = 0.004, OR = 75.147). In contrast, the CAT score was not a significant predictor (B = -0.040, p = 0.568, OR = 0.961) [Table/Fig-6].

Variable	B	p-value	OR
hs-CRP (mg/L)	4.319	0.004	75.147
CAT Score	-0.04	0.568	0.961
Constant	-25.433	0.003	0

Footnotes: High-sensitivity C-reactive protein (hs-CRP), COPD Assessment Test (CAT), Regression Coefficient (B), Odds ratio (OR). Data are presented as regression coefficients (B), p-values and odds ratios (OR). Binary logistic regression was performed. Statistical significance was set at $p < 0.05$.

[Table/Fig-6]: Logistic regression analysis of hs-CRP and CAT score

DISCUSSION

COPD is a progressive inflammatory condition characterised by airflow limitation and recurrent exacerbations, leading to significant morbidity and mortality. Hs-CRP serves as a biomarker of systemic inflammation, whereas CAT scores provide a standardised measure of symptom burden and QoL. The purpose of this study was to assess the relationship between CAT and hs-CRP values and clinical outcomes in patients with stable COPD, with an emphasis on risk prediction and exacerbation frequency.

Most patients were aged 51–60 years (50%), and most were male (81.4%). Most patients had a normal BMI (41.4%) or were overweight (40.0%), and 40% were smokers. These findings were supported by **Kang et al.,** who reported a similar age distribution, with COPD predominantly affecting individuals aged > 50 years [7]. Similarly, **Julike et al.** found that their patients with COPD had a mean age of 64.05 years, with male predominance [9]. Thus, COPD is more prevalent among older males.

Additionally, **Mandal et al.** observed that patients with COPD with a lower BMI had significantly higher CRP levels [10]. **Silva et al.** discovered a significant relationship between the BMI and CRP levels of patients with COPD (r = 0.3, p = 0.045) [11]. **Lim et al**. found a significant association between smoking and elevated hs-CRP levels in COPD patients [12]. Similarly, **Bhuvaneshwar** et al. emphasised that smokers have higher inflammatory markers and exacerbation risks [13]. Thus, smoking and BMI play an important role in systemic inflammation. In our study, 34.3% of the patients had diabetes, and 27.1% had HTN. This aligns with the findings of **Miller et al.**, who reported an increased prevalence of cardiovascular disease, diabetes, and HTN among patients with COPD. They further emphasised that comorbid conditions contribute to worse health outcomes and increased mortality risk [14].

In our study, the CAT scores showed that most patients had low (37.1%) or medium (35.7%) impact scores. Additionally, 47.1% of the patients experienced no exacerbations in the past six months, whereas 25.7% experienced two. **Stridsman et al.** identified that lower CAT scores were associated with better health-related QoL, whereas higher scores were correlated with increased fatigue and reduced physical function [15]. Furthermore, **Lee et al.** demonstrated that patients with higher CAT scores had a significantly shorter time to the first exacerbation and an increased risk of multiple exacerbations [16]. The clinical outcomes of individuals with COPD can therefore be predicted more accurately using CAT scores.

In our study, the correlation between CAT scores and hs-CRP levels was positive ($r = 0.448$, $p < 0.0001$). Compared to patients with a low-impact score (-3.41), patients with a very high-impact CAT score had significantly higher levels of hs-CRP (9.10 ± 2.24 mg/L, $p < 0.0001$). These results are consistent with those of **Kang et al.,** who showed that serum CRP levels and CAT scores were positively correlated ($r = 0.20$, $p = 0.003$). They further concluded that higher CAT scores were associated with elevated serum CRP levels [7]. **Bhuvaneshwar** reported that hs-CRP levels were significantly higher in COPD patients than healthy controls (4.82 vs. 0.8 mg/L) [13]. Higher CAT scores were associated with higher hs-CRP levels, indicating a significant association between systemic inflammation and COPD severity.

In our study, there was a significant positive association between exacerbation rates during six months and hs-CRP levels (Spearman's rho = 0.847, $p < 0.0001$). Binary logistic regression revealed that hs-CRP was a significant predictor of clinical outcomes ($B = 4.319$, $p = 0.004$, OR = 75.147). **Vassiliou et al.** reported a significant increase in CRP levels of the COPD patients during exacerbations compared to those with stable disease [17]. **Ghobadi et al.** observed that hs-CRP levels were increased significantly in COPD patients, and the BODE index was significantly correlated with it ($p = 0.008$) [8]. Furthermore, **Hassan et al.** found that patients with hs-CRP levels > 3 mg/L have a significantly higher chance of having severe COPD (GOLD stages 3 and 4, $p < 0.001$) [18]. Further strengthening our findings, **Miller et al.** reported that elevated inflammatory markers, such as CRP, IL-6, and IL-8, were associated with higher mortality and poorer QoL [14]. Thus, hs-CRP levels are significant predictors of exacerbations and clinical outcomes.

The observed correlation between CAT scores and hs-CRP suggests that using both tools together may provide precise information, helping with risk stratification and guiding more personalised management strategies in COPD.

Limitation(s)

The results' generalisability is restricted by the limited sample size and single-centre design of this study. Inflammatory assessment was restricted as hs-CRP was measured only once, and outcomes such as hospitalisation and mortality were not evaluated. Key markers like IL-6 and TNF-α were not included, and factors like medication, physical activity, and diet were not fully analysed, which might influence the findings.

CONCLUSION(S)

In patients with stable COPD, hs-CRP levels are strong independent predictors of clinical outcomes. While CAT scores provide a subjective assessment of disease burden, hs-CRP has substantial predictive value for exacerbation. Future studies should explore the interaction effects and combined predictive models to improve risk stratification and clinical decision-making in the management of COPD**.**

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