

## RELATIONSHIP BETWEEN SERUM BIOMARKERS CRP AND FIBRINOGEN WITH BODE INDEX AND SYSTEMIC COMORBIDITIES OF COPD – A CROSS-SECTIONAL STUDY

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### Abstract

**Background:** Chronic obstructive pulmonary disease (COPD), a prevalent and treatable condition, exhibits systemic effects beyond respiratory symptoms. The BODE index, incorporating biomarkers such as CRP and fibrinogen, predicts mortality and aids in treatment monitoring. Screening for comorbidities is vital for mitigating COPD-related morbidity and mortality. This study aimed to measure CRP and fibrinogen levels in patients with COPD. **Material and Methods:** This descriptive cross-sectional study included 73 patients attending our thoracic medicine outpatient clinic at the Government Thiruvoteeswarar Hospital of Thoracic Medicine (GTHTM) and Government Kilpauk Medical College (KMC), Chennai for six months. CRP and fibrinogen levels were measured using a coagulometer and the Nephelometry Minephr method, respectively. The mMRC and CAT scores were used to assess symptom severity. The BODE index incorporates BMI, FEV1, mMRC grade, and 6 MWD. **Results:** A notable correlation existed between GOLD grading and the BODE index, with higher scores corresponding to an increased severity of airflow obstruction. Statistically significant associations were found between the BODE index and the serum biomarkers CRP and fibrinogen. CRP and fibrinogen levels increased significantly as COPD severity increased, with the highest mean values observed in severe obstruction cases. FEV1 showed a highly significant negative correlation with CRP and FIBRINOGEN levels. Additionally, significant correlations were noted between mMRC grading and serum biomarker levels. Comorbidities increased progressively with COPD severity and correlated significantly with CRP and fibrinogen levels. **Conclusion:** Serum biomarkers CRP and fibrinogen are linked to FEV1, BODE score, comorbidities, exacerbation risk, and mortality in patients with COPD, enabling timely therapeutic interventions and risk stratification.

## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common, preventable, and treatable disease characterised by persistent respiratory symptoms and airflow limitation due to airway and alveolar abnormalities, usually caused by significant exposure to noxious particles or gases. The wide varieties of inflammatory mediators have increased in COPD that attract inflammatory cells from circulation (chemotactic factors), amplify the inflammatory process (pro-inflammatory cytokines) and induce structural changes (growth factors).<sup>[1]</sup>

COPD is a chronic, low-grade systemic inflammatory disease affecting the respiratory, cardiovascular, and musculoskeletal systems. It causes structural and functional changes, malnutrition, weight loss, and muscle weakness, which affect the patient's quality of life and exercise capacity. The BODE index, a combined mortality predictor, was developed to better understand the systemic nature of the disease.

The BODE index, consisting of body mass index (BMI), airway obstruction (O), dyspnoea (D) and exercise capacity (E), is a comprehensive and effective predictor of mortality and systemic

inflammation in COPD. It offers more comprehensive information than FEV1 and is a feasible clinical scoring system for COPD evaluation.<sup>[2]</sup> Therefore, it is a clinical test that can be used to evaluate the pulmonary and extrapulmonary effects of COPD. Biomarkers are required in COPD to aid diagnosis, define clinical phenotypes, and monitor responses to existing and new treatments. Therefore, an individual or composite biomarker must be useful at the individual level.<sup>[3]</sup> An ideal biomarker should possess the qualities listed to date. No single biomarker is powerful enough to be used as a diagnostic tool for COPD, but fibrinogen can be used as a composite biomarker to aid diagnosis. Various biomarkers could be used to assess the severity and progression.<sup>[4,5]</sup>

CRP level is also associated with COPD-specific and all-cause mortality. An increase in serum CRP level was independently associated with cardiovascular mortality in COPD patients with mild to moderate airway obstruction. The combination of the serum levels of CRP concentrations and the BODE score would be a better predictor for survival among patients with COPD because serum CRP is an important systemic inflammatory marker and the BODE score is a clinical parameter of great use for patients with the disease.<sup>[6]</sup> fibrinogen, along with CRP and IL-8, is linked to disease severity and predicts COPD-specific mortality risk. It is also associated with cardiovascular mortality, symptoms, exercise capacity, and BODE index. Circulating fibrinogen is moderately associated with coronary heart disease, stroke, and vascular and nonvascular mortality in a population without a history of cardiovascular disease.

fibrinogen is higher in individuals with metabolic syndrome and low physical activity, and inflammatory mediators contribute to the risk of cardiovascular disease. The measurement of serum levels can help detect subclinical disease, facilitate timely therapeutic interventions, and stratify risk.<sup>[4,5,7]</sup> Screening for comorbidities in all patients with COPD, regardless of airflow obstruction, is crucial to prevent morbidity and mortality associated with these conditions. Early diagnosis can alter the prognosis of the disease, with cardiovascular and skeletal muscular comorbidities being the most common ones. Measurements of CRP, fibrinogen, and leukocyte count can help identify individuals with increased risk and require additional diagnostic evaluation.<sup>[8]</sup>

#### **Aim**

This study aimed to measure CRP and fibrinogen levels in patients with COPD.

## **MATERIALS AND METHODS**

This descriptive cross-sectional study was conducted on 73 patients attending our thoracic

medicine outpatient clinic at the Government Thiruvoteeswarar Hospital of Thoracic Medicine (GTHTM) and Government Kilpauk Medical College (KMC), Chennai for six months. This study was approved by the institutional ethics committee before initiation, and informed consent was obtained from all patients.

#### **Inclusion Criteria**

All patients with clinical suspicion of COPD above 40 years of age; newly diagnosed or known COPD who were diagnosed according to the following GOLD guidelines: post-bronchodilator FEV1/FVC <0.70 which denotes persistent airflow limitation. Both male and female patients; smokers and alcoholics; COPD patients with other comorbidities; and second-hand smoke or biomass exposure.

#### **Exclusion Criteria**

Patients with COPD with exacerbations, asthma, active haemoptysis, inability to perform spirometry, recent eye or abdominal or thoracic surgery, lung malignancy, unwillingness to undergo echocardiography, fully completed treatment, declared cure, bronchiectasis, or interstitial lung disease were excluded.

#### **Methodology**

Among the patients attending our OPD, those who were suspected to have COPD and who fulfilled the inclusion and exclusion criteria were subjected to sputum for AFB and chest radiography to rule out TB. As explained previously, COPD patients were subjected to spirometry. They were diagnosed with stable COPD according to the following GOLD guidelines. The study followed the ATS guidelines for spirometry to assess airflow obstruction. A post-bronchodilator FEV1/FVC < 0.70 confirmed airflow obstruction. COPD (grades 1,2,3,4) grading was done according to the GOLD guidelines. Routine blood investigations, lipid profiles, blood sugar levels, and electrocardiography (ECG) were performed. CRP and fibrinogen levels were measured using a coagulometer and the Nephelometry Mineph method, respectively. Resting 2D echocardiography assessed cardiac function and pulmonary hypertension.

The TAPSE and Tei indices were used to evaluate right ventricular function. LV systolic dysfunction was assessed using EF and the E/A ratio. Smoking index-quantified smoking intensity. The mMRC and CAT scores were used to assess symptom severity. The BODE index incorporates BMI, FEV1, mMRC grade, and 6 MWD. The combined assessment considered the symptoms, airflow limitation, and exacerbation risk. Nutritional status was assessed using BMI, FFMI, and TSF. Malnutrition was defined as an FFMI of < 16 for men and < 15 for women, assessed using skinfold thickness.

#### **Statistical Analysis**

Statistical analyses were performed using Microsoft Excel SPSS with the help of a statistician. A p-value was used to assess the significance of the correlation between the variables. A statistically significant correlation was one in which the p-value was less

than 0.05. Pearson's correlation was used to assess the strength of the correlation between variables.

## RESULTS

The age range was 40-84 years, with a mean age of  $58.35 \pm 10$ . Females were non-smokers, 42.10% were light smokers, and 57.8% were moderate smokers. The mMRC grade(1,2,3,4) distributions were 10.9, 49.3, 38.4, and 1.4%, respectively. The GOLD grades(mild,moderate,severe,very severe) were 2%, 24%, 48%, and 24%, respectively. Exercise capacity dysfunction was mild (52%), moderate (34.2%), or severe (13%). Underweight BMI was observed in 32.8% of patients, primarily males, while normal BMI was found in 53.4%, predominantly males. Overweight BMI was observed in 12.3% of males. Malnourishment affected 52% of males and 13% of females. FFMI mean was  $16 \pm 2.7$ . CAT score distribution was 0-10 (18), 10-20 (32), and 20-30 (23). The BODE Index scores ranged from 1 to 10 with varying frequencies (Table 1).

There was no significant association between BMI and the various COPD grades. The distribution of FFMI in various GOLD grades showed higher FFMI values in GOLD grades with no or minimal airflow obstruction. Exercise capacity showed no limitation in GOLD grade 1. There was a progressive increase in the limitation of exercise capacity seen with the progression of GOLD grade (Table 2).

The correlation of GOLD grading with BODE INDEX showed a high statistical association ( $p < 0.05$ ). Those with a BODE index score of (8-10) who fall into GOLD GRADE 4 are 17 (94.4%). As the severity of airflow obstruction increased, the BODE index score also increased because FEV1 was included in both the GOLD grade and the BODE index (Table 3).

Of the 73 patients, patients in BODE 2, BODE3, and BODE 4 were 13(17.8%), 34 (46.6%), and 26(35.6%) patients, respectively. Their mean CRP was 2.5 mg/dl, 7.1 mg/dl and 13.8 mg/dl and the mean fibrinogen was 318.77, 339.79, and 430 respectively (Table 4).

The statistical analysis between the association of the BODE index and serum biomarkers CRP ( $p = 0.002$ ) and fibrinogen ( $p < 0.0001$ ) showed high statistical significance. Statistical analysis between FEV1 and serum levels of CRP ( $p = 0.001$ ) and fibrinogen ( $p < 0.0001$ ) showed a highly negative correlation. Our study showed an inverse relationship between fibrinogen and fev1% predicted. Higher serum fibrinogen levels were associated with a faster decline in lung function. The correlation of BMI with CRP and fibrinogen showed no significant correlation between BMI with CRP ( $p = 0.124$ ) and fibrinogen ( $p = 0.428$ ) (Table 5).

The relationship between the BODE Index and CRP, fibrinogen showed a highly significant correlation between the BODE score and CRP ( $p = 0.008$ ) and fibrinogen ( $p = 0.0005$ ) levels. There was

no significant correlation between BODE score and CRP level between BODE index groups 2 and 3 ( $p = 0.374$ ) and BODE index groups 3 and 4 ( $p = 0.064$ ). However, there was a statistically significant correlation between the BODE index groups 2 and 4 ( $p = 0.009$ ). Similarly, there was no significant correlation between fibrinogen and BODE Index in groups 2 and 3 ( $p = 0.769$ ). However, there was a highly significant correlation between BODE Index groups 3 and 4 ( $p = 0.001$ ) and between BODE index groups 2 and 4 ( $p = 0.002$ ) (Table 6).

There was a progressive increase in mean CRP and fibrinogen values from GOLD 1 to 4. The mean CRP values in GOLD grades 1, 2, 3, and 4 were 3.060 mg/dl, 4.090 mg/dl, 8.9 mg/dl, and 12.9 mg/dl respectively. The highest mean CRP level was observed in patients with severe obstruction (GOLD GRADE, 4).

The relationship between FEV1 and fibrinogen in various GOLD grades showed no significant correlation between Groups 2 and 3 ( $p = 0.103$ ). However, there was a highly statistically significant correlation between Groups 2 and 4 ( $p = 0.000$ ) and between Groups 3 and 4 ( $p = 0.018$ ) (Table 7).

The relationship of mMRC with CRP and fibrinogen levels showed a correlation between mMRC grade and CRP level ( $p = 0.019$ ). However, a significant correlation was observed between the mMRC grading and serum fibrinogen levels ( $p = 0.002$ ). There was no significant correlation between the 6 MWT and CRP levels ( $p = 0.073$ ) or fibrinogen levels ( $p = 0.061$ ). There was no significant correlation between FFMI and CRP ( $p = 0.293$ ) or fibrinogen ( $p = 0.771$ ) levels (Table 8).

There was also a significant correlation between BODE index and CRP and fibrinogen levels. There was a strong negative correlation between FEV1, CRP, and fibrinogen levels. There was a highly significant correlation between the mMRC, CRP, and fibrinogen levels. There was no significant correlation between the 6 MWT and BMI and CRP and fibrinogen levels. (Table 9).

About 48(65.7%) patients presented with comorbidities, and about 25(34.24%) had no comorbidities. The total number of comorbidities was 75 patients. One comorbidity was seen in 32% of subjects, two comorbidities were seen in 17.3% of subjects and 3 and >3 comorbidities were seen in 14.6% of subjects. The most common comorbidities seen were cardiovascular comorbidities which constituted approximately 74.6%. Among cardiovascular comorbidities, HTN constitutes approximately 60%, followed by pulmonary hypertension (16%), CHF (12.5%), dyslipidaemia (9.3%), and IHD (10.7%). Diabetes constituted approximately 16.4% of all the comorbidities (Table 10).

The prevalence of comorbidities showed a progressive increase from stage 1 to 4 COPD severity(GOLD staging) (Table 11).

The results showed a highly significant correlation between comorbidities and CRP ( $p = 0.007$ ) and fibrinogen ( $p = 0.004$ ) levels (Table 12).

There was a progressive increase in the CRP level, with the highest mean value of CRP observed in COPD patients with 3 or >3 comorbidities. The highest mean fibrinogen value was associated with COPD patients with 3 or >3 comorbidities (Table 13).

The difference in the mean CRP values of COPD patients with and without comorbidities showed no significant correlation between COPD patients without comorbidities and COPD with one comorbidity ( $p = 0.082$ ) and two comorbidities ( $p = 0.358$ ). However, there was a statistically significant correlation between COPD patients without

comorbidities and those with 3 or > 3 comorbidities ( $p = 0.005$ ).

The results showed no significant correlation between COPD patients without comorbidities and fibrinogen scores with one comorbidity ( $p = 0.389$ ) and two comorbidities ( $p = 0.598$ ). Similarly, no significant correlation was observed between COPD patients with one and two comorbidities with fibrinogen ( $p = 1$ ), and between one and 3 or >3 comorbidities ( $p = 0.065$ ) and two or 3 or >3 comorbidities ( $p = 0.093$ ) with fibrinogen. A statistically significant correlation was observed between fibrinogen levels in COPD patients without comorbidities and those with 3 or > 3 comorbidities with fibrinogen ( $p = 0.001$ ) (Table 14).

**Table 1: Demographic data of the study**

		Male	Female
Age	40-50	7	6
	50-60	17	7
	60-70	19	1
	>70	14	2
Smoking index	Non-smokers	0	16
	Light smokers	24	0
	Moderate smokers	33	0
	Heavy smokers	0	0
mMRC	Grade 1	2	6
	Grade 2	26	10
	Grade 3	28	0
	Grade 4	1	-
GOLD grades	Mild	0	2
	Moderate	11	7
	Severe	29	6
	Very severe	17	1
6MWD impairment	None	-	-
	Mild	29	9
	Moderate	19	6
	Severe	10	0
BMI	Underweight	17	7
	Normal	31	8
	Overweight	9	0
	Obese	0	0
FFMI	Malnutrition(n)	38	7
	No malnutrition(n)	19	9
Combined assessment of COPD	A	9	9
	B	37	7
	C	0	0
	D	10	1
CAT score	0-10	9	9
	10-20	29	3
	20-30	19	4
BODE index	0	0	0
	1	0	2
	2	1	6
	3	4	0
	4	9	0
	5	9	2
	6	6	3
	7	5	0
	8	5	2
	9	13	1
10	5	0	
BODE index	1-3	5 (8.8%)	8 (50.0%)
	4-7	29 (50.9%)	5 (31.3%)
	8-10	23 (40.4%)	39 (18.8%)

**Table 2: Distribution of BMI, FFMI and 6MWT in GOLD grade**

	BMI (kg/m <sup>2</sup> )	FFMI (kg/m <sup>2</sup> )	6MWT(m)
Grade 1 (2)	18±1.2	17.2±1.6	305±52
Grade 2 (18)	20.8±2.4	16.2±2.7	297±68
Grade 3 (35)	20.1±3.5	13.6±3.7	253±84
Grade 4 (18)	19.7±3.1	14.8±3.6	178.94±68

**Table 3: Correlation between GOLD grade with BODE index**

GOLD Grade	BODE index			
	0	1-3	4-7	8-10
Grade 1	0 (0%)	2(100%)	0(0%)	0(0%)
Grade 2	0(0%)	11(61.1%)	7(38.7%)	0(0.0%)
Grade 3	0(0%)	0(0.0%)	26(74.3%)	9(25.7%)
Grade 4	0(0%)	0(0.0%)	1(5.6%)	17(94.4 %)

**Table 4: Mean value of CRP and fibrinogen in BODE score**

BODE index	Number (%)	CRP	Fibrinogen
0 (BODE1)	-	-	-
1-3 (BODE2)	13 (17.8%)	2.515	318.77
4-7 (BODE3)	34 (46.6%)	7.165	339.79
8-10 (BODE4)	26 (35.6%)	13.481	430.46

**Table 5: Correlation between BODE index, FEV1, and, BMI with CRP and fibrinogen**

Biomarkers	r value		P value	
	CRP	Fibrinogen	CRP	Fibrinogen
BODE index	0.359	0.421	0.002	0
FEV1	-0.377	-0.461	0.001	<0.0001
BMI	0.124	0.428	-0.182	-0.94

**Table 6: BODE Index with CRP and fibrinogen**

Bode index grading	Mean		P-Value	
	CRP	Fibrinogen	CRP	Fibrinogen
1-3	2.515±2.5	318.77±71	0.008	0.0005
4-7	7.165±9.4	339.79±96		
8-10	13.481±13	430.46±97		
BODE Index			P-Value	
CRP	1-3	4-7	0.374	
		8-10	0.009	
		8-10	0.064	
Fibrinogen	1-3	4-7	0.769	
		8-10	0.002	
		8-10	0.001	

**Table 7: Correlation between CRP with GOLD grade and fibrinogen with GOLD grade**

GOLD Grade	GOLD Grade	GOLD Grade	P-value	
			CRP	Fibrinogen
2	3	3	0.259	0.103
		4	0.038	0
	3	2	0.259	0.103
		4	0.412	0.018
	4	2	0.038	0
		3	0.412	0.018
Mean			Mean	
GOLD Grade	GOLD Grade	1	3.060±6.4	260.24±68
		2	4.090±8.2	310.45±76
		3	8.914±11.2	364.57±98
		4	12.944±12.4	440±89

**Table 8: Correlation between mMRC, 6MWT and FFMI with CRP and fibrinogen**

mMRC grading	p		r	
	CRP	Fibrinogen	CRP	Fibrinogen
6MWT	CRP	-0.211	-0.073	
	Fibrinogen	-0.22	0.06	
FFMI	CRP	0.125	0.293	
	Fibrinogen	0.035	0.771	

**Table 9: Correlation between BODE INDEX, FEV1, mMRC, 6MWT, BMI with CRP and fibrinogen**

		<b>CRP</b>	<b>Fibrinogen</b>
BODE index	r value	.359**	.421**
	p value	0.002	0
FEV1	r value	.377**	-.461**
	p value	0.001	0
mMRC	r value	.275*	.351**
	p value	0.019	0.002
6MWT	r value	-0.211	-0.22
	p value	0.073	0.061
BMI	r value	-0.182	-0.094
	p value	0.124	0.428

**Table 10: Distribution of comorbidities**

<b>Comorbidities</b>	<b>Number (%)</b>
SHTN	34 (60%)
PHTN	9 (16%)
IHD	6 (10.7%)
CHF	7 (12.5%)
Dyslipidaemia	7 (9.3%)
Diabetes	12 (16.4%)

**Table 11: Distribution of comorbidities in GOLD grades**

<b>GOLD Grade</b>	<b>Comorbidities</b>					
	<b>HTN</b>	<b>PHTN</b>	<b>IHD</b>	<b>CHF</b>	<b>DM</b>	<b>Dyslipidemia</b>
Grade 1	0	0	0	0	1	0
Grade 2	4	0	0	3	1	1
Grade 3	19	3	4	2	7	6
Grade 4	9	6	3	3	3	0

**Table 12: Correlation between Comorbidities with CRP and fibrinogen**

<b>Comorbidities</b>	<b>Mean</b>	<b>P value</b>
	<b>CRP</b>	
Nil	3.37±3.5	0.007
1	10.84±14	
2	9.31±13	
3 and above	16.45±9	
<b>Fibrogen</b>		0.004
Nil	330.60±79	
1	374.59±94	
2	370.92±115	
3 and above	462.64±98	

**Table 13: Mean parameters of CRP and fibrinogen in comorbidities**

<b>Comorbidities</b>	<b>CRP</b>	<b>Fibrinogen</b>
COPD	3.3±0.7099	330.60±79.7
COPD + CoMb1	10.8±14	374.59±94.60
COPD + CoMb2	9.3±13	370.92±115.3
COPD + CoMb3/>3	16.4±9.5	462.64±98.3

**Table 14: Correlation of comorbidities with CRP and fibrinogen**

<b>Comorbidities</b>	<b>P value</b>	
	<b>CRP</b>	
Nil	1	0.082
	2	0.358
	3and above	0.005
1	2	0.976
1	3 and above	0.476
2	3 and above	0.354
<b>Fibrogen</b>		
Nil	1	0.389
	2	0.598
	3and above	0.001
1	2	1.00
1	3 and above	0.065
2	3 and above	0.093

## DISCUSSION

In our study, the age range was 40-84 years, with a mean age of 58.35 ± 10. Females were non-smokers,

42.10% were light smokers, and 57.8% were moderate smokers. The mMRC grade distributions were 10.9, 49.3, 38.4, and 1.4%, respectively. The GOLD grades were 2%, 24%, 48%, and 24%,



respectively. Exercise capacity dysfunction was mild (52%), moderate (34.2%), or severe (13%). Underweight BMI was observed in 32.8% of patients, primarily males, while normal BMI was found in 53.4%, predominantly males. Overweight BMI was observed in 12.3% of males. Malnourishment affected 52% of males and 13% of females. FFMI mean was  $16 \pm 2.7$ . There was no correlation seen between BMI and various GOLD stages which was like a study done by Ischaki et al.<sup>9</sup> FFMI was significantly reduced in grades 3 and 4 which was like a study done by Luo et al. and both men and women met the definition of malnutrition ( $<15.4 \pm 2.2$  kg/m<sup>2</sup>).<sup>[10]</sup>

A high incidence of malnutrition was observed in all COPD groups, especially grade 4, in our study. FFMI was strongly correlated with exercise capacity, dyspnoea, and FEV1 and could be a predictor of COPD severity. FFMI was more accurate than BMI in predicting the recent stage of the disease. The exercise capacity of our study population showed no limitation of exercise capacity in GOLD grade 1. There was a progressive increase in limitation of exercise capacity seen with progression of GOLD grade which was like a study done by Ischaki et al. on body mass and fat-free mass indices in COPD.<sup>[9]</sup>

More than half of the study population had CAT scores between 10 and 30. BODE scoring and disease staging (according to GOLD) were significantly correlated in our study which is similar to the findings of Sarioglu et al. As the severity of airflow obstruction increases the BODE index scoring will also increase due to the impact of FEV1 in both the GOLD stage and the BODE index.<sup>2</sup>

The association between the BODE index and CRP and fibrinogen levels showed high statistical significance. The statistical analysis between FEV1 and serum CRP and fibrinogen levels showed a highly negative correlation. Our study showed a progressive increase in mean CRP and fibrinogen values in patients from GOLD 1 to GOLD 4. The highest mean CRP level was observed in patients with severe obstruction (GOLD GRADE 4). The results showed significant statistical differences in the mean values of CRP and fibrinogen for various levels of airway obstruction. The results of our study are in agreement with those of Abdelsadek et al., Karadeg et al., and Corsonello et al.<sup>[11-13]</sup> There is no significant statistical correlation was observed between FEV1 and CRP between groups 2, 3, and 4. The relationship between FEV1 and fibrinogen in various GOLD grades showed no significant correlation between Groups 2 and 3. However, there was a significant correlation between Groups 2 and 4 and between Groups 3 and 4.

The highest mean value of CRP (12 mg/ml) was registered in patients with very severe obstruction (GOLD 4) in our study which was similar to the study by Simonovska et al. regarding the statistically significant correlation between CRP level and the level of bronchial obstruction and

comorbidities in COPD. The study showed significant statistical differences in the mean values of CRP in patients with different levels of bronchial obstruction.<sup>[14]</sup>

In our study, a significant correlation was found between CRP level and FEV1 (indicative of disease severity according to the GOLD criteria), as reported by De Torres et al., Groenewegan et al., and Valipour et al. found a significant correlation between the increased serum level of CRP and fibrinogen and decreased FEV1 and disease severity.<sup>[15-17]</sup>

In our study, CRP level was inversely correlated with FEV1 and COPD severity, and CRP levels increased with a decrease in FEV1. The results of our study are in agreement with those of Corsonello et al. There was a highly significant correlation between the mMRC, CRP, and fibrinogen levels. There was no significant correlation between 6 MWT and CRP or fibrinogen levels. There was a significant correlation between the BODE index and CRP and fibrinogen.<sup>[13]</sup> The correlation between BMI and FFMI and CRP and fibrinogen in our study showed no significant correlation. The correlation of FFMI with CRP and fibrinogen showed no significant correlation between FFMI with CRP and fibrinogen. About 48(65.7%) patients presented with comorbidities, and about 25(34.24%) had no comorbidities. According to a study done by Garcia et al., the overall prevalence of comorbidities in COPD was 65-81%.<sup>[18]</sup>

The most common comorbidities seen in our study population are cardiovascular comorbidities which constitute about 74.6% and it was higher than the study done by Dal Negro et al. which showed the prevalence of cardiovascular comorbidities around 40%.<sup>19</sup> Among cardiovascular comorbidities, HTN constitutes about 60% in our study followed by Pulmonary Hypertension (16%), CHF (12.5%), Dyslipidemia (9.3%) and IHD (10.7%). Diabetes constitutes approximately 16.4% of all the comorbidities.

In our study, as the severity of COPD increased, the frequency of PH also increased from 33% in GOLD III COPD to 66% in GOLD IV COPD. None of the patients had severe pulmonary hypertension. Chaouat et al. reported that the prevalence of severe PH (PPA > 40 mm Hg) was 2.7%. However, 50% of the patients had non-COPD aetiologies. Thus, the prevalence of severe PH is uncommon in COPD.<sup>[20]</sup> There was a progressive increase in the CRP and fibrinogen values, with the highest mean values of CRP and fibrinogen seen in COPD patients with 3 or >3 comorbidities. The difference in mean CRP and fibrinogen values between COPD patients with and without comorbidities showed a significant correlation between COPD patients without comorbidities and COPD patients with 3 or >3 comorbidities.

## CONCLUSION

The serum biomarkers CRP and fibrinogen which are markers of systemic inflammation, were linked with FEV1, BODE score, comorbidities, exacerbation risk, and mortality. Hence, measurement of serum levels will enable us to administer effective timely therapeutic interventions and risk stratification, and to monitor disease progression. Comorbidity screening should be performed in all COPD patients, irrespective of the degree of airflow obstruction. The combination of serum biomarkers (CRP, fibrinogen) and multidimensional score (BODE score) was superior to individual biological markers or clinical parameters for predicting disease mortality.

### Limitations

A control group was not included in this study. Most of our understudy population was male, and it would have been better if there were an equal number of males and females. Our sample size was small; therefore, we could not reach the level of significance for some understudy variables.

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