

## A STUDY OF BODE INDEX ON SEVERITY AND SYSTEMIC INVOLVEMENT IN PATIENTS WITH COPD

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### Abstract

**Background:** To determine the correlation between BODE index and the level of systemic inflammation in patients with COPD. **Material & Methods:** A total of 120 patients who attended our outpatient clinic at the Tertiary Care Hospital, Telangana State were enrolled into the study. Of these, 90 patients with symptoms suggestive of COPD were selected as cases and 30 patients who came for Master health checkup were selected as controls. **Results:** Out in all the 120 subjects (including 90 COPD patients and 30 controls) after categorizing the variable. Baseline data was collected from patients without and with mild, moderate and severe COPD. Ages, body mass index, days of hospitalization, mean hemoglobin concentration, QRS, ejection fraction, pulmonary hypertension, serum albumin concentration, and CRP of all subjects were the parameters analyzed. **Conclusion:** Thus our study concludes that BODE index is reliable method to predict hospitalisation and the severity of systemic involvement in patients with COPD. Since the assessment of BODE index requires only a spirometer, which is relatively inexpensive and can easily be made available, this index could be of great practical value in primary health care set upto identify individuals who are at need for further evaluation in a higher centre. Thus the BODE index can be used for judicious referral of patients with COPD thereby preventing the wastage of the limited resources available.

## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality throughout the world. The prevalence and burden of COPD are projected to increase in the coming decades due to continued exposure to COPD risk factors and the changing age structure of the world's population. It is projected to rank fifth in 2020 in burden of disease caused worldwide, according to a study published by the World Bank/World Health Organization.<sup>[1]</sup> The disease causes a heavy burden on the global health care resources. The costs involved in the treatment and evaluation is directly proportional to the pulmonary and the extra pulmonary components of the disease.<sup>[2]</sup>

Chronic obstructive pulmonary disease (COPD) is defined as a preventable and treatable disease with some significant extra pulmonary effects that may contribute to the severity in individual patients. Its

pulmonary component is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases.<sup>[3]</sup>

The pathogenesis and clinical manifestations of COPD are not restricted to pulmonary inflammation and structural remodeling.

Rather, this disorder is associated with clinically significant systemic alterations in biochemistry and organ function. The systemic aspects of COPD include oxidative stress and altered circulating levels of inflammatory mediators and acute-phase proteins. As in other chronic inflammatory conditions, weight loss, muscle wasting, hypo proteinemia and tissue depletion are commonly seen in COPD patients.<sup>[4]</sup> Selective wasting of fat free mass coupled with impaired respiratory and peripheral muscle function and a reduced capacity for exercise occur in COPD patients. Indeed, weight

loss may directly impact poor prognosis in COPD patients.

The severity of COPD is usually assessed on the basis of a single parameter – forced expiratory volume in one second (FEV1). However, the patients with COPD have systemic manifestations that are not reflected by the FEV1. Hence a multidimensional grading system that assessed the respiratory and systemic expressions of COPD was designed to predict outcome in these patients<sup>5</sup>. The four factors that predicted the severity most were the body-mass index (B), the degree of airflow obstruction (O) and dyspnea (D), and exercise capacity (E), measured by the six-minute-walk test. These variables were used to construct the BODE index, a multidimensional 10-point scale in which higher scores indicate a higher risk of death.

The process of allocating scarce medical resources to the most needed patients can be extremely difficult in diseases which affect a large number of patients. Decision makers need a rational and consistent scoring system that is designed to identify those who are maximally in need of a diagnostic or a therapeutic intervention under a health-care budget constraint. BODE index has been proposed to serve this purpose in patients with chronic obstructive pulmonary disease (COPD).<sup>[6]</sup>

In our study we analyzed the BODE index as a predictor of hospitalization and severity of systemic involvement.

#### Aim of The Study

1. To determine whether higher BODE index is associated with more days of hospitalisation and associated with severe disease.
2. To determine the correlation between BODE index and the level of systemic inflammation in patients with COPD.

3. To determine whether higher BODE index is associated with more severe cardiac involvement.
4. To determine whether higher BODE index correlates with poor nutritional status.
5. To determine whether higher BODE index in chronic obstructive pulmonary disease correlates with more years of cigarette smoking and associated with severe disease.

## MATERIALS AND METHODS

Out of total 120 nos. of patients Cases were seen 90 & controls 30 and to evaluate the BODE index as a predictor of hospitalization and severity of systemic involvement in patients with Chronic Obstructive Pulmonary Disease, a cross sectional study design was chosen during the study period from July 2019 to December 2021

#### Inclusion Criteria

- Patients with symptoms suggestive of COPD as cases.
- Patients who came for master health checkup as controls.

#### Exclusion Criteria

- Spirometry proved bronchial asthma defined as an increase in the FEV1 of more than 15 percent above the base-line value or of 200 ml after the administration of a bronchodilator.
- Recent myocardial infarction
- Unstable angina
- Congestive heart failure (NYHA class III or IV)
- Inability to perform spirometry or 6-minute walk test
- Unrelated life threatening major illness
- Liver disease
- Patients with acute exacerbation.

## RESULTS

**Table 1: Distribution of cases by BODE index and Smoking status**

Group	Smoker		Non Smoker		Total	Person Chi-Square
	Number	Percentage	Number	Percentage		
Control	12	15.8%	18	40.9%	30 (25%)	X <sup>2</sup> =21.787 p=0.000
Mild Cases	17	22.4%	17	38.6%	34 (28.3%)	
Severe cases	26	34.2%	2	4.5%	28 (23.3)	
Total	76	100%	44	100%	120 (100%)	

**Table 2: Distribution of cases by BODE Index and BMI**

Group	Number	Mean BMI (Kg/m <sup>2</sup> )	Standard deviation	One way ANOVA F - test	Multiple comparison (LSD)
Control	30	24.83	3.28	F= 17.221 P= 0.000	1 vs 2,3,4; p=0.398
Mild Cases	34	25.42	2.88		2 vs 1,3,4; p=0.398
Moderate cases	28	22.94	2.76		3 vs 1,2,4; p=0.010
Severe cases	28	20.81	1.67		4 vs 1,2,3 ; p=0.000
Total	120	23.62	3.25		

**Table 3: Distribution of cases by BODE Index and FEV1**

Group	Number	Mean FEV1 (%)	Standard Deviation	One way ANOVA F - test	Multiple Comparison (LSD)
Control	30	64.30	3.60		1 vs 2,3,4; p= 0.048

Mild Cases	34	62.32	3.62	F= 232.23 P=0.000	2 vs 1,3,4; p=0.048
Moderate cases	28	52.86	3.24		3 vs 1,2,4; p= 0.000
Severe cases	28	39.93	5.16		4 vs 1,2,3; p=0.000
Total	120	55.38	10.33		

**Table 4: Distribution of cases by BODE Index and CRP in mg/dl**

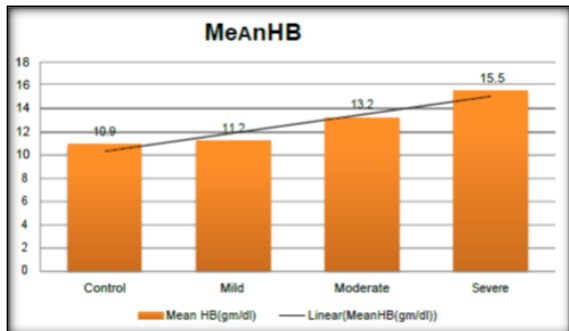
Group	Number	Mean FEV1 (%)	Standard Deviation	One way ANOVAF – test	Multiple Comparison (LSD)
Control	30	3.53	1.87	F= 3.315 P=0.022	1 vs 2,3,4; p= 0.135
Mild Cases	34	8.14	3.35		2 vs 1,3,4; p=0.135
Moderate cases	28	34.69	10.20		3 vs 1,2,4; p= 0.000
Severe cases	28	90.84	22.84		4 vs 1,2,3; p=0.000
Total	120	32.48	36.45		

**Table 5: Distribution of cases by BODE Index and Serum Albuminin gm/dl**

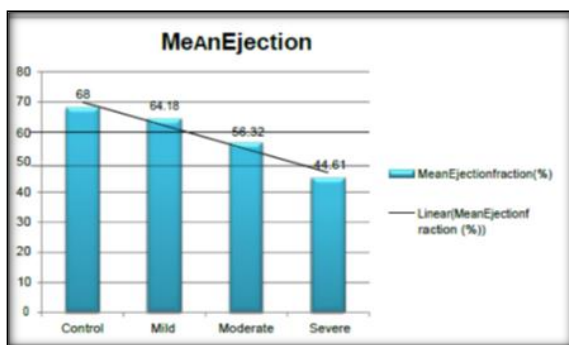
Group	Number	Mean FEV1 (%)	Standard Deviation	One way ANOVAF – test	Multiple Comparison (LSD)
Control	30	4.02	0.36	F= 3.315 P=0.022	1 vs 2,3,4; p= 0.501
Mild Cases	34	3.96	0.37		2 vs 1,3,4; p=0.501
Moderate cases	28	3.35	0.40		3 vs 1,2,4; p= 0.000
Severe cases	28	2.91	0.52		4 vs 1,2,3; p=0.000
Total	120	3.58	0.61		

**Table 6: Distribution of cases by BODE Index and Pulmonary Arterial Hypertension (PAH)**

Group	Pulmonary Arterial Hypertension (PAH)				Total	Pearson Chi-Square
	Normal	Mild	Moderate	Severe		
Control	30 (100%)	0	0	0	30 (100%)	X2= 96.422 P=0.000
Mild Cases	33 (97.1%)	1 (2.9%)	0	0	34 (100%)	
Moderate cases	0	7 (25%)	1 (3.6%)	0	28 (100%)	
Severe cases	0	13 (46.4%)	5 (17.9%)	10 (35.7%)	28 (100%)	
Total	83 (69.2%)	21 (17.5%)	6 (5%)	10 (8.3%)	120 (100%)	



**Figure 1: Distribution of cases BODE Index and HB concentration in gm/dl**



**Figure 2: Distribution of cases by BODE Index and Ejection Fraction (%)**

## DISCUSSION

COPD is predicted to be one among the most common diseases affecting a large number of

individuals by the year 2020. In the recent past, more stress has been given to formulate a simple but effective index for assessing the severity of COPD. In our study we tried to evaluate its usefulness in predicating the severity of COPD in terms of hospitalization, systemic involvement and the level of systemic inflammation. Our research has brought out many results which would have a significant impact in the management of COPD in the future. Studies by Celli et al.<sup>[5]</sup> and Kian-Chung et al.<sup>[2]</sup> has proven that grouping COPD patients into three groups with BODE scores 0-2 as first group, 3-5 as second and 6 or more as the third group correlates well hospitalization and mortality. Hence we have accepted the same classification and grouped the above groups as mild, moderate and severe COPD. Our study individuals were almost equally distributed in the various groups. 30 controls were also selected.

Kian-chung et al.<sup>[2]</sup> and Celli et al.<sup>[5]</sup> has shown in their respective studies that BODE score increases with age. But in our study doesn't show a significant increase with compared to controls. This can be supported from other studies that there is no significant progression with age. This difference is mainly due to the fact that duration of smoking was not proportional to age in those groups like in our study.

Results from this study go along with most other studies, in the relationship of smoking status to BODE index. Studies by Kian-chung et al.<sup>[2]</sup>, Celli et al.<sup>[5]</sup>, and Karoli et al.<sup>[7]</sup> have all proven beyond doubt

that higher duration of smoking is associated with higher BODE index. Our study revealed that smokers have higher BODE index compared to non-smokers. This difference between the groups was found to be statistically significant. Our study also revealed that the disease could still be reversed with the cessation of smoking. This was supported by study done by Philiptonneseni which was published in ERS JOURNALS which showed smoking cessation with help of adequate behavioural counseling and pharmacological support (varenicline or bupropion SR for 3 months) showed a significant decrease in mortality and morbidity and significant improvement in lung function.

Admission to the hospital and heavy use of health-care resources is a common feature of COPD. A clinical implication of the present study is that the BODE scoring system may prove to be helpful in health-care resource allocation and in guiding therapy for individual patients in the future. This multistage scoring system, which incorporates variables that can be evaluated easily in any office setting, should not be difficult or costly to implement routinely. As the BODE index can provide useful prognostic information of survival and hospitalization, the findings of the present study are in support of the utility of the BODE index as an assessment tool for COPD patients.

To our knowledge, this is the first study to show that the BODE staging system predicts the severity of systemic involvement in patients with COPD. The parameters that we assessed to this regard were the body mass index, hemoglobin and albumin concentration, ejection fraction and pulmonary hypertension in ECHO and systemic inflammation as assessed by the CRP value.

While considering BMI as a criterion for BODE index scoring, significance is only given to whether it is more, or less than 21. In our study we found that the BMI progressively declines with severity among the patients with COPD. Emil et al<sup>4</sup> had described the depletion of free fat mass and thereby a reduction in BMI in patients with COPD. Our finding is further supported by other study done by Lowie vanfleteren, Bernd lamprecht, Emielwouters published in ERS journal stated that the presence and severity of COPD is associated with lower BMI. Polycythemia has frequently been reported in patients with COPD, owing to the increased erythropoietin production induced by chronic hypoxia. As severity increases the mean hemoglobin concentration was found to increase. Our study also reflected the same. Mean hemoglobin concentration was found to be more in patients with severe COPD. This was further supported by ERS journal (published in 2014) and most recent BMC journal which was published in July 2021 stated that incidence of polycythemia increasing with severity of smoking.

It was also observed that there is a significant increase in days of hospitalization in patients with moderate and severe COPD but which is not

reflected the same in mild COPD cases in compared to controls. Mean days of hospitalisation is 2.21 and 7.68 in moderate and severe COPD respectively. It was also observed that there was also significant increase in number of hospital re-admissions in patients with moderate and severe COPD. It was also supported by many other studies.

The echocardiography findings in our study were generally in agreement with other studies conducted. However, studies have detected only mild reduction in ejection fraction among patients with COPD. In our study the reduction in ejection fraction was very significant especially in the group with severe COPD. This could probably be because of higher incidence of other causes of dilated Cardio myopathy in our group like ischemia, as smoking is a common risk factor. The LV dysfunction in COPD is believed to be due to Bernheim's effect which is left ventricular hypertrophy causes interventricular septum to bulge towards right ventricle causing right heart failure (paradoxical movement of the interventricular septum) in patients with COPD.

Arcasoy et al<sup>8</sup> has demonstrated an incidence of pulmonary hypertension of around 16 % in patients with COPD. Stevens et al.<sup>9</sup> showed that the proportion of patients with pulmonary hypertension is higher among patients with severe COPD. Our study revealed a total incidence of 32.5 % of PAH among patients with COPD. The proportion was higher in the severe group with 58.6% having moderate PAH and 24.1 % having severe PAH.

Li et al.<sup>10</sup> have reported direct effects of TNF  $\alpha$  and demonstrated time-dependent and concentration-dependent reductions in total protein content in patients with COPD. Wouters et al.<sup>11</sup> also demonstrated hypoalbuminemia in patients with COPD. In our study we found significant reduction in serum albumin concentrations with increase in severity of COPD as assessed by the BODE score.

Cirillo et al.<sup>12</sup> showed an increasing CRP value with worsening airflow obstruction. Our study has shown that as the severity of COPD increases, CRP levels also shows an increasing trend. Study done by Sin et al<sup>89</sup>, also revealed similar findings.

## CONCLUSION

1. BODE index can be used as a reliable index to assess the severity of chronic obstructive pulmonary disease.
2. BODE index predicts hospitalization due to causes related to COPD.
3. Cardiac effects of the disease increases with the severity of disease as assessed by BODE index.
4. BODE index directly correlates with nutritional derangement in patients with COPD as evidenced by the changes in BMI and serum albumin and CRP levels.
5. Intensity of systemic inflammation increases with increase in the severity of disease.

6. BODE index is directly correlated with the duration and intensity of smoking.
7. Polycythemia is associated with more severe disease.

### Scope for Future Studies

The study conducted in our population has many significant observations and potential implications. Our study concludes that BODE index is a reliable method to predict hospitalization and the severity of systemic involvement in patients with COPD. Future studies are needed to assess whether it can be used as a reliable index to monitor the progress of disease. Studies are also needed to assess whether reduction in BODE index improves the disease status. The incidental finding whether hemoglobin concentration decreases initially in patients with COPD could also be subjected to further research. Future research should also aim at finding the intervention measures which have the greatest impact on BODE index and thereby the severity of the disease. We do not know whether it will be a useful indicator of the outcome in clinical trials, the degree of utilization of health care resources, or the clinical response to therapy. More studies are needed in this regard.

To summarize, the BODE scoring system is a reliable index to predict hospitalizations and the severity of systemic involvement in patients with COPD. Besides its excellent predictive power with regard to outcome, the BODE index is simple to calculate and requires no special equipment. This makes it a practical tool of potentially widespread applicability.

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