Original Article

Association between BODE Index and Visceral Fat among COPD Patients Attending a Tertiary Care Hospital — A Cross Sectional Study

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Background : COPD is considered as the 2nd most common cause of death in India. "Body-Mass Index, Airflow Obstruction, Dyspnea and Exercise Capacity Index" (BODE index) predicts 4-year survival rate, making it a better tool for advanced study. So far, the degree of visceral fat accumulation in COPD patients & its effect on their survival rate has not been directly studied in Indian population.

Aims and Objective : To measure the visceral adiposity, estimate the BODE index in COPD Patients & assess the relation between Visceral adiposity & BODE Index in them.

Material and Method : 78 COPD patients were recruited. The BMI, pulmonary function, dyspnea score and the 6-minute Walk Tests were done. Visceral fat was measured by Ultrasonography. Patients were divided into 2 groups based on the presence or absence of visceral obesity. BODE index and Approximate Survival rate were compared among them.

Results : The prevalence of visceral obesity in COPD patients was 45.37%. Average BODE index Score was 4.32±1.78 and it was higher in viscerally obese patients.

Conclusion : BODE index worsens with the presence of visceral adiposity. Decreasing visceral fat will improve BODE index & survival rate and decrease cardiovascular risks. Counselling COPD patients in this regard can prevent the progression of COPD.

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Key words **: COPD, Visceral Adiposity, BODE Index.**

According to Global Initiative for Chronic Obstructive Lung Disease (GOLD), Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms such as dyspnea, cough and or sputum production. There is presence of airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases[1].

Obesity is a chronic disease which is prevalent in developed and developing countries like India and in all strata of society[2]. As the standards of living are continuing to rise, weight gain and obesity are posing a growing threat to health due to the lifestyle changes. Many theories have been put forward as to how the abdominal fat can affect the lung functions. Among them most important are :

(1) Visceral Adipose Tissue (VAT) is considered to be more metabolically active than Subcutaneous Adipose Tissue (SAT). VAT secretes more inflammatory cytokines, IL-6 and CRP. Elevated CRP and IL-6 is found to be associated with chronic inflammatory airway diseases.

(2) Activated macrophages in adipose tissues are known to cause low grade chronic inflammation;

(3) Adipose tissue in the abdominal cavity compresses the thoracic cage, diaphragm and lungs.

Editor's Comment :

- Obesity is considered as the mother of all diseases. A healthy weight is crucial in preventing spectrum of diseases, from coronary artery disease to cancer.
- Even though our study mainly focuses on the importance of reducing obesity in COPD patients, we want to reinforce the fact that obesity is the cornerstone in preventing many of the diseases plaguing the world today.
- This obesity epidemic as we call it, is an enormous burden on the healthcare system and hence should be prioritized, prevented and treated, thereby closing the gateway to all chronic diseases that ensue.
- At the community level the policymakers can organize campaigns in localities and schools to create awareness about the ill effects of obesity among parents and children alike.
- As they say Education begins at home, we should address this issue at the grass root level by enlightening the parents who in turn can lead their children into a healthier future.

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The consequences are a decrease in diaphragm displacement, a decrease in lung and chest wall compliance and an increase in elastic recoil, resulting in decrease in lung volumes and an overload of inspiratory muscles[3].

COPD has been considered as the second most common cause of death in the list of non-communicable diseases in India[4]. By 2030, COPD is predicted to be the 3rd cause of death in India. Our country ranks 5th in the list of the most polluted countries in the World. It is not only the men who travel in a polluted environment or smoke that are affected; the adult women and young children are also at a high risk as they are exposed to solid fuels due to their household roles[4].

Therefore prevention, diagnosis and early treatment play a very crucial role in preventing the mortality in an easily preventable non-communicable disease like COPD. The risk of death in patients with COPD is often graded with the use of a single physiological variable, the forced expiratory volume in first second (FEV_1). However, other risk factors, such as a short distance walked in a fixed time, a high degree of functional breathlessness and a low Body-Mass Index (BMI), are also associated with an increased risk of death. "Body-Mass Index, Airflow Obstruction, Dyspnea and Exercise Capacity Index" (BODE index) is a multidimensional grading system, which integrates body mass index, airflow limitation (forced expiratory volume in one second), dyspnea and 6-min walk distance, predicts 4-year survival rate in COPD patients[5]. In hindsight, BODE Index includes all the effective parameters for accurate mortality prediction, thereby making it a better match for a more informative & advanced study. So, we considered taking the BODE Index in our study.

Previous studies that have suggested links between COPD, cardiovascular diseases and abdominal obesity have used indirect or surrogate markers for abdominal obesity[6]. So far, the degree of visceral fat accumulation in patients with COPD & its effect on their survival rate has not been directly studied in Indian population. So, the present study aimed at assessing the relation between BODE Index, its individual parameters & visceral adiposity in COPD patients.

Material and Method

Type of Study : It was a hospital based cross sectional study.

Duration of Study : The data collection was done over a period of 2 months. Ethical clearance was taken from Institutional Ethical Committee.

Stable COPD patients (without acute exacerbation) who were attending the OPD or admitted in the wards in the Departments of General Medicine & TB and Chest were recruited in the study. The study protocol was explained to the patients in their vernacular language & the patients who agreed to be a part of the study and gave the written informed consent for the same were included in the study.

Sample Size :

(1) The sample size was obtained by purposive sampling method.

(2) The minimum sample size was set to 78 participants with study prevalence of COPD of 5.1%[7] and 5% margin of error.

(3) $n = 4pq/d^2$

$n = 4x5.1x94.9/25$

$n = 77.43 \sim 78$ (Round off to next Whole No)

Patients who fulfilled the following inclusion & exclusion criteria were included in the study.

Inclusion Criteria :

(1) Male or female COPD patients between 30 to 65 years of age.

(2) Patients with Stage 2 to Stage 4 COPD according to GOLD classification.

(3) A baseline (post bronchodilator) FEV_1<80% of predicted normal and a baseline (post bronchodilator) FEV_1/FVC ratio <0.7.

(4) A signed and informed consent was obtained prior to participation.

Exclusion Criteria :

(1) Patients who were hypertensive or diabetic.

(2) Patients who were morbidly obese.

(3) Patients with Ischemic heart disease.

(4) Patients who had musculoskeletal disorders which can limit their walking ability.

(5) Patients who had undergone previous lung surgeries.

(6) Patients who had any other lung disorder other than COPD.

Tools for Data Collection :

(1) Socio-demographic details

Age, sex, occupation, residence, smoking and Socio-economic status were recorded.

(2) Physiological parameters

Height (cms), weight (Kgs) and Resting Pulse rate were recorded.

(3) Visceral fat and subcutaneous fat:

(a) Ultrasonography (USG) has been shown to be an alternative, noninvasive, reliable method to estimate the two fat compartments[8].

(b) The two fat compartments were estimated by ultrasound method in the radiology department.

Ultrasound was done using SIEMENS ACUSON 300 with multiple frequency (2-5 MHz) convex probe for measuring visceral fat and linear probe (7-12 MHz) for measuring subcutaneous fat.

(c) Visceral and Subcutaneous fat was measured midway between the umbilicus and xiphisternum. Visceral fat was defined as the depth from the peritoneum to the lumbar spine and subcutaneous fat defined as the depth from the skin to the abdominal muscles[9]. The cut off value of Visceral Fat Thickness (VFT) of 9 cm- in men and; 6.9 cm in women was used to define visceral obesity[9].

(4) BODE Index – Body Mass Index, Airway Obstruction, Dyspnea, and Exercise.

(a) Body Mass Index (BMI) —

Patient's BMI was calculated by using formula: - kg/m^2. We classified the BMI of the patients according to the scale given by National Institutes of Health; BMI was classified as[10] :

Weight Categories BMI(kg/m^2)		
Underweight		<18.5
Normal		18.5-24.9
Overweight		25-29.9
Obesity:	Grade1	30-34.9
	Grade2	35-39.9
Extremely/Morbidlyobese:	Grade3 Obesity	>40

(b) Airway Obstruction —

Pulmonary Function Tests was performed using an RMS Medspiror. Post bronchodilator obstruction was assessed by means of FEV_1% predicted and FEV_1/ FVC values.

FEV_1% predicted: normal value of FVC is above 80% predicted.

FEV_1/FVC : The ratio of FEV_1/FVC is normally between 0.7 and 0.8. Values below 0.7 are a marker of airway obstruction[11].

(c) Dyspnea —

Interpretation of breathlessness was done using modified British Medical Research Council (mMRC) Questionnaire. This questionnaire is considered to be adequate and self-explanatory. mMRC relates well to other measures of health status and predicts future mortality risk[2].

Dyspnea was graded based on the modified MRC dyspnea scale[2] : —

Grade 0	No dyspnea	I only get breathless with strenuous exercise
Grade 1	Slight dyspnea	I get short of breath when hurrying on level ground or walking up a slight hill
Grade 2	Moderate dyspnea	On level ground, I walk slower than people of the same age because of breathlessness or I have to stop for breath when walking at my own pace on the level
Grade 3	Severe dyspnea	I stop for breath after walking about 100 yards or after a few minutes on level ground
Grade 4	Very severe dyspnea	I am too breathless to leave the house or I am breathless when dressing

d) Exercise — 6-minute Walk Distance

The 6-minute Walk Distance (6MWD) has been proven useful in assessing the functional status of patients with COPD because it is easy to perform, inexpensive and amenable to standardization[5]. Most of the day-to-day chores are performed at sub maximal levels of exertion; therefore, 6MWD would better reflect the functional exercise level for daily physical activities[12].

Patients were instructed about the procedure. Necessary precautions were taken to attend to any emergencies and equipment like pulse oximeter, oxygen cylinder, emergency drugs, etc, were kept within a hand's reach. The stop watch was set for 6 minutes. The patient was asked to walk for 6 minutes on a flat, firm surface in an empty corridor of 30 m distance. If the patient felt breathless/ tired at any point of time during the walk, he/ she was allowed to take rest without stopping the clock and encouraged to continue to finish 6-minute walk. The total distance walked in 6 minutes was noted and the points were given based on the distance covered[1].

BODE index were calculated as per the following Tables[5].

Variables	Points on BODE Index			
	0	1	2	3
FEV_1 (% of predicted)	≥65	50-64	36-49	≤35
Distance walked in 6 min (m)	≥350	250-349	150-249	≤149
MMRC dyspnea scale	0-1	2	3	4
Body-mass index	>21	≤21		

BODE Index Scoring	4 Year survival rate
0-2 points	80%
3-4 points	67%
5-6 points	57%
7-10 points	18%

Approximate 4-year survival interpretation was predicted as under (based on BODE Index Scoring)[5]:

(5) Protocol for Analysis :

COPD patients were divided into 2 groups based on the presence or absence of visceral obesity (Visceral Fat thickness >9 cm in men; >6.9 cm in women). BODE index was compared among the patients with visceral obesity & patients without visceral obesity. Approximate Survival rate were compared among the 2 groups.

(6) Statistical Analysis :

Data was expressed in terms

of actual numbers, mean ± SD, frequency and percentage. Statistical analysis was done by using SPSS software version 20. Chi-square test was used to compare the parameters between the 2 groups and P value of < 0.05 was taken as statistically significant. Descriptive statistics and Pearson's correlation were used for comparison between the factors.

Observation

A total of 78 COPD patients were recruited in the present study based on the inclusion & exclusion criteria. All of these patients completed the study protocol. Out of a total of 78 patients recruited, 55 of them were male (70.5%) and 23 (29.5%) were females. The mean age & BODE Index among the COPD patients was calculated. The results are displayed in the Table 1.

Table 1 — *Subject's mean age & BODE index parameters*

Variables	Mean±Standard Deviation
Age (years)	54.01±15.12
BMI (Kg/m^2)	24.07±4.69
Obstruction (FEV$_1$% pred)	46.38±15.61
Dyspnea (mMRC scale)	1.31±0.71
Exercise -6MWD (m)	194.99±62.59
Total points (BODE Index)	4.32±1.78

(BMI - Body Mass Index; FEV$_1$ – Forced Expiratory Volume in 1st second; 6MWD - 6-Minute Walk Distance.)

All COPD patients were subjected to ultrasound examination for measuring the amount of visceral fat as described above. We then divided the patients (n=78) into two groups, based on the visceral fat cut off values as COPD Patients with visceral adiposity and COPD patients without visceral adiposity.

It was noticed that out of all the COPD Patients (n=78), 33 patients had Visceral Adiposity and 45 Patients did not have Visceral Adiposity. We further checked the BODE Index among the two groups. It portrayed that the BODE Index was higher in the patients with Visceral Adiposity concluding that their 4-year survival rate was lesser as depicted in the Table 2.

Table 2 — *Comparison of BODE Index among viscerally Obese & Non-obese COPD patients*

Visceral Adiposity	No of Patients	Percentage	BODE Index (Mean±Standard deviation)	P value
YES	33	42.37%	4.42±1.80	0.73
NO	45	57.7%	4.24±0.10	

BODE Index Parameters & Visceral Fat :

It was observed that the BMI was significantly greater (p=0.000) in patients with visceral adiposity when compared to patients without Visceral Adiposity (Fig 1).

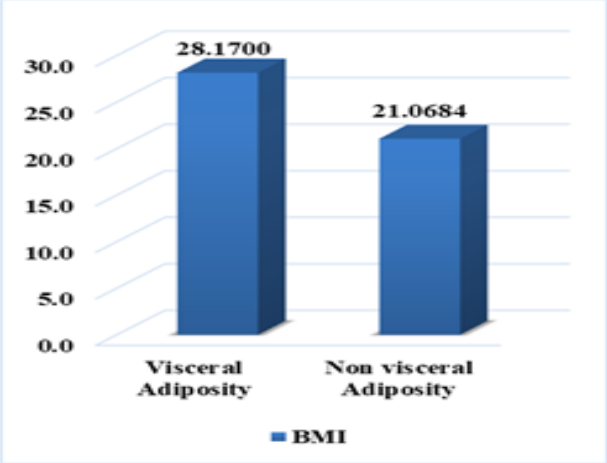

Fig 1 — Relation between BMI & Visceral fat

Patients with visceral adiposity did have more obstruction when compared to patients without visceral adiposity. But the difference was not statistically significant as p=0.888 (Fig 2).

The mean Dyspnea score among viscerally obese patients was significantly more than patients without visceral adiposity (p=0.049). The mean Dyspnea score in patients with visceral obesity was 1.48±0.7 as compared to the score of 1.18±0.06 in viscerally non-obese patients (Fig 3).

All COPD patients completed the 6-minute walk test, though some took a break while the clock was still on & later walked to complete 6 minutes. The total distance walked by patients with visceral adiposity (183±67.6m) was lesser when compared to patients without visceral adiposity (203.53±58.9m). But it was not significant as p=0.160 (Fig 4).

It was observed that patients with visceral adiposity had a higher BODE Index when compared to patients

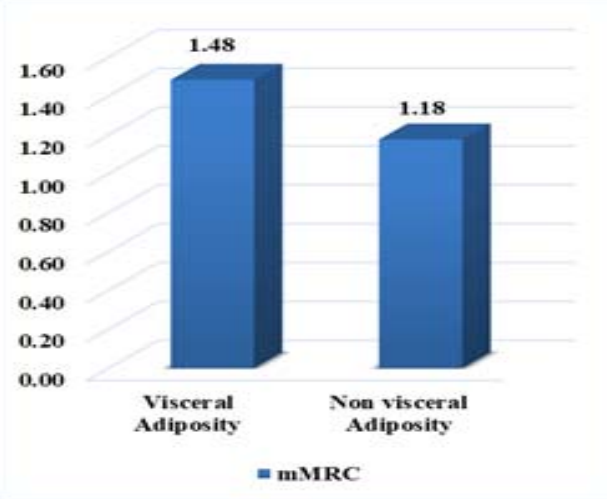

Fig 2 — mMRC Dyspnea score in COPD Patients

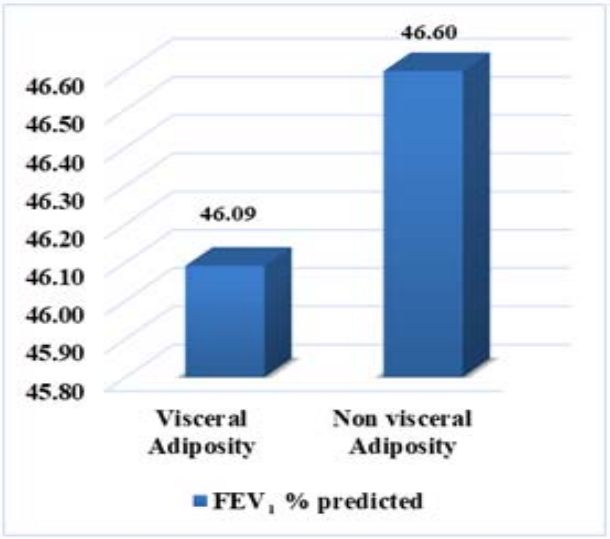

Fig 3 — FEV1 % predicted in COPD Patients

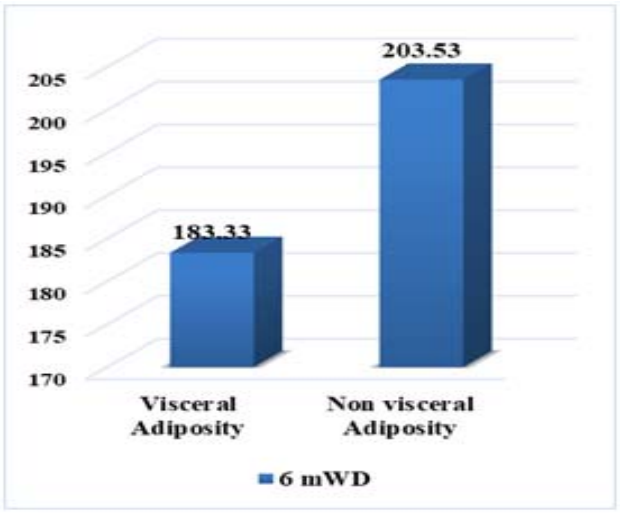

Fig 4 — 6-minute Walk Distance in COPD Patients

without visceral adiposity which was not significant as p=0.382 (Fig 5).

Higher BODE index reflects poor survival rate. So, the 4 Year survival rate in patients with visceral adiposity was lesser than that of patients without visceral adiposity, though was not statistically significant (p=0.706) (Fig 6). Figures showing the comparison of BODE Index individual parameters among the two groups.

Correlation of BMI, Obstruction, Dyspnea and 6-min Walk Test with Visceral Adiposity :

We tried to correlate BMI, Obstruction, Dyspnea and Exercise with visceral adiposity to know whether any consistent relationship existed using Pearson's correlation.

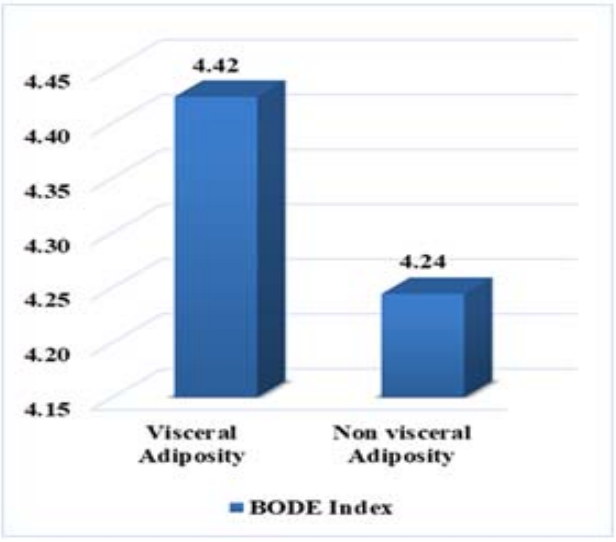

Fig 5 — Comparison of BODE Index in COPD patients

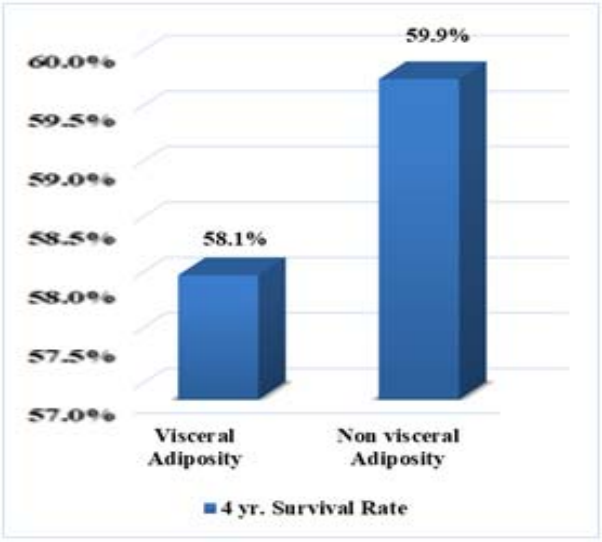

Fig 6 — 4 year Survival Rate among COPD patients

There was strong correlation of BMI with Visceral Adiposity. There was intermediate correlation between dyspnea score & Visceral adiposity and other parameters such as Obstruction and Exercise showed weak correlation with Visceral Adiposity as in Table3

Discussion

In our study the prevalence of visceral adiposity among COPD patients was 42.3%. This is in line with the findings of Furutate, *et al* where the prevalence of visceral adiposity among COPD patients was found to be 52.5% by CT measurement as compared to 38.7% in the control group[6]. Earlier studies by Steuten, *et al* reported only 18% prevalence of obesity which was based on the BMI[13].

Table 3 — *Correlation of BMI, Obstruction, Dyspnea and 6-min walk Test with visceral adiposity*

	BMI (kg/m^2)	Obstruction (FEV_1% pred)	Dyspnea (mMRC Grade)	Exercise (6 min walk test)	Total Points	4-year survival rate
Pearson Correlation	0.0753**	-0.016	0.216*	-0.160	-0.120	-0.110
Sig. (2- tailed)	0.000	0.888	0.049	0.160	0.382	0.706

**Correlation is significant at the 0.00 level
*Correlation is significant at the 0.049 level

Increase in the visceral fat in COPD may be related to physical inactivity which leads onto excessive fat accumulation in them. Along with this COPD patients are treated with glucocorticoids during exacerbations; this systemic corticosteroid therapy may cause glucocorticoids – mediated redistribution of stored energy & stimulatory effect on food intake leading to visceral obesity[6].

The BODE index which predicts the 4-year survival rate is also an important prognostic predictor of COPD. BODE Index in our study was found to be less in patients with visceral obesity as compared to non-obese individuals. These findings suggest that Visceral obesity adds on to the burden of morbidity & mortality in COPD patients[14].

In our study, the mean Body Mass Index was more in Viscerally Obese patients, this may reflect coexistence of general obesity with visceral obesity in these individuals.

Further analysis revealed that in a small fraction of patient's visceral obesity was seen though their BMI was less than normal. These were the patients in whom the obstruction was more severe (GOLD stage 3 &4). Similar findings were found by Furutate, *et al*, wherein the prevalence of non-obese subjects with increased VFA was greater in the patients with more obstruction than in those with lesser airflow limitation according to GOLD stages. In these patients there is muscle loss leading on to lesser BMI[6].

ECLIPSE, a cohort study reported that there was increased Visceral Adipose Tissue and fat accumulation in the muscle tissue in COPD patients with severe airflow limitation (mean FEV_1, 40.7% predicted). In this study, muscle fat accumulations were measured by muscle tissue attenuation on CT scan of the thorax among smoking and nonsmoking COPD patients[15].

Though FEV_1% predicted was not significantly different between the 2 groups, our study revealed that FEV_1% predicted had a negative correlation with the visceral fat.

This decrease in lung function can be attributed to the systemic inflammation triggered by adipose tissue. Visceral fat tissue is known to be more metabolically active than subcutaneous fat. This secretes or synthesizes inflammatory cytokines, such as tumor necrotic factor –α and interleukins- 6 which are known to be associated with chronic inflammatory airway disease as discussed earlier[3].

Dyspnea Scores & Visceral Fat :

Perceived breathlessness as graded by mMRC scale was significantly more severe among viscerally obese patients than the other group. Severity of dyspnea was more in Viscerally obese individuals and it positively correlated with the mMRC scale.

Exercising capacity as estimated by 6-minute Walk Test was less among the viscerally obese patients as compared to others. The total distance covered by viscerally obese patients was less. Earlier study done by Serres, *et al* showed that physical inactivity is a consequence of the so- called dyspnea spiral, in which COPD patients tend to adopt a sedentary life style to avoid dyspnea[16].

Further analysis did not show a significant correlation between 6MWD & visceral obesity. As we had ruled out other cardiorespiratory conditions which could further limit the amount of exercise may have been the reason. And also, the lung functions between the groups were not significantly different, there was not much difference in the exercise capacity also. Similar findings were observed in a Japanese study, which was explained by the fact that though 6MWD could be indicative of exercise capacity, it does not necessarily reflect the total amount of physical activity in day-to-day activities[6]. This could further be explored by using the physical activity monitors in future studies.

The present study has various strengths. First this study included participants in whom the abdominal adipose tissue was measured directly with the help of ultrasound unlike previous studies that used BMI or Waist circumference as surrogate markers of abdominal obesity. We conducted tests of all the parameters that affects a COPD patient with Visceral Adiposity which makes it a reliable and advanced study.

Limitations of the Study :

There are few limitations in our study. Firstly, as this study was done on a relatively small number of patients due to restriction of time, increasing the sample size would yield refined results. Second, in

our present study we failed to document the corticosteroid intake in our patients, as this also could affect the visceral fat deposition.

Conclusion

The National Health Policy of India 2017 recommends that premature mortality from non-communicable diseases, including chronic respiratory diseases, should be reduced by 25% by 2025[6]. As visceral fat has been proved to deteriorate the survival rate in COPD patients, steps should be taken to decrease the visceral fat, along with the standard pharmacological intervention, thereby decreasing the mortality in COPD patients.

Visceral obesity can be decreased by making certain lifestyle changes :

- Inculcating a fiber rich diet with less of fats and carbohydrate.
- Exercising on a regular basis within the capacity of the patient which depends on the stage of COPD.

The results of this study can be used by health care professionals to educate their patients regarding the importance of decreasing the visceral fat, which can improve their lung functions and prevent the progression the COPD.

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