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Metabolic Syndrome in Chronic Obstructive Pulmonary Disease (COPD) Patients and Its Association with Severity of COPD: A Study from Chhattisgarh, India

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Abstract: Metabolic Syndrome is found to be more frequent in chronic obstructive pulmonary disease (COPD) as it seems to be related to systemic inflammation. Chronic Obstructive Pulmonary Disease (COPD) is a growing cause of morbidity and mortality worldwide and will become one of the leading causes of death in near future. This study aims to detect metabolic syndrome in COPD patients and its association with the severity of COPD. The current study was Hospital based cross-sectional observational study. 60 Stable COPD patients were included. Patient of Chronic Obstructive Pulmonary Disease attending general medicine OPD, casualty, admitted to Dr. BRAM Hospital, Raipur (India) medicine ward. After obtaining informed written consent from participants, demographic details, and chief complaints, a Pulmonary Function Test for clinically suspected cases of COPD was obtained. Clinical examinations, including waist circumference, were observed. Blood investigations were done. Staging of COPD was done using GOLD criteria. The association of the severity of COPD with Metabolic Syndrome was then done using statistical tools. There is no statistically significant difference between the prevalence of Metabolic Syndrome in different COPD stages (P=0.199). There is also a significant difference in pre-FEV1 (P=0.015) and post-FEV1 (P=0.03) values in patients with and without Metabolic Syndrome. At the end of the study, it can be concluded that waist circumference (P=0.007) significantly differs in patients with and without metabolic syndrome. At the same time, other variables like weight, height, BMI, and waist-hip ratio do not show any significant difference.

Keywords: OPD, Metabolic Syndrome, Chronic bronchitis, Emphysema, Breathlessness, Waist circum

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1. INTRODUCTION

Globally, Chronic Obstructive Pulmonary Disease (COPD) is a leading cause of morbidity and mortality that induces an economic and social burden projected to increase in coming decades because of continued exposure to COPD risk factors and population aging. [1,2] The Global Initiative for Chronic Obstructive Lung Disease (GOLD) recently defined COPD as a common, preventable, and treatable disease that is characterized by Persistent respiratory symptoms and airflow limitation that is due to airway and alveolar abnormalities usually caused by significant exposure to noxious particles or gases. The prevalence of COPD is higher in smokers and ex-smokers compared to non-smokers, in those ≥ 40 years of age compared to those < 40, and in men compared to women. The prevalence of COPD increases steeply with age and is highest among those > 60 years.[2] although much of the evidence has concentrated on smokers only, it has been reported that at least one-fourth of patients with COPD are non-smokers. Risk factors of COPD in non-smokers may include genetic factors, long-standing asthma, outdoor air pollution (from traffic and other sources), environmental smoke exposure, biomass smoke, occupational exposure, diet, recurrent respiratory infection in early childhood, tuberculosis, and so on.[6] The metabolic syndrome consists of a constellation of metabolic abnormalities that confer an increased risk of cardiovascular disease (CVD)[9-11] and diabetes mellitus (DM)[12-14]. The metabolic syndrome, a state of insulin resistance also known as syndrome X or the dysmetabolic syndrome, has drawn the greatest attention because of its public health importance. Metabolic syndrome is increasing in prevalence, paralleling an increasing epidemic of obesity. Metabolic syndrome is an emerging global problem. Approximately one-fourth of the adult European population is estimated to have metabolic syndrome, with a similar prevalence in Latin America.[15] Differences in genetic background, diet, levels of physical activity, population age and sex structure, levels of over and under-nutrition, and body habitus all influence the prevalence of the metabolic syndrome and its components. Almost 40% of U.S. adults were classified as having metabolic syndrome, similarly prevalent among urban Indians (41.1 %). [16] In a study by Ameen et al. Incidence of metabolic syndrome in different levels of severity of COPD patients was (11.1%) in mild COPD, (34.8%) in moderate, (25%) in severe, and (50%) in very severe cases [8]. Another study by Akpinar et al. found that the distribution of the prevalence of MetS between GOLD stages I–IV was as follows; 38.5%, 52.8%, 30%, and 33.3%, respectively.[17]Limited studies were available evaluating the association between metabolic syndromes with the severity of COPD patients. Hence, this study was conducted to detect metabolic syndrome in COPD patients and its association with the severity of COPD.

2. MATERIALS AND METHODS

60 Stable COPD patients were included in the study. It is a Hospital based cross-sectional observational study. Patients with Chronic Obstructive Pulmonary Disease attending general medicine OPD and casualties admitted to the medicine ward of Dr. BRAM Hospital, Raipur (India) were the study subjects. GOLD (Global Initiative for Chronic Obstructive Lung Disease) criteria determined the severity level in patients with COPD. The definition of the national cholesterol education program adult treatment panel III (NCEP ATPIII) was used to diagnose metabolic syndrome.[4] We measured the characteristics of the metabolic syndrome (waist circumference, blood pressure, fasting blood glucose, serum triglycerides, and HDL).

2.1. Sample Size calculation

- The incidence of Metabolic Syndrome in COPD in a previous study was 32.9%, so taking this as a reference for the estimation of sample size for this study[3]
- The sample size was calculated by using the Metabolic Syndrome prevalence

$$n = z^2 pq/(M.E.)2$$

Where,

z = 90% confidence interval (1.645)
p= 32.9% prevalence of Metabolic Syndrome in COPD,
q=1-p=67.1%
M.E.=10% margin of error

2.2. Inclusion Criteria

1. Patient with PFT confirmed case of Chronic Obstructive Pulmonary Disease.
2. Patient age more than 18 yrs.

2.3. Exclusion Criteria

1. Any cancer within less than five years before the study.
2. Infections (including respiratory tract infections or exacerbations)
3. Systemic corticosteroid treatment within 4 weeks before the study.
4. Asthma
5. Interstitial lung diseases

Table 1: Criteria to define metabolic syndrome[10]

Presence of Central Obesity, namely waist circumference > 94 in Males and >80 cm in Females (updated ATPIII criteria) or BMI>30 kg/m2	
Elevated Triglycerides levels	(>150 mg/dL or 1.7 mmol/L) or specific treatment for this lipid abnormality
Reduced HDL-C cholesterol levels	(<40 mg/dL or 1.03 mmol/lit in M and<50 mg/dL or 1.29 mmol/L in F) or specific treatment for this lipid abnormality
Raised blood pressure	Systolic>130 or Diastolic>85 mmHg or treatment of previously diagnosed hypertension
High blood glucose level with or without insulin resistance	(Fasting plasma glucose level >100 mg/dL or 5.6 mmol/L) or previously diagnosed type 2 diabetes

2.4. *Ethical Statement*

Permission from the Ethical Committee was taken before the commencement of the study, and informed written consent was obtained from the study participants.

2.5. *Statistical Analysis*

Data was expressed as a percentage and mean ± S.D.

Kolmogorove-Smirnove analysis was performed to check the linearity of the data Pearson correlation analysis was performed to check the correlation between two categorical variables. The chi-square test and Fisher"s exact test was used to analyze the significance of the difference between the frequency distribution of the data. P value <0.05 was considered statistically significant. Suitable statistical software was used to perform the statistical analysis.

3. RESULTS

Table 2: Distribution of COPD Patients According to Gold Severity Classification

Gold Staging	Frequency	Percent
Mild	9	15.0
Moderate	36	60.0
Severe	11	18.3
Very Severe	4	6.7

Table 2 - Among the study population 60, in our study, the maximum number of patients from the moderate stage is 36 (60%) study population, followed by11 (18.3%) patients from are severe stage, followed by 9(15%) patients is mild stage and 4(6.7%) patients are very severe stage.

Table 3(a): Base Line Characteristics Of COPD Patients In Our Study

Variable	N	Minimum	Maximum	Mean	SD
Age	60	24	80	58.48	12.778
Weight(kg)	60	50	88	66.65	8.598
Height(cm)	60	146	178	164.17	6.244
BMI(kg/m2)	60	19.26	33.20	24.79	3.127
Waist Circumference	60	78	116	92.13	9.302
Waist Hip Ratio	60	.814	1.094	.941	.0510

Table 3(a) - In our study, the minimum age of the patients is 24 years, and the maximum is 80 years. Our study's mean BMI and waist circumference is 33.20± 24.79(kg/m²) and116± 92.13(cm). In our study minimum height and weight of the patients are 146 cm and 50 kg, and the maximum height and weight are 178 cm and 88 kg, respectively. The mean Waist Hip ratio in our study is 0.941± 0.051.

Table 3(B): Laboratory Characteristics of COPD Patients in Our Study

Descriptive Statistics					
Variable	N	Minimum	Maximum	Mean	Std. Deviation
SBP (mmHg)	60	106	164	133.65	14.682
DBP (mmHg)	60	68	102	84.40	8.571
HDL (mg/dl)	60	28	48	39.07	4.797
TGL (mg/dl)	60	101	254	161.22	31.565
LDL (mg/dl)	60	40	176	107.83	26.477
VLDL (mg/dl)	60	20.2	50.8	32.247	6.3115
TC (mg/dl)	60	113	265	179.18	27.762

Table 3(b) - In our study, mean systolic and diastolic blood pressure is 133.65± 14.68mmHg and 84.40 ± 8.571 mm Hg, respectively. The total Glucose level is 161.22 ± 31.565 mg/dl. Minimum and Maximum Total Cholesterol and Triglycerides levels are 113 and 265 mg/dl and 101 and 254 mg/dl, respectively. Our population's mean HDL, LDL, and VLDL cholesterol levels are 39.07, 107.83, and 32.247 mg/dl, respectively.

Table 4: Prevalence of Metabolic Syndrome in Different COPD Stages

Gold Staging * Metabolic Syndrome Cross Tabulation					
Gold Staging		Metabolic Syndrome		Total	P value
		No	Yes		
Mild	Stage 1	6 (66.7%)	3 (33.3%)	9	0.199
Moderate	Stage 2	17 47.2%)	19 (52.8%)	36	
Severe	Stage 3	6 (54.5%)	5 (45.5%)	11	
Very Severe	Stage 4	4 (100%)	0 (0%)	4	

Table 4 - There is no statistically significant difference between the prevalence of Metabolic Syndrome in different COPD stages with a p-value of 0.199. The prevalence of Metabolic Syndrome was 33.3%, 52.8%, 45.4%, and 0% in stage 1, stage 2, stage 3, and stage 4 COPD, respectively.

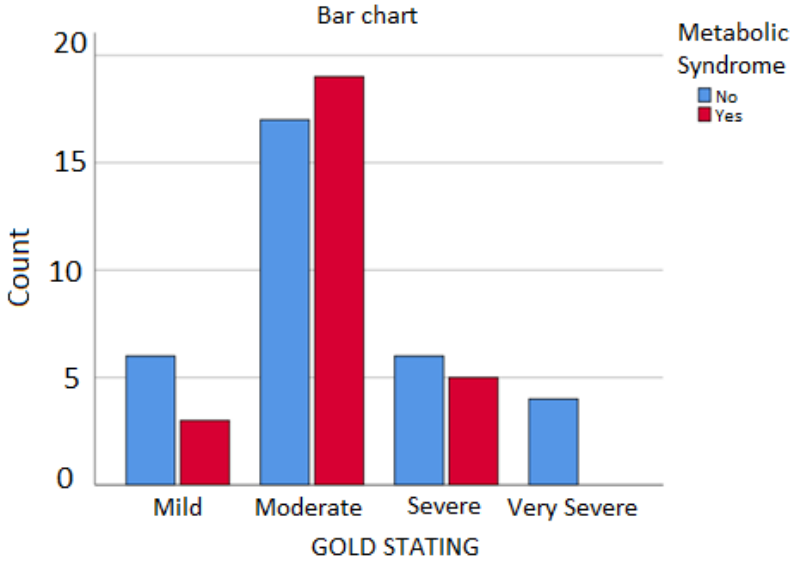

Fig 1 - Prevalence of Metabolic Syndrome in Different COPD Stages

Fig 1– In Our Study, The prevalence of Metabolic Syndrome was 33.3%, 52.8%, 45.4%, and 0% in stage 1(Mild), stage 2(Moderate), stage 3(Severe), and stage 4(Very Severe) COPD respectively.

4. DISCUSSION

Among the study population of 60, the age group most commonly affected was between 51-70years of age, which was 32(53.3%) patients, 16(26.7%) patients were from the age group of 31-50 years, 9(15%) patients belong to age group 71 years and above and 3(5%) patients belonged to age group 18-30 years. The mean age of patients in our study was 58.48+12.77 years. Similarly, in a study conducted by Akpinar EE et al. about Systemic inflammation and Metabolic Syndrome in stable COPD patients mean age of subjects in patients was 63.7 + 8.6, and that of in control group was 62.8 + 6.4 (P>0.05).[5] Among the study population of 60, 48(80%) patients are male, 12(20%) patients are female with a male predominance. Similarly, Díez-Manglano J et al., in the study of COPD patients with and without metabolic syndrome, included 375 patients, 333(88.8%) men and 42(11.2%) women.[6] Study conducted by Ahmed MEet al. Included 430 patients with stable COPD, 397(92.32%) males and 33(7.67%) females.[7] In my study, among the study population, out of 60, 51(85%) patients were above-normal systolic blood pressure, and 9 (15%) patients were normal blood pressure with a mean of 133.65+14.68. Gupta KK et al., in their study of Uncovering Metabolic Syndrome among Chronic Obstructive Pulmonary Disease Patients, observed mean Systolic BP (mmHg) of127.33±3.21 in the cases group and mean systolic BP (mmHg) of 118.98±7.81 in the control group (P<0.0001).[8] In my study population of 60, 40(66.7%) patients were above normal DBP and 20(33.3%) patients with normal DBP with a mean of 84.40+8.57. Choi HS et al. reported in a study of metabolic syndrome in early chronic obstructive pulmonary disease that mean DBP mmHg in males with no metabolic syndrome was77.4±10.1mmHg, that in males with metabolic syndrome, was 79.4±11.3 mmHg (P=0.001); mean DBP mmHg in females with no metabolic syndrome was74.3±10.0mmHg, that in females with metabolic syndrome was 76.7±10.3 mmHg(P=0.007).[9] Among the study population of 60, 32(53.3%) patients' TG levels were above normal, and 28(46.7%) were within the normal range with a mean. Ameen NM et al., in their study of metabolic syndrome in patients with chronic obstructive pulmonary disease, observed that 51.4% of patients in the patient group reported TG level above normal level and 5% in the control group reported TG level above normal level. [10] In my study population of 60, 30(50%) patients' BMI was above normal levels, and 30(50%) patients' BMI was within normal range with a mean of 24.79+3.12. Gupta KK et al., in their study of Uncovering Metabolic Syndrome among Chronic Obstructive Pulmonary Disease Patients, observed a mean BMI (kg/m2) of 23.29±3.08 in the cases group and a mean BMI (kg/m2) of 22.59±2.78 in the control group (P = 0.2011).[8] In a study on metabolic syndrome in chronic obstructive pulmonary disease conducted by Pasha MM et al., it was observed that the mean BMI (kg/m2) of 24.05±5.32 in the cases group, and the mean BMI (kg/m2) of 22.59±4.01in the control group.[11] Among the study population, 60, 30(50%) patients' waist circumference was above normal, and 28(46.7%) were within the normal range with a mean value of 92.13+9.30. Choi HS et al. reported in a study of metabolic syndrome in early chronic obstructive pulmonary disease that means abdominal circumference (cm) in patients with no metabolic syndrome was82.7±7.9 in patients with metabolic syndrome, was 89.0±7.7 (P<0.001)[9]. In my study, the minimum age of the patients was 24 years, and the maximum was 80 years. Our study's mean BMI and waist circumference were 33.20± 24.79(kg/m²) and 116± 92.13(cm). In our study minimum height and weight of the patients were 146 cm and 50 kg, and the maximum height and weight were 178 cm and 88 kg, respectively. The mean Waist Hip ratio in our study was 0.941± 0.051. Díez-Manglano Jet al in a study of COPD patients with and without metabolic syndrome, included 375 patients, 333 men, and 42 women, with a mean (SD) age of 73.7 (8.9) years, with mean height(cm) in patients with MetS was 165.6 (7.9%), that of in patients without MetS was 167.0

(9.1%) (P=0.12).The mean Weight (kg) in patients with MetS was 81.5 (15.1%), and that of patients without MetS was 69.5 (11.0%) (P=0.0001).The mean Body mass index (kg/m2)in patients with MetS was 29.8 (5.6%), and that of patients without MetS was 24.9 (3.7%) (P=0.001).[12] In our study, mean systolic and diastolic blood pressure was 133.65± 14.68mmHg and 84.40 ± 8.571 mm Hg, respectively. The total Glucose level was 161.22 ± 31.565 mg/dl. Minimum and Maximum Total Cholesterol and Triglycerides levels were 113 and 265 mg/dl and 101 and 254 mg/dl, respectively. Our Population's mean HDL, LDL, and VLDL cholesterol levels were 39.07, 107.83, and 32.247 mg/dl, respectively. Choi HS et al. reported that mean systolic and diastolic blood pressure was 126.8±17.5mmHg and 77.4±10.3 mm Hg, respectively. The mean Glucose level was 102.4±23.5mg/dl. Triglycerides levels was 155.5±36.2 mg/dl. Mean HDL-C was 44.5±9.95mg/dL.[9] In my study, the maximum number of patients from the moderate stage is 36 (60%) study population, followed by11 (18.3%) patients in our severe stage, followed by 9(15%) the patient in the mild stage, and 4(6.7%) patients are the very severe stage. Akpinar EE et al., in a study about Systemic inflammation and metabolic syndrome in stable COPD patients, reported patients in stage GOLD I was 13 (14.1%), stage GOLD II was 53 (57.6%), stage GOLD III was 20 (21.7%), and stage GOLD IV was 6 (6.5%)[5] Ameen NM et al., in the study of metabolic syndrome in patients with chronic obstructive pulmonary disease, observed that patients in mild stage with metabolic syndrome were 1 (11.1%), that without metabolic syndrome was 8 (88.9%); patients in moderate stage with metabolic syndrome was 8 (34.8%), that of without metabolic syndrome was 15 (65.2%); patients in severe stage with metabolic syndrome was 5 (25%), that of without metabolic syndrome was 15 (75%); patients in Very severe stage with metabolic syndrome was 9 (50%), that of without metabolic syndrome was 9 (50%).[10] Among the study population 60, 27(45%) patients have metabolic syndrome and 33(55%) patients have no metabolic syndrome. Ameen NM et al., in the study of metabolic syndrome in patients with chronic obstructive pulmonary disease, reported 23 (32.9%) patients with metabolic syndrome in the patient's group and 1 (5%) patients with metabolic syndrome in the control group.[10] Gupta KK et al., in their study of Uncovering Metabolic Syndrome among Chronic Obstructive Pulmonary Disease Patients, reported that there were 14 (15.56%) and 30 (33.33%) cases fulfilling the criteria of MetS. While there was no MetS in control. Of 30 MetS cases, 24 (38.71%) were dominated by males, and the rest were females.[8] There was no statistically significant difference between the prevalence of Metabolic Syndrome in different COPD stages with a p-value of 0.199. The prevalence of Metabolic Syndrome was 33.3%, 52.8%, 45.4%, and 0% in stage 1, stage 2, stage 3, and stage 4 COPD, respectively. Similarly, Ameen NM et al., in the study of metabolic syndrome in patients with chronic obstructive pulmonary disease, observed that the incidence of metabolic syndrome in different levels of severity of COPD patients was (11.1%) in mild COPD, (34.8%) in moderate (25%) in severe and (50%) very severe cases. The incidence of metabolic syndrome was higher in very severe and moderate COPD patients but less in mild and severe cases. So, the incidence of metabolic syndrome in studies, despite being highest in very severe cases, is less severe than in moderate cases. So, the incidence of metabolic syndrome is unrelated to COPD's severity.[10] In my study mean pre FEV1 and post FEV1 values in patients with Metabolic Syndrome are 1.82+0.592 and 2.08+++0.394 L and without metabolic syndrome are 1.96+0.386(P=0.015) and2.00+0.579 L (P=0.03) respectively with significant difference. In a study conducted by Küpeli E et al., it was found that the mean FEV1(L) in patients with metabolic syndrome was 1.7 ± 0.7 and that in patients without metabolic syndrome was 1.5 ± 0.6 (P=0.08), [13] Díez-Manglano J et al.et al. al in a study of COPD patients with and without metabolic syndrome reported that Patients with MetS had less airflow obstruction, either expressed by FEV1 and FEV1/FVC ratio compared with patients without MetS (p=0.01).Patients with MetS had FEV1 (% predicted) 45.5 (12.1%), and that of patients without MetS was 41.8 (12.4%) (P=0.004).Patients with MetS had FVC (% predicted) 59.9 (14.0%), and that of patients without MetS was 62.6 (17.1%) (P=0.22).Patients with MetS had FEV1/FVC 0.55 (0.10%), and that of patients without MetS was 0.51 (0.10%) (P=0.006).[12] In my study, we have found that waist circumference (P=0.007) shows a significant difference, and the other variable like weight, height, BMI, and waist-hip ratio does not show any significant difference in patients with metabolic syndrome and patients without metabolic syndrome. A study conducted by KüpeliE et al. found that Body mass index (BMI) (P=0.014) and waist circumference were significantly higher in the MetS group than in the control group. Patients in the control group were overweight yet not obese (BMI:27.2 ± 5.7).[13]

5. CONCLUSION

At the end of the study, it can be concluded that waist circumference (P=0.007) differs significantly in patients with and without metabolic syndrome. At the same time, other variables like weight, height, BMI, and waist-hip ratio do not show any significant difference. There is no statistically significant difference between the prevalence of Metabolic Syndrome in different COPD stages. (P=0.199). There is also a significant difference in pre-FEV1 (P=0.015) and post-FEV1 (P=0.03) values in patients with and without Metabolic Syndrome.

6. LIMITATION OF STUDY

This study was taken only for stable COPD patients and took less sample size, which was my study's major limitation.

7. AUTHORS CONTRIBUTION STATEMENT

Dr. A.Toppo and Dr. Jyoti conceived the presented idea, developed the theory, and performed the computations. Dr. Jyoti verified the analytical methods. Dr. A. Toppo encouraged Dr. Jyoti to investigate and supervised the findings of this study. All authors discussed the results and contributed to the final manuscript.

8. CONFLICT OF INTEREST

Conflict of interest declared none.

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