

METABOLIC SYNDROME IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE: EARLY PERCEPTION, EASY PREVENTION.

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ABSTRACT

INTRODUCTION:

Metabolic syndrome (MS) enhances the risk of cardiovascular diseases (CVD) and Diabetes Mellitus, but its frequency in Chronic Obstructive Pulmonary disease (COPD) is not yet investigated in detail. The study's aim is to assess the prevalence and its correlation to the severity stages of COPD.

METHODS:

100 COPD patients were participated in this cross-sectional study. Metabolic syndrome parameters such as high-density lipoproteins, fasting blood glucose, blood pressure, triglycerides and body mass index with waist circumference were measured. Six-minute walk distance (6MWD), COPD assessment score and spirometry were used to determine the functional capacity.

RESULTS:

Prevalence of MS was found to be 46% with most common stages of COPD were Global Initiative of Chronic Obstructive Lung Disease grade I and II. FBS, HDL and WC were statistically significant with the severity of COPD.

CONCLUSION:

MS is more common in early stages of COPD (GOLD I and II) with less advanced airflow limitation. Abdominal obesity, Hyperglycemia, Dyslipidemia were the three most prevalent metabolic parameters. Early diagnosis and appropriate management with pulmonary rehabilitation is important to prevent morbidity and mortality caused by MS in COPD.

INTRODUCTION

COPD is an irreversible progressive respiratory disorder with significant airflow limitation. Due to high prevalence and chronicity, COPD is routinely ranked among the top causes of mortality on a global scale. It has been linked to a number of comorbid conditions like skeletal muscle dysfunction, cardiovascular diseases, depression and metabolic syndrome.

Metabolic syndrome (MS) is a proinflammatory and prothrombotic condition with elevated CRP levels and increased risk for subsequent cardiovascular diseases (CVD) and type-2 diabetes. “The National Cholesterol Education Program (NCEP) Adult Treatment Panel 3 (ATP3) defines it as a cluster of five components: high blood pressure, high triglyceride (TG) level, low high-density lipoprotein (HDL), abdominal obesity and high blood glucose level”. In metabolic syndrome individuals, abdominal syndrome is associated with insulin resistance which inhibits peripheral glucose utilization leading to T2DM. Insulin resistance associated hyperglycemia, abnormal lipid levels, adipocyte cytokines all together leads to endothelial dysfunction and vascular inflammation which all promote the development of CVD.

According to studies, 30% of COPD patients estimated to have MS. Several studies observed a link between MS and COPD, in which MS is an independent risk factor for worsening lung function. Obesity, Sedentary lifestyle, Smoking and systemic inflammation may play an essential role in developing MS. Genetic factors account for 50% of the diversity in MS features in offspring, and a parent's history of the condition increases risk.^[1]

Earlier studies found that these co-morbidities are associated with increased risk of hospitalizations, death and it drastically increases the economic burden of COPD.^[2]

In this study, we studied the prevalence of metabolic syndrome in COPD patients in a tertiary care hospital. In addition, risk factors, clinical characteristics of COPD patients with and without metabolic syndrome were compared.

METHODS**STUDY DESIGN**

A cross-sectional and observational study conducted in Department of Respiratory medicine, Pune.

ETHICAL COMMITTEE

The study protocol had an Ethics committee approval (IESC/PGS/2020/67) in our tertiary care hospital. Informed consent was taken from all the participants.

STUDY CRITERIA

Male and Female aged between 40-80 years were included. GOLD diagnosed 100 COPD patients taken. Obstructive Airway diseases other than COPD, Pregnancy, Immunocompromised and other co-morbid illness patients were excluded.

PULMONARY FUNCTION TEST

At least three spirometry manoeuvres were conducted for the spirometry assessment, and the greatest forced expiratory volume (fev1) in the first second was taken into account for documentation. The day before the spirometry, inhalers were withheld.

BIOCHEMICAL AND ANTHROMETRIC MEASUREMENTS

All the selected patients underwent routine biochemical investigations, complete blood count, HbA1C, fasting lipid profile, fasting blood glucose, chest X-ray, two-dimensional Echocardiography, pulmonary function test and anthropometric measurements such as Body Mass Index, height, weight and waist circumference according to World Health Organization (WHO) protocol.

The collected data was used for diagnosing Metabolic Syndrome according to the criteria of National Cholesterol Education Programme: Adult Treatment Plan 3 (ATP3)

EXERCISE CAPACITY

Functional exercise capacity by six-minute walk distance test was done. COPD assessment test scoring and BODE (BMI, Obstruction (FEV1), Dyspnea (mMRC grading), Exercise capacity (6MWD) index was calculated.

STATISTICAL ANALYSIS

Statistical analyses was done with the Social Sciences (IBM SPSS) Version 26, Armonk for Windows. The prevalence is calculated as percentages. Proportion groups were compared by Chi-square test and Fisher's exact test if cell frequency is less than five.. Univariate Binary logistic regression analysis was done to identify risk factors for COPD and metabolic syndrome. "P <0.05 is significant."

RESULTS

A total of 100 patients were enrolled in this study. The mean age of patients was 64.61 ± 11.3 . Comparing the age in study population, minimum was 40 years and maximum was 88years. Most of the patients were in 50-59 years of age (36 patients) and 60-69 years (27 patients). Among 100 patients, males were 46% and females were 54%. Of all patients, 42% were reformed smokers with 56.1% heavy smokers and 42.9% were light smokers. 60% of study populations had biomass fuel exposure with duration of the exposure more than 20 years in 96.7% of the exposed. The percentage of patients with GOLD stages I, II, III and IV were 2%, 35%, 36% and 27% and percentage of patients in GOLD category A, B, C and D were 24%, 33%, 16% and 27%.

46% of study patients were found to have MS. There are no statistically significant association on comparing COPD with and without MS cases in smoking, biomass exposure, mMRC grade and stages of COPD.

Among 100 patients, 63 patients were normotensive and 37 patients were hypertensive with more prevalence of Grade 1 hypertension (27 patients). Comparing with GOLD severity, most of the patients fell in Grade II and III (14 patients and 15 patients). 40 patients had waist

circumference >88cm in males and >102cm in females suggestive of abdominal obesity. GOLD Grade II and III patients were more prevalent for abdominal obesity (37.5% and 35% respectively) with a statistical significance (p value 0.010). 73 patients were found diabetic with HbA1C >5.6 and FBS >100 with more prevalent in GOLD grade II and III (30 and 28 patients respectively) which is statistically significant with p-value of 0.047. Among 100 patients, only 5 patients had increased triglyceride levels >150mg/dl.

72 patients had low levels of High-density lipoprotein with more prevalent in GOLD grade IV, III and II (36.1%, 31.9% and 30.6% respectively) which is statistically significant with p value of 0.002.

The association between COPD and MS were analysed and found that hyperglycaemia, abdominal obesity and dyslipidaemia has statistical significance. Prevalence of MS were compared with severity stages of COPD and it was found to be more prevalent with GOLD I and II. Prevalence of MS with COPD was most in GOLD C, followed by GOLD B, GOLD A and least in GOLD D (62.5%,57.6%,41.7%,25.9% respectively, p <0.001).

GOLD C COPD patients have a lesser CAT score with more frequent exacerbations; and from this study it is evident that Metabolic syndrome is more common in Gold C category, making it a possible risk factor for recurrent exacerbations in COPD, a theory that needs to be studied in detail in future.

Table 1: Demographic data of study participants and parameters of metabolic syndrome in the study participants

VARIABLES	COPD WITHOUT METS (n=100)	COPD WITH METS (n=100)
Age (years)	64.57±11.61	64.72±11.33
Females	26 (26%)	28 (28%)
Males	28 (28%)	18 (18%)
Overweight/Obese [BMI >22.9]	8 (20.5%)	31 (79.4%)
Never smokers	29 (50%)	29 (50%)
Reformed smokers	25 (59.5%)	17 (46%)
Biomass fuel exposure	30 (50%)	30 (50%)
High blood glucose [Fasting glucose >100mg/dl]	29 (39%)	44 (60.3%)
High blood pressure [SBP >140, DBP >90 mmHg]	8 (21%)	29 (78.3%)

Abdominal obesity [Waist circumference >102cm in male and >88cm in females]	8 (20%)	32 (80%)
Low HDL [<40mg/dl in males and <50mg/dl in females]	31 (43.1%)	41 (56.9%)
High triglycerides [>150mg/dl]	0%	5 (100%)
GOLD I	1 (50%)	1 (50%)
GOLD II	19 (54.3%)	16 (45%)
GOLD III	21 (58%)	15 (41%)
GOLD IV	16 (59.3%)	11 (40%)
GOLD A	14 (58.3%)	10 (41.7%)
GOLD B	14 (42.4%)	19 (57.6%)
GOLD C	6 (37.5%)	10 (62.5%)
GOLD D	20 (74%)	7 (25.9%)

Data presented as mean (SD) or n (%)

Figure 1: Corelation of metabolic syndrome with severity of COPD stages

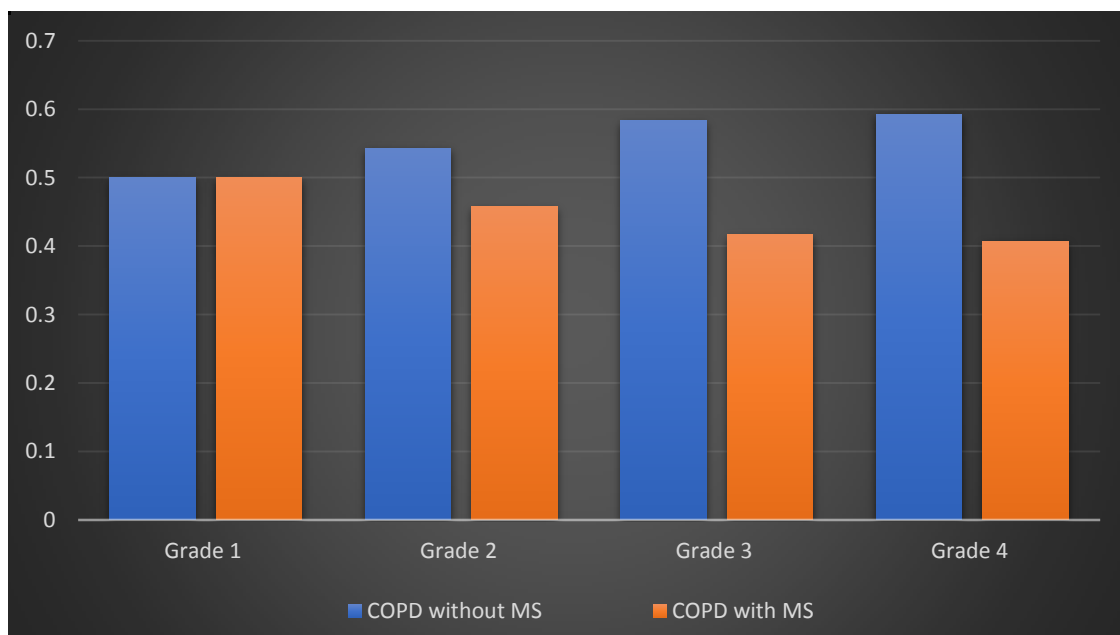


Table 2 : Metabolic syndrome parameters with severity of GOLD staging.

VARIABLES	GRADE 1	GRADE 2	GRADE 3	GRADE 4	P VALUE
High blood pressure	0 (0%)	14 (37.8%)	15 (40%)	8 (21.6%)	0.626
High blood glucose	1 (1.5%)	30 (40.5%)	29 (39.1%)	14 (18.9%)	0.047*
High triglycerides	0 (0%)	3 (60%)	1 (20%)	1 (20%)	0.573
Abdominal obesity	1 (2.5%)	15 (37.5%)	14 (35%)	10 (25%)	0.010*
Low HDL	1 (1.4%)	22 (30.6%)	23 (31.9%)	26 (36.1%)	0.002**

Data presented as n (%), p value calculated by Fisher test,

* = p value < 0.05, ** = p value < 0.005.

DISCUSSION:

The purpose of this study was to identify the frequency of MS in COPD patients and in its stages of severity. As mentioned in earlier studies, when compared to healthy individuals, COPD patients are more prone for MS. [3] We found out that the frequency of MS in COPD patients is 46%, which is same like earlier studies such as Akpınar et al. (45%) and Watz et al. (48%). [4,5]

In our study, Prevalence of metabolic syndrome with GOLD severity I, II, III, IV stages were found to be 50%, 45%, 41% and 40%, and GOLD groups A, B, C, D were 41.7%, 57.6%, 62.5%, 25.9% respectively with a statistically significant association (p value 0.04).

In their study, Diez-Manglano et al reported that frequencies of MS were 51.2%, 41.2% and 25.5% in GOLD II, III, IV respectively. [6] In the Canadian study conducted by Marquis et al, the prevalence of MS in COPD was 47%, decreasing to around 10% at GOLD stages III and IV. [7]

MS is common in mild to moderate COPD (GOLD I and II). It suggests that these patients have increased risk of developing T2DM and CVD and requires frequent follow up and careful monitoring. MS is less common in patients with severe form of COPD because advanced disease causes weight loss due to disuse atrophy and reduced calorie intake added on with increased respiratory efforts.

The average age of patients was 64.61±11.3. According to recent systemic review, frequency of COPD is more in women than men and its prevalence increases more rapidly in women. [8] This increased prevalence is due to increased exposure to tobacco and biomass fuels.

In this study, the number of female participants was 54 (54%) and 46 (46%) participants were male. Metabolic syndrome was found in 18 (39.13%) male patients and 28 (60.87%) female patients suggesting female patients are more prone for developing metabolic syndrome than males.^[9]

The smoking status of all patients in our study group was enquired and observed that 42 patients were reformed smoker where all were male patients. It was quantified by smoking index. 18 patients were light smokers (<400) and 24 patients were heavy smokers (SI>400). Even though smoking is risk factor for COPD and MS, presence of smoking is not a significant association in COPD with MS patients in this study, whereas study done by Hellas Cena et al observed that smokers has increased risk in developing MS than non-smokers and increases with number of pack years.^[10]

In our study, 45.7% of patients had metabolic syndrome with moderate obstruction and 50% of patients had MS in severe obstruction suggesting that MS patients had better FEV1. Deiz-Manglano et al showed that participants with MS had a better FEV1.^[6]

Assessing the severity of metabolic syndrome in COPD patients, 22 patients were prediabetic in COPD only group and 23 patients were prediabetic in COPD with MS group and 7 patients in COPD only were diabetic whereas 21 patients in COPD with MS group. Low HDL levels were found in 31 patients of COPD only group and 41 patients of COPD with MS group. This signifies that COPD only patients are also in high risk for developing metabolic syndrome in future. Increasing physical activity and pulmonary rehabilitation for these patients can lower the MS prevalence and prevent the morbidity and mortality of the same.

Body composition, expressed as Body Mass Index has been shown to predict the metabolic syndrome prevalence in patients with COPD. 31 patients (79.5%) were overweight in COPD with MS patients with a statistical significance of p value <0.001. MK Breyer et al has mentioned in their study that MS is more common in overweight and obese COPD patients compared to healthy individuals.^[11]

The most prevalent MS components were dyslipidaemia, hyperglycaemia and abdominal obesity with statistical significance. This can be explained by use of oral glucocorticoids which furthermore raises the blood glucose levels, HDL levels, increases appetite and weight gain, and can also cause muscle atrophy and abdominal obesity. Even smoking causes systemic inflammation which promotes insulin resistance, decrease the HDL levels and contributes to the development of metabolic syndrome.

A high MS prevalence suggests a sizable risk for developing T2DM and Cardiovascular diseases. Studies have shown COPD and MS are independent risk factors for CVD. COPD patients were more prone for cardiovascular diseases, hypertension and T2DM which causes frequent exacerbations, hospitalizations and all-cause mortality.^[12]

A “comorbidity predominant subtype” of COPD patients have been identified in recent studies, which is formed by a group of metabolic co-morbidities like obesity, CVD and T2DM.^[13] Mannino et al looked into the most common cause of death in COPD with their disease stage. They studied that GOLD I and II stages were found to have cardiovascular cause of death, whereas in advanced stages, respiratory cause were more prevalent.^[12]

Our study results support their findings, as MS was more prevalent in early stages.

Studies assessing the components of metabolic syndrome shed light on the underlying causes of extended cardiometabolic risk in COPD patients and gives us an opportunity to target those factors.

Early diagnosis and prompt follow up in these patients can prevent serious morbid conditions in future with improved quality of life. The effects of pulmonary rehabilitation, an established COPD strategy on exercises and physical training, but the effects on modifying the MS have not yet thoroughly investigated.

Our study's limitations were its small size and cross-sectional design.

Large epidemiological studies are required in light of the contentious findings of aforementioned studies.

CONCLUSION:

- In our study the prevalence of metabolic syndrome using MODIFIED NCEP ATP III criteria was 46%. MS is more prevalent in early stages of COPD (GOLD stage I and II).
- The three most prevalent MS components in COPD is hyperglycaemia, abdominal obesity and dyslipidaemia (Low HDL levels) with statistically significant association..
- The importance of the link between metabolic syndrome and COPD has highlighted the need for early diagnosis and appropriate management of both conditions in order to minimize the complications and to prevent morbidities and mortalities.

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