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Original Research Article

A study to investigate the prevalence of metabolic syndrome in Chronic Obstructive Pulmonary Disease patients from North India

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ABSTRACT

Background: Worldwide, Chronic obstructive pulmonary disease (COPD) is the one of the leading cause of chronic morbidity and mortality. COPD is one of the diseases in which smoking is the common and important risk factor when it is associated with Metabolic syndrome (MetS). The individual components of MetS, i.e., obesity, dyslipidemia, fasting hyperglycaemia, and hypertension were independently associated with impairment of lung function too. The objective of this study is to find out the prevalence of metabolic syndrome among COPD patients.
Methods: This was a cross-sectional study conducted in department of Respiratory Diseases and a total of 70 COPD patients were included in the study, which were enrolled for treatment from July 2016 to July 2017. The severity level in patients with COPD were determined according to GOLD (Global Initiative for Chronic Obstructive Lung Disease), 2015 guideline. International Diabetes Federation (IDF) guideline; (2005) was used in diagnosis of metabolic syndrome.
Results: Seventy patients with COPD were enrolled during the study period. There were 45 males (64.2%) and 25(35.7%) females. Mean age of male patients was 58.67±9.87 years, while mean age of female patients was 57.23±10.4 years (35-87 years). Mean BMI of male was 24.33±6.64 kg/m^2, while in case of female it was 30.07±6.95 kg/m^2 and overall mean BMI of study population was 26.22±7.22 kg/m^2. The mean waist circumference of male was 86.91±13.31 cm while in female it was 87.18±14.51 cm. The Overall prevalence of metabolic syndrome was 31.34% and most common in GOLD stage-3 (47.06%), followed by stage-2 (40%), followed by stage-4 (25.71%) and 7.4 % in GOLD stage -1.
Conclusions: The presence of metabolic syndrome is common in patients with COPD and, all COPD patients should be considered for screening for it.

Keywords: Chronic obstructive pulmonary disease, Metabolic syndrome, Obesity, Smoking

INTRODUCTION

Chronic obstructive pulmonary disease is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and / or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.[1] Cigarette smoking is the major risk factor for COPD.

COPD is reported to have an estimated disease burden of 210 million people worldwide.[2] Globally COPD was the fourth leading cause of death (5.1%) in 2004 and is projected to occupy the third position (8.6%) in 2030.[3]

India has a population of 1·35 billion people living in 28 states and nine union territories, and which often vary widely in terms of ecology, economy, and demography, all of which affect respiratory health.[4,5] Hence the risk factors for COPD are also likely to be different across various Indian states and regions. COPD accounts for about 500 000 deaths in India, which is more than four times the number of people who die due to COPD in USA and Europe.[6] A nationwide questionnaire-based study estimated the prevalence of COPD at 3.49% in India (ranging from 1.1% in Mumbai to 10% in Thiruvananthapuram).[7] The BOLD (Burden of obstructive lung disease) study conducted in Pune, Mumbai and Srinagar reported overall COPD prevalence estimates of 6.25%, 6.8% and 16.05%, respectively.[8]

Cigarette smoking causes not only local inflammation on lungs, but also systemic inflammation that is thought to contribute to the development of chronic diseases, like cardiovascular diseases, hypertension, osteoporosis, depression and diabetes mellitus.[9] Metabolic abnormalities like type 2 diabetes mellitus, obesity and the metabolic syndrome (MetS) are common in COPD.[10] Obesity is seen in approximately 18% of patients with COPD and is far more common in the early stage (stage - I and stage - II).[11]

Term Metabolic syndrome (MetS) is characterized by a group of risk factors (abdominal obesity, atherogenic dyslipidemia, raised blood pressure, insulin resistance) that increases the development of several diseases such as coronary artery disease, diabetes mellitus.[12,13] A link between metabolic syndrome (Met S) and COPD has been observed in several cross-sectional and longitudinal studies, and the syndrome has been identified as an independent risk factor for worsening respiratory symptoms, increasing lung function impairment, pulmonary hypertension, and asthma.[14,15]

Several studies from North America have shown a prevalence of Metabolic syndrome in COPD patients of 29 to 58%.[16-18] Tanni et al, report that Mets was found in 36 percent of their COPD patients.[19] Various other studies conducted in Europe, reported a prevalence of Mets in COPD patients of 21 to 57%.[20-25] In different studies from Middle East, the prevalence of Mets in COPD patients was 27-40%.[26-29] Some other studies from abroad, reported the prevalence of metabolic syndrome in COPD patients varies from 23% to 37%.[30-33]

Indian data on the prevalence of MetS or its components in COPD are sparse. Dave et al, reported MetS in 42% of their patients with COPD compared to 20% among age-matched controls.[34] In another study from North India, the prevalence of MetS was 27%; whereas in a yet another study from Himachal Pradesh, MetS was found in 70% of COPD cases compared to 30% among controls.[35,36]

The aim of this study was to investigate the prevalence of metabolic syndrome in COPD patients who were in different GOLD stages.

METHODS

This prospective study was conducted in 70 consecutive COPD patients attending the Department of Tuberculosis and Respiratory Diseases, G.S.V.M. Medical College, Kanpur and Government medical college, Kannauj from July 2016 to July 2017.

Inclusion criteria

COPD Patients who are clinically stable were included in the study.

Exclusion criteria

- Other respiratory diseases such as bronchial asthma, interstitial lung diseases, obstructive sleep apnea and lung cancer.
- Acute pulmonary tuberculosis infections
- Known case of Ischemic heart disease, hypertension, diabetes mellitus and chronic renal failure.
- Unstable COPD patients with acute exacerbation.

A detailed history and physical examination was carried out for every subject who entered in the study as per the pre-designed proforma. Patients were examined clinically and radiologically. All routine blood investigations were done. They were subjected to complete lipid profile after 12 hours fasting and plasma glucose estimation were done at fasting (at least eight hours fasting) glucose level and 2 hours after taking 75 grams Glucose orally (2 hours OGTT).

COPD was diagnosed with spirometry according to GOLD guideline 2015. Spirometry was performed using techniques that meet published standards. Both FEV 1 and FVC were the largest value obtained from any of the three technically satisfactory curves and FVC and FEV 1 values in these curves did not vary by more than 5% or 100 ml, whichever was greater. Bronchodilator reversibility testing was also performed by inhaled salbutamol 200 µg by metered dose inhaler via spacer, after withholding inhaled short acting bronchodilator for 6 hrs, long acting β2 agonists for 12 hrs and sustained release theophylline's for 24 hrs. Lung functions were again measured 10-15 minutes after the inhaled bronchodilator. Baseline dyspnoea was assessed using modified medical research council (MMRC) scale. Metabolic syndrome was defined as per new IDF definition; New International Diabetes Federation (IDF) definition; (2005).[37]

Central obesity (defined as waist circumference >90 cm for men and >80 cm for women, with ethnicity specific values for other groups) Plus any two of the following four factors:

- Raised TG level: >150 mg/dl (1.7 mmol/L), or specific treatment for this lipid abnormality.
- Reduced HDL cholesterol: <40 mg/dl in males and < 50 mg/dl in females, or specific treatment for this lipid abnormality.
- Raised blood pressure: systolic BP ≥130 or diastolic BP 85 mm Hg, or treatment of previously diagnosed hypertension.
- Raised fasting plasma glucose (FPG) ≥100 mg/dl (5.6 mmol/L), or previously diagnosed type 2 diabetes.

If above 5.6 mmol/L or 100 mg/dL, Oral Glucose Tolerance Test is strongly recommended but is not necessary to define presence of the syndrome.

Statistical analysis

Data was compiled using Microsoft excel and analyzed using SPSS, statistics version 20.0. Data were statistically described in terms of Mean±SD and range, or frequencies (number of cases), when appropriate. Categorical variables were analyzed using percentage and student's t test and p value less than 0.05 was considered significant.

RESULTS

Total 70 patients were taken for final analysis after exclusion criteria. Mean age of male patients was 58.67±9.87 years, while mean age of female patients was 57.23±10.4 years (35-87 years).

Majority of male were ex-tobacco smokers (46.3%) followed by tobacco smokers (13.4%) and 11.1% non-smokers. All females were nontobacco smokers and 31.3% gave history of biomass fuel exposure. (details of demographic parameter are given in (Table 1).

In present study overall percentage of obese, overweight, normal weight and underweight were 31.3%, 23.9%, 29.8% and 14.9% respectively. 50% female and 22.2% male were obese. Mean BMI of male was 24.33±6.64 kg/m^2, while in case of female it was 30.07±6.95 kg/m^2 and overall mean BMI of study population was 26.22±7.22 kg/m^2. The mean waist circumference of male was 86.91±13.31 cm while in female it was 87.18±14.51 cm.

All parameters of lipid profile were deranged in male except HDL which was more significant in female (58.3%). Among all parameters of lipid profile, raised triglyceride was found in majority of patients (69.4%) followed by LDL and total cholesterol (63.2%). HDL is considered decreased in Male <40 mg/dl and in Female <50 mg/dl. In female HDL was decreased in majority (58.3%) followed by LDL and total cholesterol (36.8%).

Diabetes were more in female (54.5%) than males (31.1%) and majority of male were nondiabetics (68.9%) than females (45.5%). Overall 38.8% patients were found diabetics or on antidiabetics drugs previously.

Maximum proportions of patients were in GOLD stage-3 (52.2%) followed by stage-2 (25.3%) followed by stage-4 (14.9%) and 7.4 % in GOLD stage -1.

Table 1: Description of study populations.

Parameter		Total populations (n=70)
Age		57.75±10.35
Sex	Male	45 (64.2%)
	Female	25 (35.7 %)
PY		8.94±15.76
FEV1/FVC ratio		57.48±7.74
Waist C		88.30±14.61
TG		161.94±73.17
HDL		53.22±12.64
SBP		133.85±23.39
FBS		104.13±20.81

Table 2: Comparison of various parameters between metabolic syndrome and non-metabolic syndrome COPD patients.

Parameter	COPD with metabolic syndrome (n=25)	COPD without metabolic syndrome (n=45)	Name of test (student t test)	p value	Significant/ Non-significant
Waist circumference	101±11.17	81.30±10.86	2.0047	0.329	Not significant
TG	202.26±97.72	140.86±94.81	2.0287	0.41	Not significant
HDL	50.26±12.12	54.77±12.76	2.0094	0.592	Not significant
Fasting blood sugar	133.22±21.06	99.39±20.06	2.0223	0.381	Not significant
Systolic BP	148.09±29.31	126.41±15.34	2.0527	0.0001	Significant

In present study, the prevalence of metabolic syndrome was most common in GOLD stage-3 (47.06%), followed by stage-2 (40%), followed by stage-4 (25.71%) and 7.4% in GOLD stage-1. The Overall prevalence of metabolic syndrome in the study was 31.34%. (Comparison of various parameters are given in (Table 2 and Table 3).

Table 3: Incidence of metabolic syndrome according to GOLD COPD staging.

GOLD COPD Stage	COPD with metabolic Syndrome (n=25)	COPD without metabolic Syndrome (n=45)	Total
Mild	2	4	6
Moderate	7	12	19
Severe	12	21	33
Very severe	4	8	12
Total	25	45	70

DISCUSSION

This prospective study was conducted on Chronic Obstructive Pulmonary Disease (COPD) patients attended Chest Hospital in Respiratory Medicine Department of GSVM Medical College Kanpur.

In present study, mean age of male patients was 58.67±9.87 years and mean age of females was 57.23±10.40 years and overall mean age of study population was 58.11±9.99 years. Alpaydin AO et al, in their study reported mean age for COPD and for control were 61.3±6.4 years and 58.4±8.4 years, respectively.[28] Bulcun E et al, had found mean age in their study 63.10±9.6 years, while in control population it was 60.9±10.6.[38] Mekov E et al, in their study had observed, mean age of patients was 65±10 years in which 71.1% were males, 28.9% were females.[39]

In present study majority of males were ex-tobacco smokers (46.3%) followed by tobacco smokers (13.4%) and 11.1% of males were non-smokers. All females were non-smokers (tobacco). Mekov E et al, found in their study that 15.8% of patients were never smokers, 57.9% ex-smokers and 26.3% current smokers.[39] In present study, maximum proportions of smokers were in GOLD stage-3 (70.6%) followed by stage-2 (60%) followed by stage-4 (57.1%) and in GOLD stage-1 smokers were 40% but the difference was not significant (p>0.05). Helvaci MR et al, had done study among COPD patients and found the prevalence of smoking in mild, moderate and severe COPD groups were 79.3%, 73.2%, 58.8% respectively.[40]

In present study, 47.5 % smoked <10 pack years, 22.5% smoked 10-19 pack years and 17.5% smoked 20-29 pack years and 12.5% smoked >40 pack years.

Lam KBH et al, found in their study Smoking exposure pack-yrs in male COPD, 30.4±26.5 while but in female COPD it was 2.1±9.1. In this study among smoker's pack years were evenly distributed among all four GOLD stages.[31] On the contrary there is mean pack years increased with the severity from mild to moderate COPD in the study of Helvaci MR et al, who found mean pack-years in mild COPD were 26.7±16.9 moderate COPD 34.8±16.7; and in severe COPD 36.8±18.6. (p <0.05 nearly in all steps).[40]

In present study Mean BMI of males was 24.33±6.64 kg/m^2, while in case of females it was 30.07±6.95 kg/m^2 and overall mean BMI of study population was 26.22±7.22 kg/m^2.

A study from Turkey had done and reported mean BMI of 28.2±4.4 kg/m^2, 29.6±4.3 kg/m^2, 26.8±5.0 kg/m^2 in mild, moderate and severe COPD groups respectively.[40] Another study reported mean BMI of 27.2±5.0 kg/m^2 and 27.6±4.7 kg/m^2 in COPD and control groups respectively.[40] Subsequent study from Netherland reported that mean BMI in COPD group and control group were 26.2±5.1 kg/m^2 and 27.3±4.2 kg/m^2 respectively.[28] Bulcun E et al, found BMI in COPD patients 26.3±4.8 kg/m^2 but in control it was 28.1±3.7 kg/m^2 in their study.[38] Yasar Z et al, found mean BMI in COPD 26.46±5.06 kg/m^2 while in control it was 27.52±3.19 kg/m^2.[41]

Prevalence of Metabolic Syndrome in the study was 31.34%. Metabolic syndrome was most common in GOLD stage two (47.06%) followed by stage one (40%) followed by stage three (25.71%) and it was only 20% in stage four but the difference between all four GOLD stages was statistically not significant.

Marquis K et al, had done a study to evaluate the presence of metabolic syndrome in 38 COPD patients and 34 control participants matched for age and gender. They further reported that 47% of COPD patients and 21% control had 3 or more determinants of metabolic syndrome.[15] Another study from France had done to evaluate the impact of overweight and obesity on the prevalence of metabolic syndrome and on the metabolic and inflammatory profiles in patients with 28 COPD patients (subdivided into overweight / obese group and normal weight group). They further concluded that metabolic syndrome was diagnosed in 50% of overweight / obese patients and none patients in normal weight group.[18] Watz et al, studied the frequency of coexisting metabolic syndrome in patients with chronic bronchitis (CB) and COPD of different stages. They included 30 patients with CB and 170 patients with COPD. Subsequently reported that frequency of metabolic syndrome in patients with chronic bronchitis and who had GOLD stages I, II, III, and IV were 53%, 50%, 53%, 37%, and 44% respectively (average, 47.5%) and it is observed a lower frequency of central obesity and lipid abnormalities among patients with severe and very severe

COPD compared to those with chronic bronchitis and mild-to-moderate COPD.[23] A study by Funakoshi et al, on 7189 Japanese males aged 45-88 years found that the prevalence of airflow obstruction was 9.0% in this study. The prevalence of airflow obstruction in this study population for GOLD stages I-IV was: 4.1% (n=297), 4.4% (n=318), 0.4% (n=26), and 0.1% (n=4), respectively.[32] Lam KBH et al, had done a study among 7,358 adults aged >50 years to know the associations between airflow obstruction and metabolic syndrome. They further reported that airflow obstruction was seen in 6.7% cases and international federation metabolic syndrome criteria were met by 20%. They further concluded that risk of metabolic syndrome was higher in those with airflow obstruction than those without (OR 1.47;95% CI).[31] Alpydin AO et al, had done study to investigate the prevalence of metabolic syndrome, carotid intima thickness (IMT) and CRP in COPD patients. They included 50 stable COPD patients and 40 healthy controls and further concluded that the risk of metabolic syndrome was 43% in COPD patients and 30% in control group.[28] DIez-Manglano J et al, had done a study among 375 hospitalize patients of COPD and found the overall prevalence of Metabolic Syndrome in COPD patients was 42.9%, being more frequent in female (59.5%) than male (40.8%), p=0.002, but with no differences in age and smoking.[20] Breyer et al, had done a study among 228 COPD patients and 156 healthy controls to know the prevalence of metabolic syndrome. they further concluded that metabolic syndrome was seen in 57% of COPD patients and 40% of healthy subjects.[22] A study from Bulgaria had been done to examine the prevalence of metabolic syndrome and its correlation with comorbidities in 152 stage 4 COPD patients. They further concluded that 25% patients with COPD have features of metabolic syndrome.[39] Amreen NM et al, had done a study to know the incidence of metabolic syndrome among 70 stable COPD patients and 20 healthy controls. They further highlighted that incidence of metabolic syndrome in mild, moderate, severe and very severe COPD groups were 11.1%, 34.8%, 25% and 50% respectively.[42]

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