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METABOLIC SYNDROME IN STABLE COPD PATIENTS AMONGST NORTH INDIAN POPULATION: A CASE CONTROL STUDY

Pulmonary Medicine

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ABSTRACT

Background: Metabolic syndrome predisposes the affected individual to cardiovascular disease and type 2 diabetes. The prevalence of metabolic syndrome in chronic obstructive airway disease (COPD) varies with ethnicity.

Aims: The aim of the present study was to investigate the frequency of metabolic syndrome in stable COPD patients compared to age and sex-matched controls from North India and to find any association of it with severity of COPD.

Settings and Design: A prospective analytical study conducted in the chest clinic of a tertiary care teaching hospital.

Material and methods: The study comprised of two groups involving 134 subjects including 67 stable COPD patients and an equal number of healthy controls for the presence of metabolic syndrome. The two groups were age and sex matched. Anthropometric measurements were taken. Fasting blood sample was collected to measure the blood glucose (FBG), triglyceride (TG), and high-density lipoprotein (HDL). The presence of metabolic syndrome was assessed using the modified NCEP ATP III criteria.

Results: The occurrence of metabolic syndrome was found to be significantly higher in the COPD patients (49.3%) than in control group (29.9%). Components of metabolic syndrome which were significantly more prevalent in the COPD patients included raised serum triglyceride, low HDL-C and hypertension. Although waist circumference, fasting glucose were more prevalent in the COPD patients but the difference was not statistically significant. The prevalence of metabolic syndrome was significantly more in obese COPD patients with GOLD stage II.

Conclusion: Metabolic syndrome is common among stable COPD patients. It is more prevalent in GOLD stage II patients who have a BMI> 25 kg/m^2.

KEYWORDS

Chronic obstructive pulmonary disease, metabolic syndrome

Introduction

The metabolic syndrome represents a cluster of risk factors that increases the risk for developing diabetes mellitus, nonfatal and fatal cardiovascular disease.[1,2] These risk factors include elevated fasting plasma glucose, abdominal obesity, dyslipidemia, and high blood pressure.[3] Chronic obstructive pulmonary disease (COPD) is among the leading causes of mortality and morbidity worldwide. In 1990, COPD ranked the sixth most common cause of mortality worldwide and was predicted to become the third most common cause of death, and the fifth most common cause of chronic disability by 2020.[4,5] COPD is a preventable and treatable disease with several extrapulmonary effects that may contribute to the severity in an individual patients. Exacerbations and co-existing morbidities further add to the overall severity in an individual patient and contribute to increased mortality [6]. Several studies from different parts of the world have shown the prevalence of metabolic syndrome in COPD patients to be between 25.6-60.9%.[7-10] Obesity, physical inactivity, cigarette smoking, corticosteroid use, systemic inflammation, oxidative stress and hypoxia are responsible mechanisms for the development of metabolic syndrome in COPD.[6,10] The prevalence of metabolic syndrome in COPD varies with ethnicity, lifestyle, severity of COPD and the criteria used to diagnose of metabolic syndrome. Indian data on the prevalence of metabolic syndrome in COPD is sparse.

In the present study we evaluated the prevalence of metabolic syndrome in COPD patients compared to healthy subjects amongst North Indian population and to see the relationship of metabolic syndrome with the severity of COPD.

Materials & Methods

Study population

This was a prospective observational analytical study involving 67 clinically stable COPD patients (COPD group) and 67 age and sex matched apparently healthy subjects (control group) attending the chest clinic of a tertiary teaching care teaching hospital in North India. The study was approved by the institutional ethical committee. An informed written consent was taken from all the subjects. Inclusion criteria for the COPD patients were: diagnosis of COPD, GOLD I–IV [11] and no respiratory tract infection or exacerbation at least 4 weeks prior to the study.

Exclusion criteria included any kind of malignancy less than 5 years prior to the study.

For all the subjects including both the COPD patients and the controls, data pertaining to demographic determinants [age, sex], personal habits [smoking, alcohol, tobacco], physical examination, anthropometric measurements [body weight, height, and waist circumference], laboratory investigations [complete blood hemogram, serum lipid profile, ECG and pulmonary function test,] were recorded on a predesigned structured performa.

Pulmonary function tests and interpretation

Pulmonary function tests were done using a dry rolling seal spirometer (Spiroflow, PK Morgan Ltd, Kent UK) as per the standard ATS guidelines. The measurements included forced expiratory volume in the first second (FEV1), forced vital capacity (FVC), and the ratio of FEV1 to FVC. The abnormalities on spirometery were categorized into normal, obstructive and restrictive pattern. The staging of COPD was made using GOLD criteria: GOLD I (mild): forced expiratory volume in 1 s (FEV1)/forced vital capacity (FVC) <70% and FEV1≥80%; GOLD II (moderate): FEV1/FVC<70% and FEV1<80 and ≥50%; GOLD III (severe): FEV1/FVC<70% and FEV1<50 and ≥30%; GOLD IV (very severe): FEV1/FVC<70% and FEV1<30% GOLD.[11]

Blood sampling and analyses

A venous blood sample was collected from each individual after a 12-h fasting. Plasma fasting glucose (FBG), triglyceride (TG), and high-density lipoprotein (HDL) were measured using fully automated analyzer Cobas 6000 (Roche Diagnostics International Ltd)

Fasting plasma glucose, serum cholesterol, triglyceride and HDL-C were measured by enzymatic, colorimetric method. Impaired fasting glucose (IFG) was defined according to 2004 ADA definition [12] as fasting plasma glucose (FPG) ≥100mg/dL to <126mg/dL, and individuals with a FPG ≥126mg/dL or history of diabetes or on hypo-

glycaemic medication were classified as having diabetes regardless of the measured FPG values.

Diagnosis of metabolic syndrome

BMI was calculated by dividing the weight by the height squared (kg/m2). The blood pressure was measured according to the American Heart Association's recommendations [13]. The waist

circumference was measured according to the procedure of Airlie Conference recommendations [14]. The revised National Cholesterol Education Program's Adult Treatment Panel III was used in the diagnosis of metabolic syndrome [15]. According to the revised NCEP criteria diagnosis of metabolic syndrome require at least three of the following:(1) abdominal obesity (waist circumference ≥90cm for Asian men or ≥80cm for Asian women), (2) triglycerides ≥150mg/dL, (3) HDL cholesterol ≤40mg/dL for men or 50mg/dL for women, (4) systolic/diastolic blood pressure ≥130/85mmHg or receiving drug treatment, and (5) fasting plasma glucose ≥100mg/dL. If the participants were using antihypertensive or antidiabetic medication, they were considered to have had high blood pressure or diabetes mellitus.

Statistical analysis:

Data were reported as mean ± SD or proportions. Statistical analysis was performed by unpaired *t* test. A p-value < 0.05 was considered statistically significant. The analysis was performed using SPSS version 20.0

Results

The study involved 67 stable COPD patients diagnosed and classified according to the GOLD criteria. There were 60 (89.5%) men and 7(10.5%) females with an overall mean age of 63.2 ± 7.5 years. The control group comprised of 67 healthy volunteers (62 men and 5 women) with a mean age of 63.7 ± 7.3 years. There was no difference in the mean age and gender distribution of the two groups (Table 1).

Table 1: Baseline characteristics of COPD patients and Healthy controls

	COPD patients (n = 67)	Healthy controls (n = 67)	p value
Age	63.2 ± 7.5	63.7 ± 7.3	0.3268
Male	60 (89.5)	62 (92.5)	0.8650
BMI, kg/m2	26.3 ± 4.5	27.3 ± 4.2	0.066
Smokingstatus			
Neversmoker, %	7 (10.4)	56 (83.6)	0.0001
Formersmoker, %	40 (59.7)	11 (16.4)	0.0001
Currentsmoker, %	20 (29.8)	0	--
Pack years, n	25.1 ± 5.8	3.5 ± 1.1	0.0001
FEV1, %pred	53.2 ± 17.8	104.4 ± 16.8	0.0001
FVC, %pred	91.8 ± 18.3	118.8± 23.3	0.0001
FEV1/FVC	43.3 ± 12.5	77.1 ± 7.5	0.0001
Waist circumference, cm	89.2 ± 14.5	84.7 ±13.6	0.9819
Fasting glucose level, mg/dL	104.5 ± 21.5	90.9 ± 12.6	0.9901
Serum triglyceride level, mg/dL	176.7 ± 16.3	138.7 ± 14.8	0.0001
HDL level, mg/dL	35.5 ±7.6	48.3±8.5	0.0001
Systolic blood pressure, mmHg	148.8 ± 20.9	134.7 ± 18.3	0.001
Diastolic blood pressure, mmHg	82.3 ± 11.3	78.3 ± 9.1	0.0118
High waist circumference, %	26 (38.8)	16 (23.9)	0.0623
High glucose level, %	28 (41.8)	18 (26.9)	0.0687
High triglyceride level, %	32 (47.7)	15 (22.4)	0.0020
Low HDL level, %	19 (28.4)	5 (7.4)	0.0016
Hypertension	29 (43.3)	22 (32.8)	0.2113
Metabolic syndrome, %	33 (49.3)	20 (29.9)	0.0214

The staging of COPD as assessed by using GOLD criteria revealed 7.5% had stage I, 47.8% had stage II, 32.8% had III and 11.9% had stage IV (Table 2) disease.

Table 2: Distribution of COPD cases based on GOLD

Severity of COPD based on GOLD	Distribution of COPD cases (n=67)
GOLD I	5 (7.5)
GOLD II	32 (47.8)
GOLD III	22 (32.8)
GOLD IV	8 (11.9)

The prevalence of metabolic syndrome in the patient with COPD was found to be much higher than in the control group (49.3 vs. 29.9%) (p=0.009).The distribution of metabolic syndrome according to GOLD stages was 3% in stage I, 57.6% in stage II, 33.3% in stage III and 6.1% in stage IV(Table 3).

Table 3: Occurrence of Metabolic syndrome according to severity of COPD based on GOLD

Severity of COPD based on GOLD	Metabolic syndrome present (n=33)	Metabolic syndrome present		
		BMI < 25 (kg/m2) (n= 11)	BMI > 25 (kg/m2) (n= 22)	p value
GOLD I	1 (3.0)	0 (0)	1 (4.5)	--
GOLD II	19 (57.6)	5 (45.4)	14 (63.6)	0.0065
GOLD III	11 (33.3)	5 (45.4)	6 (27.3)	0.5892
GOLD IV	2 (6.1)	1 (9.1)	1 (4.5)	0.9364

The parameters of metabolic syndrome were evaluated in both the COPD patients and the control groups (Table 1). The comparison of each metabolic parameter between COPD patients and control group revealed higher serum triglycerides in COPD than the control group (mean 176.7 ± 16.3 vs 138.7 ± 14.8) with statistical significance (p = 0.001). Although the fasting blood sugar and waist circumference were higher in COPD patients than control group but the difference was not statistical significance. HDL was significantly (p = 0.0001) lower in COPD patients (35.5 ±7.6) than the control group (48.3±8.5). Both the Systolic BP (mean 148.8 ± 20.9 vs 134.7 ± 18.3) and diastolic BP (mean 80.3 ± 11.3 vs 78.3 ± 9.1) were significantly higher in COPD patients than the healthy controls. The comparison of the percent of each component of the metabolic syndrome between COPD patients and control group revealed that in COPD patients, 47.7 % had elevated triglyceride levels, 43.3% had hypertension, 41.8% had elevated fasting glucose levels, 38.8 % had abdominal obesity and 28.4% had low HDL-C levels. In the control group 32.8% had hypertension, 26.9% elevated fasting glucose levels, 23.9% abdominal obesity, 22.4% elevated triglycerides and 7.4% had low HDL-C levels (Table 1). Further on comparing the occurrence of Metabolic syndrome among obese (BMI > 25 kg/m2) and non- obese (BMI< 25 kg/m2) COPD patients it was observed that metabolic syndrome was much more common in obese COPD patients and especially so in those with stage II COPD. (Table3)

Discussion:

Metabolic syndrome, also known as insulin resistance syndrome or syndrome X is not a disease but a cluster of characteristics. These characteristics include obesity, high blood pressure, elevated blood sugar levels, and high triglycerides. Metabolic syndrome is associated with the risk of developing cardiovascular disease and type 2 diabetes. [1,2] The insight in the pathogenesis of COPD has changed a lot over the last decades with the description of the disease having moved from a simple airflow limitation-centric outlook to a systemic inflammatory condition with significant extrapulmonary manifestations including cardiovascular disease, skeletal muscle dysfunction, and diabetes. Ethnicity-based regional differences in the prevalence of comorbidities in COPD may exist. In Japanese COPD patients, cardiovascular disease and metabolic syndrome were found to be less frequent while osteoporosis and malnutrition were more common.[16] In another study from Korea there was no association between COPD and a higher prevalence of diabetes among COPD patients.[17] In the present study we evaluated the prevalence of metabolic syndrome in COPD patients compared to healthy subjects amongst North Indian population. In this study, using the modified NCEP ATP III criteria, we found a strong trend of higher proportion ($P < 0.0214$) of metabolic syndrome (49.3%) in COPD patients as compared to healthy individuals (29.9%). The proportion of metabolic syndrome in COPD patients was comparable with previous studies. Several studies from different parts of the world have shown the prevalence of metabolic syndrome in COPD patients to be between 25.6-60.9%. [7-10] A meta-analysis of 19 studies involving 4208 COPD patients reported metabolic syndrome in 34% of their patients. [18] Dave *et al*. reported metabolic syndrome in 42% of their patients with COPD compared to 20% among age-matched controls.[19] In another study from Kashmir by Shah *et al*.[20] the prevalence of metabolic syndrome was 27% in COPD patients. In a study from Himachal Pradesh, metabolic syndrome was found in 70% of COPD cases compared to 30% among controls.[21]The differences in the prevalence of metabolic syndrome in COPD may partly be explained by the severity of COPD as well as by diverse criteria used to diagnose of it.

In the present study the metabolic syndrome was significantly higher in patients with stage II COPD as compared to other stages. This is in consistent with previous studies. A study by Funakoshi *et al*. found that patients with GOLD staging II - IV have a high probability of having co-existent metabolic syndrome with an odds ratio of 1.33. [7] Another study by Watz *et al*. reported the frequency of metabolic syndrome to be 53%, 50%, 37%, and 44% in GOLD stage I, II, II and IV, respectively (average, 47.5%). [10] In the Canadian study by Marquis *et al* the frequency of metabolic syndrome in COPD patients was 47 %, and the frequency reduced to about 10 % for GOLD stages III and IV. [22]Metabolic syndrome was more common in the GOLD II, COPD may be related higher influence of lifestyle on body composition and metabolic health in lesser advanced disease compared to COPD induced triggers on the wasting process in advanced disease.

Further, on analyzing the association of individual components of metabolic syndrome it was observed that serum triglycerides, systolic blood pressure and diastolic blood pressure were significantly higher in COPD as compared to apparently healthy individuals. While HDL was significantly lower in COPD patients as compared to controls. Although fasting glucose level and waist circumference were higher in the COPD group but lied outside the statistical significance. Very few studies are available on the association of COPD with individual components of metabolic syndrome. Marquis *et al.* [22] showed SBP, HDL-C, and low-density lipoprotein as statistically significant in patients with COPD.

In the present study metabolic syndrome was more prevalent in COPD patients with BMI>25 kg/m^2 than those with BMI< 25 kg/m^2. A few recent studies have shown that patients with obstructive lung disease have more visceral fat mass compared to healthy subjects [23]. It is unclear why abdominal obesity is more common in COPD patients compared to healthy volunteers, but several factors including inadequate nutrition, inactive lifestyle and ongoing inflammation may play a role [23].

Conclusion

The present study shows that metabolic syndrome is frequent in obese patients with COPD especially stage II COPD (GOLD). Primary physicians should screen COPD patients for associated metabolic syndrome and manage it aggressively to reduce the risk of cardiovascular morbidity and mortality.

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