Original Article

Prevalence of metabolic syndrome in chronic obstructive pulmonary disease and its correlation with severity of disease

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Abstract

Introduction: The understanding of chronic obstructive pulmonary disease (COPD) has changed considerably over the past decade. The metabolic syndrome (MS) represents a cluster of risk factors that increases the risk for developing various noncommunicable diseases. In COPD, it is associated with worsening respiratory symptoms, increasing lung function impairment, pulmonary hypertension, and increasing hospitalizations. **Aims:** To determine the prevalence of MS in patients with COPD and correlate it with disease severity. **Methodology:** The present study was a cross-sectional observational study. Patients confirmed by spirometry to have COPD were included in the study. All demographic data and anthropometric, radiological, and laboratory parameters were recorded. The definition stated by modified NCEP ATP III criteria proposed by the AHA/NHLB (2005) was followed to identify patients with MS. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 20 for Windows. **Results:** A total of 76 patients were included in the study. MS was recorded in 42.1% of COPD cases. The average number of exacerbations and hospitalizations due to COPD in MS cases (1.38 ± 1.95 and 0.97 ± 1.51) were more than the patients without MS (1.27 ± 1.30 and 0.68 ± 0.96). The majority of patients with MS exhibited grade 3 dyspnea based on modified medical research council grading (MMRC). MS was commonest in patients with GOLD stage III disease. High serum triglyceride level was observed in an increasing trend (25%, 30%, 35.5%, and 75%) in GOLD stages I, II, III, and IV, respectively. **Conclusion:** Patients with MS present with more severe disease and frequent exacerbations. All COPD patients should be screened for MS at the primary level.

Keywords: Blood pressure, COPD, dyspnea, metabolic syndrome, triglycerides

Introduction

Chronic obstructive pulmonary disease (COPD) is a major cause of health care burden throughout the world and the only leading cause of death that is increasing in prevalence.[1] COPD is a complex and heterogeneous condition with significant extrapulmonary manifestations, which include cardiovascular disease, skeletal muscle dysfunction, and diabetes. COPD is associated with a variety of systemic manifestations. Metabolic syndrome (MS) has been recognized to coexist with COPD.[2]

MS is generally defined as a cluster of five components: high blood pressure (BP), high triglyceride level (TG), low high-density

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lipoprotein cholesterol (HDL), abdominal obesity, and a high glucose level.[3] It was first described in 1988 by Reaven and is also known as insulin resistance syndrome or Syndrome X.[4] A link between MS and COPD has been observed in several studies, and the syndrome has been identified as an independent risk factor for worsening respiratory symptoms, increasing lung function impairment, pulmonary hypertension, and asthma.[5]

It has been postulated that obesity, smoking, sedentary lifestyle, and systemic inflammation may play a role in its development.[2] Systemic inflammation is found to be more severe in COPD patients with MS as compared to patients with COPD alone.[6] The prevalence of MS in people with COPD has been estimated to be between 21% and 53%.[2] Indian data on the prevalence of MS or its components in COPD are sparse. Dave *et al.*[7] reported MS in 42% of their patients with COPD compared to 20% among age-matched controls. COPD patients with MS have more dyspnea and are at a greater risk of hospitalization either due to acute exacerbations or other complications. In India, most COPD patients are initially treated by primary physicians. If MS is detected at the primary level by primary physicians, then the risk of hospitalization can be minimized.

Smoking, the principal risk factor for developing COPD, has been considered to be one of the main causes of increased systemic inflammation, which explains the connection between MS and COPD.[8] Systemic inflammation promotes insulin resistance, which contributes to the development of MS in people with COPD.[9] It was observed in one study that MS is more prevalent in female patients and in patients with less severe COPD and high BMI.[10] The current study was conducted to find out the proportion of MS in COPD cases and its correlation between severities of COPD. This study will help in the practice of primary physicians to search for MS components in COPD patients at an early stage so that management can be individualized.

Methodology

Study area

The present study was conducted in the Department of Pulmonary Medicine, VIMSAR, Burla, Sambalpur, Odisha.

Study population

COPD patients of both sexes attending out-patient or getting admitted to the Department of Pulmonary Medicine, VIMSAR, Burla were included in the study.

Study design

It was a hospital-based cross-sectional study.

Inclusion criteria

Patients were diagnosed with COPD based on the global initiative for chronic obstructive pulmonary disease (GOLD) guidelines, history, clinical examination, and pulmonary function test.

Exclusion criteria

Patients with asthma, other chronic respiratory diseases, active pulmonary tuberculosis, malignancy, serious comorbidities, and patients using systemic corticosteroid in the preceding 3 months were excluded from the study.

Ethical consideration

The study proposal was recommended by the ethical committee of VIMSAR, Burla.

Procedure

A total of 76 consecutive patients with a diagnosis of COPD were included. A questionnaire was prepared in the local language, and data were collected from patients ensuring their privacy and confidentiality. The data related to demographic characteristics (age, sex, ethnicity, education, occupation, and monthly income) and lifestyle (smoking habit, and exercise) were collected in a simple and understandable language. All routine investigations including lipid profile and fasting and 2-h post-prandial blood sugar (FBS and 2-h PPBS, respectively) were performed. Informed and written consent was obtained from all the participants after explaining the procedure.

The anthropometric parameters (height, weight, and waist circumference) were measured by proper procedure. Standing body height (to the nearest 0.5 cm) was measured using a commercial stadiometer. A digital weighing machine, with an accuracy of ± 100 g, was used to measure body weight (BW).

Metabolic syndrome

Systolic and diastolic blood pressure (SBP/DBP), fasting blood glucose, serum HDL, TG levels, and waist circumference were used to determine whether participants had MS. SBP and DBP were measured twice at 3-min intervals after 15-min rest for each participant, and mean SBP and DBP were calculated for analysis. Fasting blood glucose and TG levels were tested during the morning session after an 8–12-h fast. Waist circumference was measured at the uppermost lateral border of the right ileum at the end of a participant's normal expiration of breath.

The definition of MS was based on the modified NCEP ATP III criteria proposed by the AHA/NHLBI (2005), which included three or more of the following parameters to ascertain the presence of MS:

a. Abdominal obesity [waist circumference (WC): men ≥90 cm, women ≥80 cm]
b. Triglyceride (TG) levels ≥150 mg/dL or drug treatment for elevated TG levels,
c. High-density lipoprotein (HDL) levels of <40 mg/dL in men and <50 mg/dL in women or drug treatment for reduced HDL levels,
d. Systolic blood pressure (SBP) ≥130 mm Hg or diastolic blood pressure (DBP) ≥85 mm Hg or antihypertensive treatment with a history of hypertension and
e. Fasting glucose (FBS) level of ≥100 mg/dL or drug treatment for elevated glucose levels.[10,11]

Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 20 for Windows. Continuous variables were presented as mean ± standard deviation and categorical variables as percentages. Chi-square test was used to determine the associations between categorical variables. Evaluation of group differences in means for continuous variables was done using the unpaired student's *t* test and for categorical variables by Chi-square test. $P < 0.05$ was considered significant.

Results

The present study was a hospital-based cross-sectional study constituting 76 COPD cases, out of which MS was recorded in 42.1% (32) COPD cases. The majority of the patients were in the age group of 60–69 years (30 cases), followed by 50–59 years (28 cases). The mean age of COPD patients was 62.92 ± 8.97 years. The average age of the cases having MS (61.9 ± 8.03 years) was lower than that of the cases without MS (63.63 ± 9.63 years). The prevalence of COPD in females was 22.4%, but MS was observed in 37.5% of female patients. The average BMI in patients with MS was higher than that of patients without MS. A significant difference was observed between BMI in patients with MS and without MS by *t*-test analysis [Table 1].

The study revealed that the metabolic parameters were on the higher side in COPD cases with MS than those without MS, whereas serum HDL level of patients with the syndrome was found to be lower than that in the cases without MS.

The mean FEV1% in cases with MS was higher than the patients without MS (47.56 ± 11.51 and 46.36 ± 14.40). The present study revealed that the number of exacerbations and hospitalizations due to COPD in MS cases were more than those for patients without MS, which was statistically nonsignificant [Table 1].

Most of the patients were farmers by occupation (34.2%) and belonged to a lower socioeconomic class (63.2%). The majority of the patients were smokers, that is, current smokers (29%) or ex-smokers (34.2%). Unexpectedly, no significant relationship was observed between smoking status and MS in patients with COPD. Interestingly, in patients with MS, the non-smokers (53.1%) were more than the smokers.

Cough was complained by 90.8% of cases, followed by expectoration in 73.7% of patients and wheezes in 47.4% of cases. In this study, 50% patients of with MS exhibited grade 3 dyspnea.

All metabolic parameters were higher in females. Among the various components of MS, increased waist circumference was found in 70.6% of female patients, but it was observed in 16.9% of male patients, which was statistically significant. It was proved statistically that the prevalence of MS between male and female COPD cases was significant [Table 2].

Patients with or without MS presented with GOLD stage III disease predominantly [Table 3]. All components of MS were highest in patients presenting with stage III disease. Chi-square test analysis recorded the distribution of high glucose among different stages of COPD, which was significant [Table 4].

Discussion

The present study constitutes 76 diagnosed COPD cases, out of which MS was recorded in 42.1% of COPD cases as per modified NCEP ATP III criteria. This was in accordance with Dave *et al.*,[7] Díez-Manglano *et al.*,[12] and Acharyya *et al.*,[13] who reported 42%, 42.9%, and 46.7% cases of MS among COPD cases in their study, respectively. However, a slightly higher percentage of MS were reported by a few studies.[14-16]

The mean age of COPD patients was 62.92 ± 8.97 years with a M: F ratio of 3.5:1. MS was reported in 12 out of 17 (70.6%)

Table 1: Demographic and functional profile of COPD patients

Demographic and functional profile	COPD With MS	COPD Without MS	*t*	Total
No of cases (%)	32 (42.1%)	44 (57.9%)	-	76 (100%)
Sex (male %)	20 (62.5%)	39 (88.6%)	-	59 (77.6%)
Age (yrs)	61.94±8.03	63.63±9.63	0.839^{NS}	62.92±8.97
BMI (kg/m^2)	23.56±4.33	19.09±3.19	5.175^{S}	20.97±4.30
FEV1%	47.56±11.51	46.36±14.40	0.389^{NS}	46.87±13.19
FEV1/FVC	57.59±8.41	52.6±11.4	2.138^{S}	54.74±10.50
No. of exacerbation in last 1 yr	1.38±1.95	1.27±1.30	0.275^{NS}	1.32±1.59
No. of hospitalization in last 1 yr due to COPD	0.97±1.51	0.68±0.96	1.011^{NS}	0.80±1.22
WC (cm)	86.04±13.60	72.5±10.14	4.982^{S}	78.21±13.45
SBP (mm Hg)	135.69±14.34	126.93±16.45	2.415^{S}	130.61±16.10
DBP (mm Hg)	74.87±8.88	72.48±7.49	1.274^{NS}	73.49±8.14
FBS (mg/dL)	128.72±43.47	100.91±2.33	3.950^{S}	112.61±33.13
Serum TG (mg/dL)	158.56±32.99	123.82±35.51	4.337^{S}	138.45±38.36
Serum HDL (mg/dL)	38.75±9.40	49.84±9.20	−5.141^{S}	45.17±10.75

*BMI: body mass index; FEV1: forced expiratory volume in 1 second; FVC: forced vital capacity; WC: waist circumference; SBP: systolic blood pressure; DBP: diastolic blood pressure; FBS: fasting blood sugar; TG: triglycerides; HDL: high-density lipoproteins. S: significant; NS: not significant

female and 20 out of 59 (33.9%) male patients in the present study. This was in accordance with Díez-Manglano *et al.*[12] who found 40.8% male and 59.5% female cases having MS.

The average BMI in patients with MS was recorded as 23.56 ± 4.33 kg/m^2, which was higher than that of patients without MS (19.09 ± 3.19 kg/m^2), which was significant by *t*-test analysis. Previous studies have also established the connection between BMI and MS in people with COPD.[14,17]

The mean FEV1% in patients with MS (47.56 ± 11.51) was higher than the mean FEV1% of the patients without MS (46.36 ± 14.40). The average FEV1/FVC% was also higher in cases with MS than those without the syndrome. This indicated that the patients with MS had less airflow obstruction than those without it. These findings were in accordance with a study by Díez-Manglano *et al.*[12] who found mean FEV1% of MS patients (45 ± 12.1) higher than the cases without MS (41.8 ± 12.4) and also FEV1/FVC% in MS (55 ± 10) higher than those without the syndrome (51 ± 10). In a multivariate analysis, greater FEV1 and comorbidities were independently associated with MS. Weight loss associated with severity of COPD can explain the association between MS and greater spirometric values.

The average number of exacerbations and hospitalizations due to COPD in MS cases (1.38 ± 1.95 and 0.97 ± 1.51) were more than in patients without MS (1.27 ± 1.30 and 0.68 ± 0.96), which was statistically nonsignificant. The presence of comorbidities such as heart failure perhaps can partly explain this observation. This finding goes against that observed by Díez-Manglano *et al.*[12] who found no increase in exacerbations and hospitalizations due to COPD in the last 1 year.

There was a significant difference between cases with MS and without MS with respect to WC, SBP, FBS, and serum TG. The serum concentration of HDL was also significantly lower in cases with MS than that of the control group. There was a significant difference in the metabolic parameters in COPD patients with and without MS, whereas the difference in functional parameters was found to be nonsignificant. This finding was supported by Ameen *et al.*[18] However, Silviu *et al.*[19] noted a significant difference between the COPD patients with and without MS with respect to both functional lung parameters, represented mainly by FEV1 and the 6-min walk test and metabolic parameters.

Fifty percent of patients with MS exhibited grade 3 dyspnea. The difference between the grade of dyspnea of cases with and without MS was nonsignificant. This was consistent with the study by Díez-Manglano *et al.*[12] However, the study by Park *et al.*[16] found that people with MS had more dyspnea than those without MS. The more dyspnea in this study may be due to the delayed health-seeking behavior of the patients.

When metabolic parameters were compared among men and women, surprisingly, all parameters of MS were more in females than male cases. A surprising finding in this study was 70.6% female and 33.9% male COPD patients had MS. This was in contrast to the statement of Marquis *et al.*[14] who found 61% male and 27% female COPD cases with MS. The high prevalence of MS in females in this study may be due to lesser outdoor activity and sedentary lifestyle. The higher proportion of abdominal obesity among female as in this study would also have been a contributing factor.

Less number of patients with MS presented with stage IV disease, similar to previous studies.[14,20] In contrast, the study by Ameen *et al.*[18] found the highest proportion of MS cases in GOLD stage IV. Thus, the incidence of MS is not directly related to severity of COPD. Thus, all COPD patients should be screened for MS irrespective of stages.

The frequency of hospitalization and pharmacy costs were higher in patients with MS than in those without MS, especially

Table 2: Prevalence of components of MS between males and females with MS

Components of MS	Male (*n*=59)	Female (*n*=17)	χ^2	Total (*n*=76)
Increased WC (%)	10 (16.9%)	12 (70.6%)	15.945^S	22 (28.9%)
High glucose level (%)	21 (35.6%)	9 (52.9%)	1.016^{NS}	30 (39.5%)
High BP (%)	33 (55.9%)	12 (70.6%)	0.645^{NS}	45 (59.2%)
High Serum TG (%)	22 (28.9%)	6 (35.3%)	0.018^{NS}	28 (36.8%)
Low HDL level (%)	19 (32.2%)	10 (58.8%)	2.915^{NS}	29 (38.1%)
Metabolic syndrome (%)	20 (33.9%)	12 (70.6%)	7.324^S	32 (42.1%)

*WC: waist circumference; BP: blood pressure; TG: triglyceride; HDL: high-density lipoproteins. S: significant; NS: not significant

Table 3: GOLD staging in cases with and without MS

GOLD stages	With MS	Without MS	Total
I (Mild)	1 (3.1%)	3 (6.8%)	4 (5.3%)
II (Moderate)	10 (31.2%)	10 (22.7%)	20 (26.3%)
III (Severe)	19 (59.4%)	29 (65.9%)	48 (63.1%)
IV (Very Severe)	2 (6.3%)	3 (4.6%)	4 (5.3%)

N.B. Chi-square value=1.120 nonsignificant at 5% level (*P*>0.05) for D.F=3

Table 4: Components of MS by GOLD spirometric classification

Components of MS	Stage I (*n*=4)	Stage II (*n*=20)	Stage III (*n*=48)	Stage IV (*n*=4)	χ^2
Central Obesity	1 (25%)	8 (40%)	12 (25%)	1 (25%)	1.612^{NS}
High Glucose	1 (25%)	13 (65%)	14 (29.2%)	2 (50%)	8.125^S
High BP	4 (100%)	15 (75%)	23 (47.9%)	3 (75%)	7.768^{NS}
High TG	1 (25%)	6 (30%)	18 (35.5%)	3 (75%)	3.155^{NS}
Low HDL	1 (25%)	8 (40%)	18 (37.5%)	2 (50%)	0.569^{NS}

*BP: blood pressure; TG: triglyceride; HDL: high-density lipoproteins. S: significant; NS: not significant

in women.[21] Efforts must be made to identify MS in COPD patients in the early phase by primary physicians to reduce health care costs. As the prevalence of MS in COPD in our community is high and with a greater risk of exacerbation and hospitalization in those patients, it is necessary to screen for MS in all cases of COPD at the primary level for prediction of exacerbation and hence plan its management accordingly.

Conclusion

MS was recorded in approximately half of the COPD cases. The difference between the grade of dyspnea of cases with and without MS was nonsignificant. The average number of exacerbations and hospitalizations due to COPD in MS cases was more than the number of patients without MS. All the metabolic parameters in our study were higher in females than males. The highest frequency of MS was observed in GOLD stage III. Higher levels of systolic blood pressure, diastolic blood pressure, FBS, serum triglyceride, and waist circumference were recorded in COPD patients with MS. There was a significant difference in the metabolic parameters in COPD patients with and without MS, whereas the difference in functional parameters was found to be nonsignificant.

MS is associated with a greater risk of exacerbations and hospitalizations due to COPD. High blood pressure, blood sugar level, and abnormal lipid profile in these patients may add to the overall morbidity and disease outcome. Thus, screening for MS in all COPD patients should be practiced by all primary physicians at the time of diagnosis, follow-up, and treatment. Simultaneous treatment of both entities can help reduce the exacerbations and associated complications in these patients.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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