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ORIGINAL RESEARCH

Assessment of prevalence of the metabolic syndrome in COPD patients and its correlation with severity of COPD and components of metabolic syndrome

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ABSTRACT

Introduction: Extrapulmonary consequences of COPD appears to be linked to systemic inflammation. Metabolic syndrome represents a cluster of risk factors that increases the risk for developing various non-communicable diseases. It is currently unclear how metabolic syndrome, a significant factor in systemic inflammation in general population, and COPD are related.

Aim: To assess the prevalence of the metabolic syndrome in COPD patients and its correlation with severity of COPD and components of metabolic syndrome.

Methodology: The present study was a cross-sectional observational study. Patients were included after performing spirometry. All demographic data, anthropometric and laboratory parameters were recorded. COPD severity level was determined according to GOLD 2021 guideline. Metabolic syndrome was identified according to South Asian Modified National Cholesterol Education Program criteria. Statistical analysis was done using Statistical Package for the Social Sciences (SPSS) 21. Comparison of quantitative variables between the study groups was done using the Student t-test.

Results: A total of 183 COPD patients, confirmed by spirometry, from January 2021 to September 2022 were included in the study. In 34.42% of COPD patients, metabolic syndrome was recorded. Males outnumbered females. Amongst 63 COPD patients with metabolic syndrome, 74.60% were males and 25.39% were females. Amongst 120 COPD patients without metabolic syndrome 74.16% were males and 25.83% were females. COPD patients with metabolic syndrome had significant association with high BMI, more waist circumference, elevated SBP and DBP, elevated FBS, elevated serum TG and low serum HDL as compared to COPD patients without metabolic syndrome. Most of the (49.20%) COPD patients with metabolic syndrome were in GOLD stage III followed by stage II (39.68%), stage IV (9.52%) and stage I (1.58%). While most of the (50.83%) COPD patients without metabolic syndrome were in GOLD stage III followed by stage II (40.83%), stage IV (6.66%) and stage I (1.66%).

Conclusion: The present study demonstrated that there is higher prevalence of metabolic syndrome and its parameters among COPD patients.

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Key words: Metabolic syndrome, Chronic obstructive pulmonary disease

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common, preventable and treatable disease which is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities. COPD is the result of a complex interplay of long-term cumulative exposure to noxious gases and particles, combined with a variety of host factors including genetics, airway hyper-responsiveness and poor lung growth during childhood.[1-3]

Most patients with COPD are middle-aged or elderly. It is a slowly progressing disease with a long asymptomatic phase, during which lung function continues to decline. The clinical manifestations of COPD include predominantly pulmonary symptoms like cough, expectoration, breathlessness and wheeze. Patients usually present with the first acute exacerbation of COPD at an advanced stage.[4]

The pathophysiological mechanism in COPD can be explained as the inflammation [increased number of neutrophils, macrophages, and T lymphocytes (CD8 more than CD4)] in the lungs. These inflammatory cells release a variety of cytokines and mediators that participate in the disease process. Patients with COPD have evidence of systemic as well as airway inflammation with elevation of WBC, CRP, IL-6, IL-8, TNF-alpha and fibrinogen demonstrated in COPD compared to control subjects.[5] This inflammatory plethora ultimately leads to tissue destruction, impairment of the defense mechanisms that limit such destruction, and disruption of the repair mechanism. Pathological changes can be described as loss of elasticity of the alveolar attachments, or their destruction.[6] In addition to inflammation, two other processes are involved in the pathogenesis of COPD, namely an imbalance between proteases and antiproteases and an imbalance between oxidants and antioxidants (oxidative stress) in the lungs. These pathogenic mechanisms result in the pathological changes found in COPD. This amplified response may result in mucous hypersecretion (chronic bronchitis), tissue destruction (emphysema), and disruption of normal repair and defense mechanisms causing small airway inflammation and fibrosis (bronchiolitis).[7] Concomitant chronic diseases occur frequently in COPD patients, such as cardiovascular disease, skeletal muscle dysfunction, osteoporosis, depression, anxiety, lung cancer including metabolic syndrome (MetS).[8]

MetS is a cluster of metabolic risk factors such as hypertension, abdominal obesity, dyslipidemia and insulin resistance that predisposes affected patients with systemic inflammation, cardiovascular disease and physical inactivity.[9] Low grade inflammation has been described as the common pathway responsible for MetS and comorbidities in COPD.[10]

The association of MetS in various stages of COPD is still not known. Despite this crucial relationship, studies on MetS in COPD are limited. Moreover, timely diagnosing and treating the components of MetS may result in fewer exacerbations and improve quality of life in patients with COPD. However, there is paucity of data for the prevalence of MetS in patients with COPD in Kumaon region of Uttarakhand. Therefore, the present study was aimed to figure out the prevalence of the MetS in COPD patients and its correlation with severity of COPD and components of MetS.

METHODOLOGY

The present study was conducted in the Department of Respiratory Medicine, Government Medical College, Haldwani (Uttarakhand) from January 2021 to September 2022. It was a hospital based cross-sectional observational study. The targeted population were all suspected COPD patients attending Respiratory Medicine OPD of Dr. Susheela Tiwari Government Hospital, Haldwani.

Inclusion criteria

- Age ≥ 18 years of either sex
- Diagnosed case of COPD irrespective of duration of illness or treatment

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- No signs of exacerbation of COPD within 1 month of the study i.e. lack of hospitalization, urgent care visits, antibiotic use, or changes in medications
- Newly diagnosed case with spirometric findings (FEV1/FVC < 0.7, FEV1 ≤ 80% of predicted)
- Newly diagnosed case on clinic-radiological basis in which spirometry could not be performed due to any reason.

Exclusion criteria

- Seriously ill patients
- Respiratory disease other than COPD
- Patients with history of coronary artery disease and/or decompensated cardiovascular disease and stroke
- Inflammatory co-morbid illnesses such as inflammatory bowel disease, rheumatologic disease etc.
- Known Type 2 Diabetes Mellitus
- Patient immobilized for more than six months or bedridden
- Not willing individuals

Information from the participants were collected by in-depth interview using pre-designed, pre-tested semi-structured questionnaire based on the objectives in simple and understandable language. The information obtained included socio-demographic details such as age, sex, height, weight, BMI, marital status and religion, relevant history of duration of illness, smoking, alcohol, tobacco habit, education, occupation and residence status, and pre-existing respiratory or non-respiratory disease. A detailed clinical and physical examination was done. Blood pressure was checked by using sphygmomanometer in sitting position. The abdominal circumference was measured at level of iliac crest during normal expiration using a non-expandable measuring tape in standing position. Baseline investigations were performed in all study participants: Complete Blood Count (Hemoglobin, Packed Cell Volume, Total Leucocyte Count, Platelet Count), Liver Function Test (Serum Bilirubin, Alkaline Phosphatase, Serum Glutamic Oxaloacetic Transaminase, Serum Glutamic Pyruvic Transaminase), Kidney Function Test (Serum Urea, Serum Creatinine), Serum Sodium and Serum Potassium, Fasting Blood Glucose, Post-prandial Blood Glucose, Serum Triglycerides and Serum High Density Lipoprotein-Cholesterol.

COPD was diagnosed with spirometry according to GOLD guideline 2021.[11] Spirometry was done by using GANSHORN MEDIZIN ELECTRONIC PFT System with Diffusion Capacity in sitting position at Respiratory Medicine Department. Spirometry was performed before and after post-bronchodilator short acting β-agonist. Though the inclusion criteria also had patients diagnosed clinic-radiologically for COPD but later, suspected COPD patients were diagnosed as COPD only after they met spirometric criteria. Patients were categorized on the basis of airflow limitation severity using GOLD's criteria 2021.[11]

Metabolic syndrome was identified according to South Asian Modified National Cholesterol Education Program (SAM-NCEP) criteria.[12] According to SAM NCEP criteria, an individual is said to have metabolic syndrome if he/she has three or more of the following conditions:

- Central obesity: Waist circumference >90 cm (Male), >80cm (Female)
- Hypertriglyceridemia: Triglycerides ≥ 150 mg/dl or specific medication
- Low HDL cholesterol: <40 mg/dl (Male) and <50mg/dl (Female) or specific medication
- Hypertension: Blood pressure ≥130 mmHg systolic or ≥85 mmHg diastolic or specific medication
- Fasting plasma glucose ≥100 mg/dl or specific medication

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Statistical analysis

Data was described in terms of range, mean, +/- standard deviation (SD), frequencies (number of cases), and relative frequencies (percentages) as appropriate. Comparison of quantitative variables between the study groups was done using the Student t-test. For comparing categorical data, the Chi-square (X2) test was performed and an exact test was used when the expected frequency was less than 5. A probability value (p-value) less than 0.05 was considered statistically significant. All statistical calculations were done using SPSS 21 (Statistical package for the Social Science) version statistical program for Microsoft Windows.

RESULTS

A total of 183 COPD patients, confirmed by spirometry, from January 2021 to September 2022 were included in the study. Figure 1 shows that in the present study the incidence of metabolic syndrome in COPD patients was 34.42%. Males outnumbered females. Amongst 63 COPD patients with metabolic syndrome 74.60% were males and 25.39% were females. Amongst 120 COPD patients without metabolic syndrome 74.16% were males and 25.83% were females.

COPD patients with metabolic syndrome had significant association with high BMI, more waist circumference, elevated SBP and DBP, elevated FBS, elevated serum TG and low serum HDL as compared to COPD patients without metabolic syndrome. Most of the (49.20%) COPD patients with metabolic syndrome were in GOLD stage III followed by stage II (39.68%), stage IV (9.52%) and stage I (1.58%). While most of the (50.83%) COPD patients without metabolic syndrome were in GOLD stage III followed by stage II (40.83%), stage IV (6.66%) and stage I (1.66%). According to different GOLD staging, no statistically significant difference was found in between components of metabolic syndrome.

Figure 1: Pie chart of incidence of Metabolic Syndrome in COPD patients

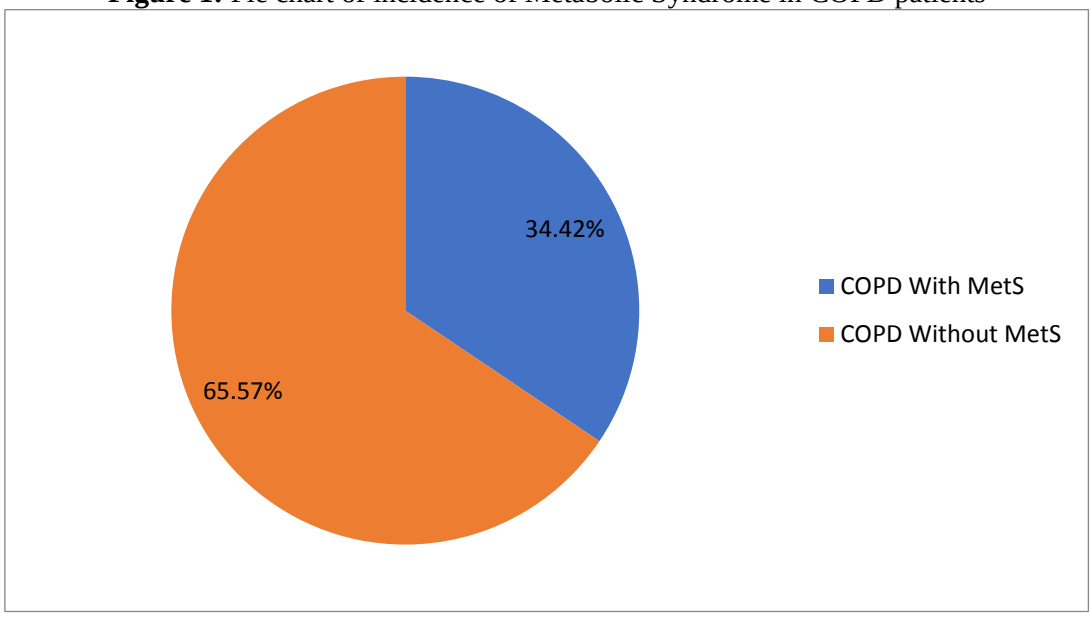

Table 1: Distribution of study subjects according to gender

Gender	**COPD With MetS (63)**		**COPD Without MetS (120)**		**Total (183)**	
	N	Percentage	N	Percentage	N	Percentage
Male	47	74.60%	89	74.16%	136	74.31%
Female	16	25.39%	31	25.83%	47	25.68%

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Table 2: Distribution of study subjects according to functional profile

Functional profile	COPD With MetS (Mean ±SD)	COPD Without MetS (Mean ±SD)	P value
Duration of disease (years)	6.80 ±4.38	6.67±4.78	0.85
BMI (kg/m2)	22.30±4.66	20.15±4.64	0.002
Waist circumference (cm)	87.84±11.88	81.55±9.84	0.002
FEV1 (liter)	1.55±0.53	1.65±0.56	0.24
FEV1/FVC	0.58±0.08	0.59±0.07	0.38
SBP (mm Hg)	128.12±18.90	116.2±16.28	0.0001
DBP (mm Hg)	83.39±10.45	75.13±9.33	0.0001
FBS (mg/dL)	115.11±43.54	93.14±15.90	0.0001
Serum TG (mg/dL)	150.12±26.97	113.74±21.06	0.0001
Serum HDL (mg/dL)	42.42±6.99	51.00±6.75	0.0001

Table 3: Distribution of study subjects according to GOLD staging

GOLD stages	COPD With MetS (63)		COPD Without MetS (120)		Total (183)	
	N	Percentage	N	Percentage	N	Percentage
I (Mild)	1	1.58%	2	1.66%	3	1.63%
II (Moderate)	25	39.68%	49	40.83%	74	40.43%
III (Severe)	31	49.20%	61	50.83%	92	50.27%
IV (Very Severe)	6	9.52%	8	6.66%	14	7.65%

Table 4: Distribution of study subjects according to components of Metabolic Syndrome by GOLD spirometric classification

Components of MetS	Stage I (Mild)		Stage II (Moderate)		Stage III (Severe)		Stage IV (Very severe)	
	N	Percentage	N	Percentage	N	Percentage	N	Percentage
Central Obesity (41)	1	2.43%	14	34.14%	22	53.65%	4	9.75%
High Fasting Blood Glucose (49)	1	2.04%	19	38.77%	25	51.02%	4	8.16%
High BP (41)	1	2.43%	15	36.58%	21	51.21%	4	9.75%
High TG (42)	0	0%	19	45.23%	18	42.85%	5	11.9%
Low HDL (36)	0	0%	16	44.44%	17	47.22%	3	8.33%
P VALUE	0.9831							

DISCUSSION

The present study constituted 183 diagnosed COPD cases out of which the incidence of metabolic syndrome was 34.42%. This was in accordance with the studies done by Dave L et al[13], Diez Manglano J et al[14] and Acharyya A et al[15] who reported 42%, 42.9%, and 46.7% cases of MetS among COPD cases in their study, respectively.

Amongst COPD patients with MetS, most common risk factor was smoking (61.90%) followed by multiple exposure (22.22%), biomass fuel exposure (14.28%), and none (1.58%). While amongst COPD patients without MetS, most common risk factor was smoking (58.33%) followed by multiple exposure (21.66%), biomass fuel exposure (15%), occupational exposure (4.16%) and none (0.83%). 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[16], found in their study that 15.8% of patients were never smokers, 57.9% ex-smokers and 26.3% current smokers.

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Most (52.38%) of the COPD patients with MetS were from urban areas and 47.61% were from rural areas. Most of the COPD patients without MetS were from rural areas (59.16%) and 40.83% were from urban areas. In COPD patients with MetS, 1 (100%) urban patient was under GOLD stage I. 11 (44%) rural and 14 (56%) urban patients were under GOLD stage II. 15 (48.38%) rural and 16 (51.61%) urban patients were under GOLD stage III. 4 (66.66%) rural and 2 (33.33%) urban patients were under GOLD stage IV. On comparison of resident status of male COPD patients with MetS with various components of metabolic syndrome, no significant difference was found in between central obesity, high fasting glucose, high blood pressure, high triglycerides and low HDL. While comparing resident status of female COPD patients with MetS with various components of metabolic syndrome, no significant difference was found in between central obesity, high fasting glucose, high blood pressure and low HDL but a significant difference was found in between high triglycerides (P value = 0.03). Female COPD patients who were residing in urban area had significant association of MetS without high TG levels.

Harikrishnan S et al[17] found prevalence of MetS to be 24% using NCEP ATP III criteria. They also found that participants living in urban areas had higher prevalence of Metabolic Syndrome (26%) than rural population (22%). It is estimated that the approximately 5.91 million and 16.3 million people in urban and rural areas are suffering from COPD respectively and approximately one-third of the urban Indian population are estimated to have Metabolic Syndrome. Metabolic Syndrome prevalence is twice common in COPD patients compared to general population. Several studies conducted across the world and India has found out the prevalence to be between 25.6 to 60.9 %.[18,19]

Most of the COPD patients with MetS were farmers (26.98%) followed by homemakers (23.80%), in service (23.80%), self-employed (15.87%), transport workers (6.34%), in business (1.58%) and 1.58% were not working. While amongst COPD patients without MetS, most of the patients were farmers (33.33%) followed by homemakers (25%), self-employed (14.16%), in service (13.33%), factory workers (6.66%), not working (3.33%), transport workers (2.5%) and in business (1.66%). Sahoo KC et al in their study also reported that most of the patients were farmers by occupation (34.2%).[20]

COPD patients with MetS had significant association with high BMI, more waist circumference, elevated SBP and DBP, elevated FBS, elevated serum TG and low serum HDL as compared to COPD patients without metabolic syndrome. Previous studies have also established the connection between BMI and MetS in people with COPD.[21,22] This finding was supported by Ameen N et al[23]. Silviu S et al[24] also noted a significant difference between the COPD patients with and without MetS. The prevalence of diabetes in COPD is approximately about 3-12%. A study by Engstrom G et al[25] described that reduced lung function is an important risk factor for the development of diabetes in COPD. An epidemiological study conducted by Lam KBH et al[26] showed results that metabolic syndrome (22.6% versus 19.8%), central obesity (34.1% versus 33.1%) and raised blood pressure (56.7% versus 53.4%) were more common in individuals with airflow obstruction than in those with normal lung function, the opposite was seen for raised fasting glucose level (34.3% versus 36.9%), raised triglyceride level (29.6% versus 33.4%) and reduced HDL–cholesterol level (15.9% versus 16.6%).

Most of the (49.20%) COPD patients with metabolic syndrome in the present study were in GOLD stage III followed by stage II (39.68%), stage IV (9.52%) and stage I (1.58%). While most of the (50.83%) COPD patients without metabolic syndrome were in GOLD stage III followed by stage II (40.83%), stage IV (6.66%) and stage I (1.66%). Less number of patients with MetS presented with stage IV disease, similar to previous studies.[27,28] In contrast, the study by Ameen N et al[23] found the highest proportion of MetS cases in GOLD stage IV. Thus, the incidence of MetS is not directly related to severity of COPD. Thus, all COPD patients should be screened for MetS irrespective of stages.

According to different GOLD staging, no statistically significant difference was found in between various components of MetS. On gender wise comparison of various components of MetS in COPD patients, no significant difference was found in between central obesity, high fasting glucose, high

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blood pressure and high triglycerides. But a statistically significant difference was found (P value = 0.00063) on gender wise comparison of low HDL. Female COPD patients with MetS had very high significant association with low HDL.

Gender wise comparison of various components of MetS with moderate airflow limitation (Stage II) in COPD patients provided no significant difference between central obesity, high fasting glucose, high blood pressure, high triglycerides and low HDL. On gender wise comparison of various components of MetS with severe airflow limitation (Stage III) in COPD patients, no significant difference was found in between central obesity, high fasting glucose, high blood pressure and high triglycerides. On gender wise comparison of low HDL with severe airflow limitation (Stage III) in COPD patients, a statistically significant difference was found (P value = 0.0036). Female COPD patients having severe airflow limitation with MetS were very high significantly associated with low HDL. On gender wise comparison of various components of metabolic syndrome with very severe airflow limitation (Stage IV) in COPD patients, no significant difference was found in between central obesity, high fasting glucose, high blood pressure, high triglycerides and low HDL.

CONCLUSION

The present study demonstrated that there is higher prevalence of metabolic syndrome and its parameters among COPD patients. Thus, considering COPD as a systemic disease and screening for components of metabolic syndrome could form a part of routine work-up of these patients. In COPD patients, the clinical management will be necessary to carefully consider, diagnose and treat all these potential co-morbidities and their underacting mechanisms.

LIMITATIONS

Small sample size due to low in-flow of patients visiting OPD because of lockdown and limited OPD hours during COVID-19 pandemic.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethical Committee

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