IMPACT OF METABOLIC SYNDROME ON SEVERITY OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) a common preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. **Aim of the study**: This study aimed to determine the impact of Metabolic Syndrome in patients with chronic obstructive pulmonary disease. **Patients and methods:** This study was carried out on 60 subjects of both sexes, who were presented to Chest Outpatient Clinic. Patients were presented with signs and symptoms of COPD and proven radiologically, according to the GOLD guidelines. Subjects were categorized into two groups; 30 COPD patients with Metabolic Syndrome (group A) and 30 COPD patients without Metabolic Syndrome (group B). **Results:** There are 22 men and 8 women in the group of COPD with Metabolic Syndrome with mean age of 56.73 years, while in the group of COPD without Metabolic Syndrome, there were 19 men and 11 women with mean age of 61.1 years. The percentage of current smokers was high in all groups. There were statistically significant differences between the studied groups regarding BMI and waist circumference**.** There were statistically significant differences between the studied groups regarding systolic and diastolic blood pressure, fasting blood glucose, HbA1c, total cholesterol, LDL cholesterol and serum triglycerides. Regarding spirometry measures, there are statistically significant differences

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between the studied groups. Regarding GOLD, there was statistically non-significant difference between the studied groups**.** The frequency of Metabolic Syndrome was the highest in COPD patients in GOLD stage II. **Conclusion**: The presence of Metabolic Syndrome is substantial among COPD patients, especially in early stages (GOLD stages I−II). When the components of Metabolic Syndrome were evaluated separately, abdominal obesity, hypertension, and hyperglycemia were significantly more in both patients'group.

Key words: chronic obstructive pulmonary disease, Metabolic Syndrome

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) a common preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients (GOLD, 2018).

Chronic Obstructive Pulmonary Disease is now one of the top three causes of death worldwide and 90% of these deaths occur in low- and middle-income countries (GOLD,2022). More than 3 million people died of COPD in 2012 accounting for 6% of all deaths globally. COPD represents an important public health challenge that is both preventable and treatable. COPD is a major cause of chronic morbidity and mortality throughout the world; many people suffer from this disease for years and die prematurely from it or its complications. Globally the COPD burden is projected to increase incoming

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decades because of continued exposure to COPD risk factors and aging of the population (GOLD, 2022).

Metabolic Syndrome is a cluster of conditions; increased blood pressure, high blood sugar, excess body fat around the waist, and abnormal cholesterol or triglyceride levels that occur together, increasing your risk of heart disease, stroke and diabetes. (National Heart, Lung, and Blood Institute, 2016).

COPD patients with Metabolic Syndrome are physically less active and have increased levels of systemic inflammation compared to COPD patients without Metabolic Syndrome (Watz et al., 2009).

COPD is complex disease with multiple systemic comorbidities and complications. The comorbidities such as diabetes, hypertension, coronary disease, heart failure, and osteoporosis are more frequent when both COPD and Metabolic Syndrome coexists, COPD patients with the Metabolic Syndrome have a severe form of disease, dyspnea, a lower forced expiratory volume in one second and require inhalational glucocorticoids to control the disease. The prevalence of Metabolic Syndrome and its comorbidities increases with advancing age (Díez-Manglano *et al*., 2014).

Aim of the study:

This study aimed to determine the impact of Metabolic Syndrome on severity of chronic obstructive pulmonary disease.

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SUBJECTS AND METHODS

1. Study setting

This comparative cross-sectional study was done in Chest Outpatient Clinic in Naser City Police Hospital from March 2017 till January 2020.

2. Study subjects:

The study was carried out on 60 COPD patients of both sexes, who were presented to Chest Outpatient Clinic for regular follow up. The patients were categorized into two groups:

Group A: 30 COPD patients with metabolic syndrome.

Group B: 30 COPD patients without metabolic syndrome.

Inclusion criteria

- Cases were selected from COPD patients attending chest outpatient clinic for regular follow up. The Diagnosis of COPD will be based on the modified criteria defined in the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines, and had irreversible/ partially reversible obstruction of airflow. COPD patients had a post-bronchodilator FEV1<80% of the predicted value, along with an FEV1/FVC% not >70%. They had an increase in FEV1< 200 mL, or < 12% of baseline value 20 minutes after 4 puffs of inhaled salbutamol (400 µg) given via a metered-dose inhaler.
- Patients were classified into COPD group with metabolic syndrome and COPD group without metabolic syndrome.

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- **The diagnosis of metabolic syndrome:**
- Body weight and height were measured and the 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. Blood pressure measurements were obtained from both arms in the supine position after a 15-min resting period and the highest measurement was used for analysis (Perloff *et al*., 1993). The waist circumference was measured according to the procedures of Airlie Conference (Lohmann and Roche, 1988). The National Cholesterol Education Program's Adult Treatment Panel III (table 1) was used in the diagnosis of metabolic syndrome (Grundy *et al.*, 2004). If the participants were using antihypertensive or antidiabetic drugs, they were considered to have had high blood pressure or high fasting glucose.

Table (1): The National Cholesterol Education Program's Adult Treatment Panel III criteria for the diagnosis of metabolic syndrome

Abdominal obesity, given as the waist circumference	
Male	>102 cm (>40 inch)
Female	>88 cm (>35 inch)
Triglycerides	≥150 mg/dl
HDL cholesterol	
Male	<40 mg/dl
Female	<50 mg/dl
Blood pressure	≥130/≥85 mmHg
Fasting glucose	≥110 mg/dl

- HDL, High-Density Lipoprotein

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- The presence of three of the five criteria explained above was diagnostic for metabolic syndrome.

Exclusion criteria: Exclusion criteria for this study are as follows:

Patients with liver disease, renal disease, chronic heart failure, malignancies, asthma, other chronic respiratory disorder and active pulmonary tuberculosis.

3. **Methods:** All patients included in the study were subjected to the followings:

A- Thorough medical history taking:

- Personal data (name, age and gender).
- Present history of medical conditions.
- Medical history.

B- Clinical examination:

Complete physical examination was done with emphasis on vital signs (heart rate, systolic and diastolic blood pressure, respiratory rate and temperature).

C- Laboratory investigations:

- Complete blood picture (hemoglobin, white blood count and platelet count).
- Arterial blood gases (ABG).
- Kidney function tests (KFTs) and liver function tests (LFTs) to exclude renal, hepatic and hematologic disorders.
- Measurement of blood glucose levels both fasting and HbA1c.
- Serum total cholesterol (TC).
- Serum triglycerides (TG).

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- High Density Lipoprotein cholesterol (HDL-c).
- Low Density Lipoprotein cholesterol (LDL-c).

D- Chest X-ray and P-A view.

E- The BODE index:

It is a tool that is used by healthcare professionals to predict the mortality rate (death rate) from chronic obstructive pulmonary disease

B - Body mass index

Body Mass Index is a simple calculation using a person's height and weight. The formula is BMI = kg/m2 where kg is a person's weight in kilograms and m2 is their height in meters squared. A BMI of 25.0 or more is overweight, while the healthy range is 18.5 to 24.9. BMI applies to most adults 18-65 years.

O - Airway obstruction

Forced expiratory volume in one second (FEV1) is a measure of the amount of air that can be forcefully exhaled in one second. The forced vital capacity (FVC) measurement shows the amount of air a person can forcefully and quickly exhale after taking a deep breath. The ratio FEV1/FVC, therefore, represents the total percentage of air that can be exhaled in one second. A normal FEV1/FVC ratio in adults is 0.70 or greater. If there is an obstruction in the airways slowing or preventing this rapid exhalation of air, the ratio decreases.

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D - Dyspnea

Dyspnea is the term that refers to the physical sensation of shortness of breath or breathlessness. The Modified Medical Research Council dyspnea scale (mMRC) is frequently used to evaluate dyspnea related to COPD. In this measurement, breathlessness is measured on a scale of 0 to 4:

- **mMRC Grade 0**: Breathless with only strenuous exercise
- **mMRC Grade 1**: Short of breath when hurrying or walking up a slight hill
- **mMRC Grade 2**: Walks slower than peers on level ground because of breathlessness or has to stop for breath when walking at own pace
- **mMRC Grade 3**: Stops for breath after walking 100 meters or after a few minutes
- **mMRC Grade 4**: Too breathless to leave the house or breathless when dressing or undressing

E - Exercise tolerance

Exercise tolerance refers to how active someone is able to be with the restrictions put forth by their lung disease. A test called a 6-minute walk test.How to **calculate BODE score?**

The BODE score ranges from 0 to 10 points. Each variable is scored as follows:

VARIABLE	0 POINTS	+ 1 POINT	+ 2 POINTS	+ 3 POINTS
FEV1 (% of predicted)	≥65	50–64	36–49	≤35
6MWD test	≥350 m	250–349 m	150–249 m	≤149 m
BMI	>21	≤21	-	-
MMRC dyspnea scale	0 or 1 point	2	3	4

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BODE index interpretation

BODE index interpretation as a 4-year survival is presented below:

- A BODE score of ***0 to 2 points*** is associated with ***80% survival***;
- A score of ***3 to 4 points - 67% survival***;
- A score of ***5 to 6 points - 57% survival***; and
- A score of ***7 to 10 points - 18% survival***.

F- Pulmonary function tests:

The amount of air inhaled and exhaled in test results are compared to the average for someone of the same age, height, sex, and race. Results are also compared to any of previous test results.

PULMONARY FUNCTION TEST	NORMAL VALUE (95 PERCENT CONFIDENCE INTERVAL)
FEV_1	80% to 120%
FVC	80% to 120%
Absolute FEV_1 /FVC ratio	Within 5% of the predicted ratio
TLC	80% to 120%

4. Statistical analysis:

Data were entered checked and analyzed using Epi-Info version 6 and SPP (Service Pack for Proliant) for Windows version 8. Data were summarized using the arithmetic mean, the standard deviation, median, student t test and chi-squared test.

Correlation between variables was done using correlation coefficient "r". This test detects if the change in one variable was accompanied by a corresponding change in the other variable or not.

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For all above mentioned statistical tests done, the threshold of significance is fixed at 5% level (p-value).

The results were considered:

- Significant when the probability of error is less than $p < 0.05$, highly significant when the probability of error is $p < 0.001$.

5. **Ethical considerations:** An informed consent was taken from every patient before conducting the study.

RESULTS

Table (2): Comparison between the two studied groups regarding demographic data

PARAMETER	GROUPS		TEST	
	COPD with Metabolic Syndrome	**COPD without Metabolic Syndrome**	χ^2 / t	p
	N=30	**N=30**		
Gender: Male Female	 22 (73.3) 8 (26.7)	 19 (63.3) 11 (36.7)	0.693	0.405
Age (year): Mean ± SD	 56.73 ±8.48	 61.1 ±8.4	-2.004	0.05
Smoking: No Yes	 10 (33.3) 20 (66.7)	 9 (30) 21 (70)	0.077	0.781
SI: Mean ± SD	 22.1 ±2.36	 21.32 ±6.92	0.499	0.622

COPD: Chronic obstructive pulmonary disease SI: Smoking index

SD: Standard deviation χ^2: Chi square test t: Independent sample t test

There is statistically non-significant difference between the studied groups regarding age, gender, history of smoking or smoking index.

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Table (3): Comparison between the two studied groups regarding anthropometric data

PARAMETER	GROUPS		TEST	
	COPD with metabolic syndrome N=30	COPD without metabolic syndrome N=30	T	P
	Mean ± SD	Mean ± SD		
BMI (kg/m^2)	27.76 ±3.23	22.22 ± **1.67**	8.32	<0.001**
Waist circumference	96.53 ±11.54	87.13±4.5	4.158	<0.001**

COPD: Chronic obstructive pulmonary disease BMI: Body mass index

SD: Standard deviation t: Independent sample t test

**p≤0.001 is statistically highly significant

There is statistically significant difference between the studied groups regarding BMI and waist circumference (both were significantly higher in the group of COPD with metabolic syndrome).

Table (4): Comparison between the two studied groups regarding blood pressure

BLOOD PRESSURE (MMHG)	GROUPS		TEST	
	COPD with metabolic syndrome N=30	COPD without metabolic syndrome N=30	T	P
	Mean ± SD	Mean ± SD		
Systolic	137.33 ± 11.72	119.67 ± 6.56	7.203	<0.001**
Diastolic	89.67 ±8.19	76.0 ±4.81	7.88	<0.001**

COPD: Chronic obstructive pulmonary disease SD: Standard deviation

t: Independent sample t test **p≤0.001 is statistically highly significant

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There is statistically significant difference between the studied groups regarding systolic and diastolic blood pressure (both were significantly higher in the group of COPD with metabolic syndrome).

Table (5): Comparison between the two studied groups regarding glycemic and lipid profile

PARAMETER	GROUPS		TEST	
	COPD with Metabolic Syndrome N=30	COPD without Metabolic Syndrome N=30	T	P
	Mean ± SD	Mean ± SD		
HbA1c (%)	5.77 ± 0.57	5.22 ± 0.5	3.996	<0.001**
Fasting blood glucose (mg/dL)	107.07 ± 14.86	95.7 ± 9.65	3.513	0.001**
Total cholesterol (mg/dL)	216.17±33.16	193.5±37.44	2.482	0.016*
LDL (mg/dl)	156.5±35.38	136.0 ±39.81	2.108	0.039*
HDL (mg/dL)	51.6±7.65	49.83±9.3	0.804	0.425
Triglycerides (mg/dL)	207.5 ± 29.91	162.33 ± 20.5	6.823	<0.001**

COPD: Chronic obstructive pulmonary disease SD: Standard deviation
Hb1Ac: Glycated hemoglobin LDL: Low-density lipoprotein
HDL: High-density lipoprotein
t: Independent sample t test *p<0.05 is statistically significant
**p≤0.001 is statistically highly significant

There is statistically significant difference between the studied groups regarding fasting blood glucose, HbA1c, total cholesterol, LDL cholesterol and serum triglycerides (all were significantly higher in the group of COPD with Metabolic Syndrome). There is statistically non-significant difference between the studied groups regarding HDL cholesterol.

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Table (6): Comparison between the two studied groups regarding spirometry measures

PARAMETER	GROUPS		TEST	
	COPD with Metabolic Syndrome N=30	COPD without Metabolic Syndrome N=30	T	P
	Mean ± SD	Mean ± SD		
FVC (%)	85.67 ± 4.33	90.4 ± 3.64	-4.588	<0.001**
FEV1 (%)	63.53 ± 9.92	69.7 ± 13.35	-2.031	0.047*
FEV1/FVC	0.74 ± 0.1	0.77 ± 0.16	-0.706	0.484
FEF_{25-75}	62.83 ± 7.68	70.1 ± 4.8	-4.393	<0.001**

COPD: Chronic obstructive pulmonary disease SD: Standard deviation
FVC: forced vital capacity FEV1: forced expiratory volume in one second
FEF: Forced Expiratory flow
t independent sample t test *$p<0.05$ is statistically significant
**$p\leq0.001$ is statistically highly significant

There is statistically significant difference between the studied groups regarding FEV1, FVC, and FEF_{25-75} (all were significantly lower in the group of COPD with Metabolic Syndrome). There is statistically non-significant difference between the studied groups regarding FEV1/FVC.

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Table (7): Comparison between the two studied groups regarding exacerbation in the last year

PARAMETER	GROUPS		TEST	
	COPD with Metabolic Syndrome	COPD without Metabolic Syndrome	Z	p
	N=30	N=30		
Exacerbation: Median Min - max	3 1 – 5	2 1 – 4	-2.577	0.01*

COPD: Chronic obstructive pulmonary disease
Z: Mann Whitney test *p<0.05 is statistically significant

There is statistically significant difference between the studied groups regarding exacerbation in the last year (it was significantly more frequent in the group of COPD with Metabolic Syndrome).

Table (8): Comparison between the two studied groups regarding GOLD stages

SPIROMETRY GRADES	GROUPS		TEST	
	COPD with Metabolic Syndrome	COPD without Metabolic Syndrome	χ^2	P
	N=30	N=30		
GOLD I (Mild)	1 (3.3)	9 (30)	2.869	0.09
GOLD II (Moderate)	23 (76.7)	15 (50)		
GOLD III (Severe)	6 (20)	6 (20)		

COPD: Chronic obstructive pulmonary disease
GOLD: Global Initiative For Chronic Obstructive Lung Disease
χ^2: Chi square for trend test

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There is statistically non-significant difference between the studied groups regarding GOLD classification (76.7% within COPD with metabolic syndrome group versus 50% within COPD only group had GOLD II class).

Table (9): Comparison between the two studied groups regarding Modified Medical Research Council (mMRC) dyspnea scale

MMRC	GROUPS		TEST	
	COPD with Metabolic Syndrome	COPD without Metabolic Syndrome	χ^2	P
	N=30	N=30		
Dyspnea on strenuous exercise	2 (6.7)	7 (23.3)	19.125	<0.001**
Dyspnea on straight hills	6 (20)	18 (60)		
Dyspnea on walking ground level	11 (36.7)	5 (16.7)		
Dyspnea after walking 100 yards	9 (30)	0 (0)		
Dyspnea on doing daily activities	2 (6.7)	0 (0)		

COPD: Chronic obstructive pulmonary disease
χ^2: Chi square for trend test **p≤0.001 is statistically highly significant

There is statistically significant difference between the studied groups regarding Modified Medical Research Council dyspnea scale (36.7% within COPD with Metabolic syndrome group versus 16.7% within COPD only group had dyspnea on walking on ground level. No patient with COPD only had dyspnea after walking 100 yards versus 30% of those within COPD with Metabolic Syndrome group).

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Table (10): Comparison between the studied groups regarding six-minute walking scale

SIX-MINUTE WALKING SCALE	GROUPS		TEST	
	COPD with metabolic syndrome	COPD without metabolic syndrome	χ^2	p
	N=30	N=30		
≥350 meters	4 (13.3)	9 (30)	4.409	0.036*
250 – 349 meters	13 (43.3)	15 (50)		
150 – 249 meters	8 (26.7)	4 (13.3)		
Less than 150 meters	5 (16.7)	2 (6.7)		

COPD: Chronic obstructive pulmonary disease
χ^2 Chi square for trend test **p≤0.001 is statistically highly significant

There is statistically significant difference between the studied groups regarding six-minute walking scale (16.7% within COPD with Metabolic Syndrome group versus 6.7% within COPD only group can walk only for <150 meters. 30% of patients with COPD versus 13.3% of those within COPD with Metabolic Syndrome group can walk for ≥350 meters).

Table (11): Comparison between the studied groups regarding BODE index

PARAMETER	GROUPS		TEST	
	COPD with Metabolic Syndrome	COPD without Metabolic Syndrome	T	p
	N=30	N=30		
BODE index				
Mean ± SD	5.23 ± **2.08**	3.07 ± **1.6**	4.528	<0.001**
Min - max	1 – 10	0 – 7		

COPD: Chronic obstructive pulmonary disease
BODE: B, Body mass index; O, airway Obstruction; D, Dyspnea; E, Exercise tolerance
t: Independent sample t test **p≤0.001 is statistically highly significant

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There is statistically significant difference between the studied groups regarding BODE index which was significantly higher in the group of COPD with Metabolic Syndrome.

Table (12): Correlations of BODE index with age, anthropometric, blood pressure and smoking index of the studied patients

PARAMETERS	BODE INDEX	
	R	P
Age (year)	-0.084	0.525
SI	-0.028	0.86
BMI (kg/m^2)	0.526	<0.001**
Waist circumference (cm)	0.469	<0.001**
Systolic blood pressure (mmHg)	0.529	<0.001**
Diastolic blood pressure (mmHg)	0.454	<0.001**

BODE: B, Body mass index; O, airway Obstruction; D, Dyspnea; E, Exercise tolerance
SI: Smoking index BMI: Body mass index
**p≤0.001 is statistically highly significant r: Spearman correlation coefficient

There is statistically significant correlation between BODE index and each of body mass index, wait circumference, systolic and diastolic blood pressure. There is statistically non-significant negative correlation between BODE index and either age or smoking index.

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Table (13): Correlation between BODE index and both glycemic and lipid profile of the studied patients

PARAMETERS	BODE INDEX	
	r	P
Fasting blood glucose (mg/dL)	0.562	<0.001**
HbA1c (%)	0.222	0.088
T. cholesterol (mg/dL)	0.490	<0.001**
LDL (mg/dl)	0.417	<0.001**
HDL (mg/dL)	0.137	00.296
Triglycerides (mg/dL)	0.355	0.009*

BODE: B, Body mass index; O, airway Obstruction; D, Dyspnea; E, Exercise tolerance
Hb1Ac: Glycated hemoglobin LDL: Low-density lipoprotein
HDL: High-density lipoprotein
**p≤0.001 is statistically highly significant *p<0.05 is statistically significant
r: Spearman correlation coefficient

There is statistically significant positive correlation between BODE index and each of fasting blood glucose, total cholesterol, LDL cholesterol, serum triglycerides. There is statistically non-significant positive correlation between BODE index and either HbA1c or HDL cholesterol.

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Table (14): Correlation between BODE index and spirometry data of the studied patients

PARAMETERS	BODE INDEX	
	r	P
FEV1	-0.556	<0.001**
FVC	-0.324	0.011*
FEV1/FVC	-0.414	0.001**
FEF_{25-75}	-0.122	0.353

BODE: B, Body mass index; O, airway Obstruction; D, Dyspnea; E, Exercise tolerance
FEV1: forced expiratory volume in one second FVC: forced vital capacity
FEF: Forced Expiratory flow
**p≤0.001 is statistically highly significant *p<0.05 is statistically significant
r Spearman correlation coefficient

There is statistically significant negative correlation between BODE index and each of FEV1, FVC and FEV1/FVC. There is statistically non-significant weak negative correlation between BODE index and FEF_{25-75}.

Table (15): Multiple linear regression analysis of factors associated with BODE index of the studied patients

	Unstandardized Coefficients		Standardized Coefficients	t	P	95.0% CI	
	B	Std. Error	B			Lower	Upper
SBP	0.047	0.015	0.284	3.154	0.003*	0.017	0.077
Total cholesterol	0.021	0.005	0.356	4.061	<0.001**	0.010	0.031
FEV1	-0.225	0.057	-1.270	-3.944	<0.001**	-0.339	-0.111
FEV1/FVC	14.439	5.045	0.906	2.862	<0.001**	4.328	24.549

SBP: Systolic blood pressure
FEV1: forced expiratory volume in one second FVC: forced vital capacity
**p≤0.001 is statistically highly significant *p<0.05 is statistically significant

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On doing multiple linear backward regression analysis of factors significantly correlated to BODE index, systolic blood pressure (unstandardized β=0.047, p=0.003), total cholesterol (unstandardized β=0.021, p<0.001), FEV1 (unstandardized β=-0.225, p<0.001), FEV1/FVC (unstandardized β=14.439, p<0.001), were significantly associated with BODE index among patients.

DISCUSSION

Chronic Obstructive Pulmonary Disease (COPD), a common preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients. The main causes of morbidity and mortality among COPD patients are cardiovascular disease (CVD) lung cancer, and osteoporosis (GOLD, 2018).

COPD is associated with increased systemic and airway inflammation, and enhanced inflammation worsens clinical symptoms and decreases lung function of patients, necessitating hospitalized treatment (Zhouetal.,2015).

Metabolic Syndrome represents a cluster of risk factors (abdominal obesity, atherogenic dyslipidemia, hypertension, and insulin resistance) that predispose affected patients to systemic inflammation, cardiovascular disease, and physical inactivity. The diagnosis of Metabolic Syndrome is based on the

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presence of central obesity, hypertension, dyslipidemia, and hyperglycemia. Various Metabolic Syndrome definitions are available and differ in specific cut points of the components. The prevalence of Metabolic Syndrome in the general population varies from 21%−31% in Asia, to 34% in the USA, and increases with increasing age and body mass index (BMI) (Suhand Lee,2014).

Predisposing factors associated with Metabolic Syndrome development are smoking and a sedentary lifestyle, which are well-described features in COPD patients. Moreover, specific factors relating to COPD as a primary lung disease, such as relative hypoxemia and steroid use may also contribute to the Metabolic Syndrome **(**S**l**a**g**t**e**r *e**t al.*,2013).

Therefore, the prevalence of Metabolic Syndrome in COPD is hypothesized to be higher compared to the general population. Furthermore, knowledge on predisposing factors may aid in characterizing the patients with the highest risk of developing Metabolic Syndrome and it may give more insight into targets for interventions aiming to reduce Metabolic Syndrome prevalence, development of T2DM and eventually CVD mortality in COPD.

However, limited data have been presented on the impact of Metabolic Syndrome on severity and prognosis of chronic obstructive pulmonary disease. The aim of this work was to evaluate the effect of metabolic syndrome on severity of chronic obstructive pulmonary disease.

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This study was carried out on 60 subjects of both sexes, who were presented to Chest Outpatient Clinic. Patients were presented with signs and symptoms of COPD and proven radiologically, according to the GOLD guidelines, based on sustained (48 hours or more) worsening of dyspnea, cough, or sputum production leading to an increase in the use of maintenance medications or supplementations with additional medications.

Subjects were categorized into two groups; 30 COPD patients with Metabolic Syndrome (group A) and 30 COPD patients without Metabolic Syndrome (group B).

In this study, there were 22 men and 8 women in the group of COPD with Metabolic Syndrome with mean age of 56.73 years, while in the group of COPD without Metabolic Syndrome, there were 19 men and 11 women with mean age of 61.1 years, with no statistically non-significant differences between the studied groups regarding age or gender.

Vujic *et al.* (2016) investigated the frequency of Metabolic Syndrome in patients with COPD and noticed no significant differences between group of COPD patients with Metabolic Syndrome and group without Metabolic Syndrome according to age and gender.

Ghatas (2017) investigated the frequency of Metabolic Syndrome as a marker of systemic inflammation in 100 stable chronic obstructive pulmonary disease (COPD) patients (86 men and 14 women) with a mean age of 62.6±7.8 years and 50 participants in an age-matched and sex-matched control group with a mean age of 63.4±8.6 years, with no statistically

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significant differences between the two groups regarding age and gender. Yao *et al*. (2017) found that there were 200 men and 103 women, and the mean age was 61 years.

Smoking is an established risk factor for COPD and has been associated with increased Metabolic Syndrome prevalence and increased CVD risk. The current smoking was high in the two studied groups, COPD group without Metabolic Syndrome included 21 smokers and COPD group with Metabolic Syndrome included 20 patients, with statistically non-significant differences between the groups regarding smoking status and smoking index (table 2).

Minas *et al.* (2011) showed significantly less smoking in the Metabolic Syndrome group expressed by pack-years. Tanni *et al.* (2015) found no significant difference between Metabolic Syndrome and non-Metabolic Syndrome patients. Vujic *et al.* (2016) found that the mean pack-year index was 52.2 ± 40.2, with no significant differences between the groups according to smoking status and the intensity of smoking. Ghatas (2017) found a smoking history of 52.4±22.3 pack-year in COPD patients.

In our study, there are statistically significant differences between the studied groups regarding BMI and waist circumference (table 3). Lipovec *et al.* (2016) reported COPD patients with a BMI of 25.1±2.0 kg/m². Patients with Metabolic Syndrome had a higher BMI compared to patients without Metabolic Syndrome.

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In our study, there are statistically significant differences between the studied groups regarding systolic and diastolic blood pressure, fasting blood glucose, HbA1c, total cholesterol, LDL cholesterol and serum triglycerides (significantly higher in the group of COPD with Metabolic Syndrome). There is statistically non-significant difference between the studied groups regarding HDL cholesterol (tables 4 and 5). Lipovec et al. (2016) found that low HDL cholesterol was significantly different between COPD patients and controls.

Vujic *et al.* (2016) noticed that fasting plasma glucose, triglycerides, total cholesterol and waist circumference were significantly higher in the group with Metabolic Syndrome. Ghatas (2017) found that TG and HDL components were higher in the control group: the ratios were TG 24.4 against 33. % and HDL 33.3 against 44%, but the difference was not significant.

Regarding spirometry measures, there are statistically significant differences between the studied groups regarding FEV1, FVC and FEF25-75 (table 6). Vujic *et al.* (2016) noticed no significant difference between the groups according to FEV1. Lipovec *et al.* (2016) found that patients with Metabolic Syndrome had a higher BMI and had higher FEV1% predicted compared to patients without Metabolic Syndrome. Yao *et al*. (2017) found that the mean FEV1% predicted value was 56%, suggesting most patients presented with moderate airflow limitation.

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Regarding GOLD, there is statistically non-significant difference between the studied groups (76.7% within COPD with Metabolic Syndrome group versus 50% within COPD only group had GOLD II class) (table 8).

Akpinar *et al.* (2012) reported the prevalence of Metabolic Syndrome between GOLD stages as follows: 38.5 %, 52.8 %, 30 %, and 33.3%. In the study of Diez-Manglano *et al*. (2014), all patients were in GOLD II, III,IV stages, and the frequencies of Metabolic Syndrome were 51.2 %, 41.2 %, and 25.5 %, respectively.

In the study of Ozgen Alpaydin *et al*. (2013) performed in Turkey, Metabolic Syndrome was assessed in 44 % COPD patients, they found significantly different Metabolic Syndrome prevalence in COPD patients in different GOLD stages: the highest prevalence was observed in stage II (59 %), and the lowest one in stage IV (4.5 %), thus Metabolic Syndrome was more frequent in the early stages of the disease.

Ghatas (2017) presented the distribution of COPD patients according to GOLD criteria as follows: stage I was presented in 15%, stage II in 58%, stage III in 20%, and stage IV in 7% of the patients. Yao *et al.* (2017) determined that the numbers of patients for each class of the Global Initiative for Chronic Obstructive Lung Disease classification were: 44, 132, 102, and 25 for classes I, II, III, and IV, respectively.

In our study, the frequency of Metabolic Syndrome was the highest in COPD patients in GOLD stage II (table 8), as observed by OzgenAlpaydin *et al*. (2013).

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Regarding modified medical research council (mMRC) dyspnea scale, there is statistically significant difference between the studied groups; 36.7% within COPD with Metabolic Syndrome group versus 16.7% within COPD only group had dyspnea on walking on ground level. No patient with COPD only had dyspnea after walking 100 yards versus 30% of those within COPD with Metabolic Syndrome group (table 9).

Regarding six-minute walking scale, there was statistically significant difference between the studied groups; 16.7% within COPD with Metabolic Syndrome group versus 6.7% within COPD only group can walk only for <150 meters. 30% of patients with COPD versus 13.3% of those within COPD with Metabolic Syndrome group can walk for ≥350 meters.

Regarding BODE index, there was statistically significant difference between the studied groups. BODE index was significantly higher in the group of COPD with Metabolic Syndrome. There are statistically significant negative correlations between BODE index and each of body mass index, wait circumference, systolic and diastolic blood pressure, FEV1, FVC, FEV1/FVC. Also, there are statistically significant positive correlations of BODE index with fasting blood glucose, total cholesterol, LDL cholesterol and serum triglycerides (tables 11, 12, 13 and 14).

On doing multiple linear backward regression analysis of factors significantly correlated to BODE index, systolic blood pressure, total cholesterol, FEV1 and FEV1/FVC were significantly associated with BODE index among patients (table 15).

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Minas et al. (2011) excluded COPD patients with DM and CVD with the exception of hypertension, reported the lowest Metabolic Syndrome prevalence (22%). In the study performed by Hosny et al. (2013) in Egypt, Metabolic Syndrome was present in 40% of COPD patients. The similar prevalence was reported by Akpinar et al. (2012) from Turkey, and Diez-Manglano et al. (2014) found the highest Metabolic Syndrome prevalence in COPD patients with more co-morbidities.

Mekov et al. (2015) from Bulgaria found a relatively low prevalence of 25%. In the research of Breyer et al. (2014), Metabolic Syndrome was detected in 57 % of COPD patients (relatively high prevalence). Lipovec et al. (2016)concluded that the prevalence of Metabolic Syndrome is higher in COPD patients compared to controls. Its most prevalent components are abdominal obesity, hypertension and hyperglycemia. Metabolic Syndrome is more prevalent in female patients, patients with less severe COPD and high BMI. Smoking does not seem to be discriminative for Metabolic Syndrome in COPD.

Ghatas (2017) found that Metabolic Syndrome is substantial among stable COPD patients, especially in the early stages (GOLD stages I–II). Abdominal obesity, hypertension, and hyperglycemia were significantly more in COPD patients with Metabolic Syndrome.

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The limitations of the present study were the small sample size (convenient sample) and absence of normal controls. These limitations make it difficult to adequately describe causal relationships of detected associations. Furthermore, this study was performed in a single center.

CONCLUSION AND RECOMMENDATIONS

From this study, it can be concluded that the presence of Metabolic Syndrome is substantial among COPD patients, especially in early stages (GOLD stages I−II). When the components of Metabolic Syndrome were evaluated separately, abdominal obesity, hypertension, and hyperglycemia were significantly high in the patient group.

In light of the results of the current study, it is recommended to conduct further studies on larger sample of patients and in multi-centers to unveil the relation of lifestyle and disease to Metabolic Syndrome prevalence as well as the best management possibilities.

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تأثير متلازمة الأيض على شدة مرض السدة الرئوية المزمنة

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المستخلص

الخلفي : مرض السدة الرئوية المزمنة هو مرض شائع يمكن الوقاية منه وعلاجه، ويتميز بتقييد مستمر لتدفق الهواء بالشعب الهوائية ويكون عادةً تقدميًا ويحدث ألتهاب مزمن في الشعب الهوائية والرئة استجابة للجزيئات أو الغازات الضارة

الهدف من البحث: هدفت هذه الدراسة لتقييم مدى تأثير متلازمة الأيض علي مرضى السدة الرئوية المزمنة.

طرق البحث: أجريت هذه الدراسة على ٦٠ شخصاً من كلا الجنسين، وعرضهم على عيادة الصدر الخارجية. وتشخيصهم بمرض السدة الرئوية المزمنة وتم إثباتها بالأشعة، وفقًا لإرشادات GOLD. تم تصنيف المرضى إلى مجموعتين. ٣٠ مريضا يعانون من مرض السدة الرئوية المزمنة وكذلك يعانون من متلازمة الايض (المجموعة أ) و ٣٠ مريضا بمرض السدة الرئوية المزمنة دون متلازمة الايض(المجموعة ب).

النتائج: يوجد ٢٢ رجلاً و ٨ نساء في مجموعة مرضى السدة الرئوية المزمنة و يعانون من متلازمة الايض بمتوسط عمر ٥٦,٧٣ سنة ، بينما في مجموعة مرضي السدة الرئوية المزمنة بدون متلازمة الايض كان هناك ١٩ رجلاً و ١١ امرأة بمتوسط عمر ٦١,١ سنة. كانت نسبة المدخنين الحاليين أكبر في جميع الفئات. توجد فروق ذات دلالة إحصائية بين المجموعات المدروسة فيما يتعلق بمؤشر كتلة الجسم ومحيط الخصر. وكذلك فيما يتعلق بضغط الدم الانقباضي والانبساطي وجلوكوز الدم الصائم ونسبة الهيموجلوبين السكري والكوليسترول الكلي وكوليسترول البروتين الدهني منخفض الكثافة والدهون الثلاثية . فيما يتعلق بوظائف التنفس توجد فروق ذات دلالة إحصائية بين المجموعات المدروسة. بالنسبة GOLD، هناك فرق غير معنوي إحصائياً بين المجموعات المدروسة. كان تكرار متلازمة الايض هو الأعلى في مرضى السدة الرئوية المزمنة في المرحلة الثانية.

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الخلاصة: وجود متلازمة الأيض كبير بين مرضى السدة الرئوية المزمنة و خاصة في المراحل المبكرة (مراحل GOLD I-II). عندما تم تقييم مكونات متلازمة الايض بشكل منفصل، كانت السمنة البطنية ، وارتفاع ضغط الدم ، وارتفاع السكر في الدم أكثر بشكل ملحوظ في مجموعات المرضى.
الكلمات الدالة: السدة الرئوية المزمنة، متلازمة الأيض .