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The prevalence of metabolic syndrome in Indonesian patients with stable chronic obstructive pulmonary disease

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EA FY BAY conceived idea, EA drafted the study, EA FY collected data, FN did statistical analysis and interpretation of data, all authors critical review manuscript and approved version to be published.

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A B S T R A C T

Background: Metabolic syndrome is a common comorbid disease in chronic obstructive pulmonary disease (COPD). Systemic inflammatory conditions can affect the condition of COPD and metabolic syndrome. Activity limitations, skeletal muscle dysfunction, and steroid use are also important causes of metabolic syndrome in COPD. The metabolic syndrome in COPD can increase mortality and morbidity.

Objective: The aim of this study is to reveal the prevalence of metabolic syndrome in stable COPD patients.

Methodology: This study is a cross-sectional study among stable COPD patients who visited COPD Outpatient Clinic at the Persahabatan Hospital, Jakarta, Indonesia, from May 2017 to November 2017 to determine the prevalence rate of metabolic syndrome among stable COPD patients. The COPD classification was based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria. The subjects were recruited to participate in the study by a consecutive sampling and were subject to medical interview, anthropometric and physical examination, and laboratory examination.

Results: A total of 64 patients participated in this study (Males = 61, Female = 3) with the mean age of the subjects was 65.81 ± 9.38. The prevalence of metabolic syndrome in all GOLD criteria of COPD patients was 15.6%, and based on GOLD criteria, the prevalence of metabolic syndrome in GOLD 1, 2, 3, and 4 were 20%, 30%, 40%, and 10%, respectively. There was a significant association between nutritional status and the prevalence of metabolic syndrome in stable COPD.

Conclusion: The prevalence of metabolic syndrome in COPD patients in this study is 15.6% especially in GOLD 3.

Key words: COPD; Metabolic Syndrome; Prevalence.

Introduction

Chronic obstructive pulmonary disease (COPD) is one of the main causes of morbidity and mortality worldwide. In the adult population, the prevalence of COPD reached 1%, increasing at the age of 40.[1] In the Persahabatan Hospital, Jakarta, Indonesia, COPD was ranked the fifth of the number of outpatients and fourth inpatients from the year 1995 to 1999.[2] The COPD influence both respiratory system and systemic organs which associated with various comorbidities, including cardiovascular disease, lung cancer, osteoporosis, depression, metabolic syndrome and diabetes.[1]

Atherosclerosis, insulin resistance, and diabetes mellitus are all symptoms of metabolic syndrome, which is a group of disorders that when combined can cause a person to develop atherosclerotic cardiovascular disease, insulin resistance, and diabetes. The effects of metabolic syndrome on a person's health and healthcare costs are significant. As smoking and changing life styles are one of the main causative reasons in both metabolic syndrome and COPD, there are greater chances of co-existence of both the problems. The rising prevalence of metabolic syndrome and COPD in the world must be identified in order to intervene and halt or reverse the disease's progression.

Metabolic syndrome is often found in stable COPD. Systemic inflammatory conditions are thought to affect COPD and metabolic syndrome.[3] Activity limitation, skeletal muscle dysfunction, and the use of steroid are also important causes of metabolic syndrome in COPD.[4] Obesity and insulin resistance are often found in mild to moderate COPD. Metabolic syndrome in COPD can increase mortality and morbidity caused by cardiovascular disease.[5] The objective of our study is to reveal the prevalence of metabolic syndrome in stable COPD who visited the Outpatient Clinic in Persahabatan Hospital, a national reference hospital for respiratory medicine in Indonesia.

Methodology

This is a cross-sectional study in group A to D of COPD subjects at the COPD Outpatient Clinic of Persahabatan Hospital, Jakarta, during May - November 2017. Chronic Obstructive Lung Disease (GOLD) 2017 classified COPD based on the history of exacerbation and based on symptoms.[6] Based on exacerbation, COPD is classified into patients without exacerbation that leads to the hospital (A-B) and those with exacerbation that leads to the hospital (C-D). As for symptoms-based classification, patients who had symptoms with CAT score <10 and/or mMRC 0-1, are classified as A-C, whereas symptomatic patients are classified as B-D.

The subjects were enrolled by consecutive sampling. All patients participating in this study provided written informed consent. This study protocol was approved by the Institutional Review Board (IRB) of the Faculty of Medicine Universitas Indonesia (Ethical Clearance No. 363/UN2.F1/ETIK/2017). Patients who visited Outpatient Clinic of Persahabatan Hospital were assessed for their history of illness and were subjected to physical examination, anthropometric assessment, lung function test and COPD Assessment Test (CAT). Data regarding patient baseline characteristics were collected including age, gender and smoking history. We excluded patients who have been diagnosed as having exacerbations, lung cancer, congestive heart failure (CHF), and chronic kidney disease (CKD).

A venous blood sample was collected from each subject after a 10-hour fasting. Plasma glucose, triglyceride (TG) and high-density lipoprotein (HDL) were measured. Body weight and height were measured and the body mass index (BMI) was calculated by dividing weight by height squared (kg/m2). Blood pressures were measured according to the American Heart Association's recommendations. Waist circumference was measured from the midpoint between the lowest ribs with the iliac crest. Indonesian Society of Endocrinology criteria (PERKENI) criteria were used in the diagnosis of metabolic syndrome as described in Table 1.[7]

Statistical analysis was carried out with the Statistical Package for Social Science (SPSS) software program version 23 (IBM Corp, Armonk, NY, USA). We used the Chi-square and Fisher's exact test to determine the associations between categorical variables. All p-value <0.05 were considered statistically significant.

Result

In the current study, 64 stable COPD patients were enrolled in which most of the subjects were males, aged 65 year-old and above, former smokers and according to Brinkman index, the smoking degree was in severe grade, as described in Table 2.

The prevalence rate of metabolic syndrome in stable COPD patients was 15.6%. The distribution of the prevalence of metabolic syndrome between GOLD stages I-IV was as follows; 20%, 30%, 40 %, and 10% respectively.

The number of metabolic syndromes in overweight and obesity group was 8 subjects (80%). There was an association between nutritional status with metabolic syndrome in stable COPD patients ($p = 0.036$). This study found that 9 subjects (90%) in metabolic syndrome were former smokers and only 1 subject (10%) was nonsmokers. There was no association between smoking status

with metabolic syndrome (p = 1). This study also discovered that 6 subjects (60%) have severe Brinkman Index, 2 subjects (20%) have moderate Brinkman index and 1 subject (10%) had mild Brinkman index. There was no association between Brinkman index with metabolic syndrome (p = 0.928).

Based on the GOLD classification, this study obtained most subjects with metabolic syndrome which considered COPD group B is about 7 subjects (70%). On the other hand, the number of metabolic syndromes in COPD group A and D was only limited to 1 (10%) and 2 (20%) subjects, respectively, while none for group C. In this study, COPD group was divided into groups without exacerbations (A-B) and with exacerbations in the past year (C-D). No association was acquired between exacerbation with metabolic syndrome (p = 0.036). This study also divided the COPD group into mild (A-C) and severe complaints (B-D) group. There was no association between complaint and metabolic syndrome. Five out of 10 subjects (50%) with metabolic syndrome were found using inhaled corticosteroids, whilst the remaining did not use any. There was no association between the uses of inhaled corticosteroids and metabolic syndrome. Table 3 shows the relationship of risk factors with the prevalence of metabolic syndrome in stable COPD patients.

Discussion

As COPD is highly associated with the systemic condition including metabolic disease, it is important to address the issue of metabolic syndrome prevalence and influencing factors among patients with stable COPD. The rate of metabolic syndrome prevalence in COPD stable patients was 15.6% in this study. This study finds the prevalence of metabolic syndrome is lower than other studies. Minas et al,[8] in Greece found a prevalence of metabolic syndrome in COPD was 21%, meanwhile, Lam et al[9] in China and Funakoshi et al[10] in Japan found the prevalence of metabolic syndrome in COPD patients were 22.6% and 23%, respectively. Furthermore, a study by Vujic et al[11] in Serbia found a prevalence of metabolic syndrome was 37.8%. Acharyya et al[12] in India found 44%, 46% and 31% metabolic syndrome respectively in COPD patients based on the National Cholesterol Education Program-Third Adult Treatment Panel (NCEP ATP-III) definition criteria, modification of NCEP ATP III and IDF. Arliny et al[13] found the prevalence of metabolic syndrome according to NCEP-ATP III modification criteria was 34.9%.

This low prevalence is influenced by different races of research subjects and the diagnostic criteria for metabolic syndrome used. This study has subjects from Asian races with smaller body postures than European and American. Central obesity which is one of the main criteria of metabolic syndrome is also more common in races other than Asia because it is related to diet and lifestyle.

In our study, the diagnosis of metabolic syndrome was established based on the criteria of PERKENI, which includes at least 3 of the following criteria: waist circumference 90 cm for male or ≥80 cm for female; fasting blood glucose 110 mg / dl or has been previously diagnosed with diabetes mellitus (DM), TG ≥150 mg / dl or in the treatment of dyslipidemia; HDL cholesterol <40 mg / dl (male), <50 (female) or in the treatment of dyslipidemia; blood pressure ≥135/85 mmHg or in anti-hypertensive drug therapy is different from other studies using the ATP-III NCEP criteria, modification of NCEP ATP III and IDF for diagnosis.

The age distribution of subjects in this study was similar to the study by Lipovec et al[14] which found the average age of COPD patients was 65 ± 4 years old. However, there was no association between age and metabolic syndrome among COPD subjects in this study. Another study by Suastika et al[15] found the prevalence of metabolic syndrome that increased in old age.

Cigarette smoke exposure is a major risk factor for COPD which is associated with an increase in the waist circumference ratio with the pelvis, which is an indicator of increased visceral fat tissue. Smoking is also associated with low HDL levels, high triglycerides and an increase in PAI. Atfall et al reported that tobacco can directly interfere with insulin action and reduce glucose uptake in tissues. Plasma glucose concentrations were reported to be higher in smokers than in nonsmokers.[4,16] Weitzman et al[17] had a higher metabolic syndrome in smokers than in nonsmokers (8.7% vs 1.2%).

Table 1. The Indonesian Society of Endocrinology (PERKENI) criteria for the diagnosis of metabolic syndrome

Metabolic syndrome component	Value
Waist circumference	≥ 90 cm (male), ≥ 80 cm (female)
Fasting glucose	≥ 110 mg/dl
Triglycerides	≥ 150 mg/dl
HDL cholesterol	< 40 mg/dl (male), < 50 mg/dl (female)
Blood pressure	≥ 135 / 85 mmHg

Table 2. Clinical characteristics of subjects

Characteristics of subjects	Metabolic syndrome		Non-Metabolic syndrome	
	N	%	N	%
Sex				
Male	8	80	53	98,1
Female	2	20	1	1,9
Age: <65 years old	3	30	28	51,9
≥65 years old	7	70	26	48,1
Smoking status				
Non-smoker	1	10	6	11,1
Former smoker	9	90	48	88,9
Brinkman index				
Mild	1	10	5	9,3
Moderate	2	20	16	29,7
Severe	6	60	27	50
Body Mass Index				
Underweight	0	0	13	24
Normal	2	20	19	35
Overweight	3	30	14	26
Obesity	5	50	8	15
COPD stage				
GOLD 1	2	20	6	11,1
GOLD 2	3	30	19	35,1
GOLD 3	4	40	18	33,4
GOLD 4	1	10	11	20,4
COPD groups				
A	1	10	9	16,7
B	7	70	13	24
C	0	0	7	13
D	2	20	25	46,3
History of exacerbation				
Yes	2	20	32	59,3
No	8	80	22	40,7
Duration of COPD				
<5 years old	4	40	41	76
≥5 years old	6	60	13	24
COPD Therapy				
LABACS	0	0	3	5,5
LAMA	5	50	15	27,8
LABACS + LAMA	5	50	30	55,6
Corticosteroid + LAMA	0	0	1	1,9
Bronchodilator	0	0	3	5,6
Without therapy	0	0	2	3,6

Abbreviations: COPD, chronic obstructive pulmonary disease; GOLD, Global for Chronic Obstructive Lung Disease, LABA, long acting beta agonist; LABACS, LABA with inhaled corticosteroid; LAMA, long-acting anti muscarinic

In our study, the prevalence of metabolic syndrome is found to be greater in the group of former smokers but there was no association between smoking status and the prevalence of metabolic syndrome. Previous study showed that smoking habits not related to the prevalence of metabolic syndrome [12]. This study also found no significant association between the numbers of cigarettes smoked in a day with the prevalence of metabolic syndrome although there was a tendency that metabolic syndrome prevalence is higher in subjects with moderate and severe Brinkman index compared with subjects with mild Brinkman index and nonsmokers.

This study finds most of the COPD subjects were obese. Average of BMI among COPD patients in China is lower as compared to those in the Western Countries and this may be related to differences in race, environment, diet, lifestyle between the two [18]. Obesity, especially central obesity, is characterized by fat accumulation in the abdomen and assessed by measuring waist circumference [4,19]. The average waist circumference of the study subjects is lower than from study by Ameen et al[20] which found the subject waist circumference was 92.9 ± 16.1

Table 3. Relationship of Risk Factors with the prevalence of Metabolic Syndrome in Stable COPD Patients

	Metabolic syndrome				P-value
	Yes		No		
	N	%	N	%	
Sex					
Male	8	80	53	98.1	0.061*
Female	2	20	1	1.9	
Age					
<65 years old	3	30	28	51.9	0.305*
≥ 65 years old	7	70	26	48.1	
Smoking status					
Former smoker	1	10	6	11.1	1.000*
Non-smoker	9	90	48	88.9	
Brinkman index#					
Mild	1	10	5	9.3	
Moderate	2	20	16	29.7	0.928**
Severe	6	60	27	50	
Nutritional status					
Underweight & normal	2	20	32	59.2	0.0356*
Overweight & obesity	8	80	22	40.8	
COPD stage					
GOLD 1 & 2	5	50	25	46.3	1.000*
GOLD 3 & 4	5	50	29	53.7	
COPD group (symptoms)					
A-C	1	10	16	29.6	0.267*
B-D	9	90	38	70.4	
COPD group (exacerbation)					
A-B	8	80	22	40.7	0.036*
D-C	2	20	32	59.3	
COPD therapy					
ICS	5	50	34	63	0.494*
Non-ICS	5	50	20	37	

Footnotes: *Fisher's Exact test; **Pearson Chi-Square test; # 1 subject non-smoker

cm. This difference might be caused by differences in race, environment, diet, and lifestyle. COPD and obesity are linked by systemic inflammation. In obese patients, adipose tissue that undergoes hypoxia activates the inflammatory pathway and releases inflammatory mediators into the circulation resulting in systemic inflammation.[21] Furthermore, chronic hypoxia in COPD patients is often accompanied by impaired glucose tolerance.[21] Mannino et al[22] found that in COPD patients with GOLD 3 and 4 were associated with an increased risk of diabetes with OR 1.5.

The COPD group with the most prevalence of metabolic syndrome is group B. This result is different from a study by Piazolla et al[23] who found the highest group was in group A. Classification of COPD based on exacerbation history shows a significant association with the prevalence of metabolic syndrome, but not in symptom-based classification.

The limitation of this study is the study design, in which it is difficult to determine a causal relationship. Another study limitation is the small number of subjects involved.

Conclusion

In conclusion, the prevalence of metabolic syndrome among Indonesian patients with stable COPD in Persahabatan Hospital, Jakarta, Indonesia is 15.6%. The most common metabolic syndrome criteria in this study are central obesity followed by hypertension. Variable that is associated with metabolic syndrome among COPD patients in this study is BMI.

Conflict of Interest Disclosure

The authors declare that there are not conflicts of interest

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