Section: General Surgery

Original Research Article

CORRELATION OF COPD AND METABOLIC SYNDROME AND ROLE OF SERUM CRP LEVEL AS A MARKER OF SYSTEMIC INFLAMMATION

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) has effects that seems to be related with systemic inflammation. There is many correlation between metabolic syndrome and of systemic inflammation in general population and stable COPD. Serum CRP level in COPD and metabolic syndrome study is one of them. The objective of the current study was to find the relationship of metabolic syndrome and C-reactive protein (CRP) levels, as a marker of systemic inflammation in stable COPD patients with different severity levels and in age and sex matched control group. **Materials and Methods:** 100 stable COPD patients and 50 control subjects were included in the study. The severity level in patients with COPD were determined according to GOLD (Global Initiative for Chronic Obstructive Lung Disease) criteria. ATP III (The National Cholesterol Education Program's Adult Treatment Panel III) was used in diagnosis of metabolic syndrome. Hs-CRP levels were measured in venous samples of patients and control subjects. **Result:** The frequency of metabolic syndrome was found higher in-patient group than control subjects, especially in GOLD stages I, II (p= 0.004). Abdominal obesity, hypertension, hyperglycemia components of metabolic syndrome were significantly more prevalent in-patient group (p< 0.0001). Increased CRP levels were higher in control and patient groups in all GOLD stages, with metabolic syndrome than without metabolic syndrome (p= 0.046, p= 0.216, p< 0.001, p= 0.05, p= 0.466). **Conclusion:** The study showed that frequency of metabolic syndrome was higher in stable COPD patients than control subjects and general Turkish population. Abdominal obesity, hypertension and hyperglycemia were significantly more prevalent in-patient group. Systemic inflammation was more intense in COPD patients with metabolic syndrome than without metabolic syndrome.

INTRODUCTION

COPD is characterized by progressive, partially reversible airflow limitation that is associated with an abnormal inflammatory response of lungs to noxious particles or gases, particularly cigarette smoke. According to GOLD guideline 2013 COPD was 5thleading cause of DALYs (DISABILITY ASSOCIATED LIFE YEARS) lost.1. By 2030 predicted 4.5 million COPD related deaths annually. Diagnosis of COPD can be established by a fixed ratio of post bronchodilator FEV1 and FVC below 0.7 measured by spirometry. Spirometric severity is graded according to percentage of FEV1 predicted (GOLD stage I-IV).[1]

Cigarette smoking is the major risk factor for COPD. It causes not only local inflammation on lungs, but also systemic inflammation that is thought to contribute to the development of chronic diseases as well as COPD, like cardiovascular diseases, hypertension and diabetes.[2]

Clinical severity of the disease is determined not only by spirometry but also by concomitant comorbidities.[3,4]

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Inflammation like high-sensitivity C-reactive protein (CRP), interleukin (IL)-6 were higher in blood of COPD patients than the ones without COPD.[3,5]

Metabolic syndrome (MetS) is characterized by a group of risk factors (abdominal obesity, atherogenic dyslipidemia, raised blood pressure, insulin resistance) that increases the development of several diseases such as coronary artery disease, diabetes mellitus.[6-8] It was first described in 1988 by Reaven, also known as "syndrome X". It was defined with the clustering risk factors for cardiovascular disease by means of underlying common path physiological findings.

The results of the study including a large number of Chinese population reported by Lam et al. suggested that both the presence of airflow obstruction was related to MetS. and the risk increased with the severity of obstruction.[9,10]

MATERIALS AND METHODS

Study Design and Subject Characteristics

The study was designed as a prospective case-control study. Group A to D of COPD subjects at the COPD Outpatient department of BBMCH BALANGIR during November 2017 to nov 2021. Chronic Obstructive Lung Disease (GOLD) 2017 classified COPD based on the history of exacerbation and based on symptoms. 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.

All though the study dose not need the approval of Ethics Committee of University, because spirometry, CRP and all the blood tests for METABOLIC SYNDROME are routine procedure and data's are collected from our lab by the permission of hospital authority, we have taken ethics committee approval at our college. Informed consents of all patients and control subjects were taken before they were included in the study

The criteria for exclusion were having an acute exacerbation (increase in cough, sputum production, worsening dyspnoea, or sputum purulence within three weeks) (1), having any infectious or inflammatory diseases such as collagen vascular diseases, inflammatory bowel disease that could cause an increase in CRP level.

The subjects who were selected for control group were smokers or non-smokers, age and sex matched with patient group, with normal spirometry and without any infectious or inflammatory diseases that could increase CRP levels.

Diagnosis of COPD

The diagnosis of COPD was made according to GOLD (Global Initiative for Chronic Obstructive Lung Disease criteria.[1]

S. The staging of COPD was made by using GOLD criteria: GOLD I (mild): FEV1/FVC < 70% and FEV1 ≥ 80%; GOLD II (moderate): FEV1/FVC < 70% and FEV1 < 80% and ≥ 50%; GOLD III (severe): FEV1/FVC < 70% and FEV1 < 50% and ≥ 30%; GOLD IV (very severe): FEV1/FVC < 70% and FEV1 < 30%.[2]

Blood Sampling and Analyses

A venous blood sample was collected from each subject after a 12-hour fasting. Blood samples were taken in stable phase of COPD patients. Plasma glucose, triglyceride (TG) and high density lipoprotein (HDL) were measured by using both a Roche COBAS INTEGRA® 400 plus analyzer (Germany, 2009) and an enzymatic calorimetric assay. High sensitivity-CRP levels were measured by using a Roche COBAS INTEGRA® 400 plus analyzer (Germany, 2009) by automatic calorimetric assay, CRP levels which were greater than 5 µg/L were accepted as "high" otherwise "low".[11-14]

Diagnosis of Body weight and height were measured and the body mass index (BMI) was calculated by dividing weight by height squared (kg/m2). 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 15 min resting period and the highest measurement was used for analysis.[15] Waist circumference was measured according to the procedures of Airlie Conference.[16] ATP III (The National Cholesterol Education Program's Adult Treatment Panel III) was used in diagnosis of MetS [Table 1].[17] If the participants were using antihypertensive or antidiabetic drugs, they were considered to have had high blood pressure or high fasting glucose.

Statistical Analysis

Statistical analyses were carried out with SPSS for Windows version 15.0 statistical software. 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. Continuous variables were examined for normality. Significance value was considered as 0.05.

RESULTS

100 stable COPD patients and 50 control subjects were included in the study. Demographic properties and smoking history of patients and control subjects were demonstrated in [Table 2].

It shows when male and female of patients and control group are compair then the result showing that male predominance of patients(74%) as well as control(35 %) group p value is >0.05 which means statistically significant. When we think the age group of COPD patients then both patients and control group having age group more than >50 yrs and p-value is >0.05. when we considered the smoking history patients group having 20 pack year and control group having 40 pack years and it is highly significant,p -value is <0.001.

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The distribution of COPD patients according to GOLD stages (I-IV) were respectively 16%, 54%, 20% and 10%. The prevalence of MetS in patient group was found much higher than control group (44.6% vs. 17.1%) (p= 0.004). The distribution of the prevalence of MetS between GOLD stages I-IV were as follows; 9%, 36%, 8% and 2% respectively. The number of the diagnostic criteria of MetS was found significantly higher in patient group (p< 0.0001) [Figure 1].

The distribution of MetS and increased CRP levels between GOLD stages were shown on Table 3 High sensitive-CRP level increased in 52% of COPD patients. Whereas high CRP levels were found only in 24.2% of control group (p= 0.005). High CRP levels seemed to be more prominent in GOLD stage II patients. But the difference was not statistically significant (p= 0.156).

The parameters of MetS were evaluated one by one in both patient and control groups. Abdominal obesity, hypertension, hyperglycemia components of MetS were significantly higher in patient group (p< 0.0001). The ratios were 51.1% vs. 13.5%, 78.1% vs. 34.5%, 45.5% vs. 8.8% respectively (p< 0.05 for all). In contrast, triglyceride and HDL components were higher in control group (28.5% vs. 25.8%, 34.8% vs. 45.8but the difference was not significant (p= 0.491, p= 0.209).

CRP levels were higher in patients who had MetS than the ones who did not have MetS in all GOLD stages. The difference was significant only in control group and patients with GOLD stage II and nearly significant in stage III. p values for control group and GOLD stages I-IV were p= 0.047, p= 0.225, p< 0.001, p= 0.05, p= 0.357 respectively [Figure 2].

Systemic inflammation and metabolic syndrome in stable COPD patients

[Table 1] The National Cholesterol Education Program's Adult Treatment Panel (ATP) III criteria for the diagnosis of metabolic syndrome*. Risk factor Abdominal obesity, given as waist circumference Male > 102 cm (> 40 in) Female > 88 cm (> 35 in) Triglycerides ≥ 150 mg/dL HDL cholesterol Male < 40 mg/dL Female < 50 mg/dL Blood pressure ≥ 130/≥ 85 mmHg Fasting glucose ≥ 110 mg/dL * Presence of three of the five criteria that is explained above diagnosed as metabolic syndrome. HDL: High density lipoprotein

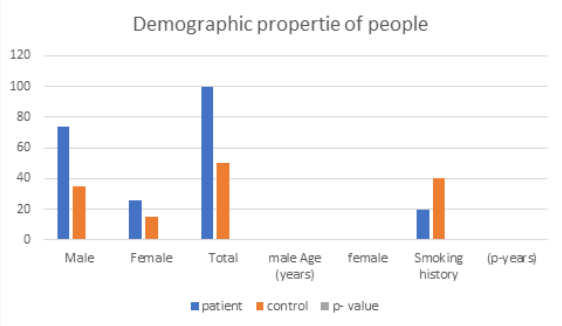

Figure 1:

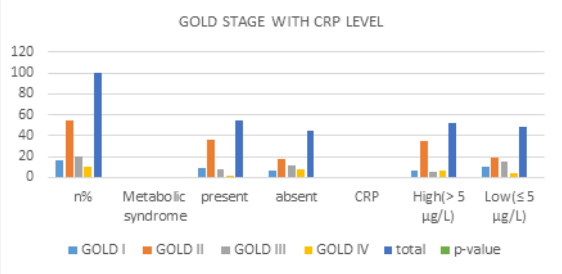

Figure 2: Metabolic syndrome and C-reactive protein levels according to GOLD stages.

Table 1:

Gender n (%)	patient	control	p- value
Male	74	35	> 0.05
Female	26	15	
Total	100	50	
male Age (years)	57 ± 8.7	56 ± 6.6	> 0.05
Female	50 ± 8.6	51 ± 6.7	
Smoking history (p-years)	20	40	< 0.001

Table 2:

Gold stages.	Gold I	Gold II	Gold III	Gold IV	Total	p-value
n%	16	54	20	10	100	> 0.05
Metabolic syndrome						
Present	9	36	8	2	55	> 0.05
Absent	7	18	12	8	45	
CRP						
High(> 5 µg/L)	6	35	5	6	52	> 0.05
Low(≤ 5 µg/L)	10	19	15	4	48	

DISCUSSION

The important finding of metabolic syndrome was found mainly in stable stage II and stage III of COPD patients than control group.[18]

When considering the CRP level the patient of COPD having metabolic syndrome have higher level.[19] Other parameter like Abdominal circumference given as waist circumference, Triglycerides, HDL cholesterol, Blood pressure, Fasting glucose, patients is considered more then control group.[20,21]

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As smoking is associated with inflammation, both systemic and local so arises various comorbid condition like cardiovascular diseases.[22]

Watz et al. investigated the prevalence of MetS in COPD patients. They reported average frequency of MetS in this group of patients as 47.5%. Frequencies according to GOLD stages (I-IV) were as follows 50%, 53%, 37%, 44%.[9]

In our study mets in patients' group is more ie 55% and GOLD stage II having higher value because may be the presence of cachexia part in higher group.[23-25] The higher mortality rates in COPD patients who were associated with MetS due to concomitant diseases like cardiovascular diseases or diabetes mellitus may also be contributed to the lower prevalence of COPD in other stage. The prevalence of MetS was reported as 17.9% in a large population-based study in Turkey.[26] Gemalmaz et al. found the prevalence as 38.1% in the study including smaller Turkish population.[27] Gundogan et al. showed the prevalence as 34.6% in a Turkish population from Mediterranean region.[28] The prevalence of MetS in COPD patient group in our study was higher than population (55%). Besides, the prevalence in control group was consistent with the result of Sanisoglu et al., but lower than the other two studies.[26-28]

Our study having hypertension in COPD 75.2%. Similarly, Watz et al. showed that hypertension was highly prevalent in COPD patients (70%).[10] Whereas, Barr et al. found that frequency of hypertension in COPD patients was 55%.[29] However, they used telephone questionnaire in contrast to objective measurement of blood pressure to determine presence of hypertension. This method may be responsible for the lower frequency of hypertension among COPD patients.

In our study, prevalence of abdominal obesity in COPD patients (55.3%) was the secondly frequent parameter of MetS just after hypertension. Visceral adipose tissue is an important source of IL-6 that induces production of high sensitivity CRP from hepatocytes.[30] The study by Poulain et al. indicated that the presence of obesity, especially abdominal obesity, was associated with increased TNF-α and IL-6, and decreased adiponectin in plasma of patients with COPD.[31] In our study, high sensitivity CRP levels were higher in COPD patients with MetS and 55.3% of COPD patients having abdominal obesity. Weight loss may be helpful to decrease the grade of systemic inflammation in COPD patients.[32]

The third common parameter of MetS in COPD patients included in our study was hyperglycemia (46.3%). It was previously shown that there was increased prevalence of diabetes in COPD patients (4,32). Gudmundsson et al. suggested that mortality rate of patients with COPD and diabetes was increased during follow-up patients hospitalized because of exacerbation of COPD.[33]

Several markers of systemic inflammation such as hsCRP, IL-6 were found higher in stable COPD patients than control subjects,[2,34-36] suggesting low grade systemic inflammation even during clinical stability. CRP is one of the most widely used serum marker of systemic inflammation. Gläser et al. showed that higher levels of CRP were associated with decreased lung volumes in a general population over a wide range of age.[37] In this study, high sensitivity CRP levels were also higher in stable COPD patients than control group.

Stanciu et al. reported that serum TNF-α and high sensitivity CRP levels were higher, whereas adiponectin levels were lower in patients with COPD and MetS than patients with COPD but without MetS.[25] Our study also revealed that high sensitivity CRP levels were higher in patients with COPD and MetS than patients with COPD but without Mets, which was in accordance with the results of Stanciu and colleagues' study.

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Our study has some limitations: First, the number of COPD patients included in the study was limited and patients were selected from only one center, to define exact prevalence of MetS in patients with COPD. Further studies that contain patients from many different centers are necessary.

Secondly, a cross-sectional study was performed to determine the effect of presence of MetS to the course of COPD. Nevertheless, prospective studies may be more useful.

Collection of data is very important point for document production in research purpose.

CONCLUSION

Metabolic syndrome known by its high CRP level ,and other parameter like abdominal circumference; abdominal obesity, hypertension and hyperglycaemia were significantly more in patient group of earlier COPD group.

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