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Original Research Article.

Microalbuminuria and COPD: A Clinical and Physiological Association

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ABSTRACT

Introduction: COPD is the major cause of mortality and morbidity in smokers and individuals exposed to risk factors associated with this disease. Microalbuminuria (MAB) in COPD is attributed to generalized endothelial dysfunction as a result of systemic inflammation, which could be a significant marker for early cardiovascular abnormality.

Objective: The aim of our study was to find out possible association of MAB in COPD patients.

Materials and Methods: A cross-sectional study of 160 patients of both sexes, of diagnosed COPD Patients in different stages as per GOLD guideline were taken. PFT, smoking history, BMI, 6Minute walk test, ABG were measured. Screening for micro albuminuria (MAB) was done by measuring urinary Albumin to Creatinine ratio in random spot urine collection. Data were thus collected and analysed. Statistical analysis was performed using the IBM's Statistical Package for Social Sciences (SPSS) software version 19.

Results: Sixty two patients (38.27%) had MAB. There is direct association between hypoxia and MAB. Regression analysis with MAB shows smoking, lower FEV_1 % pred., PaO_2, exercise capacity as independent predictor and may be associated with generalized endothelial dysfunction.

Conclusion: Gradual progression in COPD severity and symptoms must be checked for MAB and for possible generalized endothelial dysfunction.

Keywords: COPD, Microalbuminuria, BODE Index.

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INTRODUCTION

COPD is a common, preventable and treatable disease characterized by persistent airflow limitation and respiratory symptoms that is due to airways and / or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.[1] COPD is currently the fourth leading cause of death in the world[2] and usually become symptomatic in individuals more than 40 yrs of age.[3] Globally, the COPD burden is projected to increase in coming decades because of continued exposure to COPD risk factors and ageing of the population. Co – morbidities are important determinants of outcome & quality of life in COPD patients.[4] It progresses slowly and is associated with inflammatory reaction and structural changes in small peripheral airways and/or destruction of the lung parenchyma. The disease is currently defined by post-bronchodilator spirometric forced expiratory volume in 1 s (FEV1)/forced vital capacity (FVC) <0.70.[5] The excretion of small amounts of albumin in the urine, microalbuminuria, has been well documented to predict cardiovascular morbidity and mortality in both diabetic[6] and non-diabetic persons.[7] Link between microalbuminuria and atherosclerosis seems to be due the endothelial dysfunction with increased permeability and leakage of albumin through the vessel wall.[8] Microalbuminuria is today considered to be the most important renal marker for generalized damage and systemic inflammation in the vascular system.[9] We hypothesized that there was a positive association between microalbuminuria and morbidity in COPD patients.

MATERIALS AND METHODS

This was a cross-sectional study conducted on160 patients who were diagnosed with COPD as per GOLD guidelines in the Outpatient Department of Pulmonary Medicine during January – December 2015 of CCM Medical College, Durg, Chattisgarh.

All patients who came to outpatient clinic aged between thirty to seventy yrs of age, diagnosed as a case of COPD, based on GOLD guidelines (history of smoking >10 pack years and a post bronchodilator forced expiratory volume in1 s [FEV1]/forced vital capacity <0.70), who are stable for 6 weeks and received optimal therapy.

Exclusion Criteria

1. History of renal disease or presence of macroalbuminuria (urinary albumin to creatinine ratio >300 mg/g)
2. Previously diagnosed diabetes mellitus

3. Cardiovascular disease
4. Comorbidities such as malignancy, fever, urinary tract infections.
5. Asthma
6. Hypertension.

The study was approved by the Ethical and Research Committee. The selected patients were briefed about the study and written informed consent was obtained.

The enrolled patients were given a questionnaire concerning age, gender, height, weight, presenting symptoms, history and duration of COPD, history of smoking.

Lung function tests were done and COPD was classified as per GOLD guidelines. Arterial blood gases, body mass index (BMI), and BP were measured. The 6 min walk distance (6MWD) was measured according to the American Thoracic Society guidelines. Dyspnea was evaluated by the modified Medical Research Council (mMRC) scale. The FEV1%, BMI, 6MWD, and mMRC values were integrated into the BODE index. According to the American Diabetes Association, screening for MAB was done by measuring the urinary albumin-to-creatinine ratio in a random spot urine collection. MAB was defined when the urinary albumin-to-creatinine ratio was between 20 mg/g in men and 30 mg/g in women and the upper threshold of 299 mg/g for both sexes.

Statistical Analysis

Statistical analysis was performed using the IBM's Statistical Package for Social Sciences (SPSS) software version 19 (IBM SPSS, Inc. Chicago, Illinois). The results are expressed as percentages or mean ± standard deviation as specified. Stepwise logistic regression was performed using MAB as the dependent variable. $P<0.05$ was taken as statistically significant.

Table 1: COPD patients with and without microalbuminuria

Variables	Mean±SD		P value
	COPD patients without MAB (n=98)	COPD patients with MAB (*n*=62)	
Age (years)	54.14±4.54	67.39±5.12	0.0001*
BMI (kg/m2)	26.00±2.83	23.78±3.08	0.6990
Smoking pack-years	24.05±3.25	38.30±3.61	0.0001*
FEV1%, predicted	56.25±24.85	36.73±15.39	0.0001*
PaO2 (mmHg)	83.29±2.46	71.33±4.43	0.0001*
PaCO2 (mmHg)	43.02±4.19	47.78±3.87	0.0001*
6MWD (m)	480.91±87.34	376.65±112.08	0.0001*
BODE index	3.89±1.35	6.13±2.01	0.0001*
SBP (mmHg)	116.35±10.46	123.74±12.09	0.4891
DBP (mmHg)	78.46±4.38	83.04±6.33	0.0229*

* Significant

RESULTS

A total of 160 patients diagnosed were enrolled in the study. There were 140 male patients and 20 female patients. Their mean age was 59.67 years, mean smoking pack years was 32.91, and mean BMI was 23.68. There were 76(47.5%) GOLD Stage I, 50 (31.25%) Stage II, 22 (13.75%) Stage III, and 12 (7.5%) Stage IV COPD cases. The mean predicted FEV1% was 52.32 ± 22.43. The mean PaO2 was 79.48 ± 8.16 mm Hg and PaCO2 was 44.09 ± 3.97 mmHg. The mean 6MWDwas 453.02 ± 107.18 m, BODE index score 4.58 ± 3.47, systolic BP 118.54 ± 13.12 mm Hg, and diastolic BP 81.21±4.33 mm Hg. MAB was present in 62 (38.75%) patients out of 160. COPD patients having MAB were significantly higher in mean age compared to COPD patients without MAB (67.39± 4.54 vs. 54.14 ± 5.12 years P = 0.0001). Patients with COPD having MAB had low FEV1% (mean 36.73. ± 15.39 vs. 56.25 ± 24.85) and higher BODE index (mean 6.13 ± 2.01 vs. 3.89 ± 1.35) compared to COPD patients without MAB and was statistically significant.

It was observed that as the pack years increased, the risk of MAB had also increased. Application of Chi-square test showed a significant association of pack-years with MAB (P < 0.0001). Majority of COPD patients with MAB had FEV1% 50-80 (22.58%) and FEV1% ≤ 30 (51.62%), when compare to FEV1% 30-49(19.35) and FEV1% ≥ 81 (6.45%) respectively. Also it was observed, that as the FEV1% decreases, the risk of MAB had also increased MAB was significantly more in COPD patients having PaO_2 below 70 mm Hg as compared to COPD patients having PaO_2 above 70 mm Hg (87.09% vs. 12.90%, respectively, P < 0.0001), which indicates COPD patients with MAB were more hypoxemic. MAB was significantly more in COPD patients having PaCO2 ≥ 45 mm Hg as compared to COPD patients having PaCO2 <45 mm Hg (70.96% vs. 29.03%,respectively, P < 0.0001), which indicates COPD patients with MAB were more hypercapnic. The BODE index was compared with the prevalence of MAB. 38.75% of COPD patients with BODE index ≥ 4 had MAB when compared to 61.25% COPD patients with BODE index < 4, and it was statistically significant P = 0.0001. Stepwise logistic regression analysis with MAB as the dependent variable showed that smoking pack years (odds ratio 2.29; 95% CI: 1.54–3.41), lower FEV1% (OR: 1.04, 95% CI: 0.97-1.11) and PaO_2 (OR: 0.65, 95% CI 0.52- 0.78) were independent predictor of MAB.

DISCUSSION

Global burden of COPD is gradually increasing and it is becoming one of the leading causes of mortality and morbidity not only because of ageing process but also exposer to risk factors associated with this disease. COPD is a multisystem involving disease primarily involve lung parenchyma but extra pulmonary complications, especially cardiovascular disease is one of the major cause of mortality and dysfunction. Microalbuminuria (MAB) is a sensitive marker of cardiovascular risk.[10]

It reflects a state of generalized endothelial dysfunction. It is consistently associated with worse cardiovascular outcomes in patients with diabetes and hypertension in general population also.[11] Present study had 62 patients (38.75) had MAB out of 160

patients. Prevalence of 24% was noted by Casanova et al[12] in stable COPD cases. Bulcun et al[13] found prevalence of 39% MAB in COPD cases. Study done by Mahmood and Sofi[14] found that MAB appears to be more frequent in COPD compared to smokers without obstruction.(20.6% vs 7.4%). Majority of the COPD patients with in MAB in our study were from stage 3 and 4.(51.62 Vrs 22.58). Mehmood and Sofi have observed significant lower values of FEV1 in COPD patients with MAB. Casanova et al however didn't observe such correlation. MAB is found to be related directly to higher pack year of smoking exposure with significant association of pack year with MAB.(P <O.001).

Unlike our study, work done by Anand Agarwal et al showed weak co-relation of smoking with urinary excretion of Albumin in COPD cases.[15] BODE index was compared with prevalence of MAB. COPD pts with BODE index >4 had MAB (38.75%). Komurcuglu et al[16] found that the BODE index has direct relationship with levels of MAB. While Pao_2 had an inverse relationship with MAB in urine. Bulcan et al[13] reported that the presence of MAB were higher in COPD than smokers with normal spirometery and showed a inverse relationship between MAB and PaO_2, FEV1% and FVC % and a positive relationship between the presence of MAB and PaO2 and BODE index. MAB was significantly more in COPD pts having PaO2 below 70mmHg as compared to COPD with PaO2 above 70mmHg.(87.09 %v/s 12.90%, p <0.001) indicate that COPD pts are more hypoxic.as studied by Casanova et al[12] and Mehmood and Sofi[14], MAB is more in COPD pts having $PaCO_2$ > 45mmHg as compared to COPD pts having $PaCO_2$ < 45mmHg. Indicates COPD patients with MAB are more hypercapneic.

Studies conducted by Sujay and G.gajanan[17] have similar observation as well work by Casanova et al[12] and Mehmood and Sofi.[14] Kaysoydu et al[18] found that patients with COPD and MAB were more hypoxic and hypercapnic compared to those with only MAB. However Anand Kumar et al[15] found no relationship of $PaCO_2$ with MAB in his study. In 6MWT it was observed that MAB increases as exercise capacity decreases. Rakesh Kumar[19] also obtained similar result in his study. Harris et al[20] observed that albumin to creatinine ratio was inversely associated with FEV1 but not with FEV1/ FVC.

CONCLUSION

The determination of MAB is simple, inexpensive and non-invasive. COPD patients with type II respiratory failure, higher Bode index and MAB in urine should be examined regularly to identify early cardiovascular changes which start at microvascular level. Studies with larger population in different setting are needed to evaluate the role of MAB in COPD patients.

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