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Original Research Article

Prevalence and clinical significance of microalbuminuria and hypoxemia in patients with chronic obstructive pulmonary disease

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ABSTRACT

Background: Microalbuminuria is a sign of glomerular dysfunction in general and sign of tubulointerstitial disease to a lesser extent. Hypoxia induces endothelial cell to release a number of different vasoactive agents including endotheline-1, platelet derived growth factor (PDGF), nitric oxide; that causes endothelial injury and lead to microalbuminuria. This study was aimed to assess the prevalence of microalbuminuria in COPD patients and assess the Relationship of microalbuminuria with the disease severity in the forms of FEV1, PaO_2, $PaCO_2$, and BODE INDEX in COPD patients.
Methods: Total 130 COPD patients were included in our cross sectional study. Total patients were divided into two groups, 1st group was COPD with microalbuminuria while 2nd group was COPD without microalbuminuria. Lung function test, 6 min walk distance, arterial blood pressure (BP), BODE index, arterial blood gases, fasting and post prandial plasma glucose and kidney function tests were measured. Screening for microalbuminuria was done by measuring urinary microalbumin in a random spot urine collection.
Results: The prevalence of microalbuminuria was 29.23% in patients of COPD. As compared with COPD without microalbuminuria group, COPD with microalbuminuria group were more hypoxic (12% vs 74%, P=0.0001), more hypercapnic (22% vs 84%, p=0.00001) and most of the patients with grade III (16% vs 34%, p=0.00001) or grade IV (19% vs 47%, p=0.00001) severity (according to GOLD criteria).
Conclusions: Patients with severe COPD with hypoxemia or hypercapnia were significantly associated with microalbuminuria.

Keywords: Chronic obstructive pulmonary disease, Hypercapnia, Hypoxemia, Microalbuminuria

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is defined as a disease state characterized by airflow limitation that is not fully reversible. It is a preventable and treatable disease with some significant extra-pulmonary effects that may contribute to the severity in individual patient. The airflow limitation is usually progressive and associated with abnormal inflammatory response of lung to noxious particles or gases.[1] COPD is the fourth leading, but under recognized cause of morbidity and mortality worldwide.[2] and affects >10 million persons in the United States. Worldwide COPD was the sixth leading cause of death in 1990, and presently is the fifth.[3] The global burden of disease study projects that, by 2020, COPD will become the third leading cause of death worldwide.[4] The risk of eventual mortality from COPD is closely associated with reduced

level of pulmonary function (FEV1). Hypoxia induces endothelial cell to release a number of different vasoactive agents including endotheline-1, platelet derived growth factor (PDGF), nitric oxide; that can modify the contractility and proliferative state of underlying smooth muscle cells (SMCs) and can lead to increase cardiovascular diseases.[5-8] Microalbumunuria is believed to reflect a state of generalised endothelial cells dysfunction and therefore it is an emerging therapeutic target for primary prevention strategy.[9]

METHODS

This was a cross sectional study conducted on 130 patients who were diagnosed with COPD as per GOLD guidelines in the outdoor and indoor medicine department in SRNH, Prayagraj from May 2017 to August 2018. COPD patients with no other chronic illness attending medicine department of Swaroop Rani Nehru hospital, there detailed history, examination, blood investigation, urine microalbumin, PFT, chest X ray were done. All patients who have post bronchodilator (Salmeterol) FEV1/ FVC <0.70 were included and patients with Renal disease, Diabetes Mellitus, Hypertension, Cardiovascular disease or Asthma were excluded. All patients were divided into two groups, 1st group was COPD with microalbuminuria while 2nd group was COPD without microalbuminuria. 92 patients were in COPD without microalbuminuria group while 38 patients were in COPD with microalbuminuria group. Both the groups were observed for disease severity in term of degree of hypoxia, degree of hypercapnia and severity according to GOLD criteria, to find a relation with microalbuminuria. The numerical data were compared using t-test for independent variables and Chi-square tests for nonparametric variables. The level of significance was set at $p < 0.05$.

RESULTS

A total of 130 age and sex matched cases were analysed. Basic characteristics of cases are as shown in Table 1.

Table 1: Base line characteristics in COPD patients with and without Microalbuminuria.

Variables	COPD with microalbuminuria (mean±SD)	COPD without microalbuminuria (mean±SD)	t test	p value
AGE (years)	60.60±6.65	60.22±6.90	-0.286	0.775341
BMI (kg/m^2)	23.13±2.43	22.36±2.40	-3.03898	0.575341
FEV1 (%)	39.89±15.51	61.01±22.92	-5.20173	<0.00001
PaO_2 (mmHg)	66.97±5.98	80.60±8.04	-9.42194	<0.00001
$PaCO_2$ (mmHg)	56.87±10.94	43.10±7.89	-8.03898	<0.00001
BODE index	4.68±1.45	2.47±1.57	-4.03898	<0.00001

Results showed that there was significant difference in some of the base line characteristics in COPD without microalbuminuria Vs COPD with microalbuminuria, like mean FEV1 with 61.01±22.92 Vs 39.89±15.51, mean PaO_2 was 80.60±8.04 Vs 66.97±5.98; mean PaCO2 was found to be 43.10±7.89 Vs 56.87±10.94, mean BODE index was 2.47±1.53 Vs 4.68±1.45 respectively while difference between age in both the groups and BMI in both the groups were not significant (60.60±6.65 Vs 60.22±6.90 and 23.13±2.43 Vs 22.36±2.40 respectively).

Results showed that most of the patients in COPD with microalbuminuria group were having FEV1 ≤30% (i.e. maximum 47% patients) and FEV1 31-50% (34% patients) i.e. severity was severe to very severe according to GOLD criteria. In contrast to COPD with microalbuminuria group, most of the patients in COPD without microalbuminuria group were having FEV1 >80% (38% patients) and FEV1 51-80 % (27% patients) i.e. mild to moderate severity according to gold criteria. The difference was found significant (p value 0.00001) as given below in Table 2.

There was also a significant difference in the PaO_2 in both the COPD groups (p value 0.0001). Results showed that most of the patients in COPD with Microalbuminuria group were having PaO_2 <70 mmHg (i.e. 74% patients). In contrast to COPD with Microalbuminuria group, COPD without Microalbuminuria group were having most of the patients with PaO_2 >70 mmHg (i.e. 88% patients) as shown in Table 3.

$PaCO_2$ analysis in both the COPD groups showed that most of the patients in COPD with Microalbuminuria group were having $PaCO_2$ >45 mmHg (i.e. 84% patients). In contrast to COPD with Microalbuminuria group, COPD without Microalbuminuria group were having most of the patients with $PaCO_2$ <45 mmHg (i.e. 78% patients) and result was statistically significant (p value 0.0001) as shown in Table 4.

Table 2: Association between FEV1 and Microalbuminuria.

Fev1	COPD with microalbuminuria (n=38)	%	COPD without microalbuminuria (n=92)	%	Total no. of patients (n=130)	%	p value
≤30%	18	47	17	19	35	26.92	0.000017
31-50%	13	34	15	16	28	21.54	
51-80%	5	13	25	27	30	23.08	
>80%	2	6	35	38	37	28.46	
Total	38	29	92	71	130	100.0	X^2=24.78

Table 3: Association between PaO_2 and Microalbuminuria.

PaO_2	COPD with microalbuminuria (n=38)	%	COPD without microalbuminuria (n=92)	%	Total patient (n=130)	%	p value
<70 mmHg	28	74	11	12	39	30.00	0.0001
≥70 mmHg	10	26	81	88	91	70.00	
Total	38	29	92	71	130	100.0	X^2=48.79

Table 4: Association between $PaCO_2$ and Microalbuminuria.

$PaCO_2$	COPD with microalbuminuria (n=38)	%	COPD without microalbuminuria (n=92)	%	Total patient (130)	%	p value
≤45 mmHg	6	16	72	78	78	60.00	0.00001
>45 mmHg	32	84	20	22	52	40.00	
Total	38	29	92	71	130	100.0	X^2=43.73

DISCUSSION

Many studies reported a significant relationship between microalbuminuria and PaO_2, PCO_2 and FEV1 whereas some other study demonstrated that microalbuminuria had significant relationship only with PaO_2.

In this study, total 38 (29.23%) patients had Microalbuminuria. A recent study by Agrawal et al, in 2017 observe prevalence of Microalbuminuria in COPD patients to be 46%.[10] In study of Bulcon et al, in 2013 found that prevalence of Microalbuminuria to be 39%.[11] Mehmood and Sofi et al, in 2015, were also found that MAB was more frequent in COPD patients compared to smokers without obstruction (20.6% vs. 7.4%, respectively).[12] A study done by Sujay et al, in 2017 total of 46 patients (30%) out of 150 stable COPD patients had Microalbuminuria.[13]

In this study, majority of COPD patients with Microalbuminuria had GOLD stage of III (34%) and Stage IV (47%), and this association was statistically significant, P=0.0001. In a study by Sujay et al, majority of COPD patients with Microalbuminuria had GOLD stage of III (33.3%) and Stage IV (56.0%), and this association was statistically significant, p=0.0001.[13] In a study by Casanova et al, any association between MAB and spirometric severity of COPD was not observed. Mehmood and Sofi et al, were also found that COPD patients with Microalbuminuria had significantly lower levels of FEV1.[12,14]

In this study, majority of COPD patients with Microalbuminuria had MMRC dyspnea Grade IV and Grade III indicating that COPD patients with Microalbuminuria were more dyspneic and the association between Microalbuminuria and MMRC was statistically significant. In another study by Mehmood and Sofi et al in 2015, majority of COPD patients with Microalbuminuria had MMRC dyspnea Grade III-IV.[12]

This study showed that microalbuminuria was significantly more in COPD patients having PaO2 below 70 mmHg as compared to COPD patients having PaO2 above 70 mmHg (74% vs. 26%, respectively, p <0.0001), which indicates COPD patients with Microalbuminuria were more hypoxemic. A similar result was also seen in study by Sujay et al, Microalbuminuria was significantly more in COPD patients having PaO2 below 70 mmHg as compared to COPD patients having PaO2 above 70 mm Hg (100% vs. 7.14%, respectively, p <0.0001).[13] In the study of Mehmood and Sofi et al, and Agrawal et al, COPD patients having microalbuminuria were more hypoxic than those of COPD patients without microalbuminuria and it was inversely related to PaO_2.[10,12] In this study, microalbuminuria was significantly more in COPD patients having $PaCO_2$ ≥45 mmHg as compared to COPD patients having $PaCO_2$ <45

mm Hg (84% vs. 16%, respectively, p <0.0001), which indicates COPD patients with microalbuminuria were more hypercapnic. In a study by Sujay et al in 2017, Agrawal et al in 2017 and Mehmood and Sofi et al, the Microalbuminuria levels were positively related with the $PaCO_2$ level.[10,12,13] In this study, 6MWD test was also observed and found that; as exercise capacity decreases, the prevalence of Microalbuminuria increases. Kumar et al, also obtained an inverse relationship of 6MWD with Microalbuminuria levels in their study.[15] In this study, BODE index was compared with the prevalence of Microalbuminuria and found that as compared to patients with low BODE index (<3), patients with high BODE index (≥3) have more prevalence of microalbuminuria (47.76% of COPD patients with BODE index ≥3 vs. 9.52% of COPD patients with BODE index <3 had microalbuminuria) and it was statistically significant. Sujay et al, also observed BODE index and compared with the prevalence of MAB, 47.62% of COPD patients with BODE index ≥3 had MAB when compared to 9.09% of COPD patients with BODE index <3 and it was also statistically significant. Celli et al in 2004, showed that BODE index is a better predictor of mortality for COPD patients than the classical FEV1 values alone.[13,16]

CONCLUSION

In this study, majority of COPD patients with microalbuminuria were found in GOLD Stage III (34%) or GOLD Stage IV (47%) and only few patients were in GOLD stage I (6%). COPD patients (74%) with microalbuminuria were more hypoxic than COPD patients (12%) without microalbuminuria. COPD patients (84%) with microalbuminuria were more hypercapnic than COPD patients (22%) without microalbuminuria.

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