Study of Microalbuminuria in Patients with Stable COPD.

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ABSTRACT

Background: To our knowledge there are very few studies reporting a higher prevalence of microalbuminuria (MAB) in stable chronic obstructive pulmonary diseases (COPD) patients compared with age and sex matched control subjects. Present study was carried out with the purpose to find the prevalence and relationship of MAB with clinical and physiological parameters in stable COPD patients. **Methods:** Present study was done on 91 patients of COPD of either sex, aged between 30 to 80 years. A detailed history, physical examination, clinical and radiological examination was done with a view to establish diagnosis and condition made as per Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines. **Results:** Out of 51 patients, 41(80.39%) were males and 10(19.6%) were females with mean age of 58.48 ± 11.43 years and 58.20 ± 12.89 years respectively. Correlation of urine albumin creatinine ratio (UACR) values with FEV1% (r = -0.834, p=.001), BODE index (r=0.921, p=0.001), 6 MWD values (r = -0.910, p=0.001), PaO2 (r = -0.938, p=0.001) and mMRC grading (r =0.224, p=0.001) was significant in present study.**Conclusion:** MAB could be a promising biomarker to identify COPD patients at increased cardiovascular risk.

Keywords: COPD, microalbuminuria, biomarker, GOLD guidelines.

INTRODUCTION

COPD is the chronic respiratory disease that represents the most significant, and ever increasing, world public health problem. Its epidemiological, clinical, social and economic impact will increase in near future. Currently, COPD is the second most common non-infectious disease and fourth leading cause in the world, causing some 2.75 million deaths annually and global mortality is predicted to more than double by 2020.[1] COPD is associated with an abnormal inflammatory response in the lungs, with important extra-pulmonary manifestations and with the presence of multiple comorbidities.

Present study was carried out with the purpose to find the prevalence and relationship of MAB with clinical and physiological parameters in stable patients with COPD.

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MATERIALS AND METHODS

Present study was done on randomly selected 91 patients of COPD of either sex aged between 30 to 80 years in the Department of Medicine of BRD Medical College and Nehru Chikitsalya Gorakhpur from January 2014 to August 2015.

A written Informed consent from all patients and Institutional Ethics Committee approval was obtained before starting the study.

Patients were divided into a study group (51) and control group (40).

COPD was diagnosed according to criteria adopted and recommended by GOLD 2014.[2]

The clinical diagnosis was considered if any of chronic cough, chronic sputum production, breathlessness like symptoms were present along with a history of exposure to risk factors like tobacco smoke, occupational dust and chemical and biomass fuel.

Clinically stable COPD patients were included in the present study and patients with history of renal disease or presence of macroalbuminuria [urinary albumin to creatinine ratio (UACR) ≥ 300 m/g], unstable COPD patients with acute exacerbation, severe congestive heart failure, other respiratory diseases such as asthma, interstitial lung diseases, obstructive sleep apnea, acute infections and severe hepatic failure and uncontrolled comorbidities such as malignancy and patients with systemic hypertension and diabetes mellitus were excluded from the present study.

A detailed history, physical examination, clinically, radiological examination was done with a view to establish diagnosis and condition made as per GOLD guidelines.

Echocardiography, spirometry, ECG, 6 minute walk test and other investigations if required was also done. Dyspnea was assessed by using the modified British Medical Research Council (mMRC) dyspnoea scale which is based on patient's description of breathlessness as grade 0 (I only get breathless with strenuous exercise), grade 1 (I get short of breath when hurrying and the level or walking up a slight uphill), grade 2 (I walk slower than people of the same age on the level because of breathlessness or have to stop for breath when walking at my own pace on the level), grade 3 (I stop for breath after walking about 100 yards or after a few minutes on the level) and grade 4 (I am too breathless to leave the house or I am breathless when dressing).[3] The multidimensional BODE index was calculated according to BMI (grade 0 if >21 kg/m^2, grade 1 if ≤21 kg/m^2), FEV1% [grade 0 (≥65), grade 1 (50-64), grade 2 (36-49, grade 3 (≤35)], mMRC

dyspnea scale [grade 0 (0-1), grade 1 (2), grade 2 (3) and grade 3 (4)] and 6-minute walk distance (6MWD) [grade 0 (≥350), grade 1 (250-349), grade 2 (150-249) and grade 3 (≤149)].[4]

Data was compiled and analysed using IBM SPSS ver. 20.0. Categorical data was compared using percentages and paired T test was used wherever required. P values less than 0.05 was considered significant.

RESULTS

Out of 51 patients, 41 (80.39%) were males and 10 (19.6%) were females with mean age of 58.48 ± 11.43 years and 58.20 ± 12.89 years respectively. Most of the patients [16 (31.37%)] belonged to 61-70 year of age group.

Out of 40 control group patients, 30 (75%) were males and 10 (25%) were females with mean age of 59.05 ± 11.65 years and 58.23 ± 10.76 years respectively. Most of the patients belonged to 51-60 [13 (32.5%)] and 61-70 [12 (30%)] year age group.

The majority of study cases were from rural background [34 (66.66%)] and of controls were from urban areas [25 (62.5%)].

Most of the patients amongst cases were farmers [12 (23.52%)] and patients in controls had work involving travel and crowded places [9 (22.5%)].

The predominant symptom of COPD patients was cough (100%) and breathlessness (100%) followed by chest pain in 44 (86.27%) patients and in control group, 2 (5%) patients had cough and 2 (5%) had breathlessness.

Maximum [41 (80.39%)] patients amongst cases had an addiction of smoking and amongst controls all (100%) were smokers; 14 (35%) were tobacco addicts.

In cases, 7 (13.72%) patients had pallor; 2 (3.9%) had clubbing; 4 (7.8%) had edema and in controls, 4 (10%) had pallor.

In cases, 18 (35.29%) patients had a history of hospitalization in the past, whereas in control none of the patients had such history.

forced Severity of obstruction according to forced expiratory volume in one second (FEV1) values showed that most of the cases had [37 (72.54%)] FEV1 in the range of 50-80%, whereas only 2 (3.9%) cases had an FEV1 <30% and 38 (95%) of controls had FEV1>80%;2 (5%) had FEV1 in the range of 50-80%.

mMRC grading revealed that maximum [34(66.66%)] patients amongst cases had a dyspnea of grade 2, whereas 4 (10%) patients in controls had a dyspnea of grade 1; rest [36(90%)] had no dyspnea.

Amongst cases all patients had MAB whereas amongst controls only 4 (10%) had MAB ($p<0.0001$).

In the present study, 4 (7.84%) patients in cases had cor-pulmonale and all patients of cor-pulmonale had MAB levels above 200.

Amongst 3 patients who had a history of hospitalization once in the past, had MAB in the range of 101-150 whereas, out of 4 patients who had hospitalization history twice in the past, 3 (75%) had MAB in the range 151-200. Three (75%) out of 4 patients who were admitted >3 times in the past had MAB above 200.

DISCUSSION

Polatli et al studied MAB, von Willebrand factor and fibrinogen levels as markers of the severity in COPD exacerbation and concluded that the levels of plasma von Willebrand factor, fibrinogen and MAB may be helpful in grading the severity of COPD exacerbation.[5]

In our study, MAB was studied in stable COPD patients, unlike Polatli et al who studied it in COPD exacerbation. However MAB showed a positive correlation with severity in both the studies. In our study severity was assessed using various clinical and physiological parameters and these parameters were correlated with MAB levels which were found to be significant. Thus, MAB as a marker of endothelial dysfunction in COPD could make us aware of the future systemic outcomes like alterations in the microvasculature beforehand so that multi-organ damage could be prevented.

A very similar study of Cassanova et al established the prevalence and relationship of MAB with clinical and physiological parameters in stable patients with COPD and concluded that MAB is frequent in patients with COPD and is associated with hypoxaemia independent of other cardiovascular risk factors.[6] In our study, we found positive results as mentioned by Cassanova et al.

Komurcuoglu et al found that the BODE index has a direct relationship with the levels of micro-albumin in urine, while paO2 levels had an inverse relationship with micro-albumin in urine.[7] Present study had also reported the similar results. The present study also obtained a direct relationship of mMRC grading and the inverse relationship of FEV 1% and 6MWD with MAB levels which was not studied by Komurcuoglu et al.

Bulcun et al in a similar study showed that UACR was significantly higher in patients with COPD than in the control group. The rate of the presence of MAB was also higher in patients with COPD than in the control group. Urinary creatinine was significantly related with PaO2, PaCO2 and BODE index according to Pearson correlation analysis. The study suggested that MAB was related with hypoxemia and increased BODE index in patients with COPD independently.[8]

Table 1: Correlation of Different Parameters with Mircoalbumin levels.

Parameters		Mircoalbumin level (mcg/min)						Mean ±SD
		0-30	31-50	51-100	101-150	151-200	201-300	
FEV1 (liters)	>80 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 ±0
	50-80 (37)	0 (0)	0 (0)	5(13.51)	20(54.05)	12(32.43)	0 (0)	124.79 ± 9.18
	30-50 (13)	0 (0)	0 (0)	0 (0)	2(15.38)	8(61.53)	3(23.07	185.76± 32.39
	<30 (1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	199.3± 23.23
BODE Index	0-3 (18)	0 (0)	0 (0)	5 (27.77)	12(66.66)	1(5.55)	0 (0)	100.88±21.08
	4-6 (21)	0 (0)	0 (0)	0 (0)	13(61.9)	8(38.1)	0 (0)	149.56±15.61
	7-10 (12)	0 (0)	0 (0)	0 (0)	0 (0)	8(75)	4(25)	198.56 ±28.64
6MWD Test (min)	>400 (7)	0 (0)	0 (0)	4 (57.14)	3(42.85)	0 (0)	0 (0)	91.04 ±13.12
	301-400 (25)	0 (0)	0 (0)	1 (4)	21(84)	3(12)	0 (0)	130.31 ±23.84
	201-300 (10)	0 (0)	0 (0)	0 (0)	1(10)	9(90)	0 (0)	169.37 ±14.71
	101-200 (7)	0 (0)	0 (0)	0 (0)	0 (0)	5(71.42))	2(28.57)	194.63 ±21.90
	<100 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2(100)	248.75±7.42
paO2 Level	>80 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 ±0
	71-80 (15)	0 (0)	0 (0)	5(33.33)	10(66.66)	0 (0)	0 (0)	99.75 ± 21.31
	61-70 (18)	0 (0)	0 (0)	0 (0)	11(61.11)	7(38.88)	0 (0)	142.57± 13.91
	51-60 (15)	0 (0)	0 (0)	0 (0)	0 (0)	14(93.33)	1(6.66)	176.76± 17.71
	<50 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3(100)	244.63 ± 8.83
mMRC Grading	Grade 1 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 ±0
	Grade 2 (36)	0 (0)	0 (0)	5(13.8)	23(63.88)	8(22.22)	0 (0)	125.00± 8.929
	Grade 3 (12)	0 (0)	0 (0)	0 (0)	1(8.33)	10(83.33)	2(3.9)	82.79± 19.122
	Grade 4 (3)	0 (0)	0 (0)	0 (0)	0 (0)	1(33.33)	2(66.66)	232.25± 29.01

Data are expressed as no of patients (%), FEV1; forced expiratory volume in one second, 6MWD; 6-minute walk distance, PaO2**;** partial pressure of oxygen**,** mMRC; Modified Medical Research Council, BODE; Body mass index, Obstruction, Dyspnea, **E**xercise capacity. Correlation of urine albumin creatinine ratio (UACR) values with FEV1% (r = -0.834, p=.001), BODE index (r=0.921, p=0.001), 6MWD values (r = -0.910, p=0.001), PaO2 (r = -0.938, p=0.001) and mMRC grading (r =0.224, p=0.001).

In the present study difference in mean age and sex of both the groups was statistically insignificant. In the present study there was a significant difference between the MAB level in both the groups (p<. 0001). Also, there was a significant inverse relationship between UACR and PaO2 (r= -0.938, p= 0.001), FEV1% (r= -0.834, p= 0.001), 6MWD (r= -0.910, p= 0.001).

In addition, there was a positive relationship between UACR and BODE index (r= 0.921, p= 0.002) and mMRC grading (r= 0.224, p= 0.001). Hence, the present study showed significant relations between all parameters unlike Bulcan et al.

The present study also found that all patients with cor-pulmonale had MAB >200 which was highest. The study also found that COPD patients with pulmonary hypertension showed high MAB levels depicting that MAB are a marker of endothelial dysfunction.

Celli et al showed that BODE index is a better predictor of mortality for COPD patients than the classical FEV1 values alone. Increased BODE index values are observed in patients with more severe disease. Similarly, in our study, MAB which is predictive for cardiovascular disease risk, was related with BODE index and hypoxemia, and also related with pulmonary function parameters such as %FEV1 etc.[4]

John M et al studied that COPD patients have increased UACR compared to controls (asymptomatic smokers) which was related to increased aortic stiffness measured by aortic pulse wave velocity (PWV).[9]

In our study unlike above mentioned study included COPD patients without any coexisting comorbidities like renal disease, IHD, hypertension and diabetes. We found that in patients with cor-pulmonale or pulmonary hypertension MAB levels were the highest. Also significant correlation of FEV1, BODE index which includes BMI, 6MWD with UACR levels was established.

Kaysoydu E et al evaluated the presence of MAB in patients with COPD and its relationship to inflammation, arterial blood gas parameters and 24-hour ambulatory blood pressure alterations.[10] They did not find a significant relationship between MA, gender and age. Also in our study no relationship could be established between these parameters. But significant relationship was not found between MA and a history of smoking. Contrary to Kaysoydu E et al, in our study MA had a significant correlation with spirometric parameters along with a relationship with hypoxemia and pulmonary hypertension. No relationship of PaCO2 with MA was shown in our study.

Mehmood K et al found that COPD patients with MAB had significantly lower levels of FEV1 (p=0.0003) also a majority of COPD patients with MAB had GOLD stage of III and IV (33.3%), while COPD patients without MAB had GOLD stage of I and II (95.3%) (p<0.0001). The possible explanation for this is that impaired lung function, including COPD, has been associated with increased systemic arterial stiffness.[6,11] Contrary to this in our study, all COPD cases had MAB and not only PaO2 but other clinical and physiological parameters showed

significant correlation with UACR levels. Also COPD cases with mMRC grade 2 showed high MAB levels.

Harris B et al tested if microvascular changes in the retina, kidneys and heart were associated with obstructive spirometry(FEV1%) and low lung density on computed tomography, but did not find any relationship between UACR and FEV1% values.[12] In the present study, controls were asymptomatic smokers with normal spirometry and only 4 (10%) of them had MAB which is a marker of endothelial dysfunction. So no significant effect of smoking like in various other studies on endothelial dysfunction and systemic microvasculature was shown. Also, unlike Harris et al, we obtained a significant correlation of spirometric parameters (FEV1%) with UACR levels.

CONCLUSION

The determination of MABor UACR is simple, inexpensive and non-invasive and MAB can be a surrogate marker of endothelial dysfunction.

REFERENCES

1. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. Lancet. 1997; 349: 1498-504.
2. GOLD. Global Strategy for the diagnosis, management and Prevention of Chronic Obstructive Pulmonary Disease. updated 2014.
3. Nishimura K, Izumi T, Tsukino M, Oga T. Dyspnea is a better predictor of 5-year survival than airway obstruction in patients with COPD. Chest. 2002; 121:1434-40.
4. Celli BR, Cote CG, Marin JM, Casanova C, Montes de Oca M, Mendez RA et al. The body-mass index, air flow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. N Engl J Med. 2004; 350: 1005–12.
5. Polatli M, Cakir Q, Cildag O, Bolaman AZ, Yenisey C, Yenicerioglu Y. Microalbuminuria, von Willebrand factor and fibrinogen levels as markers of the severity in COPD exacerbation. J Th romb Th rombol. 2008; 26:97–102.
6. Casanova C, Torres JP, Navarro J, Jaíme AA, Toledo P, Cordoba E et al. Microalbuminuria and Hypoxemia in Patients with Chronic Obstructive Pulmonary Disease. Am J Respir Crit Care Med. 2010; 182 (8): 1004–10.
7. Komurcuoglu A, Kalenci S, Kalenci D, Komurcuoglu B, Tibet G. Microalbuminuria in chronic obstructive pulmonary disease. Monaldi Arch Chest Dis. 2003; 59: 269–72.
8. Bulcun E, Ekici M, Ekici A. Microalbuminuria in chronic obstructive pulmonary disease. COPD. 2013; 10: 186–92.
9. John M, Hussain S, Prayle A, Sims R, Cockroft JR, Bolton CE. Target Renal Damage: the microvascular associations of increased aortic stiffness in patients with COPD. Respiratory Research. 2013, 14; 31:23-9.
10. Kaysoydu E, Arslan S, Yıldız G, Candan F. Factors Related to Microalbuminuria in Patients with Chronic Obstructive Pulmonary Disease. Adv Clin Exp Med. 2014; 23 (5):749–55.
11. Mehmood K, Sofi FA. Microalbuminuria and Hypoxemia in Patients with COPD. J Pulm Respir Med. 2015; 5 (4):12-8.
12. Harris B, Klein R, Herold MJ, Hoffman EA, Ahmed FS, Jacobs DR et al. The Association of Systemic Microvascular Changes with Lung Function and Lung Density: A Cross-Sectional Study. 2012; 7(12):e50224.

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