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Research Article

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Microalbuminuria and the Presence of Hypoxemia in Patients with Chronic Obstructive Pulmonary Disease

S. M. Rezwanuzzaman[1], A. K. Al Miraj[2,*], Shuvo Majumder[3], Zakir Hasan[4], Kaoser Alam[5], Nasir Uddin Patwary[6]

[1]Medical Officer, Dept of Internal Medicine, BSMMU

[2]Research Assistant, Dept of Vascular Surgery, BSM Medical University Dhaka, Bangladesh

[3]Medical Officer, Dept of Respiratory Medicine, BSMMU

[4]Medical officer, Dept of Internal Medicine, BSMMU

[5]Medical officer, Dept of Internal medicine, BSMMU

[6]Medical officer, Dept of Internal medicine, BSMMU

Corresponding author:

A. K. Al Miraj, Research Assistant, Dept of Vascular Surgery, BSM Medical University Dhaka, Bangladesh

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Abstract

Introduction: Worldwide, the Chronic Obstructive Pulmonary Disease (COPD) is a major public health concern; On the basis of epidemiologic data, by 2020, COPD will be the third leading cause of death worldwide.

Objective: To assess the frequency of Microalbuminuria and the presence of Hypoxemia in patients with COPD.

Materials and Methods

Study Design: Cross-sectional observational study.

Place of Study: Department of Medicine & Respiratory Medicine in Dhaka Medical College Hospital (DMCH).

Study Period: Six months after approval of the protocol

Study Population: Patient suffering from COPD and admitted in Department of Medicine & Respiratory medicine, DMCH, Dhaka, Bangladesh. Total 100 samples were included in this study. COPD usually presents with a history of chronic cough with sputum production or exertional breathlessness which may be associated with relevant clinical findings and a post-bronchodilator FEV1/FVC less than 0.7. In most cases it is associated with smoking

Results: Total 100 patients of COPD were included in the study. Mean age was 58.16±5.4 years ranging from 50 to 74 years. Out of 100 patients, majority (42%) were from age group 55 to 60 years. Among all, 82% patients were male and 18% were female, of 100 patients, majority (30%) were day laborer. Only 2% were unemployed. The percentage of housewives was 18%. Other 34% were businessman and service

holders. COPD severity was assessed using GOLD guideline. Out of 100 COPD patients, 38% had severe COPD (GOLD stage III). 16 % patients were in mild (Stage I) and 32% patients were in moderate stage (Stage II). The condition was very severe for 14% patients (Stage IV). Of 100 COPD patients, 30% had microalbuminuria. Among 100 COPD patients, chance of microalbuminuria increases among COPD patients with the increase of age significantly. There is smoking history of 36 pack year for COPD patients with microalbuminuria. Of 100 patients 26% were hypoxemic. The average forced expiratory volume (FEV1%) was 37.40 with standard deviation 14.48 for patients with microalbuminuria. The PaO2 and PaCO2 is 63.06 with standard deviation 7.09 and 46.09 with standard deviation 2.43 for COPD patients with microalbuminuria respectively. All of these characteristics are significant with p-value 0.00. However, the body mass index (BMI), systolic blood pressure (SBP) and diastolic blood pressure (DBP) were not found significant. The patients who had PaO2 less than 70 mmHg were considered hypoxemic. The patients who had microalbuminuria among them 87% were hypoxemic. Only 13% patients were free from hypoxemia who had microalbuminuria. Patients without microalbuminuria had no history of hypoxemia. There is significant relation exists between hypoxemia and the presence of microalbuminuria ($p<0.5$).

Conclusion: In this study, about one-fourth of the patients have hypoxemia and more than one fourth of the patients have microalbuminuria. Stage III was more frequent among the study population but there was no association between severity grading and presence of microalbuminuria. However, significant relation is found between co-existence of both microalbuminuria and hypoxemia in COPD patients.

Introduction

Worldwide, the Chronic Obstructive Pulmonary Disease (COPD) is a major public health concern; on the basis of epidemiologic data, by 2020, COPD will be the third leading cause of death worldwide and the fifth leading cause of disability.[1-3] Like other countries, in Bangladesh, it has become an important cause of morbidity and mortality with prevalence of 21.24% at the age of 40 and above & in general population it is about 4.3%. Usually patients with COPD present to the physicians mostly due to respiratory illness, but may present with a number of non-respiratory symptoms. Among them cardiovascular morbidity and mortality are mostly highlighted.[3-5] Cardiovascular disease plays an important role in concerning morbidity and mortality in patients with COPD.[6] Studies showed that, the degree of airflow limitation was an independent predictor of cardiovascular events, implying a causal relationship between airflow obstruction and cardiovascular disease.[7,8] Although smoking is an established risk factor for both atherosclerosis and COPD, epidemiological studies have revealed that the increased cardiovascular risk in COPD patients seems to be independent of smoking habits.[8,9] The mechanisms underlying the relationship between COPD and cardiovascular disease are currently unclear. Multiple causal factors leading to vessel wall damage and atherosclerotic plaques have been suggested, including hypoxemia, concurrent systemic inflammation and oxidative stress, sympathetic activation and physical inactivity.[10-13] Hypoxemia has multiple impacts on the vascular system. The major molecular sensors for hypoxia at the cellular level are hypoxia inducible factors and haemoxygenase. Hypoxia also acts on the vasculature directly conveying its damaging effects through disruption of the control of vascular tone, particularly in the coronary circulation, enhancement of inflammatory responses and activation of coagulation pathways.[14] The impairment of endothelial function represents a potential pathophysiological link between COPD and cardiovascular disease. Endothelial function as assessed by flow mediated dilatation (FMD) of the brachial artery has been shown to provide predictive information concerning the future occurrence of cardiovascular events.[15-17] Therefore, noninvasive measures of endothelial function are of major interest, with the anticipation that patients at risk could be identified early in the absence of clinically apparent vascular disease.[18-20] A recent concept is that microalbu-

minuria (MAB) is a marker of extensive endothelial dysfunction or generalized vasculopathy, which may lead to heightened atherogenic states.[20,21] Very few studies also examined this change and found it could be a predictor of cardiovascular mortality and morbidity, particularly in COPD patients.[3,4,21] One possible explanation is that endothelial dysfunction might promote increased penetration of atherogenic lipoprotein particles in the arterial wall but glycemic status, insulin resistance, procoagulant state and adhesion molecules have all been implicated in the pathogenesis.[19] Considering this hypothesis the study is planned to see the correlation between microalbuminuria and hypoxemia in COPD patients admitted to a tertiary care hospital.

Materials and Methods

Study Design

Cross-sectional observational study.

Place of Study

Department of Medicine & Respiratory Medicine in Dhaka Medical College Hospital (DMCH).

Study Period

Six months after approval of the protocol

Study Population

Patient suffering from COPD and admitted in Department of Medicine & Respiratory medicine, DMCH

Sampling Method

Purposive convenient sampling.

Sample Size

In Bangladesh, no such relevant study is available to get the required prevalence value and data on the prevalence of microalbuminuria in hypoxemic patients with COPD in hospital settings. Considering 50% prevalence for this study (as prevalence is not known to us), sample size calculation was done by following statistical formula.

$$n = \frac{Z^2 pq}{d^2}$$

Due to shortage of the study time, total 100 samples were included in this study.

Selection Criteria

Inclusion Criteria

- Diagnosed case of COPD according to GOLD criteria
- Both genders
- Willing to participate

Exclusion Criteria

- History of renal disease in patients with COPD
- COPD patients with cardiovascular disease, diabetes mellitus, hypertension and other comorbidities such as malignancy, or other confounding diseases.

Operational Definitions

COPD

COPD usually presents with a history of chronic cough with sputum production or exertional breathlessness which may be associated with relevant clinical findings and a post-bronchodilator FEV1/FVC less than 0.7. In most cases, it is associated with smoking.

Microalbuminuria

Microalbuminuria refers to the urinary excretion of small amount of albumin (30- 300mg/24 hours).

Urinary ACR (Albumin-Creatinine Ratio): 30-300 mg/gm (or, 3-30 mg/mmol) is considered microalbuminuria

Hypoxemia

will be defined as arterial PaO2 <70 mm Hg

Severity of COPD

Stage 1 (Mild): FEV1 ≥ 80% predicted

Stage 2 (Moderate): FEV1 50-79% predicted

Stage 3 (Severe): FEV1 30-49% predicted

Stage 4 (Very severe): <30% predicted

Data Processing and Analysis

Data will be summarized as relative frequencies for categorical variables, mean (SD) for normally distributed variables, for non-normal data. Pearson chi-square, was used according to the variable type and to estimate their association. Throughout the study,

significance level was considered as the P-value of 0.05 or less. And all the calculations were made with SPSS 22.0 (Chicago, IL).

Results

Total 100 patients with COPD were included in the study. Mean age was 58.16±5.4 years ranging from 50 to 74 years. Out of 100 patients, majority (42%) were from age group 55 to 60 years. Among all, 82% patients were male and 18% were female. Of 100 patients, majority (30%) were day labourers. Only 2% were unemployed. The percentage of housewives was 18%. Other 34% were businessman and service holders. Out of 100 patients 54% were from rural areas and 46% were from urban area. Majority (34%) of the patients of the study had no education. Only 14% had completed graduation or post-graduation. The percentage of completing primary or below primary was 26%. Similarly 26% had SSC or HSC certificates. Out of 100 patients, 48% had their monthly income below 15 thousand taka. Among 100 COPD patients, 80% patients had habit of smoking. Almost 52% patients had a smoking history of 26 – 35 pack year. And the 18% patients had a smoking history of more than 35 pack-year. Only 6% patients were chronically exposed to biomass fuel. Table 1-2

COPD severity was assessed using GOLD guideline. Out of 100 COPD patients, 38% had severe COPD (GOLD stage III). 16 % patients were in mild (Stage I) and 32% patients were in moderate stage (Stage II). The condition was very severe for 14% patients (Stage IV). Of 100 COPD patients. 30% had microalbuminuria**.** Figure 1

Of 100 Patients, 26% had hypoxemia. Those patients, who had PaO2 less than 70 mmHg were considered hypoxemic. Figure 2

Among 100 COPD patients, chance of microalbuminuria increases among COPD patients with the increase of age significantly. There is smoking history of 36 pack year for COPD patients with microalbuminuria. The average forced expiratory volume (FEV1%) was 37.40 with standard deviation 14.48 for patients with microalbuminuria. The PaO2 and PaCO2 were 63.06 with standard deviation 7.09 and 46.09 with standard deviation 2.43 for COPD patients with microalbuminuria respectively. All of these characteristics are significant with p-value 0.00. However, the body mass index (BMI), systolic blood pressure (SBP) and diastolic blood pressure (DBP) were not found significant. Table 3

Among 100 COPD patients, it is observed that the majority 33% of patients with microalbuminuria had the forced expiratory volume (FEV1%) in very severe stage and 40% had it in severe stage. There is no history of patients suffering from mild stage with microalbuminuria. Table 4

The patient who had PaO2 less than 70 mmHg were considered hypoxemic. Among 100 COPD patients, almost 87% patients with microalbuminuria were hypoxemic. Only 13% patients were free from hypoxemia who had microalbuminuria. Patients without microalbuminuria had no history of hypoxemia. There is significant relation exists between hypoxemia and presence of microalbuminuria ($p<0.5$). Table 5

Discussion

Microalbuminuria is an important risk factor for cardiovascular diseases. Microalbuminuria may be seen due to hypoxemia in patients with chronic obstructive pulmonary disease (COPD) [22]. This study was designed to assess the prevalence of microalbuminuria and its relation with hypoxemia in patients with COPD. Total 100 patients were included. The mean age was 58.16±5.4 years, ranging from 50 to 74 years. This is concordant with the findings of Sujay and Gajanan [23] who found a mean age of 59.67±5.60 years in their study. Majority patients belonged to age group 55 to 60 years (42%), followed by 61 – 65 years (28%). This is slightly different from the findings of Alam et al [24] who reported that majority COPD patients were aged between 60 – 69 years (27.5%) followed by 50 – 59 years (13.6%). This difference may be due to age grouping between the reports. But both the studies confirm that age is a well established risk factor for COPD as increasing prevalence of COPD is noted in higher age groups 79. In this study 82% patients were male and 18% were female. Sujay and Gajanan [23] and Bulcan et al [25] reported a similar high prevalence of male

Table 1. Demographic profile, patients of COPD (N=100)

Age	**N**	**%**
Below 55	26	26%
55-60	42	42%
61-65	28	28%
Above 65	4	4%
Sex		
Male	82	82%
Female	18	18%
Occupation		
Service	18	18%
Business	16	16%
Housewife	18	18%
labourer	30	30%
unemployed	2	2%
Farmer	16	16%
Residence		
Urban	46	46%
Rural	54	54%

Table 2. History of respiratory irritants among COPD patients (n=100)

Characteristics	**Categories**	**Frequency**	**Percentage (%)**
Habit of smoking	Yes	80	80
	No	20	20
	Up to 25	30	30
Smoking pack year	26 to 30	26	26
	31 to 35	26	26
	Above 35	18 29.62±6.41	18
Exposure of biomass fuel	Exposure	6	6
Not exposure		94	94

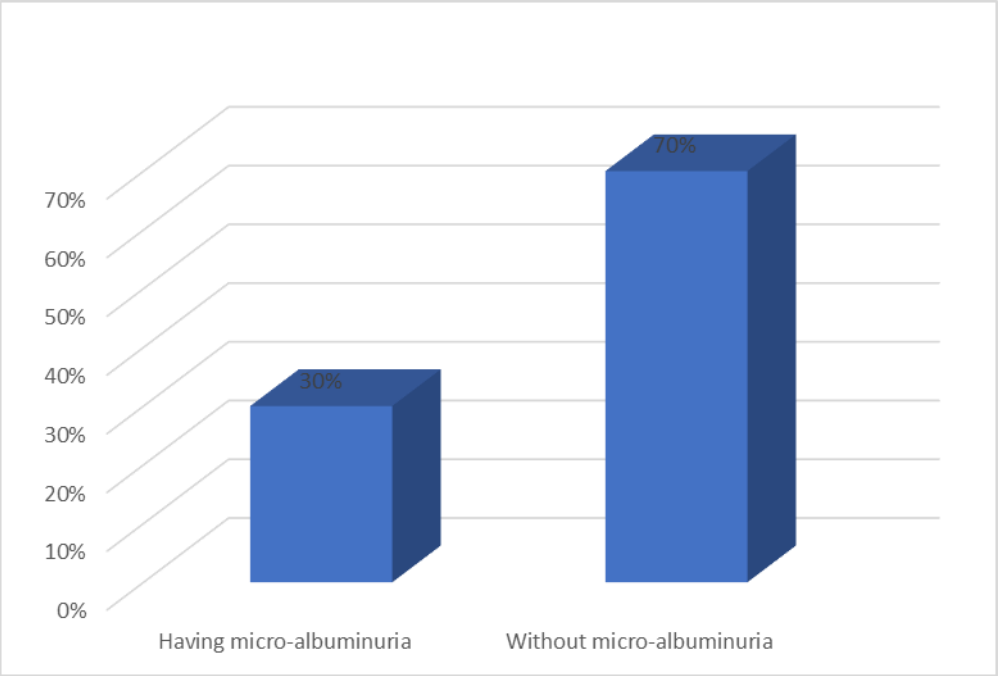

Figure 1. Distribution of COPD patients according to having microalbuminuria (n=100)

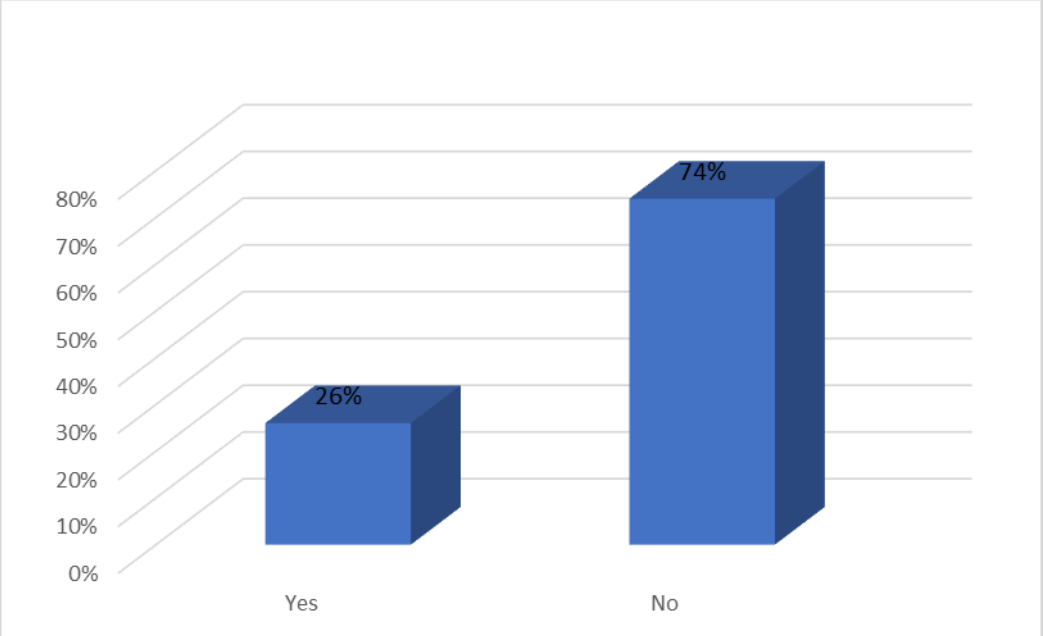

Figure 2. Distribution of COPD patients according to development of hypoxemia (n=100)

Table 3. Comparison of baseline characteristics in patients with and without microalbuminuria (n=100)

Variables	Mean ± SD		P value
	COPD patients without MAB (n=70)	COPD patients with MAB (n=30)	
Age (years)	55.89±3.76	63.47±4.99	0
BMI (kg/m2)	24.05±2.99	23.61±2.94	0.64
Smoking packyears	26.69±4.70	36.47±4.29	0
FEV1%, predicted	59.34±22.78	37.40±14.48	0
PaO2 (mmHg)	81.43±3.66	63.06±7.09	0
PaCO2 (mmHg)	38.97±4.40	46.09±2.43	0
SBP (mmHg)	111.51±12.06	112.53±10.67	0.78
DBP (mmHg)	68.86±6.54	66.20±5.63	0.18

Table 4. Association between COPD severity and microalbuminuria (n=100)

COPD severity	MAB absent n (%)	MAB present n (%)	Total n (%)	P value
Very severe (FEV_1 ≤30 % predicted)	04 (5.7)	10 (33.3)	14 (14)	
Severe (FEV_1 31-49% predicted)	26 (37.1)	12 (40.0)	38 (38)	0.025
Moderate (FEV_1 50-79% predicted)	24 (34.3)	08 (26.7)	32 (32)	
Mild (FEV_1 ≥80% (FEV1 ≥80% predicted)	16 (22.9)	0	16 (16)	

*p-value is determined by Chi-square test

Table 5. Association between hypoxemic status and microalbuminuria (n=100)

PaO2 (mmHg)	MAB absent n (%)	MAB present n (%)	Total n (%)	P value
<70	00 (0.00)	13 (86.7)	14 (14)	<0.001
≥70	35 (100)	02 (13.3)	38 (38)	

in their study. The high prevalence of male among COPD patients can be linked to high prevalence of tobacco use among male adults in Bangladesh as noted by Khandker et al [26]. Majority patients were day labourer (30%), farmer comprised 16% and businessman comprised 16% of study population. Alam et al[24] noted that COPD prevalence in Bangladeshi adults were about three times higher in manual workers than non-manual workers. This explains the high prevalence of day labourer and farmers in this study. Slightly more than half of the patients (54%) came from rural area. This was also noted in the study by Alam et al [24] in Bangladesh and Zhong et al [27] in China. Such community variability of COPD can be explained by connecting occupations like farmer living in rural area, use of biomass fuel in the village community and smoking habit among manual workers. Majority patients were illiterate (34%), followed by 26% patients appeared at primary education. This higher prevalence of lower educational qualification in COPD patients was also found in the study by Alam et al[24]. Majority of the patients came from lower income categories in this study. A similar finding was elicited by Alam et al[24] in their study COPD prevalence study among the adult population of Bangladesh. In the present study, 80% of patients were active smokers. Among them, 52% of patients smoked 26 to 35 pack-years. The mean smoking pack-year was 29.62±6.41 years. A similar mean pack-year of 28.91±6.13 was reported by Sujay and Gajanan in their study entitled "Clinical significance of microalbuminuria and hypoxemia in patients with chronic obstructive pulmonary disease" [23]. On the other hand Casanova [28] found a high mean pack-year of 58±25 among COPD patients in their study entitled "Microalbuminuria and hypoxemia in patients with chronic obstructive pulmonary disease". In the present study 38% patients had severe COPD (GOLD stage III), 32% had moderately severe COPD (GOLD stage II), 16% had mild disease (GOLD stage I) and 14% had very severe disease (GOLD stage IV). In contrast Sujay and Gajanan (2) reported 25% GOLD Stage I, 21% Stage II, 20% Stage III, and 34% Stage IV COPD cases in their study. Stage IV cases were higher in their study in comparison to present study. Alam et al (3) in their study entitled "Prevalence and determinants of chronic obstructive pulmonary disease (COPD) in Bangladesh" found that among 13.5% cases of COPD 8% had GOLD stage II disease, 2.7% had stage I disease, 2.3% had stage III disease and 0.6% had Stage IV disease. Their study was community based and depicts the proportion of COPD severity in the community. In contrast the present study as well as the study by Sujay and Gajanan[23] was conducted in a hospital setting where advanced cases COPD cases usually get admitted. Microalbuminuria (MAB) was found in 30% patients. This is concordant with other studies: Mehmood and Sofi (8) reported MAB in 20.6% COPD patients and Sujay and Gajanan[23] reported MAB in 30% patients. Casanova[27] compared presence of MAB in COPD patients and non-COPD smoker controls and found higher prevalence of MAB among COPD patients. In a study by Bulcun et al., [25] it was found that the prevalence of MAB is 39%. In the present study, majority of COPD patients with MAB had GOLD stage of III (40%) and Stage IV (33%), and this association was statistically significant; P = 0.025. In a study by Casanova et al., [28] any association between MAB and spirometric severity of COPD was not observed. Mehmood and Sofi [29] found that COPD patients with MAB had significantly lower levels of FEV_1 which is similar to finding of present study. In the present study COPD with MAB patients had mean FEV_1 % predicted of 37.40±14.48 which is significantly lower than those without MAB (59.34±22.78). 26% patients were in hypoxemic status in this study. MAB was significantly more in COPD patients having PaO2 below 70 mm Hg as compared to COPD patients having PaO2 above or equal to 70 mmHg (86.7% vs. 13.3%, respectively, $P < 0.001$), which indicates COPD patients with MAB were more hypoxemic. In a study by Sujay and Gajanan a Casanova et al. [28] and Mehmood and Sofi, [29] patients with COPD and MAB were more hypoxemic than those without MAB, and it was inversely related to PaO2.

Conclusion

In this study, about one fourth of the patients had hypoxemia and more than one fourth of the patients had microalbuminuria. Stage III were more frequently among the study population but there was no association

between severity grading and presence of microalbuminuria. However, significant relation is found between the co-existence of both microalbuminuria and hypoxemia in COPD patients.

Limitations of the Study

This was a single-center study.

The sample size was not representative

Recommendations

Depending upon the study findings, a further case-control study is recommended.

References

1. Raherison C, Girodet PO. Epidemiology of COPD. Eur Respir Rev. 2009; 18(114):213–21.
2. The Pharma World. The First & Only Pharmaceutical & Health Journal In Bangladesh". Thepharmaworld.com.bd. N.p., 2017. Web. 25 May 2017.
3. Bulcun E, Ekici M, Ekici A, Kisa U. Microalbuminuria in chronic obstructive pulmonary disease. COPD. 2013 Apr; 10(2): 186-92. doi: 10.3109/15412555.2012.735292.
4. Romundstad S, Naustda T, Romundstad R, Sorger H, Langhammer A. COPD and microalbuminuria: a 12-year follow-up study. Eur Respir J 2014; 43 (4):1042-50.
5. Sin DD, Anthonisen NR, Soriano JB, Agusti AG. Mortality in COPD:role of comorbidities. Eur Respir J 2006; 28:1245–1257.
6. McGarvey LP, John M, Anderson JA, et al. Ascertainment of cause-specific mortality in COPD: operations of theTORCH Clinical Endpoint Committee. Thorax 2007; 62: 411–415.
7. Engstro¨m G, Melander O, Hedblad B. Population-based study of lung function and incidence of heart failurehospitalizations. Thorax 2010; 65: 633–638.
8. Sin DD, Wu L, Man SF. The relationship between reduced lung function and cardiovascular mortality: apopulation-based study and a systematic review of the literature. Chest 2005; 127: 1952–1959.
9. Curkendall SM, DeLuise C, Jones JK, et al. Cardiovascular disease in patients with chronic obstructive pulmonary disease, Saskatchewan Canada: cardiovascular disease in COPD patients. Ann Epidemiol 2006; 16: 63–70.
10. Sabit R, Thomas P, Shale DJ, et al. The effects of hypoxia on markers of coagulation and systemic inflammation in-patients with COPD. Chest 2010; 138: 47–51.
11. Sin DD, Man SF. Chronic obstructive pulmonary disease: a novel risk factor for cardiovascular disease. Can J Physiol Pharmacol 2005; 83: 8–13.
12. MacNee W. Pulmonary and systemic oxidant/ antioxidant imbalance in chronic obstructive pulmonary disease. Proc Am Thorac Soc 2005; 2: 50–60.
13. Watz H, Waschki B, Boehme C, et al. Extrapulmonary effects of chronic obstructive pulmonary disease on physical activity: a cross-sectional study. Am J Respir Crit Care Med 2008; 177: 743–751.
14. Chan CK, Vanhoutte PM. Hypoxia, vascular smooth muscles and endothelium. Acta Pharm Sin B [Internet]. 2013; 3(1):1–7.
15. Rubinshtein R, Kuvin JT, Soffler M, et al. Assessment of endothelial function by non-invasive peripheral arterial tonometry predicts late cardiovascular adverse events. Eur Heart J 2010; 31: 1142–1148.
16. Lind L, Berglund L, Larsson A, et al. Endothelial function in resistance and conduit arteries and 5-year risk of cardiovascular disease. Circulation 2011; 123: 1545–1551.
17. Celermajer DS, Sorensen KE, Gooch VM, et al. Non-invasive detection of endothelial dysfunction in children and adults at risk of atherosclerosis. Lancet 1992; 340: 1111–1115.
18. Gokce N, Keaney JF Jr, Hunter LM, et al. Risk stratification for postoperative cardiovascular events via noninvasive assessment of endothelial function: a prospective study. Circulation 2002; 105: 1567–1572.

19. Naidoo DP. The link between microalbuminuria, endothelial dysfunction and cardiovascular disease in diabetes. Cardiovasc J S Afr 2002;13(4): 194-9. (Abstract citation).

20. Anthonisen NR, Skeans MA, Wise RA, Manfreda J, Kanner RE, Connett JE. The effects of a smoking cessation intervention on 14.5-year mortality: a randomized clinical trial. Ann Intern Med 2005; 142:233–239.

21. Casanova C, de Torres JP, Navarro J, Aguirre-Jaíme A, Toledo P, Cordoba E et al. Microalbuminuria and hypoxemia in patients with chronic obstructive pulmonary disease.Am J Respir Crit Care Med. 2010 Oct 15;182(8):1004-10.

22. Shayo FK, Lutale J. Albuminuria in patients with chronic obstructive pulmonary disease: a cross- sectional study in an African patient cohort. BMC Pulm Med. 2018; 18:125.

23. Sujay J, Gajanan GS. Clinical significance of microalbuminuria and hypoxemia in patients with chronic obstructive pulmonary disease. Indian J Heal Sci Biomed Res. 2017; 10(1):19.

24. Alam DS, Chowdhury MA, Siddiquee AT, Ahmed S, Clemens JD. Prevalence and determinants of chronic obstructive pulmonary disease (COPD) in Bangladesh. COPD J Chronic Obstr Pulm Dis. 2015; 12(6):658–67.

25. Bulcun E, Ekici M, Ekici A, Kisa U. Microalbuminuria in chronic obstructive pulmonary disease. COPD J Chronic Obstr Pulm Dis. 2013; 10(2):186–92.

26. Khandker NN, Biswas T, Khan ANS, Hasib E, Rawal LB. Socio-demographic characteristics and tobacco use among the adults in urban slums of Dhaka, Bangladesh. Tob Induc Dis. 2017; 15(1):1–8.

27. Zhong N, Wang C, Yao W, Chen P , Kang J, Huang S, et al. Prevalence of chronic obstructive pulmonary disease in China: a large, population-based survey. Am J Respir Crit Care Med 2007; 176 (8): 753 – 760.

28. Casanova C, De Torres JP, Navarro J, Aguirre-Jaíme A, 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.

29. Mehmood K, Sofi FA. Microalbuminuria and Hypoxemia in Patients with COPD. J Pulm Respir Med. 2015;05(04).