Association between microalbuminuria and severity of COPD at a tertiary care hospital

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***Abstract*- Background & Method: Microalbuminuria (MAB) is a sensitive marker of cardiovascular risk. MAB is believed to reflect a state of generalized endothelial dysfunction, and therefore it is an emerging therapeutic target for primary prevention strategies. Microalbuminuria can be present in COPD patients due to hypoxemia. The aim of the study was to know aassociation between microalbuminuria and severity of COPD at a tertiary care hospital. Patients with COPD who had fulfilled inclusion and exclusion criteria were included in study. They were divided into four GOLD different groups, namely A, B, C and D based on the COPD assessment (CAT) score and number of exacerbations. A CAT score of more than 10 was denoted a patient as having more symptoms and a history of exacerbations of 2 or more than 2 in a year was` denoted as patient having more risk of COPD and urine albumin creatinine ratio was taken.**

Result: Among 138 microalbuminuria cases 42% were among mmrc grade-4, 26.1% were in mmrc grade-3, 27.5% were among mmrc grade-2 and 4.3% were in mmrc grade 1. In 10 cases with absent microalbuminuria 70% were in grade-2. Association was tested using chi square test and it statistically significant (p=0.002). Among 138 microalbuminuria cases 40.5% had GOLD group -D,8.1% had GOLD group c,21.6% had group GOLD B, and 29.7% had GOLD group A and all of the cases in 10 cases with absent microalbuminuria had GOLD group A. Association was tested using chi square test and it statistically significant (p<0.001).

Conclusion: The results of this study specify a solid association between microalbuminuria and increasing severity in COPD patients. Therefore, COPD patients should undergo routine microalbuminuria screening because it increases the risk of endothelial injury, which plays a major role in the pathogenesis of Cor Pulmonale. The determination of microalbuminuria is simple and inexpensive.

***Keywords*: microalbuminuria, severity, COPD & tertiary.**

Study Designed: Cross-sectional Observational Study.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases and influenced by host factors including abnormal lung development(1).

As per World Health Organization (WHO), the third leading cause of mortality in the world by 2030 will be chronic obstructive pulmonary disease (COPD)(2). In COPD, inhaled particles and gases lead to chronic inflammation of the airways with airflow limitation, which is not fully reversible(3).

COPD is a disease having systemic inflammation. Circulating pro-inflammatory cytokines and C-reactive protein (CRP) are important label of systemic inflammation. Cardiovascular disease is most common cause of death in COPD(4–6). The likelihood of identifying cardiovascular subclinical abnormalities in patients with COPD during daily clinical practice strongly depends on the diagnostic techniques used. The widespread use of sensitive diagnostic tests, such as ultrasound scan and a new generation of computed tomography (CT) scans, are good options(5) . Recent studies have shown an association between lower FEV1 and emphysema severity with arterial stiffness (6) and endothelial dysfunction (7). Also, vascular alterations, measured from the cross-sectional area of small pulmonary vessels by CT scan, correlate with the magnitude of pulmonary hypertension(8) . However, because of the high prevalence of COPD, these investigations may not always be practical in the general population for both logistic and economical reasons.

The discovery of novel biomarkers to help identify cardiovascular risk in patients with COPD could help individualize therapy for that particular phenotype. Ideally, the biomarker should be inexpensive, noninvasive, and easily available. C-reactive protein (CRP) is one such biomarker and increased serum levels of CRP have been related to increased cardiovascular death in mild to moderate COPD (9). However, this finding was described only in epidemiological cohorts and was not replicated in patients with more severe disease. In addition, CRP appears not to provide additional prognostic information beyond traditional risk factors in the general population (10) .

Microalbuminuria (MAB) is a sensitive marker of cardiovascular risk(11) . The presence of MAB is consistently associated with arterial stiffness assessed by pulse wave velocity and worse cardiovascular outcomes in patients with diabetes and hypertension, but most importantly in the general population (12). MAB has a stronger association with cardiovascular events and mortality than

CRP(13) . MAB is believed to reflect a state of generalized endothelial dysfunction, and therefore it is an emerging therapeutic target for primary prevention strategies.
Chronic renal failure (CRF) rises in prevalence with age and is frequently associated with chronic diseases such as congestive heart failure and diabetes mellitus. When present as a comorbidity, CRF carries negative prognostic implications and impacts the therapeutic strategy(14) . It is unknown to which extent COPD is associated with CRF and the relationship between renal failure and COPD is largely undescribed. A proportion of patients with COPD has a reduced muscular mass, and thus, serum creatinine might be falsely low as the result of decreased creatine release. Also, CRF may be associated with normal serum creatinine concentration, a condition known as unrecognized or concealed CRF. It is diagnosed by glomerular filtration rate (GFR) < 60 mL/min/1.73 m^2.

Material & Method
The cross sectional study was conducted among 148 COPD patients attended to opd or admitted as ipd patients at DR.BRAMH RAIPUR(C.G.) from December2021-december 2022.
Patients with COPD who had fulfilled inclusion and exclusion criteria were included in study. They were divided into four different groups, namely A,B,C and D based on the COPD assessment (CAT) score and number of exacerbations.
A CAT score of more than 10 were denoted a patient as having more symptoms and a history of exacerbations of 2 or more than 2 in a year were denoted as patient having more risk of COPD.

- Group A included patients having less symptoms and less risk,
- Group B had patients of more symptoms, Less risk.
- Group C had patients of more risk, less symptoms .
- Group D had patients of more symptoms and more risk.

All subjects was evaluated by taking a detailed clinical history

INCLUSION CRITERIA
All diagnosed patients of COPD in department of respiratory medicine who were given written informed consent.

EXCLUSION CRITERIA
- Patients who were not given consent
- Patients with chronic history of heart failure and liver cirrhosis
- Pregnant women
- Patients who were suffering from urinary tract infection
- Patient Living with Human Immunodeficiency Virus
- Diabetes mellitus
- Ischemic heart disease

Statistical methods:
For test of significance, chi-square test is used. P-value less than 0.05 were considered statistically significant. Data was entered in MS excel sheet and analyzed using SPSS software.

RESULTS:

Table 1: Age distribution among study subjects

Age in years	Freq.	Percent
36-45 years	15	10.14
46-55 years	32	21.62
56-65 years	53	35.81
66-75 years	39	26.35
>75 years	9	6.08
Total	148	100

The mean age of study subjects was 60.62 ±11.19 years. Maximum 35.81% were b/w 56-65 years followed by 26.35% b/w 66-75 years, 21.62% b/w 46-55 years.
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Table 2: Microalbuminuria among study subjects

Microalbuminuria	Freq.	Percent
Present (30-300 mg/g)	138	93.24
Absent (0-30 mg/g)	10	6.76
Total	148	100

Among study subjects, microalbuminuria was present was in 93.24% study subjects and was absent in 6.76% of study subjects.

Table 3: Association b/w mMRC and UACR among study subjects

mMRC	UACR		Total	P value
	Absent	microalbuminuria		
Grade-1	2	6	8	0.002
	20.0%	4.3%	5.4%	
Grade-2	7	38	45	
	70.0%	27.5%	30.4%	
Grade-3	0	36	36	
	0.0%	26.1%	24.3%	
Grade-4	1	58	59	
	10.0%	42.0%	39.9%	
Total	10	138	148	
	100.0%	100.0%	100.0%	

Among 138 microalbuminuria cases 42% were among mmrc grade-4, 26.1% were in grade-3 , 27.5% were among grade-2 and 4.3% were in grade 1 . In 10 cases with absent microalbuminuria 70% were in grade-2. Association was tested using chi square test and it statistically significant (p=0.002).

Table 4: Association b/w smoking index and UACR among study subjects

Smoking index	UACR		Total	P value
	Absent	microalbuminuria		
0	4	28	32	P<0.01
	40.0%	20.3%	21.6%	
1	6	14	20	
	60.0%	10.1%	13.5%	
2	0	31	31	
	0.0%	22.5%	20.9%	
3	0	42	42	
	0.0%	30.4%	28.4%	
4	0	23	23	
	0.0%	16.7%	15.5%	
Total	10	138	148	
	100.0%	100.0%	100.0%	

Among 138 microalbuminuria cases 30.4% were in smoking index-3, 22.5% were in index-2 and 16.7% were among index-4. In 10 cases with absent microalbuminuria 60% were in index-1. Association was tested using chi square test and it statistically significant (p<0.001).

DISCUSSION

This study was designed to evaluate and investigate the relationship of MAB in patients with COPD and to correlate it with different stages of COPD. In the present cross-sectional study, during the study period, one hundred forty-eight subjects were enrolled. It further evaluated the association of microalbuminuria with smoking index, exacerbation in the last one year, CAT score, gold criteria and BMI.

The mean age of the study subjects was around sixty years and approximately eighty percent of them were males which is similar to the findings of the cross-sectional study conducted by Gupta et al., Kumar et al., and Ghobadi et al. (15) The prevalence among males can be explained in the context that the main confounding factors like tobacco usage, occupational exposure is more among males. COPD was given as the most probable diagnosis significantly more often for the male case scenario than for the female. (16) In a similar study conducted in Spain, COPD was also more likely to be the primary diagnosis for men than women. In contrast females with COPD will present differently, may have a different pattern of comorbidities, and may have improved survival after acute exacerbations. (17)Shambhu Aryal et al., studied the gender differences in COPD and concluded that female gender was associated with lung function reduction and more severe disease in patients with COPD with early onset of disease or low smoking exposure.

The main symptoms among COPD patients in our study were the presence of cough with expectoration, shortness of breath on exertion and chest pain which is similar to the findings of the study conducted worldwide. Subjects with COPD in all categories according to GOLD's criteria were included in the study, microalbuminuria was present in more than ninety percent of the study subjects; which is similar to the findings of the research carried out by Bozkus et al. (18) Similar research by Casanova et al. demonstrated that the incidence of microalbuminuria was high in subjects with stable COPD and was associated with hypoxemia independently of the other cardiovascular risk factors. Similar results were obtained by Bulcun et al. where microalbuminuria was also associated with the severity of the disease.

In the present study most COPD subjects with microalbuminuria were at GOLD stages II, III and IV, whereas those with no microalbuminuria were at GOLD stage I and the difference was statistically significant which is similar to the finding of Celli et al. (19) This could be explained by impaired lung function, including COPD, which has been associated with increased systemic arterial stiffness. Given the relationship between abnormal lung function and arterial stiffness, an increase in arterial stiffness could lead to increased kinetic energy transmission to the distal microcirculation, thus resulting in microvascular damage. Emerging evidence demonstrates that the degree of air-flow limitation is poorly predictive of dyspnea and quality of life. Therefore, the classification of severity groups, as described by the GOLD committee, has moved away from a linear approach based only on the degree of airway limitation to a 2-dimensional evaluation that includes both the risk and symptom assessment. Modified Medical Research Council(MMRC) dyspnea scale scores were 3 and 4 in COPD subjects with microalbuminuria, and the scores were 1 and 2 in COPD subjects without microalbuminuria. This was considered to be due to the increased endothelial damage caused by hypoxia in subjects with grade III and IV dyspnea leading to microalbuminuria.

CONCLUSION

The results of this study specify a solid association between microalbuminuria and severity of COPD patients. Therefore, COPD patients should undergo routine microalbuminuria screening as it can be used as marker for severity of disease and it predicts the risk of endothelial injury, which plays a major role in the pathogenesis of Cor Pulmonale. The determination of microalbuminuria is simple and inexpensive.

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