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Original Research Article

The Study Microalbuminuria in Chronic Obstructive Pulmonary Disease: A Tertiary Care Experience

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Abstract

Background: Microalbuminuria is utilized as an indicator of endothelial dysfunction and has been identified as a predictor of overall mortality and cardiovascular events. Recent research on COPD management has placed greater emphasis on comorbidities, particularly cardiovascular events. This study aimed to examine the occurrence of microalbuminuria and its correlation with physiological and clinical characteristics in a group of subjects classified according to the updated version of the Global Initiative for Chronic Obstructive Lung Disease stages.

Methods: Consecutive patients diagnosed with COPD (diagnosis of COPD conformed to Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines. The presence of microalbuminuria was defined as a UACR ranging between 20 mg/g in men and 30 mg/g in women, with an upper threshold of 299 mg/g for both sexes.

Results: In the study population, subjects with less than 30% predicted FEV1 showed a higher prevalence of microalbuminuria (88.46%) compared to subjects with 30 to 50% predicted FEV1 (73.33%) and 50 to 80% predicted FEV1 (75%). The distribution of microalbuminuria among the different levels of Gold staging was found to have a statistically significant difference ($p < 0.05$).

Conclusion: Within the limitations of the current study, it can be concluded that Microalbuminuria shows a significant association with various factors including age, BMI, Smoking Index, Gold severity staging, and acute exacerbations. However, gender does not demonstrate a significant association with microalbuminuria. After therapeutic intervention, there is no significant change in microalbuminuria, at follow-up.

Keywords: Chronic Obstructive Pulmonary Disease (COPD), microalbuminuria, FEV1% (Forced Expiratory Volume in one second).

Introduction

Chronic obstructive pulmonary disease (COPD) is a significant cause of chronic illness and mortality worldwide. Many individuals endure this disease for extended periods and experience premature death due to COPD or its complications. COPD is a preventable and treatable condition that can have notable effects beyond the lungs and may vary in severity among patients. The pulmonary aspect of COPD is characterized by persistent airflow limitation that cannot be fully reversed. [1] Pathological changes associated with COPD can be observed in various areas including the proximal and peripheral airways, lung parenchyma, and pulmonary vasculature. [2] These changes involve chronic inflammation and the increased presence of specific inflammatory cell types in different lung regions, along with structural alterations resulting from repetitive injury and healing processes. [3] While several cytokines and inflammatory mediators have been identified, the understanding of COPD and its systemic manifestations remains limited. [4]

Cardiovascular disease is the primary cause of mortality in individuals with COPD. [5] Microalbuminuria serves as a risk factor for cardiovascular diseases and emerges as a potent predictor of cardiovascular diseases and mortality

in adults. [6] The primary reason for hypoxemia in patients with COPD is the abnormal ventilation/perfusion (V/Q) ratio caused by progressive airflow limitation and destruction of the pulmonary capillary bed due to emphysema. [7] Alveolar hypoxia plays a significant role in the development of pulmonary hypertension among patients with COPD. [8] Furthermore, hypoxia contributes to endothelial dysfunction, which is characterized by an imbalance between vasodilation and vasoconstriction. Studies have observed abnormalities in endothelium-dependent relaxation of the pulmonary artery in patients with severe COPD. [9] The epidemiology of microalbuminuria highlights a strong association between systemic endothelial dysfunction, vascular disease, and glomerular endothelial dysfunction. [6] Only a few studies have examined the occurrence of microalbuminuria in individuals diagnosed with COPD. [10-12] Moreover, these studies did not establish a connection between microalbuminuria and measures of COPD severity, such as FEV1% and BODE index. Instead, they identified a correlation between microalbuminuria and hypoxemia. Consequently, this study aimed to explore the levels of microalbuminuria in patients with COPD and identify the factors contributing to its presence.

Material and Methods

This study was conducted at the Department of Pulmonary Medicine, Govt. CD & TB Hospital and KMC, Hanamkonda, Telangana State. Institutional Ethical approval was obtained for this study based on the Helsinki Declaration for Human Research Protocol. Written consent was obtained from all participants after explaining the nature of the study in vernacular language.

Inclusion criteria

1. Consecutive patients diagnosed with COPD (diagnosis of COPD conformed to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines. [13]
2. Males and Females
3. Aged 45 and above.
4. Voluntary willingness to participate in the study.

Exclusion criteria

1. Patients with renal diseases and liver diseases
2. Diabetes mellitus
3. Macroalbuminuria
4. History of Cerebrovascular Accidents
5. Ischemic heart disease/ Congestive Heart failure
6. Acute infections

A comprehensive questionnaire was administered to collect information regarding demographics, smoking history, medical background, and medication usage. Before participating in the study, all participants were adequately informed about the research objectives and procedures.

Body mass index (BMI) was calculated by measuring weight and height and dividing weight by height squared (kg/m^2). Arterial blood gases were obtained through arterial puncture in the morning, while the patient was in a seated and resting position for 15 min after at least 45 min of breathing room air. Pulmonary function tests (PFT) were conducted using a flow-sensitive spirometer following the guidelines set by the American Thoracic Society (ATS). [14] Systemic blood pressure measurements were taken on separate occasions, with systolic and diastolic readings recorded at 5-minute intervals using a conventional mercury sphygmomanometer.

To calculate the BODE index, the following parameters were considered: [15-17]

- Exercise capacity was assessed by measuring the 6-minute walk distance (6 MWD) according to ATS guidelines.
- Dyspnea was evaluated using the modified Medical Research Council (mMRC) dyspnea scale.
- The multidimensional BODE index was calculated based on BMI, FEV1% (forced expiratory volume in one second), mMRC dyspnea scale score, and 6 MWD.

The measurement of urinary albumin and creatinine levels, as well as the estimation of albumin excretion rates, was conducted using previously described methods. Creatinine levels were determined using the Jaffe method and adjusted for sex and race using the established formulas. The presence of microalbuminuria was defined as a UACR between 20 and 30 mg/g in men and women, respectively, with an upper threshold of 299 mg/g for both sexes. [10]

Statistical analysis: All available data were uploaded on an MS Excel spreadsheet and analyzed using SPSS version 21 in a Windows format. Continuous variables were represented as mean, standard deviations, percentages, and categorical variables were calculated using the chi-square test and Fisher's exact test when more than 20% of cell values had expected cell values of less than 5 and a p-value of (<0.05) was considered significant.

Results

A total of 45 cases were included in the study based on the inclusion and exclusion criteria. Out of the 45 cases, 40/45 (88.89%) were males and 5/45(11.11%) were females. Most of the cases were in the age group 61 – 71 years given in Table 1. The age range of the cases was from 43 years to 69

years. The mean age of the cases with COPD was 66.5 ± 8.5 years.

Table 1: The age-wise distribution of cases in the study

Age group	Frequency	Percentage
45 – 50	6	13.33
51 – 60	18	40.00
61 – 70	21	46.67
Total	45	100.0

In all age groups within the study population, the number of males exceeds that of females by a factor of 4-5. It was found females are more prevalent in the 51-60 years age group, and there were no females in the age group of 50 years or below. Among the case based on the BMI measurements we found 48.89% of cases were underweight, 22.22% cases were normal weight, 20% of cases were overweight and 8.89% of cases were in the obese category.

Table 2: Showing the smoking index[18] of the cases in the study

Smoking Index	Frequency	Percentage
Never smoked	8	17.78
< 100	2	4.44
100 – 300	12	26.67
300 – 600	11	24.44
> 600	12	26.67
Total	45	100.00

Within the study population, 26.67% of the participants exhibited a smoking index exceeding 600. Additionally, 26.67% of the subjects had a smoking index ranging from 100 to 300, while 24.44% had a smoking index between 300 and 600. Furthermore, 4.44% of the participants had a smoking index below 100. Notably, 13.4% of the subjects reported never having smoked depicted in Table 2.

Table 3: Distribution of Gold staging in the study population

Gold Staging	Frequency	Percentage
> 80% predicted	0	00.00%
50 - 80% predicted	4	08.89%
30 - 50% predicted	15	33.33%
< 30% predicted	26	57.78%

Among the study population, more than half of the subjects, 57.78% of the subjects had an acute exacerbation. The distribution of cases according to Gold staging is given in Table 3. Among the subjects in the study population, 61 – 70 years age group subjects had more prevalence of microalbuminuria 18/21 (85.71%) followed by 51 – 60 years 15/18 (83.33%) and 4/6 (66.67%) in 45 – 50years age group subjects. The p values were found to be significant depicted in Table 4. However, the difference in the distribution of microalbuminuria among different gender was not statistically significant ($p > 0.05$).

Table 4: Distribution of microalbuminuria in various age groups

Age group in years	Microalbuminuria		P value
	Yes	No	
45 – 50	4	2	0.0051*
51 – 60	15	3	
61 – 70	18	3	
Total	37	8	

* Significant

Among the subjects in the study population comparison of BMI and microalbuminuria showed that the underweight subjects had more prevalence of microalbuminuria 20/22 (90.90%) followed by 7/9 (77.78%) in overweight subjects, obese 3/4 (75.0%) and normal weight subjects 7/10 (70.0%). The p values were found to be significant given in Table 5.

Table 5: Distribution of microalbuminuria with BMI

BMI categories	Microalbuminuria		P value
	Yes	No	
Underweight	20	2	0.012*
Normal	7	3	
Overweight	7	2	
Obese	3	1	
Total	37	8	

* Significant

Among the subjects in the study population, subjects with a smoking index of more than 600 had a prevalence of microalbuminuria (83.33%) similarly subjects with a smoking index of 100 – 300 also had microalbuminuria (83.33%). Subjects with a smoking index of 300 – 600 had microalbuminuria in 90.90% of cases. Subjects with a smoking index of < 100 had microalbuminuria in 50% of cases and subjects who never smoked had microalbuminuria in 75% of cases details depicted in Table 6.

Table 6: Distribution of microalbuminuria with the smoking index

Smoking Index	Microalbuminuria		P value
	Yes	No	
Never smoked	6	2	0.043*
< 100	1	1	
100 – 300	10	2	
300 – 600	10	1	
> 600	10	2	
Total	37	8	

* Significant

In the study population, subjects with less than 30% predicted FEV1 showed a higher prevalence of microalbuminuria (88.46%) compared to subjects with 30 to 50% predicted FEV1 (73.33%) and 50 to 80% predicted FEV1 (75%). The distribution of microalbuminuria among the different levels of Gold staging was found to have a statistically significant difference ($p < 0.05$) Table 7.

Table 7:Distribution of microalbuminuria with the Gold Staging

Gold Staging	Microalbuminuria		P value
	Yes	No	
> 80% predicted	0	0	0.0351*
50 - 80% predicted	3	1	
30 - 50% predicted	11	4	
< 30% predicted	23	3	
Total	37	8	

Regarding the Gold staging at the six-month follow-up:

- Among the subjects who initially had a predicted FEV1 of 50-80%, all 4 subjects (100%) maintained their predicted range, and none of them experienced a deterioration to 30-50% predicted or less than 30% predicted.
- In the group with a baseline predicted FEV1 of 30-50%, after six months of follow-up, 4 subjects (26.67%) showed improvement and moved to the 50-80% predicted range, 4 subjects (26.67%) remained in the 30-50% predicted range, while 7 subjects (46.67%) experienced deterioration and their predicted FEV1 dropped to less than 30%.
- For the subjects who had a baseline predicted FEV1 of less than 30%, one subject (3.85%) showed improvement and reached the 50-80% predicted range, 11 subjects (42.30%) improved to the 30-50% predicted range, and the majority of 14 subjects (53.84%) maintained their initial classification of less than 30% predicted FEV1.

Discussion

The primary aim of this study was to assess microalbumin levels associated with COPD and determine the impact of therapeutic interventions

on microalbuminuria. In the study population, the most common age group was 61 – 71 years, and the mean age of patients with COPD was 66.5 ± 8.5 years. The higher prevalence of COPD in the older age groups can be attributed to the age-related manifestation of COPD. Generally, there is a gradual decline in FEV1 with age, with a typical reduction of half from the age of 25 to 75 years. However, in COPD patients, there is an accelerated decline of approximately two-thirds compared with the normal aging population. [19] In the current study, we found out of 45 cases 40/45 (88.89%) patients were males and 5/45(11.11%) were females. In this study, we found a notable disparity in gender distribution across all age groups, with the number of males exceeding that of females by a factor of five to seven. This difference in sex distribution can be attributed to significant confounding factors, such as tobacco usage and occupational exposure, which are more prevalent among males. Among males, there was a higher representation in the 61-70 years age group and a lower representation in the less than or equal to 50 years age group. On the other hand, females are more prevalent in the 51-60 years age group, and there are no females in the less than or equal to 50 years age group. It is important to note that women with COPD may exhibit distinct characteristics, potentially displaying different patterns of comorbidities and improved survival rates after acute exacerbations. [20] Sorheim et al. [21] conducted a study on sex differences in COPD and concluded that the female sex was associated with reduced lung function and more severe disease in patients with COPD, particularly in cases of early-onset or low smoking exposure.

In this study, male subjects exhibited a higher prevalence of microalbuminuria (87.5%) than female subjects (40.0%). This difference could be attributed to factors such as the larger sample size of male subjects and the presence of microalbuminuria resulting from other causes of endothelial injury and inflammation, which are more common in males. A cross-sectional study conducted by FK Shayo et al. [22] examined 104 patients with chronic obstructive pulmonary disease (COPD), it was found that the prevalence of albuminuria was 24% in COPD patients and 100% in patients with a history of cardiovascular disease (CVD). Additionally, the prevalence of albuminuria increased significantly with COPD severity, which aligns with the findings of our study. Furthermore, there was a statistically significant difference in the distribution of microalbuminuria among the different age groups, as indicated by a p-value of less than 0.05. Among the subjects in the study population, a comparison of BMI and microalbuminuria showed that underweight subjects had a higher prevalence of microalbuminuria 20/22 (90.90%) followed by 7/9 (77.78%), obese subjects 3/4 (75.0%), and normal-weight subjects 7/10 (70.0%). The distribution of microalbuminuria among the different BMI levels showed a statistically significant difference, with a p-value of less than 0.05. This finding was consistent with that of a study conducted by Karadag et al. [23] In a meta-analysis conducted by Guo et al. [24] it was concluded that overweight individuals with COPD have a reduced risk of all-cause mortality, whereas underweight individuals have an increased risk of all-cause mortality. These results suggest that BMI plays a role in the prognosis and outcomes of patients with COPD, with overweight individuals having a more favorable prognosis and underweight individuals being at higher risk.

Smoking, which is prevalent in up to 80% of COPD patients, is also a major risk factor for CVD. In subjects with a smoking index of > 600, the prevalence of microalbuminuria (83.33%) was similar to that of subjects with a smoking index of 100 – 300 and also had microalbuminuria (83.33%). Subjects with a smoking index of 300 – 600 had microalbuminuria in 90.90% of cases. Subjects with a smoking index <100 had microalbuminuria in 50% of cases, and subjects who never smoked had microalbuminuria in 75% of cases. In the study population, subjects with less than 30% predicted FEV1 showed a higher prevalence of microalbuminuria (88.46%) than subjects with 30–50% predicted FEV1 (73.33%) and 50–80% predicted FEV1 (75%). The distribution of microalbuminuria among the different levels of gold staging was statistically significant. Casanova et al. found no significant association between microalbuminuria and COPD severity as measured by spirometry. [25] However, K Mehmood et al. [26] reported that COPD patients with microalbuminuria had significantly lower levels of FEV1. It is important to note that reduced FEV1 is not exclusive to COPD and can be seen in other conditions, such as congestive heart failure, asthma, cystic fibrosis, thoracic kyphosis, multiple sclerosis, and other diseases. [27] In this study, more than half of the participants in this study experienced acute exacerbations. Subjects with acute exacerbation had a higher prevalence of microalbuminuria than those without acute exacerbation (60%). The difference in the distribution of microalbuminuria among the subjects experiencing acute exacerbation was statistically significant ($p<0.05$). A study by Komurcuoglu et al. [11] also established an association between exacerbations and microalbuminuria. In this study, no statistically significant difference was observed in the distribution of gold staging between the baseline and the 6-month follow-up of the study population.

Additionally, there was no statistically significant difference in the distribution of microalbuminuria between the baseline and the 6-month follow-up. These findings suggest that changes in gold staging and the presence of microalbuminuria may indicate a certain degree of irreversibility in pulmonary endothelial damage, highlighting their potential usefulness as markers for identifying Cor Pulmonale in individuals with COPD.

Conclusion

Within the limitations of the current study, it can be concluded that microalbuminuria is significantly associated with various factors including age, BMI, Smoking Index, Gold severity staging, and acute exacerbations. However, sex was not significantly associated with microalbuminuria. After therapeutic intervention, there was no significant change in microalbuminuria at follow-up. Measurement of microalbuminuria is simple and cost-effective. This marker can be valuable in the early diagnosis of cor pulmonale in patients with COPD, especially in resource-limited and emergency settings.

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