

Microalbuminuria as an Indicator of Severity and Systemic Comorbidities in Chronic Obstructive Pulmonary Disease

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Abstract

Background: Chronic Obstructive Pulmonary Disease (COPD) is a well-recognized systemic disease that is associated with extrapulmonary manifestations. Chronic inflammation leads to endothelial dysfunction, hypoxemia, and microalbuminuria. Therefore, microalbuminuria has been proposed to be a potential biomarker for the severity of disease, and it also shows the extent of systemic involvement in COPD. The current study was designed to evaluate the prevalence of microalbuminuria in COPD and its correlation with disease severity. **Material and Methods:** This prospective observational study included 60 cases of COPD evaluated with spirometry ($FEV_1/FVC < 0.70$). COPD severity was classified according to GOLD staging. Patients underwent pulmonary function testing, and details of systemic comorbidities were recorded. Early-morning urine samples were obtained for analysis of microalbuminuria by the immunoturbidimetric method. The data was compared with appropriate statistical analysis, and values of $p (< 0.05)$ were considered significant. **Results:** Out of $n=40$ cases, microalbuminuria was found to be present in $n=32(53.3\%)$ patients. The prevalence of microalbuminuria increased with severity, from 16.7% in mild COPD to 87.5% in very severe COPD ($p < 0.001$). Patients with microalbuminuria showed significantly decreased pulmonary functions, with lower mean FEV_1 (1.12 ± 0.35 L vs 1.68 ± 0.42 L), lower predicted FEV_1 percentage ($44.5 \pm 12.8\%$ vs $67.2 \pm 14.5\%$), and reduced FEV_1/FVC ratio (0.52 ± 0.09 vs 0.61 ± 0.08). Cardiovascular disease and dyslipidemia were significantly more common among patients with microalbuminuria. **Conclusion:** Microalbuminuria was found to be present increasingly with the severity of COPD, and the correlation was found to be significant. Similarly, it was also associated with decreased pulmonary function and a higher prevalence of systemic comorbidities. Therefore, microalbuminuria may be used as a non-invasive, easy-to-use biomarker to identify high-risk COPD patients and the presence of systemic disease.

Keywords: Chronic Obstructive Pulmonary Disease (COPD), Microalbuminuria, Pulmonary function test, Systemic comorbidities.

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INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a chronic respiratory disorder characterized by persistent airflow obstruction and an inflammatory response in the airways and lungs. The incidence of COPD is increasing across the world. It is now one of the significant sources of morbidity and mortality, contributing to one of the major causes of death by respiratory diseases in the near future.^[1] The contemporary understanding of the pathophysiology of COPD has shown that the disease is not restricted to the lung alone, but is now considered a systemic disease with numerous extrapulmonary manifestations and comorbidities, including cardiovascular disease, metabolic syndrome, skeletal muscle dysfunction, and renal impairment.^[2] The primary contributors to this chronic systemic inflammation are oxidative stress and endothelial dysfunction.^[3] Recent studies have also emphasized the need to identify reliable biomarkers that can quantify the severity of COPD and its associated systemic complications. Microalbuminuria, a moderate rise in the quantity of albumin in the urine between 30 and 300mg per day, is one such potential biomarker. Microalbuminuria is widely recognized as a primary indicator of endothelial cell

dysfunction and has been studied extensively in conditions such as diabetes mellitus, hypertension, and cardiovascular disease.^[4] The endothelial dysfunction is central to the pathogenesis of most systemic complications of COPD, and thus microalbuminuria could be a useful marker of the systemic effects of this disease.^[5] Chronic hypoxia, systemic inflammation, and oxidative stress in COPD patients play a role in widespread endothelial damage and increased vascular permeability. Pathological processes can lead to increased albumin leakage through the glomerular membrane, resulting in microalbuminuria.^[6] It has been proposed that microalbuminuria is more common in patients with moderate to severe COPD and possibly is associated with the severity of the

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disease, hypoxemia, and systemic inflammation.^[7] In addition, COPD patients show increased frequency of cardiovascular comorbidities, and the presence of microalbuminuria has been shown as an indicator of increased cardiovascular morbidity and mortality.^[8] Therefore, identification of microalbuminuria in patients with COPD can provide valuable information on the extent of systemic involvement of the disease. Since microalbumin estimation is simple, non-invasive, and cost-effective, microalbuminuria is considered a potential early indicator of vascular dysfunction and a predictor of disease severity and associated comorbidities.^[9] Early detection of systemic involvement will help provide timely interventions and improved management, which can reduce disease progression and prevent complications. Despite the association between microalbuminuria and COPD, there is a paucity of data in this area. With this background, we sought to determine the relationship between microalbuminuria and COPD in the current study. The data from this study can be utilised to understand the relationship and help clinicians identify high-risk patients; such cases can then be subjected to comprehensive treatment to improve patient outcomes and guide future therapeutic strategies.^[10]

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of General Medicine in coordination with the Department of Pulmonology and Biochemistry, Kakatiya Medical College and Hospital, Warangal, Telangana. Institutional ethical approval was obtained for the study after duly following the protocol for human research based on the Helsinki declaration. Written informed consent was obtained from all the participants of the study after explaining the nature of the study in the vernacular language.

Inclusion Criteria

1. Patients diagnosed with COPD based on standard clinical criteria, spirometry, and the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria.
2. Patients above 40 years of age
3. Patients are willing to sign informed consent, voluntarily agreeing to participate in the study.

Exclusion Criteria

1. Patients with congestive heart failure
2. Hypertension, diabetes mellitus
3. Renal dysfunctions
4. Acute infections
5. Urinary tract infections and Nephrotic syndrome.
6. Patients are currently on medications that can alter renal function.

Sample Size: The study included 60 patients with COPD,

selected via convenience sampling during the study period, based on the inclusion and exclusion criteria. The selected patients underwent a detailed clinical history, including age, gender, smoking history, duration of illness, symptoms, and presence of comorbidities, which was recorded in a structured questionnaire pro forma. The patients underwent a thorough general physical and systemic examination, and important findings were recorded.

Assessment of COPD Severity: Spirometry was done to evaluate Forced Expiratory Volume in one second (FEV1) and Forced Vital Capacity (FVC). Severity of COPD was categorized according to the GOLD staging system based on post-bronchodilator FEV1 values.

Microalbuminuria Estimation: All samples were collected in the early morning, and the spot urine samples were taken under aseptic conditions. Urinary albumin was measured by the immunoturbidimetric method in the hospital's biochemistry laboratory. Microalbuminuria was defined as a level of urinary albumin excretion of 30-300mg/day or its equivalent in spot urine samples.

Assessment of Systemic Comorbidities: Participants were assessed for common systemic comorbidities associated with COPD, including cardiovascular disease, metabolic abnormalities, and renal dysfunction. Relevant tests, such as blood glucose, serum creatinine, lipid profile, and electrocardiography, were performed as needed.

Outcome estimation: The main study finding was that patients with COPD had microalbuminuria. The association between microalbuminuria and the severity of COPD and the relationship of microalbuminuria with systemic comorbidities were secondary outcomes.

Statistical Analysis: The data were uploaded to Microsoft Excel and analyzed using the Statistical Package for the Social Sciences (SPSS) version 26.0. Continuous variables were presented as mean ± standard deviation, frequencies, and percentages. Categorical variables were analyzed using the Chi-square test to assess the relationship between microalbuminuria and COPD severity. A p-value of below 0.05 was taken to be significant.

RESULTS

A total of n=60 cases of COPD were included in the study. The baseline profile of the study cohort is given in Table 1. A critical analysis of the table shows that the cohort's mean age was 58.7 ± 8.4 years, indicating that most cases were in the middle-aged to elderly group. The majority of cases were males (80%), and the remaining 20% were females. Evaluation of the smoking habits showed that 58.3% were current smokers, 30% were previous smokers, and 11.7% were non-smokers. The mean duration of COPD in this study was 6.8 ± 3.5 years, indicating its chronic course in the cohort.

Table 1: Baseline Characteristics of the Study Population (N=60)

Characteristic	Category / Value
Age (Years) [Mean ± SD]	58.7 ± 8.4
Gender [n (%)]	
Male	48 (80.0%)
Female	12 (20.0%)

Smoking Status [n (%)]	
Current Smoker	35 (58.3%)
Former Smoker	18 (30.0%)
Non-Smoker	7 (11.7%)
Duration of COPD (Years) [Mean ± SD]	6.8 ± 3.5

The assessment of COPD severity was based on the GOLD staging system, using FEV₁ values. The results in Table 2 showed that 40% belonged to Stage II (moderate COPD),

26.7% to Stage III (severe COPD), and 20% to Stage I (Mild COPD). Stage IV (very severe COPD) was found to be present in 13.3% cases of COPD.

Table 2: Distribution of Study Subjects by COPD Severity (GOLD Staging) (N=60)

GOLD stage	Severity (Based on FEV1)	Number of Patients (n)	Percentage (%)
Stage I	Mild (FEV1 ≥ 80% predicted)	12	20.00%
Stage II	Moderate (50% ≤ FEV1 < 80%)	24	40.00%
Stage III	Severe (30% ≤ FEV1 < 50%)	16	26.70%
Stage IV	very Severe (FEV1 < 30%)	8	13.30%
Total		60	100%

Microalbuminuria Prevalence is depicted in Table 3. The study population comprised 32 patients (53.3%) with microalbuminuria and 28 patients (46.7%) without microalbuminuria. The result of this finding showed that

over 50% of the COPD patients showed microalbuminuria, which indicated that renal endothelial dysfunction was prevalent in these patients

Table 3: Prevalence of Microalbuminuria in the Study Population

Parameter	Number of Patients (n)	Percentage (%)
Patients with Microalbuminuria	32	53.30%
Patients without Microalbuminuria	28	46.70%
Total	60	100%

Correlation of Microalbuminuria and COPD Severity is given in Table 4. There was an apparent correlation between the degree of COPD and microalbuminuria. In Stage I (mild COPD), only 2 patients (16.7%) had microalbuminuria. Stage II (moderate COPD) had 10 patients (41.7%). It rose significantly during Stage III (severe COPD), in which 13 cases (81.3%) were

microalbuminuric. The most prevalent was Stage IV (very severe COPD), which had 7 affected patients (87.5%). The statistical analysis showed that there was a very significant correlation (p < 0.001) between the COPD severity and the prevalence of microalbuminuria, which states that microalbuminuria tends to increase with the progression of the disease.

Table 4: Association between Microalbuminuria and Severity of COPD (GOLD Staging)

COPD Severity (GOLD stage)	Total Patients (n)	Patients with Microalbuminuria (n)	Percentage within Stage (%)	P value
Stage I (Mild)	12	2	16.70%	<0.001*
Stage II (Moderate)	24	10	41.70%	
Stage III (Severe)	16	13	81.30%	
Stage IV (Very Severe)	8	7	87.50%	

*Statistically significant. There is a strong positive correlation between increasing severity of COPD and the prevalence of microalbuminuria.

Comparison of Pulmonary Function Tests according to Microalbuminuria is given in Table 5. Patients with microalbuminuria had lower FEV₁ scores than those without microalbuminuria (1.12 ± 0.35 L vs. 1.68 ± 0.42 L; p < 0.001). In addition, the mean predicted FEV₁ percentage in microalbuminuria cases was 44.5%-12.8%, versus 67.2%-14.5% without microalbuminuria; the differences were statistically significant (P < 0.001). FVC

was also lower in patients with microalbuminuria (2.21 ± 0.55 L) than in those without (2.68 ± 0.62 L), with p = 0.003. Moreover, the FEV₁/FVC ratio in the microalbuminuria group (0.52 ± 0.09) was also found to be significantly lower than in the non-microalbuminuria group (0.61 ± 0.08) (p < 0.001). This shows that lung function was very poor in patients with microalbuminuria.

Table 5: Comparison of Pulmonary Function Tests (PFTs) based on Microalbuminuria Status

Parameter	Patients with Microalbuminuria (n=32) (Mean ± SD)	Patients without Microalbuminuria (n=28) (Mean ± SD)	P value
FEV1 (Liters)	1.12 ± 0.35	1.68 ± 0.42	<0.001*
FEV1 (% predicted)	44.5 ± 12.8	67.2 ± 14.5	<0.001*
F-vc (Liters)	2.21 ± 0.55	2.68 ± 0.62	0.003*
FEV1/FVC Ratio	0.52 ± 0.09	0.61 ± 0.08	<0.001*

Statistically significant (p < 0.05). Patients with microalbuminuria have significantly poorer lung function.

The association of microalbuminuria and systemic comorbidities is given in Table 6. Evaluation of all comorbidities in this cohort, along with the presence or absence of microalbuminuria, showed that systemic disease, such as cardiovascular disease, had an OR of 3.6 and a p-

value <0.05. Similarly, the association between dyslipidemia and microalbuminuria showed an OR of 2.71 and a p-value of 0.05, considered significant. The association with other comorbidities was not found to be significant, as given in the table.

Table 6: Association between Microalbuminuria and Systemic Comorbidities

Systemic Comorbidity	Patients with Microalbuminuria (n=32)	Patients without Microalbuminuria (n=28)	Odds Ratio (OR)	P value
Cardiovascular Disease	12 (37.5%)	4 (14.3%)	3.6	0.04*
Dyslipidemia	18 (56.3%)	9 (32.1%)	2.71	0.05*
Anemia	8 (25.0%)	3 (10.7%)	2.78	0.15
Electrolyte Imbalance	6 (18.8%)	2 (7.1%)	2.93	0.18

Statistically significant (p < 0.05). The presence of microalbuminuria is significantly associated with a higher prevalence of cardiovascular disease and dyslipidemia.

DISCUSSION

The present study was conducted to evaluate the importance of microalbuminuria as a diagnostic marker of disease severity and systemic comorbidity in patients with chronic obstructive pulmonary disease (COPD). The overall results of this study showed that there was a significant association of microalbuminuria in patients with COPD, and it was also strongly correlated to progression of the disease, impaired lung function, and systemic comorbidities. The age of the study cohort revealed the mean age was 58.7 ± 8.4 years, with the male-to-female ratio of 4:1. This demographic trend is in agreement with previous epidemiological studies on COPD, which have shown older adults and males have a higher prevalence rate, primarily owing to their increased exposure to smoking and other environmental risk factors.^[1] The smoking history of our cohort found that most of the cases were current or ex-smokers, which fortifies the evidence of the role of smoking as the primary etiological determinant of COPD.^[1,2] The microalbuminuria prevalence in the current study was 53.3%, indicating that nearly half of the COPD patients had signs of renal endothelial dysfunction. Other studies in this field have observed a similar pattern and suggested that microalbuminuria is widespread in COPD patients and may indicate systemic vascular damage related to chronic inflammation and hypoxemia.^[7,10] COPD is currently viewed as a systemic inflammatory disease whereby the lung-generated inflammatory mediators could have far-reaching systemic effects on other organ systems.^[3] There was a significant correlation between microalbuminuria and progressive worsening of COPD based on GOLD staging [Table 4]. There was progressively higher microalbuminuria as the severity of COPD increased, defining a strong positive correlation between the two. Studies done in this field have also shown a similar trend, and they found the role of chronic hypoxemia in severe COPD leading to microalbuminuria due to renal endothelial dysfunction.^[7,12] It has been shown that chronic hypoxia leads to renal endothelial dysfunction and oxidative stress, which increase vascular permeability and glomerular albumin leakage, thereby contributing to microalbuminuria.^[6,13] Our study found that lung function parameters were significantly worse in patients with significant microalbuminuria than in

those without microalbuminuria. Results from cases of microalbuminuria showed reduced FEV1 and predicted FEV1, reduced FVC, and a decreased FVC/FEV1 ratio. These results show that microalbuminuria is positively associated with severe airflow restriction. Similar patterns have been reported in the literature, suggesting that decreased lung function in COPD is strongly linked to endothelial dysfunction and elevated cardiovascular risk.^[11,14]

One more interesting finding of the present research was the strong correlation between microalbuminuria and two systemic comorbidities, cardiovascular disease and dyslipidemia [Table 6]. A considerably substantial odds ratio was found in the prevalence of cardiovascular disease in patients with microalbuminuria, with an odds ratio standing at 3.6. This observation is in line with past studies that have proved that microalbuminuria is an indicator of generalized endothelial dysfunction and it is closely linked to morbidity and death due to cardiovascular disease.^[5,8] The prevalence of dyslipidemia in patients with microalbuminuria was also higher and could be a contributing factor to the vascular injury and onset of atherosclerotic complications in COPD patients.^[15] Other systemic diseases, such as anemia and electrolyte imbalance, were more commonly observed among patients with microalbuminuria, but the differences did not reach statistical significance [Table 6]. This could be due to a comparatively modest sample size or to the multifactorial etiology of the conditions mentioned in COPD patients. Altogether, the results of this study supported the fact that COPD is not only a lung disease, but a systemic disease with extensive vascular and metabolic implications. Microalbuminuria appears to be a practical, easy, and non-invasive biomarker that indicates endothelial dysfunction, disease severity, and comorbidities of the systems under study. Early detection of the presence of microalbuminuria in patients with COPD can thus assist clinicians in determining the high-risk individuals and take the necessary measures that can curb the effects of the disease and its consequences.

CONCLUSION

The present study, within its limitations, showed that microalbuminuria is very common in patients with chronic obstructive lung disease and is strongly correlated with disease progression. COPD patients with higher microalbuminuria had

poor pulmonary function, and there was increased prevalence of common systemic comorbidities, especially cardiovascular disease and dyslipidemia. These results indicate that microalbuminuria can be a useful, non-invasive biomarker of renal endothelial dysfunction and of the systemic response to COPD. Early detection of microalbuminuria among COPD patients can help determine individuals who are at greater risk of complications. Timely interventions can improve the overall clinical outcome.

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Conflicts of interest

There are no conflicts of interest.

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