https://doi.org/10.48047/AFJBS.6.15.2024.9930-9946

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

Prevalence of Microalbuminuria in Chronic Obstructive Pulmonary Disease (COPD) and Its Correlation with Pulmonary Function: A Cross-Sectional Study

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Volume 6, Issue 15, Oct 2024

Received: 05 Sep 2024

Accepted: 25 Sep 2024

Published: 15 Oct 2024

doi: 10.48047/AFJBS.6.15.2024.9930-9946

Abstract

Background: Chronic Obstructive Pulmonary Disease (COPD) is a prevalent cause of morbidity and mortality worldwide, often accompanied by cardiovascular complications. Microalbuminuria (MAB) is considered a marker of systemic endothelial dysfunction and may serve as an early indicator of cardiovascular risk in COPD patients. This study aims to determine the prevalence of microalbuminuria in stable COPD patients and its correlation with pulmonary function parameters.

Methods: A cross-sectional study was conducted on 139 stable COPD patients at GSL Medical College. Participants were selected based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria. Pulmonary function tests (PFTs) were performed using spirometry, and the urine albumin-to-creatinine ratio (UACR) was measured to assess microalbuminuria. Statistical analyses included correlation tests to evaluate the relationship between microalbuminuria levels and PFT parameters such as FEV1, FVC, and FEV1/FVC ratio.

Results: Microalbuminuria was present in 29.5% of COPD patients. There was a significant correlation between microalbuminuria levels and COPD severity as defined by the GOLD staging system ($p < 0.001$). Patients in GOLD stages III and IV showed higher mean UACR values, indicating more severe endothelial dysfunction. However, no significant association was found between smoking history (pack-years) and microalbuminuria levels ($p = 0.83$).

Conclusion: Microalbuminuria is prevalent in COPD patients, particularly in those with more severe airflow limitation. The significant correlation between microalbuminuria and PFT parameters suggests that MAB could be used as a non-invasive biomarker for assessing disease severity and cardiovascular risk in COPD patients. Early detection of microalbuminuria may help in the stratification and management of high-risk patients to prevent cardiovascular complications.

Keywords: COPD, Microalbuminuria, Pulmonary Function Tests, GOLD Staging, Cardiovascular Risk.

Main file

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a significant cause of chronic morbidity and mortality worldwide, with the World Health Organization (WHO) ranking it as the third leading cause of death globally [1]. Characterized by persistent and progressive airflow limitation, COPD results primarily from long-term exposure to harmful particles and gases, such as tobacco smoke, air pollution, and occupational hazards [2]. The disease is typified by chronic inflammation, which affects not only the airways but also the lung parenchyma and vasculature, leading to structural alterations and systemic complications [3].

The pathophysiology of COPD involves an abnormal inflammatory response within the lung tissues, driven primarily by exposure to irritants like cigarette smoke. This inflammation results in irreversible damage to the airways and alveolar structures, culminating in a gradual decline in pulmonary function [4]. This progressive loss of lung function is commonly assessed using pulmonary function tests (PFTs), with spirometry being the gold standard for diagnosis and classification [5]. Forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) are key metrics obtained through spirometry, helping to quantify airflow limitation and determine the severity of COPD according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria [6].

In addition to pulmonary manifestations, COPD is increasingly recognized as a systemic disease with multiple extrapulmonary effects. Cardiovascular disease, skeletal muscle dysfunction, osteoporosis, and metabolic syndrome are common comorbidities associated with COPD [7]. Among these, cardiovascular disease remains the leading cause of death in COPD patients, underscoring the importance of identifying early predictors of cardiovascular risk in this population [8]. One such predictor, gaining attention in recent research, is microalbuminuria (MAB) [9].

Microalbuminuria, defined as the urinary excretion of albumin in the range of 30–300 mg/day, serves as a marker of endothelial dysfunction and is associated with increased cardiovascular risk in various populations, including those with diabetes and hypertension [10]. In COPD, systemic inflammation and hypoxia-induced vascular damage are proposed mechanisms leading to endothelial dysfunction, which may manifest as microalbuminuria [11]. Given the role of MAB as an early marker of cardiovascular and renal pathology, its prevalence in COPD patients warrants investigation to establish its potential as a prognostic tool for cardiovascular risk assessment [12].

The relationship between COPD severity and microalbuminuria is hypothesized to be linked through systemic hypoxemia and the consequent impact on vascular integrity. In COPD patients, chronic alveolar hypoxia leads to pulmonary vasoconstriction, increased pulmonary artery pressure, and eventual right heart failure [13]. Hypoxia also disrupts the balance between vasodilation and vasoconstriction in the systemic circulation, contributing to endothelial injury [14]. This endothelial dysfunction may

extend to the renal vasculature, leading to increased permeability and microalbuminuria [15].

Previous studies have demonstrated a higher prevalence of microalbuminuria in COPD patients compared to control groups without pulmonary disease, suggesting that MAB may be a marker of disease severity and systemic vascular involvement [16]. For example, studies by Bulcan et al. and Mehmood et al. observed a significant association between lower oxygen levels (PaO2) and higher urinary albumin creatinine ratios (UACR) in COPD patients, reinforcing the link between systemic hypoxemia and endothelial dysfunction [17,18]. These findings highlight the potential role of microalbuminuria in identifying COPD patients at higher risk for cardiovascular events and guiding therapeutic interventions.

Despite the growing evidence, there is still a need for studies examining the prevalence and clinical significance of microalbuminuria in stable COPD patients across different severity stages. While most studies have focused on acute exacerbations or advanced stages of COPD, understanding the prevalence of MAB in stable, non-exacerbating COPD patients is crucial for establishing its utility as an early and routine screening tool [19,20]. Furthermore, correlating microalbuminuria levels with PFT parameters could provide insights into how microalbuminuria reflects pulmonary function and disease progression in COPD, potentially offering a non-invasive, easily measurable marker of disease severity.

This study aims to fill this gap by assessing the prevalence of microalbuminuria in a stable COPD population and exploring its relationship with pulmonary function parameters, such as FEV1, FVC, and the FEV1/FVC ratio. Additionally, the study examines the association between MAB levels and the severity of COPD as defined by the GOLD criteria, which classifies the disease into four stages based on spirometry results [6]. The GOLD guidelines provide a standardized method for assessing COPD severity, making it an ideal framework for correlating clinical parameters with microalbuminuria.

Materials and Methods

This study was conducted as a cross-sectional investigation at the Department of General Medicine and Respiratory Medicine at GSL Medical College and General Hospital, Rajahmundry, Andhra Pradesh, India. The study aimed to determine the prevalence of microalbuminuria in stable COPD patients and evaluate its relationship with pulmonary function parameters. The study period spanned from October 1, 2019, to March 31, 2021, and included a total of 139 participants who met the inclusion criteria.

Study Design

A cross-sectional design was chosen to evaluate the prevalence of microalbuminuria (MAB) in COPD patients and to establish any correlations with clinical and pulmonary function parameters. This design allows for the observation of associations and patterns within a specific point in time, providing insights into the impact of microalbuminuria on COPD patients.

Study Population

The study population comprised stable COPD patients attending the outpatient department of the hospital. Patients were selected based on the following criteria:

Inclusion Criteria:

1. Adults aged 35–90 years diagnosed with COPD based on the GOLD criteria (post-bronchodilator FEV1/FVC ratio < 0.7) [1].
2. Stable COPD patients, defined as those with no acute exacerbation or infection for at least four weeks prior to the study.

Exclusion Criteria:

1. Patients with a history of renal disease, diabetes mellitus, cardiovascular diseases, or urinary tract infections (UTIs).
2. Patients with other respiratory diseases like asthma, interstitial lung disease (ILD), obstructive sleep apnea (OSA), malignancies, and severe hepatic failure [2].

Data Collection

A detailed clinical history and thorough physical examination were conducted for each participant using a structured questionnaire. This included demographic data such as age, gender, duration of COPD, smoking history (measured in pack-years), and the duration of illness. Patients' clinical symptoms, including cough, dyspnea, wheezing, and other physical signs like cyanosis and clubbing, were recorded.

Pulmonary Function Testing

Spirometry was performed to evaluate pulmonary function in all participants. The spirometry measurements included:

- Forced Vital Capacity (FVC)
- Forced Expiratory Volume in 1 second (FEV1)
- FEV1/FVC ratio

These parameters were measured using standardized spirometry procedures before and after bronchodilator administration to confirm COPD diagnosis and assess airflow limitation. Based on the GOLD criteria, patients were categorized into different stages of COPD severity: mild (Stage I: FEV1 ≥ 80%), moderate (Stage II: 50% ≤ FEV1 < 80%), severe (Stage III: 30% ≤ FEV1 < 50%), and very severe (Stage IV: FEV1 < 30%) [3].

Measurement of Microalbuminuria

Microalbuminuria (MAB) was measured using the urine albumin-to-creatinine ratio (UACR) method. Spot urine samples were collected from each patient, and the albumin concentration was expressed in mg per gram of creatinine (mg/g). According to standard definitions, a UACR value between 30 and 300 mg/g was considered indicative of microalbuminuria [4].

Ethical Considerations

Ethical approval for the study was obtained from the institutional ethics review committee before commencement. Informed consent was obtained from all

participants after explaining the nature and purpose of the study, ensuring voluntary participation and confidentiality. Participants were also informed about the option to withdraw from the study at any point without any repercussions.

Statistical Analysis

The collected data were compiled and analyzed using SPSS software version 20.0 and Microsoft Excel 2010. Descriptive statistics, such as mean, standard deviation, and percentage, were used to present baseline demographic data, clinical characteristics, and microalbuminuria prevalence.

Correlation analysis was performed to assess the relationship between pulmonary function parameters (FEV1, FVC, and FEV1/FVC ratio) and microalbuminuria levels. The chi-square test was used to determine associations between qualitative variables, such as age and gender distribution of microalbuminuria. An independent t-test was utilized to compare quantitative variables like duration of smoking and UACR levels. A p-value of <0.05 was considered statistically significant.

Outcome Measures

The primary outcome measure was the prevalence of microalbuminuria among stable COPD patients. The secondary outcome was the correlation between the severity of microalbuminuria and pulmonary function parameters, as well as other clinical and demographic characteristics, such as age, gender, and smoking history.

Results

This section presents the findings from the study conducted on 139 COPD patients. The data are analyzed across various dimensions, including demographics, pulmonary function tests (PFT), smoking habits, and microalbuminuria levels. Statistical associations between these variables and microalbuminuria are explored. The results are presented with appropriate tables, summarizing key data points.

1. Demographics and Baseline Characteristics

The study population consisted of 139 COPD patients with a mean age of 62.61 ± 10.27 years, ranging from 35 to 90 years. The majority of the participants were in the age group of 51–70 years (66.2%), indicating a higher prevalence of COPD among middle-aged to elderly individuals. Males constituted 87.8% of the study population, while females accounted for 12.2%. This male predominance is in line with other studies, where smoking is the major risk factor for COPD [10].

Table 1 presents the age distribution and the prevalence of microalbuminuria (MAB) across different age groups. The highest prevalence of MAB (41.5%) was observed in the age group of 61–70 years. However, statistical analysis revealed no significant difference in the mean age between patients with microalbuminuria and those without it ($p = 0.24$).

| **Table 1: Age Distribution and Prevalence of Microalbuminuria** |

Age Group (years)	**<30 mg/d**	**30–300 mg/d**	**Total**
35–50	16 (16.3%)	7 (17.1%)	23 (16.5%)
51–60	33 (33.7%)	8 (19.5%)	41 (29.5%)
61–70	34 (34.7%)	17 (41.5%)	51 (36.7%)
71–80	12 (12.2%)	9 (22.0%)	21 (15.1%)
81–90	3 (3.1%)	0 (0%)	3 (2.2%)
Total	98	41	139

2. Pulmonary Function Test Parameters and Microalbuminuria

Pulmonary function was assessed using spirometry, and the results were classified according to GOLD staging. Table 2 provides a summary of spirometric parameters, including FEV1, FVC, and FEV1/FVC ratio, and their correlation with microalbuminuria levels. The study revealed a statistically significant association between FEV1/FVC ratio and microalbuminuria levels ($p < 0.001$). Patients with

more severe airflow obstruction (GOLD stages III and IV) exhibited higher mean urine albumin creatinine ratios (UACR), indicating a potential link between impaired pulmonary function and systemic endothelial dysfunction.

| **Table 2: Pulmonary Function Test Parameters and Microalbuminuria** |

Parameter	**Range**	**Mean ± SD**
FVC (L)	1.91 – 3.51	2.90 ± 0.44
FEV1 (L)	0.53 – 1.84	1.12 ± 0.33
FEV1 %	25.70 – 77.0	49.46 ± 13.90
FEV1/FVC %	21.50 – 70.0	52.74 ± 13.60

3. Association Between GOLD Staging and Microalbuminuria

Table 3 outlines the distribution of COPD patients across different GOLD stages (II, III, and IV) and their corresponding microalbuminuria levels. In the current study, the overall prevalence of microalbuminuria was 29.5%. Patients in GOLD stage III and IV had significantly higher mean UACR values compared to those in GOLD stage II ($p < 0.001$), suggesting that as the severity of COPD increases, so does the presence of microalbuminuria. This finding underscores the potential role of microalbuminuria as a marker of disease severity and cardiovascular risk in COPD patients.

| **Table 3: GOLD Staging and Microalbuminuria Levels** |

GOLD Stage	**Frequency (%)**	**Mean UACR (mg/g) ± SD**
Stage II (FEV1 50–80%)	69 (49.6%)	30.60 ± 49.81
Stage III (FEV1 30–50%)	59 (42.4%)	89.37 ± 98.70
Stage IV (FEV1 <30%)	11 (7.9%)	90.54 ± 94.35

GOLD Stage	**Frequency (%)**	**Mean UACR (mg/g) ± SD**
Total	139 (100%)	—

4. Smoking History and Microalbuminuria

The duration of smoking, measured in pack-years, ranged from 20 to 60 years among the study participants. As shown in Table 4, no significant association was found between smoking habits and microalbuminuria levels (p = 0.83). Despite this, the majority of the study population (87.8%) had a history of smoking, reinforcing the role of smoking as a primary risk factor for COPD. However, the lack of correlation with microalbuminuria suggests that other factors, such as the degree of lung function impairment or systemic inflammation, may play a more significant role in the development of microalbuminuria in COPD patients.

| **Table 4: Smoking Pack Years and Microalbuminuria** |

Pack Years	**<30 mg/d**	**30–300 mg/d**	**Total**
Nil	14 (14.3%)	3 (7.3%)	17 (12.2%)
20–30	7 (7.1%)	5 (12.2%)	12 (8.6%)
31–40	39 (39.8%)	17 (41.5%)	56 (40.3%)
41–50	27 (27.6%)	9 (22.0%)	36 (25.9%)
51–60	11 (11.2%)	7 (17.1%)	18 (12.9%)
Total	98	41	139

5. Clinical Symptoms and Signs

In terms of clinical presentation, all patients reported a chronic cough, with 90.6% experiencing breathlessness and 78.4% reporting wheezing. Fever was less common, affecting only 15.1% of the participants. Physical signs such as cyanosis, clubbing,

and distended neck veins were observed in a subset of patients. The presence of these symptoms and signs did not exhibit a significant correlation with microalbuminuria levels, but their prevalence highlights the diverse clinical manifestations of COPD, which often complicates its management.

Discussion

Chronic Obstructive Pulmonary Disease (COPD) is increasingly recognized as not just a pulmonary condition but a systemic disease with widespread effects beyond the lungs. The present study investigates the prevalence of microalbuminuria (MAB) in stable COPD patients and explores its correlation with pulmonary function test (PFT) parameters and disease severity. The findings demonstrate that microalbuminuria is prevalent in COPD patients, particularly those with more severe airflow limitation (GOLD stages III and IV), suggesting that MAB could serve as an early biomarker for cardiovascular risk and disease progression in this population.

Prevalence of Microalbuminuria in COPD Patients

The overall prevalence of microalbuminuria in the study population was found to be 29.5%. This figure is consistent with other studies that have reported similar prevalence rates of microalbuminuria in COPD patients, ranging from 20% to 30% [1]. The presence of microalbuminuria in COPD patients is a significant finding, as it reflects systemic endothelial dysfunction, which is a hallmark of both cardiovascular diseases and COPD [2]. The chronic hypoxia and inflammation seen in COPD may impair endothelial function, leading to increased permeability of the glomerular filtration barrier and subsequent albumin leakage into urine [3]. This systemic effect underpins the close association between COPD and cardiovascular morbidity, emphasizing the need for early markers like microalbuminuria to identify at-risk patients.

Correlation Between Microalbuminuria and Pulmonary Function

The study revealed a significant association between pulmonary function parameters and microalbuminuria levels. Specifically, the FEV1/FVC ratio was significantly

correlated with microalbuminuria ($p < 0.001$), and patients with more severe stages of COPD (GOLD stages III and IV) exhibited higher levels of microalbuminuria. This correlation suggests that as airflow limitation worsens, systemic endothelial dysfunction also intensifies, contributing to higher rates of microalbuminuria. These findings align with those from previous studies where an inverse relationship between pulmonary function (as measured by FEV1) and microalbuminuria was reported [4,5].

The GOLD criteria categorize COPD severity based on FEV1 levels, which indicate the extent of airflow limitation. As the disease progresses from mild to severe stages, patients experience a greater degree of lung function impairment, resulting in hypoxia. Chronic hypoxia is known to induce endothelial dysfunction by altering the balance between vasodilators (e.g., nitric oxide) and vasoconstrictors (e.g., endothelin-1), leading to systemic vascular damage [6]. Microalbuminuria, therefore, may be a manifestation of this vascular damage, serving as a measurable and non-invasive marker of disease severity in COPD patients.

The Role of Systemic Inflammation and Hypoxia in Microalbuminuria Development

COPD is characterized by a heightened inflammatory state, with increased levels of inflammatory cytokines like tumor necrosis factor-alpha (TNF-α), interleukins (IL-6 and IL-8), and C-reactive protein (CRP) circulating in the bloodstream. This chronic inflammation contributes not only to pulmonary damage but also to systemic vascular injury, which may manifest as microalbuminuria [7]. The link between inflammation and microalbuminuria has been well-documented, as inflammation-induced endothelial damage increases vascular permeability, leading to albumin leakage into the urine [8].

Furthermore, hypoxia in COPD exacerbates systemic endothelial dysfunction. Hypoxia-induced vasoconstriction in pulmonary arteries can extend to the systemic vasculature, affecting renal blood flow and glomerular function. The renal endothelium, under hypoxic conditions, may experience structural and functional changes, compromising its ability to maintain the filtration barrier [9]. This disruption likely explains the elevated microalbuminuria levels observed in patients with severe COPD.

Studies have shown that COPD patients with lower oxygen saturation (PaO2) levels have higher levels of microalbuminuria, supporting the role of hypoxia in the pathogenesis of microalbuminuria [10]. In the present study, the statistically significant correlation between FEV1/FVC ratios and MAB levels highlights the relationship between lung function, hypoxia, and systemic vascular damage. This further suggests that monitoring microalbuminuria levels in COPD patients could serve as a marker for both pulmonary and systemic complications, offering a comprehensive assessment of disease progression and risk.

Comparison with Existing Literature

The findings of this study are consistent with those of Kumar et al. and Gupta et al., who demonstrated that microalbuminuria is more prevalent in patients with higher GOLD stages and worse pulmonary function test outcomes [4,11]. In the study by Kumar et al., COPD patients exhibited higher microalbuminuria levels compared to control subjects, and an inverse correlation was found between FEV1 and UACR values. Similarly, Gupta et al. reported that microalbuminuria increases with the severity of COPD, particularly in patients with hypoxemia, supporting the association between airflow limitation and endothelial dysfunction.

Another significant study by Bulcan et al. reported that microalbuminuria is inversely related to PaO2 levels, further confirming that hypoxia plays a critical role in microalbuminuria development [12]. These findings align closely with the results of the present study, where patients in GOLD stages III and IV, who likely experience more severe hypoxia, exhibited higher mean microalbuminuria levels. Such consistent results across multiple studies strengthen the evidence that microalbuminuria is a reliable indicator of systemic endothelial damage and disease severity in COPD patients.

Implications for Clinical Practice

The strong association between COPD severity and microalbuminuria observed in this study suggests that MAB could be used as a prognostic marker for disease progression and cardiovascular risk. Early identification of microalbuminuria in COPD patients may allow for targeted interventions to manage and mitigate the risk

of cardiovascular complications, which are the leading cause of mortality in COPD patients [13]. Current clinical guidelines recommend monitoring COPD patients for comorbidities such as cardiovascular disease, but specific biomarkers like microalbuminuria could provide a more precise and early indication of systemic vascular involvement [14].

Microalbuminuria is a relatively simple and non-invasive test that can be incorporated into routine clinical assessments. Its presence in COPD patients could trigger further diagnostic workups, such as echocardiography or more advanced vascular imaging, to evaluate cardiovascular risk comprehensively. By integrating microalbuminuria screening in COPD management, healthcare providers can stratify patients according to their risk profile and implement appropriate cardiovascular preventive measures, such as optimizing bronchodilator therapy, using angiotensin-converting enzyme (ACE) inhibitors, or introducing lifestyle modifications aimed at reducing systemic inflammation and improving oxygenation [15].

Limitations of the Study

While the findings of this study provide valuable insights, certain limitations must be acknowledged. First, the cross-sectional nature of the study limits the ability to establish causality between microalbuminuria and COPD severity. Although a significant association was observed, longitudinal studies would be necessary to determine whether microalbuminuria precedes the development of cardiovascular complications or if it is merely a consequence of advanced COPD.

Second, the reliance on spirometry as the primary diagnostic tool for COPD assessment may introduce variability, as the test's accuracy depends on patient effort and technique. Additionally, the study did not account for potential confounding factors such as hypertension or diabetes, which could independently contribute to microalbuminuria development. Future studies should control for these variables to ensure that the observed associations are specific to COPD.

Lastly, the study population consisted predominantly of males (87.8%), which may limit the generalizability of the findings to the broader COPD population, especially considering that environmental exposures, such as indoor air pollution, are more

common in females and could influence the development of COPD and microalbuminuria differently.

Conclusion

The study demonstrates that microalbuminuria is prevalent in COPD patients, particularly those with severe airflow limitation. The significant correlation between microalbuminuria levels and pulmonary function parameters suggests that MAB could serve as a marker for systemic endothelial dysfunction and cardiovascular risk in COPD patients. Incorporating microalbuminuria screening into routine COPD management may help identify patients at higher risk for cardiovascular complications, allowing for early intervention and potentially improved patient outcomes. Further research is warranted to validate these findings and explore the prognostic value of microalbuminuria in long-term COPD management.

By addressing these considerations, healthcare providers can develop a more holistic approach to managing COPD, integrating pulmonary and systemic aspects of the disease to enhance patient care and prognosis.

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