

Correlation of the markers in patients with COPD and COR Pulmonale and the effect of therapeutic measures

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Abstract:

Chronic Obstructive Pulmonary Disease (COPD), frequently complicated by cor pulmonale, is associated with significant morbidity and mortality. Biomarkers such as microalbuminuria, serum albumin, and arterial pCO₂ have emerged as potential indicators of disease severity and treatment response. This prospective, cross-sectional study was conducted over six months at Meenakshi Medical College Hospital and Research Institute and included 100 COPD patients with cor pulmonale. Baseline clinical parameters including BMI, GOLD staging, arterial blood gas (pCO₂), serum albumin, and microalbuminuria were recorded. All patients received guideline-based management, and biomarkers were reassessed after six months. Microalbuminuria was detected in 85% of participants and showed significant associations with age, smoking index, low BMI, and severe GOLD staging ($p < 0.05$). Serum albumin levels were reduced (mean: 3.4 mg/dL) and inversely correlated with disease severity, while arterial pCO₂ levels were elevated (mean: 53.5 mmHg), especially in those with acute exacerbations. After six months of treatment, serum albumin levels significantly improved ($p = 0.002$) and pCO₂ decreased ($p = 0.001$), while microalbuminuria remained largely unchanged. These findings suggest that microalbuminuria reflects persistent endothelial dysfunction and systemic involvement in COPD with cor pulmonale, whereas serum albumin and pCO₂ are responsive to therapeutic interventions. The dynamic behavior of these biomarkers highlights their utility in monitoring disease progression, assessing treatment efficacy, and guiding individualized care in high-risk COPD populations.

Keywords: COPD, cor pulmonale, microalbuminuria, serum albumin, arterial pCO₂, GOLD staging, biomarkers, endothelial dysfunction, disease monitoring.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a significant global health burden, characterized by persistent respiratory symptoms and progressive, largely irreversible airflow limitation. It results primarily from exposure to harmful particles or gases, especially tobacco smoke, air pollution, and occupational hazards [1]. According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD), COPD remains both preventable and treatable. However, it is currently the third leading cause of death globally, accounting for over 3 million deaths annually, with nearly 90% of these occurring in low- and middle-income countries [2,3].

One of the serious complications of advanced COPD is cor pulmonale, which refers to structural and functional changes in the right ventricle due to pulmonary hypertension stemming from chronic lung disease. The World Health Organization (WHO) defines cor pulmonale as right ventricular hypertrophy and eventual failure secondary to diseases that affect lung structure or function, excluding those of left heart origin [4]. The development of cor pulmonale in COPD is multifactorial, involving chronic hypoxia, pulmonary vasoconstriction, vascular remodelling, and sustained increases in pulmonary artery pressures [5,6]. This condition significantly worsens prognosis, increases hospital admissions, and is a predictor of early mortality.

Emerging data suggest that cardiovascular involvement in COPD, including subclinical right ventricular (RV) dysfunction, may precede the clinical onset of pulmonary hypertension. The interplay of systemic inflammation, hypoxia-induced endothelial damage, and oxidative stress is believed to contribute to RV remodelling and dysfunction, even in the absence of measurable hemodynamic changes [7,8]. In fact, cardiovascular comorbidities are now recognized as leading contributors to COPD-related morbidity and mortality, necessitating early detection and holistic disease management [9].

Recent studies have emphasized that COPD is not solely a pulmonary disease, but a systemic disorder with significant extrapulmonary manifestations, such as muscle wasting, metabolic syndrome, osteoporosis, and cardiovascular disease [10,11]. This broader understanding of COPD has driven interest in identifying biomarkers that reflect systemic involvement and may assist in disease stratification and monitoring. Among these, microalbuminuria, serum albumin, and arterial partial pressure of carbon dioxide (pCO₂) have gained increasing attention.

Microalbuminuria, defined as urinary albumin excretion between 30–300 mg/day, is a sensitive marker of endothelial dysfunction and systemic microvascular injury. It has been independently associated with higher COPD severity, poor oxygenation, and increased

cardiovascular risk [12,13]. Its persistence across disease stages may reflect ongoing vascular damage and inflammation, making it a potential prognostic marker rather than one that is responsive to short-term interventions.

Serum albumin, a negative acute-phase protein, is influenced by nutritional status and systemic inflammation. Hypoalbuminemia has been correlated with increased frequency of COPD exacerbations, longer hospital stays, and higher mortality [14,15]. Furthermore, low albumin levels can impair drug transport, reduce muscle mass, and affect pulmonary defence mechanisms, thereby worsening outcomes.

Arterial pCO₂, as measured by arterial blood gas analysis, is a critical parameter reflecting ventilatory capacity, gas exchange efficiency, and acid-base status. Chronic hypercapnia is associated with advanced COPD and has been linked to poor prognosis, increased exacerbation risk, and greater need for non-invasive ventilation [16,17]. Changes in pCO₂ levels during treatment may serve as indicators of therapeutic response and disease stability.

Despite individual studies assessing these biomarkers, their combined clinical utility – particularly in patients with COPD and cor pulmonale – remains inadequately explored. The current study was designed to evaluate the prevalence and clinical correlations of microalbuminuria, serum albumin, and arterial pCO₂ in COPD patients with cor pulmonale. Furthermore, it aimed to assess the dynamic changes in these markers following six months of standardized therapy. The findings may provide evidence for incorporating these biomarkers into routine clinical evaluation, supporting risk stratification and guiding individualized management in a high-risk patient group.

MATERIAL AND METHODS

Study Design and Setting

This prospective, cross-sectional study was conducted at Meenakshi Medical College Hospital and Research Institute, Kanchipuram, over a six-month period from November 2023 to April 2024. The study aimed to evaluate the correlation of microalbuminuria, serum albumin, and arterial pCO₂ with disease severity and the impact of treatment in patients with COPD and cor pulmonale.

Study Population

A total of 100 adult patients with a confirmed diagnosis of COPD and cor pulmonale were included. Participants were either outpatients attending the General Medicine or Pulmonology departments or inpatients admitted during the study period.

Inclusion Criteria

- Adults aged ≥ 18 years

- Diagnosed with COPD and cor pulmonale based on GOLD guidelines and echocardiographic findings
- Willing to provide written informed consent

Exclusion Criteria

- Known chronic kidney disease, liver disease, or diabetes mellitus
- Presence of macroalbuminuria
- History of cerebrovascular disease, ischemic heart disease, malignancy, or symptoms suggestive of obstructive sleep apnea
- Recent urinary tract infection (within the past week)
- Persistent haematuria (within the past year)
- Unwillingness to participate

Data Collection and Clinical Assessment

After obtaining written informed consent, detailed demographic and clinical histories were recorded. A complete physical examination was conducted, including measurement of body mass index (BMI). Patients were staged according to the GOLD COPD classification.

Investigations included:

- Routine blood tests: complete blood count (CBC), liver function tests (LFT), renal function tests (RFT)
- Arterial blood gas (ABG) analysis: to measure arterial pCO₂ via radial artery puncture
- Urine microalbuminuria: assessed via a spot morning urine sample
- Electrocardiogram (ECG) and 2D-echocardiography with color Doppler: to evaluate right ventricular function and pulmonary hypertension.

Patients were managed according to GOLD guidelines for COPD and received cor pulmonale treatment as per cardiology recommendations. Follow-up was conducted at six months, during which clinical status and biomarker levels were reassessed.

Ethical Considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee of Meenakshi Medical College Hospital and Research Institute. All participants provided informed written consent before enrolment. Confidentiality and data protection measures were strictly followed throughout the study.

Statistical Analysis

Data were entered in Microsoft Excel and analysed using SPSS software version 16. Continuous variables were expressed as mean $\pm$ standard deviation (SD) or median as appropriate. Categorical variables were summarized as frequencies and percentages. Statistical comparisons were performed using:

- Chi-square test or Fisher's exact test for categorical variables

- Independent t-test or non-parametric tests for between-group comparisons
- Paired t-test for within-subject changes (pre- and post-intervention)

- One-way ANOVA for multiple group comparisons
- A p-value < 0.05 was considered statistically significant.

RESULTS AND OBSERVATIONS:

A total of 100 patients diagnosed with COPD and cor pulmonale were included in the study. Clinical, demographic, and biochemical variables were analysed at baseline and at six-month follow-up.

Table 1: Age and Gender Distribution

Age Group	Male	Female	Total
<= 50 years	14	6	20
51 - 60 years	32	8	40
61 - 70 years	38	2	40
Total	84	16	100

(Table 1): The majority of patients were male (84%) and between 51–70 years of age. This age group also reflected the highest COPD burden, consistent with known disease progression patterns.

Table 2: Smoking Index Distribution

Smoking Index	Count	Percentage
Never Smoked	15	15.0%
< 100	6	6.0%
100 - 300	24	24.0%
300 - 600	20	20.0%
> 600	35	35.0%

(Table 2): A significant portion of patients (35%) had a smoking index >600, indicating a strong association between heavy smoking and COPD severity.

Table 3: GOLD Staging Distribution

Gold Staging	Count	Percentage
> 80% predicted	0	0.0%
50 - 80% predicted	12	12.0%
30 - 50% predicted	30	30.0%
< 30% predicted	58	58.0%

(Table 3): Most patients (58%) had severe airflow limitation (FEV₁ <30%), highlighting a predominantly advanced-stage COPD cohort.

Table 4: Association of Microalbuminuria with GOLD Staging

GOLD Staging	Micro Albuminuria- Yes	Micro Albuminuria - No	Total	p-value
50 - 80% predicted	4	8	12	0.001
30 - 50% predicted	20	10	30	
< 30% predicted	61	3	64	
Total	85	15	100	

(Table 4): Microalbuminuria was present in 85% of patients and significantly associated with lower FEV₁, older age, low BMI, and higher smoking exposure (p < 0.05). Its prevalence increased with disease severity, especially in those with GOLD stage <30%.

Table 5: Mean Serum Albumin and pCO₂ by BMI

BMI	Mean Serum Albumin (mg/dL)	Std. Dev	Mean pCO ₂ (mmHg)	p-value
Underweight	3.3	7.2	54.1	0.146
Normal	3.41	8.4	51.5	
Overweight	3.68	7.9	50.9	
Obese	3.4	8.3	48.8	
Total	3.4	7.8	53.5	

(Table 5): The overall mean serum albumin was 3.4 mg/dL, showing a trend toward hypoalbuminemia. Mean pCO₂ was elevated (53.5 mmHg), particularly among underweight patients and those with severe GOLD staging or acute exacerbations.

At the six-month follow-up, 15% of the patients had died, and 10% were lost to follow-up, reflecting the high disease burden and mortality risk associated with COPD and cor pulmonale. Among the survivors, serum albumin levels improved significantly, increasing from a baseline mean of 3.38 mg/dL to 3.56 mg/dL ($p = 0.002$). This improvement may reflect better nutritional status or response to therapeutic interventions during the follow-up period.

Arterial pCO₂ levels also showed a statistically significant decrease, with values falling from 52.52 mmHg at baseline to 49.58 mmHg at follow-up ($p = 0.001$), indicating an overall improvement in ventilatory status or disease control in some patients.

Despite these biochemical improvements, microalbuminuria levels remained largely unchanged in the majority of patients, suggesting persistent endothelial dysfunction and ongoing systemic inflammation. GOLD staging reassessment revealed that only 11 patients demonstrated improvement, while 31 showed further deterioration, highlighting the progressive nature of the disease in a considerable subset of the study population despite treatment adherence.

These observations suggest that while certain biomarkers such as serum albumin and pCO₂ may respond to therapy and reflect short-term improvement, microalbuminuria appears to be a more stable marker of long-term endothelial injury and may be less amenable to reversal with standard COPD treatment over a six-month timeframe.

DISCUSSION

This study examined the correlation of microalbuminuria, serum albumin, and arterial pCO₂ with disease severity in patients with COPD and cor pulmonale and assessed the effect of therapeutic measures over a six-month period. The findings reinforce the complex and systemic nature of COPD and highlight the prognostic value of these biochemical markers.

A striking observation in our study was the high prevalence of microalbuminuria (85%), which significantly correlated with advanced GOLD stages, lower body mass index (BMI), and higher smoking index. These findings are consistent with prior studies that have identified microalbuminuria as a marker of systemic endothelial dysfunction in chronic inflammatory states like COPD [9, 12, 13]. Chronic hypoxia, oxidative stress, and persistent systemic inflammation likely contribute to this microvascular damage. Importantly, microalbuminuria levels remained largely unchanged over six months of therapy, supporting its role as a stable biomarker of chronic vascular injury rather than a dynamic marker of treatment response.

In contrast, serum albumin levels demonstrated statistically significant improvement over the follow-up period. Albumin is a negative acute-phase reactant and

reflects both nutritional status and systemic inflammation. Hypoalbuminemia is associated with worse outcomes, including increased hospitalization and mortality in COPD [14,15]. In our cohort, mean serum albumin increased from 3.38 mg/dL to 3.56 mg/dL ($p = 0.002$), indicating partial reversibility with standard therapy and improved nutritional or inflammatory control. These results are consistent with previous findings that reductions in fat-free mass and poor nutrition are common in COPD and can improve with appropriate management [26].

In this context, the role of systemic inflammation in driving poor nutritional outcomes cannot be overstated. The ECLIPSE study demonstrated that elevated inflammatory biomarkers such as fibrinogen and CRP were predictive of both exacerbations and mortality in COPD patients [22]. Therefore, the observed rise in serum albumin may not only reflect improved nutrition but also a reduction in systemic inflammatory load.

Arterial pCO₂ also showed a significant decrease from 52.52 mmHg to 49.58 mmHg ($p = 0.001$), suggesting improved alveolar ventilation and better disease control. Baseline hypercapnia was most notable in underweight patients and those with frequent exacerbations or advanced GOLD stages. Hypercapnia is not just a reflection of disease severity—it is also a therapeutic target. Malerba and Ragnoli proposed that pCO₂

elevation in COPD represents a modifiable risk factor in patients receiving long-term non-invasive ventilation (NIV), and its reduction is associated with improved clinical outcomes [25]. Similarly, Struik et al. showed that nocturnal NIV in COPD patients with persistent hypercapnia post-exacerbation led to better clinical stability, highlighting pCO₂ as a dynamic marker responsive to intervention [18].

Despite these positive changes, microalbuminuria remained persistent, pointing to its utility as a marker of long-term systemic damage. A systematic review by Machado et al. supports the combined use of biomarkers such as albumin and pCO₂, which can improve the prediction of exacerbation risk beyond conventional spirometric indices [21]. In our findings, microalbuminuria may serve as a complementary marker that reflects chronic vascular burden not easily reversed with short-term pharmacologic therapy.

Another important aspect of COPD is its multisystem involvement, especially the cardiovascular system. Right ventricular dysfunction in COPD is often underdiagnosed until advanced cor pulmonale develops [20]. Inflammation and pulmonary vascular remodelling contribute to the development of pulmonary hypertension, which further exacerbates right heart strain and impairs exercise tolerance. Sun et al. demonstrated that biomarkers of vascular injury are associated with poorer clinical outcomes in COPD, independent of airflow limitation [27]. These findings support our observation that persistent microalbuminuria may reflect a broader endothelial injury beyond pulmonary dysfunction alone.

Furthermore, this study highlighted key demographic trends: the majority of patients were male, above 50 years, with a high smoking index and advanced airflow obstruction – demographics aligned with global COPD patterns [2,3,19]. The mortality rate of 15% over six months and GOLD stage deterioration in one-third of patients despite guideline-based therapy reflect the aggressive nature of COPD with cor pulmonale and the limits of standard management in reversing advanced pathophysiology.

Lastly, it is important to acknowledge other factors that may influence biomarker behaviour in COPD patients. For example, psychological comorbidities like anxiety and depression – prevalent in COPD – were not assessed in our study. These have been shown to affect both disease outcomes and inflammatory marker expression, potentially confounding biochemical trends [23].

Taken together, our findings support the use of microalbuminuria as a prognostic marker, and serum albumin and arterial pCO₂ as dynamic markers of therapeutic response in COPD with cor pulmonale. Their combined evaluation may provide clinicians with

a cost-effective and accessible toolset for stratifying risk, tailoring therapy, and tracking disease progression. This multi-biomarker approach could enhance individualized patient care, especially in resource-limited settings.

CONCLUSION

This study reinforces the significance of using microalbuminuria, serum albumin, and arterial pCO₂ as complementary biomarkers in the evaluation and management of patients with COPD complicated by cor pulmonale. Each of these markers reflects distinct pathophysiological processes: microalbuminuria captures long-term systemic endothelial dysfunction; serum albumin reflects nutritional status and systemic inflammation; while pCO₂ provides insight into ventilatory function and gas exchange [18, 26].

Our findings demonstrated that serum albumin and arterial pCO₂ levels improved significantly after six months of guideline-based therapy, indicating their responsiveness to pharmacologic and supportive interventions. In contrast, microalbuminuria remained largely unchanged, suggesting it may serve as a stable indicator of chronic vascular injury and systemic inflammation. This divergence highlights the importance of using a multi-marker approach to monitor both acute treatment response and long-term disease burden.

Given the systemic nature of COPD, such biomarker-guided monitoring may offer a more holistic and individualized management strategy, particularly in patients with cardiovascular involvement, low BMI, or frequent exacerbations [19]. The potential prognostic role of these biomarkers is supported by findings from large cohort studies such as ECLIPSE and recent reviews indicating the utility of biomarker panels in predicting exacerbations, hospitalization, and mortality [21,22, 27].

Furthermore, the recognition of COPD as a multisystem disease – with underdiagnosis, comorbid depression, and silent cardiovascular complications – emphasizes the need for comprehensive risk assessment and monitoring tools that extend beyond pulmonary function tests [23, 24]. In this context, simple and accessible biochemical parameters like albumin, pCO₂, and microalbuminuria may bridge a critical gap in routine clinical practice.

Our study adds to the growing body of evidence advocating for routine integration of systemic biomarkers in COPD assessment protocols, particularly for high-risk subgroups such as those with cor pulmonale. While larger and longer-term studies are needed to validate these findings, the current data support the incorporation of these markers into standard care algorithms to improve risk stratification, treatment planning, and outcome prediction.

Limitations

Despite its strengths, this study has several important limitations that must be acknowledged:

1. Single-center design and limited sample size (n = 100) may reduce the generalizability of the findings to broader, more diverse COPD populations. Larger multicentric studies are needed to validate these results across various demographic and clinical settings.
2. The exclusion of common comorbid conditions such as diabetes mellitus, chronic kidney disease, and ischemic heart disease – which were necessary to isolate the effects of microalbuminuria – may not reflect real-world COPD cohorts where multimorbidity is common. The presence of these conditions could alter biomarker profiles and disease behaviour [22].
3. Cor pulmonale was diagnosed based on echocardiographic criteria, rather than invasive right heart catheterization, which remains the gold standard for confirming pulmonary hypertension. While practical and non-invasive, echocardiography may be less accurate, particularly in advanced lung disease [20].
4. The follow-up period of six months may be insufficient to assess the long-term behaviour of microalbuminuria, which appears to reflect chronic endothelial dysfunction. A longer follow-up duration would provide deeper insights into the trajectory and reversibility of these biomarkers.
5. Psychological comorbidities, such as depression and anxiety, were not evaluated. These conditions are common in advanced COPD and have been shown to independently affect disease perception, inflammatory marker levels, treatment adherence, and health-related quality of life [23].
6. Although improvements in serum albumin and pCO₂ were observed, objective measures of treatment adherence, including nutritional support and pharmacologic compliance, were not quantified. This introduces a potential confounding factor in interpreting the biochemical trends.
7. The study did not evaluate additional cardiovascular or systemic markers, such as NT-proBNP, troponins, or pro-inflammatory cytokines, which may have provided further insight into the cardiovascular and systemic inflammatory burden in these patients [27].
8. Lastly, underdiagnosis of COPD, particularly in its early stages, remains a global issue and may delay interventions that could improve biomarker trajectories and patient outcomes. This reflects a broader challenge in COPD care that extends beyond the study population [24].
9. Future studies should address these limitations by incorporating larger, multicenter cohorts, longer follow-up periods, and comprehensive biomarker panels, while accounting for comorbid psychological and systemic disease factors.

Conflict of Interest

None.

Source of Funding

None.

Authorship Contribution Statement

Nikhil Bandi: experimentation and Writing-original draft, Jayannan Jayasenan: Review and editing, Meyyammai Chidambaram: Review and editing, Mohanraj Perumaal: Conceptualization and supervision

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