Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Microalbuminuria as a Marker of Chronic Obstructive Pulmonary Disease Severity: Association with GOLD Stage, Dyspnea and CAT Score

Atkuri Sruthi

sruthiatkuri@gmail.com

Ramaiah Medical College and Hospital

D Pragati Rao

Ramaiah Medical College and Hospital

Research Article

Keywords: chronic obstructive pulmonary disease, microalbuminuria, urinary albumin-creatinine ratio, GOLD stage, mMRC, COPD Assessment Test, endothelial dysfunction

Posted Date: November 9th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-11477074/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Abstract

Background

Chronic obstructive pulmonary disease (COPD) has important systemic manifestations in addition to persistent airflow limitation. Microalbuminuria, assessed using the urinary albumin-to-creatinine ratio (UACR), may reflect generalized endothelial and microvascular dysfunction. This study evaluated the association of microalbuminuria with COPD severity assessed by GOLD spirometric stage, Modified Medical Research Council (mMRC) dyspnea grade and COPD Assessment Test (CAT) score.

Methods

A prospective observational study was conducted from March 2024 to March 2026 in the Department of Respiratory Medicine, Ramaiah Medical College and Hospital, Bengaluru. Adults with COPD diagnosed according to GOLD criteria, a documented CAT score and at least 10 smoking pack-years were enrolled. Patients with heart failure, chronic kidney disease, liver cirrhosis, ischemic heart disease, HIV infection or urinary tract infection were excluded, as were pregnant or menstruating participants at urine collection. Clinical assessment, post-bronchodilator spirometry, CAT scoring and a single midstream morning UACR measurement were performed. Associations were evaluated using chi-square/Fisher exact tests, independent-samples t-test, Pearson correlation and ANOVA as applicable.

Results

Among 166 participants, the mean age was 62.48 ± 7.83 years and 65.7% were men. Mean FEV1 was 1.45 ± 0.71 L and mean FEV1% predicted was 51.33 ± 22.42%. Microalbuminuria was present in 82 participants (49.4%), with a mean UACR of 85.77 ± 81.26 mg/g. Its prevalence increased from 16.7% in GOLD stage I to 33.3% in stage II, 62.5% in stage III and 78.1% in stage IV ($p < 0.001$). Prevalence also increased across mMRC grades, from 22.2% in grade 0 and 20.0% in grade 1 to 51.5%, 64.3% and 85.7% in grades 2, 3 and 4, respectively ($p < 0.001$). Participants with microalbuminuria had higher mean CAT scores than those without microalbuminuria (27.23 ± 9.31 vs 18.75 ± 9.05; $p < 0.001$). UACR showed a strong positive correlation with CAT score ($r = 0.655$, $p < 0.001$).

Conclusion

Microalbuminuria was common in this COPD cohort and was strongly associated with increasing airflow limitation, dyspnea and symptom burden. UACR may have potential as a simple, non-invasive marker of systemic involvement and disease severity in COPD. Larger longitudinal studies with repeated UACR measurements and adjustment for vascular and metabolic confounders are required before routine clinical use can be recommended.

Introduction

COPD is a heterogeneous respiratory disorder characterized by chronic respiratory symptoms and persistent airflow limitation resulting from abnormalities of the airways and/or alveoli. Its clinical impact extends beyond the respiratory system, with systemic inflammation, oxidative stress, hypoxemia and vascular dysfunction contributing to important extrapulmonary manifestations and comorbidities [1–4].

Albuminuria is traditionally considered a marker of renal injury, but even modest increases in urinary albumin excretion can reflect generalized endothelial dysfunction and increased vascular permeability. Moderately increased albuminuria, commonly termed microalbuminuria, corresponds to a UACR of 30–300 mg/g in a spot urine sample [5]. In COPD, chronic hypoxemia, smoking-related vascular injury, systemic inflammation and repeated exacerbations may contribute to endothelial dysfunction and glomerular albumin leakage [6, 7].

Previous studies have reported associations between microalbuminuria and hypoxemia, reduced lung function, higher GOLD stage, symptom burden and cardiovascular risk in COPD [8–15]. However, the prevalence of microalbuminuria varies substantially between cohorts, potentially because of differences in disease severity, smoking exposure, exacerbation burden and comorbidity profiles. The present study therefore evaluated microalbuminuria in patients with COPD and examined its relationship with GOLD stage, mMRC dyspnea grade and CAT score.

Materials and Methods

Study design and setting

This prospective observational study was conducted from March 2024 to March 2026 in the Department of Respiratory Medicine, Ramaiah Medical College and Hospital, Bengaluru, India. The study was designed to evaluate the relationship between microalbuminuria and COPD severity. Institutional Ethics Committee approval was obtained, and written informed consent was obtained from all participants.

Participants

Patients of either sex aged > 18 years with a clinical and functional diagnosis of COPD according to GOLD criteria, a documented CAT score and a minimum smoking exposure of 10 pack-years were eligible. Patients who did not provide consent or who had heart failure, chronic kidney disease, liver cirrhosis, ischemic heart disease, HIV infection or urinary tract infection were excluded. Pregnant women and women who were menstruating at the time of urine collection were also excluded.

Clinical and laboratory assessment

A structured clinical assessment recorded demographic characteristics, smoking exposure, COPD duration and exacerbations during the preceding year. General, respiratory and cardiovascular examinations were performed. Oxygen saturation, blood pressure and pulse rate were recorded. Laboratory evaluation included C-reactive protein, serum creatinine, serum urea, serum albumin, hemoglobin, random blood sugar and UACR.

A single midstream morning urine specimen was collected under aseptic precautions and analysed in the Biochemistry Laboratory for quantitative estimation of albuminuria. Microalbuminuria was defined according to the study protocol as UACR 30–300 mg/g.

Pulmonary function and symptom assessment

Post-bronchodilator spirometry was performed using a standardized spirometer. FEV1, FVC, FEV1/FVC and FEV1% predicted were recorded, and GOLD spirometric stage was assigned according to the degree of airflow limitation. Symptom burden was assessed using the eight-item CAT questionnaire (score range 0–40), while dyspnea was graded using the mMRC scale.

Outcomes and statistical analysis

The primary outcome was the association of microalbuminuria with COPD severity as classified by GOLD stage and CAT score. Secondary outcomes included the relationship of UACR with FEV1% predicted and the planned assessment of UACR as a potential marker of COPD severity. The sample size was calculated as 166 participants using a correlation coefficient of 0.441, 95% confidence and 80% power. Data were entered into Microsoft Excel and analysed using SPSS version 26. Continuous variables were summarized as mean ± standard deviation and categorical variables as frequencies and percentages. Pearson correlation was used for continuous associations; chi-square or Fisher exact tests were used for categorical associations, and independent-samples t-test/ANOVA were used for group comparisons as appropriate. A p-value < 0.05 was considered statistically significant.

Results

Participant characteristics

The study included 166 participants. The mean age was 62.48 ± 7.83 years; 67 participants (40.2%) were aged 60–69 years. Men constituted 109 (65.7%) and women 57 (34.3%). Mean height was 163.03 ± 7.46 cm, mean weight 60.30 ± 9.36 kg and mean BMI 22.66 ± 2.99 kg/m². Half of the participants had BMI 18.5–22.9 kg/m²; 22.3% were overweight, 20.5% obese and 7.2% underweight.

The mean smoking exposure was 26.73 ± 8.27 pack-years and mean COPD duration was 7.99 ± 3.53 years. COPD had been present for 6–10 years in 54.8% of participants. During the preceding year, 42.2% reported 0–1 exacerbations, 34.3% reported 2–3 and 23.5% reported ≥ 4 exacerbations.

Clinical, laboratory and pulmonary-function findings

Mean resting SpO2 was 90.54 ± 3.85%. Mean CRP was 15.34 ± 10.36 mg/L. Mean serum creatinine was 0.86 ± 0.17 mg/dL, serum urea 35.11 ± 6.18 mg/dL, serum albumin 3.81 ± 0.27 g/dL and hemoglobin 13.17 ± 1.27 g/dL. Mean FEV1 was 1.45 ± 0.71 L, FVC 2.50 ± 1.03 L, FEV1/FVC 56.36 ± 6.88% and FEV1% predicted 51.33 ± 22.42%.

GOLD stage III was the most frequent category (33.7%), followed by stage II (32.5%), stage IV (19.3%) and stage I (14.5%). The mean CAT score was 22.94 ± 10.09. On the mMRC scale, grade 2 was most common (39.8%), followed by grade 3 (25.3%), grade 1 (21.1%), grade 4 (8.4%) and grade 0 (5.4%).

Microalbuminuria and GOLD stage

Microalbuminuria was present in 82 of 166 participants (49.4%), while 84 (50.6%) did not have microalbuminuria. Mean UACR was 85.77 ± 81.26 mg/g. The prevalence of microalbuminuria increased progressively with GOLD stage: 4/24 (16.7%) in stage I, 18/54 (33.3%) in stage II, 35/56 (62.5%) in stage III and 25/32 (78.1%) in stage IV. This association was statistically significant (chi-square test, $p < 0.001$).

Table 1
Association between GOLD stage and microalbuminuria (chi-square test, $p < 0.001$).

GOLD stage	Microalbuminuria, n (%)	No microalbuminuria, n (%)	Total
I	4 (16.7)	20 (83.3)	24
II	18 (33.3)	36 (66.7)	54
III	35 (62.5)	21 (37.5)	56
IV	25 (78.1)	7 (21.9)	32

Microalbuminuria and dyspnea

Microalbuminuria was observed in 2/9 (22.2%) participants with mMRC grade 0, 7/35 (20.0%) with grade 1, 34/66 (51.5%) with grade 2, 27/42 (64.3%) with grade 3 and 12/14 (85.7%) with grade 4. The association between mMRC grade and microalbuminuria was statistically significant (Fisher exact test, $p < 0.001$).

Microalbuminuria and CAT score

Participants with microalbuminuria had a substantially higher mean CAT score than those without microalbuminuria (27.23 ± 9.31 vs 18.75 ± 9.05). The difference was statistically significant (independent-samples t-test, $p < 0.001$). UACR also showed a strong positive correlation with CAT score (Pearson $r = 0.655$, $p < 0.001$), indicating that higher urinary albumin excretion was associated with greater symptom burden.

Table 2
CAT score according to microalbuminuria status.

Microalbuminuria status	CAT score, mean ± SD	p-value
No	18.75 ± 9.05	< 0.001
Yes	27.23 ± 9.31	< 0.001
Total	22.94 ± 10.09	—

Discussion

The principal finding of this study was the strong graded association between microalbuminuria and COPD severity. Nearly half of the participants had microalbuminuria, and its prevalence increased from 16.7% in GOLD stage I to 78.1% in GOLD stage IV. This pattern is consistent with the concept that COPD is a systemic disease in which chronic hypoxemia, inflammation and vascular dysfunction may extend beyond the pulmonary circulation.

The prevalence of microalbuminuria in the present cohort (49.4%) falls between the rates reported in previous studies. Sahay and Prasad reported microalbuminuria in approximately 38% of patients, while other studies cited in the dissertation reported lower rates of about 18.6–30% and higher rates of approximately 70.8–81.7% [8, 10, 12, 14]. Such variation is likely to reflect differences in disease severity, smoking exposure, exacerbation burden and comorbidity profiles. The present cohort contained a substantial proportion of moderate-to-severe COPD, with 53.0% in GOLD stages III and IV, which may partly explain the relatively high prevalence.

The progressive relationship with GOLD stage is clinically important. The increase from 16.7% in stage I to 78.1% in stage IV suggests that albumin leakage is more common when airflow limitation is advanced. Prior work by Bozkus et al. and Casanova et al. similarly linked higher urinary albumin excretion with worse physiological impairment and hypoxemia [11, 13]. Studies by Bulcun et al., Shashidhar et al. and Banur et al. have also reported relationships between microalbuminuria and COPD severity [9, 14, 15].

A second important finding was the relationship with dyspnea. Microalbuminuria prevalence rose sharply at higher mMRC grades, reaching 85.7% in grade 4. This supports the observation that microalbuminuria may capture aspects of disease burden that are not represented by spirometry alone. The finding is also consistent with reports of higher mMRC scores among COPD patients with microalbuminuria.

The association with CAT score was particularly strong. Participants with microalbuminuria had a mean CAT score approximately 8.5 points higher than participants without microalbuminuria, and UACR correlated positively with CAT score (r = 0.655). Laha et al. reported a positive association between urine ACR and CAT score, while Barkati et al. also reported positive correlations with CAT and mMRC scores

[16, 17]. The present correlation was stronger than that reported in those studies, although differences in population characteristics and study methodology should be considered.

Biologically, microalbuminuria may represent increased systemic vascular permeability resulting from endothelial injury. Chronic hypoxemia, tobacco exposure, oxidative stress and inflammatory mediators may contribute to endothelial dysfunction in both pulmonary and systemic vascular beds. Albuminuria may therefore act as a readily measurable surrogate of systemic vascular involvement rather than simply representing renal disease. Importantly, however, UACR is influenced by several factors and should not be interpreted as a COPD-specific biomarker.

The study has several limitations. It was performed at a single centre and included 166 participants, limiting generalizability. The observational design demonstrates association rather than causality. Although several major conditions that can independently cause albuminuria were excluded, residual confounding by hypertension, diabetes, medication exposure and environmental factors cannot be excluded. UACR was measured from a single urine sample, so persistence of albuminuria was not established. Finally, the study did not include a broader panel of endothelial or inflammatory biomarkers, nor did it provide longitudinal outcome data.

These limitations suggest that the findings should be viewed as evidence supporting further evaluation rather than as a basis for using microalbuminuria alone to stage COPD. Multicentre longitudinal studies with repeated UACR measurements, standardized assessment of comorbidities and multivariable modelling are needed to determine whether UACR independently predicts COPD progression, cardiovascular events, exacerbations or mortality.

Conclusion

In this cohort of 166 patients with COPD, microalbuminuria was present in 49.4% and increased progressively with worsening GOLD stage and mMRC dyspnea grade. Patients with microalbuminuria had significantly greater CAT-defined symptom burden, and UACR demonstrated a strong positive correlation with CAT score. These findings support microalbuminuria as a potential non-invasive indicator of systemic vascular involvement and greater disease burden in COPD. Further longitudinal, multicentre studies are required to establish its independent prognostic value and clinical utility.

Declarations

Ethics approval and consent to participate

The dissertation states that Institutional Ethics Committee approval was obtained and written informed consent was obtained from all participants. The approval number was not stated in the source document; it should be inserted before journal submission if required by the target journal.

Consent for publication

Not applicable. No individually identifiable participant information is presented.

Competing interests

The authors should declare any competing interests according to the target journal's requirements.

Funding

No funding information was specified in the source dissertation. Insert the appropriate statement before submission.

Author Contribution

Dr Atkuri Sruthi: study conception, data collection, analysis and manuscript preparation. Dr D Pragati Rao: supervision, methodological guidance and critical review. These contributions should be confirmed by all authors before submission.

Data Availability

The underlying study data were collected as part of the dissertation. A journal-specific data-availability statement should be inserted according to institutional policy and the target journal's requirements.

References

1. Singh D, Agusti A, Anzueto A, Barnes PJ, Bourbeau J, Celli BR et al (2019) Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease: the GOLD science committee report 2019. Eur Respir J 53(5):1900164
2. Donaldson GC, Seemungal TAR, Bhowmik A, Wedzicha JA (2002) Relationship between exacerbation frequency and lung function decline in chronic obstructive pulmonary disease. Thorax 57(10):847–852
3. Donaldson GC, Seemungal TAR, Patel IS, Bhowmik A, Wilkinson TMA, Hurst JR et al (2005) Airway and systemic inflammation and decline in lung function in patients with COPD. Chest 128(4):1995–2004
4. Agustí A, Celli BR, Criner GJ, Halpin D, Anzueto A, Barnes P et al (2023) Global Initiative for Chronic Obstructive Lung Disease 2023 Report: GOLD Executive Summary. Eur Respir J. ;61(4)
5. de Zeeuw D, Parving HH, Henning RH (2006) Microalbuminuria as an early marker for cardiovascular disease. J Am Soc Nephrol 17(8):2100–2105
6. Shayo FK, Lutale J (2018) Albuminuria in patients with chronic obstructive pulmonary disease: a cross-sectional study in an African patient cohort. BMC Pulm Med 18(1):125

7. Pinto-Sietsma SJ, Mulder J, Janssen WM, Hillege HL, de Zeeuw D, de Jong PE (2000) Smoking is related to albuminuria and abnormal renal function in nondiabetic persons. Ann Intern Med 133(8):585–591
8. Sahay S, Prasad MK, Microalbuminuria COPD A Clinical and Physiological Association
9. Bulcun E, Ekici M, Ekici A, Kisa U (2013) Microalbuminuria in chronic obstructive pulmonary disease. COPD 10(2):186–192
10. Gupta KK, Kotwal M, Atam V, Usman K, Chaudhary SC, Kumar A (2020) Study of microalbuminuria in chronic obstructive pulmonary disease patients at tertiary care teaching hospital. J Family Med Prim Care 9(8):3916–3920
11. Casanova C, de Torres JP, Navarro J, Aguirre-Jaime A, Toledo P, Cordoba E et al (2010) Microalbuminuria and hypoxemia in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 182(8):1004–1010
12. Bartziokas K, Kyriakopoulos C, Dounousi E, Kostikas K (2023) Microalbuminuria on admission for acute exacerbation of COPD as a predictor of all-cause mortality and future exacerbations. Postgrad Med J 99(1169):189–197
13. Bozkus F, Dikmen N, Samur A (2017) Microalbuminuria in Subjects With COPD: Relationship to the New Version of Global Initiative for Chronic Obstructive Lung Disease Staging. Respir Care 62(3):307–314
14. Shashidhar RM, G AU (2020) Study of microalbuminuria and its correlation with severity of disease in patients with chronic obstructive pulmonary disease. Int J Adv Med 7(3):382–385
15. Banur A, Ajit E, Bondade K, Ayana K, Raikar PS, Angadi S (2024) A study on the utility of microalbuminuria as an indicator for the assessment of severity of chronic obstructive pulmonary disease and its co-morbidities. J Clin Sci Res 13(3):189–193
16. Laha S, Mohapatra A, Sarangi R, Sahoo JP, Subhankar S (2025) Urine Albumin-Creatinine Ratio (ACR) of Patients With Chronic Obstructive Pulmonary Disease (COPD): A Cross-Sectional Study. Cureus 17(6):e86974
17. Barkati Y, Mishra RS, Maqsood M, Chauhan A, Nirala P, Kumar A et al (2025) Urine microalbumin and albumin-creatinine ratio in COPD: Implications for perioperative and cardiovascular risk. IP Indian J Immunol Respir Med 10(3):146–152
18. Rakoti DC, Kusuma DPK, Dasari DL, Babu DKD, Kovi DSR, Ghantasala DMH (2024) Prevalence of Microalbuminuria in Chronic Obstructive Pulmonary Disease (COPD) and Its Correlation with Pulmonary Function: A Cross-Sectional Study. Afr J Biomed Res 27(3S):3831–3837
19. Sujay J, Gajanan G (2025) Clinical significance of microalbuminuria and hypoxemia in patients with chronic obstructive pulmonary disease. Indian J Health Sci Biomed Res KLEU 10(1):19–24
20. Gupta P, Kumar A, Chaurasia AK, Gupta A (2019) Prevalence and clinical significance of microalbuminuria and hypoxemia in patients with chronic obstructive pulmonary disease. Int J Adv Med 6(4):1299–1302

21. Khattri U, Singh L, Tandon R, Karki G, Choudhry N (2021) Study of microalbuminuria in COPD patients and its association with cardiac comorbidities. Eur Respir J 58:65