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# Original ARTICLE

## Assessment of Microalbuminuria and Its Relationship with Hypoxemia in Patients Of Chronic Obstructive Pulmonary Disease

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***ABSTRACT*:**
**Background:** Chronic obstructive pulmonary disease (COPD) is a common, preventable and treatable disease that is characterised by persistent respiratory symptoms and airflow limitation. Microalbuminuria could be a promising biomarker to identify patients with COPD at increased risk for poor cardiovascular outcomes. Hence; the present study was undertaken for assessing of microalbuminuria and its relationship with hypoxemia in patients of chronic obstructive pulmonary disease. **Materials & methods:** 100 patients of Chronic obstructive pulmonary disease diagnosed as per gold guidelines of COPD were included in the study. After taking proper history regarding hypertension, diabetes, fever, dysuria, any other co-morbid illness and smoking history (pack years), all the baseline parameters (like pulse, B.P, height, weight, BMI) shall be measured. Spirometry was recorded graphically and numerically. Microalbuminuria levels were compared between COPD cases and control groups by taking urine spot sample for analyzing UACR (urine albumin creatinine ratio) by strip method on CLINITEK urine analyser. An early morning urine sample will be preferred. Participants will be instructed to avoid heavy exercises 24 hrs before the test. All the results were analysed by SPSS software. **Results:** Microalbuminuria was found to be present in 57 percent of the COPD patients. Mean %predictive FEV1 and $Pao_2$ of the COPD patients with Microalbuminuria was found to be 31.60 and 51.48 respectively and Mean %predictive FEV1 and $Pao_2$ of the COPD patients without Microalbuminuria was found to 43.67 and 59.38 respectively. While comparing the mean % predictive FEV1 and $Pao_2$ in between COPD patients with and without Microalbuminuria, significant results were obtained. While assessing the correlation of FEV1 and Microalbuminuria among COPD patients, significant results were obtained. **Conclusion:** Microalbuminuria may be seen in patients with COPD, depending on the severity of disease and hypoxemia. The determination of microalbuminuria is simple, inexpensive, and non-invasive. As such, it could be a promising biomarker to identify patients with COPD at increased cardiovascular risk.
**Key words:** Microalbuminuria, Chronic obstructive pulmonary disease

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### INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common, preventable and treatable disease that is characterised by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases. It is progressive disease with increasing prevalence. It is a condition that progresses slowly and is associated with an inflammatory reaction and structural changes in small peripheral airways and/or destruction of lung parenchyma. COPD is currently the fourth leading cause of death in the world but is projected to be the 3rd leading cause of death by 2020. More than 3 million people died of COPD in 2012 accounting for 6% of all deaths globally. COPD burden is projected to increase in coming decades as there is high level of exposure to the risk factors and ageing of the population.[1- 3]

The disease is defined by Post-bronchodilator Forced Expiratory Volume in 1s (FEV1)/Forced Vital Capacity (FVC) <0.70. In asymptomatic individuals without any significant exposures to

tobacco or other noxious stimuli, screening spirometry is probably not indicated; whereas in those with symptoms or risk factors like >20 pack-years of smoking or recurrent chest infections, the diagnostic yield for COPD is relatively high and spirometry should be considered as a method for early case finding.[4-6]

Microalbuminuria could be a promising biomarker to identify patients with COPD at increased risk for poor cardiovascular outcomes. The presence of microalbuminuria is consistently associated with arterial stiffness, assessed by pulse wave velocity, and worse cardiovascular outcomes in patients.[5] Microalbuminuria is frequent in patients with COPD and was associated with hypoxemia independent of other cardiovascular risk factors. There are few studies that have reported a relationship between hypoxia and microalbuminuria. Studies at high altitude suggest that systemic hypoxia may cause an elevation in the urinary albumin excretion with increasing the renal capillary permeability despite unchanged tubular functions and albuminuria is strongly related with the degree of hypoxia. In vitro studies have also shown that cultured endothelial cells exposed to low oxygen concentrations become larger, and small intercellular gaps appear. These phenomenons are also reversible. Temporary proteinuria has been reported in patients with sleep apnea syndrome which regressed with oxygen therapy and the protein leakage was attributed to the increase in glomerular filtration rate resulting from tissue hypoxia.[7, 8] Hence; the present study was undertaken for assessing of microalbuminuria and its relationship with hypoxemia in patients of chronic obstructive pulmonary disease.

## MATERIALS & METHODS

The present Study was carried out in the Department of Pulmonary Medicine, Guru Gobind Singh Medical College & Hospital, Faridkot, Punjab on COPD Patients. Detailed history was recorded after taking written and informed consent and systemic examination was also carried out as per proforma attached. 100 patients of Chronic obstructive pulmonary disease diagnosed as per gold guidelines of COPD were included in the study. Those patients with Post-bronchodilator Forced Expiratory Volume in 1s ($FEV_1$)/Forced Vital Capacity (FVC) <0.70 were included in the study. As per guidelines, the patients with symptoms or risk factors like >20 pack-years of smoking or recurrent chest infections, the diagnostic yield for COPD is quite high.

### Inclusion Criteria

- Those patients diagnosed as per gold guidelines of COPD.
- COPD patients of both sexes who are willing and are able to give valid consent as study cases.
- Participants with chest X-ray changes of COPD like bilateral hyperinflation, tubular heart, flattened diaphragm, emphysematous bullae, etc.

### Exclusion Criteria

- Previous History of renal disease or presence of macroalbuminuria
- Previous History of Cardiovascular disease
- Diabetes
- Uncontrolled co-morbidities such as malignancy, HIV
- Patients less than 14 years of age
- Pregnant females
- Patients with UTI

After taking proper history regarding hypertension, diabetes, fever, dysuria, any other co-morbid illness and smoking history (pack years), all the baseline parameters (like pulse, B.P, height, weight, BMI) shall be measured.

After that Urine complete examination, **UACR** (urinary albumin to creatinine ratio), ABG(arterial blood gases), spirometry, BODE index* (body mass index, airflow obstruction, dyspnea, exercise performance) were recorded in 100 COPD patients. Hypoxemia was assessed by sending ABG samples. Patients were divided into mild, moderate and severe on the basis of following grades:- Mild : PaO2 – 60 to 79 mm Hg, Moderate : PaO2 – 40 to 59 mm Hg and Severe : PaO2 - <40 mm Hg. For dyspnea, MMRC grading of dyspnea was followed to analyse the severity of symptoms of the patient. Spirometry was recorded graphically and numerically. Microalbuminuria levels were compared between COPD cases and control groups by taking urine spot sample for analyzing UACR (urine albumin creatinine ratio) by strip method on **CLINITEK urine analyser**. An early morning urine sample will be preferred. Participants will be instructed to avoid heavy exercises 24 hrs before the test. All the results were analysed by SPSS software.

## RESULTS

29 percent of the patients belonged to the age group of 51 to 60 years, while 27 percent of the patients belonged to the age group of 61 to 70 years. Mean age of the patients was found to be 57.66 years. 93 percent of the patients were males while the remaining 7 percent were females. Microalbuminuria was found to be present in 57 percent of the COPD patients.

Table 1: Frequency of micro albuminuria among COPD patients

| Micro albuminuria | Number of patients | Percentage of patients |
|---|---|---|
| **Present** | 57 | 57 |
| **Absent** | 43 | 43 |
| **Total** | 100 | 100 |

Breathlessness was the main chief complaint found to be present in 100 percent of the patients. Cough and fever were found to be present in 69 percent and 27 percent of the patients. Chest pain was found to be present in 11 percent of the patients. Mean %predictive FEV1 and $Pao_2$ of the COPD patients with Microalbuminuria was found to be 31.60 and 51.48 respectively and Mean %predictive FEV1 and $Pao_2$ of the COPD patients without Microalbuminuria was found to 43.67 and 59.38 respectively.

While comparing the mean % predictive FEV1 and $Pao_2$ in between COPD patients with and without Microalbuminuria, significant results were obtained. While assessing the correlation of FEV1 and Microalbuminuria among COPD patients, significant results were obtained.

## DISCUSSION

Cardiovascular disease is the major cause of mortality in COPD. Microalbuminuria is a risk factor for cardiovascular diseases and it is a powerful predictor for cardiovascular diseases and mortality in adults. The principal cause of hypoxemia in patients with COPD is ventilation/perfusion (V/Q) abnormality resulting from progressive airflow limitation and emphysematous

destruction of the pulmonary capillary bed. Alveolar hypoxia is an important factor leading to the development of pulmonary hypertension in patients with COPD.

Table 2: Comparison between COPD patients with and without micro albuminuria

| Parameter | COPD with micro albuminuria | | COPD without micro albuminuria | | p- value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| **Age (years)** | 55.88 | 12.24 | 60.02 | 14.98 | 0.132 (MWUT) |
| **BMI ($Kg/m^2$)** | 19.49 | 3.65 | 20.17 | 3.78 | 0.374 (ISTT) |
| **FEV1 (%)** | 31.60 | 12.60 | 43.67 | 16.68 | <0.05 (MWUT) |
| **$PaO_2$** | 51.48 | 16.48 | 59.38 | 16.41 | 0.019 (ISTT) |

Table 3: Association between FEV1 and micro albuminuria among COPD patients

| FEV1 | COPD with micro albuminuria | COPD without micro albuminuria | p- value |
|---|---|---|---|
| **≤30%** | 31 | 12 | 0.000 |
| **31 to 50%** | 23 | 14 | |
| **51 to 80%** | 3 | 17 | |
| **More than 80%** | - | - | |
| **Total** | 100 | 100 | |

Table 4: Association between $PaO_2$ and micro albuminuria among COPD patients

| $PaO^2$ | COPD with micro albuminuria | COPD without micro albuminuria | p- value |
|---|---|---|---|
| **60 to 79 (Mild)** | 11 | 19 | 0.018 |
| **40 to 59 (Moderate)** | 27 | 12 | |
| **Less than 40 (severe)** | 15 | 8 | |
| **Total** | 100 | 100 | |

Hypoxia also appears to lead to the development of endothelial dysfunction, characterized by the loss of the physiological balance between vasodilation and vasoconstriction. In patients with severe COPD, abnormality in the endothelium-dependent pulmonary artery relaxation was observed. The epidemiology of microalbuminuria reveals a close relationship between systemic endothelial dysfunction and vascular disease, also implicating glomerular endothelial dysfunction in microalbuminuria.[9, 10] Hence; under the light of above mentioned data, the present study was undertaken for assessing frequency of microalbuminuria and it correlation with hypoxemia in COPD patients.

The present study was undertaken in the department of Chest and TB of the medical institute. A total of 100 COPD patients were analysed. In a previous study conducted by Gupta P et al, authors reported that 29.23% patients had Microalbuminuria. A recent study by Agrawal et al in 2017 observes prevalence of Microalbuminuria in COPD patients to be 46%. In study of Bulcon et al, in 2013 found that prevalence of Microalbuminuria to be 39%. Mehmood and Sofi et al, in 2015, were also found that MAB was more frequent in COPD patients compared to smokers without obstruction (20.6% vs. 7.4%, respectively). A study done by Sujay et al, in 2017 total of 46 patients (30%) out of 150 stable COPD patients had Microalbuminuria.[5, 11- 14]

Three significant studies have described the prevalence of MAB in patients with COPD. In the first study, the level of MAB was measured in 25 patients during exacerbations. It was detected in 56% of them at admission and in 28% at discharge, compared with 4% in control subjects. MAB was associated with hypoxemia but not with the FEV1. In the second study, the patients were evaluated during exacerbations and the authors reported an association between MAB and the presence of respiratory failure. However, spirometric measurements were not performed. In the third study, 33 patients with stable COPD, 26 patients with exacerbation, and 16 healthy subjects were assessed. The level of MAB was significantly increased only in the group with exacerbation. However, in the stable COPD group, the level of MAB was double that of the control group. These results suggested that MAB is frequent in COPD and that it appears to increase during exacerbations.[15- 17]

Mean %predictive FEV1 and $Pao_2$ of the COPD patients with Microalbuminuria was found to be 31.60 and 51.48 respectively and Mean %predictive FEV1 and $Pao_2$ of the COPD patients without Microalbuminuria was found to 43.67 and 59.38 respectively. While comparing the mean % predictive FEV1 and $Pao_2$ in between COPD patients with and without Microalbuminuria, significant results were obtained. Therefore; it can be inferred that in COPD patients, significant reduction in %predictive FEV1 and $Pao_2$ occurs during Microalbuminuria. The potential mechanism could be an increase in renal capillary permeability due to inflammatory mediators, such as tumor necrosis factor-a, interleukins, and free oxygen radicals. In vitro studies have reported a relation between the glomerular size and intercellular gaps and decreases in arterial $PaO_2$.[17, 18]

While assessing the correlation of $PaO_2$ and micro albuminuria among COPD patients, significant results were obtained. It was inferred that significantly higher prevalence of MAB was seen in patients with lower $Pao_2$ values. Our results were in concordance with the results obtained by previous authors who also reported similar findings in their respective studies. In a study conducted by Gupta et al, authors showed that microalbuminuria was significantly more in COPD patients having PaO2 below 70 mmHg as compared to COPD patients having PaO2 above 70 mmHg (74% vs. 26%, respectively, p <0.0001), which indicated COPD patients with Microalbuminuria were more hypoxemic.[14]

A similar result was also seen in study by Sujay et al, Microalbuminuria was significantly more in COPD patients having PaO2 below 70 mmHg as compared to COPD patients having PaO2 above 70 mm Hg (100% vs. 7.14%, respectively, p <0.0001). In the study of Mehmood and Sofi et al, and Agrawal et al, COPD patients having microalbuminuria were more hypoxic than those of COPD patients without microalbuminuria and it was inversely related to PaO2.[5, 12 13]

Kömürcüoğlu A et al, in a study, determined the presence of microalbuminuria in patients with chronic obstructive pulmonary disease (COPD) in whom no proteinuria by conventional methods. Twenty-five cases with COPD who had been hospitalized because of an acute exacerbation and 25 healthy age and sex matched volunteers were included in the study. Microalbuminuria was detected in 14 (56%) subjects at admission and in 7 (28%) subjects at discharge in the COPD

group and in 1 (4%) subject in the control group. There were statistically significant differences among these groups (admission-control $p < 0.001$, discharge-control $p = 0.023$, admission-discharge $p = 0.016$). In COPD group, mean a/c ratio was 3.9 +/- 3.8 at the time of admission, 1.7 +/- 1.9 at discharge and 0.5 +/- 0.5 mg/mmol in the control group. There were statistically significant differences among these groups (admission-control $p < 0.001$, discharge-control $p = 0.029$, admission-discharge $p = 0.002$). In the COPD group there were negative correlation between the microalbuminuria values at admission and arterial pO2 and oxygen saturation ($p = 0.031$, $r = -0.433$ and $p = 0.002$, $r = -0.596$ respectively). There were no relation between the microalbuminuria values and age, arterial pH, pCO2, FEV1 percent predicted, FVC percent predicted and FEV1/FVC. There were no statistically significant differences between the subjects with or without microalbuminuria according to the median survival time. In a quite large number of patients with COPD in whom no proteinuria were determined by conventional methods, especially at the time of exacerbation, microalbuminuria could be seen. Microalbuminuria was related with hypoxemia but has no predictive role on mortality.[18]

## CONCLUSION

Microalbuminuria may be seen in patients with COPD, depending on the severity of disease and hypoxemia. The determination of microalbuminuria is simple, inexpensive, and non-invasive. As such, it could be a promising biomarker to identify patients with COPD at increased cardiovascular risk.

## REFERENCES


1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for the Diagnosis, Management and Prevention of COPD; 2014. Available from:https://goldcopd.org/wpcontent/uploads/ 2018/11/GOLD-2019-v1.7-FINAL-14Nov2018-WMS.pdf
2. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med. 2006;3(11):e442.
3. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: A systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012; 380(9859):2095-128.
4. Paul AS, Agarwal R (2017) 'Respiratory Failure', in Jindal SK, (2nd ed.) Text book of pulmonary and critical care medicine. New Delhi: JBMP, pp.1479-87.
5. Sujay J, Gajanan GS. Clinical significance of microalbuminuria and hypoxemia in patients with chronic obstructive pulmonary disease. Indian J Health Sci Biomed Res.2017;10(1):19.
6. Eastwood PR, Naughton MT, Calverley P. How to write research papers and grants: 2011 Asian Pacific Society for Respirology Annual Scientific Meeting Postgraduate Session. Respirology. 2012;17(5):792-801.
7. Jones PW. Health status measurement in chronic obstructive pulmonary disease. Thorax. 2001;56(11):880-7.
8. Jones PW, Harding G, Berry P, Wiklund I, Chen WH, Kline Leidy N. Development and first validation of the COPD Assessment Test. EurRespir J. 2009;34(3):648-54.
9. van Eerd EA, van der Meer RM, van Schayck OC, Kotz D. Smoking cessation for people with chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2016;(8):CD010744.
10. Frazer K, Callinan JE, McHugh J, van Baarsel S, Clarke A, Doherty K, et al. Legislative smoking bans for reducing harms from second hand smoke exposure, smoking prevalence and tobacco consumption. Cochrane Database Syst Rev. 2016;2:Cd005992.
11. Bulcun E, Ekici M, Ekici A, Kisa U. Microalbuminuria in chronic obstructive pulmonary disease. COPD. J Chronic Obstructive Pulmonary Dis. 2013;10(2):186-92.
12. Agrawal A, Garg R, Sahu D, Kumar M. Study the association of chronic obstructive pulmonary disease with early endothelial dysfunction and its impact on cardiovascular system by estimating urinary albumin creatinine ratio. Lung India: official organ of Indian Chest Society. 2017;34(2):138-143.
13. Mehmood K, Sofi FA. Microalbuminuria and hypoxemia in patients with COPD. J Pulm Respir Med. 2015;5(4):12-8.
14. Gupta P, Kumar A, Chaurasia AK, Gupta A. Prevalence and clinical significance of microalbuminuria and hypoxemia in patients with chronic obstructive pulmonary disease. Int J Adv Med. 2019;6:1299-302.
15. Komurcuoglu A, Kalenci S, Kalenci D, Komurcuoglu B, Tibet G. Microalbuminuria in chronic obstructive pulmonary disease. Monaldi archives for chest disease. 2003;59(4):269-72.
16. Wachtell K, Ibsen H, Olsen MH, Borch-Johnsen K, Lindholm LH, Mogensen CE, et al. Albuminuria and cardiovascular risk in hypertensive patients with left ventricular hypertrophy: the LIFE Study. Ann Intern Med. 2003;139:901–6.
17. Ibsen H, Olsen MH, Wachtell K, Borch-Johnsen K, Lindholm LH, Mogensen CE, et al. Reduction in albuminuria translates to reduction in cardiovascular events in hypertensive patients. Hypertension. 2005;45:198–202.
18. Yan SF, Ogawa S, Stern DM, Pinsky DJ. Hypoxia-induced modulation of endothelial cell properties: regulation of barrier function and expression of interleukin-6. Kidney Int. 1997;51:419–425.