Studying Microalbuminuria In Patients With COPD In Relation To The New Version Of Global Initiative For Chronic Obstructive Lung Disease

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Abstract

Background: Microalbuminuria, used as a marker of endothelial dysfunction, is a predictor of mortality and of cardiovascular events. Microalbuminuria (MAB) in chronic obstructive lung disease (COPD) is attributed to generalized endothelial dysfunction as a result of systemic inflammation, which could be a significant marker for early cardiovascular abnormality. **Objectives:** Study the relationship between microalbuminuria and disease class in subjects with COPD classified according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2018 "A, B, C, D" classification in absence of hypertension and diabetes ,and to Evaluate the clinical features that may predict cardiovascular risk in subjects with COPD. **Setting:** Chest Department and outpatient clinic, Beni-Suef University Hospital. **Methods:** Prospective Study included 60 patients who were diagnosed as COPD by Pulmonary function tests. All patients were subjected to clinical examination, Chest x ray, spirometry and Urinary albumin/creatinine ratio. **Results:** Urinary albumin/creatinine ratios were significantly higher in subjects who have more symptoms and high future risk (categories C, D) than in those with fewer symptoms and low future risk (categories A, B). A Significant differences were noted when the subjects were grouped based on PaO_2 (<65mmHg versus >65mmHg), $PaCO_2$ (<41mmHg versus >41mmHg), arterial oxygen saturation (<92% versus >92%), FEV1 (median split <60% versus >60%). There was a statistically significant strong negative correlation between the alb/creat ratio and FEV1% (r=-0.937, p=0.000), PaO_2 (r=-0.929, p=0.000) and SaO_2(r=-0.934,p=0.000). There was a statistically significant strong positive correlation between the alb/creat ratio and Severity of COPD Gold categories (r=0.931, p=0.000), $PaCO_2$ (r=0.930, p=0.000) and number of hospital admissions last year (r=0.946, p=0.000). There was a highly significant association between high level alb/creat ratio and the presence of pulmonary hypertension (P <0.001). **Conclusions**: There is a strong correlation between microalbuminuria and the new version of GOLD A, B, C and D classification. Because the diagnosis of microalbuminuria is simple, inexpensive, and noninvasive, it can be evaluated

routinely in COPD cases, especially those with many symptoms who are at higher risk, to early predict cardiovascular morbidity and mortality.

Keywords: Copd Severity, Microalbuminuria.

1. Introduction:

COPD is an important cause of morbidity and mortality throughout the world. The mortality rate of COPD is increasing (1).

COPD is a heterogenic disease with both pulmonary and extrapulmonary symptoms characterized by long-term poor air flow. In particular, cardiovascular disease remains one of the leading causes of mortality and morbidity in subjects with COPD, independent of the well-recognized risk factors, including age, sex, and smoking status (2).

A consistent association been shown between the presence of microalbuminuria and poor cardiovascular outcomes in subjects with hypertension and diabetes mellitus and, most importantly, in the general population (4).

Studies conducted on the epidemiology of microalbuminuria have reported a close association between vascular disease and systemic endothelial dysfunction and have also suggested glomerular endothelial dysfunction in microalbuminuria (5).

In one study, lower FEV_1 and severity of emphysema have been shown to be correlated with endothelial dysfunction (6).

It has been demonstrated that microalbuminuria increases in worsening periods of COPD, suggesting an association with increased glomerular filtration, resulting in protein leakage because of increased hypoxemia during COPD episode (7).

However, to our knowledge, there is few studies investigating the association of microalbuminuria with COPD assessment tool categories and the risk of exacerbation based on the new version of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) (8).

2. Patients and Methods:

This was a Cross sectional study performed in Beni-Suef university hospital from December 2018 to November 2019 involved 60 patients complaining of dyspnea and diagnosed as Chronic Obstructive Lung Disease according to GOLD 2018,informed consents of participation were obtained.

2.1 Inclusion criteria:

Patients with Non exacerbating COPD between the age of 40 and 60 years old based on plain chest x-ray (PA) and pulmonary function.

2.2 Exclusion criteria:

1. Patients with known renal diseases.

2. Patients with a history of the presence of macroalbuminuria (urinary albumin/creatinine ratio >300 mg/g) or previously diagnosed with diabetes mellitus.

3. Patients previously diagnosed with other respiratory diseases, including obstructive sleep apnea, asthma.

4. Patients with hypertension.

2.3 All patients were subjected to:

A. Complete history taking.

- Age, occupation, drugs taken and history of smoking or Biomass.

- Presenting symptoms (onset, course and duration of the symptoms) especially: cough, breathlessness, and previous admission due to chest condition.

2. Clinical examination

General and Local examination:

3. Laboratory investigations

- CBC, Urea, Creatinine, ESR .
  Urinary Albumin /Creatinine Ratio.

- **Arterial blood gases.**

4. **Radiological examination**

- Plain CxR (PA).

5. **Spirometric testing (Flow volume loop)**

6. **Echocardiography:** for assessment of cardiac condition with special concern to left Atrium measurement, Ejection Fraction and estimation of pulmonary hypertension by estimation of pulmonary artery systolic pressure (PASP).

The studied population were divided into 4 equal groups, 15(25%) in GOLD A, 15 (25%) in GOLD B, 15(25%) in GOLD C and 15(25%) in GOLD D.

Statistical methodology

Data were described in terms of mean ± standard deviation (± SD), median and range, or frequencies (number of cases) and percentages when appropriate. Data was explored for normality using kolomogrove test. Comparison of numerical variables between the study groups was done using independent sample t test. Mann-whitney test for the non-normally distributed data. ANOVA test was used to compare between cases. For comparing categorical data, Chi-square (χ^2) test was performed. *p* values less than 0.05 was considered statistically significant.

Analysis of data was performed using SPSS v. 25 (Statistical Package for Social science) for Windows.

3. Results:

The studied population mean age was 54.72 y and 85% of them were males (Table1).

A significant difference was found between the categories in terms of albumin/creatinine ratio based on the new version of GOLD staging (A-D class) (P < 0.001)

Table (1): Baseline characteristics of the studied patients:

Characteristics	All patients no=60(%)
<u>Sex</u> Males Females	51(85%) 9(15%)
<u>Age:</u> Mean±SD	54.72±3.1

Table (2): Classifications of the studied cases regarding their pulmonary function tests and labs:

Classifications	Number (60)	Percent
<u>FEV1 median split</u> less than 60 more than or equal 60	35 25	58.3 41.7
<u>$PaCO_2$ median split</u> Less than or equal 41 More than 41	30 30	50.0 50.0
<u>PaO_2 median split</u> less than or equal 65 more than 65	16 44	26.7 73.3
<u>SaO_2 median split</u> less than or equal 92 more than 92	20 40	33.3 66.7

Table (3): Comparison between different grades of GOLD score regarding different symptomatic (mMrc), laboratory and cardiac parameters:

Parameters		N	Mean	SD	P-value
Alb/creat	Grade A	15	72.2[a]	17.8	
	Grade B	15	146.1[b]	17.8	<0.001**
	Grade C	15	257.7[c]	27.6	

	Grade D	15	426.1[d]	86.2	
ESR	Grade A	15	14.8[a]	6.5	<0.001**
	Grade B	15	32.1[b]	5.2	
	Grade C	15	50.9[c]	7.4	
	Grade D	15	88.8[d]	5.4	
EF	Grade A	15	66.4[a]	1.06	<0.001**
	Grade B	15	67.4[a]	1.5	
	Grade C	15	65.2[a]	1.3	
	Grade D	15	47.3[b]	3.7	
Lt atrium diameter	Grade A	15	3.6[a]	0.1	<0.001**
	Grade B	15	3.6[a]	0.09	
	Grade C	15	3.6[a]	0.14	
	Grade D	15	4.5[b]	0.32	
Hosp admission/last year	Grade A	15	0[a]	0	<0.001**
	Grade B	15	0[a]	0	
	Grade C	15	1.8[b]	0.4	
	Grade D	15	5.3[c]	1.4	
mMrc	Grade A	15	00[a]	0	<0.001**
	Grade B	15	1[b]	0	
	Grade C	15	2.47[c]	0.516	
	Grade D	15	5.73[d]	0.594	

Table (4): correlation between albumin /creatinine ratio and different factors:

Parameters		Alb/creat
Severity of COPD(non-parametric correlation)	R	.931**
	P-value	.000
FEV1/FVC	R	-.690**
	P-value	.000
FEV1	R	-.937**
	P-value	.000
FVC	R	-.915**
	P-value	.000

ESR	R	.954[**]
	P-value	.000
$PaCO_2$	R	.930[**]
	P-value	.000
PaO_2	R	-.929[**]
	P-value	.000
SaO_2	R	-.934[**]
	P-value	.000
EF	R	-.870[**]
	P-value	.000
Lt atrium diameter	R	.845[**]
	P-value	.000
mMrc	R	.816[**]
	P-value	.000
Hosp admission/last year	R	.946[**]
	P-value	.000

4. Discussion:

In the current study, the severity of airflow limitation varied from mild to very severe. The mean tested FEV_1/predicted % was 54.1±22.6 %. The mean PaO_2 was 71.6±11.9, mean $PaCO_2$ was 48.6±13.3, and mean SaO_2 was 91.4±7.

Similarly, **Ko¨mu¨rcuog˘lu et al., (2003)** studied a total of 150 patients diagnosed with COPD were enrolled in the study. There were 145 male patients and five female patients. Their mean age was 59.67 years; there were 38 (25%) GOLD Stage I, 32 (21%) Stage II, 30 (20%) stage III and 50 (34%) stage IV COPD cases. (9)

In the current study, COPD subject subgroups were compared in terms of urinary albumin/creatinine ratio based on GOLD stages. Urinary albumin/creatinine ratio showed a significant difference, depending on the GOLD categories of the patients (A–D class) (P <.001) with a statistically significant strong positive correlation between the alb/creat ratio and Severity of COPD Gold categories, (r=0.931, p=0.000).

Similarly, **Ko¨mu¨rcuog˘lu et al., (2003)** stated that majority of COPD patients with MAB had GOLD stage of III (33.3%) and Stage IV (56.0%), and this association was statistically significant; $P = 0.0001$. (9).

In this study, concerning hospital admission and exacerbation history showed that there were 50% of the studied cases were admitted to the hospital during the last year and the meantime of hospital admission 3.6 ± 2 times/ last year and 25% were admitted to the ICU. There were a statistically significant strong positive correlation between mMrc ($r=0.816$, $p=0.000$) and number of hospital admission/ last year($r=0.946$, $p=0.000$) with the degree of albuminuria. **(Tab.4),** similarly **Mehmood et al., (2015)** noted that majority of COPD patients with MAB had mMRC dyspnea Grade III-IV (32.5%).(10).

In this Study , the urinary albumin/creatinine ratio values showed a highly significant difference between of subjects when grouped based on median split PaO_2 levels (<65 mmHg vs> 65 mmHg), median split $PaCO_2$ levels (<41mmHg vs >41mmHg) (P-value<0.001 for both). There was also a statistically significant strong negative correlation between it and both PaO_2 ($r=-0.929$, $p=0.000$) and SaO_2 ($r=-0.934$, $p=0.000$), while there was a statistically significant strong positive correlation between it and $PaCO_2$, ($r=0.930$, $p=0.000$). **(Tab.4).**

Also, **Ko¨mu¨rcuog˘lu et al; (2003)** noted a negative relationship between microalbuminuria identified in subjects with COPD and levels of PaO_2 and arterial oxygen saturation, however they didn't find a significant correlation between microalbuminuria and levels of pH and $PaCO_2$.(9)

In this study, when we analyzed the pulmonary function tests, the urinary albumin/creatinine ratio values were found to be significantly (P-value<0.001) higher in patients with FEV_1 less than 60% percent of predicted when the subjects were grouped based on FEV_1 median split 60% percent of predicted, in addition, there was a statistically significant strong negative correlation between the alb/creat ratio and FEV_1 values ($r=-0.937$, $p=0.000$).

In contrast, **Ibsen H et al; (2005)** found that microalbuminuria was correlated with hypoxemia but not with the FEV_1 (5). Also **Casanova et al; (2010)** didn't find such correlation. (11).

In this Study, the presence of pulmonary hypertension was

significantly (P-value<0.001) more in patients with FEV_1 below 60 percent of predicted. This was also noted (P-value<0.001) in patients with PaO_2 below 65 mmHg. In patients with pulmonary hypertension, there was a highly significant association of high level of albumin/creatinine ratio (341.9±106 versus109±41.4) and presence of pulmonary hypertension (P-value<0.001). **(Fig.3)**

In a previous study by **Vinicio A et al**; (2016) of two independent cohorts of pulmonary arterial hypertension (PAH) patients were recruited from Vanderbilt University and Stanford Hospital and Clinics showed that there was a Low-grade albuminuria prevalent in patients with PAH.

5. Conclusion and Recommendations

The results of our study indicate a strong relation between microalbuminuria and the new Version of GOLD stages, presence of hypoxemia, low FEV_1 values (<60 %pred.), hypercapnia and presence of pulmonary hypertension. Because the diagnosis of microalbuminuria is simple, inexpensive and noninvasive, it can be evaluated routinely in COPD cases, especially in those with many symptoms who are at high risk to detect patients at high risk of CVS and cardiac

accidents and start their treatment early specially in patients with hypoxemia and hypercapnia and lower FEV_1.

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