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Original article

Evaluation of Serum Uric Acid in COPD Patients

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Abstract

Background: Airway inflammation and imbalance between oxidant-anti oxidant mechanisms are postulated to play a major role in the pathogenesis of COPD. The work aimed to evaluate serum uric acid among COPD patients. **Patients and methods**: A retrospective cross-sectional study included 50 COPD patients, who attended Benha University Hospital from March 2022 to November 2023. All patients were subjected to the following: written consent from the patient, full history and clinical examination, ABG, CXR (P-A), pulmonary function tests, measuring serum creatinine and urea, measuring serum uric acid by enzymatic colorimetric assay in a fully automated analyzer. **Results:** There was a highly significant negative correlation between patients' serum uric acid levels and FEV1.There was a highly significant negative correlation between patients' serum uric acid levels and FEV1/ FVC. There was no significant correlation between both urea, creatinine and COPD severity. **Conclusion:** uric acid could be used as a chemical biomarker in predicting COPD severity and staging.

Keywords: COPD, uric acid, severity

Introduction

COPD is a disease characterized by irreversible obstruction of the airways with a continuous reduction in airflow secondary to an inflammatory response of the lungs to inhalation of noxious particles or toxic gases (**1)**. COPD is a prevalent illness all over the world, and COPD exacerbations and deaths have a considerable load on the community. About 65 million people are COPD, and this adds 5% to mortality in the world (**2)**.

Serum uric acid results from purine metabolism, and constitutes a predominant, extracellular antioxidant present in the respiratory system. As the respiratory tract is exposed to high levels of oxidative stress from cigarette smoking, biomass fuel, and industrial pollution, antioxidants like UA, ascorbic acid, α-tocopherol, and ferritin in the epithelium provide a very protective defense against these injurious substances (**3).**

High uric acid level has also been associated with different diseases of the respiratory system such as elevated pulmonary arterial pressure and sleep apnea **(4)**. Hyper uricemia could be both protective as well as detrimental COPD and its exacerbations (**5)**.

Subjects and methods:

This retrospective cross-sectional study included 50 COPD patients who attended the Chest Department in Benha University Hospital from the 3/2022- 11/2023 period. Inclusion criteria included patients diagnosed with COPD. Exclusion criteria included patients with renal failure (defined as serum creatinine higher than 1.5 mg/dl), hepatic disease, congestive heart failure, diabetes mellitus, or thyroid dysfunction, or who used systemic corticosteroids, diuretics, or cytotoxic drugs. All patients were subjected to the following: -1. Written consent from the patient. 2. Full history taking and clinical examination. 3. ABG. 4. Chest X-ray (P-A) 5. Pulmonary function tests. 6. Measuring serum uric acid level by enzymatic colorimetric assay in the fully automated analyzer.

Ethical committee approval number: RC 2-12-2023

Statistical analysis:

The statistical package for the social sciences (SPSS) 22.0 for Windows was used to code, enter, analyze, and display the gathered data in appropriate tables and graphs (SPSS Inc., Chicago, IL, USA). Qualitative data were summarized using numbers and percentages. The normality of distribution for the quantitative data was tested using Shapiro Wilks test assuming normality at P>0.05. The data collected were summarized in terms of median and interquartile range (IQR) as appropriate for nonparametric data and mean & standard deviation as appropriate for parametric data. The statistical significance of the difference between the studied groups was evaluated using Mann Whitney test for comparison between 2 groups as appropriate for nonparametric data and the student t-test as appropriate for parametric data. Inter-gr○up comparison of categorical data was performed by using the chi-square test (X2-value). Spearman correlation and linear and Logistic regression were done. **(6)**

Results:

Eighty-four percentage of the studied patients were males. The mean ±SD serum uric acid level of the studied patients was 6.10±2.20 mg/ dl. The median (IQR) serum urea and creatinine level of the studied patients were 45 (39.7-52.5) and 0.90 (0.70-1.20) mg/ dl respectively. The mean ±SD FEV1 of the studied patients was 27.2±6.04. The median (IQR) FVC and FEV1/FVC of the studied patients were 46.0(41.0-49.2) and 55.0(44.7-63.2) respectively. Sixty-two percentage of the patients studied were COPD stage 4 according to GOLD classification. There was no statistically significant difference between patients GOLD stage 3 and 4 according to their age and sex (p>0.05). Serum uric acid level was significantly higher among patients GOLD stage 4 (mean ± SD=4.86±1.46 mg/dl) than GOLD stage 3 (mean ±SD=6.86±2.24 mg/dl) (p=.001). There was no statistically significant difference between patients GOLD stage 3 and 4 according to their

serum urea and creatinine levels (p>0.05) (Table 1). There was a highly significant negative correlation between patients' serum uric acid level and FEV1 (r= -.541& p =.000). There was a highly significant negative correlation between patients' serum uric acid level and FEV1/ FVC (r= -.481& p =.000). There was no significant correlation between patients' serum uric acid level and FVC (p>.05). There was no significant correlation between patients' serum urea and creatinine levels and FEV1, FVC and FEV1/FVC (p>.05) (Table 2). Figure 1. The scatter diagram shows a negative linear correlation between patients' serum uric acid level and FEV1 and linear regression correlation coefficient (R2). Figure 2. The scatter diagram shows a negative linear correlation between patients' serum uric acid level and FEV1/FVC and linear regression correlation coefficient (R2). A simple linear regression model shows that serum uric acid was a highly significant predictor of the studied patients' FEV1 (p=.000) while serum urea and creatinine levels were non-significant predictors of the studied patients' FEV1 (p>.05) (Table 3). A simple linear regression model shows that serum uric acid was a highly significant predictor of the studied patients' FEV1/FVC (p=.000) while serum urea and creatinine levels were non-significant predictors of the studied patients' FVC (p> .05) (Table 4). In a multivariable logistic regression model, serum uric acid was a highly significant predictor of the studied patient's GOLD stage (p=.004) while serum urea and creatinine levels were non-significant predictors of the studied patient's GOLD stage (p>.05) (Table 5).

Table1. Differences between the studied patients according to their characteristics and laboratory investigations

Variable		**GOLD 3**	**GOLD 4**	**Test of significance**	**P value**
N.=50		**N.=19**	**N.=31**		
Age (years) Mean ±SD		66.5±6.31	66.9±7.48	**St.t test**= 0.199	0.843
Sex	**Male**	18 (94.7%)	24 (77.4%)	**X^2** =2.62	0.10
	Female	1 (5.3%)	7 (22.6%)		
Uric acid (mg/dl) mean ±SD		4.86±1.46	6.86±2.24	**St.t test**=3.45	**0.001 (HS)**
		Median (IQR)	**Median (IQR)**	**Zmann Whitney**	**P value**
Urea (mg/dl)		45 (39-50)	45 (40-56)	0.771	0.44
Creatinine(mg/dl)		0.90 (0.7-1.2)	0.90 (0.70-1.2)	0.141	0.88

X^2: Chi-square test; HS: highly significant p< 0.001

Table 2. Spearman Correlation between PFTs and laboratory investigations

Variable	FEV1	FVC	FEV1/FVC
Uric acid (mg/dl)			
Correlation Coefficient	**-.541**	-.080	**-.481**
P value	**.000 (HS)**	.582	**0.01 (HS)**
Urea (mg/dl)			
Correlation Coefficient	-.213	-.200	.019
P value	.138	.164	.896
Creatinine (mg/dl)			
Correlation Coefficient	-.024	.051	-.079
P value	.871	.723	.587

HS: highly significant p< 0.01

Table 3. Simple linear regression between FEV1 classification and laboratory investigations of the studied patients

	B	CI	P value
Uric acid (mg/dl)	-1.36	-2.05- -.672	**0.01 (HS)**
Urea (mg/dl)	-.144	-.305 -.017	.07
Creatinine (mg/dl)	-.04	-5.01-4.92	0.98

HS: highly significant p <0.01; CI: Confidence Interval.

Table 4. Simple linear regression between FEV1/FVC classification and laboratory investigations of the studied patients

	EXP B	CI	P value
Uric acid (mg/dl)	-2.95	-4.37 - -1.53	**.000 (HS)**
Urea (mg/dl)	-.07	-.419 -.273	.67
Creatinine (mg/dl)	-.938	-11.2-9.40	.56

HS: highly significant p<.01; CI: Confidence Interval

Table 5. Multivariable logistic regression between PFTs GOLD classification and laboratory investigations of the patients studied

	EXP B	CI	P value
Uric acid (mg/dl)	1.77	1.20-2.60	**.004 (HS)**
Urea (mg/dl)	1.04	0.97-1.12	.184
Creatinine (mg/dl)	.932	.152-5.73	.940

HS: highly significant p<.01; CI: Confidence Interval

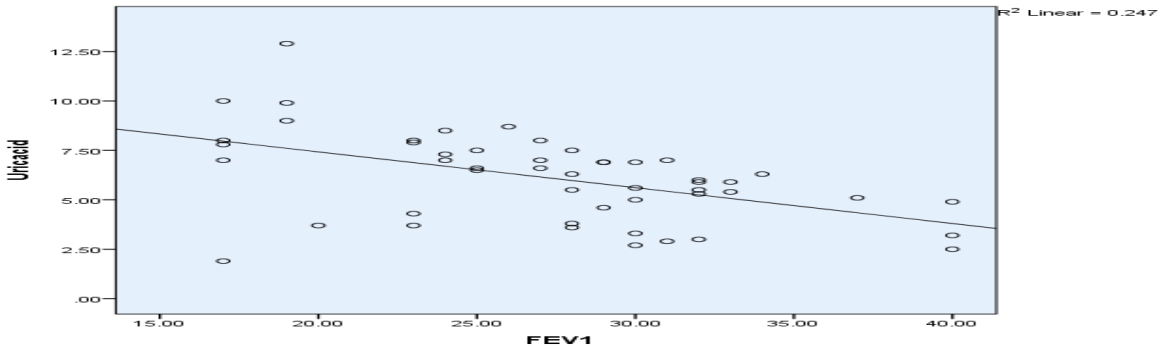

Figure 1. The scatter diagram shows a negative linear correlation between patients' serum uric acid level and FEV1 and linear regression correlation coefficient (R^2).

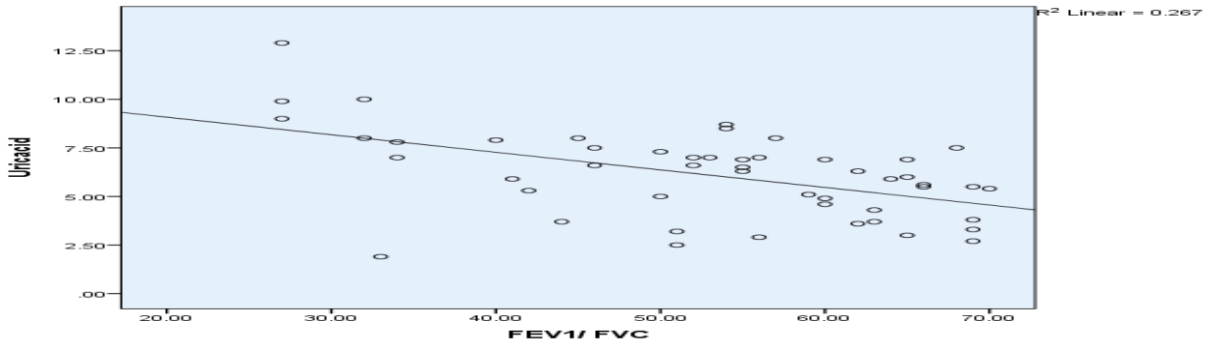

Figure 2. The scatter diagram shows a negative linear correlation between the patient's serum uric acid level and FEV1/FVC and linear regression correlation coefficient (R^2).

Discussion:

Serum uric acid is present at a high level in the epithelial lining fluid of the airway and plasma **(7)**. SUA has the double-edged characteristic of having antioxidant properties as well as pro-oxidant and pro-inflammatory properties (**8)**. Based on these characteristics, there are complicated interpretations of whether SUA has a beneficial or noxious effect on lung function (**9).** An experimental study suggested that SUA levels may only affect lung function in individuals with impaired lung tissue but not normal lung structure **(10)**.

In the current work, we found that serum uric acid level was significantly higher among patients GOLD stage 4 (mean ± SD=4.86±1.46 mg/dl) than GOLD stage 3 (mean ±SD=6.86±2.24 mg/dl) (p=.001). We also found a significant negative correlation between patients' serum uric acid level and FEV1 (r= -.541& p =.000). There was a highly significant negative correlation between patients' serum uric acid level and FEV1/ FVC (r= -.481& p =.000). There was a negative linear correlation between patients' serum uric acid level and FEV1 and negative linear correlation between patients' serum uric acid level and FEV1/FVC and it is found that serum uric acid was a highly significant predictor of the studied patients FEV1 (p=.000). This could be explained by the impairment of lung tissue which reduces oxygen intake, which may result in tissue hypoxia which in turn stimulate breakdown of adenosine and increase uric acid in the serum **(11**).

Previous research has found a negative relation between SUA level and measures of lung function, such as forced vital capacity (FVC) and the first second of forced respiratory volume (FEV1) in individuals with COPD (**12).** Another study found no effect of SUA on lung function in the same population (**13)**. For the population with normal lung structure, the effect of high SUA levels on lung function has been conflicting in cross-sectional studies; while a positive effect was found in a large Korean population (n=69,928) without any clinical diseases , this is in opposition to the Korean National Health and Nutrition Examination Survey, (**14)**, and no valuable association was shown in the age group (22‑29 years) (**15)**.

Yang et al. found that COPD patients had significantly higher serum uric acid levels than did individuals without COPD and that serum uric acid levels were significantly correlated with a decrease in FEV1%, FVC%, and FEV1/FVC% and increased risk of COPD and chronic respiratory symptoms. They found a negative association between serum uric acid and FEV1% predicted, FVC% predicted, and FEV1/FVC in the COPD group, but no significant association between lung function and serum uric acid levels was found in the non-COPD group (**16)**.

Previous research has estimated that high SUA levels do not affect reactive oxygen species levels, which can initiate inflammation or airway remodeling under normal circumstances, and do not affect lung function under the same condition (**17)**. Experimentally induced hypoxia models found that SUA levels were higher in hypoxia status compared to normal status in lung tissue, **(18)** which means that hypoxia may promote purine catabolism, which could increase the levels of SUA, and those elevated SUA levels can cause systemic inflammation, potentially damaging lung function (**19).**

Serum uric acid levels were increased in subjects with more increased airway obstruction and those with decreased oxygen tension and systemic inflammation. It was also found by Durmus Kocak et al., that serum uric acid levels were increased in COPD patients with diminished oxygen tension than those with normal ones (**20)**. It was also found by Nicks et al that lower serum uric acid levels were correlated with COPD intensity (5)**.**

A meta-analysis concluded that SUA levels might be a useful biomarker for COPD and an independent predictor of death and are associated with a higher risk of acute exacerbation of COPD. For better management of COPD, further research about the effect of SUA on lung function, especially in COPD patients, is required (**21)**.

Sarangi et al. showed an increase in uric acid levels with increasing intensity of COPD disease; though the difference was not statistically significant, and they showed that advanced GOLD stages (stages 3 and 4) COPD cases had higher uric acid levels in comparison to stage 1 and 2. And that antioxidant properties of UA decreased with increasing intensity of the disease and further exacerbation. They observed significantly higher serum uric acid levels in COPD cases with increased duration of the disease ($p<0.05$) (**22)**. COPD cases with more than 10 years' duration had the highest level of UA than those with <5 years and 6-10 years.

This might be explained by the fact that as the duration of the disease increases, lung function decreases leading to tissue hypoxia, inflammation, tissue breakdown, and increased uric acid production, which may further progress to systemic inflammatory disease.

Nicks et al., **(5)** showed a valuable inverse correlation between serum uric acid with intensity and exacerbation of COPD. A study on 59 stable COPD subjects without co-morbid conditions also reported an inverse relationship ($p<0.05$) between serum UA to creatinine ratio (UA: Cr) and respiratory functions and level of dyspnea.

As uric acid could result from tissue breakdown induced by decreased oxygen tension, oxygen therapy might be useful (**23)**. Sato et al. found that percent changes in uric acid: creatinine ratio increased in non-survivors than those who survived in those with COPD exacerbation. They found an inverse correlation between uric acid: creatinine ratio and the nadir of oxyhemoglobin saturation and this was found to be an independent predictor of death (**24**).

Conclusion:

Serum uric acid is associated with COPD severity and deteriorating lung functions, so uric acid could be used as a chemical biomarker in predicting COPD severity and staging.
Limitations of the study; the small size of the studied group, not studying the correlation between serum uric acid and COPD exacerbation; and not comparing uric acid levels between COPD males and females.
All data generated or analyzed during this study are included in this published article and its supplementary information files.

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