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Original Article

Association of Serum Uric Acid Levels in Hospitalized Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease

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Abstract

Background: Chronic obstructive pulmonary disease (COPD) is a prevalent able and progressive illness. Uric acid counteracts the effects of oxidants. It is important to assess the influence of serum uric acid levels on the clinical outcomes of hospitalized patients with chronic obstructive pulmonary disease (COPD).
Objective: To determine the association of serum uric acid levels with acute exacerbation of COPD in hospitalized patients at a tertiary care hospital in Karachi.
Methods: This observational study was carried out in the Chest Medicine Department of Jinnah Postgraduate Medical Center (JPMC), Karachi, Pakistan, from January to June 2023. It included patients presenting with acute exacerbation, diagnosed per Anthonisen's criteria. Serum uric acid levels were measured from venous blood samples at admission, and hyperuricemia was defined as a level >7 mg/dL. Data on quantitative variables (age, pack-years of smoking, systolic blood pressure (SBP), diastolic blood pressure (DBP), and COPD duration, as well as qualitative variables such as gender, residence status, hyperuricemia, and in-hospital mortality, were recorded.
Results: A total of 150 patients were examined during the study, with a mean age of 65.37±11.55 years. There were 107 (71.3%) males and 43 (28.7%) females. The mean duration of COPD was 14.33±14.65 years. The mean hyperuricemia of the patients was 7.89±2.72 mg/dl. The mean serum albumin of the patients was 3.48±0.97 g/dl. In this study, 66 (44.0%) patients were expired. It was seen that 54 (81.8%) expired patients had high uric acid versus 39 (41.9%) patients (p <0.001).
Conclusion: Hyperuricemia emerges as a promising biomarker for predicting early acute exacerbation in COPD patients, as higher uric acid levels have been linked with an augmented risk of poor clinical outcomes, including exacerbations and mortality.
Key words: COPD, in-hospital mortality, hyperuricemia, exacerbation, outcomes.

Introduction

COPD ranked 4th leading cause of death by a survey conducted in 2020 by World Health Organization.[1] Most COPD cases are triggered by smoking. Other causative factors for COPD patients are environmental pollution, bio-fuel exposure and compounds found in work environments.[2]Increased cardiovascular morbidity and death rates in individuals with COPD are caused by a sedentary lifestyle, nutrition, excessive smoking, and systemic inflammation brought on by oxidative stress and hypoxia.[3] It is a chronic progressive disease characterized by fixed or partially reversible respiratory difficulties. It is punctuated by exacerbation and remission, which is amenable to treatment.[4] Moreover, complex management and clinical courses result in poor quality of life as well as social and economic burdens.[5] Stable COPD is related to low-grade systemic inflammation as revealed by an increase in blood leukocytes, C reactive protein (CRP), and inflammatory cytokines. COPD exacerbations are an essential consequence of COPD because patients with exacerbations have compromised health status, reduced physical activity, and quicker deterioration of lung function (50-70%).[6] With other antioxidants, UA counteracts the effects of oxidants formed because of cigarette smoke and has beneficial effects in reducing the

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SAKK & NA conceptualized the project and did the drafting, revision & writing of manuscript. SAKK also did the data collection, literature search and performed the statistical analysis.

development of COPD and lung cancer.[7] In studies conducted in a general population, it was reported that individuals with lung restriction had higher serum UA levels than those without and that serum UA levels were higher in individuals with moderate and severe airflow limitation than in those without airflow limitation or mild airflow limitation.[8] Ergün et al. found the frequency of hyperuricemia and in-hospital mortality to be 47.6% and 25%, respectively.[9]

With a population exceeding 250 million and exposure to diverse and often extreme weather conditions, Pakistan faces a substantial burden of respiratory illnesses. Karachi, as one of the most densely populated cities, is particularly affected due to additional environmental and socioeconomic factors that contribute to the prevalence of COPD. In light of these considerations, the objective of the present study is to determine the connotation of serum uric acid levels presenting with acute exacerbation of COPD in hospitalized patients at a tertiary care hospital in Karachi.

Methods

This observational study was conducted at the Inpatient Chest Medicine Ward (Ward 12) of Jinnah Postgraduate Medical Center (JPMC), Karachi, from January to June 2023, after obtaining informed consent was obtained from all participants.

The study included patients of either gender, aged above 40 years, who were admitted with an acute exacerbation of chronic obstructive pulmonary disease (AECOPD). The diagnosis of AECOPD was made based on Anthonisen's criteria, which defines exacerbation by the presence of increased dyspnea, increased sputum volume, or increased sputum purulence.[10] Patients with a history of other respiratory conditions (such as asthma, tuberculosis, idiopathic pulmonary fibrosis, pneumonia, pulmonary embolism, or lung carcinoma), those taking medications that affect uric acid levels (e.g., NSAIDs or thiazide diuretics), and those with significant comorbidities (including chronic cardiac, renal, or liver failure, myocardial infarction, stroke, thyroid disorders, or obstructive sleep apnea) were excluded. Pregnant patients were also omitted from the study.

The sample size was calculated as 150 patients using the World Health Organization's sample size calculation software. This calculation was based on a reported hyperuricemia prevalence of 47.6% among patients with acute COPD exacerbation[12], with a 95% confidence level and an 8% margin of error.

Upon enrollment, a detailed history was recorded from each participant, encompassing demographic data (age, gender, residence), smoking history, duration of COPD, and history of biomass exposure. Smoking status was categorized as 'smoker' (current smoker), 'no smoker' (former smoker), or 'non-smoker' (never smoked). Anthropometric measurements were taken at hospital admission to calculate Body Mass Index (BMI).

A 5 ml blood sample was collected from a peripheral vein of each patient using a disposable syringe at the time of study inclusion. The sample was transported to the hospital's standardized laboratory for analysis. Serum uric acid levels were measured, and hyperuricemia was defined as a level greater than 7 mg/dL, according to the operational definition.[11] The outcome of interest was all-cause in-hospital mortality.

Data on quantitative variables (age, systolic and diastolic blood pressure, duration of COPD, pack-years of smoking) and qualitative variables (gender, residence status, hyperuricemia, and in-hospital mortality) were recorded. Data analysis was performed using SPSS Version 20. Continuous variables were presented as mean±standard deviation, and categorical variables as frequencies and percentages. To control potential effect modifiers, the data were stratified by age, gender, and duration of COPD. Post-stratification, the chi-square test (or Fisher's exact test where appropriate) was used for categorical variables, and the independent sample t-test was used for continuous variables. A *p*-value of ≤0.05 was considered statistically significant.

Results

About 150 patients were examined during the research, with a mean age of 65.37±11.55 years. There were 107 (71.3%) males and 43 (28.7%) females. Of the 150 patients, 64 (42.7%) were smokers, and the mean pack-years of smoking was 28.87±18.39 years. The mean duration of biomass exposure of the patients was 6.46±7.21 years. The mean duration of COPD of the patients was 14.33±14.65 years. The mean serum UA level of the patients was 7.89±2.72 mg/dl. Whereas the mean serum albumin of the patients was 3.48±0.97 g/dl. In current study, 66 (44.0%) patients were expired. (Table-1).

The mean duration of exposure to biomass was high in high uric acid patients compared to the normal uric acid patients, 8.56±8.80 years and 4.02±3.45 years, respectively (p <0.001). The mean duration of COPD was less in high uric acid patients than in normal uric acid patients, 11.91±14.06 years and 22.18±14.18 years, respectively (p =0.011). Mean serum albumin was less in high uric acid patients than in normal uric acid patients, 3.32±1.12

g/dl and 3.73±0.58 g/dl, respectively (*p* =0.011). Further, it was seen that 54 (81.8%) was expired among high uric acid patients than normal uric acid patients 12 (18.2%), *(p* <0.001). (Table-2).

Table 1: Demographics and baseline profile of the patients.

Variable	*N (%) / Mean±S.D**
Age (years)	65.37±11.55
Male	107 (71.3)
Female	43 (28.7)
Smoking status	
Smoker	64 (42.7)
Non-smoker	56 (37.3)
No smoker	30 (20.0)
Pack-years smoking (years)	28.87±18.39
Biomass exposure(years)	6.46±7.21
Duration of COPD(years)	14.33±14.65
Hyperuricemia (mg/dl)	7.89±2.72
S. albumin (g/dl)	3.48±0.97
Outcome	
Expired	66 (44.0)
Discharge	84 (56.0)

*S.D = standard deviation

The mean age of the expired patients was greater than the non-expired patients, 68.64±10.43 years and 62.80±11.78 years, respectively (*p* =0.002). Mean duration of biomass exposure was greater than the non-expired patients, 8.40±9.81 years and 4.91±3.45 years, respectively, (*p* =0.008). The mean duration of COPD was greater in expired patients than in non-expired patients, 31.94±9.72 years and 8.46±10.81 years, respectively (*p* <0.001) (Table-3).

The association between in-hospital mortality and uric acid is shown in Table-1. It was seen that 54 (58.1%) expired patients had high uric acid versus 39 (41.9%) discharged patients (*p* <0.001) (Table-3).

Discussion

Several prognostic factors for mortality in patients with COPD have been identified, including acute exacerbations, alcohol abuse, diabetes, and cerebrovascular disease. Uric acid (UA), a metabolic end product of purine nucleotide breakdown, is noteworthy due to its antioxidant properties, as highlighted in previous studies.[13] Billiet et al[14] reported that hyperuricemia might contribute to the worsening of COPD by increasing oxidative stress and inflammation in the body, providing necessary information about the link between early mortality of COPD patients and hyperuricemia.

Previous study carried by Rock et al[15] and Alvarez-Lario et al[16] highlights the dual role of uric acid (UA) in the human body. On one hand, UA is a potent antioxidant, playing a protective role by neutralizing free radicals and reducing oxidative stress. On the other hand, UA exhibits pro-inflammatory properties, particularly in individuals with elevated serum UA levels, where it can support systemic inflammation and is implicated in the pathogenesis of conditions such as gout, hypertension, and metabolic syndrome. This dichotomy underscores the complex and context-dependent nature of UA's physiological effects.

A study by Sato et al[17] evaluated the analytical significance of the ratio of serum uric acid (UA) and creatinine concentrations in a cohort of 91 patients diagnosed with COPD. The findings suggested that this ratio is reliable for predicting disease prognosis. Similarly, research by Garcia-Pachonet al[18] demonstrated that the UA-to-

Table 2: Association of uric acid with baseline and demographic profile.

Variable	*Uric Acid*		*Sig. (p)*
	Normal 57 (38.0%)	High 93 (62.0%)	
Age (years)	65.37±11.71	65.37±11.50	0.999
Gender			
Male	43 (40.2)	64 (59.8)	0.384
Female	14 (32.6)	29 (67.4)	
Smoking status			
Smoker	24 (37.5)	40 (62.5)	0.501
Non-smoker	24 (42.9)	32 (57.1)	
No smoker	9 (30.0)	21 (70.0)	
Pack-years smoking (years)	30.09±17.33	28.12±19.07	0.527
Biomass exposure (years)	4.02±3.45	8.56±8.80	<0.001
Duration of COPD (years)	22.18±14.18	11.91±14.06	0.011
S. albumin (g/dl)	3.73±0.58	3.32±1.12	0.011
Outcome			
Expired	12 (18.2)	54 (58.1)	<0.001
Discharge	45 (53.6)	39 (41.9)	
N (%), mean±standard deviation			

n (%), mean±standard deviation

Table 3: Association of in-hospital mortality with baseline and demographic profile.

Variable	*In-hospital Mortality*		*Sig. (p)*
	Expired	No	
	66 (44.0)	84 (56.0%)	
Age (years)	68.64±10.43	62.80±11.78	0.002
Gender			
Male	47 (43.9)	60 (56.1)	0.977
Female	19 (44.2)	24 (55.8)	
Smoking status			
Smoker	25 (39.1)	39 (60.9)	0.570
Non-smoker	27 (48.2)	29 (51.8)	
No smoker	14 (46.7)	16 (53.3)	
Pack-years smoking (years)	29.64±18.96	28.48±18.03	0.766
Biomass exposure (years)	8.40±9.81	4.91±3.45	0.008
Duration of COPD (years)	31.94±9.72	8.46±10.81	<0.001
S. albumin (g/dl)	3.51±1.27	3.45±0.64	0.686

N (%), mean±standard deviation

creatinine ratio was meaning fully linked with lung function in COPD patients, highlighting its potential utility as a biomarker for assessing disease severity and functional impairment in this population.

This study revealed that hyperuricemia serves as a significant biomarker associated with an increased risk of mortality in patients with COPD. It was seen that 54 (58.1%) expired patients had high uric acid versus 39 (41.9%) patients (p <0.001). Similarly, a 2014 study conducted by Bartziokas et al[19] demonstrated that elevated serum uric acid (UA) levels were an independent predictor of 30-day mortality in patients with COPD; however, the study did not find a significant association between high UA levels and 1 year mortality in this patient population.

Zhang et al [20] conducted a study to assess the association between mortality risk in patients with COPD and hyperuricemia. In their univariate analysis, they found that hyperuricemia was significantly associated with an increased risk of mortality, with a hazard ratio of 2.29 (95% confidence interval. Furthermore, in the multivariate analysis, which adjusted for potential confounding variables, hyperuricemia was identified as an independent predictor of higher mortality risk in COPD patients, underscoring its potential role as a prognostic biomarker in this population. Hwang et al[21] conducted a study that demonstrated hyperuricemia is not an independent predictor of mortality in patients admitted with acute exacerbation of COPD. This study was conducted at a single tertiary care hospital with a relatively small sample size, which may limit the generalizability of findings, reduce statistical power, and restrict the ability to detect subtle associations or perform subgroup analyses.

Conclusion

Hyperuricemia emerges as a promising biomarker for predicting early acute exacerbation of in COPD patients, as higher uric acid levels have been associated with an increased risk of poor clinical outcomes, including exacerbations and mortality.

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Availability of Data: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethical Approval: The Institutional Review Board Committee of Jinnah Postgraduate Medical Centre, Karachi approved the study via letter no. F.2-81/2022-GENL/335/JPMC.

Conflict of Interest: None declared.

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