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ORIGINAL ARTICLE

Association of Serum Uric Acid with the Degree of Severity and Prognostic Outcomes in Patients with Acute Exacerbation of COPD

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ABSTRACT

Background: *Serum uric acid levels rise in response to systemic infections and hypoxic states. Given this, an association between elevated uric acid and COPD has been established, leading to the hypothesis that it may serve as a prognostic predictor for outcomes in Acute Exacerbations of COPD (AECOPD).* ***Objective:*** *To determine the association of serum uric acid with the degree of severity and prognostic outcome in patients with AECOPD.* ***Methods:*** *This one-year observational analytic study was conducted at the National Institute of Diseases of the Chest and Hospital (NIDCH) from July 2019 to June 2020. After screening, 96 AECOPD patients were enrolled based on inclusion/exclusion criteria. Following informed consent, all participants underwent a physical examination, relevant investigations, and a severity assessment using the GOLD criteria. Serum uric acid levels were measured. Ethical and health standards were strictly maintained, and data were analyzed using SPSS version 20.* ***Results:*** *The mean ages of Groups A and B were comparable (54.42±8.14 vs. 55.94±8.9 years; p>0.05), as were other socio-demographic profiles. Uric acid was significantly higher in Group B (8.42±1.02 vs. 5.7±0.77 mg/dl). Levels increased with GOLD stage severity (P < 0.001). Hyperuricemia was significantly associated with longer hospital stays, more ICU referrals, and a 10.42% mortality rate in AECOPD patients (p<0.05 for all).* ***Conclusion:*** *Elevated serum uric acid is a significant biomarker for predicting both disease severity and short-term outcomes in patients experiencing an Acute Exacerbation of COPD (AECOPD).*

Keywords: *Acute exacerbation, Biomarker, COPD, Hyperuricemia, Prognostic outcome, Serum uric acid, Spirometry*

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is one of the leading causes of morbidity and mortality with increasing prevalence worldwide. An acute exacerbation of COPD (AECOPD) is characterized by a significant change in symptoms that is acute in onset and may warrant a change in regular medication. [1] COPD encompasses chronic bronchitis and emphysema and is characterized by airflow limitation, breathing difficulty, coughing, and other symptoms/signs. It has high morbidity and mortality rates and is the third leading cause of death in developed countries. [2] COPD is still a smoking-related disorder and one of the most common causes of death. Although COPD mainly affects persons in the age group of 40–50 years, the pathogenesis of this disease can begin in early life and result in early death. There are several risk factors associated with COPD in later life, such as smoking, diabetes, and vitamin D deficiency. According to the World Health Organization (WHO), 64 million people were estimated to have moderate to severe COPD, and more than 3 million or 5% of deaths in 2005 were attributed to COPD worldwide. Almost 90% of COPD deaths occur in low- and middle-income countries. [3] Generally, COPD has a poor prognosis. Several studies have been done to determine the prognostic factors that can assist in various areas, such as grading the severity of COPD, further management, predicting lung function decline, clinical practice for educating patients, and providing patients with realistic expectations. Decreased forced expiratory volume in one second (FEV1) is a well-established prognostic factor along with variables such as smoking, low body mass index (BMI), exercise capacity, male gender, and comorbid

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diseases, especially heart failure. The BODE index (Body mass index, airflow Obstruction, Dyspnoea, and Exercise) was developed specifically for COPD patients to evaluate mortality and hospitalization risk. [4] Serum uric acid is the final product of purine degradation, which increases significantly during hypoxia. Elevated serum uric acid levels have been associated with the presence of systemic inflammation and increased cardiovascular risk. In this context, increased levels of serum uric acid have been shown in respiratory disorders, including obstructive sleep apnea and pulmonary hypertension. In COPD, cigarette smoke induces oxidative stress and lung inflammation, resulting in lung tissue damage and decline of pulmonary function. Impairment of pulmonary function reduces oxygen intake, resulting in tissue hypoxia, which is more prominent during AECOPD. [4] UA is one of the main non-enzymatic antioxidants found in the lungs. UA, together with other antioxidants, counteract the effects of oxidants produced by cigarette smoke. The antioxidant property of UA has been shown to have beneficial effects in reducing the development of COPD and lung cancer. [5] The present study aimed to evaluate the possible role of serum uric acid as a biomarker for the prediction of the outcome of patients hospitalized for AECOPD. The outcomes included the duration of hospitalization and (elaboration) NIV support.

METHODS & MATERIALS

Study population: This observational analytical study was conducted in the Department of Respiratory Medicine at the National Institute of Diseases of the Chest and Hospital (NIDCH). The study population consisted of all patients admitted to NIDCH with a primary diagnosis of Acute Exacerbation of COPD (AECOPD) during the one year from July 2019 to June 2020. A final cohort of 96 patients was selected through purposive sampling based on predefined criteria.

Inclusion and exclusion criteria: Patients were included if they were aged over 40 years and were admitted with a confirmed diagnosis of AECOPD. Key exclusion criteria were a history of gout, chronic kidney disease, hepatic failure, other significant respiratory diseases, or being debilitated or disoriented. These criteria were applied to minimize confounding variables that could influence serum uric acid levels.

Study procedure: After obtaining ethical permission from the institutional review board, 96 eligible patients provided informed written consent. Participants were categorized into two groups based on their serum uric acid levels: Group A (low, <6.9 mg/dL) and Group B (high, ≥6.9 mg/dL), each containing 48 patients. Data collected included socio-demographic details (age, sex, occupation, economic status), disease-related variables (symptoms, smoking history, severity via GOLD criteria), and results from investigations like spirometry, arterial blood gas, chest X-ray, and comprehensive blood tests.

Data collection: A structured questionnaire was used to systematically gather all data points. For each patient, the severity of AECOPD was recorded as an input variable, while the serum uric acid level was the primary outcome variable measured. All relevant clinical investigations were performed uniformly for every participant in the study.

Data analysis: Collected data were verified, compiled in Microsoft Excel 2016, and analyzed using SPSS version 20. Categorical variables were expressed as percentages, and continuous variables as mean ± standard deviation. Statistical significance was determined using Pearson's chi-square, Student's t-test, independent samples t-test, and Pearson's correlation test, where appropriate, with a p-value <0.05 considered significant.

RESULT

The mean age of the entire study cohort was 55.18 ± 8.52 years. No significant differences were observed in the mean age, age group distribution, sex distribution, or mean BMI (21.83 ± 3.23) between Group A (low serum uric acid) and Group B (high serum uric acid), as all corresponding p-values were greater than 0.05. A stark contrast was evident in COPD severity between the groups. The majority of patients in Group A (77.08%) were classified with mild or moderate COPD (GOLD stages I-II), with over half (54.17%) in stage II. Conversely, the majority in Group B (83.33%) had severe or very severe COPD (GOLD stages III-IV), with 58.33% in stage III. This difference in GOLD stage distribution was highly significant ($p < 0.001$). Consequently, complications were more frequent in Group B; 64.58% of these patients presented with acute respiratory failure upon admission, a significantly higher proportion compared to the 22.92% in Group A ($p = 0.001$). Laboratory findings revealed significant differences between the groups. All measured parameters, including arterial blood gases, showed statistically significant variations ($p < 0.05$). Most notably, a direct correlation was found between serum uric acid levels and COPD severity. The median serum uric acid level exhibited a progressive and significant increase with each advancing GOLD stage, from 4.79 mg/dL in stage I to 9.67 mg/dL in stage IV ($P < 0.001$). Correlation analyses further solidified this relationship. Serum uric acid demonstrated a highly significant negative correlation with FEV1 ($R=-0.922$, $p < 0.001$) and SpO2 ($R=-0.776$, $p < 0.001$). It also showed a strong positive correlation with PaCO2 ($R= 0.956$, $p < 0.001$) and a moderate negative correlation with PaO2 ($R= -0.656$, $p < 0.001$). These results consistently indicate that elevated uric acid is strongly associated with worse lung function and impaired gas exchange.

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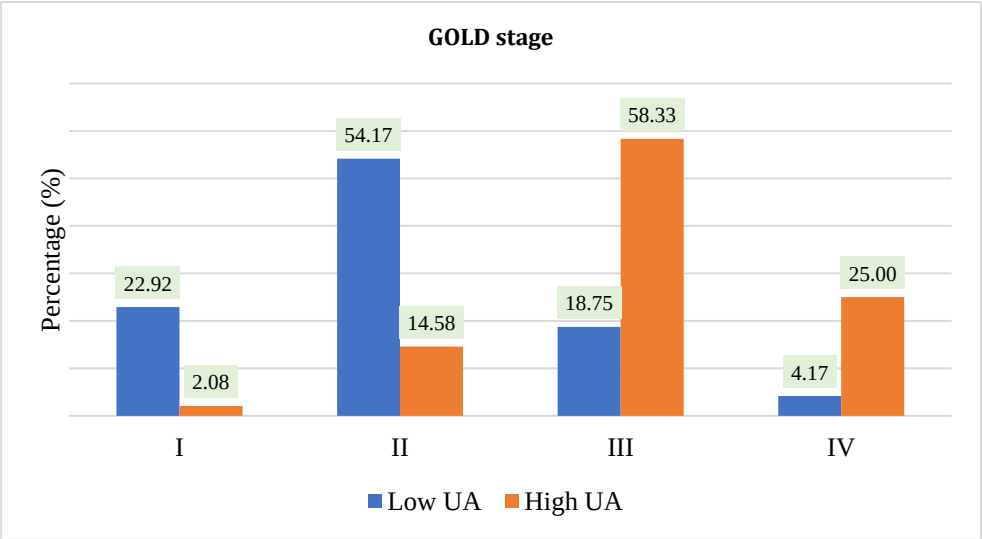

Figure – 1: GOLD stage of COPD among patients (*n*=96)

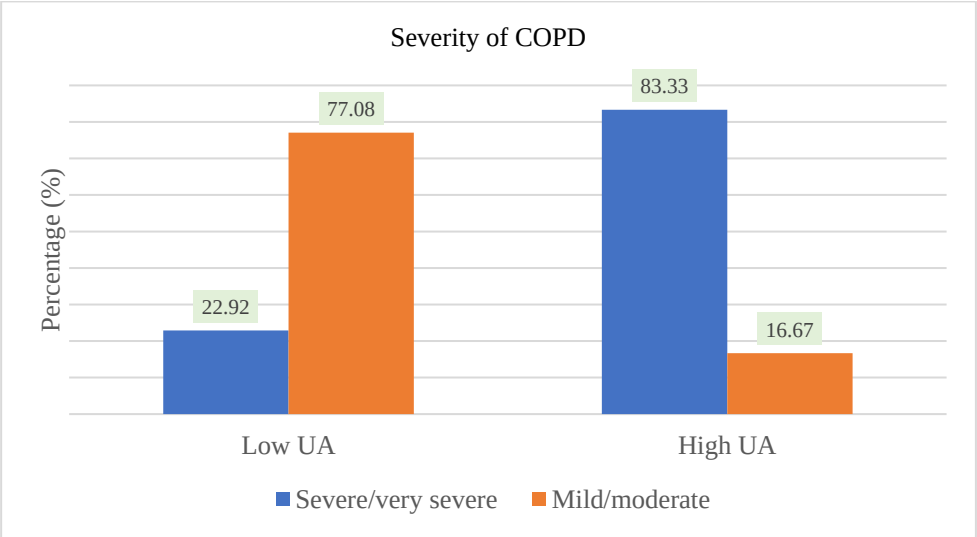

Figure – 2: Severity of COPD among patients (*n*=96)

Table – I: Classification of acute exacerbation of COPD patients (*n*=96)

Types	Group A (n=48) No. (%)	Group B (n=48) No. (%)	Total (n=96) No. (%)	p value
Mild	11 (22.92%)	0 (0%)	11 (11.46%)	<0.001
Moderate	26 (54.17%)	8 (16.67%)	34 (35.42%)	
Severe	11 (22.92%)	40 (83.33%)	51 (53.13%)	
Classes of severe types of acute exacerbation of COPD				
No respiratory failure	9 (18.75%)	9 (18.75%)	18 (18.75%)	<0.001
Acute respiratory failure is non-life-threatening	2 (4.17%)	19 (39.58%)	21 (21.88%)	
Acute respiratory failure life life-threatening	0 (0%)	12 (25%)	12 (12.50%)	

p-value was determined by the Pearson Chi-square test

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Table – II: Laboratory findings of both groups (*n*=96)

Variables	Group A(n=48) n (%)	Group B(n=48) n (%)	P value
Uric acid	5.7±0.77	8.42±1.02	<0.001**
FEV1 (%)	62.10±14.91	37.92±12.03	<0.001**
pH	7.40±0.03	7.37±0.04	<0.001**
PaO_2	64.73±5.34	61.60±6.82	0.014**
$PaCO_2$	41.02±3.26	43.38±4.77	0.006**
SpO_2 (%)	95.19±2.62	92.21±3.92	<0.001**

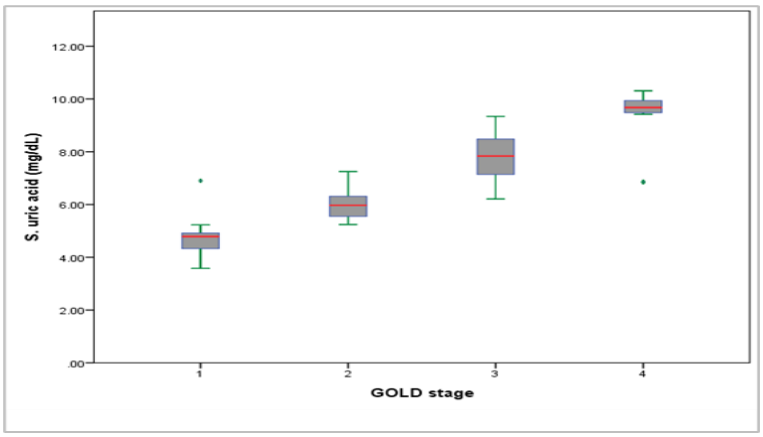

Figure – 3: Serum uric acid levels on admission in all studied patients according to GOLD stage (*n*=96)

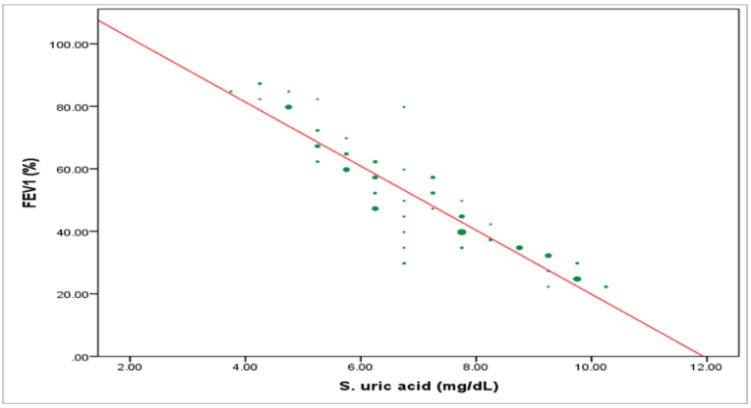

Figure – 4: Correlation between serum uric acid level and FEV1 among patients. (*n*=96)

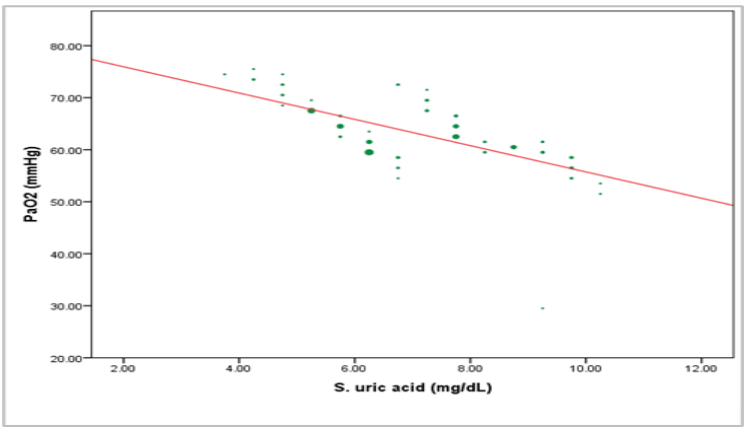

Figure – 5: Correlation between serum uric acid level and PaO2 among patients (*n*=96)

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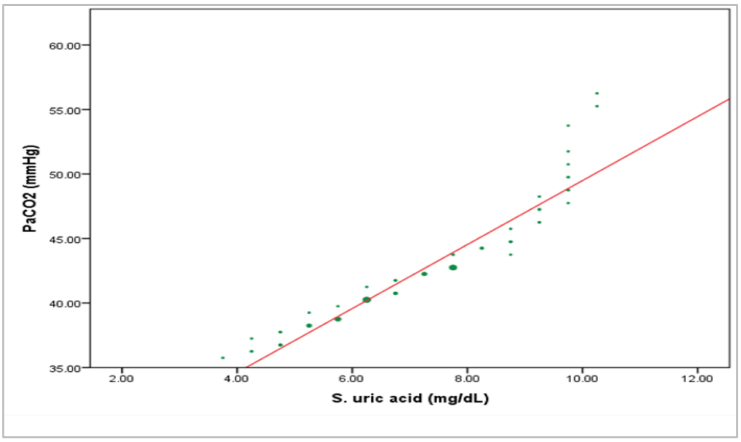

Figure – 6: Correlation between serum uric acid level and PaCO2 among patients (*n*=96)

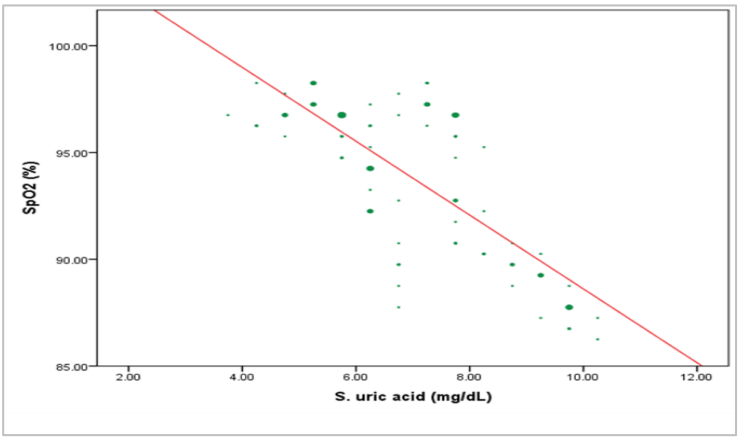

Figure – 7: Correlation between serum uric acid level and SpO2 among patients (*n*=96)

Table – III: Outcome of both groups (*n*=96)

Characteristics	Group A (n=48) n (%)	Group B (n=48) n (%)	p value
Length of hospital stay (days)	4.75±1.78	9.71±2.63	<0.001**
Need for ICU admission	1 (2.08%)	8 (16.67%)	0.031*
In hospital mortality	-	5 (10.42%)	0.022*

DISCUSSION

Chronic obstructive pulmonary disease (COPD) remains a leading cause of global morbidity and mortality, ranking as the third most common cause of death in developed nations. [6] The identification of reliable prognostic biomarkers is therefore critical, as it could facilitate early, intensified therapeutic interventions for high-risk patients, potentially improving survival outcomes. In this study, the mean patient age was 55.18 ± 8.52 years, with a majority (36.46%) aged 40-49. While no significant age difference existed between the comparison groups, this demographic aligns with the natural history of COPD, where a physiological decline in lung function begins around ages 30-40, leading to increased prevalence with advancing age. [7] A pronounced male predominance (82.29%) was observed, consistent with classical epidemiological patterns attributing higher historical COPD risk in males to greater smoking rates and occupational exposures, though no significant difference was found between the groups in our cohort (p=0.189). The distribution of disease severity, assessed by GOLD criteria, revealed a highly significant disparity between patients with normal and elevated serum uric acid (SUA) levels. The majority of patients with normal SUA (54.17%) were classified as GOLD stage II, whereas most with high SUA (58.33%) were in stage III. The mean SUA level across all patients was 7.06 ± 1.63 mg/dL, with a stark and highly significant difference between the groups (5.7 ± 0.77 vs. 8.42 ± 1.02 mg/dL, p<0.001). Receiver operator curve analysis further established a clinically robust cut-off value of 7.38 mg/dL for assessing COPD severity, demonstrating 76.5% sensitivity and 100% specificity (p<0.001). These findings are strongly supported by existing literature. Our results concord with those of Bartziokas et al., [5] who identified SUA as a predictor of severity, noting higher levels in patients with severe airflow limitation, cardiovascular comorbidity, and frequent exacerbations. Similarly, some other studies reported a significant correlation between SUA, hypoxemia, and COPD severity, a result bolstered by several other studies. [8,9] The pathophysiological link is believed to be increased purine catabolism secondary to tissue hypoxia, leading to elevated SUA. [10,11] The correlation analysis in our

study provides mechanistic insight, revealing a highly significant, strong negative association between SUA and both FEV1 (R=-0.922, p<0.001) and SpO2 (R=-0.776, p<0.001). A strong positive correlation was found with PaCO2 (R= 0.956, p<0.001), and a moderate negative correlation with PaO2 (R= -0.656, p<0.001). These results position SUA as a strong indicator of impaired gas exchange and ventilatory function, consistent with cross-sectional studies that have linked uric acid to clinical and functional characteristics in COPD. [1,12] However, the relationship between SUA and hypoxia is complex. While our study found significant differences in blood gas parameters between groups, other studies have reported no direct correlation between SUA and arterial oxygen saturation.[13,14] This inconsistency might arise because tissue hypoxia depends not only on arterial oxygen saturation but also on a complex combination of factors such as hemoglobin levels, cardiac output, blood flow to tissues, and how much oxygen the tissues require.[15] Furthermore, several key limitations should be noted. Uric acid (SUA) levels are affected by multiple confounding variables, including pre-existing heart disease, dietary habits, alcohol intake, and genetic predispositions affecting purine processing or inflammation.[16] Although we excluded patients with renal failure, hepatic failure, and gout, residual confounding from unmeasured variables may persist. Despite these limitations, the cumulative evidence from this study strongly suggests that serum uric acid serves as a valuable biomarker, reflecting disease severity and identifying AECOPD patients with a worse prognosis, including longer hospital stays, higher ICU referral rates, and increased mortality. Its integration into clinical assessment could enhance risk stratification and guide more aggressive management strategies for this vulnerable patient population.

Limitations:

The limitations of this study include the lack of comparison between different pre-hospital treatment modalities and the exclusion of patients with other significant co-morbid conditions, which may affect the generalizability of the results.

CONCLUSION

Elevated serum uric acid is a significant biomarker in Acute Exacerbations of COPD (AECOPD), demonstrating a strong positive correlation with the severity of airflow limitation (lower FEV1) and disease severity as classified by GOLD criteria. Higher levels are predictive of worse clinical outcomes, including prolonged hospitalization, increased need for ICU admission, and higher mortality. Its measurement provides valuable prognostic information that can aid in risk stratification and management planning for AECOPD patients.

Recommendation:

Future prospective studies should compare serum uric acid levels during exacerbation and stable COPD phases. Research should also include heterogeneous populations, incorporating various treatment histories and co-morbid conditions to enhance the generalizability of the findings.

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