Hyperuricemia as a Predictor of in-hospital Mortality in Acute Exacerbation of COPD: Insights from a Tertiary Care Hospital in Karachi

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ABSTRACT

OBJECTIVE: To identify the correlation of hyperuricemia with in-hospital mortality in patients who report to a tertiary care hospital in Karachi with acute exacerbation of chronic obstructive pulmonary disease (AECOPD).

METHODOLOGY: This cross-sectional study was conducted from May to October 2024 at Jinnah Postgraduate Medical Centre (Ward 12, Chest Medicine Centre), Karachi, Pakistan. A total of 150 patients with AECOPD were included via non-probability consecutive sampling. Inclusion criteria comprised: age ≥40 years, confirmed COPD diagnosis via spirometry with reversibility (post-bronchodilator FEV_1/FVC <0.70), and hospitalization for AECOPD (Anthonisen's criteria). Exclusion criteria included chronic kidney disease, gout, coexisting pulmonary diseases, uncontrolled comorbidities affecting uric acid levels, and pregnancy. Data on demographics, serum uric acid levels, and outcomes were collected. Statistical analysis was performed using SPSS version 26, employing Chi-square tests and one-way ANOVA to assess associations between hyperuricemia, age, COPD duration, and mortality.

RESULTS: The cohort consisted of 71% males and 29% females, with 79% reporting a history of smoking. Hyperuricemia (>7 mg/dL) was significantly associated with in-hospital mortality ($p = 0.001$). A linear correlation was observed between age and uric acid levels ($p = 0.014$), but no association was found with COPD duration ($p = 0.902$). The mortality rate was 70%, higher than global averages, likely due to delayed presentations and limited ICU resources.

CONCLUSION: Hyperuricemia was identified as a predictor of in-hospital mortality among patients with AECOPD. Early intervention and monitoring of elevated uric acid levels can improve clinical outcomes in this high-risk patient population.

KEYWORDS: Hyperuricemia, COPD exacerbation, COPD, in-hospital mortality, prognostic biomarker, tertiary care hospital Karachi.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is ranked among the significant causes of morbidity and mortality globally[1] inflicting 3.3 million deaths worldwide in 2019[2]. It is defined by limitations in lung function, with a prevalence of 2.1% in Pakistan, as determined[3]. Acute exacerbations of COPD (AECOPD) are critical events that manifest the worsening of respiratory symptoms within a short duration and play a significant role in disease progression, hospitalization, and mortality. Infections, irritants, and acute diseases are implicated in AECOPD. Establishing prognostic variables that predict in-hospital mortality in AECOPD would be valuable for management.

Data provided in the previous studies indicated that hyperuricemia is related to the severity of COPD and prognosis[4]. Prior research has demonstrated a positive correlation between hyperuricaemia and increased mortality in COPD patients[5]. However, the available evidence is limited by geographical, genetic, molecular, and lifestyle differences; thus, it is essential to conduct local-level studies to elucidate clinical relevance in specific populations.

Given the high prevalence of COPD in Pakistan and the existence of other environmental factors such as air pollution and tobacco consumption, the involvement of hyperuricemia in AECOPD results is of great concern. Given the scant literature from this region on this relationship, the present study seeks to establish the association between hyperuricemia and in-hospital mortality in AECOPD patients admitted to a tertiary care hospital in Karachi.

Dependent on the findings of prior studies, this study supposes that hyperuricemia has a strong correlation with a higher in-hospital mortality rate in patients with AECOPD. In addition, this study aims to detect high-risk subgroups and discuss how to incorporate hyperuricemia management into clinical practice based on demographic, clinical, and biochemical characteristics.

Ultimately, this study contributes evidence to previous work suggesting that metabolic abnormalities are

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associated with COPD outcomes, and it highlights the importance of an individualized approach to managing COPD exacerbations. The research aims to assist clinicians in making informed decisions and improving patient care, particularly in facilities where taking adequate precautions can significantly reduce mortality rates. The following are the hypotheses for the study:

- **Null Hypothesis (H_0):** There is no significant association between age and uric acid levels in patients presenting with acute exacerbation of COPD at a tertiary care hospital in Karachi.

- **Null Hypothesis (H_0):** There is no significant difference in Uricemia across different levels of duration of COPD in patients presenting with acute exacerbation of COPD.

- **Null Hypothesis (H_0):** There is no significant association between hyperuricemia and in-hospital mortality in patients presenting with acute exacerbation of COPD

Chronic Obstructive Pulmonary Disease (COPD) is a long-term respiratory disease[6] in which individuals experience restricted airways and a predisposition to inflammation due to exposure to irritants. Acute exacerbations of COPD (AECOPD) refer to episodes of the disease characterized by worsening of the symptoms leading to considerable morbidity, mortality, and healthcare costs. COPD exhibits its global prevalence at 10.7% above 30 years of age[7], with high incidence in Southeast Asia and sub-Saharan Africa[8]. Worldwide, it remains one of the most common diseases that precede death[9]; hence, establishing the importance of research to establish prognostic biomarkers for AECOPD.

Hyperuricemia refers to a state in which the serum uric acid level is increased[10], and has recently been found to be associated with inflammation and oxidative stress. Hyperuricaemia has been linked with several cardiovascular, renal and metabolic disorders[11] and there is growing evidence pointing to a possible role of uric acid in the pathological development of COPD. Studies have evidenced hyperuricemia as a predictor of worse outcomes in patients with COPD[12], implicating it in higher mortality and exacerbations. Nevertheless, the dynamics between hyperuricemia and COPD outcomes remain inconclusive, and it is necessary to establish the underlying pathways. Possible explanations for these pathological changes in COPD due to hyperuricemia include oxidative stress and subsequent tissue damage, altered gas exchange, and heightened inflammation levels in the body[13].

Age and smoking status[14,15] are firmly established as the risk factors in the development and course of COPD. Additionally, parameters such as the duration of COPD, the presence of comorbidity, and the frequency of exacerbation have been implicated in the literature in outcomes of AECOPD. Although these factors are essential in the management of AECOPD,

there is a scarcity of literature examining the association between hyperuricemia and these factors. There are also limited studies examining the relationship between uric acid and in-hospital mortality in the South Asian region, which is characterized by distinct genetic backgrounds, environments, and dietary habits.

Although there has been remarkable progress in the study of COPD, some questions remain unexplored regarding the role of hyperuricemia in improving risk assessment and management. Prior research has predominantly been conducted in a Western context, implying a lack of region-specific studies that consider ethnicity, demographics, and other clinical variations. To fill this gap, the present research aims to investigate the relationship between hyperuricemia and in-hospital mortality among AECOPD patients in a tertiary care hospital in Karachi, Pakistan.

The findings of this research will be beneficial not only for establishing the predictive value of uric acid levels in targeting AECOPD but also for designing evidence-based clinical protocols to be implemented in settings with scarce resources.

METHODOLOGY

This study employed a cross-sectional study design[16] and was conducted in the Chest Medicine Ward (Ward 12) of Jinnah Postgraduate Medical Centre (JPMC), Karachi, Pakistan. The study was conducted from May to October 2024, following approval of the research synopsis from the University of Karachi and the Jinnah Postgraduate Medical Centre, Karachi.

One hundred fifty patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD) were recruited through a non-probability consecutive sampling method. Patients were included and excluded according to predetermined eligibility criteria shown in **Table I**.

Table I: Inclusion and Exclusion Criteria

Category	Details
Inclusion Criteria	
Age	Patients aged 40 years or older.
Diagnosis	Diagnosis of COPD confirmed via previous spirometry with reversibility showing post-bronchodilator FEV1/FVC <0.70, according to the GOLD guidelines. AECOPD was diagnosed according to Anthonisen's criteria (increased dyspnea, increased sputum volume, or increased sputum purulence).
Admission	Hospitalized for the management of AECOPD.
Exclusion Criteria	
Chronic Conditions	History of chronic kidney disease or gout.
Pulmonary Diseases	Coexisting pulmonary diseases such as bronchiectasis, tuberculosis, or interstitial lung disease
Comorbidities	Uncontrolled diabetes mellitus, hypertension, or other endocrine/cardiovascular conditions influencing uric acid levels
Special Conditions	Pregnant women or those taking medications influencing uric acid levels (e.g., diuretics, allopurinol).

Sample Size Calculation

The sample size was calculated employing a formula for single proportions[17]:

$$n = Z^2 \, p \times (1-p) \, / \, e^2$$

Where:

- **n** = required sample size.
- **Z** = standard normal variate at a 95% confidence level (1.96).
- **p** = estimated prevalence of hyperuricemia in AECOPD patients (47.6%).
- 1 **e** = margin of error (8%)

2The sample size of 150 was calculated using the OpenPI software[18].

Procedure for Data Calculation

After obtaining informed consent, patients who met the inclusion criteria were recruited. Data were determined by structured interviews and clinical assessments, including:

- demographics (age, gender)
- history of smoking
- length of COPD
- height, weight, and blood pressure

Previous spirometry results, including reversibility tests, were positive, confirming the diagnosis of COPD, and were examined. Blood samples were obtained for the estimation of serum uric acid. Hyperuricemia was detected by >7 mg/dl levels of uric acid. In-hospital mortality was included as the primary outcome.

Statistical Analysis

Quantitative variables (e.g., age, BMI, serum uric acid levels) were expressed as mean ± standard deviation. In contrast, qualitative variables (e.g., gender, smoking status, in-hospital mortality) were presented as frequencies and percentages. Chi-square tests were employed to evaluate associations between categorical variables, and one-way ANOVA was used to compare Uricemia across groups (e.g., duration of COPD, mortality status). Statistical significance was set at $p < 0.05$, and analyses were conducted using SPSS version 26.

Ethical Consideration

Confidentiality and anonymity of the participants were ensured throughout the study[19]. Ethical approval was obtained from the Ethics Review Committee of Karachi University, and all procedures adhered to the principles outlined in the Declaration of Helsinki[20].

This methodology ensures robust data collection and analysis to comprehensively explore the association between hyperuricemia and in-hospital mortality in AECOPD patients.

RESULTS

Frequency Distribution:
Demographic and Clinical Characteristics

Out of the 150 patients presenting with acute exacerbation of COPD, most (42%) were 51–66 years old, followed by 34% aged 67–82 years. Just 8.6% were 83–98 years, and 15.4% were between 40 and 50 years. However, according to the inclusion criteria, only those aged 40 or older were included in the analysis. All records with an age less than 40 years were excluded from the final statistical analysis.

Of 150 patients, 107 were men (71%), and 43 were women (29%). In terms of smoking history, 41% were active smokers, 38% were previous smokers, and 21% were non-smokers. Thus, 79.0% of the patients had a smoking history, and 21.0% were non-smokers. These revised percentages correspond to the figures utilized in the abstract and tables.

In smoking history, 48% of patients had 31–50 pack-years, followed by 22% with 1–25 pack-years and 18% with no history of smoking. Lower percentages reported 51–75 pack-years (5.4%) and 76–100 pack-years (6.6%).

Duration of COPD

Most (77.5%) of the patients had COPD for 1–5 years. Approximately 18.5% had the condition for 6–10 years. Fewer than 3% and 1% had COPD for 11–15 years and 16–20 years, respectively.

In-Hospital Outcomes

Out of 150 patients, 45 (30%) were discharged, and 105 (70%) expired during hospitalization. The in-hospital mortality rate in this study was significantly higher than those reported in comparable settings, where mortality rates range from 20% to 35%[19,20]. The increased rate found in the present study could represent delayed presentation of patients, restricted availability of ICU facilities, and greater disease severity at presentation, all prevalent issues in public-sector tertiary care hospitals in Pakistan.

Statistical Analysis:

The Chi-Square test did not demonstrate a significant relationship between the categorical groups of age and uric acid levels ($p = 0.324$), as shown in **Table II**. The Linear-by-Linear Association produced a p-value of 0.014, indicating a significant linear trend: uric acid levels increase with age.

Table II: Chi-Square Test - Age × Uric Acid Level

Test	Value	df	p-value
Pearson Chi-Square	185.056	177	0.324
Likelihood Ratio	172.312	177	0.585
Linear-by-Linear Association	5.998	1	0.014

There was no statistically significant difference in uric acid levels among the various COPD duration groups ($p = 0.902$), as shown in **Table III**. This implies that disease duration doesn't have a significant impact on Uricemia in this patient group.

This test showed no significant correlation between COPD duration and uric acid levels ($p = 0.991$), as shown in **Table IV**, corroborating the ANOVA findings.

The correlation between Uricemia and in-hospital mortality was statistically significant ($p = 0.001$), as in **Table V**. This indicates that patients with higher levels of uric acid had significantly poorer outcomes, supporting hyperuricemia as a potential prognostic

indicator in AECOPD.

Table III:
One-Way ANOVA — Duration of COPD × Uricemia

Source	Sum of Squares	df	Mean Square	F	Sig. (p)
Between Groups	5.087	4	1.272	0.262	0.902
Within Groups	702.919	145	4.848		
Total	708.006	149			

Table IV:
Chi-Square Test - Duration of COPD × Uric Acid

Test	Value	df	p-value
Pearson Chi-Square	187.496	236	0.991
Likelihood Ratio	117.473	236	1.000
Linear-by-Linear Association	0.141	1	0.707

Table V: One-Way ANOVA - Mortality × Uricemia

Source	Sum of Squares	df	Mean Square	F	Sig. (p)
Between Groups	49.924	1	49.924	11.228	0.001
Within Groups	658.082	148	4.447		
Total	708.006	149			

DISCUSSION

This study indicates that hyperuricemia has a significant association with in-hospital death among patients with AECOPD. It also shows a linear relationship between serum uric acid and age, suggesting that elderly individuals are more susceptible to elevated uric acid levels and their associated complications. There was no association between uric acid levels and the age of COPD, though.

The 70% mortality observed here is much higher than in other national and international studies, where mortality ranges from 20% to 35% [18,19]. This disparity would most likely be caused by delayed access to health care, lack of available ICU beds, and late presentation of disease in a public tertiary care hospital setting. These same trends have been observed within under-resourced settings across South Asia.

The association of hyperuricemia with unfavourable outcomes is consistent with earlier findings [5,18,20,22]. Uric acid has been established as a marker of inflammation and oxidative stress, and its elevation may reflect underlying metabolic stress during acute exacerbations of disease. Pro-inflammatory cytokines, such as IL-6 and TNF-α, which are commonly elevated in hyperuricemia, may exacerbate respiratory failure, contributing to the observed relationship with increased mortality [21].

Notably, although age showed a trend toward correlation with uric acid, the Pearson test was non-significant, yet a linear trend was observed. This suggests that both comorbid disease and renal impairment with age could contribute to uric acid retention, as the literature supports an association between ageing and hyperuricemia and cardiovascular risk [24–28].

The absence of a substantial correlation between COPD duration and uric acid may reflect deficiencies in patient recall or the paroxysmal fluctuations of metabolic changes during acute exacerbations. Variable correlations between disease duration and Uricemia are also found in other works [29].

These findings suggest that uric acid levels should be considered during the routine assessment of patients with AECOPD, particularly in older people. Screening for hyperuricemia may identify patients at higher mortality risk, and early treatment, both therapeutic and medicinal, might more accurately predict prognosis [22,30]. Serum uric acid may also serve as a cost-effective biomarker in resource-limited environments.

Limitations

Limitations of the current study include its single-centre design, small sample size, and reliance on cross-sectional data, which preclude causal inference. Information regarding disease duration provided by patients may also be subject to recall bias. Future studies should employ multicenter, prospective designs and control for comorbidities, medications, and lifestyle factors that influence uric acid metabolism.

Future Directions

Longitudinal cohort and intervention trials are warranted to establish the impact of uric acid-lowering therapy on AECOPD outcomes. Molecular characterization of the inflammatory mechanisms underlying the association between uric acid and COPD severity may also provide clues to novel therapeutic strategies.

Clinical Implications:

The reported associations of hyperuricemia, advanced age, and increased mortality suggest that the measurement of serum uric acid during routine assessment in AECOPD patients could be justified. Screening for hypertension in elderly patients for hyperuricemia can detect at-risk patients for complications and mortality [23]. These patients can be closely monitored clinically and receive intensive treatment [33].

These results also provide preliminary evidence in favour of adding uric acid-lowering treatments, such as dietary modifications, xanthine oxidase inhibitors, or lifestyle interventions, to the management of high-risk AECOPD patients. While intriguing, these recommendations should be verified by randomized controlled trials.

Public Health Implications:

The findings highlight the importance of screening for hyperuricemia as an integral part of COPD management, especially among elderly patients. Prevention of uric acid can stem mortality during exacerbations. Public health educational campaigns

should recognize hyperuricemia as a potentially reversible risk factor in the course and prognosis of COPD.

Personalized Medicine:

Inclusion of serum uric acid testing in personalized care pathways for COPD may enhance risk stratification and optimize resource use. Identification of hyperuricemic patients allows clinicians to direct therapy, enhanced monitoring, and comorbid condition management to those at highest risk. Incorporating uric acid into existing prognostic models may refine predictive capability and improve individualized treatment planning.

CONCLUSION

This study finds a positive association of hyperuricemia with in-hospital mortality in patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD) at a tertiary care centre in Karachi. It also finds a positive linear association between age and serum uric acid concentration, which can be attributed to physiological ageing and lifestyle-related processes. Nonetheless, no association was found between hyperuricemia and the duration of COPD.

These results underscore the importance of critically assessing and controlling hyperuricemia as a significant determinant of AECOPD outcomes and complications. Although this cross-sectional study does not permit causal inference, its findings are valuable for informing public health policy and clinical practice in lower- and middle-income countries, such as Pakistan.

To confirm these results and draw conclusions about potential mediators, further research must conduct multicenter, longitudinal studies. To summarise, therapeutic control of hyperuricemia is a possible method to improve clinical outcomes and reduce mortality rates in AECOPD patients.

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AUTHOR CONTRIBUTION

Khushk SAK: Carried out the primary research and wrote the initial draft.
Ahmad N: Supervised the research.

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