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# 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 in the study. Early intervention and monitoring of elevated uric acid levels can lead to improved 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 functioning, with prevalence recorded at 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 during AECOPD would be valuable for management practices.

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 studies at the local level to elucidate the 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. Since there is scant literature available from this region exploring this relationship, the present study seeks to establish the link 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 its evidence to the previous works suggesting that metabolic abnormalities are 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

## LITERATURE REVIEW

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 have relations 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 outcome are still 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 investigations that have focused on the relationship between uric acid and the in-hospital mortality rate in the South Asian region, 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 in establishing the predictive value of uric acid level in targeting AECOPD but also in 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 $FEV_1/FVC < 0.70$, according to the GOLD guidelines. AECOPD was identified using Anthonisen's criteria (increased dyspnea, sputum volume, or 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]:

$$\mathbf{n=Z^2\ p\ x\ (1-p)\ /\ e^2}$$

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%).
- **e** = margin of error (8%)

The 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 uric acid in serum. 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, as per the inclusion criteria, only those above 40 years were considered for analysis. All records with an age less than 40 years were excluded from the final statistical analysis.

Of 150 patients, there were 107 men (71%) and 43 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 vary between 20% and 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.

**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 | | | |

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

**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 |

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 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 presents a linear relationship between serum uric acid and age, suggesting that elderly individuals are more susceptible to elevated uric acid and its resulting complications. There was no association between uric acid levels and the age of COPD, though.

70% mortality observed here is much higher than has been observed in other national and international studies, where mortalities range 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 was trending to correlate with uric acid, the Pearson test was non-significant, although 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 patient recall deficiencies or the paroxysmal fluctuation 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 the 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 through which uric acid is linked to COPD severity may also give clues about 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 utilization. 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 make conclusions regarding potential mediators, further research must conduct multicenter and 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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**Data Sharing Statement:** The corresponding author can provide the data proving the findings of this study on request. Privacy or ethical restrictions bound us from sharing the data publicly.

## AUTHOR CONTRIBUTION

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

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