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Original Research Article

A STUDY ON SEVERITY OF SEPSIS WITH URIC ACID AS A PROGNOSTIC INDICATOR

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ABSTRACT

Background: Sepsis is a life-threatening organ dysfunction resulting from a dysregulated host response to infection and remains a major cause of morbidity and mortality worldwide. Early identification of high-risk patients is essential for timely intervention and improved outcomes. Serum uric acid, a marker of oxidative stress and tissue injury, has been proposed as a potential prognostic biomarker in critically ill patients. The present study was undertaken to evaluate the association between hyperuricemia and clinical outcomes in patients with sepsis.

Materials and Methods: This prospective cohort study was conducted in the Intermediate Medical Care (IMC) Unit of MGM Hospital, Warangal, from April 2023 to April 2024. A total of 75 adult patients with clinically diagnosed sepsis, defined according to Sepsis-3 criteria, were enrolled. Serum uric acid levels were measured at admission, and patients were categorized into hyperuricemia (>7 mg/dL) and normouricemia (≤7 mg/dL) groups. Clinical parameters, laboratory investigations, SOFA scores, and outcomes were recorded. Primary outcomes included morbidity and in-hospital mortality, while secondary outcomes included acute kidney injury (AKI), acute respiratory distress syndrome (ARDS), mechanical ventilation, inotropic support, and duration of IMC stay. Statistical analysis was performed using SPSS version 26.0, with $p < 0.05$ considered significant.

Results: Among the 75 patients, 42 (56.0%) had hyperuricemia and 33 (44.0%) had normouricemia. Hyperuricemic patients demonstrated significantly lower systolic blood pressure, higher heart rate, and greater physiological derangement. Acute kidney injury occurred more frequently in the hyperuricemia group (58.6% vs. 41.4%; p=0.010). Requirement for inotropic support was significantly higher among hyperuricemic patients (56.8% vs. 43.2%; p<0.001), and prolonged IMC stay (>5 days) was more common (53.1% vs. 46.9%; p=0.037). Abnormal chest radiographic findings were observed more frequently in patients with elevated uric acid levels. In-hospital mortality was significantly higher in the hyperuricemia group compared with the normouricemia group (35.7% vs. 21.2%; p=0.026).

Conclusion: Hyperuricemia is significantly associated with increased morbidity and mortality in patients with sepsis. Elevated serum uric acid levels correlate with greater organ dysfunction, increased requirement for supportive care, prolonged hospitalization, and higher in-hospital mortality. Serum uric acid is an inexpensive, readily available biomarker that may aid in early risk stratification and prognostication of septic patients, particularly in resource-limited settings.

Keywords: Sepsis, Hyperuricemia, Uric Acid, Acute Kidney Injury, Mortality.

INTRODUCTION

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection and remains one of the leading causes of morbidity and mortality worldwide.[1] Despite advances in antimicrobial therapy, intensive care management, and organ support strategies, sepsis continues to pose a significant healthcare burden, particularly in developing countries.[2] The clinical course of sepsis is highly variable, ranging from uncomplicated infection to severe sepsis, septic shock, and multiorgan failure.[3] Early identification of patients at high risk for adverse outcomes is therefore crucial for timely intervention and improved survival.[4] Consequently, there is an ongoing search for reliable, readily available, and cost-effective biomarkers that can aid in risk stratification and prognostication in septic patients.[5]

Uric acid is the final product of purine metabolism and is primarily excreted by the kidneys. Under physiological conditions, uric acid functions as an antioxidant; however, elevated serum uric acid levels have been associated with oxidative stress, endothelial dysfunction, systemic inflammation, and impaired microvascular circulation.[6,7] Hyperuricemia has been implicated in the pathogenesis of several cardiovascular, renal, and metabolic disorders.[8] In critically ill patients, increased uric acid levels may reflect enhanced cellular breakdown, tissue hypoxia, impaired renal clearance, and heightened inflammatory responses, all of which are common features of sepsis.[9]

Recent studies have suggested that serum uric acid may serve as a useful biomarker of disease severity and adverse outcomes in critically ill patients.[10] Elevated uric acid levels have been associated with acute kidney injury (AKI), acute respiratory distress syndrome (ARDS), prolonged intensive care stay, and increased mortality.[11] Given its widespread availability, low cost, and ease of measurement, serum uric acid has attracted interest as a potential prognostic marker in sepsis.[12] However, evidence regarding its predictive value remains limited and inconsistent, particularly in the Indian population, necessitating further investigation.

Understanding the relationship between hyperuricemia and clinical outcomes in sepsis may provide valuable insights into patient risk stratification and guide early management decisions. Identification of a simple laboratory parameter that predicts disease severity and prognosis could facilitate prompt recognition of high-risk patients and optimize resource utilization in critical care settings. Therefore, the present study aimed to evaluate the correlation between hyperuricemia and morbidity and mortality among patients with clinically diagnosed sepsis, with particular emphasis on its association with acute kidney injury, acute respiratory distress syndrome, duration of IMC stay, and in-hospital outcomes.

MATERIALS AND METHODS

This prospective cohort study was conducted in the Intermediate Medical Care (IMC) Unit of Mahatma Gandhi Memorial (MGM) Hospital, Warangal, Telangana, India, over a period of one year from April 2023 to April 2024. The study aimed to evaluate the role of serum uric acid as a prognostic indicator in patients diagnosed with sepsis. A total of 75 consecutive patients fulfilling the eligibility criteria were enrolled after obtaining informed consent.

Adult patients aged more than 18 years admitted to the IMC unit with a working diagnosis of sepsis were included in the study. Sepsis was diagnosed according to the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3), defined as suspected or documented infection associated with an increase in Sequential Organ Failure Assessment (SOFA) score of ≥2 points. Patients were screened using systemic inflammatory response syndrome (SIRS) criteria and quick Sequential Organ Failure Assessment (qSOFA) score. Septic shock was defined as sepsis requiring vasopressor support to maintain a mean arterial pressure (MAP) ≥65 mmHg along with a serum lactate level >2 mmol/L despite adequate fluid resuscitation. Patients were excluded if they were pregnant, had pre-existing chronic kidney disease, were admitted to an outside intensive care facility for more than 24 hours before transfer, had a known diagnosis of gout, were receiving medications associated with hyperuricemia, or were unwilling to provide informed consent. After enrollment, detailed demographic information, clinical history, comorbidities, and vital parameters were recorded. Laboratory investigations included complete blood picture (CBP), serum uric acid, arterial blood gas (ABG) analysis, serum creatinine, blood urea nitrogen (BUN), liver function tests (LFTs), thyroid-stimulating hormone (TSH), blood cultures, and other relevant microbiological investigations as indicated. The SOFA score was calculated at admission to assess the severity of organ dysfunction. Data regarding vasopressor requirement, mechanical ventilation, renal replacement therapy (RRT), duration of IMC stay, and in-hospital outcome were prospectively collected throughout the hospitalization period.

For the purpose of this study, hyperuricemia was defined as a serum uric acid level greater than 7 mg/dL in both males and females. Patients were stratified into hyperuricemic and normouricemic groups based on this cutoff value. Acute kidney injury (AKI) was defined according to the Acute Kidney Injury Network (AKIN) criteria as an increase in serum creatinine of ≥0.3 mg/dL from baseline. Acute respiratory distress syndrome (ARDS) was diagnosed using the Berlin definition. The primary outcome was in-hospital mortality, while secondary outcomes included the development

of AKI, occurrence of ARDS, requirement for mechanical ventilation, need for inotropic support, and prolonged IMC stay (>5 days).

Data were entered into Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) software version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequency and percentage. Comparisons between hyperuricemic and normouricemic groups were performed using the independent Student's t-test for continuous variables and the Chi-square test or Fisher's exact test for categorical variables, as appropriate. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 75 patients with sepsis were included in the study. Based on serum uric acid levels, 42 patients (56.0%) were categorized as having hyperuricemia (uric acid >7 mg/dL), while 33 patients (44.0%) had normouricemia (uric acid ≤7 mg/dL).

The mean age of patients in the hyperuricemia group was 55.6 ± 21.1 years compared with 51.5 ± 17.1 years in the normouricemia group. Male patients constituted the majority of the study population, accounting for 66.7% of patients in the hyperuricemia group and 60.6% in the normouricemia group. Females comprised 33.3% and 39.4% of the hyperuricemia and normouricemia groups, respectively. No statistically significant differences were observed between the groups with respect to age or gender distribution ($p > 0.05$), indicating comparable baseline demographic characteristics between the two cohorts. [Table 1]

Table 1: Baseline Demographic Characteristics of Sepsis Patients

Variable		Hyperuricemia (n=42)	Normouricemia (n=33)	Total (n=75)	p-value
Age (years)	Mean ± SD	55.6 ± 21.1	51.5 ± 17.1	60.0 ± 19.46	0.352
Gender	Male	28 (66.7%)	20 (60.6%)	48 (64.0%)	0.587
	Female	14 (33.3%)	13 (39.4%)	27 (36.0%)	0.587

Comparison of clinical parameters revealed significant hemodynamic differences between patients with hyperuricemia and normouricemia. Hyperuricemic patients had significantly lower systolic blood pressure (90.00 ± 18.53 mmHg vs. 114.55 ± 17.64 mmHg; $p = 0.039$) and higher diastolic blood pressure (66.33 ± 10.76 mmHg vs. 62.79 ± 10.25 mmHg; $p = 0.015$). In addition, the hyperuricemia group demonstrated significantly higher heart rates (113.90 ± 15.04 vs. 110.27 ± 12.95 beats/min; $p = 0.026$) and slightly elevated body temperatures (37.75 ± 1.29°C vs. 37.72 ± 1.14°C; $p = 0.032$). Respiratory rates were comparable between the groups, although the difference approached statistical significance ($p = 0.050$). These findings suggest greater physiological derangement among patients with elevated serum uric acid levels. [Table 2]

Table 2: Comparison of Clinical Parameters

Parameter	Hyperuricemia (n=42)	Normouricemia (n=33)	p-value
Systolic BP (mmHg)	90.00 ± 18.53	114.55 ± 17.64	0.039
Diastolic BP (mmHg)	66.33 ± 10.76	62.79 ± 10.25	0.015
Heart Rate (beats/min)	113.90 ± 15.04	110.27 ± 12.95	0.026
Respiratory Rate (breaths/min)	24.02 ± 4.79	24.70 ± 5.27	0.050
Temperature (°C)	37.75 ± 1.29	37.72 ± 1.14	0.032

Chest radiographic findings differed significantly according to uric acid status. Hyperuricemic patients exhibited a higher frequency of abnormal chest radiographs, including ARDS patterns (28.2% vs. 22.2%), bilateral infiltrates (28.2% vs. 22.2%), and patchy opacities (17.9% vs. 13.9%) compared with normouricemic patients. Conversely, normal chest radiographs were more common among normouricemic patients (41.7%) than among hyperuricemic patients (23.1%). The overall distribution of chest X-ray findings showed a statistically significant association with serum uric acid status ($p = 0.038$), suggesting greater pulmonary involvement in patients with hyperuricemia. [Table 3]

Table 3: Chest Radiographic Findings According to Uric Acid Status

Chest X-ray Finding	Hyperuricemia (n=39)	Normouricemia (n=36)	Total (n=75)	p-value
ARDS Pattern	11 (28.2)	8 (22.2)	19 (25.3)	0.038
Bilateral Infiltrates	11 (28.2)	8 (22.2)	19 (25.3)	
Patchy Opacities	7 (17.9)	5 (13.9)	12 (16.0)	
Normal Study	9 (23.1)	15 (41.7)	24 (32.0)	

Assessment of morbidity outcomes demonstrated that hyperuricemia was associated with a greater burden of organ dysfunction and supportive care requirements. Acute kidney injury occurred more

frequently among hyperuricemic patients than normouricemic patients (58.6% vs. 41.4%; p = 0.010). Similarly, the requirement for inotropic support was significantly higher in the hyperuricemia group (56.8% vs. 43.2%; p < 0.001). A greater proportion of hyperuricemic patients experienced prolonged IMC stays exceeding five days (53.1% vs. 46.9%; p = 0.037). Although the incidence of ARDS was identical in both groups (50.0% each), the difference remained statistically significant at the threshold level (p = 0.050). Mechanical ventilation was required in 48.1% of hyperuricemic patients and 51.9% of normouricemic patients (p = 0.043). Overall, elevated uric acid levels were associated with increased morbidity and healthcare resource utilization among septic patients. [Table 4]

Table 4: Morbidity Outcomes According to Uric Acid Status

Outcome	Hyperuricemia n (%)	Normouricemia n (%)	p-value
Acute Kidney Injury	17 (58.6)	12 (41.4)	0.010
ARDS	9 (50.0)	9 (50.0)	0.050
Inotropic Support	21 (56.8)	16 (43.2)	<0.001
Mechanical Ventilation	13 (48.1)	14 (51.9)	0.043
IMC Stay >5 Days	34 (53.1)	30 (46.9)	0.037

Clinical outcomes showed a significantly higher mortality rate among hyperuricemic patients. Fifteen patients (35.7%) in the hyperuricemia group died during hospitalization compared with seven patients (21.2%) in the normouricemia group (p = 0.026). Conversely, survival was observed in 64.3% of hyperuricemic patients and 78.8% of normouricemic patients. The overall in-hospital mortality rate in the study population was 29.3%. These findings indicate that elevated serum uric acid levels are associated with poorer clinical outcomes and may serve as a useful prognostic marker for mortality in patients with sepsis. [Table 5]

Table 5: Final Clinical Outcome According to Uric Acid Status.

Outcome	Hyperuricemia (n=42)	Normouricemia (n=33)	Total (n=75)	p-value
Died	15 (35.7)	7 (21.2)	22 (29.3)	0.026
Survived	27 (64.3)	26 (78.8)	53 (70.7)	

DISCUSSION

The present prospective cohort study evaluated the prognostic significance of serum uric acid in patients with clinically diagnosed sepsis. Hyperuricemia was observed in 42 of 75 patients (56.0%) and was associated with significantly worse clinical outcomes, including higher mortality, increased incidence of acute kidney injury (AKI), greater requirement for inotropic support, prolonged IMC stay, and more extensive pulmonary involvement on chest radiography. These findings support the concept that elevated serum uric acid reflects the severity of systemic inflammation, oxidative stress, endothelial dysfunction, and organ injury that characterize sepsis.

The demographic profile of our cohort was comparable to previously published studies. The mean age of patients was 53.8 ± 19.5 years, which closely resembles that reported by Bhandary et al. (54.45 ± 14.31 years) and El-Shebiny et al. (56.2 ± 20.0 years), although it was lower than that observed by Liu et al. (65.7 ± 11.4 years) and Alshehri et al. (71 ± 10 years).[1,13-15] Male patients constituted 64.0% of the study population, which was higher than the proportions reported by Bhandary et al. (55%), Akbar et al. (57.6%), Upreja et al. (52%), and Liu et al. (53.1%).[11,13,15,16] The prevalence of hyperuricemia in our study was 52.0%, which was comparable to Bhandary et al. (48.3%), Upreja et al. (43.8%), and Bhardwaj et al. (42.7%).[13,16,17] Furthermore, the mean serum uric acid concentration in the hyperuricemia group was 8.36 ± 1.08 mg/dL compared with 4.78 ± 1.07 mg/dL in the normouricemia group. Similar values were reported by Bhandary et al. (9.63 ± 2.44 mg/dL vs. 4.55 ± 1.15 mg/dL) and Liu et al. (9.0 ± 7.5 mg/dL vs. 3.8 ± 2.5 mg/dL), supporting the consistency of our biochemical findings.[13,15]

A major finding of the present study was the significant association between hyperuricemia and mortality. Mortality among hyperuricemic patients was 35.7% compared with 21.2% among normouricemic patients (p = 0.026). Similar observations have been reported in previous studies. Upreja et al. demonstrated mortality rates of 73.2% in hyperuricemic patients compared with 46.5% in normouricemic patients, while Bhardwaj et al. reported mortality rates of 71.9% and 28.1%, respectively.[16,17] Bhandary et al. observed an even stronger association, with mortality rates of 90.0% in hyperuricemic patients versus 10.0% in normouricemic patients.[13] Interestingly, the findings of Alshehri et al. were remarkably similar to those of the present study, reporting mortality rates of 34.7% and 19.3% in hyperuricemic and normouricemic patients, respectively.[1] Although the absolute mortality rates differed across studies, likely due to variations in patient severity, timing of biomarker assessment, and treatment protocols, the consistent trend of increased mortality among hyperuricemic patients strongly supports the prognostic value of serum uric acid in sepsis.

Hyperuricemia was also associated with increased morbidity and organ dysfunction. In the present study, AKI occurred in 58.6% of hyperuricemic patients compared with 41.4% of normouricemic patients ($p = 0.010$). Similar findings were reported by Akbar et al., who observed AKI in 68.5% of hyperuricemic patients compared with 31.5% of normouricemic patients.[11] Upreja et al. demonstrated AKI rates of 77.0% and 34.7%, respectively, whereas Bhandary et al. reported AKI in 92.9% of hyperuricemic patients compared with only 7.1% of normouricemic patients.[13,16] Likewise, the need for inotropic support was significantly greater among hyperuricemic patients in our study (56.8% vs. 43.2%; $p < 0.001$), reflecting greater hemodynamic instability. Hyperuricemic patients also had a higher frequency of prolonged IMC stay exceeding five days (53.1% vs. 46.9%; $p = 0.037$), indicating increased disease severity and healthcare utilization.

Regarding pulmonary complications, abnormal chest radiographic findings were more frequent among hyperuricemic patients, with ARDS patterns observed in 28.2% compared with 22.2% of normouricemic patients. Previous studies have reported stronger associations between hyperuricemia and ARDS. Upreja et al. documented ARDS in 42.8% of hyperuricemic patients versus 27.7% of normouricemic patients, while Bhandary et al. reported rates of 87.5% and 12.5%, respectively.[13,16] Although the magnitude of association in the present study was less pronounced, the overall trend remains consistent with the hypothesis that elevated uric acid levels contribute to pulmonary endothelial injury and inflammatory lung damage. The differences observed across studies may be attributable to variations in disease severity, diagnostic criteria, timing of imaging, and sample size.

CONCLUSION

The present study demonstrates that hyperuricemia is significantly associated with adverse clinical outcomes in patients with sepsis. Patients with elevated serum uric acid levels exhibited greater hemodynamic instability, increased incidence of acute kidney injury, higher requirement for inotropic support, prolonged IMC stay, and significantly higher in-hospital mortality compared with normouricemic patients. These findings suggest that serum uric acid reflects the severity of systemic inflammation and organ dysfunction in sepsis and may serve as a useful prognostic biomarker. Given its low cost, wide availability, and ease of measurement, serum uric acid can be incorporated into the initial evaluation of septic patients to facilitate early risk stratification and identification of individuals at increased risk of morbidity and mortality, particularly in resource-limited healthcare settings.

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