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Role Of Serum Uric Acid as A Prognostic Marker for Sepsis and Development of Acute Kidney Injury

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ABSTRACT

Background Sepsis remains one of the leading causes of morbidity and mortality worldwide despite advances in critical care medicine. Early identification of patients at risk of severe disease, acute kidney injury (AKI), prolonged intensive care unit (ICU) stay, and mortality is essential for improving outcomes. Serum uric acid, a product of purine metabolism, has emerged as a potential biomarker reflecting oxidative stress, inflammation, endothelial dysfunction, and tissue hypoxia. Elevated serum uric acid levels may therefore serve as an early predictor of adverse outcomes in sepsis.
Methods This prospective observational study was conducted at Dr B R Ambedkar Medical College and Hospital, Bangalore, from June 2025 to December 2025. A total of 100 adult patients diagnosed with sepsis according to qSOFA criteria were included. Serum uric acid levels were measured at admission. Clinical parameters including SOFA score, APACHE II score, development of AKI according to KDIGO criteria, duration of ICU stay, and in-hospital mortality were recorded. Statistical analysis was performed to determine associations between admission uric acid levels and clinical outcomes.
Results Elevated serum uric acid levels (>7 mg/dL) were observed in 48% of patients. AKI developed in 42% of patients during hospitalization. Patients with hyperuricemia demonstrated significantly higher SOFA scores, APACHE II scores, longer ICU stays, increased incidence of AKI, and higher mortality rates compared to patients with normal uric acid levels ($p < 0.001$). Admission serum uric acid showed a positive correlation with disease severity and adverse outcomes.
Conclusion Serum uric acid is a readily available, inexpensive, and reliable biomarker that demonstrates significant association with sepsis severity, development of AKI, prolonged ICU stay, and mortality. Measurement of serum uric acid at admission may aid in early risk stratification and prognostication in patients with sepsis.

***Keywords**: Sepsis, Serum Uric Acid, Acute Kidney Injury, SOFA Score, APACHE II Score, Prognostic Marker, Mortality, Critical Care*

INTRODUCTION

Modern medicine has witnessed remarkable advances in antimicrobial therapy, intensive care monitoring, organ support technologies, and evidence-based critical care practices. Despite these achievements, sepsis continues to represent one of the greatest challenges faced by healthcare systems worldwide. It remains a major cause of hospitalization, intensive care unit admission, multi-organ dysfunction, and mortality across both developed and developing nations. The burden is particularly significant in low- and middle-income countries, where delayed diagnosis, limited healthcare resources, and high infectious disease prevalence contribute substantially to poor outcomes.

Sepsis is currently defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. Unlike uncomplicated infections, sepsis represents a complex interaction between invading pathogens and the host immune system. The resulting cascade of inflammatory mediators, endothelial injury, microvascular dysfunction, coagulation abnormalities, and metabolic derangements often culminates in organ failure. Even with aggressive treatment, mortality rates remain unacceptably high, ranging from 20% to over 50% depending on disease severity and the presence of septic shock.

One of the greatest difficulties in sepsis management is the unpredictable nature of disease progression. Some patients respond rapidly to treatment and recover without significant complications, while others develop severe organ dysfunction despite seemingly similar clinical presentations. Acute kidney injury (AKI) is among the most common and devastating complications encountered during sepsis. The development of AKI not only increases mortality but also prolongs hospitalization, escalates healthcare costs, and predisposes survivors to chronic kidney disease in the future.

Given this variability in clinical outcomes, considerable effort has been directed toward identifying biomarkers that can assist clinicians in early risk stratification. An ideal prognostic marker should be inexpensive, easily available, reproducible, and capable of predicting disease severity before irreversible organ damage occurs. While biomarkers such as procalcitonin, lactate, C-reactive protein, interleukins, and presepsin have been extensively studied, many remain expensive or unavailable in resource-limited settings.

In this context, serum uric acid has attracted growing interest as a potential prognostic indicator in critically ill patients. Traditionally regarded merely as a metabolic by-product associated with gout and renal stones, uric acid is now recognized as an important mediator of oxidative stress, endothelial dysfunction, inflammation, and tissue injury. Elevated serum uric acid levels have been linked to cardiovascular disease, hypertension, chronic kidney disease, metabolic syndrome, and adverse outcomes in critical illness.

Recent evidence suggests that hyperuricemia may reflect the severity of cellular injury and tissue hypoxia occurring during sepsis. Increased cellular turnover, enhanced purine degradation, mitochondrial dysfunction, and impaired renal clearance contribute to elevated uric acid levels in critically ill patients. These mechanisms overlap significantly with the pathophysiological processes responsible for sepsis-induced organ dysfunction, making uric acid a biologically plausible prognostic marker.

The relationship between serum uric acid and acute kidney injury deserves particular attention. Uric acid is not merely a marker of impaired renal function but may actively contribute to kidney injury through several mechanisms. Experimental studies have demonstrated that elevated uric acid levels induce endothelial dysfunction, activate inflammatory pathways, stimulate oxidative stress, and promote renal vasoconstriction. These effects may exacerbate the already compromised renal perfusion observed during sepsis, thereby increasing susceptibility to AKI.

The growing interest in uric acid stems from its potential utility as a simple laboratory parameter capable of identifying high-risk patients early in the disease course. Since serum uric acid estimation is inexpensive and routinely available even in peripheral healthcare settings, its incorporation into sepsis assessment protocols could provide significant clinical value.

THE GLOBAL BURDEN OF SEPSIS

Sepsis affects millions of individuals annually and remains a leading cause of death worldwide. According to recent estimates, nearly 49 million cases of sepsis occur globally each year, resulting in approximately 11 million deaths. This accounts for almost one-fifth of all global deaths.

The burden is disproportionately higher in developing countries where infectious diseases remain prevalent and access to critical care services may be limited. India contributes substantially to the global sepsis burden due to its large population, high prevalence of infectious diseases, and increasing rates of antimicrobial resistance.

Sepsis affects individuals across all age groups, although extremes of age, immunocompromised states, diabetes mellitus, malignancy, chronic kidney disease, and chronic liver disease significantly increase susceptibility. Respiratory tract infections, urinary tract infections, abdominal infections, and bloodstream infections remain the most common sources of sepsis.

The economic implications are equally profound. Sepsis-related hospitalizations are associated with prolonged ICU stay, increased resource utilization, repeated investigations, expensive therapies, and long-term rehabilitation needs among survivors. Consequently, identifying reliable predictors of disease severity remains an important clinical priority.

ACUTE KIDNEY INJURY IN SEPSIS

Among the numerous complications associated with sepsis, acute kidney injury occupies a particularly important position because of its frequency and prognostic significance.

Sepsis accounts for nearly half of all AKI cases encountered in intensive care units worldwide. Depending on disease severity and patient characteristics, the incidence of sepsis-associated AKI ranges from 30% to 60%.

Historically, sepsis-induced AKI was attributed primarily to renal hypoperfusion. However, contemporary evidence suggests a much more complex pathophysiology involving inflammatory injury, endothelial dysfunction, microvascular abnormalities, mitochondrial impairment, tubular cell apoptosis, and immune-mediated damage.

The occurrence of AKI in sepsis substantially increases mortality. Studies have consistently demonstrated mortality rates exceeding 40–50% among septic patients who develop AKI. Furthermore, survivors frequently experience prolonged hospitalization and increased risk of chronic kidney disease.

Given these serious consequences, early identification of patients at risk for AKI remains a crucial aspect of sepsis management.

URIC ACID: MORE THAN A METABOLIC BY-PRODUCT

Uric acid is the final product of purine metabolism in humans. Under physiological conditions, approximately two-thirds of uric acid is excreted by the kidneys, while the remaining third is eliminated through the gastrointestinal tract.
Traditionally, uric acid was considered merely a biochemical marker associated with gout and nephrolithiasis. However, advances in molecular biology and experimental medicine have revealed its broader role in inflammatory and oxidative processes.

At physiological concentrations, uric acid possesses antioxidant properties. However, under pathological conditions, elevated uric acid may act as a pro-inflammatory mediator. It stimulates activation of the NLRP3 inflammasome, promotes cytokine release, enhances oxidative stress, induces endothelial dysfunction, and contributes to microvascular injury.
These mechanisms closely mirror the pathological events observed during sepsis. Consequently, elevated serum uric acid may serve as an indirect marker of the intensity of systemic inflammation and tissue injury.

PATHOPHYSIOLOGICAL BASIS FOR HYPERURICEMIA IN SEPSIS

Several mechanisms contribute to elevated serum uric acid levels during sepsis.

Firstly, severe infection increases cellular turnover and tissue breakdown, resulting in accelerated purine metabolism. The degradation of nucleic acids generates large quantities of uric acid.

Secondly, tissue hypoxia and mitochondrial dysfunction promote ATP depletion. ATP degradation leads to accumulation of hypoxanthine and xanthine, which are subsequently converted into uric acid by xanthine oxidase.

Thirdly, oxidative stress stimulates xanthine oxidase activity. This enzyme not only generates uric acid but also produces reactive oxygen species, amplifying tissue injury.

Fourthly, renal dysfunction commonly encountered during sepsis reduces uric acid excretion, further contributing to hyperuricemia.

Finally, inflammatory cytokines alter renal tubular handling of uric acid and impair glomerular filtration, resulting in progressive accumulation.

The convergence of these pathways provides strong biological plausibility for the association between elevated uric acid levels and adverse clinical outcomes in sepsis.

METHODOLOGY

Study Design

This study was designed as a prospective observational study aimed at evaluating the role of serum uric acid as a prognostic marker in patients with sepsis and its association with the development of acute kidney injury.

Study Setting

The study was conducted at Dr B R Ambedkar Medical College and Hospital, Bangalore, a tertiary care teaching hospital catering to a diverse patient population.
The study duration extended from June 2025 to December 2025.

Study Population

A total of 100 consecutive adult patients admitted with sepsis were included in the study.

Inclusion Criteria

Patients fulfilling all the following criteria were included:

- Age ≥18 years
- Clinical diagnosis of sepsis
- qSOFA score ≥2 at presentation
- Willingness to participate in the study

Exclusion Criteria

- Known chronic kidney disease stage 4 or 5
- Chronic dialysis patients
- Known gout or hyperuricemia on treatment
- Hematological malignancies
- Current use of uric acid lowering drugs
- Pregnancy
- Recent chemotherapy

Data Collection

After obtaining informed consent, demographic and clinical details were recorded.
Parameters documented included:

1. Age
2. Gender
3. Source of infection
4. Comorbidities
5. qSOFA score
6. SOFA score
7. APACHE II score
8. ICU stay duration
9. Mortality outcome

Laboratory Assessment

Blood samples were collected at admission.
Investigations included:

- Complete blood count
- Renal function tests
- Liver function tests
- Serum electrolytes
- Arterial blood gas analysis
- Serum uric acid level

Hyperuricemia was defined as serum uric acid >7 mg/dL.

Outcome Measures

1. Primary Outcome:
2. Development of AKI according to KDIGO criteria
3. Secondary Outcomes:
    - SOFA score severity
    - APACHE II score severity
    - ICU length of stay
    - In-hospital mortality

Statistical Analysis

Data were analysed using SPSS software version 26.
Continuous variables were expressed as mean ± standard deviation.
Categorical variables were expressed as percentages.
Chi-square test and Student's t-test were used where appropriate.
Pearson correlation coefficient was calculated to assess associations between serum uric acid and clinical outcomes.
A p-value <0.05 was considered statistically significant.

RESULTS

Demographic Characteristics

A total of 100 patients were included.

Table 1: Baseline Characteristics

Variable	Value

Mean Age	54.8 ± 15.2 years
Male	64 (64%)
Female	36 (36%)
Diabetes Mellitus	41 (41%)
Hypertension	37 (37%)
Mean qSOFA	2.4 ± 0.5
Mean SOFA	8.2 ± 3.4
Mean APACHE II	18.5 ± 7.2

Table 2: Sources of Sepsis

Source	**Number (%)**
Pneumonia	38 (38%)
Urinary Tract Infection	24 (24%)
Intra-abdominal Infection	18 (18%)
Skin and Soft Tissue Infection	12 (12%)
Bloodstream Infection	8 (8%)

Table 3: Serum Uric Acid Distribution

Uric Acid Category	**Number**
≤7 mg/dL	52 (52%)
>7 mg/dL	48 48%)

Mean serum uric acid level was 7.3 ± 2.1 mg/dL.

Table 4: Association Between Uric Acid and AKI

Uric Acid	**AKI**	**No AKI**
≤7 mg/dL	10	42
>7 mg/dL	32	16

p <0.001

AKI developed in 42% of study participants. Patients with elevated serum uric acid had significantly higher incidence of AKI.

Table 5: Association With Disease Severity

Parameter	**Uric Acid ≤7**	**Uric Acid >7**
SOFA Score	6.1 ± 2.4	10.5 ± 3.1
APACHE II	14.3 ± 5.2	23.1 ± 6.3

p <0.001

Table 6: ICU Stay

Uric Acid Group	ICU Stay
≤7 mg/dL	5.6 ± 2.1 days
>7 mg/dL	10.2 ± 4.8 days

p <0.001

Table 7: Mortality Analysis

Uric Acid	Survived	Died
≤7 mg/dL	48	4
>7 mg/dL	31	17

Mortality Rate:
- Normal uric acid: 7.7%
- Elevated uric acid: 35.4%

p <0.001

DISCUSSION

The present study demonstrates a significant association between admission serum uric acid levels and adverse outcomes among patients with sepsis. Elevated serum uric acid was associated with increased disease severity, higher incidence of acute kidney injury, prolonged ICU stay, and increased mortality.

Nearly half of the study population exhibited hyperuricemia at admission. This finding is consistent with previous studies suggesting that elevated uric acid levels are common in critically ill patients and reflect underlying metabolic stress and tissue injury.

The strongest association observed in our study was between serum uric acid and development of AKI. Patients with hyperuricemia had more than three times greater risk of developing AKI compared to those with normal uric acid levels. Similar findings have been reported by Ejaz et al. and Lapsia et al., who demonstrated that elevated uric acid independently predicts acute kidney injury in critically ill populations.

Several biological mechanisms may explain this relationship. Elevated uric acid contributes to endothelial dysfunction, reduced nitric oxide bioavailability, renal vasoconstriction, oxidative stress, and inflammatory activation. These processes may exacerbate the microvascular abnormalities already present in sepsis, thereby increasing susceptibility to renal injury.

A significant correlation was also observed between serum uric acid and severity scores. Patients with elevated uric acid demonstrated markedly higher SOFA and APACHE II scores. This observation supports the hypothesis that serum uric acid reflects the overall burden of organ dysfunction and systemic inflammation.

The association between hyperuricemia and prolonged ICU stay further emphasizes its clinical relevance. Patients with elevated uric acid required almost twice the duration of intensive care support compared to those with normal levels. Prolonged ICU stay is frequently associated with greater healthcare expenditure, increased nosocomial infections, and poorer long-term outcomes.

Perhaps the most clinically important finding was the significant association between admission uric acid and mortality. Mortality among patients with hyperuricemia exceeded 35%, compared to less than 10% among patients with normal uric acid levels. This substantial difference highlights the potential utility of serum uric acid as an early prognostic marker.

The relationship between uric acid and mortality may be explained by its association with oxidative stress, endothelial dysfunction, mitochondrial injury, and progressive organ failure. Elevated uric acid likely reflects the cumulative impact of these pathological processes rather than serving solely as a marker of renal impairment.

One of the major strengths of the present study is its prospective design and comprehensive assessment of clinically relevant outcomes including AKI, ICU stay, severity scores, and mortality. Furthermore, serum uric acid measurement is inexpensive, widely available, and easily reproducible, making it particularly attractive for use in resource-limited settings.

However, certain limitations should be acknowledged. The study was conducted at a single tertiary care center, potentially limiting generalizability. The sample size, although adequate for detecting significant associations, remains relatively modest. Serial uric acid measurements were not performed, and therefore dynamic changes during hospitalization could not be assessed. Future multicenter studies with larger populations and longitudinal follow-up may provide additional insights.

Despite these limitations, the findings strongly support the role of serum uric acid as a useful prognostic biomarker in sepsis.

CONCLUSION

Serum uric acid measured at admission demonstrates significant association with sepsis severity, development of acute kidney injury, prolonged ICU stay, and in-hospital mortality. Patients with elevated serum uric acid levels are more likely to develop organ dysfunction and experience adverse clinical outcomes.

As a simple, inexpensive, and universally available laboratory parameter, serum uric acid offers considerable potential for early risk stratification in sepsis. Incorporation of serum uric acid into routine sepsis evaluation may help identify high-risk patients who require closer monitoring and aggressive management.

Further large-scale multicentric studies are warranted to validate these findings and establish optimal cut-off values for prognostic use. Future research should also explore whether interventions targeting hyperuricemia can influence outcomes in patients with sepsis.

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