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ASSOCIATION BETWEEN HYPERURICEMIA AND ACUTE KIDNEY INJURY IN CRITICALLY ILL PATIENTS WITH SEPSIS

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Abstract

Objective:
To determine the association between hyperuricemia and acute kidney injury in critically ill patients with sepsis.

Methods:
This prospective cohort study involved 60 patients and was carried out at the Department of Medicine, Nishtar Hospital in Multan between December 2024 and April 2025. The study included patients aged 20 to 65 years who were admitted with sepsis. The patients were categorized as exposed (hyperuricemia) and unexposed (no hyperuricemia). All the patients were managed for sepsis as per hospital protocol. Daily serum creatinine levels were measured for up to 7 days after admission to determine the occurrence of AKI.

Results:
The study participants had a mean age of 55.1 ± 6.4 years. There were 32 males (53.3%) and 28 females (46.7%). Regarding hyperuricemia, 17 participants (28.3%) had the condition while 43 (71.7%) did not. In the group with hyperuricemia (exposed group, n=17), 13 participants (76.5%) developed AKI, while 4 (23.5%) did not. In the non-exposed group (n=43), 16 participants (37.2%) developed AKI, and 27 (62.8%) did not. The relative risk (RR) of developing AKI in the exposed group compared to the non-exposed group was 2.05 (1.28 to 3.28). This association was statistically significant (P = 0.003).

Conclusion:
Hyperuricemia significantly increases the risk of AKI in patients of sepsis. So serum uric acid can be used as a potential predictive marker to predict AKI in sepsis patients.

INTRODUCTION:

Sepsis is a critical and potentially fatal condition in which the body's response to infection leads to widespread organ dysfunction.[1] It occurs when infection or suspected infection results in a significant increase in the Sequential Organ Failure Assessment (SOFA) score by at least two points.[2] Globally, sepsis affects over 19 million individuals annually, contributing to high mortality rates and substantial healthcare expenses.[3] Despite advances in medical care, sepsis remains a major challenge in intensive care units, accounting for more than 30% of short-term ICU deaths.[4]

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Acute kidney injury (AKI) is a common complication of sepsis, occurring in 40–50% of patients. The mortality rate for septic patients with AKI is 50% higher than for those without AKI.[5] The mechanisms behind sepsis-related AKI are complex. Uric acid, the end product of purine breakdown, is excreted by the kidneys and can cause renal damage via crystal-dependent and non-crystal-dependent mechanisms, including vasoconstriction, oxidative stress, and inflammation.[6] Hyperuricemia has been identified as an independent risk factor for the initiation and progression of CKD and AKI.[7]

Uric acid results from purine breakdown, mainly excreted through urine. During sepsis, hyperuricemia occurs due to increased production and decreased excretion. Uric acid may cause AKI by activating systemic pro-inflammatory cytokines like tumor necrosis factor and inducing oxidative stress.[8] Furthermore, uric acid crystals can block renal tubules, causing direct tubular injury.[9]

The aim of this study was to determine the association between hyperuricemia and acute kidney injury in critically ill patients with sepsis.

METHODS:

This prospective cohort study involved 60 patients and was carried out at the Department of Medicine, Nishtar Hospital in Multan between December 2024 and April 2025. The study included patients aged 20 to 65 years who were admitted with sepsis. Exclusion criteria encompassed individuals with a history or medical records indicating end-stage renal disease or renal transplantation, patients with acute kidney injury (AKI) or those who underwent renal replacement therapy (RRT) on the day of ICU admission, patients whose serum creatinine levels were not re-evaluated after ICU admission, and individuals treated with aminoglycoside antibiotics or vancomycin. Informed consent was obtained from each participant.

All the enrolled patients had blood samples drawn by standard techniques for measurement of serum uric acid and serum creatinine. All the tests were performed from a single laboratory through standard methods. The patients were categorized as exposed (hyperuricemia) and unexposed (no hyperuricemia). Serum uric acid >7 mg/dL in men and >6 mg/dL in women on admission were labelled as having hyperuricemia.

All the patients were managed for sepsis as per hospital protocol. Daily serum creatinine levels were measured for up to 7 days after admission. Presence of any one of the following in a patient with sepsis was deemed positive for sepsis-related acute kidney injury (a). Increase in serum creatinine > 0.3 mg/dl within 48 hrs. Or (b) an increase in serum creatinine >1.5 times from baseline.

The data was analyzed using SPSS version 23. Normality of numerical data was checked with Shapiro-Wilk test. Age, uric acid, and serum creatinine levels are shown as mean ± SD. Gender, obesity, diabetes, smoking, hypertension, AKI, and hyperuricemia are displayed as counts and percentages. The risk of AKI between hyperuricemia and no-hyperuricemia groups was evaluated by calculating relative risk with 95% CI. P-value < 0.05 was considered significant.

RESULTS:

The study participants had a mean age of 55.1 ± 6.4 years. There were 32 males (53.3%) and 28 females (46.7%). Obesity was observed in 23 participants (38.3%), and 11 (18.3%) were smokers. Diabetes was present in 5 individuals (8.3%), and hypertension was found in 14 (23.3%). Regarding hyperuricemia, 17 participants (28.3%) had the condition while 43 (71.7%) did not (Table 1).

In the group with hyperuricemia (exposed group, n=17), 13 participants (76.5%) developed AKI, while 4 (23.5%) did not. In the non-exposed group (n=43), 16 participants (37.2%) developed AKI, and 27 (62.8%) did not. The relative risk (RR) of developing AKI in the exposed group compared to the non-exposed group was 2.05 (1.28 to 3.28). This association was statistically significant (P = 0.003) [Table 2].

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Table 1. Baseline Characteristics.

Age (Y)	55.1±6.4
Gender (Male/Female) (%)	32 (53.3%)/28 (46.7%)
Obesity (%)	23 (38.3%)
Smoking (%)	11 (18.3)
Diabetes (%)	05 (8.3%)
Hypertension (%)	14 (23.3%)
Hyperuricemia (%)	
Yes	17 (28.3%)
No	43 (71.7%)

Table 2. Association of Hyperuricemia with Acute Kidney Injury (AKI).

AKI	Exposed Group (N=17)	Non-Exposed Group (N=43)	RR (95% CI)	P-value
Yes (%)	13 (76.5%)	16 (37.2%)	2.05 (1.28-3.28)	0.003
No (%)	04 (23.5%)	27 (62.8%)		

DISCUSSION:

Uric acid is a waste product from purine metabolism that acts as an antioxidant by neutralizing free radicals. During sepsis, hyperuricemia occurs due to increased tissue breakdown and systemic oxidative stress. Sepsis-related ischemic-reperfusion injury also impairs uric acid metabolism. As kidney function declines, uric acid clearance decreases, leading to buildup. High uric acid levels switch its role to a proinflammatory agent, worsening oxidative stress and causing hemodynamic instability. Uric acid can crystallize as monosodium urate, activating the NLRP3 inflammasome and releasing cytokines like IL-1β and IL-18, which increase inflammation, damage the endothelium, and may cause organ failure, especially in kidneys and lungs.[10, 11]

Patients with sepsis face a higher chance of developing AKI because systemic hypotension can decrease blood flow to the kidneys, which may lead to kidney problems.[12] In addition, hyperuricemia can contribute to AKI through various pathways, including direct tubular damage from crystal buildup and indirect injury caused by vasoactive mediators, pro-inflammatory markers, and oxidative stress.[13] Uric acid might also contribute to AKI by causing renal vasoconstriction, a process that can be triggered by activation of the renin-angiotensin system, catecholamine release, and reduced nitric oxide levels.[14]

In our study, we found a significant association of hyperuricemia with the occurrence of AAKI. This finding is corroborated by the research conducted by Akbar et al. They performed a prospective study involving 144 patients diagnosed with sepsis and determined that uric acid levels of ≥ 7 mg/dL serve as independent risk factors for acute kidney injury (AKI) as well as AKI-associated mortality upon admission to the intensive care unit (ICU). The probability of hyperuricemia occurring alongside AKI is approximately 68.5%, whereas the likelihood of hyperuricemia occurring without AKI is approximately 31.5%. These findings are statistically significant, with a P value of less than 0.001.[15]

Jiang Y and colleagues studied 634 adult sepsis patients in the ICU. They found that 25.7% developed hyperuricemia, while 51.5% experienced AKI. The AKI incidence was significantly higher in patients with hyperuricemia at 76.7%, compared to 42.3% in those without ($p<0.05$).[16] Cheungpasitporn W and team examined 1,435 hospitalized adults, among whom 263 (18%) developed AKI. The rate of AKI increased with higher serum uric acid levels at admission: 7.4% for <3.4 mg/dl, 9% for 3.5-4.5 mg/dl, 16% for 4.5-5.8 mg/dl, 20.3% for 5.8-7.6 mg/dl, 22.2% for 7.6-9.4 mg/dl, and 36.7% for >9.4 mg/dl.[17]

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Furthermore, in 2017, Xu et al. published a meta-analysis encompassing 18 cohort studies involving 75,200 participants. They identified that hyperuricemia serves as a significant predictor of acute kidney injury (AKI).[18] Similarly, Yeter et al. established that uric acid levels exceeding 7 mg/dL were associated with AKI in critically ill patients, $P<0.001$.[19]

This study has certain limitations, such as a relatively small sample size and a brief follow-up duration. It is possible that some patients may have had elevated uric acid levels before developing sepsis, which could have contributed to increased risks of morbidity and mortality. Consequently, there is a rationale for screening the general population for hyperuricemia and considering treatment, aiming to enhance overall health outcomes.

The other limitations include the fact that we did not have baseline creatinine levels for the patients before admission, so we couldn't be certain about the percentage who had CKD prior to presentation. Therefore, to minimize potential errors, we used the patient's admission creatinine as the baseline to determine AKI.

CONCLUSION:

Hyperuricemia significantly increases the risk of AKI in patients of sepsis. So serum uric acid can be used as a potential predictive marker to predict AKI in sepsis patients.

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