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Original Article

# Prevalence of in Hospital Acute Kidney Injury in Patients Having Admission Hyperuricemia

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## Abstract

**Objective:** To determine the prevalence of acute kidney injury among patients admitted to tertiary-care hospital with hyperuricemia, secondary to any cause.

**Methods:** This descriptive study was conducted in a tertiary-care hospital from January, 2022 to June, 2023. A total of 118 patients were selected by using non-probabilistic consecutive sampling. Patients having admission serum uric acid levels ≥ 7 mg/dl were labeled as having admission-hyperuricemia. Patients developing AKI during hospital stay were diagnosed using KDIGO guidelines as after-mentioned.

**Results:** The prevalence of AKI in patients having hyperuricemia at the time of admission to our hospital was recorded in 25.42%(n=30) whereas 74.58%(n=88) had no findings of AKI.

**Conclusion:** It has been shown that there is a greater risk of developing AKI in patients who have hyperuricemia upon admission. Nevertheless, it is essential to do multicenter trials in order to authenticate our findings.

**Keywords:** Acute kidney injury, hyperuricemia, serum uric acid level, serum creatinine

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## Introduction

Uric acid is the last byproduct of the metabolic breakdown of purines and has limited solubility in aqueous solutions. Approximately two-thirds of the body's uric acid is synthesised internally, whilst the remaining one-third is derived through the metabolic breakdown of dietary purines.[1] Approximately 70% of the uric acid is removed via renal excretion, with the remaining portion through the intestines.[1,2] Hyperuricemia may arise as a result of either excessive uric acid synthesis or by insufficient excretion. The primary aetiology of hyperuricemia in the majority of cases is attributed to insufficient excretion. Renal insufficiency is characterized by a reduction in the filtration of uric acid via glomerulus. Patients with acidosis have a reduction in tubular secretion, as a result of competition between organic acids and the production of uric acid. Increased tubular reabsorption of uric acid is seen in diuretic use and diabetes inspidus. Over-production of uric acid accounts for only a minority of the cases. Lesch Nyhan syndrome is one of the causes of over production of uric acid.[3]

The prevalence rate of asymptomatic hyperuricemia is around 2-13% in the United States. It is associated with increased morbidity and mortality. Symptomatic hyperuricemia presents as gout and nephrolithiasis.[4] The retention of urea and nitrogenous waste products is the hallmark symptom of AKI, also known as acute renal failure. The amount and composition of extracellular fluid and intracellular electrolytes are also disrupted.[5] The most important causes of AKI include acute tubular necrosis, pre-renal disease, urinary tract obstruction, glomerulonephritis and acute interstitial nephritis. Various diagnostic criteria have been used to assess acute kidney damage, such as the RIFLE criteria and the AKIN criteria.[6]

Uric acid has been hypothesized to have a role in the pathogenesis of AKI, with the potential to cause renal damage via crystal-dependent and crystal-independent mechanisms. Elevated amounts of uric acid have been shown to induce renal vasoconstriction and disrupt renal

autoregulation. It further exacerbates renal injury by promoting renal inflammatory pathways, resulting in chemokine expression and leukocyte infiltration. Crystal dependent pathway results in stone formation and acute uropathy seen in tumor lysis syndrome.[7] Previous research have posited a potential correlation between hyperuricemia and the onset of acute renal damage. The incidence of acute renal damage in individuals presenting with hyperuricemia at admission is around 22%.[8]

However, no local study for estimation of this prevalence has been done in our population. International studies done to calculate this prevalence are not applicable to our community. This study shall help us to ascertain the significance and impact of hyperuricemia on AKI and possibly suggest a role of uricosuric agents in it's prevention. The purpose of this research is to determine the prevalence of AKI among patients admitted to tertiary-care hospital with hyperuricemia, secondary to any cause.

## Methods

**Study design:** It was descriptive case series.

**Study place:** Study was conducted in a tertiary-care hospital.

**Duration of study:** 18 months (From: January, 2022 to June, 2023).

**Sample size:** Using the World Health Organization (WHO) calculator for the sample size 'n' estimation. The sample size is of 118 by using 95% confidence level and 7.5% Margin of Error with expected prevalence of in-hospital AKI in patients having admission hyperuricemia to be 22.2%8.

**Sampling technique:** It was non-probability consecutive sampling.

**Inclusion criteria:** All participants aged between 18 to 80 years, both genders, whose uric acid levels were over 7 mg/dl at admission were enrolled. An eGFR of less than 60 ml/min/1.73 m2 indicates that a patient has impaired filtration of blood via the kidneys.

**Exclusion criteria:** Patients who are on treatment for hyperuricemia, with history of renal stones were excluded from the study.

**Data collection:** After taking informed consent from each participant, 118 patients were enrolled in the study. Data was then gathered based on predetermined criteria for inclusion and exclusion, use a Proforma. Patients having admission serum uric acid levels ≥7 mg/dl were labeled as having admission hyperuricemia. Patients developing AKI during hospital stay were diagnosed using KDIGO guidelines as mentioned earlier. AKI was defined by a sudden decline in renal function, resulting in a decrease in the filtration of urea and other nitrogenous waste substances.

- According to the KDIGO recommendations, AKI encompasses any of the following conditions.
- Serum creatinine (SCr) levels that have risen by 0.3 mg/dl or more (26.5 mol/l or more) during the course of 48 hours; alternatively.
- An elevation in serum creatinine (SCr) levels to a value equal to or more than 1.5 times the individual's baseline, which is either confirmed or believed to have taken place during the preceding seven days; OR.
- The urine volume has been consistently below 0.5 ml per kilogram per hour for a duration of 6 hours.

Hyperuricemia was labeled when patients having serum uric acid levels ≥7 mg/dl.

**Data analysis:** Data was collected and compiled in the computer SPSS version 21 for windows. In-hospital acute renal injury was represented in terms of frequency and percentage.

## Results

An analysis was conducted to determine the age distribution of the patients. The results indicate that 35.59% (n=42) fell within the age range of 20-50 years, while 64.41% (n=76) fell within the age range of 51-75 years. The analysis of gender distribution reveals that 48.31% (n=57) of the participants were identified as male, while 51.69% (n=61) were identified as female. The study conducted was to determine the prevalence of AKI in patients with hyperuricemia upon admission. Out of the total sample size of 118 patients, 30 individuals (25.42%) were found to have AKI, whereas the remaining 88 patients (74.58%) did not exhibit any signs of AKI. (Table No. 1)

The age stratification analysis revealed that of the 30 cases examined, 7 were into the 20-50 years age range, while 23 were in the 51-75 years age range. The obtained p-value was 0.000, indicating a statistically significant difference. The process of stratification based on gender

**Table 1:** *Demographics of patients enrolled in the study (n = 118)*

| | | No. of patients |
|---|---|---|
| **Age (in years)** | 20-50 | 42 (35.6%) |
| | 51-75 | 76 (64.4%) |
| | Mean ± SD | 53.66 ± 7.98 |
| **Gender** | Male | 57 |
| | Female | 61 |
| **BMI** | $Kg/m^2$ | 29.61 ± 3.14 |
| **AKI** | Yes | 30 (25.4%) |
| | No | 88 (74.6%) |

was conducted, revealing that out of a total of 30 instances, 14 were classified as male and 16 as female. The resulting p-value obtained from the analysis was 0.17. The stratification for BMI was done, it shows that out of 30 cases 18 were upto 30 BMI and 12 had >30 BMI, p value was 0.72. The stratification for serum uric acid levels was done, it shows that out of 30 cases 19 had >7-8 and 11 had >8 mg/dl, p value was 0.76. (Table No. 2)

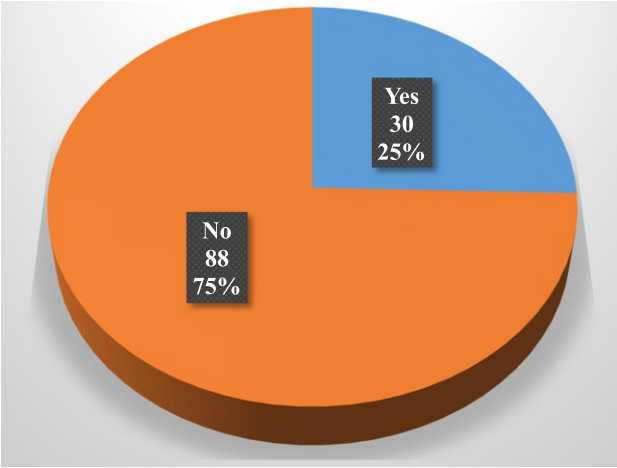


Figure 1: *Presence of Acute Kidney Infection*

**Table 2:** *Comparison of AKI in different groups*

| | | AKI | | P value |
|---|---|---|---|---|
| | | Yes | No | |
| **Age** | 20-50 | 7 | 35 | 0.10 |
| | 51-75 | 23 | 53 | |
| **Gender** | Male | 14 | 43 | 0.84 |
| | Female | 16 | 45 | |
| **BMI** | Up to 30 | 18 | 56 | 0.72 |
| | >30 | 12 | 32 | |
| **Serum uric acid levels** | >7-8 | 19 | 53 | 0.76 |
| | >8 | 11 | 35 | |

## Discussion

AKI often occurs after cardiac surgery, in patients with sepsis, and following the injection of several nephrotoxic drugs, including contrast agents. The occurrence of AKI has a substantial impact on the results. The implementation of preventive measures before to any surgery is of utmost importance due to the lack of established treatments for successfully managing AKI. Hence, in the event that high-risk patients were subjected to early screening, clinicians would be afforded more opportunity to mitigate the occurrence of AKI and thereby improve patient outcomes. Uric acid is a metabolic byproduct resulting from the breakdown of purines, and its elimination occurs mostly by renal excretion. High blood pressure, cardiovascular issues, diabetes, and the progression of chronic renal disease are just some of the many illnesses and conditions that have been linked to hyperuricemia in several epidemiological studies. In addition, hyperuricemia is linked to AKI in a number of settings.

This descriptive case series was planned with the view that no local study for estimation of this prevalence has been done in our population. International studies done to calculate this prevalence is not applicable to our community. The purpose of this research was to determine the true prevalence in our set of patients. The importance and effect of hyperuricemia on acute renal damage may then be evaluated. This may indicate that uricosuric drugs may be considered early for use in the treatment of acute renal damage.

In our study, out of 118 cases, 35.59%(n=42) were between 20-50 years of age whereas 64.41%(n=76) were between 51-75 years of age mean+sd was calculated as 53.66+7.98 years, 48.31% (n=57) were male and 51.69%(n=61) were females, the prevalence of AKI in patients having hyperuricemia at the time of admission presenting to us was recorded in 25.42%(n=30). Our findings are supported by another study where the prevalence of AKI in patients having hyperuricemia at admission is around 22%.8

In a meta-analysis, it was shown that the incidence rates of AKI in the hyperuricemia group were significantly greater compared to those in the control group. The fundamental factors were examined and evaluated in the following manner. First and foremost, it is noteworthy that the kidneys play a significant role in the excretion of the bulk of uric acid, amounting to around 70% of the total expelled amount. It is important to acknowledge that a significant proportion, namely about 90-95%, of the uric acid that is subjected to filtration by the glomerular apparatus is reabsorbed, mostly by the proximal tubules.[9] Renal tubules produce a little quantity of uric acid. The amount of serum uric acid in the blood depends on glomerular filtration and the subsequent role of tubular reabsorption. Serum uric acid is increasingly being investigated as a potential biomarker or independent risk factor for chronic kidney disease.[10,11] Several studies have shown that there is an increased risk of acute kidney damage when preexisting chronic renal illness is present. According to the findings of Ishani et al, the occurrence of AKI was seen to be 8.8% among individuals with chronic renal disease, in contrast to a lower prevalence of 2.3% among people without chronic kidney disease.[12] Pannu et al. (year) observed a significantly elevated risk of AKI in patients with an estimated glomerular filtration rate (eGFR) below 30 ml/min/1.73 $m^2$ compared to those with an eGFR above 60 ml/min/1.73 $m^2$, with a magnitude of 18-fold increase in risk.[13] Hence, individuals exhibiting elevated serum

uric acid levels may potentially possess underlying subclinical chronic renal impairment, rendering them more susceptible to AKI.

Multiple research' findings lend credence to the idea that uric acid is a separate risk factor for cardiovascular illness. Patients with hyperuricemia have a greater risk of cardiovascular disease than the general population.[14] The results of a meta-analysis indicated that there was a significantly elevated prevalence of coronary heart disease in those with hyperuricemia, with a relative risk of 1.34 (95% CI 1.19-1.49) compared to those with normal uric acid levels.[15] Individuals diagnosed with coronary heart disease in conjunction with hyperuricemia have an elevated prevalence of myocardial infarction. The annual incidence of cardiac operations or percutaneous coronary intervention worldwide is estimated to be over 2 million. Among the several postoperative consequences, AKI is recognized as one of the most prevalent and severe.[16,17] A comprehensive investigation revealed that the global prevalence of AKI after cardiac surgery was shown to be 22.3% (95% CI 19.8-25.1).[18] The prevalence of percutaneous coronary intervention-induced AKI has been reported to range from 2% to 30%, mostly influenced by the baseline renal function of patients. This incidence is rising in tandem with the growing prevalence of coronary heart disease over time.[17] The incidence of AKI after cardiac surgery is influenced by a greater number of intricate risk factors and processes compared to percutaneous coronary intervention. As a consequence, the gap between the incidence of AKI in those with hyperuricemia and those without it narrows. Additionally, serum uric acid needs additional investigation to establish its prognostic importance in the development of AKI after cardiac surgery. Uric acid has the potential to elicit AKI via many pathways, including direct tubular toxicity resulting from crystal-induced injury, as well as indirect harm caused by vasoconstriction, oxidative stress, inflammation, and other factors.[19] In several animal and human models, it has been shown that uric acid has the ability to impede the proliferation and migration of endothelial cells, as well as induce malfunction and death in these cells. Animal experimental research have shown that uric acid has the potential to induce renal vasoconstriction. This effect is believed to occur via two mechanisms: firstly, by inhibiting renal nitric oxide synthase, which leads to a decrease in nitric oxide production in endothelial cells; and secondly, by activating the reninangiotensin system.[20,21] The narrowing of blood vessels in the kidneys is a frequent pathologic mechanism that contributes to the onset of AKI. AKI is known to have several causes, although inflammation and oxidative stress are two of the more prominent ones. The stimulation of the pro-inflammatory nuclear factor-B signaling pathway has been empirically linked to uric acid.[22-24] The kidney's production of pro-inflammatory systemic cytokines like tumour necrosis factor and local chemokines like monocyte chemotactic protein 1 is induced by an increase in serum uric acid.[25,26] Elevated serum uric acid levels have been shown to initiate oxidative damage in proximal tubule cells via the activation of nicotinamide adenine dinucleotide phosphate oxidase. The numerical value provided is 27. Hence, it is plausible that Serum uric acid plays a role in the development of AKI and contributes to an increased prevalence of AKI in individuals with hyperuricemia. Irrespective of whether increased serum uric acid serves only as a predictive factor for AKI or functions as an independent risk factor for AKI, it is crucial to exercise caution and provide due consideration.

## Conclusion

It has been shown in our study that there is a greater risk of development of Acute Kidney Injury in patients who have hyperuricemia upon admission. Nevertheless, it is imperative to do multicenter trials in order to authenticate our findings.

Conflict of Interest: *None*

Funding Source: *None*

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