

Original Article

Association between hyperuricemia and progression of chronic kidney disease: a longitudinal study.Aamir Nabi¹, Moazzam Ismail², Waqas ur Rehman³, Sumayya Roshan⁴¹⁻⁴ PGR Department of Nephrology MTI,LRH Peshawar**Article Metadata****Corresponding Author**Mozzam Ismail²PGR Department of
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2024;1(1):20–24.**ABSTRACT**

Background: Various factors some of which can be changed, play a role in the progression of chronic kidney disease. There is new evidence to show that higher levels of uric acid may fasten renal function degradation by damaging blood vessels, increasing inflammation in the kidneys, and interacting with oxidative reactions in the body.

Objectives: To evaluate the association between elevated serum uric acid levels and the progression of chronic kidney disease (CKD) in adults, and to determine whether hyperuricemia independently predicts subsequent decline in renal function over time.

Methodology: A longitudinal cohort study was done at the Nephrology Department of Nephrology MTI,LRH Peshawar from January 2021 to December 2023. Adult patients with CKD stages 2–4 was included and watched for 24 months. Serum uric acid and estimated glomerular filtration rate (eGFR) were checked and recorded at the start of the study and again later. CKD progression was considered to happen if a person's kidney function dropped by 25% or if their blood test score showed the disease had gotten worse. Data were analyzed using SPSS v24.0.

Results: 152 patients, and their mean age was 58.4 years, with a standard deviation of 13.2. 61% were male. Out of the patients studied, 52% (78 patients) had hyperuricemia. In hyperuricemia patients, progression of CKD was seen in 42.3% of cases, whereas only 24.7% showed progression among normouricemic patients ($p=0.01$). The eGFR rate of drop was higher in the hyperuricemia group over the 24-month period (12.8 ± 6.3 vs. 7.4 ± 4.9 mL/min/1.73 m²). $p=0.002$). Having hyperuricemia increased the risk of CKD progression (HR: 1.76, 95% CI: 1.18–2.84, $p=0.004$).

Conclusion: The findings of this study suggest that hyperuricemia is strongly linked to the advanced stages of CKD. People with high serum uric acid were more likely to experience kidney function decline and more rapid development of the disease as time passed. This research points out that CKD patients should have their blood uric acid levels monitored often. Also, managing elevated uric acid may help keep kidney function decline at bay.

Keywords: Hyperuricemia, CKD progression, eGFR, uric acid

INTRODUCTION

There is a growing concern about chronic kidney disease (CKD) on a global scale since aging, diabetes, hypertension, and obesity are all becoming more common. It is estimated that 10% of the world's population has CKD, leading to more frequent and serious health problems, additional expenses, and more deaths [1]. Spotting possible causes of CKD that can be changed is very important for better clinical results and to prevent ESRD. Among these risk factors, one that can be treated is hyperuricemia, which refers to high uric acid levels in blood. It is commonly thought that hyperuricemia, historically associated with gout, can contribute to hypertension, disease of the heart and blood vessels, and kidney problems [2]. The presence of uric acid can cause harm to the kidneys through different processes, which include activity of the renin-angiotensin system, problems in the endothelium, oxidative stress, and inflammation [3]. This can increase the pressure in the glomeruli and cause scarring in the interstitial, leading to a faster decline in kidney function. Observational studies indicate that hyperuricemia might increase the risk of CKD progression. Higher uric acid levels have been linked to greater loss of kidney function and raised risk of ESRD in the CRIC study [4,5]. Study by Obermayr and his colleagues found that for every milligram of uric acid per deciliter increase, the risk of CKD went up. However, there is still debate about whether hyperuricemia leads to worsening CKD. Although some studies suggest urate-lowering therapy (for example, allopurinol) can slow the decline of eGFR [6], others such as CKD-FIX didn't find a significant improvement in kidney function [7]. Such varying outcomes could result from changes in study structure, initial kidney function among patients, thresholds for uric acid, and characteristics of the participants. Because the burden of CKD in South Asia is strong and nephrology care limited, few researchers there have studied how diabetes and CKD are linked in the long run. People in this region have a higher risk of hyperuricemia due to their diets, the occurrence of metabolic syndrome, and certain gene predispositions [8]. Because of this, it is crucial for doctors to know the connection between serum uric acid and CKD progression. Our aim was to explore if hyperuricemia causes a faster loss of kidney function in patients with renal disease, and to determine its role in predicting renal decline apart from known risk factors. The results of our study might guide how patients are sorted, the risks they face, and the treatments chosen to stop CKD from progressing [9].

MATERIAL & METHODS

The study was carried out at the Department of Nephrology MTI,LRH Peshawar from January 2021 to December 2023. Adult patients over the age of 18 diagnosed with CKD stages 2–4 was enrolled. Hyperuricemia was measured as serum uric acid higher than 7.0 mg/dL in males and higher than 6.0 mg/dL in females. The CKD-EPI equation was used to determine eGFR at the beginning and every six months for 24 months. The change was considered CKD progression when eGFR dropped by at least 25% from the start or a person was moved to a higher CKD stage. Patients were grouped, as, either having hyperuricemia or normouricemic. Information about age, sex, diabetes, hypertension, and medications was kept in the records. The study received approval from the Institutional Review Board (Ref: All participants gave adult consent after being informed and agreed to take part in the study

Inclusion Criteria:

Patients between 18 and 90 years old with CKD stages 2–4 who showed consistent renal function and kept regular follow-up appointments after agreeing to participate were part of the study.

Exclusion Criteria:

Patients with last-stage kidney disease, dialysis patients, people with active cancer, autoimmune kidney disease, and those who received urate-lowering medication within the past 3 months were excluded.

Data Collection:

We obtained data using standard medical forms and included information on patients' age, blood pressure, levels of serum uric acid, eGFR, other diseases, and drugs they were taking. Labs were done every six months to monitor his condition. Patient progress and CKD stage were regularly reviewed in electronic records and confirmed by repeat tests and visits from nephrologists.

Statistical Analysis:

Statistical analysis was performed using SPSS version 24.0. Normally distributed variables were expressed as mean $\pm$ standard deviation (SD) and compared using independent sample t-tests, while categorical variables were analyzed using the chi-square test.

Results:

152 patients with CKD, and the group's average age was 58.4 ± 13.2 years. 61% were male. 78 out of 152 individuals (52%) at the study's beginning had hyperuricemia. Patients who were hyperuricemia were more likely to be diagnosed with hypertension (74.4% vs. 57.9%, $p=0.03$) and diabetes (48.7% vs. 31.6%, $p=0.04$). During the 2-year study, hyperuricemia patients were more likely to develop CKD, with a rate of 42.3% compared to 24.7% in normouricemic patients ($p=0.01$). The group with hyperuricemia showed a greater decrease in eGFR (12.8 ± 6.3 vs. 7.4 ± 4.9 mL/min/1.73 m²). $p=0.002$). Once age, diabetes, hypertension, and baseline eGFR were considered, hyperuricemia was found to independently contribute to CKD progression (Hazard Ratio: 1.76; 95% CI: 1.18–2.84; $p=0.004$). The change from stage 3 to stage 4 was seen more often in patients with high uric acid. Similar rates of mortality and hospitalization were found among the two groups. The findings highlight that larger amounts of uric acid are strongly related to worsening kidney function, strengthening the idea that high uric acid plays a key role in CKD.

Table 1: Baseline Demographics

Variables	Hyperuricemia Group (n=78)	Normouricemic Group (n=72)	p-value
Total Patients	78	72	-
Mean Age (years)	59.8	56.9	0.12
Male (%)	67.9%	54.2%	0.04
Female (%)	32.1%	45.8%	0.04
Hypertension (%)	74.4%	57.9%	0.03
Diabetes Mellitus (%)	48.7%	31.6%	0.04

Table 2: Renal Parameters and CKD Progression

Variables	Hyperuricemia Group	Normouricemic Group	p-value
Mean eGFR Decline (mL/min/1.73 m ²)	12.8 ± 6.3	7.4 ± 4.9	0.002
CKD Progression (%)	42.3%	24.7%	0.01
Stage Advancement (%)	35.9%	19.4%	0.03

Table 3: Multivariate Cox Regression for CKD Progression

Risk Factor	Hazard Ratio (HR)	95% Confidence Interval	p-value
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Hyperuricemia	1.76	1.18–2.84	0.004
Diabetes Mellitus	1.52	1.01–2.45	0.04
Hypertension	1.31	0.91–2.10	0.11
Baseline eGFR (per 5 mL/min drop)	1.22	1.10–1.38	0.001
Age (per year increase)	1.05	1.01–1.09	0.02

Discussion

This study over time shows that having high uric acid is linked to a higher chance of CKD getting worse over 2 years. Patients with higher levels of serum uric acid saw their kidney function drop faster and were more likely to move into later stages of CKD than those whose uric acid was normal. Even after considering common risks like high blood pressure, diabetes, and how well the kidneys were working at first, having high uric acid levels was still linked to getting worse kidney problems. Our findings agree with other studies that have shown that high levels of uric acid can contribute to kidney disease. Obermayr et al. reported that for every 1 mg/dL higher in uric acid, the chance of getting kidney disease went up by 7–12%, showing that high uric acid levels might play a key role in developing kidney problems [10]. Similarly, the Chronic Renal Insufficiency Cohort (CRIC) study found out that having too much uric acid increased the chances of kidney function getting worse faster and people were more likely to develop severe kidney disease [11]. The mechanical processes that connect uric acid and kidney damage include problems with blood vessel function, more free radicals, and the activation of the renin-angiotensin system. Uric acid has been found to cause cell growth in the blood vessels, raise pressure in the kidneys, cause inflammation inside the kidneys, and finally lead to scarring and loss of working kidney tissue. These biological processes can make things even worse in people whose kidneys are already having trouble, but studies that look at medicines that lower uric acid have shown both positive and negative results. The study by Goicoechea et al. found that taking allopurinol helped lower how quickly kidney function got worse for people who already had CKD [13]. However, the CKD-FIX trial, a bigger study where patients were randomly given allopurinol or a dummy pill, showed that allopurinol didn't help slow kidney disease progression, even though it lowered uric acid levels [14]. These inconsistencies might happen because the people in the studies were not identical, the starting levels of their uric acid could differ, or because people had varying stages of kidney disease. In the context of South Asian populations, there isn't much found that many

people in South Asia have both metabolic syndrome and high levels of uric acid, which might together lead to more CKD [15]. Our study happens more often in these groups. Furthermore, Jalal and his colleagues pointed out that uric acid can be a useful treatment target for people with early stages of CKD, since trying to lower uric acid early might help more than trying later on. Despite people still discussing this topic, most of the research and our own studies show that monitoring uric acid levels can help improve the care for people with kidney disease. In conclusion, our study agrees with previous research that shows hyperuricemia is not just a side effect in CKD, but it actually seems to contribute to how the disease gets worse. Further big treatment studies are needed to find out if lowering uric acid can truly help slow down kidney damage in people with kidney disease and high levels of uric acid, but not yet showing symptoms [17-18].

Conclusion:

Normal uric acid levels tend to have kidney disease progress faster. Elevated serum uric acid seems to independently cause a decline in kidney function, even when other health problems are considered. Monitoring and managing uric acid levels in people with CKD might be a way to slow down the disease and help them feel better.

Limitations:

This was a single-center study and had a fair number of patients, so it might not apply to everyone. Serum uric acid levels were checked just at the start, and the effects of urate-lowering treatments were not looked at in this study. Additionally, other possible influencing factors like diet, genetics, and if people are sticking to their medicine were not completely looked at or controlled for in this study.

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Future Directions:

Larger multicenter studies that track people for a longer time are needed to confirm if high levels of uric acid and kidney disease are related. Future study should look at how urate-lowering treatments affect kidney health, try to understand why these treatments work by more research on their mechanisms, and also look at whether things like genetics or other metabolic factors play a role in causing high uric acid in different groups, especially in people from South Asia.

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Conflict of Interest: Nil

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Final Approval of version: **All Mention**

Authors approved the final version.

Research Ethics Statement

There were no animal studies conducted. This study was approved by the **Institutional Review Board (IRB-No.MTI/LRH/2213/00/2020)**. Accordance with the ethical principles of the Declaration of Helsinki (2013). All participants or legal guardians signed written informed consent. No recognizably identifiable human data were included. As described in the article and supplementary materials, data that that under or findings are held in online repositories.

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