

ORIGINAL ARTICLE

ASSESSMENT OF SERUM URIC ACID LEVELS IN CHRONIC KIDNEY DISEASE PATIENTS: A CROSS-SECTIONAL STUDY IN A TERTIARY CARE HOSPITAL**Arun Bahadur Chand^{1*}, Bindu Sen², Rajendra Dev Bhatt³, Mahendra Prasad Bhatt⁴, Santosh Cheetri⁵**¹*Department of Clinical Biochemistry, KIST Medical College and Teaching Hospital, Lalitpur, Nepal*²*Department of Dentistry, Good Smile Dental Clinic, Kathmandu, Nepal*³*Department of Clinical Chemistry and Laboratory Medicine, Kathmandu University School of Medical Sciences, Dhulikhel Hospital-Kathmandu University Hospital*⁴*Department of Laboratory Medicine, Manmohan Memorial Institute of Health Sciences, Kathmandu, Nepal*⁵*Department of Internal Medicine (Nephrology Unit), KIST Medical College and Teaching Hospital, Lalitpur, Nepal***ABSTRACT**

Introduction: Chronic kidney disease (CKD) is a major public health concern worldwide, notably impacting Nepal, where increased blood uric acid levels are common and may magnify the risks of glomerulosclerosis, interstitial fibrosis, and atherosclerosis. The purpose of this study was to measure uric acid levels among CKD patients at a Nepalese tertiary care hospital.

Method: A cross-sectional study was conducted at the Kist Medical College and Teaching Hospital (KISTMCTH), Lalitpur, Nepal, on 242 CKD patients with stages IIIB to V from 14 April 2021 to 12 April 2024. Ethical approval was obtained from the Institutional Review Committee of KISTMCTH (Reference number: 078/079/75). Blood samples were collected, and uric acid and creatinine levels were measured using a fully automated biochemistry analyzer. Data analysis was performed using SPSS version 17.0.

Results: Among the 242 CKD patients, hyperuricemia was found in 131(54.13%) patients with stage V CKD, 19(7.85%) patients with stage IV CKD, and 12(4.96%) patients with stage IIIB CKD. Hypouricemia was most common in stage V CKD, affecting 9 patients (3.72%), followed by stage IV, 3 patients, (1.24%), the majority of patients 163(67.36%) were adults (17-59 years). Of the 242 CKD patients, 179(73.97%) patients were in stage V, 38(15.70%) in stage IV, and 25(10.33%) in stage IIIB CKD patients. Out of the total CKD patients, 162(66.94%) had hyperuricemia, while 12(4.96%) had hypouricemia. Both hyperuricemia and hypouricemia were more common in males, with 97(40.08%) and 11(4.55%) of cases, respectively.

Conclusion: Hyperuricemia is common among CKD patients, particularly in men. Hyperuricemia and hypouricemia were more prevalent among patients with stage V CKD.

Key words: Creatinine, Uric acid, Hyperuricemia, Hypouricemia, Chronic kidney disease

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*Corresponding Author: Arun Bahadur Chand, Kist Medical College and Teaching Hospital, Lalitpur, Nepal

Email: arunbchand@gmail.com

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INTRODUCTION

Uric acid, the end product of purine metabolism, is primarily eliminated by the kidneys. The kidneys typically remove 70% of daily uric acid production (500 mg/day), while the remaining 30% is excreted via the intestines. In chronic kidney disease (CKD), impaired renal function leads to increased plasma uric acid levels due to decreased glomerular filtration rate (GFR) ¹⁻³. chronic kidney disease affecting approximately 850 million people globally, is expected to become a leading cause of premature mortality by 2040, with one in ten adults worldwide affected and millions dying annually from CKD-related complications ^{4,5}. Common risk factors include diabetes, hypertension, glomerulonephritis, obesity, and aging ⁶⁻⁸.

Previous studies have suggested a potential correlation between elevated serum uric acid levels and the onset or progression of CKD ⁹⁻¹¹. A study conducted in Nepal found that almost half (48.07%) of CKD patients on hemodialysis had hyperuricemia, with an average uric acid level of 6.76 ± 2.62 mg/dL ¹². Hyperuricemia, often caused by excessive production or impaired renal excretion, accounts for over 90% of cases ^{13,14}. Notably, hyperuricemia has been associated with CKD progression even in patients with normal kidney function at baseline ¹⁵. Despite these insights, the precise mechanisms underlying uric acid regulation and its specific relationships with kidney and cardiovascular diseases are still not fully clear ¹⁶. Furthermore, research on uric acid levels in CKD patients in the Nepalese population is limited. Therefore, this study aims to assess serum uric acid levels among CKD patients at a tertiary care hospital in Lalitpur, Nepal.

METHODS**Study Design and Population**

This cross-sectional study was conducted at the Department of Clinical Biochemistry, KIST Medical College and Teaching Hospital

(KISTMCTH), focusing on patients diagnosed with chronic kidney disease (CKD) who visited the hospital from 14 April 2021 to 12 April 2024.

Inclusion Criteria

Patients aged 10 years and above with confirmed chronic kidney disease, diagnosed from 14 April 2021 to 12 April 2024, were included in this study.

Exclusion Criteria

Patients with diseases such as active gout and hypothyroidism, those on hyperuricemia medication, and cancer patients were all excluded based on the clinical history provided on the test requisition slip.

Ethical Approval

The study was initiated after obtaining ethical approval from the Institutional Review Committee of KISTMCTH (Reference number: 078/079/75).

Data Collection

Patient socio-demographic data was retrieved from hospital records. Serum uric acid and serum creatinine levels were extracted from the clinical laboratory software (Midas version 3.2). The CKD stage was determined using the CKD-EPI Creatinine (2021) equation formula ¹⁷. The data were meticulously validated and anonymized by checking the

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MIDAS database for new registrations and repeat tests using hospital and lab IDs. Additionally, medication data and comorbidity details were extracted from the clinical history on the test requisition slip. The data were then entered into Microsoft Excel 2010.

Specimen Processing and Laboratory Diagnosis

Approximately three milliliters of venous blood were collected from each patient using a serum-separating tube. After clotting, the samples were centrifuged at 4000 revolutions per minute for five minutes to obtain serum. Serum samples were analyzed using the fully automated integrated biochemistry analyzer (SIEMENS RxL Max, USA).

Diagnostic Criteria for Uric Acid

Hyperuricemia was defined as serum uric acid concentration >7.0 mg/dL ($416.4 \mu\text{mol/L}$) in men and >6.0 mg/dL ($356.9 \mu\text{mol/L}$) in women¹⁸. Hypouricemia is defined as serum uric acid levels below 2 mg/dL ($119 \mu\text{mol/L}$)¹⁹.

Diagnostic Criteria for the Definition of CKD

Chronic kidney disease (CKD) is characterized by either kidney damage or a decrease in glomerular filtration rate (GFR) less than $60 \text{ mL/min/1.73 m}^2$ for more than three months based on evidence or inference. Kidney damage is defined as structural and functional abnormalities other than decreased GFR. The baseline eGFR and CKD stage were based on the first available eGFR²⁰. Chronic kidney disease severity is classified into 5 categories according to the level of the GFR²⁰.

Stage (GFR category)	GFR, ml/min per 1.73m^2	Terms
I	>90	Normal or High
II	60-89	Mildly decreased
III	30-59	Mild to moderately decreased [Stage 3 CKD is divided into 3A (GFR is 45 to 59) and 3B (GFR is 30 to 44)]
IV	15-29	Severely decreased
V	<15	Kidney Failure

An estimate of the glomerular filtration rate (GFR) was obtained using the CKD-EPI equation, expressed as a single equation,

$$\text{GFR} = 141 * \min(\text{Scr}/\kappa, 1)^\alpha * \max(\text{Scr}/\kappa, 1)^{-1.209} * 0.993^{\text{Age}} * 1.018 [\text{if female}] * 1.159 [\text{if Black}]$$
 Here, Scr represents serum creatinine (mg/dL), κ is 0.7 for females and 0.9 for males, and α is -0.329 for females and -0.411 for males. The min function indicates the minimum of Scr/κ or 1, while the max function indicates the maximum of Scr/κ or 1²¹.

Statistical analysis

The data were analyzed using the Statistical Package for the Social Sciences (IBM SPSS version 17.0). Descriptive statistics, such as mean (\pm SD), number, and percentage, were used to illustrate study variables. A p-value of <0.05 was considered as statistically significant.

RESULTS

Socio-demographic details of patients

Among the 242 CKD patients, the median age \pm SD was 55 ± 13.47 years (IQR: 45.65; range: 19-80). There were 163(67.36%) male and 79(32.64%) female patients. The highest number of patients, 153 (63.22%), belonged to the 17-59 years age group (Table 1).

Table 1: Socio-demographic details of patients

Variable	Category	Number	Percentage
Age group (years)	Mean	51.46 (14-94)	
	≤ 16 : Children	3	1.24
	17-59: Adult	153	63.22
Gender	≥ 60 : Elderly	86	35.54
	Male	163	67.36
	Female	79	32.64

Distribution of CKD patients according to CKD stage

Among the 242 CKD patients, 73.97% had stage V CKD, followed by 15.70% with stage IV CKD and, 10.33% with stage IIIB CKD. The mean \pm SD for stage V CKD was 4.4 ± 1.9 mg/dL, for stage IV CKD was 6.5 ± 4.1 mg/dL, and for stage III CKD was 8.8 ± 3.1 mg/dL ($p < 0.05$). The differences between CKD stages IIIB, IV, and V were statistically significant ($p < 0.05$) (Figure 1).

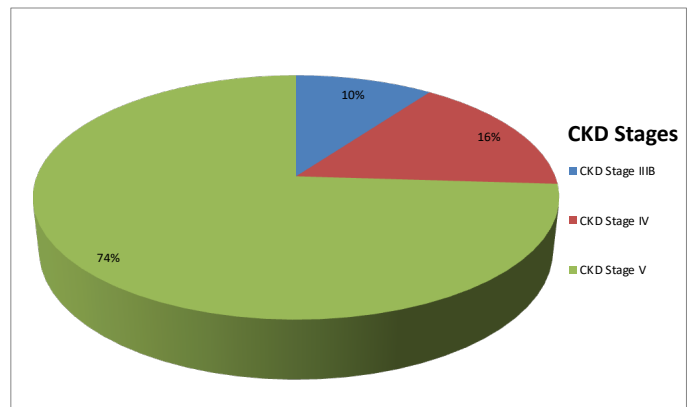


Figure 1: Distribution of patients according to CKD stage

Distribution of CKD patients according to gender, age group, and CKD stage

Among the 242 CKD patients, hyperuricemia was observed in 162 (66.94%) of cases, with a higher prevalence among males (97, 40.08%). Hyperuricemia was most common in stage V CKD 131(54.13%), followed by stage IV CKD 19(7.85%) and stage IIIB CKD 12(4.96%). Hypouricemia was most common in stage V CKD, followed by stage IV CKD and stage IIIB CKD. Out of 242 CKD patients, 68(28.10 %) had normal uric acid levels (Table 2).

Distribution of patients according to uric acid level and age group

The Median age \pm SD was 55 ± 13.47 years (IQR: 45.65; range: 19-80) (Figure 2).

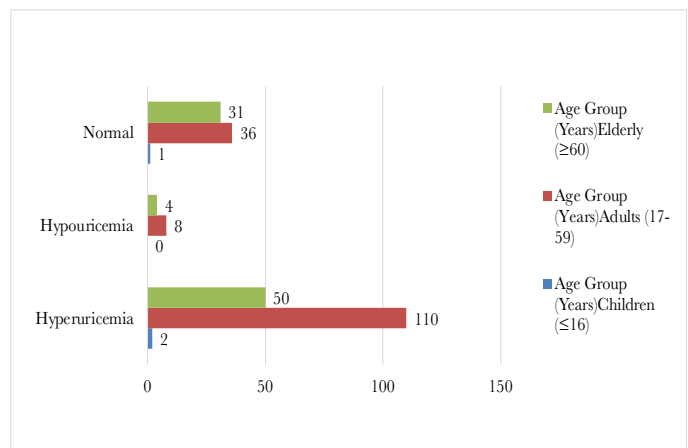


Figure 2: Uric acid levels according to age group

Table 2: Distribution of CKD patients according to gender, age group, and CKD stage

CKD	Age Group	Hyperuricemia		Hypouricemia		Normal	
		Male (%)	Female (%)	Male (%)	Female (%)	Male (%)	Female (%)
IIB (30-59)	≤ 16 Children		1(0.41)	--	--	--	--
	17-59: Adult	9(3.72)	--	--	--	--	6(2.48)
	≥ 60: Elderly	1(0.41)	1(0.41)	--	--	--	7(2.89)
IV (15-29)	≤ 16: Children	--	--		--	--	--
	17-59: Adult	7(2.89)	4(1.65)	1(0.41)	--	5(2.07)	3(1.24)
	≥ 60: Elderly	6(2.48)	2(0.83)	2(0.83)	--	8(3.31)	--
V(<15)	≤ 16: Children	--	1(0.41)	--	--	1(0.41)	--
	17-59: Adult	53(21.90)	36(14.88)	6(2.48)	1(0.41)	16(6.64)	6(2.48)
	≥ 60: Elderly	21(8.68)	20(8.26)	2(0.83)	--	12(4.96)	4(1.65)

Distribution of patients according to uric acid level and gender

Out of the 242 CKD patients, 162 (66.94%) had hyperuricemia, 12 (4.96%) had hypouricemia, and 68 (28.10%) had normal uric acid levels. Hyperuricemia was more common in males (97, 40.08%) than in females (65, 26.86%), while hypouricemia was found in 11 (4.55%) of males and 1 (0.41%) of females. The difference in uric acid levels between males and females was statistically significant ($p < 0.05$) (Figure 3).

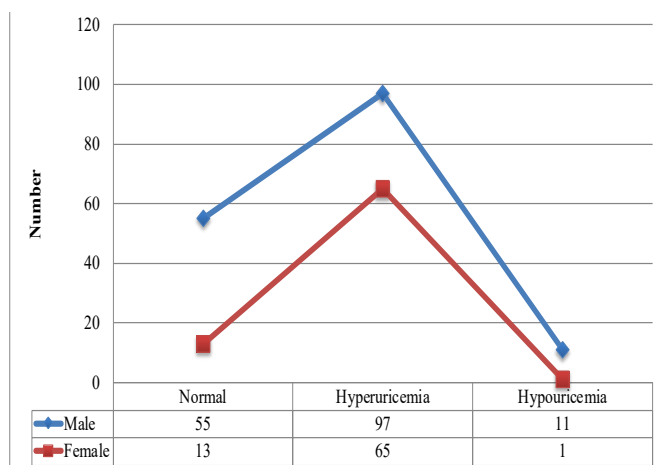


Figure 3: Uric acid levels according to gender

DISCUSSIONS

Elevated serum uric acid levels are closely associated with increased mortality risk in CKD patients²². Additionally, serum uric acid levels within the high-normal range are independently associated with CKD²³. Numerous clinical and experimental studies have investigated the relationship between hyperuricemia and the development of CKD^{24,25}. This study analyzed the alterations in uric acid levels among individuals with chronic kidney disease.

Our study highlighted significant findings regarding serum uric acid levels among CKD patients at various stages of the disease. Similarly, research from the University of Benin Teaching Hospital in Benin City, Nigeria, found that hyperuricemia was present in 47.5% of CKD patients, compared to only 15% in the control group ($P=0.001$)²⁶. In contrast, Chonchol et al. found no statistically significant association between uric acid levels and incident CKD²⁷. Other studies have reported a correlation between elevated uric acid levels and the progression of kidney disease, or vice versa²⁸⁻³⁰. Sheikhabaei et al. (2014) investigated the relationship between serum uric acid (SUA) levels, metabolic risk factors, albuminuria, and CKD, finding a significant, graded increase in CKD odds with rising SUA levels and the number of metabolic syndrome risk factors ($p < 0.001$)³¹. Mok

et al. (2012), in a prospective cohort study involving 14,939 Koreans, observed that higher SUA levels increased the risk of CKD (defined as an estimated glomerular filtration rate [GFR] of <60 mL/min/1.73 m)³². Ching et al. (Taiwan, 2017) studied 739 patients and concluded that elevated uric acid levels were associated with a significantly faster decline in eGFR and a higher risk of kidney failure³³. The relationship between uric acid and reduced kidney function has been explored in 13,338 participants with intact kidney function from two community-based cohorts in the USA: the Atherosclerosis Risk in Communities Study and the Cardiovascular Health Study³⁴. Although there is debate regarding the association between uric acid levels and CKD, there are various possible mechanisms by which higher uric acid levels might contribute to the development of CKD. Initially, hyperuricemia was supposed to induce CKD by deposition of urate crystals in the renal interstitium, known as urate nephropathy. However, it was eventually shown that hypertension was probably the main cause of renal insufficiency, not gout or hyperuricemia alone³⁵. More recently, it has been proposed that hyperuricemia might contribute to hypertension, which in turn leads to renal injury³⁶.

In our study, the abnormal uric acid levels were more prevalent among the CKD patients, with a higher prevalence in males than females. Additionally, hyperuricemia was more common with a higher prevalence in males than females. A recent study from Bangladesh reported a similar hyperuricemia prevalence of 16.6%, with 21.3% in males and 8.3% in females³⁷. Prevalence rates in other Asian countries include 13.3% in mainland China (19.4% in males and 7.9% in females) and 25.8% in Japan (34.5% in males and 11.6% in females)³⁸. Satirapoj et al. found a mean blood uric acid level of 7.82 ± 1.80 and reported a higher prevalence of hyperuricemia among males (77.1%) in a study conducted at the Armed Forces Research Institute of Medical Sciences in Bangkok, Thailand. They also found that elevated uric acid levels were associated with a higher incidence of CKD³⁹. Similarly, Nivedita et al. found that hyperuricemia was more prevalent among males with CKD⁴⁰. However, Chini et al. found that asymptomatic hyperuricemia was not an independent risk factor for CKD progression⁴¹. The higher prevalence of hyperuricemia in males may be attributed to their greater tendency for smoking and alcohol consumption compared to females⁴². In our study, hyperuricemia was more common in the adult age group, which also had a higher prevalence of CKD. Hyperuricemia has been identified as an independent risk factor for CKD in middle-aged and elderly adults in the Taiwanese population⁴³. Additionally, both uric acid levels and the likelihood of developing kidney disease increased with age, consistent with findings from previous research⁴⁴.

CONCLUSIONS

Our study showed that nearly half of the chronic kidney disease patients had hyperuricemia. Around three-fourths of the study participants with hyperuricemia were aged 17-59 years, with the majority being male. Hyperuricemia and hypouricemia were more prevalent

among patients with stage V chronic kidney disease.

LIMITATIONS

The research has some limitations. This study was conducted on hospital patients, therefore, it may not be representative of the entire nation or generalizable to the general community. There was no detailed food history obtained, and calorie consumption may have influenced the uric acid levels.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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