

# Prevalence and clinical characteristics of hyperuricemia among patients with chronic kidney disease under haemodialysis in a tertiary care center: a cross-sectional study

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**Background:** Hyperuricemia is common in chronic kidney disease patients. This study aimed to investigate the prevalence and clinical characteristics of hyperuricemia in patients with chronic kidney disease undergoing haemodialysis.

**Materials and methods:** This cross-sectional study was conducted among 104 patients with chronic kidney disease who visited the haemodialysis unit of a tertiary centre hospital from 11 September 2022, to 11 November 2022. A convenience sampling technique was used. The data were collected using a proforma form, entered into, and analyzed using the Statistical Package for Social Sciences version 21.

**Results:** The mean age group of the study participants was  $54.02 \pm 14.03$  years, and around two-thirds were male (n = 70, 67.3%). Almost half of the participants (50, 48.07%) had hyperuricemia with a mean uric acid level of  $6.76 \pm 2.62$  mg/dl. The majority of the participants had associated hypertension (n = 100, 96.2%). More than three-fourths of the respondents (83, 79.8%) had haemoglobin levels below the target range.

Conclusion: Nearly half of the study participants had hyperuricemia.

Keywords: chronic renal insufficiency, cross-sectional study, hyperuricemia, Nepal, renal dialysis

# Introduction

Chronic kidney disease (CKD) is defined as the abnormalities of the kidney structure or function for greater than three months, with health implications<sup>[1]</sup>. Hyperuricemia is defined by the serum uric acid level greater than 7.0 mg/dl in males and greater than 6.0 mg/dl in females<sup>[2]</sup>. CKD results in electrolyte abnormalities including but not limited to hyperuricemia, hyperkalemia, hypocalcemia, hyperphosphatemia, and metabolic acidosis<sup>[3,4]</sup>. Hyperuricemia is common in CKD patients with its severity increasing with the progression of the chronic kidney disease.

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# HIGHLIGHTS

- Chronic kidney disease (CKD) refers to abnormal kidney structure or function for 3 or more months.
- There is decreased urinary excretion of uric acid in CKD patients.
- Hyperuricemia is common in CKD patients.

Hyperuricemia has been associated with the development of several cardiovascular diseases and hypertension<sup>[5,6]</sup>. However, there are some controversies regarding hyperuricemia as a risk factor for CKD. Some studies have shown asymptomatic hyperuricemia to be a risk factor for its progression<sup>[7,8]</sup>. Untreated hyperuricemia is an independent risk factor for the onset of CKD<sup>[9,10]</sup>. Some studies suggest that hyperuricemia with crystalluria and not asymptomatic hyperuricemia alone contributes to the disease progression<sup>[11]</sup>.

Elevated serum uric acid is significantly associated with the risk of mortality; a 1 mg/dl increase in serum uric acid level correlates with an 8% increase in mortality<sup>[12]</sup>. Hence it is important to acknowledge hyperuricemia in CKD patients and manage it appropriately. Our study aimed to find the prevalence and clinical characteristics of hyperuricemia in patients with end-stage kidney disease (ESKD).

### Methods

# Study design and setting

This study was conducted in a haemodialysis unit of a tertiary care hospital where it receives a high volume of CKD patients

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representing different social and economic backgrounds visiting the haemodialysis unit for dialysis.

## Study participants

A descriptive cross-sectional study was conducted among all the patients with chronic kidney disease who gave consent and underwent haemodialysis at the haemodialysis unit of a tertiary care hospital. The study took place from 11 September 2022 to 11 November 2022.

## Sampling and sample size

With a convenience sampling approach, the study included patients with CKD who visited the haemodialysis unit of a tertiary care hospital during the research period and those who were receiving medical therapy. Patients aged more than 18 years who were diagnosed with CKD attending the haemodialysis, and willing to participate were included. Patients less than 18 years of age, known cases of hyperuricemia, and gout, and those who were unwilling to participate were excluded from the research.

## Study instrument

A semi-structured pre-designed proforma prepared by the investigators themselves after studying other similar studies was used to collect the data. The proforma was pre-tested in 10% of the sample before being conducted, and necessary modifications were made.

Demographic data including age, sex, address, educational status, and duration of dialysis were gathered from the interviews of the patients. Data regarding co-morbidities like hypertension, diabetes, dyslipidemia, hyperuricemia, evidence of atherosclerosis, and others along with their durations were extracted from the patient's hospital record book. A complete physical examination was performed including vital signs such as blood pressure, pulse rate, respiratory rate, and temperature, and pertinent systemic examinations.

Laboratory investigations including complete blood count (CBC), serum calcium, serum phosphate, serum uric acid, serum sodium, serum potassium, total iron, serum ferritin, total reticulocyte count, mean corpuscular volume (MCV), mean corpuscular haemoglobin concentration (MCHC), and serology for HIV, hepatitis B, and hepatitis C were sent. Serum uric acid estimation was done by the uricase method. Different medical treatments including Erythropoietin supplements, allopurinol, non-steroidal anti-inflammatory drugs (NSAIDs), and thiazides along with dietary restrictions were collected from the personal record book.

# Statistical analysis

Data were entered into and analyzed using Statistical Package for Social Sciences (SPSS) version 21. Descriptive statistics like frequency, percentages, mean  $\pm$  SD, and/or median (minimummaximum) were calculated wherever required and depicted accordingly in bar diagrams and pie-chart. The association of hyperuricemia with selected background characteristics was assessed using the chi-square test and binary logistic regression. A *P* value less than 0.05 was considered significant. The 95% CI of prevalence was estimated using OpenEpi version 3.

### Ethical consideration

A letter of ethical approval was obtained from the Institutional Review Committee (IRC) of the institution (IRC Reg. No. 647). Written informed consent was taken from the participants. Anonymity and privacy of patient information were maintained.

The manuscript has been reported in line with the STROCSS criteria<sup>[13]</sup>.

# Results

Among 104 patients visiting the haemodialysis unit on an outpatient basis, 50 (48.07%, 95% CI 38.72–57.57) were found to have hyperuricemia with a mean uric acid level of 6.76  $\pm$  2.62 mg/dl [6.85 (0.4–13)].

Most of the people visiting the haemodialysis unit were of the age group 40–59 years (44, 42.3%) with a mean age of 54.02  $\pm$  14.03 years. Around two-thirds of the participants were male (70, 67.3%). The most common associated comorbidity was hypertension (100, 96.2%). Most of the patients (45, 43.3%) had a history of haemodialysis started in the past 5 years, while half of the patients (54, 51.9%) had a history of erythropoietin use for anaemia in previous months. Complete blood counts and peripheral blood smears of the patients showed, mean haemoglobin of 9.19 $\pm$  1.42 g/dl, MCV of 87.21 $\pm$  15.87 fl, and MCHC of 32.90 $\pm$  1.06 g/dl. Analysis of serum electrolytes profile revealed, Na<sup>+</sup> of 136.64 $\pm$  5.69 mEq/l, K<sup>+</sup> of 5.10 $\pm$  1.08 mEq/l, Ca<sup>2+</sup> of 8.54 $\pm$  1.52 mg/dl and PO4<sup>3-</sup> of 5.95 $\pm$  2.14 mg/dl (Table 1).

# Distribution pattern of haemoglobin and red blood cell indices

79.8% of the total patients had haemoglobin levels below the target range. However, most of them had normal MCV (85.6%) and all the patients had normal MCHC (Fig. 1).

## Distribution pattern of electrolytes

Most of the patients had normal sodium (52.9%) and potassium (61.5%) levels, lower calcium levels (48.1%), and higher phosphate level (74%) (Fig. 2).

## Serum uric acid profile

Among all those patients visiting the haemodialysis unit on an outpatient basis, 48.1% of the patients had increased uric acid levels (Fig. 3).

## Effects of different variables on serum uric acid level

We used the  $\chi^2$  test and binary logistic regression to analyze the effect of different variables on serum uric acid levels. As shown in Table 2, there were statistically non-significant lower odds of hyperuricemia in those aged 40–59 years [odds ratio (OR) 0.76, 95% CI 0.27–2.12) and aged older than or equal to 60 (OR 0.67, 95% CI 0.23–1.94) than those aged 20–29 years, those with dialysis 5–10 years (OR 0.42, 95% CI 0.16–1.15) and older than 10 years (OR 0.75, 95% CI 0.30–1.85) than those for younger than 5 years and non-erythropoietin use in previous months (OR 0.62, 95% CI 0.29–1.36) than erythropoietin users. The male participants had non-significant higher odds of hyperuricemia (OR 1.27, 95% CI 0.56–2.89) than female participants.

#### Table 1

Background clinical characteristics of participants with ESKD attending haemodialysis on an outpatient basis

Variables	Frequency, <i>n</i> (%)	
Age		
20–39	22 (21.2)	
40-59	44 (42.3)	
> 60	38 (36.5)	
Sex		
Female	34 (32.7)	
Male	70 (67.3)	
Co-morbidities		
Hypertension	100 (96.2)	
Diabetes	13 (12.5)	
Dyslipidemia	6 (5.8)	
Others <sup>a</sup>	9 (8.7)	
Dialysis duration (years)		
<5	45 (43.3)	
5–10	26 (25.0)	
> 10	33 (31.7)	
Erythropoietin use <sup>b</sup>		
No	50 (48.1)	
Yes	54 (51.9)	
	Normal values	Mean $\pm$ SD or [Median (Min–Max)]
Age (years)	—	54.02 ± 14.03 [55 (22–87)]
Dialysis duration (years)	_	7.31 ± 5.68 [6 (1-20)]
SBP <sup>c</sup> , mm Hg	≤130	148.94 ± 20.99 [140 (110-200)]
DBP <sup>c</sup> , mm Hg	≤80	88.15± 10.48 [90 (70–120)]
Hemoglobin <sup>c</sup> , g/dl	10-11.5 (KDIGO 2012)	9.19 ± 1.42 [9 (6.20–13.80)]
MCV, fl	80-100	87.21 ± 15.87 [90.40
		(8.10–104)]
MCHC, g/dl	$33 \pm 3$	32.90 ± 1.06 [33.10 (30-35.1)]
Na+, mEq/l	135–145	136.64 ± 5.69 [136 (113-158)]
K <sup>+</sup> , mEq/l	3.5-5.2	5.10 ± 1.08 [5 (3.5-8.60)]
Ca <sup>2+</sup> , mg/dl	8.4-10.2	8.54 ± 1.52 [8.43 (3.79–13)]
PO4 <sup>3-</sup> , mg/dl	3-4.5	5.95 ± 2.14 [5.52 (2.37–12.08)]

COPD, chronic obstructive pulmonary disease; DBP, Diastolic blood pressure; ESKD, end-stage kidney diseas; Max, maximum; MCHC, mean corpuscular haemoglobin concentration; MCV, mean corpuscular volume; Min, minimum; SBP, systolic blood pressure.

<sup>a</sup>Others co-morbidities: thyroid dysfunction, COPD, asthma

<sup>b</sup>Erythropoietin use in previous months.

<sup>c</sup>Optimal targets defined as in this study.

# Discussion

Our cross-sectional study included 104 patients with chronic kidney disease stage 5 under haemodialysis. In our study, more than three-fourths of the study participants (82, 78.8%) were aged 40 years and above, with a mean age of  $54.02 \pm 14.03$  years and the majority being male (70, 67.3%). The demographic findings in our study were similar to other studies from Nepal. A study conducted among CKD V visiting the haemodialysis unit of a teaching hospital in Nepal showed the mean age of the participants was  $46.9 \pm 17.9$  years, with male predominance (57, 57%)<sup>[14]</sup>. Similarly, another observational study from a tertiary hospital in Nepal showed the mean age of end-stage kidney disease patients on maintenance haemodialysis was 52.2 ± 15.6 years, with male predominance (96, 61.5%)<sup>[15]</sup>. A nationwide population-based cross-sectional study from Nepal showed that CKD was independently associated with older age, with the odds of having CKD being 1.4 (95% CI 1.0-1.8) and 2.6 (95% CI 1.9-3.6) times higher for 40-59 years and older than or equal to 60 years compared to 20-39 years people<sup>[16]</sup>. Likewise, a study from Pakistan also supports the demographic findings of our study, which showed the mean age of CKD patients undergoing maintenance haemodialysis was  $50.3 \pm 12.1$  years with a higher prevalence in males (47, 64.4%)<sup>[17]</sup>.

CKD and hypertension are closely related conditions, the latter can worsen kidney function while the former can, in turn, make it more difficult to control blood pressure<sup>[18]</sup>. Hypertension in CKD could be due to various factors such as reduced nephron mass, endothelial dysfunction, sympathetic overactivity, activation of the renin-angiotensin-aldosterone system, and increased sodium and water retention<sup>[18]</sup>. Longer haemodialysis sessions were associated with a highly statistically significant decrease in mean systolic and diastolic blood pressure  $(p \text{ value } < 0.001)^{[19]}$ . Our study showed that hypertension (100, 96.2%) was the most commonly associated comorbidity followed by diabetes (13, 12.5%). A nationwide population-based representative study from Nepal showed that there are higher odds of occurrence of CKD among patients with diabetes and hypertension, 3.2 (95% CI 2.5-4.1) and 2.4 (95% CI 2.0-3.0) times higher than normal participants, respectively<sup>[16]</sup>. A study among CKD patients under haemodialysis from Pakistan and Nepal showed similar results, the former study showed hypertension (38, 52.1%) and diabetes  $(30, 41.1\%)^{[20]}$  to be the most commonly associated comorbidity, and similar results in the latter study with 54% of hypertension and 18% of diabetes patients<sup>[14]</sup>. In contrast to our study, other studies from Nepal showed that 42 (30.4%)<sup>[21]</sup> and 68 (43.6%)<sup>[15]</sup> patients undergoing maintenance haemodialysis had diabetes mellitus as a leading cause of ESKD.

Anaemia is a very common complication associated with reduced quality of life and cardiovascular abnormalities in chronic kidney disease patients<sup>[14]</sup>. Looking at the haematological parameters in our study, 79.8% of patients had haemoglobin levels below the target range. However, most of them had normal MCV (85.6%) and all the patients had normal MCHC (100%). Our findings were supported by other studies from Nepal which showed that anaemia was present among 85 (85%)<sup>[14]</sup> and 127 (92%)<sup>[21]</sup> CKD patients on haemodialysis respectively. Likewise, a cross-sectional study from India conducted among chronic kidney disease patients under haemodialysis also showed that 124 (96.8%) CKD patients were anaemic, with normocytic normochromic anaemia (113, 91.1%) being the most common type<sup>[22]</sup>.

Lack of erythropoietin is one of the several mechanisms for the development of anaemia in CKD patients<sup>[14]</sup>. Half of our study population (54, 51.9%) also used erythropoietin, similar to a cross-sectional study from Nepal where 78 (43.5%) end-stage kidney disease patients under haemodialysis were regularly using erythropoietin analogues<sup>[21]</sup>. The clinical use of erythropoietin in the correction of anaemia among CKD patients has been successful in reducing related morbidity and mortality, improving functioning, exercise tolerance, cognitive function, and overall quality of life, through its anti-apoptotic, anti-inflammatory, angiogenetic, and cytoprotective effects in kidneys, cardiovascular system, brain and retina<sup>[23]</sup>. However, higher dose requirement may exert toxic effects and is an independent mortality predictor in haemodialysis patients, and adjuvant therapies should be considered for poor responders to erythropoietin<sup>[23,24]</sup>.

In our study, almost half of the CKD patients undergoing haemodialysis (50, 48.07%) were found to have hyperuricemia, which is higher compared to another study from Nepal (43, 31.2%), conducted among end renal stage disease patients



undergoing haemodialysis<sup>[21]</sup>. However, the prevalence of hyperuricemia in our study was lower compared to the study from Pakistan that showed nearly three-fourths of patients (56, 76.7%) who were under thrice weekly haemodialysis had hyperuricemia<sup>[17]</sup>. In our study, hyperuricemia was more prevalent in males (35, 70%). The higher prevalence of hyperuricemia in males could be due to their habit of smoking and alcohol consumption tendency than females<sup>[25]</sup>.

In various studies, evidence has shown hyperuricemia is not only a marker of renal dysfunction but also plays role in the progression and pathogenesis of CKD<sup>[17,26,27]</sup>. Hyperuricemia is associated with an increased risk of all causes of mortality (especially cardiovascular) among patients with CKD and on haemodialysis<sup>[12,26–28]</sup>. A study done by Selllamyr et al showed asymptomatic hyperuricemia does not particularly affect CKD progression unless uric acid crystallizes in the kidney which contributes to CKD progression<sup>[29]</sup>. However, urate-lowering therapies have shown evidence to slow the progression. A systematic review and meta-analysis of 12 randomized controlled trials reported that the treatment group (uric acid lowering therapy) had a reduced risk of worsening kidney function or ESKD or mortality than the control group (RR 0.39, 95% CI 0.28–0.52, P < 0.01)<sup>[30]</sup>.

Malnutrition might adversely affect the outcome in haemodialysis patients <sup>[15]</sup>; however, nutritional status and body mass index (BMI) of the participants were not accounted for in our study, which is a limitation of the study. Likewise, dietary regimens that might influence serum uric acid, alcohol consumption habits, and medication that might alter the serum uric acid level weren't considered during the study. This study being a single centred cross-sectional study, the findings mightn't be generalized, highlighting the need for multi-centric studies in the future.



Figure 2. Distribution pattern of electrolytes.



#### Table 2

Effect of selected clinical variables on serum uric acid level of participants with ESKD attending haemodialysis on an outpatient basis

	Hyperuricemia (≥7 mg/dl)	Binary logistic regression		
Variables	No, <i>n</i> (%)	Yes, <i>n</i> (%)	OR (95% CI)	Pª
Age (years)				0.541
20–39	10 (45.5)	12 (54.5)	1 (Ref.)	
40-59	23 (52.3)	21 (47.7)	0.76 (0.27-2.12)	
$\geq 60$	21 (55.3)	17 (44.7)	0.67 (0.23-1.94)	
Sex				0.314
Female	19 (55.9)	15 (44.1)	1 (Ref.)	
Male	35 (50.0)	35 (50.0)	1.27 (0.56-2.89)	
Duration of				0.235
haemodialysis				
< 5	20 (44.4)	25 (55.6)	1 (Ref.)	
5–10	17 (65.4)	9 (34.6)	0.42 (0.16-1.15)	
> 10	17 (51.5)	16 (48.5)	0.75 (0.30–1.85)	
Erythropoietin use				0.233
(prior month)				
Yes	25 (46.3)	29 (53.7)	1 (Ref.)	
No	29 (58.0)	21 (42.0)	0.62 (0.29–1.36)	

ESKD, end-stage kidney diseas; OR, odds ratio.

<sup>a</sup>*P* value from the  $\chi^2$  test.

# Conclusion

Our study showed that nearly half of the chronic kidney disease patients under haemodialysis had hyperuricemia. Around three-fourths of the study participants with hyperuricemia were aged 40 years and above, the majority being male. The most commonly associated comorbidity was hypertension and normocytic normochromic anaemia was common in the study participants.

## **Ethical approval**

The study was approved by the Institutional Review Committee (IRC) of the institution (Reference no. 647) on July 2022.

## Consent

Written informed consent was obtained from the participants for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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This study did not receive any grant from any funding agencies in public or organizations.

# **Author contribution**

A.M.B.: literature review, conceptualization, methodology, data collection, writing-original draft, review and edit. S.G.: literature review, conceptualization, methodology, data collection, formal analysis, writing-original draft, review and edit. A.A.: literature review, conceptualization, methodology, data collection, writing-original draft, review and edit. S.K.: literature review, conceptualization, methodology, data collection, writing -original draft, review and edit. B.D.P.: literature review, conceptualization, methodology, data collection, writing-original draft, review and edit. B.R.: literature review, methodology, data interpretation, writing-original draft, review and edit. M.K.: literature review, methodology, data interpretation, writingoriginal draft, review and edit. G.K.Y .: literature review, methodology, data interpretation, writing-original draft, review and edit. S.B.: literature review, methodology, data interpretation, writing-original draft, review and edit. All the authors approved the final version of the manuscript.

# **Conflicts of interest disclosure**

The authors declare that they have no conflicts of interest.

# Research registration unique identifying number (UIN)

- 1. Name of the registry: research registry.
- 2. Unique Identifying number or registration ID: research-registry9269.
- 3. Hyperlink to your specific registration (must be publicly accessible and will be checked): research registry.

## Guarantor

Dr. Ayush Mohan Bhattarai.

## **Data availability statement**

The datasets generated during and/or analyzed during the current study are publicly available.

### Provenance and peer review

Not commissioned, externally peer-reviewed.

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