Original Article

Prevalence of High Serum Uric Acid Level in Patients with Chronic Kidney Disease Stage II-V

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ABSTRACT

Background: Chronic kidney disease (CKD) has emerged as a significant public health issue affecting millions of individuals of all races and ethnic groups. It's also a major health burden in Nepal. Hyperuricemia is widely established as a risk factor for glomerulosclerosis, interstitial fibrosis, and atherosclerosis. However, reversing and preventing it in CKD will delay the course of chronic renal failure. Therefore, this research was designed to examine the uric acid profile in CKD patients who are receiving conservative therapy to avoid the worsening of CKD.

Methods: The study included a total of 90 CKD patients at stages II-V. The complete history taking, clinical examination, and laboratory testing were done and the data were analyzed using SPSS version 22. The prevalence of hyperuricemia was determined and compared at various stages of CKD.

Results: Among the enrolled patients (n = 90), the majority were male (66%) in gender. The maximum number of patients (44%) were elderly (60-80 years). Hyperuricemia was present in 80% of patients. Among them, two patients were in stage II (7.4±0.42), five in stage IIA (8.8±1.22), 25 in stage IIIB (8.59±1.63), 36 in stage IV (9.21±1.49), and three patients were in stage V (10.70±1.609).

Conclusion: Serum uric acid levels were elevated in various stages of CKD patients. Thus, serum uric acid may be used as a predictive indicator of CKD. However, large-scale cohort research of the Nepalese population is suggested to corroborate the results of this study.

Keywords: Uric Acid, Hyperuricemia, Prevalence, Nepal, Kidney Failure, Chronic

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INTRODUCTION

Chronic Kidney Disease (CKD) is defined by Kidney Disease Improving Global Outcomes (KDIGO) as kidney damage or a glomerular filtration rate (GFR) of less than 60 ml/min/1.73m^2 for three months or longer, regardless of the cause.[1-3] Millions of people around the globe die each year of end-stage chronic renal disease and acute renal failure.[4,5] According to the Global Burden of Disease 2015 study, 1.2 million individuals died of renal failure in 2015.[6] In Nepal, CKD has only recently been recognized as a severe public health concern.[7] In metropolitan regions, the estimated

prevalence of CKD is around 10.6%. According to research conducted by the International Society of Nephrology's Kidney Disease Data Center (ISN-KDDC) across 12 low- and middle-income countries, the prevalence of CKD was found much more significant in the Nepali population.[8]

Uric acid is the purine metabolism's ultimate oxidation product, which is eliminated by the kidneys.[9] Elevated blood uric acid levels are reported in individuals with decreased GFR owing to impaired nephron clearance. It was recently discovered that uric acid has a causative role in the pathogenesis of chronic kidney disease (CKD) and perhaps acute renal damage (AKI).[10] Hyperuricemia is a significant factor in advancing chronic kidney disease (CKD) and the development of hypertension.

Shree Birendra Hospital receives a high volume of CKD patients, and CKD is regarded as one of the primary causes of death and morbidity. This is the first research undertaken at Shree Birendra hospital to provide a crude estimate of the frequency of hyperuricemia in CKD patients throughout the various age groups of militaries and their families. Thus, this research was conducted to determine the incidence of hyperuricemia in patients with CKD stages II-V, which may be beneficial in predicting future outcomes related to the development of CKD and end-stage renal disease (ESRD). This research will aid in the prevention and treatment of hyperuricemia in CKD patients to slow the course of the disease.

MATERIALS AND METHODS

Study design and setting

Cross-sectional and observational research was conducted at Shree Birendra Hospital, Chhauni, Kathmandu, on CKD patients. The study took place between 15 June 2018 and 17 December 2019.

Sampling

Patients with CKD receiving medical therapy and visiting the Shree Birendra Hospital's department of internal medicine throughout the research period were included using a non-random sample approach. A total enumerating sample was utilized to select a total of 90 patients (N = 90) from the medicine department of Shree Birendra Hospital. This research comprised patients with CKD stages II, III, IV, and V who were admitted to the internal medicine department of Shree Birendra Hospital in Chhauni, Nepal. Patients of both sexes who were >18 years of age and willing to agree were included. Whereas the patients of <18 years of age, HIV-positive cases, gout, known hyperuricemic cases, and the patients taking anti-tubercular and/or thiazides drugs were excluded. Similarly, CKD patients on dialysis and those who refused to give consent were also excluded from the study.

Criteria for definition of CKD (KDIGO 2012)[11]

Duration: More than three months, based on documentation or inference

GFR: Less than 60 ml/min/1.73m^2 (GFR categories G3a-G5)

Kidney damage is defined by structural or functional abnormalities other than decreased GFR.

Markers of kidney damage

Albuminuria (≥30 mg/24 hours, approximately equivalent to urine albumin to creatinine ratio (ACR) ≥30 mg/g (≥3mg/mmol)), urinary sediment abnormalities, renal tubular disorders were considered markers of the kidney damage. Similarly, pathologic abnormalities detected by histology or inferred, structural abnormalities detected by imaging (ultrasound, computed tomography, and magnetic resonance with or without contrast, isotope scans, angiography), and history of kidney transplantation were also considered.

CKD staging

CKD staging is done using the Cockroft and Gault equation.

Creatinine clearance = [{(140-age) x wt in kg} / (72 x Serum Creatinine mg\dl)] x 0.85 (if female).

CKD staging was done as described in table 1.

Table 1: CKD staging based on estimated GFR[11,12]

Stage (GFR category)		GFR, mL/min per 1.73 m^2	Terms
1		≥90	Normal or high
2		60-89	Mildly decreased
3	a	45-59	Mildly to moderately decreased
	b	30-44	Moderately to severely decreased
4		15-29	Severely decreased
5		<15	Kidney failure

Ethics approval

The Institutional Review Committee of the Nepalese Army Institute of Health Sciences (NAIHS – IRC, Ref. No. 245) authorized the research. Before patients were included in the study, informed written consent was taken. A complete clinical history, examinations, and investigations were conducted, including uric acid testing.

History and clinical examination

The patients completed a full clinical history in the predesigned proforma. Data were collected regarding demographic characteristics such as age, gender, residence, and profession. The presenting symptoms including a history of smoking, alcohol intake, and major history of diabetes mellitus, hypertension, and treatment were recorded. A complete physical examination was conducted, including vital signs such as blood pressure and pulse rate, height and weight, and pertinent systemic examinations.

Laboratory investigations

Routine laboratory tests for CKD were performed on out-patient and in-patient CKD patients, including complete blood count, blood sugar, urea, creatinine, sodium, potassium, calcium, phosphorus, total protein, albumin, urine analysis, abdominal ultrasonogram, and electrocardiogram. After confirming the diagnosis of CKD with staging, a blood sample for uric acid was sent.

Estimation of serum uric acid was done by Kabasakalian method (uricase method) in Shree Birendra Hospital.[13]

Serum uric acid of >7 mg/dl in males and >6 mg/dl in females were considered hyperuricemia.

Data processing

The data were tabulated, and an interim analysis was performed using SPSS 22. The findings were presented in the form of tables, graphs, and diagrams. The prevalence of hyperuricemia was determined and compared among CKD stages. The unpaired t-test (for continuous variables) and the χ^2 tests (for categorical variables) were used in the statistical analysis. A 95% confidence interval was used in this investigation, and a p-value of 0.05 was considered significant.

RESULTS

A systematic evaluation of the various literature and comparison with this study was done to establish the impact of hyperuricemia in CKD patients.

Demographic and physical assessment of the study population

According to the study population's age distribution, a maximum of 40 patients (44%) were found to be between the ages of 60 and 80 years, and a minimum of 6 patients (7%) were found to be between the ages of 80 and 100 years (Figure 1).

Physical assessment of the study population

Hypertension was present in most of the patients with chronic kidney disease. The p-value of systolic blood pressure was found to be 0.037 and diastolic blood pressure was found to be 0.026 which was significant (Table 2). Comparing the weight in kg among males and females, mean weight in males was 55.75±6.91,

and mean weight in females was 53.74±6.45 (P-value > 0.05, Table 2).

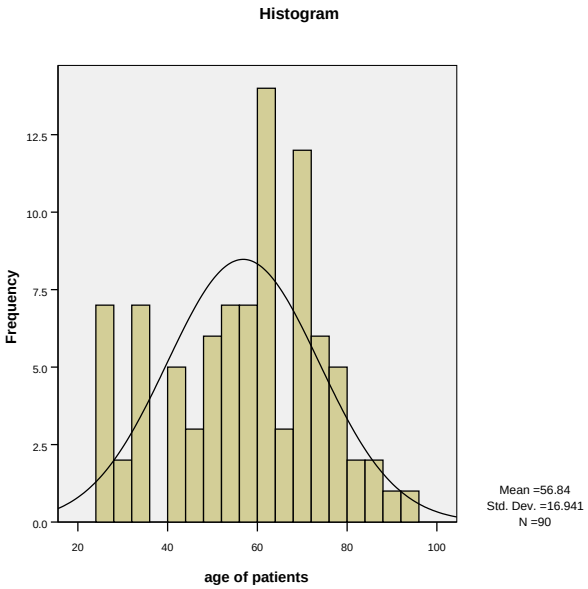

Figure 1: Age-wise distribution of patients

Table 2: Gender wise assessment of physical parameters of patients

Parameters	Gender	Mean	SD	P-value
Systolic BP (mmHg)	Male	149.83	16.24	0.037
	Female	142.26	15.856	
Diastolic BP (mmHg)	Male	96.10	9.28	0.026
	Female	91.61	8.20	
Weight (kg)	Male	55.75	6.91	0.185
	Female	53.74	6.45	

Among the study populations, most of the patients had hypertension. Out of 90 CKD patients, 82 patients (91.2%) had hypertension, and eight patients (8.8%) did not have hypertension (Table 3). Similarly, 26 patients (28.8%) had diabetes mellitus (Table 4).

Table 3: Association between chronic kidney diseases and hypertension

CKD stage	Hypertension		Total
	Yes	No	
II	3 (3.3)	0 (0)	3 (3.3)
IIIA	8 (9)	0 (0)	8 (9)
IIIB	33 (36.7)	2 (2.2)	35 (38.9)
IV	36 (40)	5(5.5)	41 (45.5)
V	2(2.2)	1 (1.1)	3 (3.3)
Total	82 (91.2)	8 (8.8)	90 (100)

Table 4: Association between chronic kidney diseases and diabetes mellitus

CKD stage	Diabetes mellitus		Total	P-value
	Yes	No		
II	1 (1.1)	2(2.2)	3(3.3)	0.224
IIIA	1(1.1)	7 (7.8)	8 (8.9)	
IIIB	7 (7.8)	28 (31.1)	35 (38.9)	
IV	15 (16.6)	26 (29)	41 (45.6)	
V	2 (2.2)	1 (1.1)	3 (3.3)	
Total	26 (28.8)	64 (71.2)	90(100)	

Hyperuricemia in various stages of CKD

Out of the total 90 CKD patients, 71 patients (80%) had hyperuricemia, whereas, the remaining 19 patients (20%) had normal uric acid levels (Figure 2).

One-way analysis of variance (ANOVA) was performed to test the mean differences among the CKD stages. P-value was found to be 0.024, which was <0.05. Hence, it is statistically significant (Table 5).

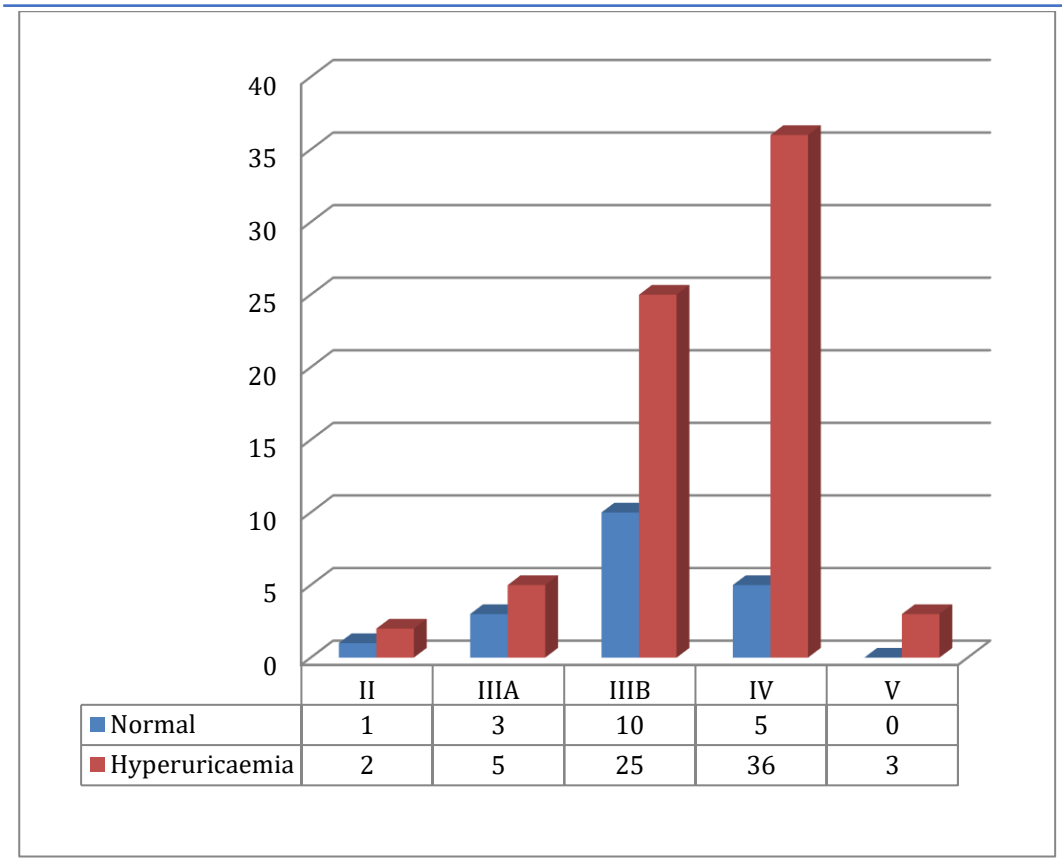

Figure 2: Prevalence of hyperuricemia according to CKD stage

Table 5: Mean and SD of the uric acid level in normal and hyperuricemia patients

Stages	Normal (Mean±SD)	Hyperuricemia (Mean±SD)	P-value
II	6.1	7.4±0.42	0.024
IIIA	5.56±1.40	8.8±1.22	
IIIB	5.74±0.35	8.59±1.63	
IV	5.18±0.268	9.21±1.49	
V	0	10.70±1.609	

DISCUSSION

This research examined the incidence of hyperuricemia in a total of 90 CKD patients, 59 of whom were male (66%) and 31 were female (34%). The participants were with mild to severe CKD (i.e. CKD stages II, III, IV, and V) on conservative therapy of medications.

In our study, hyperuricemia was present in 71 patients (80%), while 19 patients (20%) had normal uric acid levels. According to the stages of CKD, hyperuricemia was present in 2 patients (66%) (7.4±0.42), five patients (62.5%) (8.8±1.22), 25 patients (71%) (8.59±1.63), 36 patients (88%) (9.21±1.49) and 3 patients (100%) (Mean 10.70±1.609) in stages II, IIIA, IIIB, IV, and V respectively.

The findings of this study were comparable to a cross-sectional study conducted in Cameroon with 103 patients by Doualla et al. In such study, the mean age was 55.78±12.58, 61 patients were male, and hyperuricemia was present in 69 patients, with mean serum uric acid being 7.6 mg/dl ± 2.02.[14]

Similarly, the result of this study was comparable to the findings of Jolly et al. who studied 1078 individuals in the Genetics of Coronary Artery Disease in Alaska Natives (GOCADAN) research, which followed the patients for four years. There were 75 individuals with chronic kidney disease in total. The mean age of patients with chronic kidney disease was 63 years; 47 (63%) had hypertension, and 7 (9%) had

diabetes mellitus. The mean blood uric acid level was 6.5±1.9 mg/dl in the research subjects.[15]

Satirapoj et al. found that the mean blood uric acid level was 7.82±1.80, and hyperuricemia was considerably greater in the male population (77.1%) in observational research conducted at Armed Forces Research Institute of Medical Sciences in Bangkok, Thailand. Additionally, the study discovered that high blood uric acid was related to an increased incidence of chronic kidney disease.[16]

Similarly, cross-sectional descriptive research was undertaken on 120 consecutive pre-dialysis chronic kidney disease patients at the University of Benin Teaching Hospital in Benin City, Nigeria. The research lasted two years. The mean patient age was 48.77 years, and 76% of the study group was male. 36.7% of the sample group had hypertension, whereas 30% had diabetes. In this study, the mean uric acid concentration was 6.91±3.78 mg/dl. Hyperuricemia was prevalent in 47.5% of CKD participants, much greater than the 15% reported in the control group (P 0.001).[17] Similarly, hyperuricemia was detected in 71 patients (80%) in our research, with a P-value of 0.024, which was 0.05. As a result, the difference is statistically significant.

Limitations This research has drawbacks since it was conducted on a limited scale with different groups inside the army and their beneficiaries, which may not reflect the whole nation. As a result, the study's results may not be generalizable to the entire population. There was no detailed food history obtained, and calorie consumption may have influenced the uric acid levels. The research excluded patients on maintenance hemodialysis and peritoneal dialysis.

CONCLUSION

The majority of individuals with chronic kidney disease were found to have hyperuricemia in this research. Hyperuricemia was connected with the stage of CKD in this research, indicating that serum uric acid may be used as a predictive indicator in CKD patients. Given the research's limited sample size and inherent limitations as a cross-sectional study, more large-scale cohort studies among the Nepalese population are required to bolster the findings of this study.

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