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Uric acid level in Chronic Kidney Disease patients and its association with other established CKD risk factors

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ABSTRACT

Introduction: Chronic Kidney Disease (CKD) is a rising global health concern with increased cardiovascular risks. Hyperuricemia, linked to CKD and related conditions, warrants investigation.

Objectives: This study examines the uric acid in different stages of CKD and the association between uric acid levels and established CKD risk factors.

Methodology: A hospital-based prospective cross-sectional study was conducted at Birat Medical College Teaching Hospital from 10 June 2023 to 30 August 2023. We enrolled 90 patients with non-dialytic chronic kidney disease (CKD) by complete enumeration sampling method. Ethical approval was obtained from the institutional review committee of the college. Written informed consent was obtained from each participant. Data was collected by means of a self developed questionnaire. Blood samples were obtained for estimation of serum creatinine and uric acid level and recorded in Microsoft excel sheet and analyzed by using SPSS software version 23.

Results: Hyperuricemia was seen in 33(36.7%) ranging from 3.5-12 mg/dl with an average uric acid level of 6.38 mg/dl and a standard deviation of 1.43 mg/dl of total 90 patients. The mean serum uric acid level was highest in stage 2 CKD which includes 6.88±2.10 ranging from 4.3-12 mg/dl. CKD patients with a history of alcohol intake had increased risk of hyperuricemia and it was statistically significant (p value 0.005). Different stages of CKD (p value: 0.70), age groups, (p value 0.17), gender(P value 0.082), diabetes(p value 0.954), hypertension(p value 0.364), other CVDs(p value 0.649)and anemia(p value 0.0602)had no statistical significant association with hyperuricemia.

Conclusion: In conclusion, hyperuricemia prevalence was observed in CKD patients, with the highest levels in stage 2 CKD. Notably, alcohol intake significantly correlated with hyperuricemia, while other studied factors did not show significant associations.

INTRODUCTION

Chronic Kidney Disease (CKD) is a significant global health concern characterized by the gradual loss of kidney function over time. Its prevalence has been on the rise by 29·3% (26·4 to 32·6) from1990 to 2017, leading to a substantial burden on healthcare systems and public health efforts.[1] As of 2019, the global prevalence was 9.1%.[1] A population based survey in 2019 stated the 6% prevalence of CKD in Nepal.[2] CKD not only impacts kidney function but also elevates the risk of cardiovascular disease, end-stage renal disease, and mortality.[3] Among the numerous risk factors associated with CKD, hyperuricemia has garnered increasing attention in recent years. Uric acid, a metabolic byproduct of purine metabolism, is primarily excreted by the kidneys.[4] Elevated levels of uric acid have been linked to the development of various health conditions, including gout, hypertension, metabolic syndrome, and cardiovascular diseases.[5,6] Emerging evidence suggests that hyperuricemia may play a pivotal role in the pathogenesis and progression of CKD.[7] The intricate relationship between uric acid levels and CKD is multifaceted. While the exact mechanisms underlying this

association are not yet fully elucidated, several hypotheses have been proposed. Uric acid has been suggested to contribute to renal damage through various pathways, including endothelial dysfunction, inflammation, oxidative stress, and activation of the renin-angiotensin-aldosterone system.[8] Moreover, uric acid has been implicated in promoting renal fibrosis and tubulointerstitial injury, which are hallmark features of CKD.[8] CKD is a complex disorder influenced by a multitude of factors, thus exploring the correlation between uric acid levels and established CKD risk factors is crucial for comprehending the disease's underlying mechanisms. Hypertension and diabetes mellitus are established risk factors for CKD. Investigating the interplay between these risk factors and uric acid levels could provide valuable insights into the potential synergistic effects and interactions that contribute to CKD development and progression. Hence, this study delves into the evaluation of uric acid level in CKD patients and its association with other established CKD risk factors.

METHODOLOGY

We conducted a hospital based prospective cross-sectional study design from 10 June 2023 to 30 August 2023 in the hemodialysis unit, Department of Internal Medicine, at Birat Medical College Teaching Hospital. Patients diagnosed with chronic kidney disease, nondialytic and willingness to participate in the study were enrolled for the study. Patients with known cases of hyperuricemia and those on dialysis were excluded from the study. A total of 90 samples were consecutively taken during the study period by complete enumeration sampling. Ethical approval was taken from the institutional review committee of Birat medical college prior to conducting research (IRC-PA-312/2023). Written informed consent was obtained from each participant before collecting data. Participants were interviewed using a self-developed questionnaire on sociodemographic characteristics that includes age, sex, comorbid illness, smoking, alcoholic history. Blood samples were obtained for estimation of serum creatinine and uric acid level and recorded. The eGFR was calculated using the National Guideline al Kidney Foundation app-based Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI)

calculator.[9]Participants were then staged for CKD as per the Kidney Disease Improving Global Outcomes (KDIGO) criteria by National Kidney Foundation. Chronic kidney disease was defined as abnormalities in kidney structure or function present for ≥ three months, with implication for health or GFR < 60 ml/min/1.73 m^2 for three or more months, irrespective of cause. CKD was graded on stage 1, stage 2, stage 3a, 3b, stage 4 and stage 5 based on the KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases 2021. [10] Hyperuricemia was defined as serum uric acid concentration > 7mg/dl in men and > 6mg/dl in women.[11]

The collected data were entered in Microsoft excel sheet and analyzed by using SPSS software version 23. Frequency, Mean and standard deviation was calculated for univariate analysis. Mean comparisons of values of parameters in between patients with five stages of CKD and age groups were done by using ANOVA (Analysis of Variance Test). Pearson's chi square test was used to find the association between CKD risk factors and uric acid level. P value less than 0.05 at 95% confidence interval was considered statistically significant.

RESULTS

Table 1: Baseline characteristics of patients (n=90)

Baseline characteristics	n(%)
Age groups in years	
30-45	28(31.1)
46-60	33(36.7%)
61-75	22(24.4)
>75	7(7.7)
Sex	
Male	52(57.8)
Female	38(42.2)
Risk factors	
Hypertension	63(70)
Anemia	66(72.5)
Alcohol	60(66.7)
Smoking	55(61.1)
Other cardiovascular diseases (CVD)	49(53.4)
Diabetes	44(48.9)

The study included 90 patients with chronic kidney disease with a mean age of 53.9±12.6 years. Maximum number of the patients were from the age group 46-60 years 33(36.7%) followed by the age group 30-45 years 28(31.1%). More than half 52(57.8%) were male. Seventy Percent had hypertension and nearly 49% had diabetes. Table 1.

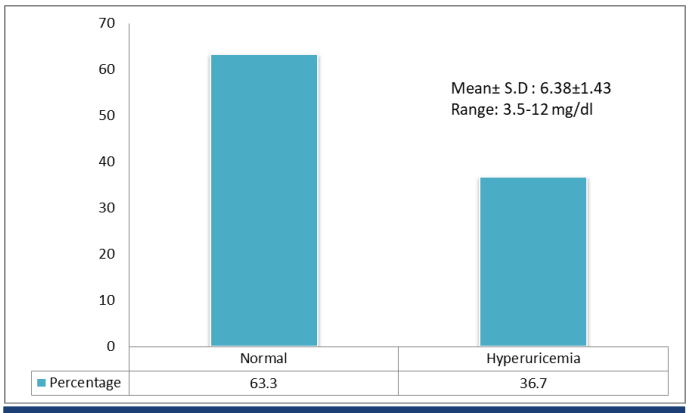

Fig 1: Prevalence of serum uric acid in patients with chronic kidney diseases (n=90)

Among the 90 patients with Chronic Kidney Disease (CKD), 33(36.7%) exhibited hyperuricemia, with mean uric acid concentration of 6.38 mg/dl and a standard deviation of 1.43. The serum uric acid levels within this group varied between 3.5 mg/dl and 12 mg/dl, figure 1.

Table 2: Evaluation of uric acid in different stages of chronic kidney disease and different age group of patients (n=90)

Stages	No. of patients	Uric acid level (mg/dl)			P value
		Mean± SD	Minimum	Maximum	
Stage 2	9 (10)	6.88±2.10	4.3	12	0.70
Stage 3	16 (17.7)	6.26±0.93	4.6	7.4	
Stage 4	19 (21.1)	6.46±1.38	4.7	9	
Stage 5	46 (51.1)	6.30±1.45	3.5	9.8	
Age groups in years					
30-45	28(31.1)	5.9±1.1	3.5	8	0.17
46-60	33(36.7)	6.4±1.6	3.8	12	
61-75	22(24.4)	6.62±1.25	4.3	9	
> 75	7(7.7)	6.97±1.98	4.4	9.7	

The mean serum uric acid level is highest in stage 2 CKD which includes 6.88±2.10 ranging from 4.3-12 mg/dl. Also, the mean serum uric acid level was increased with increasing age highest in the age >75 years. However, there was no statistically significant association of uric acid level with different stages of CKD (p value: 0.70) and different age groups (p value 0.17), table 2.

Table 3: Association of uric acid level with various risk factors for Chronic kidney diseases n (%)

Parameters		High uric acid group (n=33)	Normal uric acid group (n=57)	Total	P value
Age in years	30-60	20(32.79)	41(67.21)	61	0.268
	≥ 61	13(44.83)	16(55.17)	29	
Gender	Male	23(44.2%)	29(55.8%)	52	0.082
	Female	10(26.3%)	28(73.7%)	38	
Diabetes	Yes	16(36.4%)	28(63.6%)	44	0.954
	No	17(34.0%)	29(66.0%)	46	
Hyperten-sion	Yes	25(39.7%)	38(60.3%)	63	0.364
	No	8(29.6%)	19(70.4%)	27	
Alcohol	Yes	28(46.7%)	32(53.3%)	60	0.005
	No	5(16.7%)	25(83.3%)	30	
Smoking	Yes	16(29.1%)	39(70.9%)	55	0.062
	No	17(48.6%)	18(51.4%)	35	
CVD	Yes	19(38.8%)	30(61.2%)	49	0.649
	No	14(34.1%)	27(65.9%)	41	
Anemia	Yes	28(42.1%)	38(57.6%)	66	0.0602
	No	5(20.8%)	19(79.2%)	24	

CKD patients with a history of alcohol intake had increased risk of hyperuricemia and it was statistically significant (p value 0.005). There was increased prevalence of hyperuricemia in the age ≥ 61 years, male, patients with history of diabetes, hypertension, other CVDs and anemia however no statistical significant association was found, Table 3.

DISCUSSION

We conducted an observational study with the objective to evaluate uric acid level at different stages of chronic kidney disease patients and its asssociation with CKD risk factors. Nearly 37% of patients had hyperuricemia in our study. The mean value

of uric acid was 6.3± 1.4 mg/dl.We found that there were no statistical association of serum uric acid level and different stages of CKD, age group, sex, comorbidities like hypertension and diabetes. A study conducted in Shree Birendra Hospital Chhauni among 90 patients stated that hyperuricemia was present in 71(80%)patients which is significantly higher compared to our study.[12] Studies conducted by Hariharan C and Suresh CH in 2017 found the mean SUA level of 8±1.3 mg/dl, which was higher than ours. The difference might be due to geographical variation, diet and lifestyle changes.[12] In our study, the maximum percentage of patients were in stage 5 CKD 46(51%) followed by stage 4, 19(21%). We found that the mean uric acid level differs in different stages of CKD and it was higher in stage 2 and stage 4 in our study. Contrast to our finding, mean serum uric acid level was increasingly higher with increasing age in a study from Shree Birendra Hospital Chhauni where the stage 5 CKD had an increasing percentage of hyperuricemia compared to other stages (mean +/- S.D. 10.70±1.609). [12] Our study demonstrated that the mean serum uric acid level increases with increasing age which is 5.9±1.1 in 30-45 years to 6.97±1.98 in age above 75 years. However there was no statistical significant association between the increased level of uric acid and different age groups. Similar finding was observed in a study by Shrawan kumar Yadav etal. which stated that the mean uric acid level was increased with increasing age ≥ 65 years (7.61 +/- 2.39)[13]

We observed that the prevalence of hyperuricemia was higher in CKD patients with hypertension 25(39.7%) than those without hypertension which was 8 (29.6%) though there was no statistically significant association (p value: 0.36). Research suggests that there is a bidirectional relationship between uric acid, hypertension, and CKD. This means that each condition can contribute to the development or exacerbation of the other. Uric acid, an antioxidant, helps to control blood pressure during a low sodium diet through activation of the renin angiotensin system.[14,15] Uric acid has also been associated with endothelial dysfunction, oxidative stress, inflammation, and impairment of nitric oxide function—all of which can contribute to high blood pressure.[15] On the other hand, hypertension can also contribute to the development of hyperuricemia. High blood pressure can affect kidney function, leading to reduced clearance of uric acid from the bloodstream. Hyperuricemia can further exacerbate the relationship between hypertension and CKD. High uric acid levels contribute to kidney damage by promoting inflammation, oxidative stress, and kidney tissue fibrosis. Thus increasing the risk of developing CKD, as well as an increased risk of progression of CKD to more advanced stages.[15-17] In this study, prevalence of hyperuricemia was more in male patients (44.2%) compared to female patients (26.3%) however there was no statistically insignificant (p value: 0.082). We observed that CKD patients with diabetes had an increased prevalence of hyperuricemia, (36.4%) than those without diabetes 34%. There was a statistically significant association between alcohol intake history and hyperuricemia in our study. Consistent with our finding, a study from Morang District had a similar finding where the prevalence of hyperuricemia was higher in males (30.06%) and alcoholic group.[13] A study showed that older, males, diabetic, alcohol drinkers and former smokers had hyperuricemia. It also showed that hyperuricemic patients had increased systolic blood pressure and an increased percentage of chronic kidney disease.[18] The low prevalence of hyperuricemia in females might be due to uricosuric action of estrogen, genetic influence, dietary habits, lifestyle choices, and age-related hormonal changes.[19] Diabetes, hyperuricemia, and chronic kidney disease can collectively contribute to each other's development and progression. Elevated uric acid levels in individuals with diabetes might further exacerbate kidney damage and the risk of CKD by damaging the renal blood vessels, impairing their ability to filter waste products and regulate fluid and electrolyte balance. [20,21] Excessive alcohol consumption leads to the increased production of uric acid, causes diuretic effect resulting in dehydration and higher uric acid concentration in the body. Excessive and chronic entail also have detrimental effects on kidney function.[22,23]

Conclusion: In conclusion, hyperuricemia prevalence was observed in CKD patients, with the highest levels in stage 2 CKD. Notably, alcohol intake significantly correlated with hyperuricemia, while other studied factors did not show significant associations.

RECOMMENDATIONS

We recommend conducting long-term follow-up and a more diverse and larger cohort study to enhance the robustness and applicability of the conclusions.

Limitation of the study: While this study provides valuable insights into the relationship between hyperuricemia and different stages of CKD, certain limitations should be acknowledged. The sample size of 90 patients, while providing useful data, might not fully represent the diversity of CKD patients. The study's cross-sectional design restricts our ability to establish causal relationships or assess the impact of temporal changes. Additionally, relying on self-reported data for factors such as alcohol intake and sociodemographic characteristics could introduce recall bias. The study's single-center nature might limit the generalizability of findings to broader populations.

LIMITATIONS OF THE STUDY:

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CONFLICT OF INTEREST None

FINANCIAL DISCLOSURE None

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