

## Original Research Article

# Uric acid levels in chronic kidney disease- a hospital based cross-sectional study in RIMS, Ranchi, Jharkhand

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### ABSTRACT

**Background:** Uric acid is the final end product of purine metabolism and is excreted mainly by proximal tubules of the kidney. Raised uric acid levels may lead to proximal tubular injury, endothelial dysfunction, oxidative stress and intra renal inflammation in patients with normal renal function. Uric acid has been deemed as an independent risk factor for progression of CKD. Aim was to study the uric acid levels in different stages of chronic kidney disease and its association with age, sex and other co-morbidities.

**Methods:** 140 patients of chronic kidney disease admitted in RIMS, Ranchi were included in this study and their serum uric acid level were analyzed. Uric acid level more than 7 mg/dl was considered as hyperuricemia. The study was approved by the Institutional Ethics Committee, Rajendra Institute of Medical Sciences, Ranchi, Jharkhand, India. Informed consent was taken from every patient included in the study.

**Results:** Median age±SD was 55±13.47 years (IQR: 45,65; Range: 19-80). Mean±SD uric acid levels in stage 3 CKD was 4.4±1.9 mg/dl, stage 4 CKD was 6.5±4.1 mg/dl, stage 5 CKD was 8.8±3.1 mg/dl (p<0.05). Females were 31.4% and males were 69.6%. Male to female ratio was 2.2:1. The prevalence of hyperuricemia was 50% in females and 66.6% in males.

**Conclusions:** Hyperuricemia is common among CKD patients and more common among males. Uric acid levels increase with progressive decline in eGFR. Monitoring and follow-up of such patients by may lead to delay in onset and progression of complications of CKD.

**Keywords:** CKD, Nephropathy, Uric acid

### INTRODUCTION

CKD is defined as the presence of kidney damage, manifested by abnormal albumin excretion or decreased kidney function, quantified by measured or estimated glomerular filtration rate (GFR), that persists for more than three months.<sup>1,2</sup> Both complications and likelihood of progression to end-stage renal disease requiring renal replacement therapy are more likely to occur in patients with additional co-morbidities. Early intervention will more commonly reduce serious CKD sequelae and slow CKD progression. To facilitate assessment of CKD severity, the National Kidney Foundation developed a

criteria as part of its Kidney Disease Outcomes Quality Initiative (NKF KDOQI™) to stratify CKD patients:<sup>3</sup>

Stage 1: normal eGFR  $\geq$  90 mL/min per 1.73 m<sup>2</sup> and persistent albuminuria. Stage 2: eGFR between 60 to 89 mL/minute per 1.73 m<sup>2</sup>. Stage 3: eGFR between 30 to 59 mL/minute per 1.73 m<sup>2</sup>. Stage 4: eGFR between 15 to 29 mL/minute per 1.73 m<sup>2</sup>. Stage 5: eGFR of <15 mL/minute per 1.73 m<sup>2</sup> or end-stage renal disease.

Uric acid is the final product of purine metabolism and is excreted primarily by the kidney and to a lesser extent, the gut.<sup>4</sup> Therefore, elevated serum uric acid levels are

seen in patients with reduced glomerular filtration rate (GFR). However, in recent years, it has been proposed that uric acid itself plays a causal role in the pathophysiology of chronic kidney disease or it may be a consequence of CKD. Elevated uric acid level is known to cause endothelial dysfunction, vascular smooth muscle cell proliferation, increased IL-6 synthesis, and impairment of nitric oxide production, all of which may contribute to the progression of chronic kidney disease.<sup>5</sup> Some patients with elevated uric acid level experience joint pains, joint stiffness with restricted movement of that particular joint. Uric acid lowering therapy in CKD has been reported to delay the disease progression, however some studies have suggested no benefits.<sup>6-9</sup>

We aim to study the uric acid levels in different stages of chronic kidney disease and its association with age, sex and other co-morbidities.

**METHODS**

Our study was a single centre, observational study in indoor ward, department of medicine, Rajendra Institute of Medical Sciences, Ranchi, Jharkhand.

The study was approved by the Institutional Ethics Committee, Rajendra Institute of Medical Sciences, Ranchi, Jharkhand, India. Informed consent was taken from every patient included in the study.

**Inclusion criteria**

All the patients above 15 years of age with confirmed chronic kidney disease and those diagnosed with CKD following evaluation between February 2020 and July 2020 were included in this study.

**Exclusion criteria**

Patients with other causes of hyperuricemia like gout, hypothyroidism, alcoholics, history of drugs causing hyperuricemia, iron overload, tumor lysis syndrome were excluded from this study after performing relevant investigations.

Serum uric acid was measured using colorimetric method and eGFR was estimated using CKD EPI equation.<sup>6</sup> Serum uric acid levels more than 7 mg/dl was considered as hyperuricemia.

**Statistical analysis**

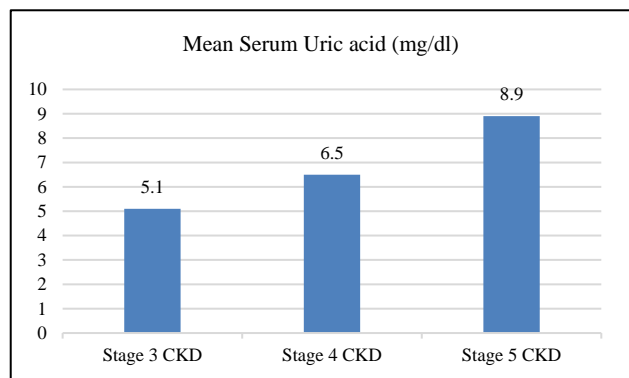
The data thus obtained was analyzed using statistical methods in which quantitative variables were summarized using mean and standard deviation while categorical variables were tabulated using frequencies and percentages and compared using the chi-square ( $\chi^2$ ) test. The level of statistical significance was  $p < 0.05$ . All hypothesis tests were 2-tailed. SPSS software version 21.0 was used to perform the analysis.

**RESULTS**

Median age $\pm$ SD was 55 $\pm$ 13.47 years (IQR: 45.65; range: 19-80). Females were 31.4% and males were 69.6%. Male to female ratio was 2.2:1 in our study. The prevalence of hyperuricemia was 50% in females and 66.6% in males. Mean $\pm$ SD uric acid level in our study was 7.9 $\pm$ 3.6 mg/dl. Uric acid levels in stage 3, stage 4 and stage 5 was statistically significant ( $p < 0.05$ ).

**Table 1: Serum uric acid levels in different stages of CKD.**

S. uric acid (mg/dl)	Stage 3	Stage 4	Stage 5
<7 mg/dl	10 (100%)	26 (68.6%)	26 (28.3%)
7-10 mg/dl	Nil	6 (15.7%)	26 (28.3%)
>10 mg/dl	Nil	6 (15.7%)	40 (43.4%)
<b>Total % (out of 140)</b>	10 (7.1%)	38(27.2%)	92 (65.7%)



**Figure 1: Mean serum uric acid levels in different stages of CKD.**

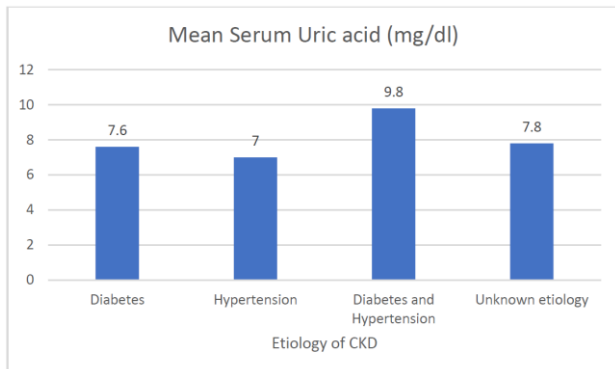
Hyperuricemia was seen in 31.4% cases with stage 4 CKD and 71.7% of cases with stage 5 CKD patients (Table 1). Mean $\pm$ SD uric acid levels in stage 3 CKD was 4.4 $\pm$ 1.9 mg/dl, stage 4 CKD was 6.5 $\pm$ 4.1 mg/dl, stage 5 CKD was 8.8 $\pm$ 3.1 mg/dl ( $p < 0.05$ ). Among cases with stage 3 CKD, all the cases had uric acid levels below 7 mg/dl. Among those with stage 4 CKD, 68.6% had uric acid levels <7 mg/dl, 15.7% had levels between 7-10 mg/dl, 15.7% had levels more than 10 mg/dl. While in those with stage 5 CKD 28.3% had uric acid levels <7 mg/dl, 28.3% had levels between 7-10 mg/dl, 43.4% had levels more than 10 mg/dl.

**Table 2: Mean uric acid levels in different stages of CKD.**

Uric acid levels (mg/dl)	Stage 3 CKD	Stage 4 CKD	Stage 5 CKD	P value
<b>Mean<math>\pm</math>SD</b>	5.1 $\pm$ 1.9	6.5 $\pm$ 4.1	8.8 $\pm$ 3.1	$p < 0.05$

In our study hyperuricemia was seen 32% cases in the age group of 46-60 years with CKD followed by 31.4%

in those with more than 60 years. Age group of 15-30 years was found to be least associated with hyperuricemia. Mean±SD serum uric acid levels in mg/dl in various causes of CKD is as represented in Figure 2. Hyperuricemia was seen in 52% cases with hypertensive nephropathy, 47.3% cases of diabetic nephropathy, in 77% cases with both diabetes-hypertension associated CKD and in 46.6% cases with unknown etiology of CKD.



**Figure 2: Mean serum Uric acid levels in various etiologies of CKD.**

## DISCUSSION

Median age was  $5\pm 13.47$  years (IQR: 45,65; range: 19-80) in our study which is consistent with median age of  $55.80\pm 13.49$  years (range: 14-82) as reported by Jha et al.<sup>10</sup> The proportion of males and females in our study was 69.6% and 31.4% respectively with male: female ratio of 2.2:1 which is similar to a previous report.<sup>11</sup> Mean uric acid levels in stage 3, stage 4 and stage 5 CKD was statistically significant ( $p<0.05$ ) as also suggested by a previous longitudinal study.<sup>12</sup> In this study, it was observed that uric acid level increases with progressive decline in eGFR and hyperuricemia among CKD patients is more common among males. However, a study by Chini et al reported that asymptomatic hyperuricemia was not an independent risk factor for progression of CKD.<sup>13</sup> Another study by Chonchol et al reported no statistically significant association between uric acid levels and incident CKD.<sup>14</sup> Various studies have reported elevated uric acid levels with progressive evolution of kidney disease, or vice versa.<sup>15-17</sup> Hyperuricemia as a cause of CKD or rather a consequence is still a matter of discussion. Multiple RCTs have demonstrated that uric acid lowering therapy can delay the progression of CKD.<sup>6-8</sup> A randomized control trial by Shi et al concluded no benefit from uric acid lowering therapy in CKD patient.<sup>9</sup> In our study, hyperuricemia was observed in 47.3% cases of diabetic nephropathy and 52% cases of hypertensive nephropathy which is similar to a previous report.<sup>18</sup>

Assessment of uric acid levels in CKD patients is an important aspect of management of CKD at a primary level of care. Monitoring and follow-up of such patients

by primary care physicians may lead to delay in onset and progression of complications of CKD. Treatment with uric acid lowering drugs may further decrease the morbidity and mortality associated with CKD.

This study has some limitations. Duration of CKD was unknown. Patients of CKD with hyperuricemia could not be followed up.

## CONCLUSION

There has been an association between stages of CKD and increasing level of serum uric acid level. Most patients with late stage of CKD have increased level of serum uric acid level, some symptomatic complaining of joint pain. Uric acid lowering agents help in improving symptoms.

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*Ethical approval: The study was approved by the Institutional Ethics Committee*

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