

Study on serum uric acid levels in patients with chronic kidney disease and associated factors

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Abstract

Introduction: Hyperuricemia, previously thought as a consequence of renal impairment, has been recently identified as an independent risk factor for the development of Chronic Kidney disease. (CKD) This study was done to find out the prevalence of hyperuricemia and the various clinical, demographic and social factors associated with hyperuricemia in patients with CKD.

Material and methods: This descriptive study was conducted at Chengalpattu medical college. The study population included 102 patients with CKD and 60 subjects without CKD as controls from the department of General medicine. Detailed history, anthropometry and clinical examination were recorded from all patients and uric acid levels were compared between the two groups. Other study parameters were analysed within the CKD group.

Results: Comparison was done between patients with CKD and the control group. Mean uric acid level in CKD group was 8.0 mg/dl and in non CKD group was 5.03 mg/dl which was found to be statistically significant (p value<0.001).

Among the CKD group Uric acid level is significantly higher in obese subjects (with raised waist hip ratio, high body mass index (BMI)). Uric acid level is significantly higher in diabetic and hypertensive CKD patients. Prevalence of coronary artery disease is significantly higher in CKD subjects with higher uric acid level.

Conclusions: Prevalence of hyperuricemia is significantly higher in CKD patients compared to normal subjects. Significantly high uric acid levels were recorded in subjects with raised waist hip ratio, higher BMI, those with diabetes and hypertension.

Keywords: hyperuricemia, CKD, T2DM, Hypertension

Introduction

Although high uric acid level is often seen in CKD patients, it was not clear whether hyperuricemia per se is an individual risk factor in development and progression of CKD. Studies have shown that increased uric acid decreases the levels of nitrite and nitrous oxide in body [1]. It also causes afferent renal arteriopathy and tubulointerstitial fibrosis through renin-angiotensin-aldosterone mechanism [2].

Hyperuricemia has been identified in diseases like obesity, diabetes mellitus, atherosclerosis, systemic hypertension, coronary artery disease, cerebrovascular disease, low physical activity, increased intake of purine rich diet like meat, leguminous vegetables and yeast and high socio economic status.

Literature from India is much scarce on the association of CKD with hyperuricemia. This study was undertaken to estimate the prevalence of hyperuricemia inpatient with CKD. It also evaluated the various clinical, demographic and social factors associated with hyperuricemia in CKD patients

Aim

1. To estimate the prevalence of hyperuricemia in patients with chronic kidney disease.
2. To evaluate the various clinical, demographic and social factors associated with hyperuricemia in CKD patients.

Material and Methods

Type of study: Hospital based descriptive study
Study Setting
 The study was undertaken in the Department Of General

Medicine and Department of Nephrology, Chengalpattu Medical College and hospital, Chengalpattu.

Duration of study: One year.

Inclusion criteria

Cases: Patients aged >18 years and diagnosed as chronic kidney disease

Controls: Age and sex matched patients without renal disease from the medicine outpatient department for minor illness.

Exclusion Criteria

1. Stage 1 and stage 2 CKD and stage 5 CKD on renal replacement therapy(RRT)
2. Patients with gout.
3. Patients on drugs affecting serum uric acid levels(thiazide diuretics, pyrazinamide, allopurinol)
4. Post renal transplant patients.
5. Patient on chemotherapy.
6. Pregnant women.
7. Patients with malignancy
8. Patients with chronic liver disease
9. Patients on lipid lowering drugs

Maneuver

Subjects were selected for the study based on the inclusion, exclusion criteria criteria. Patients with CKD were considered as cases and those without renal disease were considered as controls.

A detailed history, anthropometry, vital signs, clinical examination and laboratory parameters were recorded for both the study group.

1. Height: Height was measured with the help of a metric scale attached to a vertical board. The individual was made to stand bare foot. Measurement was recorded to the nearest 0.1cm
2. Weight: Dial type bathroom scale weighing machine was used for weight measurement. Weight was measured in kilogram.
3. Body mass index: Calculated using Quetelet index
 $BMI = \frac{W}{H^2}$
 Underweight <18
 Normal 18-24.9
 Grade I (over weight) 25-29.9
 Grade II (obese) 30-39.9
 Grade III (very obese) >40
4. Waist circumference, hip circumference and waist hip ratio: Waist and hip circumferences were measured in centimeters using a measuring tape. The least measurement in a horizontal plane between the costal margin and the iliac crest was taken as waist circumference. With thin clothes on, the largest protrusion of the buttock without compressing the skin was taken as hip circumference. Waist circumference • 88 cm in females and • 102 cm in males and WHR • 0.85 in females and • 0.90 in males were considered obese
5. Blood pressure recording: Sphygmomanometer is used to record the BP. BP is recorded in the sitting posture in the right upper limb using a proper sized cuff. Phase I Korokoff sound was taken as the systolic BP and disappearance of sound (phase IV) was taken as the diastolic BP.
6. Coronary artery disease: Cases are said to have coronary artery disease with any one of the following.
 - i) Past history of coronary artery disease with a documented evidence
 - ii) ECG changes of past or present myocardial infarction confirmed by an echocardiography by an experienced cardiologist.
7. Diabetes: Participant is diagnosed to be diabetic if any one of the following is present:
 - x FBS>126 mg/dl
 - x PPBS>200 mg/dl
 - x Patient already on anti diabetic drugs

Detailed history regarding patient's education, occupation, family income, daily physical activities, smoking, alcohol intake and family history of hypertension were asked. The socio economic status of the patient was determined using "Modified Kuppaswamy scale". Participants with daily physical activity of ≤ 2 MET (Metabolic Equivalent of Task) were considered as sedentary. Those who smoke • 5 cigarettes » day were considered as smokers.

Investigations included complete blood count, Renal function test (RFT), serum uric acid levels and lipid profile. Serum uric acid levels were measured using phosphotungstic acid method, caraway method. Study was undertaken after Institutional ethics committee approval and informed written consent from the subjects

Statistical Analysis

Data were analyzed using SPSS statistical software and proportion, mean and standard deviations were calculated. Serum uric acid levels were compared between the two groups to look for any statistically significant difference using unpaired – T test, double tailed with unequal variance. Among those with CKD study parameters were analysed for significance. For continuous variables, sub grouping was done and analysed by Analysis of Variance (ANOVA). The p value of less than 0.05 was considered as statistically significant.

Results

Study group comprised of 102 cases and 60 controls. Among the cases 38 were males and 64 were females the male female ratio was 2:3. The control group had 24-- males and 36--females with a male female ratio of 2:3

Age distribution to be given-40 to 79

The mean uric acid level in CKD group was 8.0 (\pm SD) mg/dl and in non CKD subjects it is 5.03 mg/dl. This was statistically significant with $P < 0.001$, (give the actual value)

Mean uric acid level among the CKD patients in different age groups were compared as shown- The age groups and their mean uric acid values were 40-49, 50-59, 60-69 and 70-79 years and 7.5, 8.41, 7.92 and 7.88 mg/ dl respectively.). There was no significant relationship between age and uric acid levels in this study. ($p=0.282$)

The mean serum uric acid level in males and females were 7.64 and 8.22 mg/dl respectively. Though mean serum uric acid (SUA) level was higher in males as compared to females but, this was not statistically significant ($P= 0.079$).

Influence of smoking: Mean SUA level in nonsmokers and smokers was 8.29 mg/dl and 6.44 mg/dl respectively. P less than 0.05, indicating that serum uric acid level was significantly lower in smokers compared to non-smokers.

Influence of alcohol

In this study among non-alcoholics and alcoholics, the mean uric acid levels were 7.92 mg/dl and 8.03 mg/dl respectively. Uric acid levels were higher in the non-alcoholic group. But this was not statistically insignificant ($p= 0.75$).

Influence of obesity:

Body mass index

The mean SUA levels among under weight, normal weight and overweight were 6.71 mg/dl, 7.57 mg/dl and 9.18 mg/dl respectively. Serum uric acid level showed an increasing trend with an increase in BMI, which was highest in overweight category and least in underweight category. The variation of uric acid with BMI was statistically significant with a P value < 0.001 .

Waist-hip ratio

Subjects with normal waist-hip ratio had a mean uric acid level of 7.70 mg/dl and subjects with increased waist hip ratio ($\bullet 0.85$ in females and $\bullet 0.90$ in male) had a mean uric acid level of 8.76 mg/dl. The P value was statistically significant (0.011) suggesting SUA levels are higher in people with increased waist-hip ratio compared to subjects with normal waist hip ratio.

Influence of life style

Mean uric acid in sedentary and non sedentary subjects were 9.02 mg/dl and 7.49 mg/dl, which was statistically significant (P<0.001)

Influence of hypertension

Mean Serum uric acid values in normotensive, prehypertensive, stage 1 hypertensive and stage 2 hypertensive were 7.04 mg/dl, 7.24 mg/dl, 8.45 mg/dl and 9.48 mg/dl respectively. P value for this relation was <0.001 indicating a statistical significance. In this study subjects with higher systolic BP (mean 136.94 mmHg) and diastolic BP(mean 86.23 mmHg) with uric acid level (mean 8 mg/dl) with a p value of < 0.001 for both.

Table 1: Parameters influencing serum uric acid level in CKD

Parameter		S. Uric Acid	P Value
Age	40-49	7.8	0.282
	50-59	8.41	
	60-69	7.92	
	70-79	7.88	
Sex	Female	7.64	0.079
	Male	8.22	
Smoking	No	8.29	0.02
	Yes	6.44	
Alcohol	Yes	7.92	0.75
	No	8.03	
Waist hip ratio	No obese	7.70	0.001
	Obese	8.83	
Body Mass Intex	Under weight	6.71	0.002
	Normal	7.57	
	Over weight	9.18	
Life style	Non-sedentary	7.49	0.001
	Sedentary	9.02	
Stage of Hypertension	Normal	7.04	0.001
	Pre-Ht	7.24	
	Stage 1	8.45	
	Stage 2	9.48	
Total Cholesterol	<200 mg/dl	7.77	0.278
	200-239	8.21	
	≥ 240	8.46	
T2DM	No	7.38	0.001
	Yes	8.76	
CAD	No	7.75	0.009
	Yes	8.67	
CVA	No	7.97	0.471
	Yes	8.47	

Uric acid and Total cholesterol

Mean uric acid level in subjects with normal total cholesterol (<200 mg/dl), borderline high (200-239 mg/dl) and high total cholesterol (> 240 mg/dl) was 7.77 mg/dl, 8.21 mg/dl and 8.48 mg/dl. Mean value of SUA increased with the increase in total cholesterol level. But these changes were not statistically significant (P =0.278).

Influence on diabetes mellitus

In Non diabetic and diabetic subjects, mean uric acid level was 7.38 mg/dl and 8.53 mg/dl respectively with a P value of <0.001. Thus in our study prevalence of diabetes mellitus was higher in subjects with high serum uric acid level.

Influence on coronary artery disease:

In our study mean serum uric acid level was significantly higher in subjects with coronary artery disease (8.67 mg/dl) as compared to subjects without coronary artery disease (7.75 mg/dl) with a P value of 0.009.

Influence on cerebro vascular diseases:

In our study we did not get a significant relationship between cerebro vascular events and uric acid level (P = 0.471). Mean uric acid level in CVA group and non CVA group was 8.47 mg/dl and 7.97 mg/dl respectively.

Discussion

There are few studies indicating the potential benefit of decreasing uric acid level in CKD. A randomized control trial was conducted by Siu *et al.*, with 54 hyperuricemic patients with mild to moderate CKD. Study was conducted for one year. Cases were given allopurinol (100-300mg/day) and controls were not given therapy. Patients with high uric acid level with CKD and was randomly assigned into either allopurinol (100mg/day) or control group with no therapy. Patients were followed for 2 years. At the end of the study GFR increased by 1.3±1.3ml/min/1.73m2 [P= 0.018] in the allopurinol group whereas decreased by 3.3±1.2ml/min/1.73m2 in the control group.

A randomized double blinded placebo controlled study was conducted on patients of diabetic nephropathy 100 and showed a significant decrease in proteinuria with allopurinol therapy. Few studies also suggest that onset of CKD can be prevented or can be delayed by reducing uric acid level.

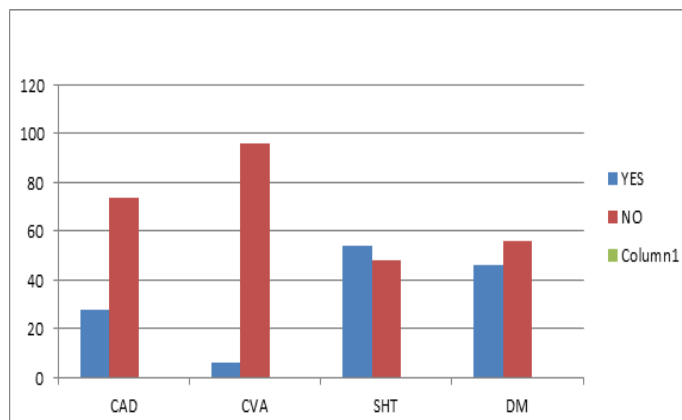


Fig 1: Prevalence of various conditions in CKD

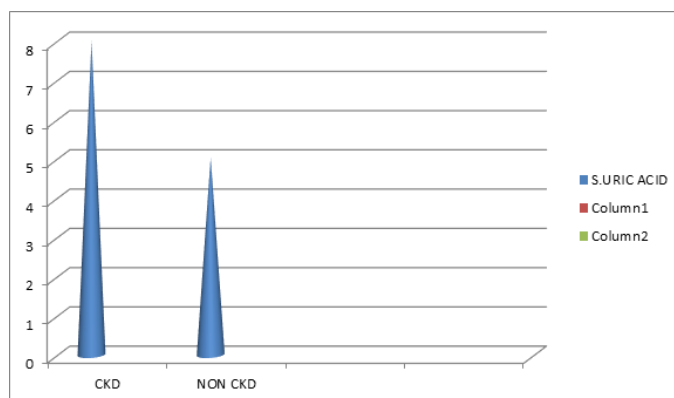


Fig 2: URIC ACID in CKD and non CKD subject

Conclusion

Prevalence of hyperuricemia is significantly higher in chronic kidney diseases patients compared to normal subjects. Uric acid level is significantly higher in obese CKD subjects with raised waist hip ratio, high body mass index. Uric acid level is significantly higher in diabetic and hypertensive CKD patients. Prevalence of coronary artery disease is significantly higher in CKD subjects with higher uric acid level.

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