Original Article

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A Study on Uric Acid Levels in Type 2 Diabetes Mellitus with Chronic Kidney Disease

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Abstract

Background: The classification of stages of CKD is based on the level of kidney function measured by GFR, stage 1 represents kidney damage with normal or elevated GFR and stage 5 represents a GFR of less than 15 ml/min or who require treatment with dialysis. In recent times a new equation the Chronic Kidney Disease-Epidemiological Collaboration (CKD-EPI) has been introduced. The CKD-EPI equation has lower bias, especially at an estimated GFR greater than 60 mL/min per 1.73 m2; however, precision remains limited. **Subjects and Methods:** The study was undertaken in the Department Of General Medicine,and a total 64 CKD patients are included in study who fulfilled the inclusion and exclusion criteria. These cases taken are not overlapped with other postgraduate students. The patients were randomly divided into two groups according group chosen by time of enrollment. **Results:** The Study reveals that, there was no statistical significant difference of mean serum uric acid among smokers and non-smokers in Type 2 diabetes mellitus with CKD(P>0.05). **Conclusion:** Study reveals that, there was no statistical significant difference of mean serum uric acid among alcoholic and non-alcoholic cases in Type 2 diabetes mellitus with CKD(P>0.05).

Keywords: Uric Acid Levels, Type 2 Diabetes Mellitus, Chronic Kidney Disease.

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Introduction

Chronic kidney disease (CKD) encompasses a spectrum of different pathophysiologic process associated with abnormal kidney function and a progressive decline in glomerular filtration rate (GFR). The term chronic renal failure applies to the process of continuing significant irreversible reduction in nephron number and typically corresponds to CKD stage 3-5. The dispiriting term end stage renal disease represents a stage of CKD where the accumulation of toxins, fluid, and electrolytes normally excreted by the kidneys results in the uremic syndrome.[1]

The most common screening test for CKD is the measurement of serum creatinine. However, it as an insensitive measure, since as much as 50% of the nephron mass may be lost before creatinine concentration increases and levels are influenced by several factors such as sex, age, body mass, and diet.[2]

CKD is defined as abnormalities of kidney structure or function, present for > 3 months, with implications for health. CKD is classified based on cause, GFR category (G1–G5), and albuminuria category (A1–A3), abbreviated as CGA.

The National Kidney Foundation Dialysis Outcome Quality Initiative (NKF/DOQI) (National Kidney Foundation, 2002) and European Best Practice Guidelines (European Best \ Practice Guidelines for Haemodialysis, 2002) recommend the use of prediction equations to estimate the GFR from serum creatinine.In adults, the most commonly used formulae are those derived from the Modification of Diet in Renal Disease (MDRD) study population [3] and that by Cockcroft and Gault. The MDRD equations were derived from patients with varying degrees of renal impairment employing a stepwise regression technique, with GFR measured from the renal clearance of [125I] iothalamate.[3] In its original form, the MDRD formula used six variables (serum creatinine, albumin and urea nitrogen, gender, age and ethnicity), although two simpler equations requiring either five variables (excluding serum albumin) or four variables (excluding serum albumin and urea nitrogen) were proposed to offer a similar performance. The Cockcroft and Gault formula, in marked contrast, was constructed from hospitalized patients to predict creatinine clearance from the serum creatinine in the absence of urine collection. The NKF has suggested the following definition of CKD: established kidney damage with structural or functional abnormalities or a glomerular filtration rate <60 ml/min/1.73 m2 for three months or more.[4]

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introduced. The CKD-EPI equation has lower bias, especially at an estimated GFR greater than 60 mL/min per 1.73 m2; however, precision remains limited. The enhanced accuracy of the CKD-EPI equation overcomes some of the limitations of the MDRD study equation and has important implications for public health and clinical practice. where stage 1 represents kidney damage with normal or elevated GFR and stage 5 represents a GFR of less than 15 ml/min or who require treatment with dialysis. In recent times a new equation the Chronic Kidney Disease-Epidemiological Collaboration (CKD-EPI) has been introduced[5]. The CKD-EPI equation has lower bias, especially at an estimated GFR greater than 60 mL/min per 1.73 m2; however, precision remains limited. The enhanced accuracy of the CKD-EPI equation overcomes some of the limitations of the MDRD study equation and has important implications for public health and clinical practice.

Subjects and Methods

The study was undertaken in the Department Of General Medicine,and a total 64 CKD patients are included in study that fulfilled the inclusion and exclusion criteria. These cases taken are not overlapped with other postgraduate students.
The patients were randomly divided into two groups according group chosen by time of enrollment. By using simple random method, 64 study subjects were taken, and the study subject was divided into following 2 groups:

Group 1: Comprised of 32 cases suffering from type 2 diabetes mellitus.
Group 2: Comprised of 32 controls not suffering from type 2 diabetes mellitus.

Inclusion Criteria

- Patients of both the sexes >18 years of age.
- Non Diabetic and Type 2 Diabetic renal disease.

Exclusion Criteria

- All the patients <18 years of age.
- Patients who are taking anti tubercular drugs and thiazide diuretics.
- Liver disorders, Alcoholics, Smokers, and others with secondary hyperuricemia cases and uncontrolled hypertension.

A written informed consent was obtained from all patients. History regarding the duration of hypertension, the medications being taken, coexisting medical problems, and symptomatology suggestive of ischemic heart disease, transient ischemic attacks and that of renal involvement were documented.

Results

The Study reveals that, there was no statistical significant difference of mean serum uric acidamong smokers and non-smokers in Type 2 diabetes mellitus with CKD(P>0.05).Study revealsthat, there was no statistical significant difference of mean serum uric acid among alcoholic andnon-alcoholic cases in Type 2 diabetes mellitus with CKD(P>0.05)

Table 1: Comparison of serum uric acid among smokers and alcoholics in Type 2 diabetes mellitus with CKD

Variables	Serum uric acid	t- test values	P-value & significance
	Mean ± SD		
Smokers (N=11)	8.98 ± 3.03	t = 0.763	P = 0.766, NS
Non- smokers(N=21)	9.99 ± 3.47		
Alcoholic(N=13)	9.45 ± 2.19	t = 0.563	P = 0.612, NS
Non- alcoholic(N=19)	9.79 ± 3.92		

Table 2: Characteristics of hyperuricemic patients stratified by baseline serum uric acid categories

Variables	Serum Uric Acid levels(mg/dl)				ANOVA-test P-value & significance
	<6	6-8	8-10	>10	
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Age(years)	48.0 ± 10.58	53.5 ± 9.54	46.71 ± 5.18	54.58 ± 10.65	F= 1.55 P = 0.232, NS
Body mass index (kg/m2) BMI	24.23 ± 3.64	26.06 ± 3.62	27.24 ± 2.06	28.21 ±3.65	F= 2.97 P = 0.037, S
Serum creatinine (mg/dL)	1.74 ± 0.28	2.08 ± 0.37	2.11 ± 0.53	4.90 ± 2.75	F= 5.84 P = 0.000, VHS
eGFR (ml/min/1.73m2)	71.41 ± 6.62	67.35 ± 5.06	61.35 ±9.22	32.07 ± 20.17	F= 14.57 P = 0.000, VHS
Total count	40.67 ± 49.13	13.46 ± 10.21	10.74 ± 8.59	13.0 ± 2.24	F= 2.06 P = 0.113, NS
HB(g/dl)	9.38 ± 2.25	9.40 ± 2.71	8.30 ± 2.07	7.23 ± 1.17	F= 2.42 P = 0.087, NS
Total cholesterol (mg/dL)	190.33 ± 20.59	195.33 ± 31.27	205.20 ± 10.03	209.83 ± 19..23	F= 2.93 P = 0.041, S
Triglycerides(mg /dl)	192.83 ± 28.84	202.32 ± 16.19	205.0 ± 30.85	211.58 ± 28.22	F=3.04 P =0.032, S
$HBA1_C$(%)	6.86 ± 1.26	7.51 ± 1.53	7.29 ± 1.01	6.79 ± 1.21	F= 2.63 P = 0.200, NS
Durationof DM2(years)	6.67 ± 4.17	7.16 ± 3.71	4.71 ± 1.38	1.17 ± 2.71	F= 1.495 P = 0.238, NS

The Study reveals that, there was no statistical significant difference of mean age, TC, HB, $HBA1_C$ and duration of DM2 with levels of serum uric acid in Type 2 diabetes mellitus with CKD cases (P>0.05).There was an increasing trend in the mean serum creatinine concentration with a corresponding decreasing trend in eGFR across increasing UA categories There is significantly sloping down of GFR with increase of SUA level as model.

Table 3: Distribution of cases according to serum uric acid levels in CKD cases

Serum uric acid Levels	Type 2 diabetes mellitus with CKD		Total	
	No.	%	No.	%
<6	6	18.8	10	15.6
6-8	6	18.8	17	26.6
8-10	7	21.8	16	25.0
>10	13	40.6	21	32.8
Total	32	100.0	64	100.0

Discussion

Hyperuricemia is seen when kidney function declines. Whether elevated uric acid (UA) levels play a role in the initiation and progression of kidney disease is a subject of a great debate. Animal studies demonstrate that elevated UA level is a risk factor for kidney disease. In humans, the relationship between UA and kidney disease is more complicated. Cross-sectional studies show an association of hyperuricemia with the presence of CKD; however, from cross-sectional studies, one cannot determine which came first—the elevated UA level or the kidney disease. UA levels are also associated with other risk factors for kidney disease, including hypertension, metabolic syndrome, and microalbuminuria, but it is not clear whether these are mediators or confounders of a relationship. Observational studies suggest a relationship of UA level with incident CKD, but studies evaluating the relationship with decline in kidney function in established CKD are conflicting.[6]

Our study supports that hyperuricemia is associated with a greater decline in renal function and a higher risk of progressing to kidney failure. The influences of hyperuricemia on renal function decline and the risk of kidney failure are greater in both patients of CKD with type 2 DM and without .High serum uric acid level remains independent risk factor for CKD in both CKD in type 2 DM and ckd without diabetes. Our findings suggest hyperuricemia is a potential modifiable factor of CKD progression.

On analyzing the uric acid level in 64 CKD patients, where 32 patients of chronic kidney diseases with type 2DM and 32 patients of chronic kidney disease without Type 2DM comparing in different level of GFR it is found that the mean uric acid level in CKD group is high with declining GFR in progression of CKD in both the groups suggestive of hyperurecemia remains as independent risk factor for CKD.. The concept of hyperuricemia in CKD patients is proved by many studies.

The concept of hyperuricemia in CKD patients is proved by many studies. Similar results were obtained by Ansari et al[7]. Yan et al reports that increased uric acid levels is a risk factor for the development of diabetic nephropathy and predict that uric acid is independently associated with diabetic kidney disease.[8]

The concept of hyperuricemia in CKD patients is proved by many studies. One such study was done by Iseki K,Ikemiya Y, Inoue T, et al,[9] in which along with hyperuricemia in CKD they went on to show the relationship between high uric acid level and development of end stage renal disease.

Effect of age on serum uric acid has been evaluated in various studies. KuzuyaM et al[10] did a longitudinal population based study which showed that uric acid level increased with the age except in the youngest cohort. Increase in serum uric acid level with age was also proved by Mark A. Reynolds et al in their study. The mean serum uric acid level in males and females were 7.64 and 8.22 mg/dl respectively. Though mean SUA level was higher in males as compared to females, this was not statistically significant with a P value of 0.079. A study conducted by Anton FM et al[11] on 9 normal adult women and 9 age matched men showed a significantly low uric acid level, higher fractional excretion of urate and a lower post secretory reabsorption of urate at tubules in women as compared to men.

The effect of smoking and alcohol on SUV level are shown results Mean SUA level in group1 non smoker mean is 7.98mg/dl and and smoker 10.02mg/dl and in group2 nonsmokers and smokers was 9.9mg/dl and 8.99 mg/dl respectively. P value was less than 0.062 and 0.766 non significant. In group2 serum uric acid level is slightly less in smoker but non significant. A study was conducted by Dhouha Haj Mouhamedet al[12] to know the effect of smoking cigarette on serum uric acid. At the end of the study it was found that plasma uric acid level was significantly lower in smokers as compared to non smokers.The effect of alcohol and nonalcoholic patients shows 8.49mg/dl and 8.78mg/dl in group 1and respectively which is non significant. In group 2 alcoholic 9.45mg/dl and Non-alcoholic 9.79mg/dl. The other study shows Ethanol enhances adenine nucleotide degradation and increases lactic acid level in blood, leading to hyperuricemia.

With respect to BMI, in our study we found that mean SUA level for under-weight, normal weight and overweight was in all models of SUA levels 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. This variation of uric acid with BMI was statistically significant with a P value <0.001in group 2 and non-significant in group 1.

Conclusion

There was an increasing trend in the mean serum creatinine concentration with a corresponding decreasing trend in eGFR across increasing UA categories There is significantly sloping down of GFR with increase of SUA level as model.

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