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Serum uric acid levels in diabetic kidney disease and its correlation with left ventricular hypertrophy and eGFR

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Abstract:

Background: Serum Uric acid is a known anti-oxidant, it has a beneficial role in diseases**.** But it has been found that elevated levels of uric acid are associated with high risks of cerebrovascular complication of type 2 diabetes mellitus.Serum uric acid level was also strongly associated with microalbuminuria and reduced glomerular filtration rate in renal diseases.There are contradicting statements on the relationship between uric acid and CKD in patients with type 2 diabetes. Hence this study was undertaken with the objectives to determine serum uric acid levels in diabetic kidney disease patients and to determine the association between serum uric acid levels and Left ventricular hypertrophy and eGFR.

Methodology: Cross sectional study was conducted among 53 Patients with Type 2 DM associated with kidney disease admitted at Adhichunchanagiri Hospital and Research centre. BG Nagara. Nagamangala taluk. Mandya districtwere included.Data was collected using predesigned questionnaire by interviewing the patients. Participants demographic, social and medical details were recorded in proforma.serum uric acid,urine albumin creatinine ratio and eGFR was calculated using Modification of diet in renal disease formula. Data was entered into Microsoft excel data sheet and was analyzed using Epi Info version 7.2.6 software.**p value** of <0.05 was considered as statistically significant.

Results: Majority of subjects were in the age group 51 to 60 years (43.4%). Male: female ratio was 1.52. 71.7% of subjects had Hyperuricemia (Uric acid >6.5 mg/dl). 64.15% had LVH, 62.26% had HTN and 28.3% had IHD. UACR and LVMI was significantly high among subjects with hyperuricemia and eGFR was significantly low among subjects with hyperuricemia. Among subjects with hyperuricemia Odds of developing LVH was 62, 3.682 for HTN and 8.167 for IHD.

Conclusion: From the study findings it was concluded that the higher serum uric levels were associated with significantly higher Urine albumin creatinine ratio, lower eGFR, higher LVMI. Elevated serum uric acid was associated with increased risk for LVH, hypertension and IHD. Hence serum uric acid can predict the cardiovascular morbidities among Type 2 DM with Chronic kidney disease.

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Keywords: Serum Uric Acid, left ventricular hypertrophy, eGFR, Type 2 Diabetes Mellitus, Chronic Kidney disease

Introduction:

Chronic kidney disease (CKD) encompasses a spectrum of different pathophysiologicprocess associated with abnormal kidney function and a progressive decline in glomerularfiltration rate (GFR). Serum Uric acid is a known anti-oxidant, it has a beneficial role in diseases.[1] But it hasbeen found that elevated levels of uric acid are associated with high risks of cerebrovascularcomplication of type 2 diabetes mellitus.[2] Studies have reported a strong association betweenelevated uric acid levels and obesity, metabolic syndrome, diabetes mellitus, hypertension,cardiovascular and renal disorders.[3]Several prospective studies have suggested that hyperuricemia is associated withan increased risk of incident cardiovascular events and death in both nondiabetic and type 2diabetic individuals.[4,5,6]Hyperuricemia also is largely prevalent in patients with chronickidney disease(CKD).[7,8]

Uric acid (UA) is consistently overproduced by ischemic tissues and has beenassociated withendothelial dysfunction by inhibiting nitric oxide release. Hence it washypothesized that Uric acidand/or its precursors might serve as injury signals in renalischemia.[3,9] Serum uric acid level was also strongly associated with microalbuminuriaand reduced glomerular filtration rate in renal diseases.[10] Chronic kidney disease patients who have reduced estimated glomerular filtration rate, frequently have volume retention and electrolyte imbalance which may cause abnormal cardiac function, increased left ventricular mass index and adverse cardiac events.[11]

There are contradicting statements on the relationship between uric acid and CKD in patients with type 2 diabetes. Hence this study was undertaken with the objectives to determine serum uric acid levels in diabetic kidney disease patients and to determine the association between serum uric acid levels and Left ventricular hypertrophy and eGFR.

Material and Methods:

Cross sectional study was conducted among 53 Patients with Type 2 DM associated with kidney disease admitted at Adhichunchanagiri Hospital and Research centre. BG Nagara. Nagamangala taluk. Mandya districtwere included. Inclusion Criteria:Type 2 DM patients, aged >18 years who were diagnosed with Diabetic Kidney disease as defined by KDOQI 2007 guidelines.[12] Patients on Diuretics, uric acid lowering drugs, patients on hemodialysis and peritoneal dialysis and other known conditions causing hyperuricemia were excluded. Study was conducted between December 2022 to December 2023 (1 year). Non-Probability sampling method was used to select the samples.

Method of Data Collection:

Institutional Ethical clearance was obtained prior to the start of the study. Written informed consent was obtained from all the patients fulfilling the inclusion criteria. Data was collected using predesigned questionnaire by interviewing the patients. Participants demographic, social and medical details were recorded in proforma. The diagnostic probability was based on clinical data obtained from patient charts and the results of relevant investigations. Following laboratory investigations were done in all the patients ECG, 2D Echocardiography, Renal function tests – Blood urea, serum creatinine and serum uric acid, serum electrolytes, Spot Urine Albumin Creatinine ratio, Urine routine and urine albumin creatinine ratio, Complete hemogram, fasting plasma glucose, post prandial glucose, HbA1c, Liver function

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tests and eGFR was calculated using Modification of diet in renal disease formula.[13]Data was entered into Microsoft excel data sheet and was analyzed using Epi Info version 7.2.6 software. Categorical data was represented in the form of Frequencies and proportions. **Chi-square test** was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation.**Independent t test or Mann Whitney U test** was the test of significance to compare quantitative data.**p value** (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.[14,15]

Results:

In the present study 53 subjects with diabetic kidney disease were included. Majority of subjects were in the age group 51 to 60 years (43.4%). Male:female ratio was 1.52. 71.7% of subjects had Hyperuricemia (Uric acid >6.5 mg/dl). 64.15% had LVH, 62.26% had HTN and 28.3% had IHD [Table 1].

Table 1: Profile of subjects in the study

		Count	Percentage
Age	40-50 years	5	9.4%
	51 to 60 years	23	43.4%
	61 to 70 years	18	34%
	71 to 80 years	7	13.2%
Gender	Male	32	60.4%
	Female	21	39.6%
Serum Uric acid (mg/dl)	<6.5 mg/dl	15	28.3%
	>6.5 mg/dl	38	71.7%
LVH	Present	34	64.15%
HTN	Present	33	62.26%
IHD	Present	15	28.3%

Table 2: Comparison of UACR, eGFR, LVMI and HbA1c with respect to Uric acid levels

		UACR (mg/gm)		eGFR ml/min/1/73 m^2		LVMI (g/m2)		HbA1c (%)	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
Serum Uric acid (mg/dl)	<6.5 mg/dl (n = 15)	1181.4	756	62.86	4.6	89.6	10.4	9.36	2.20
	>6.5 mg/dl (n = 38)	1807.9	818	32.43	3.2	117.1	16.2	8.74	1.46
	P value	0.013*#		<0.001*		<0.001*		0.236	

Independent t test* or Mann Whitney U test#

Mean UACR among subjects with serum uric acid <6.5 mg/dl was 1181.4 ± 756 and among subjects with serum uric acid >6.5 mg/dl was 1807.9 ± 818. UACR was significantly high among subjects with hyperuricemia. Similarly Mean eGFR among subjects with serum uric acid <6.5 mg/dl was 62.86 ± 4.6 and among subjects with serum uric acid >6.5 mg/dl was

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32.43 ± 3.2. eGFR was significantly low among subjects with hyperuricemia. Similarly Mean LVMI among subjects with serum uric acid <6.5 mg/dl was 89.6 ± 10.4 and among subjects with serum uric acid >6.5 mg/dl was 117.1 ± 16.2. LVMI was significantly High among subjects with hyperuricemia. Mean HbA1c among subjects with serum uric acid <6.5 mg/dl was 9.36 ± 2.20 % and among subjects with serum uric acid >6.5 mg/dl was 8.74 ± 1.46%. There was no significant difference in HbA1c with respect to Serum uric acid [Table 2].

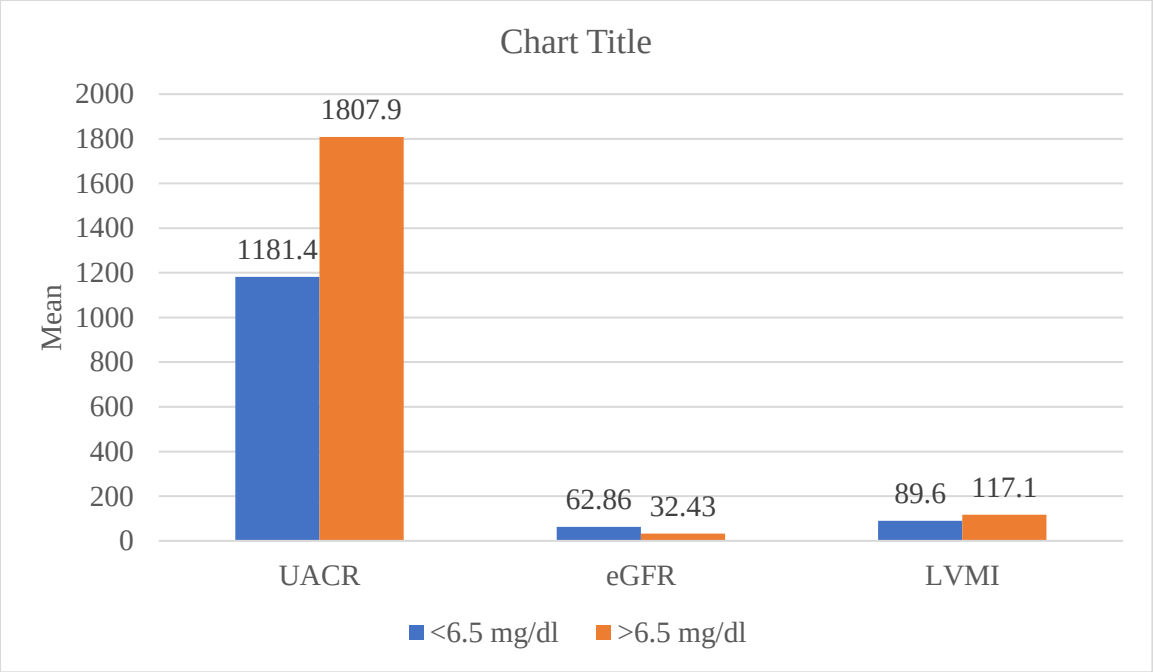

Figure 1: Column diagram showing UACR, eGFR, LVMI and HbA1c with respect to Uric acid levels

Table 3: Association between Serum uric acid and cardiovascular disease

		Serum Uric acid (mg/dl)				OR (95% CI)	P value
		>6.5 mg/dl (n = 38)		<6.5 mg/dl(n =15)			
		Count	%	Count	%		
LVH	Yes	31	81.6%	1	6.7%	62 (6.952 – 553)	<0.001*
	No	7	18.4%	14	93.3%		
HTN	Yes	27	71.1%	6	40%	3.682 (1.057-12.83)	0.036*
	No	11	28.9%	9	60%		
IHD	Yes	14	36.8%	1	6.7%	8.167 (0.967 – 68.93)	0.028*
	No	24	63.2%	14	93.3%		

In the present study among subjects with Serum uric acid >6.5 mg/dl, 81.6% had LVH, 71.1% had HTN and 36.8% had IHD and among subjects with Serum uric acid <6.5 mg/dl,

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6.7% had LVH, 40% had HTN and 6.7% had IHD. There was significant association of serum uric acid with LVH, HTN and IHD.

Odds of developing LVH among subjects with hyperuricemia was 62. times higher compared to subjects with normal Uric acid levels. Similarly, odds of developing HTN among subjects with hyperuricemia was 3.682 times higher compared to subjects with normal Uric acid levels and Odds of developing IHD among subjects with hyperuricemia was 8.167 times higher compared to subjects with normal Uric acid levels [Table 3].

Discussion:

Hyperuricemia is seen when kidney function declines. Whether elevated uric acid (UA) levelsplay 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. Inhumans, the relationship between Uric acid and kidney disease is more complicated. Cross-sectionalstudies show an association of hyperuricemia with the presence of CKD. Uric acid levels are also associated with other risk factors for kidney disease, includinghypertension, metabolic syndrome, and microalbuminuria, but it is not clear whether these aremediators or confounders of a relationship.Studies finding association of Uric acid with LVH and eGFR among Diabetics is sparse in databases, hence this study was conducted.

In the present study age of subjects ranged from 40 to 80 years, mean age was 61.09 ±8.53 years. Mean age was similar in studies by Behradmanesh et al[16] and Sunita Neupane et al[17] at 57±8.3 years and 58.94±13.8 years respectively. Male: Female ratio was 1.52:1 in the present study were as Sunita Neupane et al[17] observed M:F ratio of 1.38:1, Beena Unnikrishnan et al,[18]0.66:1 and Hina Latif et al[19] at 0.9:1.

In the present study mean UACR (mg/gm) was significantly high among subjects with SUA >6.5 mg/dl. Similar observations were made by Suryawanshi KS et al,[20] Michiaki Fukui et al[21] and Hina Latif et al.[19] The UACR levels were dependent on micro and marco albuminuria among diabetic patients. Nonethelessin the present study micro and marco albuminuria was not evaluated.

Mean eGFR among subjects with SUA >6.5mg/dl was 32.43 ± 3.2 ml/min/1.73 m^2. Were as in the studies by Chang et al,[22] SUA at 6.9 ± 1.8 mg/dl, mean eGFR was 64.8 ± 23.5 and in the study by Chuchu Zeng et al,[23] SUA at 6.99 ± 1.101 mg/dl, mean eGFR was 49.82 ± 9.56. Higher values of eGFR was observed in these studies. This can be due to factors such as duration of DM, stage of CKD and cutoff of Serum Uric acid considered.

Mean LVMI among subjects with SUA >6.5mg/dl was 117.1 ± 16.2 (g/m^2). Were as in the study by Chuchu Zeng et al,[23] SUA at >7.9, mean LVMI was 110.12 ± 30.08 g/m^2 and in study by Szu-Chia Chen et al,[24] SUA at 9.6 ± 1.6, mean LVMI observed was 193.1 ± 45.1 g/m^2.

Present study observed that among subjects with Serum Uric acid >6.5 mg/dl, 81.6% had LVH. Were as in the studies by Chuchu Zeng et al,[23] 38.07% had LVH at serum uric acid at >6.71, Fujita et al[25] observed LVH in 41.4% at serum uric acid >6.9 and Tsioufis C et al,[26]observed LVH in 36% at serum uric acid 4.88 respectively. Among subjects with Hyperuricemia in the present study, 71.1% had HTN and 36.8% had IHD. In the similar study by Chanchal Shrivastav et al,[27] among subjects with hyperuricemia (SUA >6.8 mg/dl), 37.33% had HTN. From the literature it is evident that Serum uric acid levels were not

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constant while determining the Outcomes. Hence the variability in outcomes was observed. Hence optimal cut off of Serum uric acid should be determined to evaluate the complications such as LVH, HTN and IHD in Type 2 DM.

Conclusion:

From the study findings it was concluded that the higher serum uric levels were associated with significantly higher Urine albumin creatinine ratio, lower eGFR, higher LVMI. Elevated serum uric acid was associated with increased risk for LVH, hypertension and IHD. Hence serum uric acid can predict the cardiovascular morbidities among Type 2 DM with Chronic kidney disease. Hence it recommended that Serum uric acid levels should be closely monitored among Type 2 DM with CKD to determine the cardiovascular complications. This study also recommends for further studies on large population to the confirm the results obtained from a large sample size and by adjusting cofounding factors.

Limitation:

Non-probability sampling and small sample size does not allow for generalization of results.

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