J Nepal Health Res Counc 2023 Apr-Jun;21(59): 271-6

Serum Uric Acid to Creatinine Ratio with Estimated Glomerular Filtration Rate in Type 2 Diabetes Patients

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ABSTRACT

Background: Diabetes mellitus is a metabolic disorder associated with cardiovascular and renal complications. The serum uric acid to creatinine ratio and estimated glomerular filtration rate are important markers used to assess kidney function in patients with type 2 diabetes. This study aimed to find the correlation between serum uric acid to creatinine ratio and estimated glomerular filtration rate to various parameters among the diabetes patients.

Methods: It is an observational hospital-based, cross-sectional study. Patients with a diagnosis of diabetes for three years or more duration were selected. This study designed to serum uric acid to creatinine ratio with estimated glomerular filtration rate and its relationship with other biochemical parameters. The Modification of Diet in Renal Disease formula was used to calculate estimated glomerular filtration rate (eGFR). eGFR (mL/min·1.73 m^2) = 186 × (Scr) −1.154 × (age) − 0.203 × (0.742 female). Low eGFR was defined as eGFR<60 mL/min·1.73 m^2. The data were analyzed by SPSS version 20. Mean values of different variables, standard deviations and p-values were calculated.

Results: Mean serum uric acid to creatinine ratio was 6.09±1.71 and elevated among 49.1%. Mean blood urea and serum creatinine levels were 28.0±10.72 and 1.01±0.18, respectively. There was a significant positive correlation between eGFR and serum uric acid : serum creatinine (r = 0.246, p = 0.007) in this study.

Conclusions: The serum uric acid to creatinine ratio can serve as an early marker for renal injury, showing a positive correlation with estimated glomerular filtration rate (eGFR). Monitoring serum uric acid to creatinine ratio levels alongside eGFR can assistance in the identification and management of kidney damage in its early stages.

Keywords: Creatinine; glomerular filtration rate; glycated hemoglobin; serum uric acid; type 2 diabetes

INTRODUCTION

Diabetes is known as chronic hyperglycemia linked with cardiovascular and renal complications. HbA1c is used for monitoring tool for glycemic control. [1] Serum uric acid is consider as independent predictor and early indicator of renal complications in diabetes.[2,3] Recently, a higher serum uric acid to creatinine ratio was used to predict chronic kidney disease incidence in diabetes.[4-6] The Kidney Disease Improving Global Outcomes recommends that glomerular filtration rate is a determinant for diagnosis, classification, and staging CKD. Serum creatinine is a crucial marker for detecting renal diseases. Because of the many formulas of the eGFR, including sex, weight, race, and many mathematic numbers were used in the clinical practice and provided different results.[7] But serum uric acid to creatinine ratio is a more straightforward calculation by using general biochemical markers with no additions.[8,9] This study helps to find the relationship between serum uric acid: creatinine and eGFR of diabetes patients.

METHODS

This was a descriptive cross-sectional hospital based study conducted on patients with diagnosis of diabetes for three years or more duration with aged 30 years above who attended Department of Internal Medicine, Bir hospital, Kathmandu, Nepal from August 10 , 2021 to August 9 2022.

A total of 120 patients were enrolled in this study after

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taking informed consent based on the set inclusion and exclusion criteria. Inclusion criteria were; Overt diabetes more than 3 years, patients receiving regular treatment with glycemic lowering, lipid lowering, and anti-hypertensive medication.Exclusion criteria were Heart failure,CKD, Peripheral vascular disease, Recent myocardial infarction , Unstable angina, Stroke, Acute or chronic infection, Cancer and hematological disorders, Hepatic disease and Acute illness

The following variables were obtained using a questionnaire filled through direct interview with the study participants: duration of diabetes ,age, sex, family history of hypertension and diabetes mellitus, comorbid illnesses, and type of diabetes therapy along with relevant biochemical parameters. Body mass index (BMI)) and blood pressure were measured using standard methods. Body mass index (BMI) was divided into underweight, Normal weight, over weight and obese with BMI of <18.5, 18.50-22.9, 23.00-27.99, and >28 for Asian population. BMI calculation-calculated applying the formula, i.e.,BMI = (Weight in Kilograms/ (Height in Meters X Height in Meters).

The Modification of Diet in Renal Disease formula was used to calculate estimated glomerular filtration rate (eGFR) - eGFR (mL/min·1.73 m^2) = 186 × (Scr) -1.154 × (age) – 0.203 × (0.742 female). Low eGFR was defined as eGFR<60 mL/min/1.73 m^2 and Uric acid: Creatinine was obtained by calculation formula. While on diabetes treatment, Glycated hemoglobin (HbA1c) <7%; post prandial and fasting blood glucose below 180 mg/dl and 120 respectively were considered a good control of sugar.

The data were analyzed by statistical package for social sciences (SPSS). Mean and standard deviation values of serum glucose, HbA1c, Uric acid, and UACR, Cr and these all variables correlated with eGFR. To correlated eGFR, was calculated using a modified MDRD formula. Patient anthropometric measurements were collected using standardized protocols, Pearson's correlation coefficient r was calculated to evaluate the relationship between uric acid, Uric acid: serum creatinine ratio. This study was approved by the ethical review committee of the Bir hospital, NAMS, Kathmandu.(ref no 148/2078/79)

RESULTS

A total of 120 diagnosis patients of T2DM were included in the study. The mean for age in the study subjects was 54.16±10.36 years predominated by age group of 41-50 years (35%), followed by 5-60 years (27.5 %). There were 61-70 years (20 %), 33-40 years (9.2 %) 70-76 years was (8.3 %). Among them, 61 (50.8%) were males, and the remaining 59 were females (49.2 %) with Male to female ratio was 1. 033.

Table 1. Baseline characteristics of Total Study Subjects (n=120).

Parameters	Mean Values(±SD)
Age (Range 33-76 years)	54.16±10.36
Male (n=61)	55.13±10.47
Female (n=59)	53.16±10.24
Duration of diabetes, (years)	6.07±2.81
Urea (mg/dl)	28.0±10.72
FBS (mg/dl)	182.55±58.09
PPBS (mg/dl)	271.60±76.75
HbA1c (%)	9.73±1.98
S.creatinine (mg/dL)	1.01±0.18
Serum uric acid (mg/dl)	5.95±1.03
eGFR (ml/min/1.73m^2)	73.01±17.01
Sodium (mEq/L)	137.02±4.62
Potassium (mEq/L)	4.15±0.57
SUA:S.Cr	6.09±1.71
BMI kg/m^2	23.67±3.19

The Mean duration of diabetes was 6.07±2.81 (3-15 years). The fasting blood sugars (FBS) of the subjects had a mean of 182.55±58.09 mg/dl. The majority number of people 65.8% had elevated fasting blood sugar levels (>126-250mg/dl), some (22.5%) had fasting blood sugar levels of less than 126 mg/dl while few (11.7%) had between 250-350 mg/dl range

The postprandial blood sugars (PPBS) of the subjects had mean 271.60±76.75mg/dl. Significant number of subjects (83.3%) had raised PPBS (>200-450 mg/dl) where as 16.5% had PPBS of 140–199 mg/dl. Similarly, the mean HbA1c was 9.73±1.98 and were increased in 77.5%(HbA1c>8%) and 22.5% had less than 8%. There was strong positive correlation between HbA1c with FBS(r= 0.644,p=0.000) and PPBS(r=0.669,p=000). The Mean Serum Uric acid was 5.95±1.03mg/dl, and hyperuricemia was present in 15%, and the remaining 85% had normal serum uric acid level, i.e., <7mg/dl. The mean eGFR was 73.01±17.01 ml/min/1.73m^2. In this study, eGFR stage 1 was 13.33%, whereas stage 2 (61.6%)and stage 3a+b (25%), so must of diabetes patients belong in stages 2 and 3. The mean SUA:S.Cr was 6.09±1.71, which showed 50.8% had less than 5.8, and 49.1% had more than 5.8. The mean urea and creatinine was 28.0±10.72 and 1.01±0.18mg/dl.In which 10.8% had increased Urea level >40mg/dl and 11.7% had increased Creatinine level>1.2mg/dl.

The Mean BMI was 23.67±3.19 kg/m^2 in which 42.5% of diabetes patient had healthy BMI, and 45.8% was overweight, and 10% was Obese whereas 1.7% were underweight according to Using Asian specific BMI cut-offs underweight was defined as <18.5 kg/m^2, healthy weight as 18.5–22.99 kg/m^2, overweight as 23–27.49 kg/m^2 and obese ≥27.5 kg/m^2. The character of the patient was shown in table 1

Table 2. Correlation between Serum Uric acid /S. Cr with other measured parameters in T2DM.

Parameters	r	p-value
Age(years)	-0.275**	0.002
BMI(kg/m^2)	0.273**	0.003
FBS(mg/dl)	0.77	0.405
PPBS mg/dl)	0.306**	0.001
eGFR(ml/min/1.73^2)	0.246**	0.007

The study showed the correlations between SUA/ S.Cr, and other measured parameters are summarized in Table 2. Serum UA/Cr is inversely correlated with age (r=−0.275, p=0.002), urea (r=−0.253, p=0.005) and Creatinine (r=−0.738, p=0.000). A significant positive correlation was found between serum UA/Cr and BMI (r=0.273, p=0.003), and eGFR (r=0.246, p=0.007). Similarly, there was strong positive correlations of eGFR with serum uric acid (r=0.239, p=0.009) and SUA: S. Cr (r=0.246, p=0.007) as shown in table-3

Table 3. Correlation of eGFR with Uric Acid, Urea, Creatinine, SerumUA: S.Creatinine.

Variable	eGFR	Urea	Creatinine	Uric Acid	SUA:S. cr
eGFR	1				
Urea	0.41	1			
Creatinine	-147	0.273**	1		
Uric acid	0.239**	-0.155	-0.211*	1	
SUA:S.cr	0.246**	-0.253**	-0.738**	0.782**	1

*** Correlation is significant at the 0.01 level (2-tailed), *Correlation is significant at the 0.05 level (2-tailed).*

DISCUSSION

Diabetes is a common disease presented with various complications. Early detection and proper management diminish complications. So this study aims to find the association between SUA:S.Cr and eGRF in diabetes patients.

In our study, the prevalence of diabetes was estimated higher among 41-60 years of age, which is similar to previous study findings for developing countries between 45 and 64 years conducted by Yoon KH et al. and Asaduzzaman M et al.[10,11] So this may indicate that complications occur with an increases in age. The Mean duration of diabetes was 6.07±2.81 (3-15 years). Pendurthi AK et al. study shows a similar period of our study finding.[12]

The mean blood sugar value is found to be high in our diabetes patients. The mean fasting blood sugar value was 182.55±58.09 mg/dl. Zarei M et al show similar findings among uncontrolled diabetes patients who had high fasting blood sugar.[13] The postprandial blood sugars (PPBS) in diabetes patients had a mean of 271.60 ±76.75mg/dl. Significant number of subjects (83.3%) had raised PPBS (>200-450 mg/dl) whereas 16.5% had PPBS of 140–199 mg/dl. Similarly, the mean HbA1c was 9.73±1.98 and was increased by 77.5% (HbA1c>8%), and 22.5% had less than 8%, which had similar findings in Kumar SP et al. study.[14] This finding indicates that the majority of the diabetic population is controlled poorly.

There was strong positive correlation between HbA1c with FBS (r= 0.644,p=0.000) and PPBS(r=0.669,p=000). The result showed that the correlation between FBS and PPBS with HbA1c was significant. Our study revealed that both FBS and PPBS are important to achieve optimal glycemic control, which is similar to the studies reported by Abrahamson et al. and Monnier et al.[15-17] In various meta-analysis study showed a significantly increased risk of long-term mortality in patients with a high HbA1c level than those with a low HbA1c level.[18,19]

Lin et al. performed a retrospective cohort study among 3,220 type 2 diabetes patients with a mean follow-up duration of 4.4 years to assess the relationship between annual variation in A1C and incident diabetic nephropathy (eGFR <60 ml/min/1.73 m^2). After multivariate adjustment, the yearly A1C-CV were associated significantly with the incidence of diabetic nephropathy.[20]

There are mechanisms to explain the association between A1C variability and nephropathy. First, increased A1C variability could be a signal of previous poor glycemic control. The metabolic memory phenomenon suggests that diabetic nephropathy continues to occur even after reasonable control has established. Second, highly variable A1C was associated with some baseline factors, such as increased smoking, higher blood pressure, and an increased prevalence of peripheral neuropathy and peripheral vascular disease.[21] Thus Glycemic control among diabetic people around the world seems to be

worsening despite the newer additions to the medical treatment and diet control. So Greater HbA1c variability predicts retinopathy, early nephropathy, and coronary artery neuropathy.[20,22]

The Mean Serum Uric acid was 5.95±1.03mg/dl, and hyperuricemia was present in 15% which was similar to the finding of Rao TM et al., in which 11.43% had hyperuricemia in diabetes patients.[23]

The mean eGFR was 73.01±17.01 ml/min/1.73m^2 In this study, eGFR stage 1(>90 ml/min/1.73 m$^{2)}$ was 13.33% whereas stage 2(60-89 ml/min/1.73 m$^{2)}$ was 61.6% and Stage 3a+b (30-60 ml/min/1.73 m$^{2)}$ was (25%), so must of diabetes patient had decline eGFR by using MDRD equation. Fontela PC et al. study showed that the prevalence of decreased renal function was greater in diabetic patients assessed by MDRD which was similar to our study.[24]

Using eGFR by MDRD equation, which is considered a more effective result decrease of 50% in healthy kidney function in diabetes patients, which was support by the finding of Bastos MG et al.[25] Still, there is about 25% of diabetes patient had < 60 ml/min/1.73 m$^{2.}$ Prabhu at el. study findings suggest that 21.9% of diabetes had decreased eGFR (<60 ml/min/1.73 m^2). 22.22% of diabetes with decreased eGFR had SCr values within the reference range (0.6-1.2 mg/dl) which was similar to our finding.[26]

After analyzing the results, the prevalence of individuals with reduced renal function based on serum creatinine was lower. Using these equations to determine GFR has lower cost and greater convenience in clinical practice, facilitating early screening and diagnosis of CKD among diabetic in primary care in our setting hospital.[26] It is most relevant since CKD is considered a global public health problem, DM being the most common cause of CKD in the world, and the second most common etiology among dialysis patients in Nepal.

The mean serum uric acid: Sr Creatinine ratio was 6.09±1.71, which showed 50.8% had less than 5.8, and 49.1% had more than 5.8. This mean value of SUA:S.Cr corresponded to the study done by AI-Daghri NM et al. in which serum UA/Cr was divided into tertile to find the significant.[4]

The Mean BMI was 23.67±3.19 kg/m^2 in which 42.5% of diabetes patients had healthy BMI, and 45.8% was overweight, and 10% was Obese, whereas 1.7% was underweight, according to Asian specific BMI cut-offs. This finding was supported by Joshi B et al.[27] These results showed that most of the diabetes patients are overweight and obese, which many consider as a contributing factor for the uncontrolled glycemic level in our study. Similarly, find was seen by a study done by Venugopal & Lyer (2010) where the majority of subjects were overweight or obese.[28]

In this study, Serum UA/Cr is inversely correlated with age ($r=-0.275$, $p=0.002$), urea ($r=-0.253$, $p=0.005$) and Creatinine ($r=-0.738$, $p=0.000$). Similarly, a positive correlation is found between serum UA/Cr and BMI ($r=0.273$, $p=0.003$), and eGFR ($r=0.246$, $p=0.007$).

In a study done by Al-Daghri N.M et al., higher BMI was observed in the most top serum UA/Cr, which was confirmed by a strong positive relationship of serum UA/Cr with BMI, which was similar to our finding.[4] Similarly, a positive correlation between eGFR with and Serum Uric acid and SUA: Scr has corresponded to our study done by AI-Daghri N.M and Qin Q et al. and et al [4,29] which shows a significant positive correlation between eGFR and SUA:Scr ($r=0.359$, $p<0.001$).

The limitations of our study include its single-center nature and small sample size, which prevent from generalizing the findings to the wider population.

CONCLUSIONS

The positive correlation between the serum uric acid to creatinine ratio (SUA/S.Cr) and estimated glomerular filtration rate (eGFR) in diabetes patients suggests that the SUA/S.Cr ratio can serve as an early indicator of renal injury. This early recognition can help prevent the progression of renal impairment to chronic kidney disease (CKD) in diabetes patients.

COMPETING INTERESTS

The authors declare no competing interest

ACKNOWLEDGEMENTS

We would like to thank all the patients for their valuable time and support. Also would like to thank Department of Internal Medicine, Bir hospital, NAMS, Kathmandu, Nepal for approval of conducting this research work.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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