

## Original Research Article

# Association of serum uric acid-creatinine ratio with microalbuminuria and glycemic status (HbA1c) as an early indicator of diabetic nephropathy

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### ABSTRACT

**Background:** The serum uric acid is a good predictor of renal injury in both diabetes patients and non-diabetes. Creatinine is the marker to detect the renal function. Aim of our study was to assess the correlation of the serum uric acid to creatinine ratio with the Microalbuminuria and glycemic status (HbA1c) in diabetes mellitus patients.

**Methods:** It is analytical observational study conducted in urban tertiary care hospital attached to medical college between July to August 2019 after obtaining the ethics clearance. Participants aged between 18 to 60 years with type 2 diabetes mellitus and healthy controls were included in present study. The patients with diabetic nephropathy with grade 3 and above and non-diabetes patients with history of ischemic heart disease, advanced hypertension, Chronic or acute kidney disease, liver disease, known case of hyperuricemia/gout, alcoholics, acute febrile illness, urinary tract infection, cancer were excluded from present study.

**Results:** Total of 131 individuals were included in present study that fulfilled inclusion criteria. The mean age of the participants was  $56.70 \pm 11.9$  with 64 females and male 67 (male: female ratio of 1). Among 131 participants, 60 were with T2DM and 71 were normal control. Our study showed a significant strength of association between the UACr with the urine MAU ( $r=0.760$ ,  $p<0.001$ ), where-as the SAU was associated with MAU excretion in urine ( $0.52$ ,  $p<0.001$ ). The UACr was also significantly associated with the HbA1c ( $r=0.25$ ,  $p=0.01$ ).

**Conclusions:** Urine microalbuminuria and HbA1c were significantly correlated with the ratio of uric acid to creatinine in the serum. The serum uric acid creatinine ratio (UACr) is a good predictor for predicting renal damage in patients with diabetes mellitus at an early stage of illness.

**Keywords:** Microalbuminuria, Uric acid-creatinine ratio, T2DM, Serum uric acid, HbA1c

## INTRODUCTION

Diabetes mellitus (DM) is one of the most prevalent health issues worldwide, with increasing prevalence of more than 180 million people to 366 million by the year 2030.<sup>1</sup> Diabetic nephropathy (DN) is the most common cause of chronic kidney disease worldwide, its pathogenesis is not fully understood.<sup>2</sup> Diabetes is responsible for 30-50% of all the chronic kidney disease (CKD) and one among the major cause for the renal

failure requiring renal replacement treatment worldwide.<sup>3</sup> Many risk factors have already been associated with development and progression of diabetic nephropathy, such as elevated level of HbA1c, duration of disease, presence of other microvascular complications and elevated level of albumin excretion rate in urine.

In recent years, increasing evidences shows that the serum uric acid is a good predictor of renal injury in both diabetes patients and non-diabetes.<sup>4</sup> Uric acid (UA) is one

of the greatest interests in the research related to the oxidative marker and the marker for the endothelial damage, cardiovascular disease and the kidney injury. Uric acid is produced by the enzymatic activity of xanthine oxidase and is the final degradation product of the purine metabolism.<sup>5</sup> Albuminuria is a well-known predictor of poor renal outcomes in patients with diabetes mellitus and sign of kidney disease.<sup>6</sup> The estimation of the microalbumin in urine requires the collection of the urine for 24 hrs. This is subjected for the errors of the urine collection by the patients or the individual with diabetes mellitus. The creatinine is constantly excreted in the urine, and is not influenced by the diet or the daily routine; hence the uric acid level in the blood with the creatinine excretion would give a comparable constant ratio for the interpretation. The glycemic status will influence the microvascular and macrovascular endothelial damage to the kidneys, leading to the inefficiency in reabsorption or filtration of the albumin and appearing in urine in measurable level.

However, the influence of the serum uric acid level on renal function has been insufficiently investigated in the patients with diabetes mellitus in context with the developing country populations. Aim of our study was to assess the correlation of the serum uric acid to creatinine ratio with the microalbuminuria and glycemic status (HbA1c) in diabetes mellitus patients.

## METHODS

It is analytical observational study conducted in urban tertiary care hospital attached to medical college between July to August 2019 after obtaining the ethics clearance. Participants aged between 18 to 60 years with type 2 diabetes mellitus and healthy controls were included in present study. The patients with diabetic nephropathy with grade 3 and above and non-diabetes patients with history of ischemic heart disease, advanced hypertension, chronic or acute kidney disease, liver disease, known case of hyperuricemia/gout, alcoholics, acute febrile illness, urinary tract infection, cancer were excluded from present study.

Before starting the study, clearance from the Institutional Ethics Committee was sought. The healthy individuals who come for routine health checkups and individuals with diabetes mellitus attending endocrine/medicine outpatient were selected for the study after obtaining informed consent. The blood and urine specimen of the included patients were collected from the biochemistry section of central laboratory, and analysed for the additional parameters after obtaining informed consent. Estimation of serum uric acid (SUA) (mg/dl) by uricase kinetic method, serum creatinine (mg/dl) by modified kinetic Jaffe's method and urine microalbumin (mg/24hr) by immunoturbidometric method are analysed in fully automated Roche Cobas® 6000 analyser (Roche diagnostics & Hitachi), Glycated haemoglobin (HbA1c) measured by cation exchange HPLC method by bio-rad

variant™ II turbo instrument. The serum uric acid-creatinine ratio (UACr) was calculated as serum uric acid (mg/dl)/serum creatinine (mg/dl). Fasting plasma glucose, previous levels of HbA1c, creatinine (Scr), urea, triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) measured in the last visit or on same visit assessed from the patient's medical records or the hospital information system (HIS). Renal estimated glomerular filtration rate (eGFR) was estimated by CKD-EPI equation in adults and expressed as GFR in millilitres per min per 1.73m<sup>2</sup> (ml/min).<sup>7</sup>

The sample size was calculated using the SPSS sample-power calculator for the power of >80% and p-value<0.05. The data were entered in the sophisticated statistical software SPSS version 23 institution licensed, and results are presented as mean and SD. The mean difference between continuous variables was analyzed by student t-test and strength of association between the measurements was analyzed by Pearson's correlation. A p value of<0.05 was considered statistically significant.

## RESULTS

Total of 131 individuals were included in present study that fulfilled inclusion criteria. The mean age of the participants was 56.70±11.9 with 64 females and male 67 (male: female ratio of 1). Among 131 participants, 60 were with T2DM and 71 were normal controls. Compared to those without T2DM, patients with T2DM had higher systolic BP, higher serum creatinine and uric acid. SUA and Scr was significantly higher in T2DM than compared to normal healthy control. (p<0.001) the correlation analysis showed a significant strength of association between the UACr with the urine MAU (r=0.760, p<0.001), whereas the SAU was associated with MAU excretion in urine (0.52, p<0.001). (Table 1) The UACr was also significantly associated with the HbA1c (r=0.25, p=0.01) (Table 2).

**Table 1: The results of the Variables in T2DM and healthy controls.**

	T2DM	Healthy controls	P value
<b>Age (years)</b>	54.26±10.92	55.14±11.05	0.648
<b>FBS (mg/dL)</b>	189.18±29.1	98.01±12.7	0.001
<b>Serum creatinine (mg/dL)</b>	1.12±0.62	0.82±0.21	0.001
<b>Serum uric acid (mg/dL)</b>	7.65±1.22	4.21±1.8	0.001
<b>MAU (mg/day)</b>	218±21.17	29.01±6.17	0.001
<b>UACr</b>	6.83±1.16	5.13±1.01	0.001
<b>HbA1c (%)</b>	7.96±2.43	5.62±0.92	0.001

**Table 2: Pearson's correlation between the serum uric acid-creatinine ratio and microalbuminuria in both groups.**

		MAU	HbA1c
UACr	r	0.76	0.25
	Sig	0.01	0.01

## DISCUSSION

Nephropathy remains the most common cause of end-stage renal disease, following recent advancements in diabetes treatment (ESRD). Inflammation and endothelial dysfunction play an important part in diabetic nephropathy (DN's) onset and progression. Serum uric acid is recently considered an inflammatory factor that may play a significant role in endothelial dysfunction. Serum creatinine is one of the important markers for the function of the renal. Renal impairment is an established microvascular complication in diabetes mellitus with reduction in GFR. The eGFR is estimated in present study, which was reduced in the patients with diabetes mellitus progressing into the renal impairment. The excretion of albumin in urine is important marker to detect the present of the renal basement damage. The urine albumin excretion is estimated by microalbuminuria (MAU) in urine. The spot urine is compliant with the patient, which does not require the preparation of the patient as with the collection of urine for 24-hour urine specimens.

Studies have reported the significant relation between the serum uric acid and the urine MAU. Hyperuricemia is also prevalent in patients with chronic renal failure. Indeed, many studies have shown that hyperuricemia can have a pathogenic role in the development and progression of chronic renal failure, rather than merely indicating reduced uric acid excretion. In diabetic patients, serum uric acid is significantly associated with macroalbuminuria later development early in diabetes.<sup>8-12</sup> The serum uric acid-creatinine ratio was recently associated with the patient with diabetes mellitus. Impaired renal function itself is an independent and good indicator of progression of renal disease and elevated SUA also occurs as a result of CKD, those patients with lower eGFR are more likely to have higher SUA rates and are at higher risk of progression of renal disease.<sup>13-15</sup>

The serum UACr was previously used as a marker as important marker as an independent and significant association with future renal function and decline in the GFR among the diabetes patients. In present study, we summarize the presence of a significant strength of association with the presence of the MAU in urine and progressing to the renal impairment.<sup>13-15</sup>

## CONCLUSION

The urine microalbuminuria and HbA1c was significantly correlated with the serum uric acid-creatinine ratio. The

serum uric acid creatinine ratio (UACr) is a good marker in predicting the renal injury in the diabetes mellitus patients at an early stage of disease and provides the physician for modification in medication to control the glycemic status at early stage of renal disease.

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