Serum uric acid and its association with hypertension, early nephropathy and chronic kidney disease in type 2 diabetic patients

Ácido úrico sérico e sua associação com hipertensão, nefropatia precoce e doença renal crônica em pacientes diabéticos tipo 2

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ABSTRACT

Introduction: Early detection diabetic nephropathy (DN) is important. Whether serum uric acid (SUA) has a role in the development of DN is not known. **Objective:** To study the relationship between SUA and hypertension, early nephropathy and progression of chronic kidney disease (CKD) in type 2 *diabetes mellitus* (T2DM). **Methods:** The total number of the study was 986 participants, according to presence and duration of diabetes were classified into three groups. Group I; including 250 healthy participants. Group II; including 352 with onset of diabetes < 5 years. Group III; including 384, with the onset of diabetes > 5 years. All participants were submitted to complete clinical examination, anthropometric measurements, laboratory investigations, including glycosylated hemoglobin (HbA1C), as well triglycerides to high-density lipoprotein ratios (TG/HDL-C), SUA, urinary albumin/creatinine ratio (ACR) and estimated glomerular filtration rate (eGFR). **Results:** SUA, BP, HbA1c, TG/HDL-C ratio, and ACR levels were significantly higher in group III than group I, II and in II than I. eGFR significantly lower in group III than group I, II and in II than I (p < 0.001). Age, BMI, BP, HbA1c, TG/HDL-C, ACR, were positively correlated with SUA, while GFR negatively correlated. SUA at level of > 6.1 mg/dl, > 6.2 mg/dl and > 6.5 mg/dl had a greater sensitivity and specificity for identifying hypertension, early nephropathy and decline eGFR respectively. **Conclusion:** Even high normal SUA level, was associated with the risk of hypertension, early nephropathy and decline of eGFR. Moreover SUA level may identify the onset of hypertension, early nephropathy and progression of CKD in T2DM.

Keywords: *diabetes mellitus*, type 2; diabetic nephropathies; hypertension; uric acid.

RESUMO

Introdução: A detecção precoce da nefropatia diabética (ND) é importante. O ácido úrico sérico (AUS) tem um papel ainda desconhecido no desenvolvimento de ND. **Objetivo:** Estudar a relação entre AUS e hipertensão, nefropatia precoce e progressão da doença renal crônica (DRC) no diabetes mellitus tipo 2 (DM2). **Métodos:** O estudo contou com 986 participantes, de acordo com a presença e a duração do diabetes, os pacientes foram classificados em três grupos. O Grupo I incluiu 250 participantes saudáveis. O Grupo II incluiu 352 pacientes com início de diabetes < 5 anos. O Grupo III incluiu 384 pacientes com o aparecimento de diabetes > 5 anos. Todos os participantes foram submetidos a exame clínico completo, medidas antropométricas, exames laboratoriais - incluindo hemoglobina glicosilada (HbA1C), bem como a razão entre triglicérides e lipoproteína de alta densidade (TG/HDL-C), AUS, razão creatinina/albumina (RCA) urinária, e taxa estimada de filtração glomerular (eTFG). **Resultados:** A razão AUS, PA, HbA1c, TG/HDL-C e RCA foi significativamente maior no grupo III do que no grupo I, II e em II do que I. A eTFG foi significativamente menor no grupo III do que nos grupos I, II e no II do que no I (p < 0,001). Idade, IMC, PA, HbA1c, razão TG/HDL-C, RCA, foram positivamente correlacionados com AUS, enquanto que a TFG esteve negativamente correlacionada. O AUS a níveis > 6,1 mg/dl, > 6,2 mg/dl e > 6,5 mg/dl apresentou maior sensibilidade e especificidade para identificar hipertensão, nefropatia precoce e declínio da eTFG, respectivamente. **Conclusão:** Mesmo elevados níveis de AUS, foi associado ao risco de hipertensão, nefropatia precoce e declínio da eTFG. Além disso, o nível de AUS pode identificar o início da hipertensão, nefropatia precoce e progressão da DRC em DM2.

Palavras-chave: ácido úrico; *diabetes mellitus* tipo 2; hipertensão; nefropatias diabéticas.

Introduction

The prevalence of type 2 *diabetes mellitus* (T2DM) has significantly increased worldwide, which has resulted in an increased burden on individuals and health care systems.[1] Diabetic nephropathy (DN) is a common complication of diabetes and its earliest clinical sign is a slight elevation of urinary albumin excretion microalbuminuria (MA). Such leakage was believed to progress inexorably to gross proteinuria, which destroyed nephrons and led to end stage renal disease (ESRD).[2]

Chronic kidney disease (CKD) is a worldwide public health issue, with increasing prevalence, poor outcomes, and high treatment costs.[3] Early detection of CKD is crucial to prevent its progression, and thereby, to potentially improve its outcome.[4]

Uric acid (UA) is the end product of purine metabolism in humans, and approximately 70% of UA are eliminated by the kidney.[5] Several prospective studies have documented that the elevated serum uric acid (SUA) level is associated with the development of T2DM itself,[6] hypertension,[7] cardiovascular disease[8] and the risk factors of metabolic syndrome (MS).[9] UA has several reported effects by which it may cause DN. Including endothelial dysfunction,[10] increased activity of the renin-angiotensin aldosterone system (RAAS),[11] and induction of inflammatory cascades,[12] in addition to profibrotic cytokine activation,[13] all of which have been demonstrated to contribute to the progression of microvascular disease and thereby renal injury in DN.

Despite the strides that had made in understanding the factors that contribute to the evolution and the progression of diabetic kidney disease. The pathophysiology of diabetic nephropathy is complex and still not fully elucidated.[14] Beside MA may not be as sensitive and specific a predictor of the DN as previously suggested.[15] So we conducted this study to investigate the relationship between SUA and hypertension, early nephropathy and progression of CKD in patients with T2DM.

Patients and methods

Study design and population

A case-control study was carried out among patients with T2DM attending the Zagazig University hospital in between January 2015 and February 2016. The study was approved by the local Institutional Ethics Committee and conformed to the Helsinki Declaration. The aim of the study was explained, and informed consent was obtained.

Demographic information was collected; the enrolled number of the study was 986 participants, among them 484 males and 502 females, with mean age of 49.8 ± 10.6 years.

The inclusion criteria included the following: patients with T2DM attending at the Zagazig University hospital outpatient clinic for treatment and their current age ≥ 18 years. Patients were excluded from the study if they suffered from other chronic systemic inflammatory or autoimmune disease or malignancy, type 1 diabetes patients, undetermined onset of diabetes, patients with other causes of CKD were excluded, patients receiving medications for hyperuricemia or drugs known to influence both uric acid levels or urinary albumin excretion were also excluded. However hypertensive patients were not excluded if there was no evidence of a causal role of hypertension in proteinuria.

According to the presence and duration of diabetes the study populations were categorized into three groups. Group I; control group was selected of healthy 250 healthy subjects with comparable age, sex and BMI to other participants. Group II; including 352 type 2 diabetic patients, with onset of diabetes less than 5 years. Group III; including 384 type 2 diabetic patients, with onset of diabetes more than 5 years. Among diabetic patients 486 on oral hypoglycemic drugs, and the remaining 250 on insulin therapy.

Physical examination and measurements

All participants in this study were subjected to complete clinical examination and anthropometric measurements. Height (height was measured using calibrated height meters while subjects stood erect and barefooted, with feet, placing together, and looking forward). Weight (the weight scale was calibrated daily). Waist circumference (WC) the circumference below the costal margin at the level of the umbilicus). Body mass index (BMI) = BW/H^2 kg/m), patients with BMI ≥ 30 considered obese.[16] Fundus examination was performed to confirm diabetic retinopathy in participants with overt proteinuria to confirm the diagnosis of DN. Blood pressure was measured with a mercury sphygmomanometer on the right arm with the patient in a sitting position after a rest of 5 min. Hypertension was defined as a systolic blood pressure

≥ 130 mmHg and/or a diastolic blood pressure ≥ 85 mmHg and/or the current use of antihypertensive medication.

Laboratory measurements

Venous blood was drawn in the morning after an overnight fast. All participants were subjected to routine investigations, including SCr, $HbA1_C$, lipid profile, including HDL-C, low-density lipoprotein (LDL), total cholesterol (TC), and TG beside TG/HDL-C ratio. Finally SUA was measured by uricase/peroxidase enzymatic method. Hyperuricemia was defined as SUA level 7.0 mg/dl.[17] Metabolic syndrome (MS) was defined by the presence of at least three of the following: HDL-C < 40 mg/dl for men or 50 mg/dl for women, fasting blood sugar (FBS) > 100 mg/dl, fasting TG level over 150 mg/dl, BP ≥ 130/85 mmHg, WC ≥ 102 cm for men or ≥ 88 cm for women.[18]

All participants were instructed how to obtain a fresh, clean first morning urine specimen to exclude orthostatic proteinuria. Urine samples examined for urinary ACR. Early nephropathy defined urine ACR ≥ 30 mg/g, and overt nephropathy was defined as the data urinary ACR ≥ 300 mg/g. Albuminuria was measured by immunoturbidimetry. All positive cases re-examined after three months to confirm diagnosis.

GFR is estimated by CKD-EPI equation formula, as follows: CKD-EPI formula = $141 \times \min(Scr/\kappa,1)^{\alpha} \times \max(Scr/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018$ [if female] × 1.159 [if black].[19] CKD was defined according to KDIGO guidelines for the evaluation and management of CKD by glomerular filtration rate (G1-5) G1 Normal or high ≥ 90 but with active urinary sediment, G2 mildly decreased 60-89, G3a mildly to moderately decreased 45 - 59, G3b moderately to severely decreased 30 - 44, G4 severely decreased 15 - 29, and G5 Kidney failure < 15, as well albuminuria category (A1-3) A1 normal to mildly increased < 30 mg/g < 3 mg/mmol, A2 moderately increased 30 - 300 mg/g 3-30 mg/mmol, and A3 severely increased > 300 mg/g > 30 mg/mmol.[4]

Statistical analyses

Results were expressed as mean ± standard deviation (SD), analysis of variance by ANOVA and post hoc analysis with LSD tests were applied for comparing differences among groups. Data of SCr and ACR were expressed as median because of skewed distribution and analyzed by KruskalWallis test. Qualitative data were expressed in the form of numbers and percentages and comparison between data was performed by using the Chi-square test. The correlation between variables was calculated using the Pearson's and the Spearman correlation tests. Predictive values were assessed by the area under curve/the receiver operator characteristic curve (AUC/ROC). The AUC/ROC was used to determine the discriminatory ability of risk factor in detecting CKD. The criterion for statistical significance was set at $p < 0.05$. All calculations were carried out using a standard statistical package (SPSS version 19, Inc., Chicago, USA).

Results

Demographic data and characteristic of study

The existent studied number was 986 participants, their mean age 47.9 ± 11.8, male gender represented by 484 (49%) and female gender represented by 502 (51%) of the total study. The age, gender, smoking and BMI did not differ between the 3 studied groups. SUA significantly higher in diabetic patients than the healthy control group, meanwhile SUA levels were significantly higher in diabetic patients over 5 years duration than lesser duration of diabetes. Similarly systolic, diastolic, mean arterial BP, duration of diabetes, $HbA1_C$, TG, TC, LDL, TG/HDL-C ratio, SCr and ACR levels were significantly higher in group III than group I, II, likewise higher in group II than group I. Lastly eGFR significantly lower in group III than group I, II, likewise lower in group II than group I (Table 1).

Prevalence and significance of SUA

In the cohort of type 2 diabetic patients we found, the overall prevalence of hyperuricemia was 32% and the mean value of SUA was significantly higher among hypertensive, obese, poor glycemic control, high TG/HDL-C ratios patients as well as patients with ACR ≥ 300 mg/g, followed by ACR ≥ 30 mg/g. Meanwhile, there was non-significant difference of SUA level regarding genders and line of treatment (Table 2).

Correlates of SUA with study parameters

Although age, gender, duration of diabetes, BMI, WC, mean BP, HbA1c, TC, HDL-C, LDL, TG, TG/HDL-C, SCr, ACR and GFR were assessed in for association with SUA. Only age (r = 0.30; $p = 0.05$),

Table 1 Demographic and laboratory characteristics of the study

Variable	Control 250	Diabetic < 5 years 352	Diabetic > 5 years 384	*p*
Age (years)	48.5 ± 10.13	49.72 ± 11.07	50.38 ± 11.38	NS
Gender:				NS
Male %	122 49%	175 49.7%	187 49%	
Female %	128 51%	177 50.2%	197 51%	
Smoking:	63 25%	95 27%	92 24%	NS
BMI: (Kg/m^2)	30.5 ± 9.48	31.28 ± 6.45	31.95 ± 7.89	NS
Systolic BP (mm Hg)	119.59 ± 11.46	126.88 ± 14.95[a]	141 ± 18.72[ab]	< 0.001
Diastolic BP (mm Hg)	74.31 ± 9.54	78.75 ± 5.04[a]	84.88 ± 9.19[ab]	< 0.001
MAP (mm Hg)	92.95 ± 8.62	94.59 ± 8.6[a]	104.22 ± 10.97[ab]	< 0.001
Duration of diabetes: (y)		4.01 ± 0.88	11 ± 5.31	< 0.001
$HbA1_C$	5.12 ± 0.54	7.72 ± 1.44[a]	8.83 ± 1.99[ab]	< 0.001
T.G mg/dL	100.5 ± 40.5	155.5 ± 60.5[a]	182.4 ± 78.6[ab]	< 0.001
Cholesterol mg/dL	189.5 ± 32.9	201.3 ± 45.9[a]	210.1 ± 49.6[ab]	< 0.001
LDL mg/dL	104.7 ± 25.7	113.6 ± 31.4[a]	122.2 ± 38.8[ab]	< 0.001
HDL mg/dL	50.6 ± 5.9	45.1 ± 6.3[a]	39.5 ± 7.1[ab]	< 0.001
TG/HDL-C ratio	1.91 ± 1.2	3.44 ± 0.98[a]	4.15 ± 1.8[ab]	< 0.001
SCr: (mg/dl)	0.90 ± 0.17	1.1 ± 0.21[a]	2.04 ± 1.44[ab]	< 0.001
Alb.creat.ratio(mg/gm)	6.55 ± 3.93	36.06 ±57.89[a]	940.52 ± 2007.71[ab]	< 0.001
eGFR: (ml/min/m^2)	105.34 ± 18.8	82.31 ± 16.9[a]	56.37 ± 20.4[ab]	< 0.001
Uric acid: (mg/dl)	4.61 ± 1.8	5.26 ± 1[a]	7.40 ± 1.32[ab]	< 0.001

[a] significant difference as compared to control group. [ab] significant difference as compared to group II.

duration of diabetes (r = 0.47; *p* = 0.001), BMI (r = 0.42; *p* = 0.001), WC (r = 0.44; *p* = 0.001), mean BP (r = 0.35; *p* = 0.01), HbA1c (r = 0.4; *p* = 0.001), TC (r = 0.31; *p* = 0.05), HDL-C (r = 0.36; *p* = 0.01), LDL (r = 0.33; *p* = 0.05), TG (r = 0.45; *p* = 0.001), TG/HDL-C (r = 0.59; *p* = 0.001), SCr (r = 0.6; *p* = 0.001), ACR (r = 0.51; *p* = 0.001), were positively correlated with SUA, while HDL (r = 0.-0.36; *p* = 0.01) and eGFR (r = -0.65; *p* = 0.001), were negatively correlated with SUA. Hence SUA was significantly associated with all components of MS (Table 3).

Sensitivity and specificity of UA

In the cohort of type 2 diabetic patients we found, SUA at level of > 6.1, > 6.2 and > 6.5 had a greater sensitivity 86.8%, 81.25%, 65.4% and specificity 82.8%, 85.94%, 77.1% for identifying hypertension, early nephropathy and diminished GFR respectively (Table 4).

Demographic, clinical and laboratory features of the patients with SUA above and below 6.2 mg/dL.

The mean age, duration of diabetes, BP, BMI, HBA1C, TG/H.D.L-C ratio and SCr were significantly higher in patients with elevated SUA > 6.2 mg/dl. Similarly the prevalence of hypertension, ACR ≥ 30 mg/g and ACR ≥ 300 mg/g were significantly higher among patients with elevated SUA > 6.2 mg/dl. Moreover, patients with elevated SUA > 6.2 mg/dl had lesser eGFR (Table 5).

Discussion

Early detection of DN has a pivotal role in the prevention of ESRD.[20] Conflicting data exist about the role of SUA in patients with T2DM; the present study was addressed to evaluate the relation between SUA and hypertension, albumin excretion rate and CKD in a cohort of T2DM patients.

Hyperuricemia is usually defined as an SUA level of 7.0 mg/dl and of ≥ 6 mg/dl in women.[17] In the current study, we demonstrated that that solely 32% of diabetic patients were hyperuricemic, but in contrast to healthy control subjects SUA levels were higher in T2DM patients with onset of diabetes less than 5 years and continue to rise with disease progression and clinical presentation of DN. Moreover, we also observed a positive correlation between SUA and $HbA1_C$. Our findings were consistent with other

Table 2 Comparative difference of SUA levels

Variable No.	Uric acid M ± SD	*p*
Sex		
Male 362	6.5 ± 1.58	NS
Female 374	6.3 ± 1.41	
BP		
Normotensive 455	6.13 ± 0.82	< 0.001
Hypertensive 281	6.81 ± 1.42	
BMI		
< 30 485	5.76 ± 0.72	< 0.001
≥ 30 251	6.91 ± 1.25	
$HbA1_c$		
< 7.0%	5.1 ± 1.09	< 0.001
≥ 7.0%	6.95 ± 1.28	
TG/H.D.L ratio		
< 4	5.3 ± 0.93	< 0.001
≥ 4	7.2 ± 1.4	
Treatment		
Insulin 250	6.2 ± 1.7	NS
Oral Hyopglycemic 486	6.4 ± 1.66	
ACR		
< 30 253	4.97 ± 0.97	< 0.001
≥ 30 mg/g 276	6.11 ± 0.75	
≥ 300 mg/g 207	7.51 ± 1.3	

Table 3 Correlates of SUA with other study parameters

Variable	R	*p*
Age	0.30	0.05
Gender	0.14	NS
Duration of diabetes	0.47	< 0.001
BMI	0.42	< 0.001
WC	0.44	< 0.001
Mean BP	0.35	0.01
$HbA1_C$	0.40	< 0.001
Total cholesterol (mg/dl)	0.31	0.05
HDL-C (mg/dl)	-0.36	0.01
LDL-C (mg/dl)	0.33	0.05
Triglycerides (mg/dl)	0.45	< 0.001
TG/HDL-C ratio	0.59	< 0.001
ACR (mg/gm)	0.51	< 0.001
SCr (mg/dl)	0.6	< 0.001
eGFR (ml/min/m^2)	-0.65	< 0.001

reports that link not only a positive association between elevated SUA levels and diabetes[21] but also with DN.[22]

Contrary to our results other studies found higher SUA levels were inversely associated with *diabetes mellitus*.[23] The excuse of such contradictory results is hyperinsulinemia/insulin resistance, which is the cardinal feature of T2DM.[24] It has been proposed that elevated plasma insulin concentrations may decrease urinary uric acid clearance in insulin-resistant individuals.[25] Contrary, hypouricemia may be the consequence of glomerular hyperfiltration, typically defined by a GFR of between 125 mL/min and 140 mL/min/1.73 m^2, consequently increasing renal clearance of the urate,[26] while the mean GFR of our patients study much lesser.

Unexpectedly, we failed to find a correlation between SUA levels and sex; however, the possible reason that may explain these conflicting results, is the mean age of women was significantly higher and most of them older than 50 years, moreover most of them were menopausal, as menopausal women have higher SUA levels than premenopausal women.[27] Estrogen is known to promote excretion of uric acid, so reduce the prevalence of hyperuricemia in premenopausal women.[28]

Table 4 Validity of SUA in prediction of, hypertension, early nephropathy and impaired GFR

Cutoff	Parameter	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy
> 6.1 mg/dl	Hypertension	0.90	86.8	82.8	76.7	90.6	84.4
> 6.2 mg/dl	Early nephropathy	0.94	81.25	85.94	74.3	90.2	84.4
> 6.5 mg/dl	Impaired GFR	0.93	80.4	84.1	71.5	89.7	82.5

Table 5 Demographic, clinical and laboratory features of the patients with SUA above and below 6.2 mg/dl

Variable	Uric acid ≤ 6.2 402	Uric acid > 6.2 334	*p*
Age (years)	47.23 ± 11.35	53.34 ± 10.47	< 0.001
Sex %			
Male	193 48%	169 50.5%	NS
Female	209 52%	165 49.5%	
Duration of diabetes (years):	6.63 ± 3.82	11.97 ± 5.55	< 0.001
Smoking %			
No	71.4%	75.9%	NS
Yes	28.6%	24.1%	
HPT %			
No	74.3%	37.9%	0.003
Yes	25.7%	62.1%	
Blood pressure			
Systolic	127.43 ± 16.19	141.79 ± 17.73	< 0.001
Diastolic	78.43 ± 5.22	85.9 ± 8.85	< 0.001
Mean	102.93 ± 9.81	113.84 ± 12.08	< 0.001
BMI	28.9 ± 6.04	32.5 ± 7.2	< 0.001
$HBA1_C$	7.82 ± 1.72	8.81 ± 1.81	< 0.001
TG/H.D.L-C ratio	2.72 ± 1.1	3.35 ± 1.4	< 0.001
ACR ≥ 30 mg/g	37.1%	93.1%	< 0.001
ACR ≥ 300 mg/g	22.9%	82.8	< 0.03
SCr (mg/dl)	1.17 ± 0.29	2.04 ± 1.53	< 0.001
GFR: (ml/min/m^2)	86.46 ± 18.3	50.17 ± 22.6	< 0.001

In the Current study, we found, a higher level of SUA among hypertensive patients, SUA levels were associated with the risk of hypertension, and furthermore SUA at level 6.1 mg.dl identify the onset of hypertension in T2DM. Our findings were consistent with other studies which reported that higher UA concentrations were independently associated with increased odds of developing hypertension.[29] Potential mechanisms behind the link between hyperuricemia and the development of hypertension have included nitric oxide and RAAS pathways. UA could lead to endothelial cell dysfunction via nitric oxide synthetase and stimulate vascular smooth muscle cell proliferation.[10] Furthermore, UA may also directly stimulate the RAAS.[11]

Hyperuricemia has gained attention as it has been reported that it plays an important role in the development of MS. It has been suggested that the plasma TG/HDL-C ratio can serve as a simple and easily accessible marker for the diagnosis of MS and insulin resistance.[30] In the current study, we found SUA negatively correlated with HDL-C and positively correlated with other components of MS as, BMI, WC, BP, $HbA1_C$, TG, TG/HDL-C. Moreover diabetic patients with a higher SUA level > 6.2 mg/dl have a higher BMI, BP, TG/HDL-C. So, increased SUA concentration may be an additional risk factor for MS. The underlying mechanisms may explain the association between UA and MS includes deleterious effects of UA on endothelial function [10], oxidative

metabolism,[31] and the systemic inflammatory state.[32] Our findings were consistent with other reports that the link between UA and MS.[33]

UA is produced by xanthine oxidoreductase. Oxidoreductase activity also contributes to macrophage foam cell formation and inflammation and macrophage activation is thought to be involved in the pathogenesis of DN.[34] MA is a marker of endothelial dysfunction and associated with an increased risk of cardiovascular morbidity in patients with diabetes.[35] In the present study, we have evaluated the relationships between UA concentration and degree of urinary albumin excretion. We demonstrated not only a higher level of SUA in patients with ACR ≥ 30 mg/g, but also a positive correlation with ACR ≥ 30 mg/g, and at a cutoff level of > 6.2 mg/dl identify the onset of early nephropathy in type 2 diabetic patients. Moreover SUA level continues to raise with progression of overt diabetic nephropathy patients with ACR ≥ 300 mg/g, and still positively correlated with ACR ≥ 300 mg/g. Generally, these results appear compatible with other studies which found, SUA concentration was associated with microalbuminuria and increased progression to overt nephropathy in patients with T2DM[36] as well SUA levels, even within the normal range > 6.3 mg/dl can predict the onset of overt nephropathy.[37]

Overt nephropathy resulted in an increased risk for declining renal function in T2DM. The role of UA in patients with T2DM is still not well studied, particularly in association with declining renal function. In the present study, we demonstrated that higher levels of SUA were associated with declines of eGFR and identify the onset of rapid progression of CKD, furthermore at a cutoff level of > 6.5 mg/dl may link to progression of CKD in T2DM patients. Our results were consistent with previous findings, which registered that hyperuricemia seemed to be an independent risk factor for the development of incident CKD rather associated with overt nephropathy[37] and even in normalbuminuria patients with T2DM.[38]

Collectively in the current study we, achieved that T2DM patients with UA ≤ 6.2 mg/dl were, younger, recently diabetic, better glycemic control, normotensive, lesser BMI, comparatively ideal TG/HDL-C, lower prevalence of early and overt nephropathy and preserved GFR. The current data give an important, highlighting to maintain SUA ≤ 6.2 mg/dl.

Conclusion

Even the high normal SUA level, was associated with the risk of hypertension, MS, early nephropathy and decline of eGFR. Moreover SUA level may identify and link with the onset of hypertension, early nephropathy, a procession of nephropathy and progression of CKD in T2DM. Measuring SUA levels routinely may help to identify high risk patients, as well as great attention to maintain SUA ≤ 6.2 mg/dl. Further studies are needed to examine the impact of lowering SUA levels on diabetic complications.

Conflict of Interest. No conflict of interest has been declared by the authors.

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