Section: Biochemistry

Original Research Article

SERUM URIC ACID TO CREATININE RATIO AND RISK OF METABOLIC SYNDROME IN TYPE 2 DIABETIC PATIENTS

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ABSTRACT

Background: Metabolic syndrome is a cluster of metabolic disorders including abdominal obesity, hypertension, high triglycerides, low HDL-Cholesterol and hyperglycemia. As a major worldwide public health problem, the prevalence of MetS has grown markedly over the past decades. MetS is associated with the increasing mortality of type 2 diabetes mellitus. Uric Acid is the final product of purine metabolism. It has been demonstrated that SUA level is closely related to conditions such as obesity, endothelial dysfunction, impaired glucose metabolism and hypertension. Evidence demonstrates that uric acid may have a key role in the pathogenesis of MetS. Serum creatinine is a commonly used indicator for detecting small changes in GFR, hence a good biomarker of early-stage CKD. This biomarker is studied before; however it is yet to be studied in relation to metabolic syndrome and in a population where the prevalence of Mets and T2DM are high. This is a cross-sectional study, Aim to estimate the correlation between serum UA/Cr ratio and metabolic syndrome in Diabetic patients.

Materials and Methods: Serum UA/Cr ratio and components of metabolic syndrome will be measured and then correlating these values with diabetic patients.

Results: Serum UA/Cr ratio was positively with BMI, CRP, waist circumference, triglycerides, and hypertension. In the highest quartile of UA/Cr levels, the risks were substantially higher for MetS compared with that in the lowest quartile of UA/Cr levels.

Conclusion: Levels of serum UA/Cr in T2DM are strongly associated with risk of MetS and its components.

Keywords: Type-2 Diabetes Mellitus, Serum uric acid, creatinine.

INTRODUCTION

Type-2 Diabetes Mellitus (T2DM) is a long-term condition that has become epidemic globally, impacting millions of people and posing a considerable public health challenge. T2DM is mainly defined by insulin resistance and impaired beta-cell function, resulting in Persistent high blood sugar. With time, this unmanaged blood sugar may result in various microvascular and macrovascular issues. Diabetic nephropathy, a complication caused by kidney damage, is among the most frequent and serious consequences of prolonged diabetes.[1]

A significant global public health issue is metabolic syndrome (MetS), a group of cardiovascular risk factors that includes insulin resistance, hypertension, glucose intolerance, hypertriglyceridemia, and low levels of HDL cholesterol.[2] Because of the westernization of the lifestyle, which includes eating a high-fat, high-calorie diet and engaging in less physical activity, the prevalence of MetS is rising in India. The final byproduct of human purine metabolism is uric acid. Excess serum buildup can cause a number of illnesses, most notably gouty arthritis, which is caused by uric acid.[3-5] Recent research indicates that uric acid may play a significant role in the pathophysiology of MetS.[6]

Recent research using animal models suggests that uric acid may contribute to the development of MetS, and lowering uric acid levels can stop or reverse MetS symptoms.[7] Serum Cr has been linked to an increased risk of obesity, CAD, hypertension, and type 2 diabetes.[8] Recently, renal function normalized SUA (UA/Cr) has appeared as a new biomarker and is considered to reflect endogenous UA levels more precisely than SUA level. Several studies have suggested that serum UA/Cr ratio was significantly associated with chronic obstructive pulmonary disease, chronic kidney disease, b-Cell function in type 2 diabetes mellitus patients.[9–11] However, there are limited studies focused on the relationship between serum UA/Cr ratio and MetS.

Aims and Objectives

To estimate the correlation between serum uric acid to creatinine ratio and metabolic syndrome in Diabetes Mellitus patients.

MATERIALS AND METHODS

The cross-sectional study was conducted in Nootan medical College and Research centre, Visnagar, Gujarat during July 2022 to November 2022. Altogether 300 participants were involved in this study. Ethical clearance was obtained by institution's Human Research Ethics Committee. (Ref: IEC/NMCRCAPPROVAL/52/2022)

Inclusion Criteria

1. Participants aged 18 years or older diagnosed with Type-2 Diabetes Mellitus.
2. Participants willing to provide valid informed consent for the study.

Exclusion Criteria

1. Use of drugs known to cause hyperuricemia
2. Presence of liver disease / CKD / Muscle disorder / Gout
3. Patients with active urinary tract infections (UTIs)
4. History of malignancy

Definition of MetS

The MetS was defined based on the updated National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) criteria for Asian-Americans,[12]: (1) as presenting at least three of the following components:

1) Waist circumferences 90 cm or greater in men or 80 cm or greater in women;

2) Triglycerides 1.7 mmol/liter or greater;

3) HDL cholesterol less than 1.03 mmol/liter in men or less than 1.30 mmol/liter in women;

4) Blood pressure 130/85 mm Hg or greater or current use of antihypertensive medications; or

5) Fasting plasma glucose (FPG) 5.6 mmol/liter or greater or previously diagnosed type 2 diabetes or on oral antidiabetic agents or insulin.

A total of 300 subjects with T2DM were recruited for in this cross-sectional study. The mean age of the study population was 53.94 ± 11.4; 40.6% of whom were males. Subjects were divided into serum UA/Cr tertiles (Ter). Ter1 ranged from 2.0 to 3.9 [N = 110, mean ± standard deviation (SD) 3.24 ± 0.5], Ter2 ranged from 4.0 to 5.0 (110, 4.50 ± 0.3) and Ter3 ranged from 5.1 to 11.1 (112, 6.16 ± 1.0). The results are presented in [Table 1]. Anthropometry included height, waist and hips (cm) and weight (kg) measured using Digital Pearson Scale (ADAM equipment Inc., USA). A standard procedure was utilized to measure resting blood pressure (measured twice by a qualified nurse).

About 5 ml of blood samples were collected and allow to clot then centrifuged to obtain the serum. Serum uric acid was measured by Colorimetric enzymatic method (Uricase -POD). Serum Creatinine was measured by Colorimetric enzymatic method (creatinase). Serum Urea was measured by Colorimetric enzymatic method (Urease-GLDH). Serum Glucose was measured by Colorimetric enzymatic method (GOD-POD). Serum HbA1c was measured by particle enhanced immunoturbidimetric method. Serum Triglyceride was measured by Colorimetric enzymatic method (GPO-PAP). Serum HDL Cholesterol was measured by Colorimetric enzymatic method (Direct HDL-C).All parameters were done on Erba XL 640 fully auto analyzer.

RESULTS

With respect to metabolic parameters, the patients in the higher uric acid quartiles exhibited higher levels of systolic blood pressure, BMI, waist circumference, creatinine and triglycerides (all $P < 0.05$). The overall prevalence of MetS was 58.3%. The prevalence of MetS significantly increased in parallel with increasing tertiles, from 42.8% (Ter1) and 58.8% (Ter2) to 68.6% (Ter3) ($p = 0.003$).

Remarkably, serum UA/Cr levels increased gradually with increasing number of MetS components [Figure 1].

Analysis was performed using the commercially available Statistical Software STATA (14.2), and Microsoft Excel 2016. The p-value of less than 0.05 was considered statistically significant.

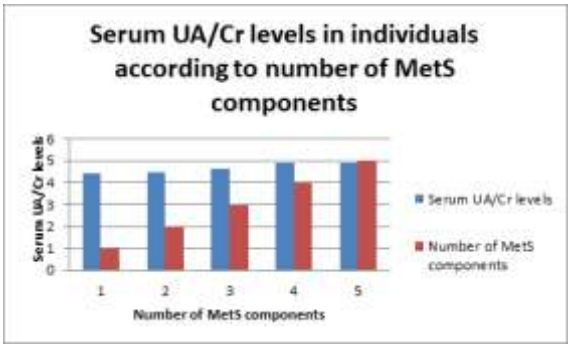

Figure 1: Serum UA/Cr levels in individuals according to number of MetS components. The mean serum UA/Cr value for the subjects with 1, 2, 3, 4 and 5 MetS components is 4.44 (0.2), 4.49 (0.1), 4.64 (0.1), 4.89 (0.2) and 4.91 (0.4) respectively.

Table 1: General Characteristic of Subjects based on Serum UA/Cr Tertiles

Characteristics	Ter 1 (2.0–3.9)	Ter 2 (4.0–5.0)	Ter 3 (5.1–11.1)	P- Value
MetS (%)	42.8	58.8	68.6	0.003
UA/Cr	3.1 ± 0.5	4.4 ± 0.3	6 ± 0.9	<0.001
Age (yr)	54.2 ± 10.8	52.8 ± 10.1	53.1 ± 11	0.005
Duration of diabetes (yr)	9.72 ± 7.84	7.74 ± 7.04	7.24 ± 6.69	<0.001
SBP (mmHg)	136 ± 15.8	137.8 ± 16.1	139.2 ± 14.1	0.92
DBP (mmHg)	80 ± 8.9	81.2 ± 9.1	82.22 ± 8.3	0.92
BMI (kg/m2)	26.5 ± 4.3	27.9 ± 4.5	30.1 ± 5	<0.001
Waist circumference (cm)	94.2 ± 9.9	95.6 ± 9.4	96.4 ± 10.1	0.04
Glucose (mmol/L)	9.25(7.20-12.30)	7.70(6.40-9.60)	7.80(6.60-9.70)	<0.001
HbA(%)1C	7.91 ± 1.94	7.10 ± 1.59	6.96 ± 1.42	<0.001
Uric acid	239.5 ± 61.6	273.2 ± 62.5	338.3 ± 94.5	0.001
Creatinine (µmol/L)	76.3 ± 22.6	61.4 ± 13.9	55.6 ± 12.6	0.001
Triglycerides (mmol/l)	1.6 ± 0.9	1.6 ± 0.9	1.5 ± 0.7	0.81
HDL-Cholesterol (mmol/l)	1.1 ± 0.4	1.0 ± 0.3	1.0 ± 0.3	0.006
Urea (mmol/l)	5.0 ± 1.5	4.7 ± 1.7	4.6 ± 1.3	0.003

Table 2: Correlation between Serum UA/Cr and other measured parameters in T2DM

Variable	Correlation coefficient	P value
Age (years)	-0.204	<0.001
BMI (kg/m)2	0.326	<0.001
Waist (cm)	0.147	0.05
SBP (mmHg)	-0.016	0.76
DBP (mmHg)	-0.001	0.99
Fasting Glucose (mmol/l)	-0.140	0.01
Urea (mmol/l)	-0.116	0.04
Triglycerides (mmol/l)	-0.030	0.59
HDL-Cholesterol (mmol/l)	-0.134	0.02

DISCUSSION

Increased risk in all MetS components was associated with higher serum UA/Cr values.

The odds of having central obesity, hypertriglyceridemia, low HDL-cholesterol and hypertension for the highest serum UA/Cr tertile compared to the lowest were significant at 2.62, 1.41, 1.45 and 1.18 respectively (p<0.001in all) even after adjustment for age, gender, MI and the rest of MetS components. Previous research has demonstrated a substantial correlation between hyperuricemia and greater BMI, dyslipidemia, and hypertension.[13-14] Although insulin resistance is thought to be the mechanism connecting hyperuricemia with the emergence of various metabolic diseases, the underlying process is still poorly understood. It has recently been discovered that elevated serum Cr levels are likewise linked to the components of MetS.[15-16] In our study, higher BMI, waist and hip circumference was observed in the highest tertile of serum UA/Cr which was confirmed by a strong positive correlation of serum UA/Cr with BMI, waist and hips. In contrast, HDL-cholesterol was significantly lowest in the highest tertile of serum UA/Cr and confirmed by the significant inverse correlation of SrUa/Cr with HDL-cholesterol. Serum UA/Cr levels significantly rose in those with greater cradiometabolic risk factors, suggesting that it could be helpful in predicting the prognosis for MetS. In various population studies, the relationship between serum UA and full MetS has been investigated.[6,17] Similarly, a recent study showed serum Cr to be associated with MetS.[18] The prevalence of MetS also Increased from lower to higher Serum UA/Cr tertiles [Table 1].

This may be partially explained by the endocrine imbalance in adipose tissue caused by hyperuricemia, which ultimately leads to the low-grade inflammation associated with MetS.[19] Additionally, it has been noted that UA increases the synthesis of pro-inflammatory cytokines such as tumor necrosis factor and C-reactive protein, which may influence long-term inflammatory processes.[20] Over the past few decades, there has been a noteworthy increase in the consumption of fructose and purine-rich foods, which may have contributed to elevated serum uric acid levels and a strong correlation with the increased incidence of MetS.[21] Renal function is identified as the primary confounding variable in the relationship between blood uric acid and metabolic syndrome along with its components.[14,6,7] A byproduct of purine metabolism, UA is mostly excreted in the urine. Therefore, greater levels of serum UA are correlated with poorer renal function linked to reduced eGFR and higher blood creatinine levels.

In this study, serum UA shows a significant and positive correlation with creatinine. Increased serum UA levels may suggest impaired kidney function, which has been identified as an independent predictor of MetS and CVD occurrences.[22-23] Renal function-normalized serum UA such as serum UA/Cr, reflecting the net production of UA, may thus turn out to be a good marker in pathogenesis of MetS and related diseases. The association between SUA and MetS has long been recognized. A meta-analysis encompassing 54,970 people and 8,719 instances of MS revealed that elevated SUA levels

corresponded to an augmented risk of MetS, demonstrating a linear dose-response association.[24] Yadav et al performed a population-based cohort study 1590 healthy adults aged 40 to 70 years, and found that SUA may predicted as a risk factor for developing MetS during a mean2.6 years of follow-up.[25] Yang et al performed a prospective study of 3857 subjects who were free of MetS and found that hyperuricemia was an independent risk factor for MetS in women during a mean follow-up of 5.41 years.[26] Uric acid (UA) is the ultimate oxidation product of purine metabolism in humans, and serum uric acid (SUA) levels are affected by renal function. However, most previous studies ignored the contribution of kidney on UA levels. Serum UA/Cr, a function-normalized SUA index, is considered to be better representative of endogenous serum uric acid and may be better correlated with metabolic diseases. The following description may explain the mechanisms that link SUA to MetS. First, Endothelial function may be compromised and endothelial cells may emit less nitric oxide as a result of hyperuricemia. However, increasing blood flow, which is facilitated by the release of nitric oxide from endothelial cells, is partially responsible for the uptake of glucose in skeletal muscle. Therefore, by reducing nitric oxide's bioavailability, UA may worsen insulin resistance.[27–28]

The inflammation and oxidative stress brought on by SUA could be the second mechanism. Previous research has shown that the metabolic syndrome in obese mice is largely caused by oxidative alterations brought on by hyperuricemia in adipocytes.[29]

CONCLUSION

In conclusion, our data suggest that levels of serum UA/Cr in T2DM are strongly associated with risk of MetS and its components. Consequently, lowering serum UA/Cr levels by adopting a healthier lifestyle may prove to be a useful strategy for lowering MetS burden. Further research is needed to address the causal relationship of serum UA/Cr in the pathogenesis of MetS.

REFERENCES

1. Warjukar P, Jain P, Kute P, Anjankar A, Ghangale S. Study of microalbuminuria and uric acid in type 2 diabetes mellitus. Int J Cur Res Rev. 2020 Jul;2020.
2. Yamaoka-Tojo M, Tojo T, Takahira N, Matsunaga A, Aoyama N, Masuda T,Izumi T: Elevated circulating levels of an incretin hormone, glucagon-likepeptide-1, are associated with metabolic components in high-riskpatients with cardiovascular disease. Cardiovascular Diabetology 2010,9(17).
3. Moriarity JT, Folsom AR, Iribarren C, Nieto FJ, Rosamond WD: Serum Uric Acid and Risk of Coronary Heart Disease: Atherosclerosis Risk in Communities (ARIC) Study. Annals of Epidemiology 2000, 10(3):136-143.
4. So A, Thorens B: Uric acid transport and disease. Journal of Clinical Investigation 2010, 120(6):1791-1799.
5. Koenig W, Meisinger C: Uric acid, type 2 diabetes, and cardiovascular diseases: Fueling the common soil hypothesis? Clinical Chemistry 2008, 54(2):231-233.
6. Ishizaka N, Ishizaka Y, Toda E-I, Nagai R, Yamakado M: Association Between Serum Uric Acid, Metabolic Syndrome, and Carotid Atherosclerosis in Japanese Individuals. Arterioscler Thromb Vasc Biol 2005, 25(5):1038-1044.
7. Nakagawa T, Hu H, Zharikov S, Tuttle KR, Short RA, Glushakova O, Ouyang X, Feig DI, Block ER, Herrera-Acosta J, Patel JM, Johnson RJ: A causal role for uric acid in fructose-induced metabolic syndrome. American Journal of Physiology - Renal Physiology 2006, 290(3):F625-F631.
8. Fried LF, Shlipak MG, Crump C, et al. Renal insufficiency as a predictor of cardiovascular outcomes and mortality in elderly individuals. J Am Coll Cardiol 2003;41:1364–72.
9. Durmus Kocak N, Sasak G, Aka Akturk U, et al. Serum uric acid levelsand uric acid/creatinine ratios in stable chronic obstructive pulmonarydisease (COPD) patients: are these parameters efficient predictors ofpatients at risk for exacerbation and/or severity of disease? Med SciMonit 2016;22:4169–76.
10. Al-Daghri NM, Al-Attas OS, Wani K, et al. Serum uric acid to creatinine ratio and risk of metabolic syndrome in Saudi type 2 diabetic patients. Sci Rep 2017;7:12104.
11. Li M, Gu L, Yang J, et al. Serum uric acid to creatinine ratio correlates with b-cell function in type 2 diabetes. Diabetes Metab Res Rev 2018;34: e3001.
12. Liu J, Grundy SM, Wang W, Smith SC, Vega GL, Wu Z, Zeng Z, Wang W, Zhao D: Ethnic-Specific Criteria for the Metabolic Syndrome. Diabetes Care 2006, 29(6):1414-1416.
13. Rathmann, W., Funkhouser, E., Dyer, A. R. & Roseman, J. M. Relations of hyperuricemia with the various components of the insulin resistance syndrome in young black and white adults: the CARDIA study. Ann Epidemiol8, 250–261 (1998).
14. Conen, D. et al. Prevalence of hyperuricemia and relation of serum uric acid with cardiovascular risk factors in a developing country. BMC Public Health4, 9 (2004).
15. Chen, N. et al. Community-based study on CKD subjects and the associated risk factors. Nephrology Dialysis Transplantation24, 2117–2123 (2009).
16. Chang, I. H. et al. Association between metabolic syndrome and chronic kidney disease in the Korean population. Nephrology14, 321–326 (2009).
17. Kim, E. S. et al. Serum uric acid level is associated with metabolic syndrome and microalbuminuria in Korean patients with type 2 diabetes mellitus. J Diabetes Complications25, 309–313 (2011).
18. Wang, J. et al. Serum creatinine levels and risk of metabolic syndrome in a middle-aged and older Chinese population. Clinica Chimica Acta440, 177–182 (2015).
19. Baldwin, W. et al. Hyperuricemia as a mediator of the proinflammatory endocrine imbalance in the adipose tissue in a murine model of the metabolic syndrome. Diabetes60, 1258–1269 (2011).
20. Kanellis, J. & Kang, D. H. Uric acid as a mediator of endothelial dysfunction, inflammation, and vascular disease. Seminars innephrology25, 39–42 (2005).
21. Cirillo, P. et al. Uric acid, the metabolic syndrome, and renal disease. JASN17, S165–S168 (2006).
22. Ruilope, L. M. & Garcia-Puig, J. Hyperuricemia and renal function. Curr Hypertens Rep3, 197–202 (2001).
23. Baker, J. F., Krishnan, E., Chen, L. & Schumacher, H. R. Serum uric acid and cardiovascular disease: recent developments, and where do they leave us? Am J Med118, 816–826 (2005).
24. Yuan H, Yu C, Li X, et al. Serum uric acid levels and risk of metabolic syndrome: a dose-response meta-analysis of prospective studies. J Clin Endocrinol Metab 2015;100:4198–207.
25. Yadav D, Lee ES, Kim HM, et al. Prospective study of serum uric acid levels and incident metabolic syndrome in a Korean ruralcohort. Atherosclerosis 2015;241:271–7..
26. Yang T, Chu CH, Bai CH, et al. Uric acid level as a risk marker for metabolic syndrome: a Chinese cohort study. Atherosclerosis 2012;220: 525–31.
27. Khosla UM, Zharikov S, Finch JL, et al. Hyperuricemia inducesendothelial dysfunction. Kidney Int 2005;67:1739–42.
28. Feig DI, Kang DH, Johnson RJ. Uric acid and cardiovascular risk. NEnglJ Med 2008;359:1811–21.
29. Sautin YY, Nakagawa T, Zharikov S, et al. Adverse effects of theclassical antioxidant uric acid in adipocytes: NADPH oxidase-mediatedoxidative/nitrosative stress. Am J Physiol Cell Physiol 2007;293:C584–96.