



## A Study of Relationship Between Serum Uric Acid, and Fasting Plasma Glucose in Type 2 Diabetes Mellitus Patients

Anuradha G, Santhini Gopalakrishnan S\*, Vinodakumar H R

Department of Biochemistry, Chettinad hospital and research institute, Kelambakkam, Chengalpattu district-603103, Tamil Nadu, India

### Article History:

Received on: 21 Aug 2020

Revised on: 21 Sep 2020

Accepted on: 28 Sep 2020

### Keywords:

Lipid profile,  
cardiovascular disease,  
Antioxidant,  
Obesity

### ABSTRACT

The current study was conducted to observe the relationship between serum uric acid, lipid profile and fasting plasma glucose in type 2 DM patients. It was a cross-sectional study. A total of 618 participants were included in the study (203-healthy, 206-prediabetic and 209-T2DM). One way analysis of variance was used to compare the mean between these three groups. A linear regression model was used to find the relationship between SUA and FPG in T2DM. The mean values of serum uric acid in pre-diabetes and T2DM ( $4.929 \pm 1.33$  and  $4.69 \pm 1.41$  mg/dl, respectively) were lower compared to healthy ( $5.40 \pm 1.08$  mg/dl). SUA showed a significant positive correlation with serum triglycerides in T2DM ( $p < 0.05$ ). The linear regression model showed that SUA was inversely associated with FPG in T2DM after adjustment for age and gender. The biological interrelationship observed in the current study raises the possibility of potential pathogenic overlap between SUA and FPG. SUA might be involved in a metabolic imbalance which in turn leads to T2DM.



### \*Corresponding Author

Name: Santhini Gopalakrishnan S

Phone: 7299069636

Email: [santhini.research@gmail.com](mailto:santhini.research@gmail.com)

ISSN: 0975-7538

DOI: <https://doi.org/10.26452/ijrps.v11i4.3854>

Production and Hosted by

IJRPS | [www.ijrps.com](http://www.ijrps.com)

© 2020 | All rights reserved.

urban area, and lifestyle modifications may also be the causative factors. Among the various risk factors, obesity plays a significant role [3]. Indians with lower body mass index (BMI) has a high proportionate of diabetes (Rao, 2011; Mohan and Deepa, 2006). Hence they are at equal risk as those who are in western countries with obesity (Zargar et al., 2000). Moreover, Indians are genetically predisposed to coronary artery disease because of dyslipidemia (Misra and Khurana, 2011). To reduce the cardiovascular disease burden that diabetes creates, diabetes patients must be screened at an early stage itself.

Many previous studies have found the relationship between serum uric acid (SUA) and various risk factors that cause cardiovascular disease. But there is a lack of clear causal mechanism.

Uric acid (UA) is obtained as the final product of purine metabolism. UA reacts to oxidative stress based on its localization. Intracellular Uric acid has anti-oxidant role while extracellular have pro-oxidant property (Kang and Ha, 2014). Being

### INTRODUCTION

Diabetes mellitus is a potential epidemic in India. The prevalence of Type 2 Diabetes mellitus (T2DM) may increase drastically from 171 million in the year 2000 to 366 million by the year 2030 (Wild et al., 2004; Whiting et al., 2011). The aetiology for the development of T2DM is multifactorial. It is a genetic disease. Various environmental factors such as obesity, migration from rural to an

an anti-oxidant, uric acid protects the cardiovascular system. It prevents the peroxidation of proteins and lipids, scavenges free radicals, and chelates transitional metal ions (Glantzounis *et al.*, 2005). Its intrinsic anti-oxidant activity has been confirmed by the administration of UA in healthy volunteers and athletes, which, in turn, reduced reactive oxygen species production (ROS) (Waring *et al.*, 2001). UA also acts as a pro-oxidant. The Xanthine-oxidase, which is an isoform of Xanthine-oxidoreductase enzyme, generates ROS, which in turn induce endothelial dysfunction. This has been observed in an animal study on a rat. In rats, oxonic acid, which is an inhibitor of the enzyme, uricase has been administered. This has induced hyperuricemia which in turn raised blood pressure (Sanchez-Lozada *et al.*, 2007).

Some studies have found a positive relationship between elevated SUA and diabetes (Dehghan *et al.*, 2008; Chien *et al.*, 2008), few reported no correlation (Taniguchi *et al.*, 2001; Modi and Sahi, 2018), and some have reported inverse relationship (Bandaru and Shankar, 2011; Bonakdaran and Kharraqani, 2014). The current study was undertaken to know the actual trend of SUA in healthy, prediabetic, and T2DM and the relationship between SUA and Fasting plasma glucose (FPG) in T2DM.

### Study design

It was a cross-sectional study. The study was done after getting approval from the Institutional Human Ethics Committee, Chettinad hospital and research institute, Kelambakkam.

### Inclusion criteria and exclusion criteria

Those who underwent a volunteer health check-up at Chettinad hospital and research institute from 1<sup>st</sup> August 2019 to 30<sup>th</sup> August 2020 were included in the study. The study participants included both genders from the age of 35 to 65 years.

Based on the American diabetes association criteria, study participants were classified as normoglycemic (n=203), prediabetic (n=206), and T2DM (n=209).

A standard questionnaire was used to obtain personal history. Smokers and chronic alcoholics were excluded from the study. Those who suffer from systemic disorders like hypertension, renal disease, cardiovascular disease, and pulmonary disease were excluded from the study.

### Anthropometric measurement and blood collection

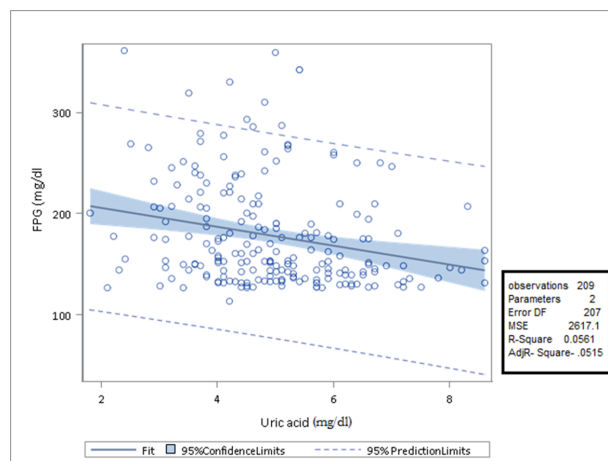
Height, weight, and blood pressure were measured using a standard protocol. The formula used for calculating Body mass index was weight in Kg divided

by height in meter squared. After ensuring that participants were under 12hours fasting, a venous blood sample was drawn under aseptic precautions. Baseline variables like glycated haemoglobin, FPG, Blood urea nitrogen, creatinine, uric acid, total cholesterol, Triglycerides, and High- density cholesterol were measured using Siemens RXL automated chemistry multi dimension system. The Calculated parameters were LDL-C and VLDL-C. The Friedewald formula was used to calculate LDL-C. VLDL-C was calculated by dividing TGL by 5.

### Statistical analysis

SPSS software was used for doing statistical analysis. One way analysis of variance (ANOVA) was used to find the p-Value between the mean of the variables between healthy, pre-diabetes, and T2DM. The correlation between serum uric acid and TC, TGL, HDL-C, LDL-C, and VLDL-C was found using Pearson's correlation coefficient test. The relationship between SUA and FPG was found using a simple linear regression model.

## RESULTS



**Figure 1: Shows a scatter plot with regression data between SUA and FPG. The Dependent variable was FPG. The figure shows a significant negative correlation between SUA and FPG in T2DM patients.**

Table 1 shows the mean values of healthy, pre-diabetes, and T2DM patients. A Statistically significant p-Value was obtained for the biochemical parameters HbA1c, FPG, UC, Creatinine, TC, TGL, LDL-C and VLDL-C. Variables such as age, BMI, WC and SBP also showed statistically significant p values.

Table 2 shows Pearson's correlation analysis between SUA and Lipid profile among T2DM. A Significant and positive relation existed between

**Table 1: Baseline variables of Healthy, Pre-diabetes and T2DM**

	Healthy Mean $\pm$ SD (N=203)	Pre-diabetes Mean $\pm$ SD (N= 206 )	Type 2 DM Mean $\pm$ SD (N= 209 )	P-Value
Age (years)	43.18 $\pm$ 7.53	45.2 $\pm$ 9.04	51.48 $\pm$ 9.47	<.0001*
BMI (kg/m <sup>2</sup> )	24.9 $\pm$ 0.42	26.1 $\pm$ 0.51	28.51 $\pm$ 0.98	<.0001*
WC(cm)	77.43 $\pm$ 1.97	91.83 $\pm$ 2.44	96.17 $\pm$ 5.39	<.0001*
SBP(mmHg)	108.6 $\pm$ 8.2	114.1 $\pm$ 10.1	116.2 $\pm$ 11.6	<.0001*
DBP(mmHg)	72.9 $\pm$ 8.2	74.4 $\pm$ 8.2	74.9 $\pm$ 9.8	0.057
HbA1C(%)	5.18 $\pm$ 0.22	6.2 $\pm$ 0.12	9.02 $\pm$ 1.74	<.0001*
FPG(mg/dl)	93.53 $\pm$ 4.72	107.29 $\pm$ 3.08	177.45 $\pm$ 52.16	<.0001*
BUN(mg/dl)	10.48 $\pm$ 3.09	10.29 $\pm$ 3.06	10.5 $\pm$ 3.26	0.755
Uric acid(mg/dl)	5.4 $\pm$ 1.08	4.929 $\pm$ 1.33	4.69 $\pm$ 1.41	<.0001*
Creatinine(mg/dl)	0.95 $\pm$ 0.17	0.93 $\pm$ 0.18	0.98 $\pm$ 0.2	0.021*
TC(mg/dl)	169.97 $\pm$ 32.51	182.03 $\pm$ 39.53	188.48 $\pm$ 45.65	<.0001*
TGL(mg/dl)	109.07 $\pm$ 68.71	122.59 $\pm$ 61.78	151.72 $\pm$ 74.99	<.0001*
HDL-C(mg/dl)	38.16 $\pm$ 8.55	37.36 $\pm$ 8.43	37.02 $\pm$ 8.19	0.369
LDL-C(mg/dl)	110.04 $\pm$ 29.53	119.71 $\pm$ 33.43	121.27 $\pm$ 40.07	0.002*
VLDL-C(mg/dl)	21.77 $\pm$ 13.78	24.16 $\pm$ 11.39	30.19 $\pm$ 15.06	<.0001*

\*p-value less than 0.05 was considered statistically significant

BMI: Body mass index

WC: Waist circumference

SBP: Systolic blood pressure

DBP: Diastolic blood pressure

**Table 2: Correlation analysis between Serum Uric acid (SUA) and Lipid profile among T2DM**

		SUA
TC(mg/dl)	r	0.1022
	p	.14089
TGL(mg/dl)	r	0.1878
	p	.00647*
HDL-C(mg/dl)	r	-0.0966
	p	0.195
LDL-C(mg/dl)	r	0.068
	p	.327925
VLDL-C(mg/dl)	r	0.1824
	p	0.00821*

\*p-value less than 0.05 was considered statistically significant

**Table 3: Simple Linear Regression for FPG/SUA**

Variable	Label	Number of T2DM Patients-209 Parameter Estimates				
		DF	Parameter Estimate	Standard Error	t Value	Pr >  t
Intercept	Intercept	1	223.91366	13.61729	16.44	<.0001
Uric acid	Uric acid	1	-9.35542	2.66768	-3.51	0.0006

\*p-value less than 0.05 was considered statistically significant

SUA and TGL. Also, there was a negative but not significant relation between SUA and HDL-C. VLDL-C also shows a significant positive correlation with SUA.

Table 3 shows that serum uric acid was statistically significant and negatively related to FPG.

Figure 1 shows a scatter plot with regression data between SUA and FPG. The Dependent variable was FPG. The figure shows a significant negative correlation between SUA and FPG in T2DM patients.

## DISCUSSION

Previous few studies have shown a positive relationship between SUA and FPG (Dehghan *et al.*, 2008; Chien *et al.*, 2008), and a recent study has shown no correlation between SUA and FPG (Modi and Sahi, 2018). The inconsistent findings seen in previous studies might be due to the small sample size, more of aged participants, selection of participants from a particular group rather than the general population, influence other factors like food habits, lifestyle, genetic and environmental factors, etc.

In the current study, as shown in Figure 1, a simple linear regression model adjusted for age and sex showed a negative and significant association between SUA and FPG in T2DM. These findings were supported by the previous study (Bandaru and Shankar, 2011).

A possible mechanism for the negative correlation between SUA and FPG may be due to inhibition of uric acid reabsorption in the proximal convoluted tubule by the high level of glucose concentration in the kidney (Tuomilehto *et al.*, 1988; Herman *et al.*, 1976). The kidney mainly regulates glucose homeostasis. In normal circumstances, plasma glucose is freely filtered, and the majority of them are reabsorbed by sodium-dependent glucose transporter. Both Uric acid and glucose are reabsorbed at the same site in the proximal tubule. Hence, Glucose levels influence the uric acid excretion by regulating the reabsorption of uric acid in the proximal tubule of the kidney.

Uric acid, which has intrinsic anti-oxidant activity, is reduced in pre-diabetes and T2DM. It may be one of the potential causes of oxidative stress in T2DM.

## CONCLUSION

Our study has confirmed that there exists an inverse relationship between SUA and FPG in T2DM patients. Further studies with data on the levels of uric acid in the urine of T2DM patients would better reveal the underlying mechanisms for the associa-

tion between SUA and FPG.

## Conflict of interest

The authors declare that they have no conflict of interest for this study.

## Funding Support

The authors declare that they have no funding support for this study.

## REFERENCES

- Bandaru, P., Shankar, A. 2011. Association between Serum Uric Acid Levels and Diabetes Mellitus. *International Journal of Endocrinology*, 2011:1-6.
- Bonakdaran, S., Kharaqani, B. 2014. Association of Serum Uric Acid and Metabolic Syndrome in Type 2 Diabetes. *Current Diabetes Reviews*, 10(2):113-117.
- Chien, K. L., Chen, M. F., Hsu, H. C., Chang, W. T., Su, T. C., Lee, Y. T., Hu, F. B. 2008. Plasma Uric Acid and the Risk of Type 2 Diabetes in a Chinese Community. *Clinical Chemistry*, 54(2):310-316.
- Dehghan, A., van Hoek, M., Sijbrands, E. J., Hofman, A., Witteman, J. C. 2008. High Serum Uric Acid as a Novel Risk Factor for Type 2 Diabetes. *Diabetes Care*, 31(2):361-362.
- Glantzounis, G., Tsimoyiannis, E., Kappas, A., Galaris, D. 2005. Uric Acid and Oxidative Stress. *Current Pharmaceutical Design*, 11(32):4145-4151.
- Herman, J. B., Medalie, J. H., Goldbourt, U. 1976. Diabetes, prediabetes and uricaemia. *Diabetologia*, 12(1):47-52.
- Kang, D. H., Ha, S. K. 2014. Uric Acid Puzzle: Dual Role as Anti-oxidant and Pro-oxidant. *Electrolytes and Blood Pressure*, 12(1).
- Misra, A., Khurana, L. 2011. Obesity-related non-communicable diseases: South Asians vs White Caucasians. *International Journal of Obesity*, 35(2):167-187.
- Modi, A. S., Sahi, N. 2018. Serum uric acid levels in type 2 diabetes mellitus. *Indian J Basic Appl Med Res*, 7:459-63.
- Mohan, V., Deepa, R. 2006. Obesity and abdominal obesity in Asian Indians. *The Indian Journal of Medical Research*, 123(5):593-596.
- Rao, C. 2011. A cross-sectional analysis of obesity among a rural population in coastal Southern Karnataka. *India. Australasian Medical Journal*, (1):53-57.
- Sanchez-Lozada, L. G., Tapia, E., Soto, V., Avila-Casado, C., Franco, M., Zhao, L., Johnson, R. J. 2007. Treatment with the xanthine oxidase inhibitor febuxostat lowers uric acid and alleviates sys-

- temic and glomerular hypertension in experimental hyperuricaemia. *Nephrology Dialysis Transplantation*, 23(4):1179–1185.
- Taniguchi, Y., Hayashi, T., Tsumura, K., Endo, G., Fujii, S., Okada, K. 2001. Serum uric acid and the risk for hypertension and Type 2 diabetes in Japanese men: The Osaka Health Survey. *Journal of Hypertension*, 19(7):1209–1215.
- Tuomilehto, J., Zimmet, P., Wolf, E., Taylor, R., Ram, P., King, H. 1988. Plasma uric acid level and its association with diabetes mellitus and some biologic parameters in a biracial population of fiji. *American Journal of Epidemiology*, 127(2):321–336.
- Waring, S. W., Webb, D. J., Maxwell, S. R. J. 2001. Systemic Uric Acid Administration Increases Serum Antioxidant Capacity in Healthy Volunteers. *Journal of Cardiovascular Pharmacology*, 38(3):365–371.
- Whiting, D. R., Guariguata, L., Weil, C., Shaw, J. 2011. IDF Diabetes Atlas: Global estimates of the prevalence of diabetes for 2011 and 2030. *Diabetes Research and Clinical Practice*, 94(3):311–321.
- Wild, S., Roglic, G., Green, A., Sicree, R., King, H. 2004. Global Prevalence of Diabetes: Estimates for the year 2000 and projections for 2030. *Diabetes Care*, 27(5):1047–1053.
- Zargar, A. H., Khan, A. K., Masoodi, S. R., Laway, B. A., Wani, A. I., Bashir, M. I., Dar, F. A. 2000. Prevalence of Type 2 diabetes mellitus and impaired glucose tolerance in the Kashmir Valley of the Indian subcontinent. *Diabetes Research and Clinical Practice*, 47(2):135–146.