Correlation of serum uric acid with lipid profile in patients with type 2 diabetes mellitus with normal creatinine level: 
Report from a tertiary care hospital in India

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ABSTRACT

Background: Increased serum uric acid (SUA) level is considered a risk factor for kidney diseases in type 2 diabetes mellitus (T2DM) patients. Deranged lipid profile in T2DM is an overall risk factor for cardiovascular complications. Aim: This study aimed to find the correlation between SUA and serum lipid profile in T2DM patients who had serum creatinine levels within normal limits. Materials and Methods: This cross-sectional observational study was conducted in a tertiary care hospital in eastern India. Serum creatinine level was measured first. Then, patients with serum creatinine levels within normal limits were recruited as the final sample. Anthropometric measurements were conducted by an experienced clinician. A 12-h fasting venous blood sample was used to measure serum urea, lipids, sugar, and glycated hemoglobin. Results: A total of 176 (male = 104 [59.1%], female = 72 [40.9%]) T2DM patients with a median age of 46 (Q1–Q3 = 40–55) years participated in the study. There was no gender difference in fasting blood sugar (FBS) (P = 0.57), SUA (P = 0.42), and high-density lipoprotein-cholesterol (HDL-C) (P = 0.17). Females showed higher total cholesterol (TC) (P < 0.0001), triglyceride (TG) (P = 0.002), low-density lipoprotein-cholesterol (LDL-C) (P = 0.0002), and very-low-density lipoprotein-cholesterol (VLDL-C) (P = 0.01). SUA showed significant positive correlation with TG (r = 0.65, P < 0.0001) and VLDL-C (r = 0.63, P < 0.0001) and significant negative correlation with HDL-C (r = −0.35, P < 0.0001) and FBS (r = −0.45, P < 0.0001). Conclusions: A higher level of SUA, an indicator for kidney disease in T2DM patients, may be associated with a higher TG and VLDL-C and lower FBS and HDL-C. Thus, SUA should be monitored along with lipid profile for early detection of the risk of kidney diseases.

Keywords: Blood glucose, creatinine, kidney diseases, lipids, type 2 diabetes mellitus, urea, uric acid
Deranged levels of low-density lipoprotein cholesterol (LDL-C) and very-low-density lipoprotein cholesterol (VLDL-C) are established risk factors for overall cardiovascular diseases. Various types of cardiovascular diseases are one of the most common complications in T2DM patients. Dyslipidemia, commonly elevated levels of triglyceride (TG), and low levels of high-density lipoprotein cholesterol (HDL-C) are major problems in T2DM patients.7

Previous studies have evaluated the relationship between the SUA and lipid profile in India (Assam state), Bangladesh, the USA, and the Italian population.8,11 However, no previous study was conducted in this region of India on patients suffering from T2DM without any existent kidney disease. In the current study, we first evaluated the creatinine level of the patients to know if there is already any kidney disease the patient is suffering from. With this, we excluded patients already suffering from kidney disease. Then, the SUA and lipid profile were measured and compared. The result of this study would help us to understand any correlation of SUA with lipid profile in patients suffering from T2DM and help plan treatment strategies. Family physicians and primary care physicians may be benefitted from the result as many patients are treated for T2DM by them.

Materials and Methods

Type and setting
This was a cross-sectional observational study conducted from July 2018 to October 2018 in the Department of Physiology of a teaching hospital in eastern India.

Ethics
This study was approved by the institutional ethics committee (reference number: 107 IARC/IEC RIMS). We declare that the study was conducted in full accordance with the World Medical Association Declaration of Helsinki (updated in 2013). All the patients were adults (i.e., age >18 completed years) and were recruited after obtaining written informed consent in vernacular language.

Minimum sample
A study conducted on Assamese people showed correlation coefficient of SUA versus TC = 0.85, SUA versus TG = 0.87, and SUA versus HDL = 0.79.10 Considering these three values, we calculated the sample size for our study with \( \alpha = 0.05 \) and \( \beta = 0.05 \) (95% power) to be 35.15 However, we aimed to recruit more patients according to our logistics.

Recruitment of sample
We used a convenience sample from the outpatient department of Medicine. Patients suffering from T2DM and being treated for >1 year were included in the study. All of them were on oral hypoglycemic medications. Patients who were on insulin or had gout or other pathologies of increased cell turnover (such as leukemia, lymphoma, hemolytic anemia, polycythemia, and renal disease) were excluded. Pregnant females were also excluded. After the initial recruitment, research participants were tested for serum creatinine. Male participants with creatinine <1.35 mg/dL and female participants with creatinine <1.04 mg/dL were taken as the final sample.13

Measurement
All of the research participants were first measured for height (cm), weight (kg), and waist circumference (cm) by a single expert clinician who had previous anthropometric measurement experience. BMI (kg/m²) and waist-to-height ratio (WHR) were calculated from the measured data. The measurements were done with the presence of the same-sex attendant while maintaining utmost privacy. The research participants were on 12-h fasting. Venous blood was collected from the antecubital vein in a commercially available vacutainer. The blood sample was immediately transferred to the laboratory for tests – SUA, total cholesterol (TC), TG, LDL-C, VLDL-C, HDL-C, fasting blood sugar (FBS), and glycated hemoglobin (HbA1c).

Statistical analysis
All the data were first tested for normality by Shapiro–Wilk test. The data sets were found to be not normally distributed. Thus, we expressed the data in median and 1st quartile (Q1)–3rd quartile (Q3) and used non-parametric statistical tests.14 For comparing the variables between males and females, the Mann–Whitney U test was used. For correlation, Spearman correlation coefficients were calculated. For all the tests, \( P < 0.05 \) was considered to be statistically significant.

Results
A total of 104 (59.1%) male and 72 (40.9%) female T2DM patients participated in the study. The median age was 46 (Q1–Q3 = 40–55) years. Age and anthropometric data are shown in Table 1. Females had higher age than males. The height and weight were higher in males; however, BMI was higher in females. Although the waist circumference was not significantly different, the WHR was higher in females.

Blood tests parameters are shown in Table 2. The median serum creatinine level was 0.9 (Q1–Q3 = 0.8–1.1) and 0.8 (Q1–Q3 = 0.7–0.98) in males and females, respectively (\( P = 0.0002 \)). The mean SUA in overall sample was 6.75 (Q1–Q3 = 4.39–8) mg/dL, and males (6.75 [Q1–Q3 = 4.24–7.9]) and females (6.75 [Q1–Q3 = 4.5–8.19]) showed no gender difference (\( P = 0.42 \)). There was no gender difference in FBS (\( P = 0.57 \)) and HDL-C (\( P = 0.17 \)). Females showed higher TC (\( P < 0.0001 \)), TG (\( P = 0.002 \)), LDL-C (\( P = 0.0002 \)), and VLDL-C (\( P = 0.01 \)).

The Spearman correlation coefficient between SUA and other variables is shown in Table 3. The SUA showed significant positive correlation with TG (\( r_s = 0.65, P < 0.0001 \)), VLDL-C (\( r_s = 0.63, P < 0.0001 \)) and significant negative
Table 1: Age and anthropometric variables of the sample

| Variable                  | Overall (n=176) | Male (n=104) | Female (n=72) | P       |
|---------------------------|-----------------|--------------|---------------|---------|
| Age (years)               | 46 (40-55)      | 45 (37.25-54.5) | 48.5 (42.5-55) | 0.03*   |
| Height (cm)               | 158.5 (154-165.75) | 162.5 (160-169) | 152 (149-155.75) | <0.0001* |
| Weight (kg)               | 64 (56.25-70)   | 65 (59.25-75)   | 59 (55-65)    | <0.0001* |
| BMI (m/kg²)               | 25.62 (22.31-27.33) | 25.19 (22.03-27.03) | 26.58 (23.25-27.89) | 0.02* |
| Waist Circumference (cm)  | 95.5 (86-100)   | 95 (86-100)     | 96.5 (85-100) | 0.86    |
| Waist-to-height ratio     | 0.59 (0.54-0.64) | 0.58 (0.51-0.61) | 0.63 (0.57-0.67) | <0.0001* |

Table 2: Variables measured from the blood sample of the research participants

| Variable                         | Overall (n=176) | Male (n=104) | Female (n=72) | P        |
|----------------------------------|-----------------|--------------|---------------|---------|
| Fasting blood sugar (mg/dL)      | 166.67 (135-206.39) | 178.29 (135-200) | 163.64 (135-228.57) | 0.57    |
| Glycated hemoglobin (%)          | 8.4 (6.98-10.25)  | 8.6 (6.7-10.3)  | 8.35 (7.5-10.1) | 0.26    |
| Serum uric acid (mg/dL)          | 6.75 (4.39-8)    | 6.75 (4.24-7.91) | 6.75 (4.5-8.19) | 0.42    |
| Total Cholesterol (mg/dL)        | 150 (133.33-178.95) | 146.67 (125.33-162.5) | 171.43 (139.79-200) | <0.0001* |
| Triglyceride (mg/dL)             | 171.43 (133.33-228.57) | 144.16 (133.33-228.57) | 200 (147.37-272.73) | 0.002*  |
| Low-density lipoprotein-cholesterol (mg/dL) | 76.96 (58.12-101.91) | 71.35 (53.57-90.18) | 87.68 (68.07-116.55) | 0.0002* |
| Very-low-density lipoprotein-cholesterol (mg/dL) | 34.29 (26.67-45.71) | 28.83 (26.67-45.71) | 40 (28.14-54.89) | 0.01* |
| High-density lipoprotein-cholesterol (mg/dL) | 40 (33.93-43.75) | 40 (33.33-43.53) | 40.83 (36.16-48.44) | 0.17    |
| Serum creatinine (mg/dL)         | 0.9 (0.8-1)      | 0.9 (0.8-1.1)  | 0.8 (0.7-0.98) | 0.0002* |

Correlation with HDL-C (r = −0.35, P < 0.0001) and FBS (r = −0.45, P < 0.0001). Scatterplot with a trend line is shown in Figure 1a (SUA vs. FBS), 1b (SUA vs. TG), 1c (SUA vs. VLDL-C), and 1d (SUA vs. HDL-C).

Multiple regression was run to predict SUA from age, height, weight, BMI, WC, WHR, FBS, creatinine, HbA1c, TC, TG, LDL-C, VLDL-C, and HDL-C. All these variables statistically significantly predicted SUA, F (14, 161) = 12.254, P < 0.0001. R² = 0.516. Among the anthropometric variables, age, weight, BMI, WC, WHR, and FBS in blood variables added statistically significantly to the prediction, with P < 0.05.

**Discussion**

With an aim to find the correlation between the SUA and lipid profile in T2DM patients having serum creatinine within the normal range, we found that SUA has a positive correlation with TG and VLDL-C. In contrast, there was a negative correlation with HDL-C and FBS. This indicates that although there is no underlying kidney disease in the patients, higher levels of TG and VLDL-C indicate a higher SUA level. Additionally, a higher HDL-C indicates a possible lower level of SUA. Thus, SUA should be tested at an early date if a T2DM patient is suffering from dyslipidemia.

Obesity is an overall risk factor for T2DM patients, and hyperuricemia is associated with obesity. From multiple regression analysis, we found that the weight, surrogate marker for obesity - BMI, and central obesity parameters such as WC and WHR predict the level of SUA level. Obesity, dyslipidemia, and hyperuricemia contribute to the increased production of uric acid. This, in turn, increases purine catabolism and that increases the level of uric acid. Although age is a factor that may increase the SUA, it is beyond our control. However, obesity may be controlled with a proper diet plan and exercise program. A strict glucose control with diet and exercise would be beneficial to reduce kidney disease risk among the patients on oral hypoglycemic medications. The SUA is also found to be a risk factor for developing T2DM, hypertension, and impaired fasting glucose.

Sarmah et al[9] found that the Indian Assamese sample of the population has a positive correlation of SUA with TC, TG,
and LDL-C and a negative correlation with HDL-C.\(^{[16]}\) A study from Bangladesh by Ali et al.\(^{[17]}\) also supports the above study. In comparison, we found a positive correlation of SUA with TG and VLDL-C. A slight discordant finding may be attributed to the different levels of lipids that contribute to TC. Peng et al.\(^{[19]}\) from the USA also reported the positive association of dyslipidemia with SUA. Lippi et al.\(^{[20]}\) also reported similar results from Italy; however, they reported the association with plasma uric acid level and lipid profile. Thus, the measurement of SUA remains an important clinical entity along with lipid profile.

The underlying reason for higher SUA and lipids is as follows. Higher central obesity is linked with insulin resistance and leptin production. These two factors reduce uric acid excretion. Along with this, increased production of TG is associated with higher production of uric acid. An optimum level of plasma uric acid is a protective factor, but a higher than optimum level is considered a risk factor.\(^{[18]}\)

Primary care physicians treat the majority of T2DM patients.\(^{[21]}\) They are a major source of credible health information. A previous study showed that young and educated people adhere to regular follow-up for their diabetes treatment and rely on the information provided by their physicians.\(^{[22]}\) Thus, an additional SUA test may be suggested to patients with high lipids to early detect the future possibility of kidney disease. There is a difference in fasting and postprandial serum lipids and selectively there is higher postprandial hypertriglyceridemia. Thus, estimation of postprandial lipid status may also be suggested to get overall lipid derangements.\(^{[23]}\)

**Limitations**

This study has several limitations. This is a single-center study. We used a purposive sample from a hospital outpatient department. Although we calculated the minimum sample size and achieved an adequate sample for statistical analysis, a higher number would increase the power of the study. However, we had limited resources. The result of this study should be interpreted with caution as the sample size from a hospital from a particular state has limited generalizability.

**Conclusion**

In T2DM patients, with normal level of serum creatinine, SUA shows a positive correlation with TG and VLDL-C. Being a promoter of inflammation and indicator of future kidney damage, SUA should be monitored along with serum lipid profile in T2DM patients for timely management of complications.

Multiple regressions showed that age, weight, BMI, WC, WHR, and FBS are the variables that predict the level of SUA in T2DM patients having normal creatinine levels. Thus, along with sugar control, a lifestyle modification to reduce weight and central obesity should be stressed to reduce the risk of kidney disease in the future.

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**Conflicts of interest**

There are no conflicts of interest.

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**Table 3: Spearman correlation coefficient between serum uric acid and blood tests parameters**

| Statistical test parameter | Total cholesterol | Triglyceride | Low-density lipoprotein-cholesterol | Very-low-density lipoprotein-cholesterol | High-density lipoprotein-cholesterol | Serum creatinine | Fasting blood sugar | HbA1c |
|---------------------------|------------------|-------------|-------------------------------------|------------------------------------------|-------------------------------------|----------------|------------------|-------|
| r                         | 0.09             | 0.65        | -0.04                               | 0.63                                     | -0.35                               | 0.02           | -0.45            | -0.09 |
| 95% confidence interval   | -0.06-0.24       | 0.54-0.72   | -0.19-0.12                          | 0.52-0.71                                | -0.48-0.21                          | -0.13-0.17     | -0.56-0.31       | -0.24-0.06 |
| P (two-tailed)            | 0.24             | <0.0001*    | 0.64                                | <0.0001*                                 | <0.0001*                            | 0.82           | <0.0001*         | 0.23  |

*Statistically significant Spearman correlation coefficient (r, or ρ). Data were not normally distributed; hence, Spearman correlation coefficient was calculated.

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95% confidence interval = lower limit to upper limit
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