Section: Biochemistry

Original Research Article

# STUDY OF CORRELATION OF SERUM URIC ACID WITH THE PARAMETERS OF METABOLIC SYNDROME IN TYPE2 DIABETES MELLITUS

**S. Sindu Priya[1], S. Ramya[2], M. Mohamed Khalidh[3]**

[1]Associate Professor, Department of Biochemistry, Annapoorana Medical College and Hospitals, Salem, Tamil Nadu, India.
[2]Associate Professor, Department of Biochemistry, Annapoorana Medical College and Hospitals, Salem, Tamil Nadu, India.
[3]MBBS, Thenkasi, Tamil Nadu, India.

*Received* : 02/06/2023
*Received in revised form* : 15/07/2023
*Accepted* : 29/07/2023

*Keywords:*
*Hyperuricemia, diabetes mellitus, metabolic syndrome, cardiovascular disease, parameters.*

Corresponding Author:
**Dr. S. Ramya,**
Email: drramyasathish@gmail.com

DOI: 10.47009/jamp.2023.5.4.306

Source of Support: Nil,
Conflict of Interest: None declared

*Int J Acad Med Pharm*
2023; 5 (4); 1538-1542

## Abstract

**Background:** Elevated serum uric acid levels are a major risk factor for the development of cardiovascular disease in type 2 diabetic patients. Studies have proven the relationship between serum uric acid and the individual components of metabolic syndrome, which also precipitates the cardiovascular risk in diabetics. Hence it is important to monitor the serum uric acid level in type2 diabetics since it is a good predictor of CVD risk and its correlation with metabolic syndrome thereby reducing the death due to CVD in those patients. **Objectives:** 1. To estimate the serum uric acid levels in type 2 diabetic patients. 2. To establish the correlation between serum uric acid and the parameters of metabolic syndrome in those patients. **Materials and Methods:** This was an observational analytical study which included 100 known T2DM patients. Further these patients were categorized into two groups based on the presence of metabolic syndrome. Glucose, Uric acid, Total cholesterol, Triglyceride, High-density lipoprotein cholesterol (HDL) by the direct enzymatic method were measured and low-density lipoprotein cholesterol (LDL) was calculated by Friedewald's formula. **Results:** All analysis were performed with SPSS statistical package version 20. In our study, Serum uric acid levels were significantly higher in group II compared to group I. No significant correlation was found between uric acid levels and other parameters in group I. Serum uric acid levels have significant positive correlation with waist circumference, systolic blood pressure, fasting glucose and triglycerides and a significant negative correlation with HDL in group II. **Conclusion:** Hence, it is very important to monitor all T2DM patients for uric acid levels in order to prevent the complications related to hyperuricemia mainly metabolic syndrome and cardiovascular disease.

## INTRODUCTION

Diabetes mellitus has become the cardinal never-ending metabolic endocrine disorder in most of the countries. Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia that occurs due to defects in insulin secretion, insulin action, or both.[1] The prevalence of diabetes mellitus and cardiovascular disease as a complication of diabetes are increasing globally.[2]

Uric acid is the end product formed by the breakdown of purine nucleotides. High levels of serum uric acid are known as hyperuricemia. Hyperuricemia is probably associated with glucose intolerance and the most important mechanism is the association between insulin and renal resistance to the absorption of urates.[3] Diabetes mellitus patients with hyperuricemia, appear to be at an increased risk to develop diabetic complications, in particular the cardiovascular disease (CVD).[2]

Metabolic syndrome refers to a cluster of risk factors that accelerate the risk for the development of type 2 diabetes mellitus (T2DM) and cardiovascular diseases. This syndrome is distinguished by central obesity, glucose intolerance, hypertension and dyslipidemia.[4,5] Epidemiological studies have revealed the relationship between uric acid and metabolic syndrome[6] and also with the individual components of metabolic syndrome such as obesity, hypertension, dyslipidemia.[7]

Based on this background, the present study is designed to study the serum uric acid levels in type2 diabetic patients and to evaluate its correlation with the individual parameters of metabolic syndrome in those patients.


ISSN (O): 2687-5365; ISSN (P): 2753-6556

## MATERIALS AND METHODS

**Source of Data**

This is an observational analytical study which included 100 known T2DM patients admitted to or treated on outpatient basis in our medical college hospital. The study period was 2 months from 20.8.2021 to 20.10.2021. This study was conducted after getting ethical committee clearance. Informed written consent was obtained from all the participants selected for our study. All the patients were age and sex matched.

**Inclusion Criteria**

Known cases of type 2 diabetes mellitus patients in the age group of 40-70 years.

Further these patients were categorized into two groups based on the presence of metabolic syndrome.

**Exclusion Criteria**

Subjects with Gout, arthritis, cancerous conditions, cardiac failure, renal failure, thyroid disorders and on drugs that alter uric acid level in the blood will be excluded from the study.

Detailed medical history and clinical examination was done for all the study participants. Height, weight, systolic blood pressure (SBP) and diastolic blood pressure (DBP) were recorded and Body mass index (BMI) was calculated for all the study participants.

**Collection of Samples**

The study subjects are instructed not to take a protein-rich diet the previous day of blood collection. Fasting blood samples will be collected from the study groups after 8-12hrs of overnight fasting. 2ml of blood is collected in a fluoride tube for analyzing glucose and 3ml of blood collected in a plain tube and analysed for lipid profile and uric acid. Post-prandial blood is collected after 1 1/2 hrs in all the study subjects.

Glucose is analyzed by the glucose oxidase-peroxidase (GOD-POD) method, Uric acid is analyzed by the uricase method, Total cholesterol is analyzed using cholesterol-oxidase method, Triglyceride by glycerol phosphate oxidase-peroxidase (GPO-POD) method, High-density lipoprotein cholesterol (HDL) by the direct enzymatic method and low-density lipoprotein cholesterol (LDL) is calculated by Friedewald's formula. According to NCEP ATP III criteria, a case of metabolic syndrome is defined as having three or more of the following parameters.[8] The parameters of metabolic syndrome are 1) Waist circumference >90cm for men, >80cm for women (For Asians), 2) Serum Triglycerides >150mg/dl, 3) HDL Cholesterol <40mg/dl in men, <50mg/dl in women, 4) Fasting blood glucose >100mg/dl,5) Blood pressure >130/85 mmHg.

**Statistical Analysis:** All analysis were performed with SPSS statistical package version 20. Data was expressed as mean ± standard deviation (SD) for quantitative variables. Comparison between groups was done by student's t-test. P value <0.05 was considered statistically significant. Correlation was done by calculating Pearson's correlation coefficient.

## RESULTS

A total of 100 known type 2 diabetic patients were selected for this study. Further the study participants were grouped according to the existence of metabolic syndrome. There were 59 subjects without metabolic syndrome (group I) and 41 subjects with metabolic syndrome (group II).

A total of 100 known T2DM patients which includes 48 females and 52 males were selected for our study. [Table 1] shows that there were 28 males(53.84%) and 31 females(59.6%) in the T2DM without metabolic syndrome group and 24 males(46.15%) and 17 females(35.41%) in the T2DM with metabolic syndrome group.

[Table 2] shows the comparison of clinical parameters expressed as mean ± SD between the two groups. No significant difference was observed in the mean of age and BMI between the two groups. Statistically significant difference was observed in the mean of duration, WC, SBP and DBP between the two groups ($p< 0.05$).

[Table 3] shows that the mean of fasting glucose and postprandial glucose were increased in group II compared to group I. Statistically significant difference was found in the mean of fasting glucose and postprandial glucose between the two groups ($p<0.05$).

[Table 4] shows the mean of total cholesterol, triglyceride, HDL and LDL between the two groups. Statistically significant difference was found in the mean of total cholesterol, triglyceride and HDL between the two groups ($p<0.05$). Whereas the difference in the mean of LDL between two groups is not statistically significant.

[Table 5] shows the mean of serum uric acid between the two groups. Statistically significant difference was observed in the mean of uric acid between the two groups ($p<0.05$).

[Table 6] shows that uric acid has no statistically significant association with other parameters in group I.

[Table 7] shows that uric acid has no association with duration, BMI, DBP and LDL. Statistically significant positive correlation was observed between uric acid and SBP, fasting glucose, postprandial glucose, TC and TGL. In contrast, strong negative correlation was achieved between uric acid and HDL.

**Table 1: Gender Distribution Between the Two Groups.**

| Gender | Group I No (%) | Group II No (%) |
|---|---|---|
| Male | 28(53.84%) | 24(46.15%) |
| Female | 31(59.6%) | 17(35.41%) |


ISSN (O): 2687-5365; ISSN (P): 2753-6556

**Table 2: comparison of clinical parameters between the two groups**

| Parameters | Group I Mean ± SD | Group II Mean ± S D | P value |
|---|---|---|---|
| AGE (years) | 57.50 ± 5.49 | 56.53 ± 6.97 | 0.50 NS |
| DURATION (years) | 6.30 ± 2.67 | 8.07± 3.2 | 0.004* |
| BMI (kg/m$^2$) | 24.20 ± 2.21 | 24.70 ± 2.70 | 0.33 NS |
| WC (cm) | 82.36 ± 5.89 | 94.28 ± 6.31 | <0.0001 * |
| SBP (mmHg) | 123.86± 3.11 | 130.12 ± 6.07 | <0.0001 * |
| DBP (mmHg) | 83.77 ± 4.51 | 87.02 ±6.46 | 0.007* |

NS- Non-significant; P value < 0.05 Significant

**Table 3: comparison of fasting glucose and postprandial glucose between the two groups**

| Parameters | Group I Mean ± S D | Group II Mean ± S D | P value |
|---|---|---|---|
| Fasting glucose(mg/dl) | 131.05 ± 16.82 | 192.14± 33.05 | <0.0001 * |
| Postprandial glucose(mg/dl) | 168.44±19.64 | 204.60±34.86 | <0.0001 * |

NS- Non-significant; P value < 0.05 Significant

**Table 4: Comparison of Lipid Profile Between the Two Groups**

| Parameters | Group I Mean ± S D | Group II Mean ± S D | P value |
|---|---|---|---|
| Total cholesterol(mg/dl) | 199.07± 29.64 | 212.94± 21.93 | <0.001 * |
| Triglyceride(mg/dl) | 116.82 ± 12.38 | 208.62 ± 38.03 | <0.0001 * |
| HDL( mg/dl) | 51.73 ± 7.16 | 40.46 ± 6.1 | <0.0001 * |
| LDL(mg/dl) | 111.58 ± 27.85 | 126.72± 22.78 | 0.092 NS |

NS- Non-significant; P value < 0.05 Significant

**Table 5: comparison of uric acid between the two groups**

| Parameters | Group I Mean ± S D | Group II Mean ± S D | P value |
|---|---|---|---|
| Serum uric acid (mg/dl) | 6.58 ± 1.19 | 7.87± 0.94 | <0.0001 * |

NS- Non-significant; P value < 0.05 Significant

**Table 6: correlation coefficient of uric acid with other parameters in group I**

| Parameter | Correlation coefficient (r value) with significance |
|---|---|
| Duration | 0.054 |
| BMI | 0.017 |
| WC | 0.182 |
| SBP | 0.113 |
| DBP | 0.009 |
| Fasting glucose | 0.126 |
| Postprandial glucose | 0.123 |
| TC | 0.144 |
| TGL | 0.026 |
| HDL | -0.148 |
| LDL | 0.105 |

*p value < 0.05 (2 tailed)

**Table 7: correlation coefficient of uric acid with other parameters in group II**

| Parameter | Correlation coefficient (r value) with significance |
|---|---|
| Duration | 0.147 |
| BMI | 0.103 |
| WC | 0.412 * |
| SBP | 0.313 * |
| DBP | 0.177 |
| Fasting glucose | 0.325* |
| Postprandial glucose | 0.341* |
| TC | 0.274* |
| TGL | 0.307* |
| HDL | -0.248 * |
| LDL | 0.175 |

* p value < 0.05 (2 tailed)

## DISCUSSION

The present study included 100 known cases of type 2 diabetic patients in the age group of 40-70 years and further these patients were categorized into two groups based on the presence of metabolic syndrome. Group I with T2DM without metabolic syndrome (59 subjects) and T2DM with metabolic syndrome (41 subjects). The mean difference of all the studied parameters were significantly higher in group II compared to group I except for age, BMI and LDL. In group I, no significant correlation was found between uric acid and other parameters. In group II, statistically significant correlation was observed between uric acid and other studied parameters except for age, BMI, DBP and LDL.


ISSN (O): 2687-5365; ISSN (P): 2753-6556

Serum uric acid, a diprotic acid produced by xanthine oxidase from xanthine and hypoxanthine, which in turn are the products formed from purine.[34] Hyperuricemia is an increasingly common medical problem in both advanced and developing countries. Hyperuricemia is associated with metabolic syndrome components like obesity, dyslipidemia, hyperglycemia and hypertension.[9,10,11] In our study, serum uric acid levels were higher in group II with mean±S.D of 7.87±0.94 compared to group I with mean±S.D of 6.58±1.19, which is statistically significant.

Hyperinsulinemia in subjects with metabolic syndrome reduces renal excretion of serum uric acid which leads to hyperuricemia.[12] Insulin may increase the renal urate reabsorption through stimulation of the urate-anion exchanger URAT1[13] and/or the sodium dependent anion co-transporter in the renal proximal tubules brush border membranes.[14] Duman TT et al, has shown that increased uric acid was associated with poor diabetic control in type 2 diabetic patients.[15]

In our study also, statistically significant higher values were observed in the mean of fasting glucose, postprandial glucose, in group II compared to group I. A significant positive correlation was obtained in group II patients between uric acid and fasting glucose. In our study, no significant correlation was observed between uric acid concentration and duration of diabetes in group II. Hence, it is evident serum uric acid levels increases in poorly controlled diabetic patients and is not associated with duration of diabetes.

Obesity is found to be associated with serum uric acid levels via increased production pathways.[16] The underlying mechanism for development of metabolic syndrome is visceral obesity and it can be measured by waist circumference. Increased uric acid levels induce redox-dependent signaling and oxidative stress in adipocytes. Oxidative stress in the adipose tissue has been considered as a major cause of insulin resistance and cardiovascular disorder. Hence hyperuricemia-induced changes in oxidative homeostasis in the adipose tissue might play an significant role in these derangements.[17]

In our study, a significant positive correlation was observed between uric acid levels and waist circumference, whereas correlation was not observed between uric acid levels and BMI. This is in accordance with Ciarla et al study,[18] they found a positive correlation between uric acid levels and waist circumference. Further in their study, waist circumference correlated better with uric acid levels than that of BMI.

Mundhe SA et al,[19] study has shown that uric acid level has significant positive correlation with blood pressure. In our study, a significant positive correlation was found between uric acid level and systolic blood pressure, whereas no correlation observed between uric acid level and diastolic blood pressure.

In our study, Uric acid was found to be positively correlated with serum triglyceride and negatively correlated with HDL-cholesterol levels which are statistically significant. This is in accordance with Peng et al,[20] and many other studies. It has been discussed that hyperuricemia induces insulin resistance. The main underlying cause for the development of dyslipidemia in diabetic patients is insulin resistance.[21] Adipose tissue releases free fatty acids which is accelerated as a consequence of peripheral insulin resistance and are further entrapped by the liver, which in turn results in elevated synthesis of triglycerides by the hepatocytes.[22] Low HDL level is a strong risk factor for the development of cardiovascular disease and the cardioprotective role of HDL is due to its function in reverse cholesterol transport.[23]

Many studies have suggested hyperuricemia to be an additional component of the metabolic syndrome.[24,25,26] In our study also, serum uric acid is significantly associated with all the components of metabolic syndrome in group II except for diastolic blood pressure.

## CONCLUSION

In our study, Serum uric acid were significantly higher in group II compared to group I. No significant correlation was found between uric acid and other parameters in group I. Serum uric acid has significant positive correlation with waist circumference, systolic blood pressure, fasting glucose and triglycerides and a significant negative correlation with HDL in group II. Serum uric acid has no significant correlation with diastolic blood pressure in group II. Hence serum uric acid is increased in group II than group I and also associated with all the components of metabolic syndrome in group II except for diastolic blood pressure. Hence, it can be considered as the sixth component for diagnosing metabolic syndrome. So, it is important to monitor all T2DM patients for uric acid in order to prevent the complications related to hyperuricemia mainly metabolic syndrome and cardiovascular disease. Further studies in a larger sample size are needed to emphasize the association of uric acid with metabolic syndrome and cardiovascular disorder in T2DM.

**Acknowledgement**

We would like to express our sincere gratitude to our college management for logistic and technical support.

**Financial Support**

We would like to thank ICMR for providing the stipend for STS on completion of this study.

## REFERENCES

1. Dabla PK. Renal function in diabetic nephropathy. World Journal of Diabetes. May 15, 2010; 1(2): 48-56.
2. Zoppini G, Tanger G, Negri C, Perrone F. Elevated serum uric acid concentrations independently predict cardiovascular


ISSN (O): 2687-5365; ISSN (P): 2753-6556

mortality in type 2 diabetes. Diabetes care.2009;32:1716-1720.
3. American diabetes association. Diagnosis and classification of diabetes mellitus. Diabetic care.2012;35.(1),64-71.
4. Da Silva VN, Fiorelli LN, Da Silva CC, Kurokawa CS, Goldberg TB. Do metabolic syndrome and its components have an impact on bone mineral density in adolescents?Nutr Metab (Lond) 2017; 14:1.
5. Hidaka T, Hayakawa T, Kakamu T, Kumagai T, Hiruta Y, Hata J, Tsuji M, Fukushima T. Prevalence of metabolic syndrome and its components among Japanese workers by clustered business category. PLoS One 2016;11:e0153368.
6. X. Sui, T. S. Church, R. A. Meriwether, F. Lobelo, and S. N. Blair, "Uric acid and the development of metabolic syndrome in women and men," Metabolism: Clinical and Experimental, 2008;57(6):845–852.
7. L. Vavrova, J. Kodydkova, M. Zeman et al., "Altered activities of antioxidant enzymes in patients with metabolic syndrome," Obesity Facts, 2013;6(1):39–47.
8. Grundy SM, Cleeman J I, Stephen R. Daniels SR, Donato KA, Eckel R H, Franklin B A, Gordon D J, Krauss RM, Savage P J, Smith SC, Spertus J A, Costa F. Diagnosis and Management of the Metabolic Syndrome An American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement Executive Summary. Circulation. 2005;112: e285-e290.
9. Nakagawa T, Hu H, Zharikov S, Tuttle KR, Short RA, Glushakova O, et al. A causal role for uric acid in fructose-induced metabolic syndrome. Am. J. Physiol. Renal Physiol. 2006;290(3):625-31.
10. Conen D, Wietlisbach V, Bovet P, Shamlaye C, Riesen W, Paccaud F, et al. Prevalence of hyperuricemia and relation of serum uric acid with cardiovascular risk factors in a developing country. BMC Public Health. 2004;4(1):9.
11. Schachter M. Uric acid and hypertension. Curr Pharm Des. 2004;11(32):4139-43.
12. F Facchini, Y D Chen, C B Hollenbeck, G M Reaven. Relationship between resistance to insulin-mediated glucose uptake, urinary uric acid clearance, and plasma uric acid concentration. JAMA. 1991; 266(21): 3008-11.
13. Enomoto A, Kimura H, Chairoungdua A, Shigeta Y, Jutabha P, Cha SH, et al. Molecular identification of a renal urate anion exchanger that regulates blood urate levels. Nature. 2002; 417:447– 452.
14. Choi HK, Mount DB, Reginato AM. Pathogenesis of gout. Ann Intern Med. 2005;143: 499-516.
15. Duman TT, Kocak MZ, Atak BM, Erkus E. Serum uric acid is correlated with HbA1c levels in type 2 diabetes mellitus. Exp Biomed Res. 2018;1(1):6-9.
16. Hikita M, Ohno I, Mori Y, Ichida K, Yokose T, Hosoya T. Relationship between hyperuricemia and body fat distribution. Intern Med. 2007;46(17):1353-8.
17. Sautin YY, Nakagawa T, Zharikov S, Johnson RJ. Adverse effects of the classic antioxidant uric acid in adipocytes: NADPH oxidase-mediated oxidative/nitrosative stress. Am J Physiol Cell Physiol 2007;293:C584-96.
18. Ciarla S, Giorgini P, Struglia M, striuli r, Necozione S, Desideri G, Properzi G, Ferri C: Associations between low levels of serum uric acid and cardiometabolic parameters. Arch Physiol Biochem 2015; 121: 139-143.
19. Sanjay A. Mundhe, Dinkar R. Mhasde. The study of prevalence of hyperuricemia and metabolic syndrome in type 2 diabetes mellitus. Int J Adv Med. 2016 May;3(2):241-249.
20. Peng TC, Wang CC, Kao TW, Chan JY, Yang YH, Chang YW, et al. Relationship between hyperuricemia and lipid profiles in US adults. Biomed Res Int. 2015;2015(2015):127596.
21. Sheth J, Shah A, Sheth F, Trivedi S, Nabar N, Shah N, Thakor P, Vaidya R. The association of dyslipidemia and obesity with glycated hemoglobin. Clin Diabetes Endocrinol 2015;1:6.
22. Bays HE, Maki KC, McKenney J, Snipes R, Meadowcroft A, Schroyer R, Doyle RT, Stein E. Long-term up to 24-month efficacy and safety of concomitant prescription omega-3-acid ethyl esters and simvastatin in hypertriglyceridemic patients. Curr Med Res Opin 2010;26:907–915.
23. Mosaad A. Abou-Seif. Evaluation of some biochemical changes in diabetic patients. Clinica Chimica Acta. 2004;346:161–170.
24. Liou TL, Lin MW, Hsiao LC, Tsai TT, Chan WL, Ho LT, et al. Is hyperuricemia another facet of the metabolic syndrome? J Chin Med Assoc. 2006;69:104–9.
25. Sheu WH, Tseng YH. Uric acid: an additional component of metabolic syndrome? J Chin Med Assoc. 2006;69:99–100.
26. Nejatinamini S, Ataie-Jafari A, Qorbani M, Nikoohemat S, Kelishadi R, Asayesh H, Hosseini S. Association between serum uric acid level and metabolic syndrome components. J Diabetes Metab Disord. 2015 Sep 14;14:70.


ISSN (O): 2687-5365; ISSN (P): 2753-6556