Journal of Cardiovascular Disease Research

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 12, 2023

Original research article

TYPE 2 DIABETES MELLITUS AND SERUM URIC ACID AS AN INDICATOR OF CORONARY ARTERY DISEASE: A CROSS-SECTIONAL STUDY

[1]Dr. T. Sanath Kumar, [2]Dr. Jyotsna Ale

[1]Associate Professor, Department of General Medicine, GMC/GGH Jayashankar, Bhupalpally, Telangana, India

[2]Associate Professor, Department of Biochemistry, GMC, Mahabubabad, Telangana, India

Corresponding Author:

Dr. Jyotsna Ale

Abstract

Background and Objectives: One of the symptoms of Type-2 diabetes mellitus Syndrome X is hyperuricemia. However, the precise pathophysiology of coronary heart disease and uric acid is unknown. The study's objective was to determine whether higher serum uric acid concentrations in type 2 diabetic patients are indicative of coronary artery disease.

Material and Methods: This study was conducted at the Department of Biochemistry, GMC, Mahabubabad, Telangana, India between October 2022 to September 2023. The study comprised around 83 patients, with 7 being eliminated due to the presence of ischemia alterations exclusively in the ECG. The study had two groups of individuals, all of whom had diabetes. Another group consisted of patients who had clinical and electrocardiographic indications of prior myocardial infarction.

Results: Diabetic patients with coronary artery disease had notably elevated blood levels of inflammatory biomarkers and oxidative malondialdehyde. Conversely, they displayed considerably reduced levels of serum total antioxidant capacity compared to both the control group and diabetic patients without CAD. There were strong positive associations between levels of serum uric acid and levels of inflammatory biomarkers and malondialdehyde. Conversely, there was a significant negative link between SUA levels and total antioxidant capacity in the serum. SUA exhibited a proficient capacity to discern and differentiate.

Conclusions: Our results show that triglyceride levels are much higher in people with coronary heart disease compared to those without the condition. Additionally, hypertriglyceridemia has been linked to increased uric acid levels.

Keywords: Type 2 diabetes mellitus, serum uric acid, coronary artery disease

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 12, 2023

Introduction

Over the past few decades, Type 2 Diabetes Mellitus has become an epidemic in India. Diabetes mellitus is a significant risk factor that is strongly linked to a two to four time's higher occurrence of coronary heart disease. While small blood vessel disease is exclusive to diabetes mellitus, large vessel disease is highly prevalent in managed diabetes and is responsible for around 70% of all fatalities [1, 2].

Hyperuricemia is a constituent of Syndrome X in individuals with Type-2 diabetes mellitus. However, the precise involvement of uric acid in the pathophysiology of coronary heart disease remains unknown. Uric acid has been identified as a marker for atherosclerosis in individuals with type-2 diabetes mellitus. It has been found to be associated with the development of coronary heart disease, regardless of the presence of hypertension and nephropathy. The combination of risk factors in coronary disease contributes to the morbidity and mortality rates in patients with type-2 diabetes mellitus and coronary heart disease. Among these risk factors, diabetic dyslipidemia plays a significant role [3].

Uric acid (UA) is the final result of the metabolic process of purine nucleotides in humans. The homeostasis of uric acid (UA) levels in the body is upheld through an intricate interplay between its synthesis and excretion via the renal system and gastrointestinal tract. The kidneys play a crucial role in controlling the amounts of uric acid in the bloodstream. Around 66% of UA is eliminated through renal excretion, whereas the remaining 33% is excreted into the intestines. Uric acid (UA) is a powerful natural antioxidant [4]. However, elevated levels of UA, known as hyperuricemia, have been associated with oxidative stress, inflammation and damage to the inner lining of blood vessels (endothelial vascular damage). Elevated levels of uric acid (UA) are linked to several medical diseases including gout, chronic renal disease, hypertension, atherosclerosis, coronary artery disease (CAD), and heart failure. An increased concentration of uric acid in the blood (serum uric acid level) is associated with the onset of type 2 diabetes mellitus (T2DM) in individuals with diabetes. In the early phases of impaired glucose metabolism, there is a tendency for serum uric acid (SUA) levels to rise. Hyperuricemia is linked to both microvascular and macrovascular problems in individuals with diabetes [4-6].

The objective of the study was to determine the correlation between high levels of uric acid in the blood and the presence of coronary artery disease in patients with type 2 diabetes. The objective is to determine the correlation between uric acid levels and other risk factors of coronary artery disease in patients with type 2 diabetes.

Materials and Methods

The study comprised around 83 patients, with 7 being eliminated due to the presence of ischemia alterations exclusively in the ECG. This study was conducted at the Department of Biochemistry, GMC, Mahabubabad, Telangana, India between October 2022 to September 2023. The study had two groups of individuals, all of whom had diabetes. One cohort consisted of patients who had no clinical or electrocardiographic signs of coronary heart disease. They were designated as the control group. Another group consisted of patients who had clinical and electrocardiographic indications of

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 12, 2023

previous myocardial infarction.

Exclusion Criteria

The study excluded patients with any type of renal failure, whether it was acute or chronic. Patients with volume excess or volume depletion were excluded from the study due to the potential impact of these disorders on serum uric acid levels.

Biochemical Parameters

In order to detect early kidney damage caused by diabetic nephropathy, a urine spot protein/creatinine ratio test was performed on all patients. The main focus of our study was to analyze the blood uric acid level in relation to coronary artery disease and its related risk factors. Consequently, fundamental biochemical measurements such as blood urea and serum creatinine were conducted in all patients to exclude the presence of obvious renal failure.

Results

An analysis was conducted separately for males and females to examine the presence of hyperuricemia and coronary artery disease risk factors. The subgroups were compared with coronary artery disease patients who did not have evidence of coronary artery disease or its associated risk factors. The analysis was conducted utilizing the standard error of the difference between the means.

Table 1: Hyperuricemia and its clinical manifestations in men

Sr. No.	Medicinal indicators	Individuals who exhibit typical SUA	Hyperuricemic patients
1.	Age	58.4	60.2
2.	Obesity	8.1	26
3.	Smoking	55	40
4.	Alcohol	21	14
5.	Hypertension	18	22
6.	CAD	36	80

Patients with normal serum uric acid levels were less likely to have hypertension, coronary artery disease, and obesity, as shown in the preceding table. The levels of serum uric acid were unrelated to smoking and alcohol consumption. Although the findings in the male and female analyses were identical, there was a statistically significant increase in the incidence of coronary artery disease in patients with high uric acid levels. The female patients did not have any alcohol consumption. An increased uric acid level was more commonly associated with obesity and hypertension.

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 12, 2023

Table 2: Hyperuricemia and its clinical manifestations in women

Sr. No.	Medicinal indicators	Patient who do not have hyperuricemia	Patient suffering from hyperuricemia
1.	Age	45.5	51.3
2.	Obesity	01	20
3.	Hypertension	10	24
4.	CAD/CVA	10	80

The average age of the diabetics in the normal uric acid group is 45.5 years, whereas in the hyperuricemia group it is 51.3 years. Females had significantly higher levels of uric acid at an earlier stage of diabetes compared to males, as indicated by the statistically significant difference in the mean age between the sexes. Additionally, as the majority of the females were in the postmenopausal era, there was no discernible difference in the serum uric acid levels of the sexes. What follows is a comparison of the biochemical values between the two groups that reveals significant differences.

Table 3: Comparing biochemical profiles of hyperuricemic men

Sr. No.	Analyses of Biochemistry	Patients who do not have hyperuricemia	Patient suffering from hyperuricemia
1.	BS-F	128±59.3	160±41.8
2.	BS-PP	256.3±62.2	268.3±61.1
3.	TC	177.1±41.6	208.4±50.4
4.	TGL	128.1±40.6	178.7±76.8
5.	LDL	113.5±41.2	132.2±43.1
6.	HDL	36.8±3.8	36.4±5.7

The mean blood sugar levels were elevated in the hyperuricemia group compared to the normouricemic group. The hyperuricemic group had a substantial increase in total cholesterol, triglycerides, and low-density lipoprotein compared to the normouricemic group.

Table 4: The biochemical profile of hyperuricemic women

Sr. No.	Analyses of Biochemistry	Patients with Normal uric acid	Patients with Hyperuricemia
1.	BS-F	171.2±37.2	195.7±93.5
2.	BS-PP	280.8±75.2	284.3±82.7
3.	TC	181.3±33.0	202.8±56.1
	TGL	144.6±61.2	184.6±74.3
4.	LDL	113.1±31.3	131.2±44.5
5.	HDL	36.2±3.5	41.1±2.9

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 12, 2023

The results showed that all biochemical values were significantly different in the female group as well, with the exception of postprandial blood sugar, which did not differ significantly from the normouricemic group. All of these things point to the idea that uric acid levels are significantly higher in patients who have several risk factors. The intricate interplay between uric acid metabolism and the various risk factors is likely to blame for the elevated uric acid levels associated with these conditions.

Patient characteristics in the context of coronary artery disease

There was a positive correlation between age, smoking, and hypertension in both the normal ECG and elderly infarction groups when looking at risk variables. This was true for both males and females.

Table 5: Differential diagnosis of coronary artery disease in men

Sr. No.	Medicinal indicators	With CAD	Without CAD
1.	Age	61.2±3.4	55.7±10.4
2.	Obesity	22	25
3.	Smoking	76	59
4.	Alcohol	26	17
5.	Hypertension	34	13

The percentage of risk variables for both the CAD and non-CAD groups are shown in the table above. Both the CAD and no-CAD groups had a similar prevalence of diabetes (63.2 years old), smoking (76 percent) and alcoholism (26 percent) among men.

Table 6: Cardiovascular disease (CAD) clinical characteristics in women

Sr. No.	Medicinal indicators	With coronary artery disease	Without coronary artery disease
1.	Age	54.5±8.1	48.5±7.5
2.	Obesity	22	8
3.	Hypertension	35	26
4.	Smoking	8	1

The average age of diabetes in females was 54.5 years, compared to 48.5 years in the non-CAD group; 22.0% were obese; 35.0% had hypertension; and 8.0% smoked. These data are shown in Table 6.

Analysis of biochemical markers in patients with coronary artery disease

Overall, glycemic control was poor in both sexes, and there was a marked increase in total cholesterol, triglycerides and low-density lipoprotein cholesterol in both groups. There was no statistically significant correlation between age, BMI, or glycemic control and coronary artery disease in females either. Total cholesterol levels were found to be

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 12, 2023

correlated. While there was a statistically significant difference in triglycerides, HDL cholesterol, and low-density lipoprotein cholesterol between the two groups, there was no such difference in total cholesterol in the hyperuricemia group. Both the hyperuricemia and coronary artery disease groups had relatively high levels of high-density lipoproteins [7, 8].

No statistical link was found for age, sex, or body mass index when comparing hyperuricemia risk variables with coronary artery disease risk factors overall. Despite being statistically significant, glycemic control was subpar in both groups. Although there was no statistically significant total cholesterol, both groups did have hypertriglyceridemia. Overall, our study found that hyperuricemia is significantly associated with risk factors for coronary artery disease. The existence of coronary artery disease was associated with a considerable rise of uric acid. Taking everything into account, it appears that hyperuricemia is a marker for coronary artery disease and that its existence in type 2 diabetes is associated with an increased incidence of the condition [8].

Discussion

Data were presented in the current population-based study of type 2 diabetes in a manner that was specific to each gender and was stratified according to SUA quartiles. Based on the findings of the investigation, it was discovered that SUA levels had a positive correlation with BMI, BUN, Scr, and TG, while having a negative correlation with eGFR, HDL, and TG. FBG, 2h-PG, and HbA1c% were measured in either gender. In light of the fact that BUN, Scr, and eGFR are the measures that indicate the ability of glomeruli to clear waste, it is possible to draw the conclusion that the deterioration in kidney function in terms of UA clearance is the primary cause of the elevation of SUA levels in type 2 diabetes. With the exception of a limited number of studies, there is a lack of research on the significance of blood uric acid levels as a crucial indicator of type-2 diabetes mellitus, a dysmetabolic syndrome. The presence of hyperuricemia in patients with type-2 diabetes mellitus, in the absence of gout, is a significant marker and an additional risk factor for atherosclerosis [9].

While there is ongoing debate over the association between increased serum uric acid and its role as a risk factor, certain research have provided evidence supporting this relationship. There have been a limited number of studies that have examined the role of this marker in conjunction with other risk factors, including high levels of triglycerides. Elevated triglyceride levels have been found to be an important risk factor in the progression of atherosclerosis, as indicated by current research [10, 11]. Our study additionally shown a notable correlation between increased levels of uric acid in the blood and hypertriglyceridemia. A study conducted by Pearl A. *et al*. discovered that uric acid acts as a scavenger for free radicals. This was determined by examining the correlation between serum uric acid levels and the Molar Equivalent Serum Antioxidant (MESA) in both diabetic and non-diabetic persons. The study revealed a direct association between serum uric acid and MESA. The two groups exhibited notable disparities in both the average MESA values and the average uric acid readings [12-14].

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 12, 2023

A recent study conducted at the Lomo Medical Clinic, The Heart of Africa, Cardiovascular Center in Kinshasa, Congo by Longo-Mbenza B *et al*., found that high levels of uric acid in the blood (hyperuricemia) are a significant predictor of heart attacks, strokes, and overall mortality. The study suggests that uric acid stabilizes platelet aggregation and increases the risk of blood clot formation [15-17].

Tkac *et al*., conducted a study similar to our present investigation, with 91 individuals with type-2 diabetes. Among these participants, 57 had both clinical and ECG indications of previous myocardial infarction, while the other 34 diabetics in the control group showed no signs of coronary heart disease. The entire group with the Ml had markedly elevated average blood uric acid levels. Biserial regression analysis demonstrated the enduring statistical importance of the blood uric acid level, even after controlling for age and serum creatinine levels [18].

There is evidence that UA can cause damage to the microvascular system, which is a process that contributes to the development of DN. To be more specific, hyperuricemia causes a decrease in the generation of endogenous nitric oxide (NO) as well as the damage of endothelial cells, which in turn leads to an increase in oxidative stress and inflammation at the glomerulus. In addition, evidence from animal and human research demonstrated that UA-mediated RAS activation is a unique mechanism of UA-induced endothelial dysfunction. This dysfunction is closely associated with cardiovascular and renal disorders, such as atherosclerosis or DN [19, 20].

Our study focuses on hypertriglyceridemia as a significant risk factor for coronary heart disease. We have found that hypertriglyceridemia is independently associated with an increase in serum uric acid levels. This study adds to the existing knowledge on emerging risk factors for coronary heart disease, such as Hypertriglyceridemia, Lipoprotein (a), and small dense LDL. Diabetic dyslipidemia significantly contributes to the development of atherosclerosis in individuals with type-2 diabetes mellitus, both in the control group and the group with infarction. The following is a comparison between the serum lipids of Indians, our research population, and the American population [21-24].

Conclusion

The average serum uric acid level in the diabetic population in our study was similar to the normal range observed in the general population. There was no notable disparity in serum uric acid levels between diabetics without any indication of coronary heart disease and the overall population. Elevated serum uric acid in diabetics can serve as a marker for coronary heart disease in diabetics. Elevated uric acid levels may be a secondary phenomenon caused by the presence of other risk factors for coronary heart disease. Our investigation revealed a notable increase in Triglycerides levels in all the groups, with and without coronary heart disease. However, this increase was more pronounced in patients with coronary heart disease. Furthermore, it has been noted that increased levels of uric acid are linked to hypertriglyceridemia.

Funding: None.

Conflict of Interest: None.

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 12, 2023

References

1. Hu Y, Li Q, Min R, Deng Y, Xu Y, Gao L. The association between serum uric acid and diabetic complications in patients with type 2 diabetes mellitus by gender: a cross-sectional study. PeerJ. 2021 Jan 13;9:e10691.
2. Khairnar SJ, Rudrapal M, Ahire ED, Jagtap MR, Kshirsagar SJ. Role of Functional Foods in Cardiovascular Diseases. In Applications of Functional Foods in Disease Prevention Apple Academic Press, 2024 Jan, p. 119-138.
3. Yan P, Zhang Z, Wan Q, Zhu J, Li H, Gao C, Ma H, Xu Y. Association of serum uric acid with bone mineral density and clinical fractures in Chinese type 2 diabetes mellitus patients: a cross-sectional study. Clinica Chimica Acta. 2018 Nov 1;486:76-85.
4. Keservani RK, Sharma AK, Kesharwani RK. Nutraceutical and functional foods for cardiovascular health. InFood Process Engineering 2016 Dec 8 (pp. 291-312). Apple Academic Press.
5. Rao TM, Vanukuri NK. A study on serum uric acid levels in type 2 diabetes mellitus and its association with cardiovascular risk factors. IAIM. 2016 Dec 1;3(12):148-55.
6. Kesharwani RK, Keservani RK, Sharma AK, editors. Nutraceuticals and Functional Foods in Immunomodulators. Springer Nature; 2023.
7. Han M, Kim H, Kim HJ, Kang E, Kim YS, Choi KH, Kim SW, Ahn C, Oh KH. Serum uric acid is associated with coronary artery calcification in early chronic kidney disease: a cross-sectional study. BMC nephrology. 2021 Dec;22(1):1-6.
8. Ahire ED, Sonawane VN, Surana KR, Talele SG, Talele GS, Kshirsagar SJ, *et al*. Preventive Measures of Type 2 Diabetes via Nutrition. In The Metabolic Syndrome. Apple Academic Press, 2023, pp. 71-99.
9. Yan L, Li XM, Xin G. Cross-sectional association of serum C-reactive protein and uric acid with albuminuria in Chinese type 2 diabetic patients. Chinese Medical Journal. 2013 Nov 5;126(21):4023-9.
10. Li LX, Wang AP, Zhang R, Li TT, Wang JW, Bao YQ, Jia WP. Decreased urine uric acid excretion is an independent risk factor for chronic kidney disease but not for carotid atherosclerosis in hospital-based patients with type 2 diabetes: a cross-sectional study. Cardiovascular diabetology. 2015 Dec;14:1-9.
11. Pathan AS, Ahire MR, Diwane SA, Jain PG, Pandagale PM, Ahire ED. Functional Foods in Prevention of Diabetes Mellitus. In Applications of Functional Foods in Disease Prevention Apple Academic Press, 2024 Jan, pp. 139-164.
12. Keservani RK, Tung BT, Singh S, Kesharwani RK, editors. Nutraceuticals in Cancer Prevention, Management, and Treatment. CRC Press; 2023 Oct 20.
13. Pathan AS, Wagh PP, Jain PG, Sonawane GB, Ahire ED. Functional Foods in Health and Diseases. In Applications of Functional Foods in Disease Prevention. Apple Academic Press, 2024 Jan, pp. 103-117.
14. Ghorbani Z, Mirmohammadali SN, Shoaibinobarian N, Rosenkranz SK, Arami S, Hekmatdoost A, Mahdavi-Roshan M. Insulin resistance surrogate markers and risk of hyperuricemia among patients with and without coronary artery disease: a cross-sectional study. Frontiers in Nutrition. 2023;10.

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 12, 2023

15. Ali N, Miah R, Hasan M, Barman Z, Mou AD, Hafsa JM, Trisha AD, Hasan A, Islam F. Association between serum uric acid and metabolic syndrome: a cross-sectional study in Bangladeshi adults. Scientific reports. 2020 May 12;10(1):7841.
16. Kim H, Kim SH, Choi AR, Kim S, Choi HY, Kim HJ, Park HC. Asymptomatic hyperuricemia is independently associated with coronary artery calcification in the absence of overt coronary artery disease: a single-center cross-sectional study. Medicine. 2017 Apr;96(14).
17. Ito H, Abe M, Mifune M, Oshikiri K, Antoku S, Takeuchi Y, Togane M. Hyperuricemia is independently associated with coronary heart disease and renal dysfunction in patients with type 2 diabetes mellitus. PloS one. 2011 Nov 18;6(11):e27817.
18. Zhang J, Xiang G, Xiang L, Sun H. Serum uric acid is associated with arterial stiffness in men with newly diagnosed type 2 diabetes mellitus. Journal of endocrinological investigation. 2014 May;37:441-7.
19. Jankar JS, Harley KN, Jha RK. Correlation between serum uric acid with type 2 diabetes mellitus and its complications. Journal of Pharmaceutical Research International. 2021 Sep 6;33(43A):335-45.
20. Li Y, Xu C, Yu C, Xu L, Miao M. Association of serum uric acid level with non-alcoholic fatty liver disease: a cross-sectional study. Journal of hepatology. 2009 May 1;50(5):1029-34.
21. Ahmad MF, Keservani RK, Babu DJ. Interaction study between Ocimum sanctum and Glimepiride (sulfonylurea derivative) in diabetic rats. J. Chin. Pharm. Sci. 2015 Jan 8;24(3):156-63.
22. Gaita L, Timar R, Lupascu N, Roman D, Albai A, Potre O, Timar B. The impact of hyperuricemia on cardiometabolic risk factors in patients with diabetes mellitus: a cross-sectional study. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy. 2019 Oct 3:2003-10.
23. Huang R, Tian S, Han J, Lin H, Guo D, Wang J, An K, Wang S. U-shaped association between serum uric acid levels and cognitive functions in patients with type 2 diabetes: a cross-sectional study. Journal of Alzheimer's Disease. 2019 Jan 1;69(1):135-44.
24. Chuengsamarn S, Rattanamongkolgul S, Jirawatnotai S. Association between serum uric acid level and microalbuminuria to chronic vascular complications in Thai patients with type 2 diabetes. Journal of diabetes and its complications. 2014 Mar 1;28(2):124-9.
25. Chuengsamarn S, Rattanamongkolgul S, Jirawatnotai S. Association between serum uric acid level and microalbuminuria to chronic vascular complications in Thai patients with type 2 diabetes. Journal of diabetes and its complications. 2014 Mar 1;28(2):124-9.
26. Ren Y, Jin N, Hong T, Mu Y, Guo L, Ji Q, Li Q, Yang X, Ji L. Interactive effect of serum uric acid and total bilirubin for cardiovascular disease in Chinese patients with type 2 diabetes. Scientific reports. 2016 Nov 2;6(1):36437.