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Original Research Article

A STUDY OF URIC ACID LEVELS AS AN EARLY MARKER OF TYPE 2 DIABETES MELLITUS AND ITS CORRELATION OF THE SAME IN A PRE-DIABETIC STATE

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Abstract

Background: Type 2 diabetes mellitus (DM) is strongly associated with hyperuricaemia. Recent data suggest that uric acid clearance (UA) is reduced with increased insulin resistance and that UA is a marker of the prediabetes period. This study aimed to assess uric acid levels as an early marker of type 2 diabetes mellitus and its correlation of the same in a pre-diabetic state. **Material and Methods**: This descriptive study was conducted from January 2017 to April 2018 at the Department of General Medicine, Meenakshi Medical College Hospital and Research Institute, Kanchipuram, Tamil Nadu. Of the 100 patients, 50 age- and sex-matched healthy subjects were included in the control group (CR group) and the remaining 50 volunteers were included in the DM group. A detailed history of the participants, such as past medical history, surgical history, personal history, and family history, was collected through personal interviews. **Results**: Fasting, postprandial glucose, and serum uric acid levels were significantly higher in the DM group than in the CR group. Hyperuricaemia was also observed among the patients of both groups. Hyperuricaemia was reported in 13 (26%) patients in the DM group whereas it was absent in the CR group. The effect was statistically significant ($p<0.0001$) in both groups. In addition, the serum uric acid levels were found to be significantly ($p<0.001$) higher with a longer duration of diabetes than with a shorter duration of diabetes mellitus in the DM group. **Conclusion:** Our study found a positive correlation between serum uric acid level and type 2 diabetes mellitus.

INTRODUCTION

Diabetes mellitus is a metabolic disease characterised by hyperglycaemia, resulting from defects in insulin secretion, insulin action, and insulin resistance. Chronic hyperglycaemia in diabetes mellitus is associated with long-term damage, dysfunction, and failure of various vital organs, especially the eyes, kidneys, nervous system, and cardiovascular system.[1] Individuals with undiagnosed type 2 diabetes are also at significantly higher risk of stroke, and peripheral vascular disease than non-diabetes is more prevalent in individuals with a family history of diabetes and members of certain racial or ethnic groups, especially Indians.[2] Type 2 diabetes mellitus has been the most common type of diabetes in India over the past few decades. Diabetes Mellitus is the most important risk factor associated with a two to fourfold increased incidence of coronary artery disease.[2-3]

Diabetes also increases the likelihood of severe carotid atherosclerosis and an almost threefold increase in stroke-related mortality in patients with diabetes. Therefore, both type 1 and type 2 diabetes mellitus are powerful independent risk factors for

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coronary artery disease (CAD), stroke, and peripheral arterial disease.[3-4] Type 2 diabetes mellitus affects more than 150 million adults worldwide. India has more than 30 million diabetics, who are known to affect Indians at a much younger age. The prevalence of diabetes is increasing worldwide and is expected to affect approximately 300 million adults worldwide and 57 million adults in India by 2025.[5]

Coronary artery disease is a major cause of mortality, with many risk factors, such as hypercholesterolaemia, hypertension, diabetes mellitus, and cigarette smoking, of which diabetes mellitus is the most important. Hence, early detection of diabetes mellitus, even before it is exhibited, will help in the prevention of CAD.[4] Approximately 120 years have elapsed since uric acid was first described as a potential risk factor for the development of chronic disease. Hyperuricemia as a potential risk factor for Type 2 Diabetes mellitus has ballooned in the last several years with numerous abstracts, research papers, multiple editorials, and review articles.[6] The end product of purine ring degradation is uric acid, which is excreted in urine. Uric acid has limited solubility; if it were to accumulate, uric acid crystals would precipitate in body tissues at a reduced temperature (such as in the big toe). Acute painful inflammation of specific soft tissues and joints is called gout. People with higher uric acid levels were more likely to get Type 2 Diabetes mellitus.[7]

Hyperuricaemia is a component of syndrome X in Type-2 diabetes mellitus. However, the exact mechanism underlying the role of uric acid in coronary heart disease. Uric acid was recognized as an atherosclerosis marker in type-2 DM and was correlated with the presence of CHD independently of hypertension and nephropathy.[8-9] Much but not all epidemiological research identifies hyperuricemia as an independent risk factor for the development of cardiovascular disease and renal disease, particularly in patients with hypertension or congestive heart failure and in women.[10]

We aimed to study the level of serum uric acid in patients with type 2 diabetes mellitus and the correlation between elevated serum uric acid levels and the components of metabolic syndromes such as obesity, hypertension, and dyslipidaemia.

MATERIALS AND METHODS

This descriptive study was conducted with 100 patients from January 2017 to April 2018 in the Department of General Medicine, Meenakshi Medical College Hospital and Research Institute, Kanchipuram, Tamil Nadu. Written consent and institutional ethics committee approval were obtained before the start of the study.

Inclusion Criteria

Patients of both sexes had normal glucose levels and type 2 diabetes mellitus (patients were taken irrespective of their glycaemic control and duration of diabetes). and patients 30-70 years old were included in this study.

Exclusion Criteria

Patients with renal failure and pregnancy and lactating mothers; patients who were on long-term diuretics, steroids, anti-metabolites, and chemotherapy drugs; patients who regularly consumed alcohol had hepatic and metabolic disorders; and patients who had PVD/CVA/pulmonary tuberculosis were excluded.

Materials

In this study 4-Aminoantipyrine, p-Hydroxyl Benzoic Acid, Glucose Oxidase, Peroxidase, Glucose Standard, Uricase, Uric acid Standard, Latex, Glycine Buffer, Mouse anti-human HbA1c Monoclonal antibody, Goat anti-Mouse IgG Polyclonal antibody were required to perform the study.

Methodology

A total of 100 patients were enrolled in the study, and 50 age- and sex-matched healthy subjects were included in the control group. The remaining 50 volunteers were in the type-2 Diabetes mellitus (DM) group. In addition, a detailed history of the participants, such as past medical, surgical, personal, and family history, was collected through personal interviews.

Fasting and postprandial plasma glucose, serum uric acid, glucose tolerance, and glycated haemoglobin (HbA1c) levels were the biochemical parameters estimated in the study population. The blood samples of the respondents were collected after an overnight fast: 1 ml in sodium fluoride-coated sugar tubes, and 3 ml in plain tubes between 8 am and 9 am. In addition, 1 ml of postprandial blood sugar was collected 2 hours after breakfast. The blood drawn was allowed to coagulate, and the serum was separated by centrifugation and stored at -20°C until assayed. Blood sugar was determined by the GOD/POD method, uric acid was determined by the uricase method, and HbA1c was measured using the nephelometry method.

Statistical Analysis

The individual student t-test was performed to evaluate the significance of the difference in means between two groups, using the Statistical Package for Social Science (SPSS) statistical package, version 17. The data were also subjected to an independent samples test (unpaired) whenever necessary to evaluate the significance of the difference between the means of the control and study groups using SPSS software. Values are presented as mean ± SD, and a p-value <0.05 was considered significant.

RESULTS

The maximum number of patients was reported in the age group of 51–60 years in the DM group (42%) and 41–50 years in the CR group 22(44%).

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The mean age was reported to be 58.72 years and 57.93 years for Group DM and CR, respectively. Male predominance was reported in both groups. The fasting and postprandial glucose levels were significantly higher in the DM group than in the normal CR group. [Table 1]

Serum uric acid in the DM and CR groups varied from 3.4 to 6.8 and 2.8 to 5.5 mg/dl, respectively. The mean and standard deviation of uric acid in the DM group was 5.8 ± 0.83, whereas, in the control CR group, it was 4.15 ± 0.45, respectively. This effect was statistically significant ($p<0.0001$) among the groups. HbA1c was 9.8% in the DM group and 5.4% in the CR group. Glucose tolerance was positive and negative in the DM and control groups, respectively. [Table 1]

Hyperuricaemia was also observed among the patients of both groups in our study. Hyperuricaemia was reported in 13 (26%) patients in the DM group, whereas it was absent in CR group patients. [Table 2] The effect was statistically significant ($p<0.0001$) in both groups.

The serum uric acid levels were found to be significantly ($p<0.001$) higher in patients with a longer duration of diabetes than in those with a shorter duration of diabetes mellitus. [Table 3]

Table 1: Demographic variable of the patients of both groups

Particulars	DM Group (Type 2 Diabetes Mellitus Group)	CR Group Control Normal Group
Gender		
Male	32 (64%)	37 (74%)
Female	18 (36%)	13 (26%)
Age Group		
30-40	9 (18%)	5 (10%)
41-50	12 (24%)	22 (44%)
51-60	21 (42%)	16 (32%)
61-70	8 (16%)	7 (14%)
Mean age (years)	58.72	57.93
Fasting Blood Glucose (mg/dL)	110 -170	76 – 110
Postprandial Blood Glucose (mg/dL)	155-310	126-145
Serum Uric Acid (mg/dL)	3.4-6.8	2.8-5.5
HbA1c	9.8%	5.4%
Glucose Tolerance Test	Positive	Normal

Table 2: Observation of hyperuricemia among patients of both groups

Hyperuricemia	DM Group		CR Group	
	Number (%)	Mean ± S.D	Number (%)	Mean ± S.D
Presence	13 (26%)	6.2 ± 0.68	-	-
Absence	37 (74%)	5.53 ± 0.06	50 (100%%)	4.15 ± 0.45

Table 3: Observation of duration of diabetes mellitus for the uric acid level in both groups

Duration of diabetes mellitus (years)	Number of DM patients	Uric acid Mean ±SD
2-4	9	4.83±0.49
5-8	23	5.56±0.64
9-12	18	6.80±0.75

DISCUSSION

Diabetes mellitus is a group of disorders characterised by chronic hyperglycaemia associated with disturbances in carbohydrate, fat, and protein metabolism due to absolute or relative deficiency in insulin secretion or its action. Type 2 diabetes mellitus is a risk factor for cardiovascular disease, and it also presents in an average of 25% of adults and increases in prevalence with age and gender type.[1-3] Hyperuricaemia is a component of metabolic syndrome. "In the absence of gout, the presence of hyperuricemia in patients with type 2 diabetes mellitus is an important marker as well as an added risk factor for atherosclerosis".[8]

In the present study, we examined the relationship between serum uric acid levels and type 2 diabetes mellitus. Uric acid, the end product of purine metabolism, is a strong reducing agent and marker for coronary artery disease and other risk factors for type 2 diabetes mellitus.[7-9] Serum uric acid (SUA) levels in the diabetic group were significantly lower than those in the pre-diabetic group ($p<0.001$). These findings were consistent with those a of previous study, which demonstrated that people with diabetes have lower serum uric acid levels and that pre-diabetics have higher levels of uric acid than non-diabetics. The reduced urate level in severe hyperglycaemia has been attributed to the uricosuric effect of glycosuria, which may explain the low uric acid concentration among patients with diabetes. Furthermore, changes in plasma glucose and insulin concentrations might influence uric acid concentration. Thus, uric acid fluctuations during prediabetes and diabetes are regarded as secondary metabolic phenomena.[10-11]

In this study, we found an inverse relationship between diabetes mellitus and increased serum uric acid levels in men (3.98 mg/dl) and women (3.93 mg/dl); however, the relationship was stronger in men. We found that SUA concentration increased with increasing fasting plasma levels up to 140

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mg/dl but remarkably decreased when fasting plasma levels were over 140 mg/dl. An increasing trend in the SUA concentration at the 2h PG of 220 mg/dl and a decreasing trend thereafter was also observed, and an increasing trend up to HbA1c, 7%, and a decreasing trend thereafter. Nan et al. supported this observation.[12] Very few studies have evaluated the association between 2h postprandial glucose and UA since two-hour OGTTs have not been widely applied. In a study by Kodama et al., it was reported that SUA was strongly related to 2h postprandial glucose in diabetic men and women ($p<0.001$ for both).[8] In the current study, we have reported that the UA-2h postprandial glucose association seems stronger in men and women both. Nan et al. reported that SUA is inversely related to DM.[12]

Most of these studies were partial due to smaller sample sizes, including either women or men and not both, from selected populations such as industrial workers or not having data on confounding factors as opposed to general population samples. A reasonable mechanism for the observed inverse relationship between increased SUA levels and diabetes mellitus may be related to uric acid inhibition and reabsorption in the proximal tubule by high glucose levels in patients with diabetes. Epidemiologically and pathologically, it has been shown that decreased SUA concentration correlates with FBS, RBS and HbA1C, typically considered diagnostic criteria for type 2 diabetes. Therefore, it is promising to establish a positive association between the risk of type 2 diabetes and decreased SUA levels.[9-10]

Therefore, the results of this study strongly suggest that SUA level is an independent predictor of the development of type 2 diabetes. This study had some limitations. The participants' average age was 58.72 years at baseline; therefore, the role of uric acid in predicting type 2 diabetes among younger adults requires further study. Because of the lower number of new type 2 diabetes cases, this study had limited power to exclude the complete effectiveness of uric acid prediction in the IGT and normoglycaemia groups.

Although uric acid levels and age were independent, the duration of the illness may have an impact on uric acid levels. Our study also shows that a higher level of serum uric acid was seen in patients with longer duration of diabetes when compared with shorter duration of diabetes, 7.01±0.75 (9-12 years) vs 4.83±0.49 (2-4 years) this difference was statistically significant ($p<0.05$).[13]

Uric acid level >4 mg/dl should be considered a "Red flag" in patients at risk for cardiovascular disease. In this study, 78.57% of the diabetic patients had serum uric acid levels >4 mg/dl, while only 30% of the controls had serum uric acid levels >4 mg/dl. In these patients, clinicians should strive to utilise a global risk reduction program to reduce the complications of the atherogenic process.[9-11] Hyperuricaemia was observed in 13 (26%) of the 50 patients with type 2 diabetes mellitus. Rao and Vanukuri reported the prevalence of hyperuricaemia in 22% of patients with longstanding uncontrolled diabetes. However, in this study, many of the cases were on treatment which might have affected the results.[14]

CONCLUSION

Our study showed that uric acid levels are significantly elevated in patients with type 2 diabetes. The serum uric acid level was an independent risk factor for both age and sex. The serum uric acid level is a marker of the duration of diabetes mellitus. We conclude that uric acid levels > 4 mg/dl in the diabetic population are prognostic and diagnostic markers for type 2 diabetes mellitus.

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