Original Research Article

Study of serum uric acid levels in type 2 diabetes mellitus in tertiary care hospital in south Gujarat

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ABSTRACT

Background: The need for early indicators of diabetic complications is essential to prevent late complications and their deleterious effects. There is a need for sensitive serum markers that are associated with diabetes and its complications. Estimation of these parameters helps in early intervention, thereby delaying the chronic complications of diabetes in the early stages. Hyperuricemia has been shown to be linked to a number of diseases and conditions including gout, hypertension, cardiovascular disease, myocardial infarction, stroke and renal disease. Uric acid has long been associated with delayed complications of diabetes mellitus. This study was conducted on 357 patients of diabetes mellitus to investigate the significance of serum uric acid levels and its correlation with it.
Methods: This is an observational cross-sectional study carried out amongst 357 patients with T2DM attending out-patient department as well as indoor patients under medicine department at Surat Municipal Institute of Medical Education and Research (SMIMER) Hospital, of south Gujarat.
Results: There is highly significant association seen between HbA1c (glycated hemoglobin) and uric acid levels in present study (p<0.001). There is significant association seen between fasting blood sugar (FBS) levels and uric acid levels in the study (p=0.0253).
Conclusions: There is increase in uric acid levels in diabetic patients with increased levels of HbA1c. Thus, serum uric acid may serve as a potential biomarker of the deterioration of glucose metabolism.

Keywords: Serum uric acid, Diabetes mellitus, HBA1c

INTRODUCTION

Diabetes comprises disorders characterized by hyperglycemia. According to the current classification there are two major types: type 1 diabetes (T1DM) and type 2 diabetes (T2DM). The distinction between the two types has historically been based on age at onset, degree of loss of β cell function, degree of insulin resistance, presence of diabetes-associated autoantibodies, and requirement for insulin treatment for survival.[1] However, none of these characteristics unequivocally distinguishes one type of diabetes from the other, nor accounts for the entire spectrum of diabetes phenotypes.

At present, many studies have shown that the relevant pathological mechanisms showing correlation between serum uric acid levels and diabetes mellitus and its complication.

Inflammation

Increased uric acid levels in the blood promoted the expression of interleukin-1β (IL-1β), interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and CRP production, which activate the classical inflammatory pathway.[2-4]

Oxidative stress

Excessive uric acid will lead to an increase in reactive oxygen species (ROS) production, which leads to inflammation and dysfunction in the vessel.[5] UA is a powerful antioxidant that can remove superoxide and hydroxyl radicals in plasma, and UA has prooxidant effects in vascular tissue by increasing ROS production, such as H_2O_2.[5] UA-mediated oxidative stress-induced lipid peroxidation, DNA damage, and activation of inflammatory factors finally lead to cellular damage.[5] Oxidative stress also can affect the expression of insulin gene, causing a decrease in insulin secretion.[6]

Endothelial dysfunction

Endothelial dysfunction is characterized by deficiencies in the synthesis and/or bioavailability of endothelium-derived nitric oxide (NO).[7] In addition, UA reduces endothelial NO bioavailability in humans.8 Uric acid inhibits proliferation and migration of endothelial cells and NO secretion.[3] Uric Acid (UA) can react with NO to form 6-aminouracil, UA-dependent ROS reacts with NO to form peroxynitrite, and UA can hold back L-arginine uptake and stimulate L-arginine degradation.[9] As a result of the effects of hyperglycemia and neurohormonal activation, UA levels are independently associated with endothelial dysfunction in animals and humans, thereby promoting hypertension.[10]

Inhibiting insulin pathway

UA directly inhibits the trigger of insulin signalling pathway by an ectonucleotide pyrophosphatase/phosphodiesterase 1 (ENPP1) recruitment at the receptor level.11 All factors interference with glucose homeostasis and insulin sensitivity promotes the development of diabetes.[12-14]

This study is about estimation of serum uric acid levels in patients with type 2 diabetes mellitus (T2DM) and to find out correlation between serum uric acid & glycemic status in patients with T2DM.

METHODS

This is an observational cross-sectional study carried out amongst 357 patients with T2DM attending out-patient department and indoor patients under medicine department at Surat Municipal Institute of Medical Education and Research (SMIMER) Hospital, of south Gujarat, which was carried out after getting approval from Institutional Ethics Committee. Patients included are of age group between 30-70 years having T2DM, which is defined as fasting blood glucose (FBS) concentration ≥126 mg/dl and on oral hypoglycaemic medication or insulin for treatment. Patients with hypertension, coronary artery disease, cerebrovascular disease, renal disease, suffering from gout and taking any drugs that alters uric acid levels are excluded. 5 ml of plain venous blood sample after

overnight fasting was obtained by venepuncture. For post prandial blood sugar (PPBS), blood sample was collected 2 hours after the breakfast. For HbA1C estimation 2 ml of EDTA blood sample was collected. This was followed by centrifugation and then sample was processed immediately after collection. Serum uric acid estimated by uricase method. HBA1c is estimated by immunoturbidimetric method. FBS and PPBS by oxidase / peroxidase method. Data entry and statistical analysis was performed with the help of IBP Statistical package for social sciences (SPSS) version 22. In the present study, the statistical methods used for quantitative data were descriptive statistics presented by n, Mean, Standard Deviation and Range. For qualitative data, frequency count, n and percentage were put in tabular columns. To analyse the data, appropriate statistical tests were applied. To compare the difference between variances in the subjects, unpaired Student's t test and Chi square test were used.

RESLUTS

In the present study, the mean and standard deviation for age in the study subjects is 52.0 ± 8.46 years respectively. The age distribution is as shown in table 1 below.

Table 1: Age wise distribution.

Age (in years)	No of patients (n=357)
31-40	31 (8.68%)
41-50	140 (39.22%)
51-60	115 (32.22%)
>60	71 (19.88%)
Total	357 (100%)
Mean Age	52.0±8.46

Table 2: Distribution based on duration of DM.

Duration of DM (years)	No of patients(n=357)
<1	0 (0%)
1-5	132 (36.97%)
6-10	166 (46.50%)
>10	59 (16.53%)
Total	357 (100%)
Mean duration of DM (years)	7.44±4.52

In the present study, the number of male patients is 234 (65.55%) which is higher than number of females i.e., 123 (34.45%). The ratio of male:female is 1.90:1.

In the present study, majority of patients (n=166(46%)) have duration of diabetes between 6-10 years, the least duration of diabetes is 12 months while the maximum duration is 25 years. The mean duration of diabetes was 7.44±4.52 years. The distribution is displayed in table 2.

The following table 3 shows various biochemical parameters in this study.

Table 3: Distribution based on biochemical parameters.

Biochemical parameters	Mean±SD
Haemoglobin (Hb) (gm/dL)	11.08±1.68
Total count (cmm^3)	6758.76±1784.14
Platelet (cmm^3)	253604.48±106542.6
FBS (mg/dL)	169.44±42.68
PPBS (mg/dL)	246.75±67.44
Hb1Ac (%)	8.20±1.68
Uric acid (mg/dL)	5.98±1.30
S. creatinine (mg/dL)	0.94±0.13
S. bilirubin (mg/dL)	0.91±0.25
Total cholesterol (mg/dL)	198.11±44.94
High density lipoprotein (HDL) (mg/dL)	41.88±5.05
Low density lipoprotein (LDL) (mg/dL)	106.52±31.56
Alanine phosphatase (ALP) (IU/L)	21.14±7.85
Alanine transaminase (AST) (IU/L)	21.53±7.96

In the present study, it is found that number of patients with abnormal levels of uric acid levels are 133 (37.25%) (i.e. male 81 (22.68%) and female 52 (14.56%)), while normal levels of uric acid are found in 224 (62.75%) patients.

In the present study, there is significant association seen between HbA1c and uric acid levels. Also, significant association is seen between FBS levels and uric acid levels. High uric acid levels were seen more in subjects with raised FBS levels and similarly there is significant association between PPBS levels and UA levels. The distribution is as show in table 4 below.

DISCUSSION

The need for early indicators of diabetic complications is essential to prevent late complications and their detrimental / deleterious effects. There is a need for sensitive serum markers that are associated with diabetes and its complications. Estimation of these parameters helps in early intervention, thereby delaying / reverting the chronic complications of diabetes in the early stages.

Hyperuricemia has been shown to be linked to a number of diseases and conditions including gout, hypertension, cardiovascular disease, myocardial infarction, stroke and renal disease.

The mean age of the present study is correlated with others studies mentioned in table 5 below.

The male:female ratio of the present study is correlated with the other studies mentioned in table 6 below.

Table 5: Comparison between other studies and present study for age.

	Mean age (years)
Rao et al[15]	55.89 years
Talwar et al[16]	56.51±12.95 years
Shrishanth et al[17]	59.04±13.47 years
Sidhu et al[18]	54.6±10.05 years
Present study	52.0±8.46 years

Table 6: Comparison between other studies and present study for gender.

	Male : Female Ratio
Talwar et al[16]	1.17:1
Marwah et al[21]	1.18:1
Shrishanth et al[17]	1.35:1
Grover et al[19]	1.38:1
Datta et al[20]	2.08:1
Present study	1.90:1

Table 7: Comparison between other studies and present study for uric acid levels.

Authors	Prevalence of uric acid
Rao et al[15]	29.58%
Shrishanth et al[17]	36.6%
Datta et al[20]	35.3%
Marwah et al[21]	47.2%
Grover et al[19]	64%
Present study	37.25%

In the present study, the proportion of T2DM patients is almost unequal (approximately ranges from 20-45%) for different durations of T2DM since diagnosis (<5 years, 5-10 years, and >10 years). The mean duration of T2DM is 7.44±4.52 years compared to the study by Oshin et al, where the mean duration of diabetes was found to be 9.06±4.121 years i.e. maximum population was having diabetes of duration 5-10 years.[22]

In the present study, 106 (29.69%) patients were suffering from anaemia and 54 (15.12%) patients with dyslipidemia. However, mean Hb (11.08±1.68 gm/dL) and Lipid profile (Total Cholesterol-198.11±44.94 mg/dL; HDL 41.88±5.05 mg/dL; LDL 106.52±31.56 mg/dL) were found to be in normal range respectively. Moreover, blood sugar profile was also found higher from normal range such as FBS (169.44±42.68 mg/dL), PPBS (246.75±67.44 mg/dL) and HbA1C (8.20±1.68gm%). In similar study done by Barma et al, the mean FBS was 132.5±68.2 mg% and PPBS was 193.9±100.1 mg%, the mean HbA1c was 7.7±2.2%, total cholesterol was 188.5±25.8 mg%, triglyceride 146.0±32.2 mg%, low density lipoprotein (LDL) 106.5±25.5 mg%,

high density lipoprotein (HDL) 49.8±7.1 mg% and very low density lipoprotein (VLDL) 32.1±7.0 mg%.[23]

In addition, Oshin et al had observed the mean FBS was 196.12±4.12 mg/dL, mean PPBS was 303.26±115.38 mg/dL and HbA1c was 10.95±2.36%.[22] The mean total cholesterol was 155.55±51.37 mg/dL, mean HDL 41.05±6.98 mg/dL, mean LDL 84.50±24.21 mg/dL, and mean triglyceride was 131.46±62.300 mg/dL.

In this study, the percentage of patients with abnormal uric acid was 37.25% which was higher compared to Rao et al, Shrishanth et al and Datta et al while lower compared to other studies such as Marwah et al and Grover et al as shown in table 7 below.[15,17,19,20]

The increase in uric acid levels is not associated with age, gender, duration of DM and family history of DM in the present study (p>0.05) which is similar with other study by Datta et al.[20]

In present study, there is highly significant association seen between HbA1c and uric acid levels (p<0.001). There is significant association seen between FBS and uric acid levels (p=0.0253). High uric acid levels are seen more in subjects with raised FBS and similarly there is significant association between PPBS levels and uric acid levels (p=0.0209). Similarly, study done by Sidhu GK et al[18], Marwah et al, Talwar et al, and Shrishanth et al states that increased FBS, PPBS and HbA1C levels are statistically significant with raised uric acid levels in diabetic patients (p<0.01).[16,17,21]

The major limitation of the study is the cross-sectional nature of the data which may preclude the findings regarding the temporal nature of the relationship between SUA and diabetes. Therefore, even though there were some independent traditional confounders such as age, bodymass index, total cholesterol and triglycerides, but it was difficult to confirm the cause-effect relationship.

CONCLUSION

The present study is predominated by male gender and older adult age years. About one-third subjects with high serum uric acid levels were associated with diabetes mellitus. Our data is suggestive of positive correlation between altered blood glucose and serum uric acid levels and also between serum uric acid and HbA1c levels. There was an increase in uric acid levels in diabetic patients with increased levels of HbA1c. Thus, serum uric acid may serve as a potential biomarker of the deterioration of glucose metabolism.

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