Comparative Study of Level of Serum Uric Acid in Type 2 Diabetes Mellitus Associated with Hypertension

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ABSTRACT

Background: The role of uric acid in the progression of prediabetes to diabetes has been known. Serum uric acid has been shown to be associated with cardiovascular disease, hypertension, and chronic kidney disease. However, conflicting data exist as regards the serum uric acid (UA) levels in type 2 diabetes mellitus, which are associated with risk factors and complications.

Material & Methods: The present study was designed to look for any association of serum uric acid with hypertension in type 2 diabetes mellitus, taking into consideration the relevant clinical, biochemical and the anthropometric data. 110 patients with type 2 male diabetes mellitus as case and 100 healthy male controls were included in this study.

Results: This study shows that there were significant differences in mean of age, duration of DM, exercise time, waist hip ratio, systolic blood pressure and diastolic blood pressure within case and control but no significant differences of mean BMI was found between and control. The mean age, duration of DM, exercise time, waist hip ratio, systolic blood pressure and diastolic blood pressure and BMI were (51.83±9.911 years, 6.87±5.54 years, 1.94±.831 hours, .92±0.3, 140±6.75 mm of Hg, 90±2.41 mm of Hg and 25.43±3.19 Kg/m² respectively), where as in controls these were (44.81±9.66 yrs, 00 years, 1.12±.327 hours, .91±.03, 130±1.28 mm of Hg, 80±6.18 mm of Hg and 24.96±3.02 Kg/m² respectively). This table also shows that significant differences in mean of FBS, ABF, HbA1C and S. Uric acid between case and control, but there was no significant differences of mean TG, Cholesterol, HDL and LDL. The mean of FBS, ABF, HbA1C and S. Uric acid among the cases were (8.19±2.48 mmol/L, 11.29±3.47 mmol/L, 7.96±6.04 mg%, 189.72±111.36 mg/dl, 179±43 mg/dl, 38.38±13.77 mg/dl, 102.10±35.79 mg/dl and 8.39±2.61 mg/dl respectively, on the other hand among the control these were 5.91±1.13 mmol/L, 9.19±1.95 mmol/L, 5.93±1.01 mg%, 200±104.49 mg/dl, 183±42.25 mg/dl, 38.14±5.52 mg/dl, 110±33.23 mg/dl and 5.14±.84 mg/dl respectively.

Key Words: Type 2 D. M, Hypertension, and Uric Acid.

Introduction

Diabetes mellitus is a clinical syndrome which is characterized by persistent hyperglycaemia due to an absolute or a relative deficiency of insulin. It may be associated with a number of complications which include macro and micro vascular diseases. Uric acid (UA) is the end product of the purine metabolism. The association between the blood glucose and the serum uric acid levels has been known for quite some time.¹ A positive association between the serum uric acid levels and the development of type 2 diabetes mellitus (T2DM) has been reported.² In individuals with an impaired glucose tolerance, an elevated Serum Uric Acid (SUA) level was found to increase the risk for
developing T2-DM. Although uric acid can act as an antioxidant, excess serum accumulation is often associated with cardiovascular disease. It is not known whether this is causative (e.g., by acting as a prooxidant) or a protective reaction taking advantage of urate’s antioxidant properties. The same may account for the putative role of uric acid in the etiology of stroke. Uric acid can act as an oxidant and it may thus be a marker of oxidative stress, but it may also have a therapeutic role as an antioxidant. Urate, the soluble form of uric acid, can scavenge the superoxide and the hydroxyl radicals and it can chelate the transition metals. Hyperuricaemia has been also added to the set of metabolic abnormalities which are associated with insulin resistance and/or hyperinsulinaemia in the metabolic syndrome. While an increase in the uric acid levels in prediabetes and diabetes was demonstrated by some studies, a declining trend of the serum uric acid levels with increasing blood glucose levels was observed by other research workers. Hypouricaemia has also been implicated in the development of diabetic nephropathy. Although some studies have demonstrated the role of UA in the progression of prediabetes to diabetes, conflicting data exist about the uric acid levels in T2DM, which are associated with risk factors and complications. Thus, the role of UA in the pathogenesis and the development of the diabetic complications is controversial. Therefore, the present study was designed to look for any association of serum uric acid with hypertension in T2DM, taking into consideration the relevant clinical, biochemical and the anthropometric data.

Materials & Methods
A case control study was conducted on 110 patients with known type 2 male diabetics and on 100 healthy male control that were in the age group of 30-70 years at BIRDEM outpatient department from the period of 1st June 2015 to January 2016 and controls were collected from healthy working men of BIRDEM. All the data were collected in a prescribed proforma and they were compiled. The questionnaire contained questions regarding the duration of diabetes, the family history of diabetes, the dietary history and the history of hypertension, smoking, alcohol drinking, fast food habit etc.

Inclusion criteria: Individual having history of diabetes and taking treatment with either oral antidiabetic drugs or insulin were considered to have diabetes.

Exclusion criteria: Individual having history of gout and cardio-vascular or renal diseases and those who were on drugs (other than antidiabetics) that could alter the blood glucose levels were excluded from the study. The controls were non-diabetic.

The patients who gave a history of hypertension and were on antihypertensive treatment or whose blood pressure was more than or equal to 140/90 mm of Hg were considered to have hypertension. The height and the weight of cases and the controls were measured. The body mass index (BMI) was calculated. The waist/hip ratio (W/H ratio) was also calculated. All the patients were asked to fast overnight for a period of minimum 10 hours. The blood samples which were taken for analysis were obtained from the antecubital vein. The analysis of plasma glucose was done by the glucose oxidase method, while the serum uric acid, cholesterol and triglycerides were evaluated by enzymatic methods. These tests were performed on a Roche cobas c-311 biochemical analyser. The statistical analysis was done by the unpaired two-tailed ‘t’ test and the Pearson’s correlation coefficient by using online calculator. The data were presented as mean with SD. The statistical significance was kept as a P value of <0.05.

Results

Table 1: Distributions of study population according to age

| Age (years) | Case (Type-2DM) n=110 | Control (Healthy Individual) n=100 |
|-------------|------------------------|-----------------------------------|
| 30-40       | 16                     | 40                                |
| 41-50       | 39                     | 33                                |
| 51-60       | 36                     | 21                                |
| 61-70       | 19                     | 6                                 |
| Total       | 110                    | 100                               |
Table 1 shows the distributions of study population according to age and it indicates that 41-50 years study subjects more in Type-2 DM (39) whereas in control 30 -40 years study subjects are more (40).

**Table 2: Different range of uric acid levels and their distributions in study subjects**

| Uric acid (mg/dl) | Case (Type-2DM) n=110 | Control (Healthy Individual) n= 100 |
|-------------------|------------------------|-------------------------------------|
| 3.5-6.4           | 28                     | 94                                  |
| 6.5-9.4           | 48                     | 6                                   |
| 9.5-12.4          | 26                     | 0                                   |
| ≥ 12.5            | 8                      | 0                                   |
| Total             | 110                    | 100                                 |

Table 2 shows the different range of uric acid levels and their distributions in study subjects. It shows that uric acid level ranges from 6.5-9.4 mg/dl distribution more in cases (type -2 male DM) and it was 48 study subjects whereas in control it was 6 study subjects and in control more study subjects uric acid ranges from 3.5-6.4 mg/dl and it was 94 study subjects.

**Table 3: Comparison of different characteristics and biochemical parameters of study subjects**

| Variables                  | Case (Type-2 DM) | Control (Healthy Individual) | P value |
|----------------------------|------------------|------------------------------|---------|
| Age (years)                | 51.83 ±9.911     | 44.81 ±9.66                  | .000    |
| Duration of diabetes (years) | 6.87 ±5.54   | 00                           | .000    |
| Body mass index (kg/m2)    | 25.43 ±3.19      | 24.96 ±3.02                  | .274    |
| Exercise time (hours)      | 1.94 ± .831      | 1.12 ± .327                  | .000    |
| Waist (cm)                 | 94 ±7.06         | 90.95 ±9.51                  | .000    |
| Hip (cm)                   | 102 ±6.19        | 98.48 ±8.24                  | .000    |
| Waist: Hip                 | .92 ±.03         | .91 ±.03                     | .035    |
| Systolic BP (mm of Hg)     | 140 ± 6.75       | 130 ±14.28                   | .002    |
| Diastolic BP (mm of Hg)    | 90 ±2.41         | 80 ±6.18                     | .000    |
| Fasting blood sugar (mmol/l) | 8.19 ±2.48    | 5.91 ±1.13                   | .025    |
| After break fast (ABF) (mmol/l) | 11.29 ±3.47 | 9.19 ±1.95                   | .033    |
| HBA1C (mg%)                | 7.96 ±6.04       | 5.93 ±1.01                   | .026    |
| TG (mg/dl)                 | 189.72 ±111.36   | 200 ±104.49                  | .468    |
| Cholesterol (mg/dl)        | 179 ±.43         | 183 ±42.25                   | .495    |
| HDL-C (mg/dl)              | 38.38 ±13.77     | 38.14 ±5.52                  | .870    |
| LDL-C (mg/dl)              | 102.10 ±35.79    | 110 ±33.23                   | .088    |
| Uric acid (mg/dl)          | 8.39 ±2.61       | 5.14 ± .84                   | .000    |

Table 3 shows Comparison of different characteristics and biochemical parameters of study subjects. It shows that there were significant differences in mean of age, duration of DM, exercise time, waist hip ratio, systolic blood pressure and diastolic blood pressure within case and control but no significant differences of mean BMI was found between and control. The mean age, duration of DM, exercise time, waist hip ratio, systolic blood pressure and diastolic blood pressure and BMI were (51.83±9.911 years, 6.87±5.54 years, 1.94±.831 hours, .92±.03, 140±6.75 mm of Hg, 90±2.41 mm of Hg and 25.43±3.19 Kg/m² respectively), where as in controls these were (44.81±9.66 yrs, 00 years, 1.12±.327 hours, .91±.03, 130±1.28 mm of Hg, 80±6.18 mm of Hg and 24.96±3.02 Kg/m² respectively). This table also shows that significant differences in mean of FBS, ABF, HbA1C and S. Uric acid between case and control, but there was no significant differences of mean TG, Cholesterol, HDL and LDL. The mean of FBS, ABF, HbA1C and S. Uric acid among the cases were (8.19±2.48 mmol/L, 11.29±3.47 mmol/L, 7.96±6.04 mg%, 189.72±111.36 mg/dl, 179±43 mg/dl, 38.38±13.77 mg/dl, 102.10±35.79 mg/dl and 8.39±2.61 mg/dl respectively, on the other hand among the control these were 5.91±1.13 mmol/L, 9.19±1.95 mmol/L, 5.93±1.01mg%, 200±104.49 mg/dl, 183±42.25 mg/dl, 38.14±5.52 mg/dl, 110±33.23 mg/dl and 5.14±.84 mg/dl respectively.

**Table 4: serum uric acid level associated with hypertension in T2 DM as Mean±SD**

| Variable                  | Case (Type-2 DM) | Case (Type-2 DM) | NonHypertensive Case | P value |
|----------------------------|------------------|------------------|----------------------|---------|
| Uric acid (mg/dl)          | 7±1.61           | 5±.25            | 5±1.4                | .002    |

(Significant p value < .001)

Table 4 shows that mean serum uric acid level in type-2DM hypertensive study subjects is significantly increased than non-hypertensive type-2DM and it was 7±1.61mg/dl and 5±.25 mg/dl respectively.
Table 5: Correlations of serum uric acid level associated with duration of DM and BP

| Uric acid | Systolic BP | Diastolic BP |
|-----------|-------------|--------------|
| r = .416** | r = .56   | r = .141    |
| p = .000   | p = .418   | p = .041    |

Table 4 shows the correlations of Serum uric acid with Blood pressure and duration of DM. It shows that serum uric acid is significantly correlated with duration of DM. It also shows that serum uric acid is positively correlated with diastolic blood pressure where $r = .141$ and significance level was .041 but in systolic BP it was not significantly correlated.

Discussion

Uric acid is the final product of the purine metabolism in humans. The 2 final reactions in its production which catalyze the conversion of hypoxanthine to xanthine and the latter to uric acid are catalyzed by the enzyme xanthine oxidoreductase, which may attain 2 inter-convertible forms, namely xanthine dehydrogenase or xanthine oxidase. The latter uses molecular oxygen as an electron acceptor and it generates a superoxide anion and other Reactive Oxygen Species (ROS), thus favoring an antioxidant - prooxidant urate redox shuttle. Uric acid is also a physiological free radical scavenger and one of the major contributors of the plasma antioxidant capacity. Thus, UA plays a dual role, both as a prooxidant and as an antioxidant. T2DM is associated with oxidative stress and increased free radical formation. While on one hand, hyperglycaemia generates free radicals, on the other hand, it also impairs the endogenous antioxidant defense system. Under the condition of increased oxidative stress, there occurs the depletion of the local antioxidants, which causes a reduction in the antioxidant status of the body. Studies have reported the association of hypouricaemia with T2DM. A positive relationship has been described between glycosuria and uricosuria. Further, a higher degree of hyperuricaemia was observed to be associated with an increased rate of uric acid excretion and lowering of the plasma uric acid levels. Hypouricaemia and risk factor for type 2 diabetes mellitus. Diabetes Care the tubular transport of uric acid have been thoroughly reviewed. An increased urate clearance due to increased glomerular hyperfiltration which is a result of an abnormality in the tubular urate handling has been reported. The Serum uric acid levels were found to be higher in males than in females. We reported a similar finding in our study. The findings of the BMI, age, duration of DM and the waist hip ratio in the diabetic males in our study were in accordance with the findings of others. Our study reported a significant difference in mean of diastolic and systolic blood pressure in type-2DM and healthy individual and it was $(90 \pm 8.41, 80 \pm 6.18)$ mm of Hg and $(140 \pm 16.75, 130 \pm 11.28)$ mm of Hg respectively and p value was .000 and .002 which were in agreement with the findings of other studies. While the incidence of hypercholesterolaemia and hypertension and a family history of diabetes were more in the female diabetics, the incidences of hypertriglyceridaemia, smoking, and alcohol drinking were more in the male diabetic patients. These findings were in corroboration with those of other studies. According to study by Johnson and colleagues, they have reported a positive association of hyperuricaemia with hypertension in T2DM with complications. In contrast, a statistically significant decrease in the serum uric acid levels in the hypertensive diabetics (both males and females) in comparison with the non-hypertensive diabetics, was observed in our study. As a increase in the serum uric acid levels was seen with high plasma glucose levels in diabetes which was complicated with hypertension, as was observed in our study, may be of pathogenic significance. Several factors are known to alter the serum uric acid levels in T2DM.

Conclusion

Hyperglycemia with long term duration of type 2 diabetes mellitus is a major risk factor for macro and micro vascular complications which causes retinopathy, neuropathy and cardiovascular disease. Many factors like family history of diabetes, lifestyle, obesity, hypertension and mixed diet are contributing in type 2 diabetic patients. In present study the serum uric acid and blood pressure were measured and evaluated and there is a significant
difference in mean uric acid level in type 2 DM hypertensive and significant correlation of uric acid level with diastolic blood pressure was found.

**Conflict of interest:** no.

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