Plasma Level of Urate among Sudanese with Type 2 Diabetes in Khartoum state, Sudan. Salma H.Elhassan, Bader Eldien H. Elabid and Sara O. Yousif

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ABSTRACT

Background: *Type 2 diabetes mellitus is an independent risk factor for cardiovascular disease and the risk for cardiovascular disease is increased three to four fold in type 2 diabetes mellitus as compared to non-diabetic population. Hyperuricaemia has been reported to be a potential risk factor for cardiovascular disease in type 2 diabetes mellitus. The objective of this study was to assess the plasma level of urate in Sudanese patients with type 2 diabetes in comparison with apparently healthy (non-diabetic) volunteers as controls.*

Methods: *This is a descriptive, cross- sectional and hospital-based study conducted during the period from March to May 2011 in Jabir Abu Elez diabetic center and Nurein medical center, both in Khartoum state, Sudan. The study group included 52 NIDDM cases and 30 healthy controls of either sex matched for age and gender. Fasting venous samples were collected from both cases and controls. Serum levels of uric acid, and lipid profile were assayed using commercial reagent kits from Biosystem Company.*

Results: *In the current study there was a significant increase in plasma urate in type 2 diabetic patients as compared to the control group. There was a significant increase in lipid profile with exception to high density lipoprotein which was significantly reduced. There was insignificant correlation of plasma urea, and lipid profile with both; body mass index and the duration of diabetes.*

Conclusion: *Hyperuricemia is significantly associated with type 2 diabetes mellitus and can increase the morbidity and mortality of diabetes if not managed in time. Elevated plasma urate levels are associated with increased risk of cardiovascular mortality in type 2 diabetes.*

Key words: Type 2 diabetes mellitus, Plasma urate, and cardiovascular disease.

Introduction

Diabetes mellitus is a clinical syndrome characterized by hyperglycemia due to absolute or relative deficiency of insulin.[1, 2] It may be associated with a number of complications including nephropathy, neuropathy, retinopathy, diabetic foot and macro and micro vascular diseases. [3]

Type 2 diabetes is characterized by a group of abnormalities: hyperinsulinemia, dyslipidemia, obesity and vascular abnormalities. These groups of abnormalities are associated with increased risk for cardiovascular disorder. The cardiovascular risk is increased three to four fold in patients with type2 diabetes as compared to non-diabetic population.[4]

Uric acid is the final oxidation product of purine catabolism, Excess serum accumulation can lead to various diseases, and most notably uric acid is involved in the pathogenesis of gouty arthritis. [5, 6] Also, for more than 50 years, increased serum concentrations of uric acid have been implicated in cardiovascular disease[5,6] .Hyperuricemia has been found to be associated with obesity and insulin resistance, and consequently with type 2 diabetes. [7, 8]

The actual mechanism of hyperuricemia found in patients with type 2 diabetes mellitus is not known but it has been observed that compensatory hyper-insulinemia in insulin resistant individuals impose an antiuricosuric effect on the kidney. [1, 9, 1o]

Recently, elevation of serum uric acid has been found to be associated with subsequent morbidity and mortality in the general population among patients with congestive heart failure, diabetes and hypertensive patients[1, 11] .It has been proposed that the serum uric acid levels are linked to the other risk factors, such as dyslipidaemia and diabetes.[1, 12]

Materials and Methods

The study included 52 type2 diabetes cases in the age group of 40-55 years of either sex with no complications who visited Jabir Abu Elez diabetic center and Nurein medical center, both in Khartoum state, Sudan.

Thirty apperantly healthy subjects (non-diabetic) matched for age and sex were recruited as controls for the study. Patients with type 1 diabetes mellitus, gout, hypertension, renal impairment, familial hyperlipidaemia, and coronary heart disease had been excluded from this study. After consent was given, venous blood samples were collected after 12 hours overnight fasting. The samples were then centrifuged at 3000rpm for 5 minutes and the supernatant was separated.

Plasma urate, total cholesterol, triglyceride, and high density lipoprotein (HDL), were assayed using enzymatic endpoint kits from Biosystem Company(**E**nzymatic- spectrophotometric uricase / peroxidase method for plasma urate). The LDL concentration was calculated using Friedwald formula. Body Mass Index (BMI) was taken into consideration from both cases and controls. Body mass index was calculated from the formula

BMI= weight in kilograms/ square of height in meters.

Patients where considered as obese if there body mass index was $\geq$ 30 kg/m^2.

Results

The average age of the study group was 51.35± 11.3yrs in cases and 49.63± 10.05 yrs in controls. BMI (kg/m2) was significantly elevated in cases as compared to controls (Table 1).mean plasma urate in diabetic patients was 6.294±1.8 and in control was 4.6±1.1, it is significantly raised in diabetics (Table 2). Mean plasma T.cholesterol, triglyceride, and LDL were significantly increased in diabetics as compared to controls (Table 2). HDL was significantly decreased in cases as compared to controls. There were insignificant weak positive correlations between the duration of diabetes, the BMI and the plasma levels of urate (Figure 1, 2).

Table 1: Comparison of anthropometric variables between cases andControls

Parameters	Control	Cases	P-value
Age in years	49.63± 8.31	51.35± 11.3	0.47
BMI (kg/m2)	23.42±4.01	27.68±6.3	0.002

Results are expressed as Mean±SD.

Table 2: Comparison of biochemical parameters between cases and controls

Parameters	Control	Cases	P-value
Plasma Urate (mg/dl)	4.607±1.1	6.294±1.8	0.000
T. Chol (mg/dl)	171.90±35.62	189.90±40.33	0.039
TGL (mg/dl)	100.19±42.23	146.40±52.32	0.000
HDL (mg/dl)	66.33±20.94	26.79±12.47	0.000
LDL (mg/dl)	92.78±34.05	122.38±35.20	0.000

Results are expressed as Mean±SD.

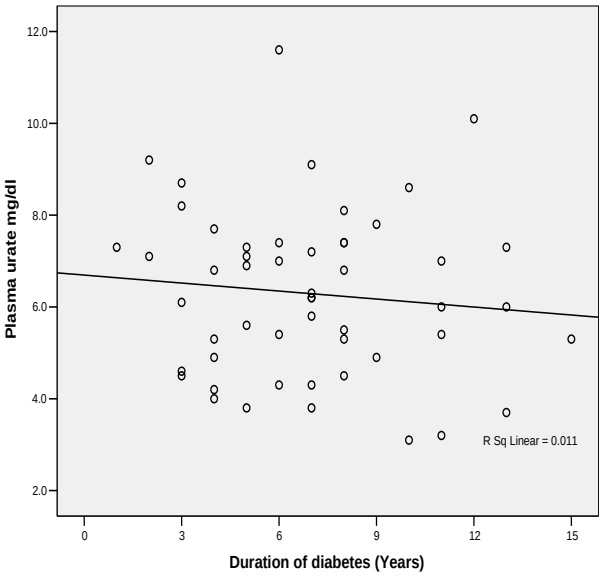

Figure (1):

A scatter plot shows the relationship between the duration of diabetes and the plasma levels of urate (r = 0.10) , (p= 0.46).

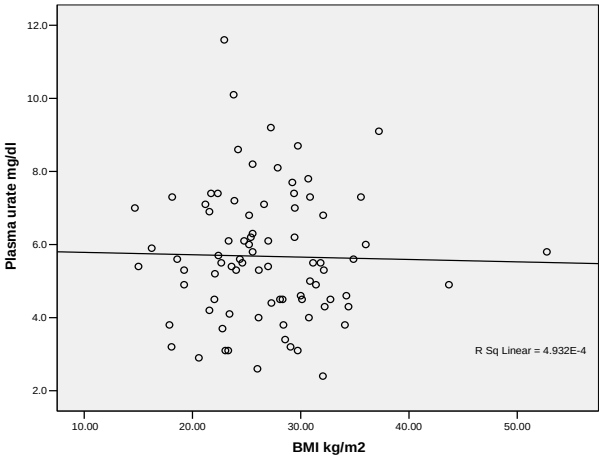

Figure (2):
A scatter plot shows the relationship between the body mass index and the plasma levels of urate (r = 0.02), (p = 0.58).

Discussion

Type 2 diabetes is a heterogeneous syndrome characterized by insulin resistance and / or defective insulin secretion. Glucotoxicity places an additional burden of redox stress on the capillary endothelium and arterial vessel wall. Hyperglycemia induces oxidative stress by reactive oxygen species (ROS) oxidation and reductive stress through pseudohypoxia with the accumulation of NADH and NADPH in the vascular intima. [13,14]Oxidative redox stress results in impaired endothelium dependent vasodilatation with quenching of endothelial nitric oxide (NO). Reduced level of NO has a central role in the induction of insulin resistance as insulin requires NO for its action. In the present study there was a significant elevated mean of plasma urate in type 2 diabetics as compared to controls (Table 2). Hyperuricaemia is found to be associated with impaired glucose tolerance, insulin resistance syndrome and hyperinsulinemia as in type 2 diabetes[4]. In the present study there was a significant increase in BMI in diabetes as compared to controls. Zang et al. have reported a positive correlation between BMI and cardiovascular disease.[15] High BMI itself is a potential risk factor for type 2 diabetes. In the present study the mean of plasma urate levels was found to be significantly increased in patients with type 2 diabetes when compared with the control group. These results agree with that obtained in a study done by Safi etal[1], who found the average level of serum uric acid in the diabetic patients was 6.07 mg/dl as compared to 5.01 mg/dl in the control group. It was seen that serum uric acid is positively associated with type 2 diabetes mellitus and the association was relatively more significant in females, obese patients and patients with hyperlipidemia. Also these results were comparable in most aspects to similar studies performed by different research workers [16,17,18,19]

Pathologically and epidemiologically, it has been indicated that elevated plasma urate concentration is correlated with lifestyle factors and various metabolic profiles specially high values of BMI, blood pressure, fasting plasma glucose and triglycerides, and low HDL-c values, which are typically considered to be diagnostic criteria for metabolic syndrome.[20]

In the present study all lipid fractions with exception to HDL are significantly elevated in type 2 diabetes cases supporting the fact that high morbidity and mortality in diabetes may be due to derangement in lipid profile. Uric acid can promote LDL oxidation, a key step in progression of atherosclerosis by stimulating granulocyte adherence to the endothelium. High range of glycaemia can promote non enzymatic glycosylation of LDL which

in turn can be phagocytosed into the arterial wall independent of receptor mechanism.[21, 22] Phagocytosed uric acids can transverse through
dysfunctional endothelium, this in turn can act as nidus for plaque formation.[23.24] Diabetics with elevated uric acid levels are at increased risk for developing nephropathy and cardiovascular disease.[25]The link between elevated serum uric acid and cardiovascular disease may arise through its non causal relationship with insulin resistance syndrome.
The current study shows weak correlations between the plasma urate levels and both the duration of diabetes and body mass index. In a study done by Talat, etal, [26] they found a moderate correlation between the duration of diabetes, plasma urate and hyperlipidaemia.

Conclusion

Hyperuricemia is a common finding in type 2 diabetes mellitus adding to the morbidity and mortality of these patients. In this study it was found that plasma urate is significantly associated with type 2 diabetes mellitus in general and in particular independent of body mass index and duration of diabetes and hyperlipidemia.

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