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COMPARATIVE STUDY OF LEVEL OF SERUM URIC ACID IN TYPE 2 DIABETES MELLITUS ASSOCIATED WITH HYPERTENSION

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ABSTRACT
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. 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. Fifty patients with type 2 diabetes mellitus and 50 healthy controls were included in this study. They were further divided into different groups, based on the sex, the duration of diabetes, and the diabetes which was complicated with hypertension. The circulatory levels of glucose, total cholesterol and triglycerides were found to be elevated in the diabetics of either sex as compared to those in the controls. There was no significant difference in the serum uric acid levels between the diabetics and the non-diabetics, either in males or females. A negative correlation was observed between the fasting plasma glucose and the serum uric acid levels in both male [$r = -0.60$] and female [$r = -0.60$] diabetic patients. The serum uric acid levels marginally decreased with an increased duration of diabetes. The hypertensive male and female diabetics were found to have significantly decreased ($P < 0.05$) serum uric acid levels as compared to the corresponding non-hypertensive diabetics. It was concluded from the present study that there occurs a significant decrease in the serum uric acid levels in hypertensive diabetics (both in males and females) in comparison with the non-hypertensive diabetics.

KEY WORDS: Type 2 D.M, Hypertension, Uric Acid

INTRODUCTION

Diabetes mellitus is a clinical syndrome which is characterized by hyperglycaemia due to an absolute or a relative deficiency of insulin. It may be associated with a number of complications which include macro and microvascular 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 T2DM [3]. 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 strokeUric acid can act as a prooxidant and it may thus be a marker of oxidative stress, but it may also have a therapeutic role as an antioxidant [4]. Urate, the soluble form of uric acid, can scavenge the superoxide and the hydroxyl radicals and it can chelate the transition metals [5]. Hyperuricaemia has been also added to the set of metabolic abnormalities which are associated with insulin resistance and/or hyperinsulinaemia in the metabolic syndrome [6]. 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 [7]. Hypouricaemia has also been implicated in the development of diabetic nephropathy [8]. 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[9,10]. 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 cross- sectional study was conducted on 50 patients with known type 2 diabetes mellitus and on 50 healthy controls that were in the age group of 30 -60 year at Geetanjali Medical college and hospital, Udaipur. The patients and the controls were further divided into different groups, based on

(i) The sex of the individual,
(ii) The duration of diabetes - group I (1- 5 years) and group II (5.1-10 years)
(iii) The patients with and without hypertension.

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, 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, non-hypertensive, non-smokers and non-alcoholics with normal plasma glucose levels.

The patients who gave a history of hypertension and were on antihypertensive treatment or whose blood pressure was more than 140/90 mm of Hg were considered to have hypertension. The height and the weight of patients 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

The mean ages (in years) of the male and female diabetic patients were 51.5±1.51 and 50.4±1.46 against 43.9±1.60 and 41.8±1.86 in the controls (males and females) respectively. The BMI, the W/H ratio, the fasting and the postprandial plasma glucose (FPG, 2hPG) levels and the total serum cholesterol and the serum triglycerides levels were higher in the diabetics as compared to the controls in both males and females. The serum uric acid levels in the diabetic males and females were marginally lower as compared to those in the controls, although this was not statistically significant [Table-1].

TABLE 1: Comparison of various parameter between cases and control [*significant p- value <0.05]

	Male		Female	
Variable	Control (35)	Cases (25)	Control (35)	Cases (25)
Age	43.9 ± 1.60	51.5 ± 1.51	41.8± 1.86	50.4±1.46
BMI	23.9 ± 0.75	25.2 ± 0.62	25.4±0.77	27±0.79
W/H ratio	0.90 ± 0.01	0.92 ± 0.01	0.80±0.01	0.83±0.01
FPG	4.5 ± 0.13	8.6 ± 0.48*	4.3±0.12	9.5±0.83*
PP2BS	6.1 ± 0.19	13.4 ± 0.69*	5.7±0.21	14.4±0.81*
T. cholesterol	3.1 ± 0.16	4.2 ± 0.35*	3.3±0.16	4.7±0.33*
Triglyceride	1.1 ± 0.04	1.6 ± 0.11*	1.2±0.04	1.5±0.04*
Uric Acid	314.5 ±16.48	306.8 ±14.27	265±18.45	250.1±10.85

A negative correlation was observed between the fasting plasma glucose and the serum uric acid levels in both male [r = −0.60] and female [r = −0.60] diabetic patients [Table-2], [Table-3]. The serum uric acid levels decreased with an increased duration of diabetes, although it was not statistically significant [Fig-1].

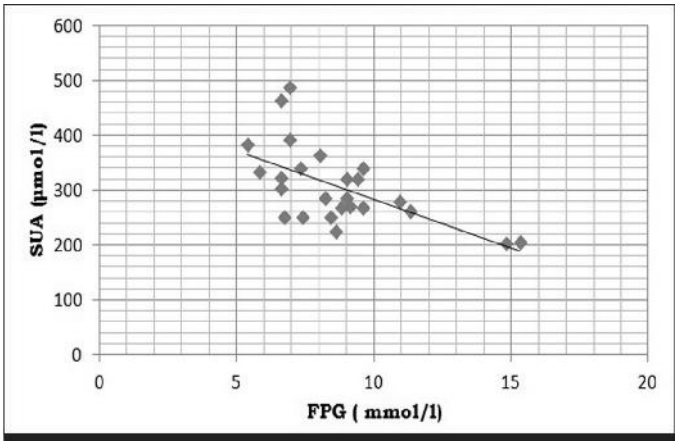

FIGURE 1: correlation (r = -0.60) between FPG and S. Uric acid level in Male

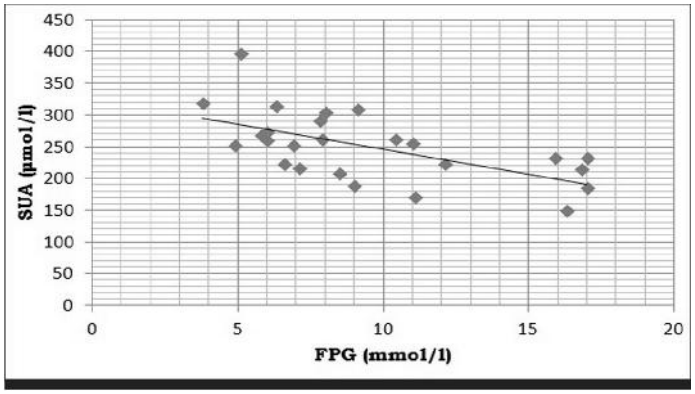

FIGURE 2: correlation (r = -0.60) between FPG and S. Uric acid level in Female

TABLE 2: S. uric acid level associated with duration of DM (i= 1-5 yr, ii = 5-10 yr)

Group	I	I I
Female diabetics	285.7±28.68 (15)	236.6±13.76 (10)
Male diabetics	308.5±18.82 (15)	262.5±10.25 (10)

TABLE 3: S. uric acid level associated with Hypertension in T2DM as Mean ± SD (*significant P-value <0.05)

Group	Non Hypertensive	Hypertensive
Female diabetics	320.3 ± 35.01	235.5 ± 17.63*
Male diabetics	311.9 ± 18.58	257.3 ± 8.24*

The comparison of the non-hypertensive and the hypertensive male and female diabetics showed decreasing serum uric acid levels, which was statistically significant (P<0.05). The decrease in the uric acid levels was more pronounced in the female diabetics (P<0.02) than in the male diabetics (P<0.03) [Fig-2]. The percentage of the diabetics who gave a positive family history of diabetes and a history of hypertension was more among the females than among the males, while smoking and alcohol drinking were predominantly seen in the males. Dyslipidaemia in the form of increased serum total cholesterol levels was more pronounced in the female diabetics and hypertriglyceridaemia was more common in the male diabetics

DISCUSSION

Uric acid is the final product of the purine metabolism in humans. The 2 final reactions in its production which catalyze the conver-sion 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 favouring an antioxidant – prooxidant urate redox shuttle [10,11]. UA is also a physiological free radical scavenger and one of the major contributors of the plasma antioxidant capacity [12]. Thus, UA plays a dual role, both as a prooxidant and as an antioxidant[13,14]. T2DM is associ-ated with oxidative stress and increased free radical formation [15]. While on one hand, hyperglycaemia generates free radicals, on the other hand, it also impairs the endogenous antioxidant defense system [16]. 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[17]. Studies have reported the association of hypouricaemia with T2DM[18,19]. A positive relationship has been described be-tween glycosuria and uricosuria [20]. Further, a higher degree of hyperglycaemia was observed to be associated with an in-creased rate of uric acid excretion and lowering of the plasma uric acid levels [20]. Hypouricaemia and the tubular transport of uric acid have been thoroughly reviewed[21]. An increased urate clearance due to increased glomerular hyperfiltration which is a result of an abnormality in the tubular urate handling has been reported [22]. The Serum uric acid levels were found to be higher in males than in females [23]. We reported a similar finding in our study. The findings of the BMI, and the waist hip ratio in the diabetic males and females in our study were in accordance with the findings of others [24, 25]. Our study reported a negative relationship between the fasting plasma glucose and the serum uric acid levels which were in agreement with the findings of other studies[26]. 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 [24]. Although it was not statistically significant, the lowering of the serum uric acid levels with an increase in the duration of diabetes was ob-served in our study and this was in agreement with the findings of another study [1]. According to study by Johnson and collegues, they have reported a positive association of hyperuricaemia with hypertension in T2DM with complications[27]. 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 decrease in the serum uric acid levels was seen with high plasma glucose

levels/increased glycosuria, hyperfiltration and a decreased antioxidant status, the lowering of the serum uric acid 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. From the present study, it appears that uric acid alone cannot act as an independent risk marker for type 2 diabetes mellitus. Taking up more studies on the renal clearance and the uric acid excretion and on the antioxidant status in the hypertensive diabetics, by taking the glycaemic status into consideration, may help in better defining the role of uric acid in type 2 diabetes mellitus. Further, as the decrease in the serum uric acid levels is more significant in the hypertensive diabetic females with a family history of diabetes, it would be pertinent to perform genetic studies in order to clarify the gender differences in the serum uric acid concentrations in relation to type 2 diabetes mellitus which is associated with hypertension.

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