



URIC ACID IN TYPE 2 DIABETES MELLITUS

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ABSTRACT

Whether Uric acid is an antioxidant or pro oxidant has been a topic of debate since long. The antioxidant activity of uric acid has been proved by various studies. This study was carried out among a group of Type 2 Diabetic patients attending Sree Balaji Medical College and Hospital. The FPG, PPPG levels were assayed along with Uric acid levels. We found a minimal decrease in serum uric acid levels among the diabetic patients in comparison with Healthy controls. The results support the idea that uric acid is an antioxidant which is being used up in combating the oxidative stress.

KEYWORDS: Uric acid, Type 2 Diabetes Mellitus, antioxidant.



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INTRODUCTION

Uric acid is the end product of purine metabolism in humans. The last two reactions of its production are catalyzed by the enzyme xanthine oxidase. Xanthine oxidase uses molecular oxygen as electron acceptor and generates superoxide anion and other reactive oxygen species (ROS)¹. Evidence based on various studies suggests that increased serum levels of uric acid are a risk factor for cardiovascular disease & Diabetes mellitus where oxidative stress plays an important pathophysiological role². However, there is increasing experimental and clinical evidence showing that uric acid has an important role as an antioxidant in vivo³. Diabetes mellitus has been known to be a state of oxidative stress with excess generation of free radicals contributed by several mechanisms, including hyperglycemia⁴. Oxidative stress is defined as a condition in which the rate of generation of ROS exceeds the ability of the normal levels of antioxidant machinery to combat the ROS¹. Studies have revealed a depleted level of the extracellular antioxidant status in the type 2 diabetics, regardless of any complications, in favor of an oxidative stress in such patients. These results were in agreement with those of previous studies^{5, 6} which demonstrated a strong association between poor glycaemic control and the depletion of the protective antioxidant defence mechanisms in diabetes mellitus. Antioxidant systems include enzymes such as superoxide dismutase, catalase, and glutathione peroxidase, macromolecules such as albumin, ceruloplasmin and ferritin: and an array of small molecules including ascorbic acid, α tocopherol, β carotene, reduced glutathione, uric acid and bilirubin⁷. Uric acid is a chain breaking antioxidant. They intercept the peroxy free radical and inactivate it before a PUFA can be attacked⁸. The ability of urate to scavenge oxygen radicals and protect the erythrocyte membrane from Lipid oxidation was originally described by Kellogg and Fridovich⁹ and was characterized further by Ames et al¹⁰. In the above studies the effects of uric acid was

shown under specific conditions where exogenously added uric acid protected cells from oxidants, which were also added exogenously to aqueous incubation media. This kind of condition is relevant to a variety of physiological situations when circulating uric acid can scavenge reactive radicals released into the blood by deleterious reactions, such as autoxidation of hemoglobin or peroxide production by macrophages¹¹. The antioxidant effect of Uric acid is second next to Vitamin C. A vast literature on the epidemiology of cardiovascular disease, hypertension, and metabolic syndrome overwhelmingly shows that, at least among modern Humans, a high level of uric acid is strongly related and in many cases alarms development of hypertension^{12,13,14} visceral obesity,^{2,15,16} insulin resistance,¹⁷ dyslipidemia,^{2,17,18,19} type II diabetes,¹⁷ kidney disease,¹³ and cardiovascular and cerebrovascular events^{13,20}. Some studies reported that there is a positive association between high serum uric acid levels and diabetes²¹⁻²⁷ whereas other studies reported no association²⁸ or an inverse relationship^{29, 10}.

AIMS AND OBJECTIVES

1. To estimate FPG & PPPG as diagnostic of Diabetes.
2. To estimate Uric acid in patients with Type 2 Diabetes Mellitus.

MATERIALS & METHODS

A total of ninety three (93) - type 2 diabetic patients in the age group 30-50yrs attending the Diabetic OP of SBMC&H were included in the study and were compared with eighty nine (89) age and sex matched healthy controls.

Exclusion Criteria

Patients with chronic illness other than Type 2 Diabetes Mellitus Post-menopausal women.

Smokers and alcoholics. Ethical clearance was obtained from the Ethical Clearance Committee of SBMC&H. Informed consent was signed by patients and healthy controls. 2ml venous blood was drawn from the patients in the fasting condition for the following investigations: Fasting plasma glucose (FPG), serum uric acid . 2 ml blood was drawn 2 hours after food for estimation of Post prandial plasma glucose (PPPG). FPG & PPPG were estimated using Glucose Oxidase Peroxidase (GOD POD) Method (Enzymatic method).

Uric Acid

Enzymatic photometric test using (TBHBA) 2, 4, 6-tribromo-3- hydroxybenzoic acid. Principle: Uric acid is oxidized to allantoin by uricase and liberates H₂O₂. The generated hydrogen peroxide reacts with 4- aminoantipyrine and 2, 4, 6-tribromo-3-hydroxybenzoic acid (TBHBA) to form quinoneimine. Incubate at 37 C for 10 minutes. The intensity of the colour is read at 520 nm. The intensity of the colour is directly proportional to the concentration of Uric acid in the sample.

RESULTS

Table 1
A Comparison of Glucose levels in two groups

Parameter	Controls	Cases	Significance
FPG (mg/dl)	88.22±13.25	169.63±69.43	t=10.753; P<0.001**
PPPG (mg/dl)	112.33±24.35	244.46±88.19	t=13.499; P<0.001**

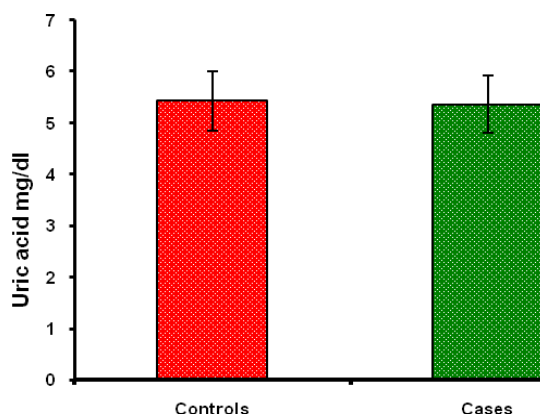
*Student t test (two tailed, independent) has been used to find the significance of glucose levels. The p value is ** strongly significant for the plasma glucose levels.*

Table 2
Uric acid levels in controls and cases

Parameter	Controls	Cases	Significance
Uric acid mg/dl	5.43±0.58	5.36±0.56	t=0.828; p=0.409

Student t test (two tailed, independent) has been used to find the significance of serum uric acid level. Normal value for serum uric acid is 3.5-7 mg/dl. Actually there was a minimal decrease in case of Diabetic patients. The value expressed as Mean +/- S.D was 5.36±0.56 mg/dl. The healthy controls had a value expressed as mean ± SD to be 5.43±0.58 mg/dl. The p value is 0.409. There was a definite minimal decrease in uric acid levels among Diabetic subjects, though the difference in levels between healthy controls and diabetic subjects was not significant.

Graph
1 Uric acid levels in controls and cases



DISCUSSION

In our study we have seen results in favor of the antioxidant activity of Uric acid. There has been a marginal decrease in Diabetics as 5.36 ± 0.56 in comparison to healthy controls as 5.43 ± 0.58 showing that Uric acid as an antioxidant is used up in combating the oxidative stress in Type 2 Diabetes Mellitus. Similar results have been observed by Shabana *et al* among a population in Andhra³⁰. In a multiethnic sample of US adults, higher serum uric acid levels were found to be inversely associated with diabetes mellitus in both men and women³¹. This is in correlation with our study. Uric acid is an antioxidant only in

the hydrophilic environment, which is probably a major limitation of the antioxidant function of uric acid

CONCLUSION

In our study, the level of serum uric acid is decreased in Diabetes mellitus. This may be due to its antioxidant property. Uric acid as an antioxidant should be considered a topic of further research in a large population

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