

SERUM URIC ACID AND TYPE 2 DIABETES MELLITUS COMPLICATIONS

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ABSTRACT

BACKGROUND

Diabetes mellitus is a leading public health problem with increasing incidence and long-term complications. Hyperuricemia is an independent risk factor for developing micro and macro vascular complications.

MATERIALS AND METHODS

The study was conducted in 100 cases diagnosed with Type 2 diabetes mellitus.

RESULTS

Out of 100 patients, 60 patients showed elevated serum uric acid. Complications were more in patients with hyperuricemia.

CONCLUSION

Elevated serum uric acid levels in type 2 diabetes mellitus cause more micro vascular and macro vascular complications. Frequent monitoring of serum uric acid levels and early detection helps in the treatment of kidney disease

KEYWORDS

Serum uric acid, type 2 diabetes mellitus, micro vascular and macro vascular complication.

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BACKGROUND

World Health Organization (WHO) defines the term Diabetes Mellitus (DM) as a metabolic disorder of multiple aetiology, characterized by chronic hyperglycaemia with disturbances of carbohydrate, protein and fat metabolism, resulting from defects in insulin secretion or insulin action or both.¹ Diabetes mellitus is a leading public health problem with increasing incidence and long-term complications such as diabetic nephropathy, diabetic neuropathy, diabetic retinopathy etc. These complications are mainly a consequence of macro vascular and micro vascular damages of the target organs. The top three countries are India, China and U.S. India is called Diabetic Capital of World as there are going to be eighty per cent of all diabetics from the entire world population, concentrated here.² In 2000 the number of people with diabetes was 31.7 million and it is expected that by 2030 this will increase to 79.4 million.³ Several factors contributing to this include greater longevity, obesity, unsatisfactory diet, sedentary lifestyle. The cause of clinical diabetes is absolute or relative deficiency of insulin. Diabetes mellitus of Type 2 or NIDDM, is characterized by insulin

resistance and impaired insulin receptors.⁴ It is common type of diabetes and usually develops after the age of 40 years.

Uric acid is end product of purine metabolism. Hyperuricemia is a condition that is significantly associated with markers of metabolic syndrome such as dyslipidaemia, glucose intolerance, insulin resistance, high blood pressure, and central obesity, which are accepted as risk factors for developing cardiovascular and other complications.⁵ Because it has paradoxical action, it acts as an antioxidant at physiological level but shows a pro-oxidant property while the levels are elevated. Hyperuricemia has been described as a strong predictor of well-defined cerebrovascular complications (stroke) in patients with type 2 diabetes.⁶ Hyperuricemia is an independent risk factor for kidney dysfunction in diabetes mellitus. Increased uric acid will damage the kidney by causing Hyperuricemia induced endothelial injury.⁷ Association between Hyperuricemia and diabetes includes: (a) uric acid induced activation of renin - angiotensin system and action on glomerular apparatus (b) increased insulin resistance and hyperinsulinemia, causing decreased excretion of uric acid, sodium, potassium from renal tubules; and (c) uric acid action in proliferation of vascular smooth muscle, endothelial dysfunction with decreased nitric acid production.

Urinary micro albumin assesses glomerular endothelial function and micro vascular integrity. The higher the urinary micro albumin level, the higher the risk for development of kidney disease, particularly in type 2 diabetes mellitus and hypertension.⁸

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MATERIALS AND METHODS

The study was conducted in Jhalawar Medical College and SRG Hospital, Jhalawar (Rajasthan) from July 2017 to Dec 2017 in Department of General Medicine. The Ethics committee clearance was obtained. The study included 100 cases of Type 2 diabetes mellitus. After an overnight fasting 10 ml blood was taken from a forearm vein which was used for the determination of FBS and serum uric acid concentrations. After 2 hours of lunch 2 ml of blood for post prandial blood sugar was obtained. Urine sample also collected from patients for estimation of urine sugar and urinary micro albumin. Urine micro albumin was done by turbidometry.

Patients with type 2 diabetes mellitus with age > 40 years and both sexes were included in the study. Patients with Renal failure, Chronic alcoholics, hepatic disorders, on long term diuretics, steroids, xanthine oxidase inhibitor, antimetabolite, chemotherapy and uricosuric drugs, patients of renal transplant, pregnant and lactating women were excluded from the study.

After informed written consent, selected data were taken from the patients. Information was filled in Performa having patients name, age, sex, Clinical parameters like duration of diabetes, family history of diabetes, CAD, HTN and Physical examination was done to record Clinical parameters like Systolic and Diastolic blood pressure. 10 ml of blood was collected and sent to the laboratory for assessment of Fasting blood sugar levels and 2 hours after lunch 5 ml of blood was sent for post prandial blood sugar levels estimation by using glucosoxidase-peroxidase (GOD/POD) method, Serum uric acid was done by using phosphor tungstic acid method.

Definitions

Diabetes Mellitus- FPG -126 mg/dl (7.0 mmol/l) and fasting is defined as no caloric intake for at least 8 h. OR symptoms of hyperglycaemia and casual plasma glucose >200 mg/dl (11.1 mmol/l). Casual is defined as any time of day without time regard since last meal.⁹ The classic symptoms are polyuria, polydipsia, and unexplained weight loss. OR 2-h plasma glucose >200 mg/dl (11.1 mmol/l) during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.

Hyperuricemia- Hyperuricemia has been arbitrarily defined as >7.0 mg/dL in men and >6.0 mg/dL in women.¹⁰

Micro Albuminuria- Micro albuminuria refers to an abnormally increased excretion rate of albumin in the urine in the range of 30-299 mg/g creatinine.

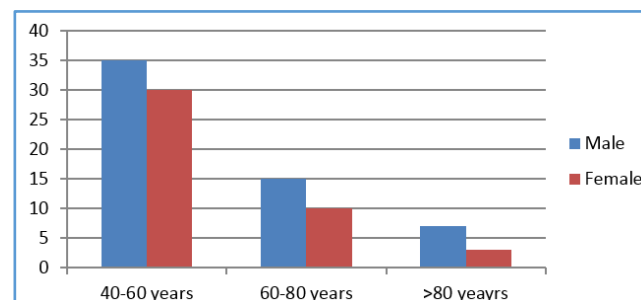
RESULTS

A total of 100 diabetic patients were studied out of these 100 patients, 60 patients showed elevated serum uric acid.

Age Groups	Male	Female	Total
40-60 years	35	30	65
60- 80 years	15	10	25
>80 years	7	3	10

Table 1. Showing Age and Sex Distribution among Study Population

A total 100 patients were studied out of them 57 were male and 43 were female. Most of them came under the age of 40-60 years and the number was 65.



Graph 1. Age and Sex Distribution of the Subjects Studied

Hyperuricemia	Frequency	(Percentage)%
POSITIVE	60	60%
NEGATIVE	40	40%

Table 2. Association between Hyperuricemia and Diabetes Mellitus

Table 3. Association between Serum Uric Acid Levels and Cardiovascular Complications Hypertension and ECG Changes in Diabetic Subjects

Hypertension	Serum uric acid		Total	P value
	High	Normal or low		
Yes	45 (45%)	10 (10%)	55 (55%)	.001
No	15 (15%)	30 (30%)	45 (45%)	

Table 3A. Association between Hypertension and Serum Uric Acid Levels

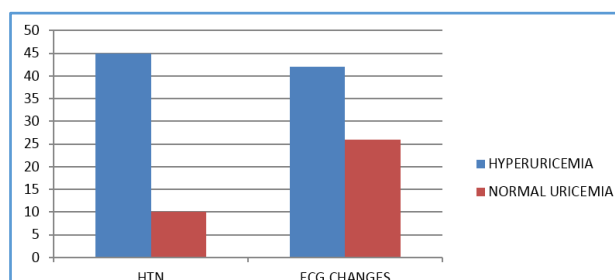
Table 3A. Represents the association between Hypertension and serum uric acid levels. We found Hypertension in 55 patients, among them 45 had elevated serum uric acid levels.

ECG Changes	Serum uric acid		Total	P value
	High	Normal		
Present	42 (42%)	26 (26%)	68 (68%)	0.038
Absent	18 (18%)	14 (14%)	32 (32%)	

Table 3B. Association Between ECG Changes and Serum Uric Acid Levels

Table 3B represents the association between ECG changes and serum uric acid levels and we found 68 patients showed ECG changes among them 42 patients had elevated serum uric acid and value were statistically significant (P

value – 0.038). We observed that diabetic patients with elevated serum uric acid showed ECG changes than those having normal value.



Graph 2. Showing Diabetic Patients with Cardiovascular Complication in Percentage

Fundus Changes.	Serum Uric Acid		Total	P value
	High	Normal		
Present	43 (43%)	11 (11%)	54	.001
Absent	17 (17%)	29 (29%)	46	

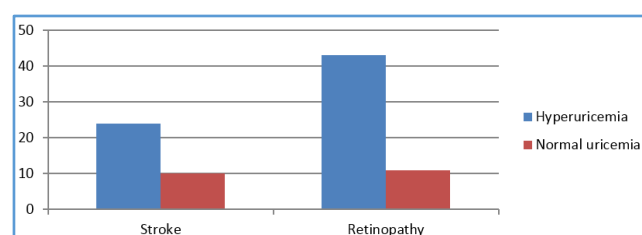
Table 4. Represents the Association between the Fundus Change and the Serum Uric Acid Level

There is a positive correlation between elevated serum uric acid and the fundus changes (p value .001).

Stroke.	Serum Uric Acid		Total	P value
	High	Normal		
YES	24 (48%)	10 (19%)	34	.001
NO	1 (2%)	15 (31%)	16	

Table 5. Represents the Association between the Serum Uric Acid and Cerebrovascular Accident Patients (Stroke)

Patients who had cerebrovascular accident (stroke) showed increased serum uric acid levels:

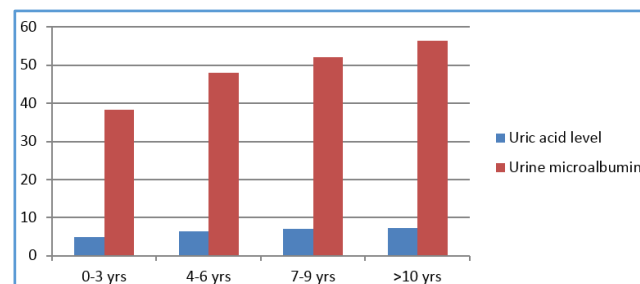


Graph 3. Shows Stroke and Retinal Complications in Percentage

Duration of Diabetes	No. of Patients	Uric Acid (mg %) Mean	Urine Micro Albumin (mg/L) Mean
0 to 3 years	40	5.01	38.21
4 to 6 years	35	6.34	47.93
7 to 9 years	15	7.12	52.01
≥10 years	10	7.24	56.31

Table 6. Correlation between Serum Uric Acid and Urine Micro Albumin in Diabetes Patients

We found that serum uric acid and urine micro albumin levels were elevated more with duration of diabetes mellitus.



Graph 4. Shows Serum Uric Acid and Urine Micro Albumin Level were Markedly Increased in Type 2 DM Patients

DISCUSSION

Type-2 diabetes mellitus is a metabolic disorder. The hyperglycaemia causes biochemical and structural changes which lead to many complications due to organ dysfunction including micro and macro vascular diseases.¹¹ The extent and duration in diabetic patients may contribute to the severity of diabetic complications like Hyperuricemia, renal and cardiovascular dysfunction.¹²

Serum uric acid levels were markedly increased in type 2 diabetic (p<0.001). Biologically uric acid plays an important role in worsening of insulin resistance by inhibiting the bioavailability of nitric oxide, which is essential for insulin-stimulated glucose uptake.

Hyperinsulinemia as a consequence of insulin resistance causes an increase in serum uric acid concentration by both reducing renal uric acid secretion and accumulating substrates for uric acid production.^{13,14} The mean serum uric acid levels were elevated statistically highly significant in type 2 diabetic (p<0.001). Hyperuricemia is caused by muscle wasting and weight loss in diabetes mellitus¹⁵ Chronic high glucose concentration causes tissue injury, in turn leads to increasing non-protein nitrogen substances.³ This phenomenon accounts for increased uric acid levels. Diabetic patients have a high risk of kidney disease due to hyperglycaemia, Hyperuricemia etc. Increased glycaemic index related with Hyperuricemia lead to changes in glomerular permeability. The highly significant values seen were due to dysfunction of the rennin-angiotensin system in long term diabetes.¹⁶ Type 2 diabetic patients have a long asymptomatic period of hyperglycaemia and many other conditions causing micro albuminuria but hypertension and long term diabetes are main risk factors.^{17,18} Considering the strong association between the levels of serum uric acid and the occurrence of coronary atherosclerosis in subjects with type 2 diabetes mellitus, the current study has been undertaken to assess the factors influencing the serum uric acid levels in patients with type 2 diabetes mellitus. The study has shown Hyperuricemia higher in diabetic patients and its complications.

Among the 100 patients selected for our study, 60 patients had elevated serum Uric acid levels and the remaining 40 patients had normal or less than normal serum uric acid levels. In our study all the patients underwent complete clinical examination and relevant laboratory and radiological investigations. After the detailed evaluation of the results of the study it was observed that the elevated

levels of serum uric acid is associated with higher incidence of both micro vascular and macro vascular complications.

In our study complications are found to have been increased in diabetic patients with Hyperuricemia. The mean serum uric acid and urine micro albumin levels were elevated statistically highly significant in type 2 diabetic. ($p < 0.001$). The presence of micro albuminuria is an indicator of the early stages of kidney disease in diabetic patients.^{19,20} These results were supported by other studies as follows, same finding observed by Cai xiao-ling (2011).¹⁹ Chonchol M, (2007)²¹ and Saeed Behradmanesh et al (2012).²²

In our study, there is a strong association of elevated uric acid levels with micro vascular involvement of Kidneys,²³ Fundus, and macro vascular involvement of coronary artery and cerebral vessels. Hyperuricemia is also associated with hypertension.

CONCLUSION

Elevated serum uric acid levels in type 2 diabetes mellitus cause more micro vascular and macro vascular complications. Frequent monitoring of serum uric acid levels and early detection helps in the treatment of kidney disease.

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