

Plasma Uric Acid Levels in Patients with Diabetes Mellitus and Impaired Glucose Tolerance Test in Comparison with Normal Subjects

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Abstract: *Background:* Plasma uric acid has been shown to be associated with an increased risk of hypertension, cardiovascular disease, chronic kidney disease, insulin resistance and metabolic syndrome. However the putative association between serum uric acid level and diabetes mellitus is not clear. This study aimed to investigate the plasma uric acid levels in patients with Type 2 DM and patients with IGT in comparison with normal subjects. *Methodology:* This is a case control study conducted in M.B.S. Hospital over a period of years 2012-13. Serum uric acid and serum glucose concentration were measured in both control and patients groups (Group 1 – patients of Type 2 DM, Group 2 – patients with IGT and Group 3 – normal subjects). *Results:* Serum uric acid concentration was lower in diabetic group (3.32 ± 0.882) as compared with control group (4.74 ± 1.51) and was significant ($p < 0.001$). Serum uric acid concentration was higher in IGT group (6.19 ± 1.13) when compared with control group (4.74 ± 1.51) ($p < 0.001$) and was significant. *Conclusion:* Serum uric acid concentration is slightly reduced in patients with Type 2 DM and this may be due to increased excretion of uric acid during hyperglycemia and glycosuria. Serum uric acid concentration is increased in patients with IGT and factors contributing to it are still unclear

Keywords: Serum uric acid; type 2 DM; Impaired glucose tolerance, IGT, hyperglycemia

1. Introduction

Uric acid is formed by the breakdown of purins and by direct synthesis from 5-phosphoribosyl pyrophosphate and glutamine. Serum urate levels vary with age and sex. Most children have serum urate concentrations of 180 to 240 $\mu\text{mol/L}$ (3.0 to 4.0 mg/dl). Levels begin to rise in males during puberty but remain low in females until menopause. Mean serum urate values of adult men and premenopausal women are 415 and 360 $\mu\text{mol/L}$ (6.8 and 6.0 mg/dl), respectively. After menopause, values for women increase to approximate those of men. In adulthood, concentrations rise steadily over time and vary with height, body weight, blood pressure, renal function, and alcohol intake.^{1,2}

Serum uric acid has been shown to be associated with an increased risk of Hypertension^{3,4} Cardiovascular diseases^{5,6} Chronic kidney disease⁷ insulin resistance and metabolic syndrome⁸ However the putative association between serum uric acid level and diabetes mellitus is not clear. Some studies have been recognised that serum uric acid is positively associated with diabetes^{9,10,11,12,13,} where as other studies reported no association¹⁴ or an inverse association^{15,16}.

Recent studies have demonstrated that uric acid level is higher in subject with pre-diabetic and early diabetics than in healthy⁸. As the diabetic status progress there is gradual decline of uric acid level in many patient^{9,17}. An elevated uric acid level was found to increase chances for developing of diabetics in individual with impaired glucose tolerance test¹¹

2. Aim of the Study

- 1) To define the relationship between serum uric acid and glucose levels in patients with impaired glucose tolerance test and diabetes mellitus.

- 2) To assess the prevalence of hyperuricemia in patients with impaired glucose tolerance test.
- 3) To assess the prevalence of hypouricemia in patients with diabetes mellitus.
4. Compare the serum uric acid levels between male and female diabetic subjects

3. Materials and Methods

Source of Data

Patients, with known diabetes mellitus or newly detected patients of diabetes or impaired glucose tolerance treated on OPD basis or in patients admitted in M.B.S. Hospital Kota. A detailed history was taken and thorough physical examination was done and BMI was calculated.

Inclusion Criteria

- 1) Patients already on treatment or newly detected diabetes mellitus (ADA criteria for Diabetes).
- 2) Patients found to be detected to have impaired glucose tolerance test.
- 3) Non diabetes
- 4) All age group and both sexes

Exclusion Criteria

- 1) B.M.I. > 30
- 2) Hypertension.
- 3) Patients with serum creatinine > 1.0 mg/dl
- 4) Patient is an alcoholic.
- 5) Myeloproliferative disorders.
- 6) Lymphoproliferative disorders.
- 7) Psoriasis.
- 8) Patient on drug which increase serum uric acid eg. salicylate, diuretics, ethambutol, pyrazinamide

Method of uric acid estimation

Uric acid level was measured by uricase – pap methodology.

Test Principle

Uric acid is degraded by uricase to allantoin and H₂O₂. The product H₂O₂ is then quantitated by the use of catalase and aldehyde dehydrogenase. The increase in NADPH concentration, measured by the change in absorption at 339 nm or 334 nm is proportional to the amount of uric acid.

Oral Glucose Tolerance Test

Procedure

- 1) A zero time (baseline) blood sample is drawn.
- 2) The patient is then given a 75g of glucose solution to drink within a 5 minute time frame.
- 3) Blood is drawn at intervals for measurement of glucose (blood sugar), for simple diabetes screening, the most important sample is the 2 hour sample and the 0 and 2 hour samples may be the only ones collected.

4. Result

In this study 100 patients who presented M.B.S.Hospital Kota, 40 patients with Type 2 DM (20male & 20 female) and 10 patients with IGT(4male&6female) formed the study group and 50 normal patients (33male & 17 female) were taken as controls.(table-1)

Study was made in detail regarding age, sex, history, glycemic status, duration of diabetes and investigations. Age distribution of the study ranged from 32-80 years. There was no significant difference among cases and controls in relation to age and sex. (table2)

The present study showed that there is a mild decrease in serum uric acid levels in patients with Type 2 DM. Study also showed that as the duration of diabetes increases there is decrease in serum uric acid levels. The mean serum uric acid level is lower in control group (4.74±1.51), rose in IGT(6.19±1.13) and again decreased in diabetics (3.32±0.88). The result were statistically significant.

The factors contributing to decreased level of serum uric acid in diabetics are increased excretion of uric acid during hyperglycemia and glycosuria. The present study showed that IGT patients had high serum uric acid values. Factors contributing to hyperuricemia are still unclear. Higher serum uric acid levels was observed in males than females in every group of study. (Type2DM,IGT&control group) .

5. Discussion

The patients were grouped into study group (patients with type 2 DM and patients with IGT) and control group (normal patients). The purpose of the study was to study the serum uric acid levels in patients with type 2 DM and patients with IGT in comparison with normal subjects.

The main finding of our study was that plasma uric acid levels were elevated in patient with impaired glucose tolerance. The lowest plasma uric acid levels were found in diabetic patients. A negative association of plasma uric acid with overt diabetes was found earlier in several other studies^{-11,18,19}. Our results confirm this finding despite the

methodological differences and the various diagnostic criteria for diabetes mellitus used in these studies. In a prospective study of 10,000 Israeli men, it was found that diabetic men had lower plasma uric acid levels than "prediabetic" men, who had higher levels than nondiabetic men^{11,17}. Our study used the WHO criteria and showed that patients with impaired glucose tolerance had the highest plasma uric acid levels. An interesting finding in our study was that plasma uric acid levels were clearly reduced in diabetic patients when compared with nondiabetic patients.

In our study the mean serum uric acid was high in patients with IGT when compared to controls and diabetic subjects. The mean serum uric acid level was 3.32± 0.88, 6.19± 0.13 and 4.74±1.51 in patients with Type 2 DM, patients with IGT and controls respectively. The results were statistically significant. (Table-1)

Kodama S Et al⁹, in their study assessed systematical evaluation of association between serum uric acid level and subsequent development of Type 2. DM and concluded that serum uric acid level is positively associated with subsequent development of Type 2 DM regardless of various study characteristics and also concluded that further research should be attempted to determine whether it is effective to utilize serum uric acid level as a predictor of Type 2DM for its primary prevention. In this study patients with longer duration of diabetes were more susceptible to develop various complications including hypouricemia (table-6).

Our study also shows that lower levels of serum uric acid was seen in patients with longer duration of diabetes, 2.58±0.56 (>8yrs) when compared with shorter duration of diabetes, 3.59±0.98(0-5yrs). The difference was statistically significant. The possible reason may be due to increased excretion of uric acid over the years (table-6).

In our study hyperuricemia was observed in 5(50%) patients of IGT and 3(6%) patients in control group (table-5) The results were statistically significant. Daniel felg¹⁹ et al in their study concluded that 40-60% subjects with IGT had hyperuricemia. In our study hypouricemia was observed in 17 (42.5%) patients of Type 2 DM and 5(10%) patients in control group. The results were statistically significant (table-4).

According to Masoo Kanuchi Et al¹⁸, glomerular hyperfiltration, which accompanies diabetic nephropathy and, functional abnormality of renal tubular urate handling lead to tubulointerstitial involvement which contributes to hypouricemia in diabetic patients.

In our study when we compare males and females distribution of serum uric acid levels it was observed that males had higher serum uric acid level than females in every group (Type2DM,IGT,&controlgroup). The difference was statistically not significant (Table-3)

Table 1: Details of Subjects included in the study

Parameter	Type 2 dm	Impaired glucose tolerance	Controls
Total No	40	10	50
Age	35-74	42-72	32-80
Mean Age	53.15	56.5	53.6
Sex	M =20 F =20	M=4 F=6	M=33 F =17
B.M.I.	25.04	27.2	24.8
FBS	128.02	107.8	78.6
PPBS	175.02	156.2	92.48
RBS	168.1	143.7	97.96
SUA	3.32 ± 0.882	6.19 ± 1.13	4.74 ±1.51

Table 2: Cases and control in relation to age

Age Group	Type 2 dm		IGT		Controls	
	No	%	No	%	No	%
32-41	6	15	0	0	9	18
42-51	10	25	4	40	13	26
52-61	11	27.5	3	30	13	26
62-71	11	27.5	1	10	12	24
> 72	2	5	2	20	3	6
Mean	53.15		56.5		53.26	
S.D.	11.18		10.29		12.26	

Table 3: The Serum uric acid levels in relation to gender

	Type 2 DM			IGT			Controls		
	Age	S.U.A.	B.M.I.	Age	S.U.A.	B.M.I.	Age	S.U.A.	B.M.I.
Male	57.75 ± 9.92	3.53± 1.01	25.07 ± 0.89	59.75 ± 10.53	6.97± 1.02	27.77 ± 0.85	51.06± 12.84	4.97 ± 1.57	24.81 ± 1.17
Females	48.55 ± 10.66	3.12 ± 0.68	25.01 ± 0.87	54.33 ± 10.67	5.66 ± 0.92	26.81 ± 0.59	57.52 ± 10.04	4.30 ± 1.34	24.76 ± 1.16

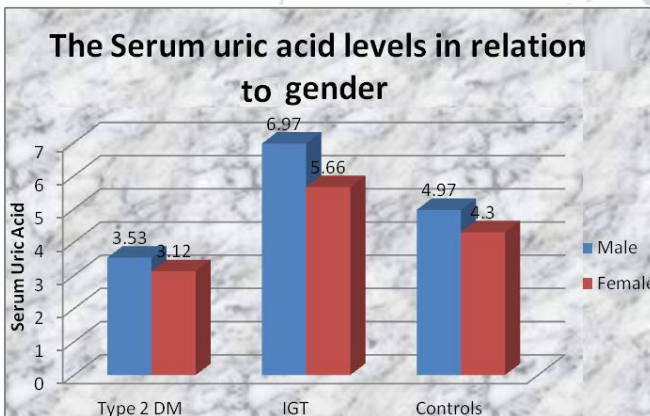


Table 5: Analysis of Hyperuricemia in Cases and Controls

Hyperuricemia	Impaired glucose tolerance	Controls
Positive	5	3
Negative	5	47

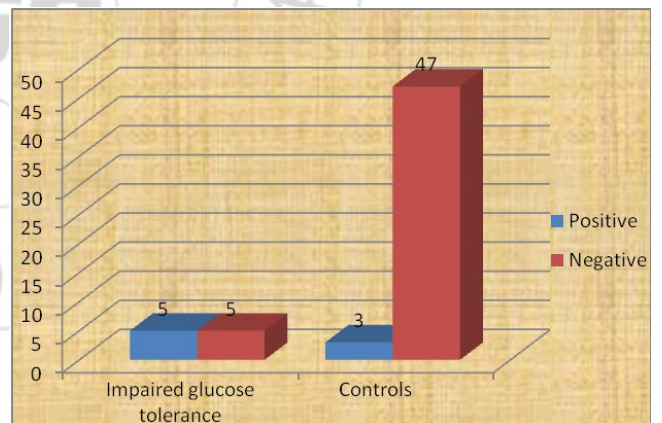


Table 4: Analysis of Hypouricemia in Cases and Controls

Hypouricemia	Type 2 dm	Controls
Positive	17	5
Negative	23	45

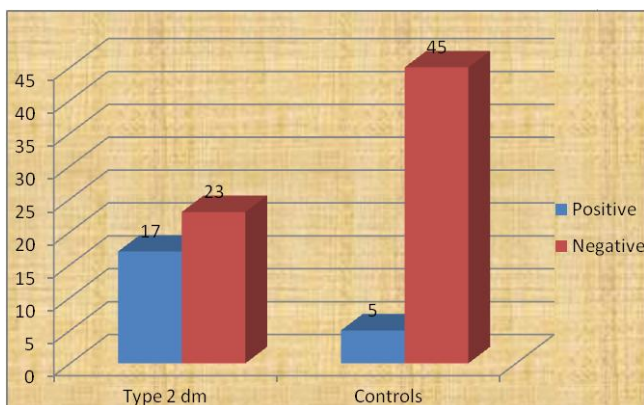
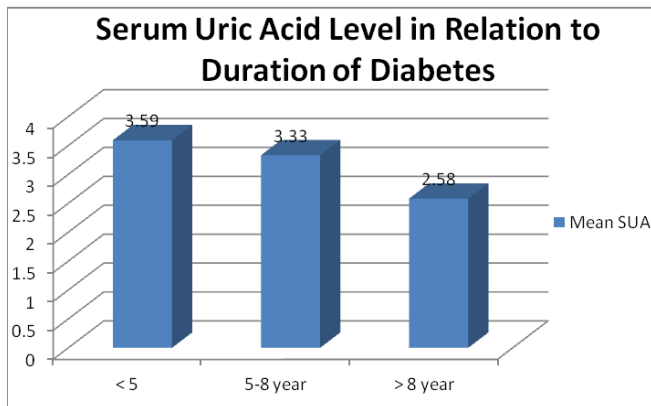


Table 6: Serum Uric Acid Level in Relation to Duration of Diabetes

Duration of Diabetes	No	Mean SUA	S.D.
< 5	22	3.59	0.98
5-8 year	10	3.33	0.46
> 8 year	8	2.58	0.56



6. Conclusion

- 1) Plasma uric acid level was higher in IGT group than controls and lower in diabetes mellitus.
- 2) Plasma uric acid decreased in patients with Type 2 DM of longer duration and the degree of reduced plasma uric acid levels were directly proportional to the duration of Type 2 DM.
- 3) Plasma uric acid was significantly elevated in patients with IGT
- 4) Males had higher uric acid level in every group of study when compared to females

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