Plasma Uric Acid Level and its Association with Type II Diabetes Mellitus

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Abstract: _Introduction: Hyperinsulinemia as a consequence of insulin resistance causes an increase in serum uric acid (SUA) concentration by both reducing renal uric acid secretion and accumulating substrates for uric acid production. Therefore, it remains controversial whether SUA is independently associated with the development of type 2 diabetes.Aim: Plasma uric acid level and its association with Diabetes Mellitus II._ _Method: Analytical case control study with 145 cases and controls with uric acid level and blood sugar levels and duration of Diabetes._ _Result: baseline parameters of the study population with the studied cases were overweight with uncontrolled Diabetes Mellitus II. As compared to controls the cases had high Glycosylated Hemoglobin levels and raised mean serum uric acid levels. Diabetic cases ~27% had high uric acid levels as compared to controls. None of the cases in control group had raised serum uric acid levels. Duration of Diabetes has a direct relationship with the levels of raised uric acid._ _Conclusion: Serum uric acid levels were significantly elevated in Diabetic population. Significant positive correlation between serum uric acid levels and duration of Diabetes Mellitus II was seen._

Keywords: Diabetes Mellitus II, Uric Acid

1. Introduction

Plasma uric acid is the end product of the purine metabolism and is related to the purine bases of the nucleic acids; plasma uric acid levels are genetically determined but are influenced by multiple environmental factors. Several studies have been carried out in various populations in order to study the distribution of plasma uric acid in different ethnic groups and to establish whether an association exists between plasma uric acid and such diseases as clinical gout, diabetes mellitus, coronary heart disease and hypertension[1].Uric acid over-production anddecreased excretion through kidneys lead to hyperuricemiain humans[2].

The prevalence of hyperuricemiain the general population is estimated at about 10–25%.In recent decades, the prevalence of hyperuricemia hasincreased substantially in the world with a rising trendboth in the developed and developing nations[3]. Some studies reported a positive associationbetween elevated Serum Uric Acid (SUA) and diabetes, whereas,other studies reported no correlation, or aninverse relationship[4].A meta-analysis reported an association betweenSUA and increased risk of development of type 2 diabetes (T2D)[5].

International Diabetic Federation data shows that worldDiabetes & Pre-diabetes prevalence in 2007 is 5.7% and7.5% respectively. In India Diabetes mellitus prevalenceranges from 0.4 to 3.9% in rural areas and from 9.3 to 16.6%in urban areas. Diabetes causes long term dysfunction ofvarious organs like heart, kidneys, eyes, nerves and blood1 vessels. Age adjusted mortality rates among diabetics is1.5 to 2.5 times higher than general population. Much ofthis excessive mortality is attributable to cardiovasculardisease[6].With the above background, this study was done to examine theserum level of uric acid in diabetics andcontrols.

2. Material and Methods

Study setting: The study was conducted in MGM Medical College and Hospital, Aurangabad in Department of General Medicine.
Study design: The study was analytical cross sectional study.
Study period: The study was conducted from November 2017 to September 2019.
Sample size: The study has included 145 cases diagnosed with Type 2 diabetes mellitus and 145 healthy controls.

Inclusion criteria
1) Patients with type 2 diabetes mellitus (irrespective of their glycemic status and duration of diabetes and ADA criteria for diabetes).
2) Patient's age > 40 years.
3) Both sexes were included.

Exclusion criteria -
Patients with the following conditions were excluded from the study -
1) Renal failure.
2) On long term diuretics and steroids.
3) Regularly consuming alcohol.
4) On antimetabolite and chemotherapy drugs.
5) Hepatic disorders.
6) Peripheral vascular disease/ cerebrovascular disease/ pulmonary tuberculosis.
7) Renal transplant patients.
8) Pregnancy and lactating mothers

Ethical Approval: Approval taken from Ethical Committee of MGM Hospital.

Study procedure: After informed written consent was obtained, selected data were elicited from the patients and controls and recorded in structured proforma.

Estimation of serum uric acid and various blood parameters as per NABL protocol of MGM laboratory.

Operational definitions-

Diabetes Mellitus [7]
1) FPG -126 mg/dl (7.0 mmol/l). Fasting is defined as no caloric intake for at least 8 h.* OR
2) Symptoms of hyperglycaemia and casual plasma glucose -200 mg/dl (11.1mmol/l). Casual is defined as any time of day without regard to time since last meal. The classic symptoms of hyperglycaemia include polyuria, polydipsia, and unexplained weight loss. OR
3) 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. *

*In the absence of unequivocal hyperglycemia, these criteria were confirmed by repeat testing on a different day Hyperuricemia[8]

Hyperuricemia has been arbitrarily defined as >7.0 mg/dL in men and >6. mg/dL in women.

3. Statistical Analysis

Descriptive analysis of all variables was done using mean and standard deviation for quantitative variables. The categorical variables were compared across the groups by chi square test. P value < 0.05 was considered as statistically significant. IBM SPSS version 21 was used for statistical analysis.

4. Result

1) Comparison of cases and controls with respect to baseline parameters

S.No.	Parameters	Cases (n = 145)		Controls (n = 145)	
		Male (n=87)	Female (n=58)	Male (n=87)	Female (n=58)
1.	Gender				
2.	Mean Age (years)	54±6.7	49±7.9	56 ±8.8	48 ±9.2
3.	Mean BMI	25.11±2.2	26.21±2.8	23.1± 2.5	22.5±3.2
4.	Mean FBS (mg/dl)	176±22	159±35	98.7± 09	102.2±8.8
5.	Mean PBS (mg/dl)	256±39	268±42	139.9± 21	146.7± 24
6.	Mean HbA1c	8.1±3.3	7.9±2.9	5.1± 0.5	4.9± 0.9
7.	Mean Serum Uric Acid (mg/dl)	5.6± 2.1	5.7±1.6	4.4±0.4	4.7±0.5

n= Number of cases, HbA1c – Glycosylated Hemoglobin; BMI – Body Mass Index
FBS – Fasting blood sugar; PBS – Post prandial blood sugar.

The above table shows baseline parameters of the study population with the studied cases were overweight with

uncontrolled Diabetes Mellitus II. As compared to controls the cases had high Glycosylated Hemoglobin levels and raised mean serum uric acid levels.

2) Association between Hyperuricemia and Diabetes Mellitus II.

S. No.	Hyperuricemia	Cases		Controls	
		Male	Female	Male	Female
1.	Positive	23 (26.44%)	16 (27.58%)	0 (0 %)	0 (0 %)
2.	Negative	64 (73.56%)	42 (72.42%)	87 (100%)	58 (100%)
	Total	87 (100%)	58 (100%)	87 (100%)	58 (100%)

The above table shows that in the studied population, Diabetic cases ~27% had high uric acid levels as compared to controls. None of the cases in control group had raised serum uric acid levels.

3) Duration of Diabetes Mellitus type II and Hyperuricemia

Sr. No.	Duration of DM II	Cases		Hyperuricemia	P Value
		Male (n=87)	Female (n=58)		
1.	2-4 years	21	13	4.4±0.3	>0.05
2.	5-8 years	35	27	5.2±0.9	<0.05
3.	>8 yeas	31	28	6.8±1.2	<0.05

n- number of cases; P value >0.05 is non-significant; P value <0.05 significant.

The above table shows as duration of Diabetes Mellitus increases mean values of uric acid increases. Duration of Diabetes has a direct relationship with the levels of raised uric acid.

5. Discussion

Hyperuricemia hasbeen found to be associated with obesity and insulinresistance, and consequently with type2 diabetes. Furtherpotentially important biological effects of uric acid relate toendothelial dysfunction by inducing anti-proliferativeeffects on endothelium and impairing nitric oxideproduction and inflammation, through increased C-reactiveprotein expression, although these issues areconsidered controversial. Uric acid may play a role inimmune activation with subsequent increased chemokine6 and cytokine expression [9],[10].

This is a hospital based case control study including 145 cases of which 87 were male and 58 were female. The study also included matched 145 controls with 87 males and 58 females. The mean age of cases was 54 ± 6.7 years in males and 49 ± 7.9 in females. T. Rao et.al.[9] in their study had 42 males and 28 females with a total of 70 cases, which has a mean age of 59.55 years. BMI in our case is 25.11 ± 2.2 in males and 26.21± 2.8 in females while in study by T. Rao et.al.[9] has 24.38±2.80.

In our study mean FBS was 176±22 mg/dl in males and 159±35 mg/dl in females. While PBS was 256±39 mg/dl in males and 268±42 mg/dl in females. Mean HbA1c in males

was 8.1±3.3 and 7.9±2.9 in females. Mean serum uric acid levels in males is 5.6± 2.1mg/dl and 5.7±1.6 mg/dl in females.The findings were consistent with the findings in the study conducted by T. Rao et.al.[9]which had FBS 102-206 mg/dl and PBS was162-304 mg/dl. Range of Serum Uric acid levels was 3.3-8.2 mg/dl.

The current study has demonstrated that the proportion of subjects with hyperuricemia was much higher in diabetic population 26.44% in males and 27.58% in females and none of the controls had hyperuricemia, which was according to findings of hyperuricemia in a study conducted by Rao et.al. (11.43%)[9]. In their review, Katsiki N. et al.[11] have concluded a strong association between the serum uric acid levels and diabetes and it's complications. Keenan T., et al.[12] have reported increased by Serum urate levels were not associated with T2DM, CHD, ischemic stroke, or HF.

Choi H. K., et al.[13] have evaluated the correlation between gout and the future risk of type 2 diabetes among men with a high cardiovascular risk profile and confirmed that, among men with a high cardiovascular risk profile with gout, there is a higher risk of future risk of type 2 diabetes independent of other known risk factors. These study findings suggest a reverse causality and raises further questions on nature of the association of diabetes, serum uric acid and the diabetes related complications.

In the current study, the mean uric acid level increased from 4.4±0.3 in people with duration diabetes 2 to 4 years to 5.2±0.9 in people with duration of diabetes 5 to 8 years. Among people who had diabetes for 9 to 12 years, the mean uric acid level was 6.8±1.2. The association between duration of diabetes and serum uric acid level was statistically significant.Studies by T. Rao et.al[9],Gagliardi A. C., et al.[14], Javorsky, et al.[15], Kramer C. K., et al.[16] have reported similar association.

6. Conclusion

Serum uric acid levels were significantly elevated in Diabetic population. Significant positive correlation between serum uric acid levels and duration of Diabetes Mellitus II was seen. The uric acid may serve as a potential biomarker of deterioration of glucose metabolism. A large community based prospective study in Indian population is needed to verify the findings and to evaluate multiple factors which are associated with increased uric acid levels.

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