Research Article

"Serum Uric Acid Levels in Type II diabetes Mellitus"

Dr. Sharan A Patil[1] and Dr. M Satya Prathik[1*]

[1]Assistant professor, Department of General medicine, Navodaya medical college, Raichur India

*Corresponding Author
Dr. M Satya Prathik

Abstract: **Objective:** To investigate Serum Uric Acid levels, HbA1c levels in patient's withType II Diabetes mellitus and compare with normal subjects. **Methodology:** The present study is a case control study conducted at Navodaya Medical College Hospital and Research Centre, over a period of 1 year. 100 participants were divided into 2 different groups, Cases and Controls. Cases included 50 patients with Type II Diabetes Mellitus and controls included 50 matched participants who didn't have Type II Diabetes mellitus, both the groups fulfilling the inclusion criteria and exclusion criteria. Serum uric acid, blood sugar levels, HbA1c levels were measured in both controls and patients. **Results:** The serum uric acid levels were low in cases, compared to controls (mean in cases 3.4890 mg/dl compared to 4.8600 mg/dl in controls). The HbA1c levels negatively correlated with serum uric acid, i.e.; as HbA1c increased, serum uric acid levels decreased (p value < 0.001; highly negatively correlated). **Conclusion:** Serum Uric Acid levels were low in patients with Type 2 Diabetes Mellitus, particularly in those who had poor glycemic control. This may be due to increased excretion of serum uric acid during hyperglycemia and glycosuria.
Keywords: Serum uric acid, Type 2 Diabetes Mellitus, HbA1c.

INTRODUCTION:

Diabetes mellitus is a syndrome with disordered metabolism and inappropriate hyperglycemia due to either a deficiency of insulin or to a combination of insulin resistance and inadequate insulin secretion to compensate for the resistance. Uric acid is the end product of purine metabolism in humans. Humans convert the major purine nucleosides, adenosine and guanosine to uric acid through intermediates. It is then excreted unchanged via the renal system and the gastrointestinal system as humans lack the enzyme uricase. Uric acid acts as a pro-oxidant, particularly at increased concentration.

Serum uric acid has been shown to be associated with production of Tumor Necrosis Factor alpha6 (TNF-α), which are both related to the development of diabetes. Uric acid decreases endothelial nitric oxide production and leads to endothelial dysfunction and insulin resistance. Consequently, uric acid induces vascular inflammation and artery damage, which in turn leads to increased risk of diabetes and atherosclerosis. Increased levels of uric acid have been associated with insulin resistance and with established Type II Diabetes Mellitus. The present study was done to study the levels of Serum Uric Acid in Type II Diabetes Mellitus and the correlation between Serum Uric Acid levels and Glycemic control (HbA1c) in Type II Diabetes Mellitus.

AIMS AND OBJECTIVES:

- To compare Serum Uric Acid levels in patients with Type II Diabetes Mellitus to the levels of Serum Uric Acid in controls.
- To correlate Serum Uric Acid levels in patients with Type II Diabetes Mellitus with their Glycemic control (HbA1c).

MATERIALS AND METHODS:
Source of Data:

Patients presenting to Out Patient and In Patient Department, Department of General Medicine with Type II Diabetes Mellitus at Navodaya Medical College Hospital & Research Centre, Raichur.

Study Subjects:

100 subjects presenting to the Department of General Medicine were randomly taken and divided into two groups, each comprising of 50 subjects each.

Quick Response Code

The first group consisted of 50 subjects who had Type II Diabetes Mellitus and fulfilled the inclusion and exclusion criteria as discussed below. They were labeled as cases.

The second group comprised of 50 subjects, who were matched to the subjects in the first group and fulfilled the inclusion and exclusion criteria. The subjects belonging to the second group did not have Type II Diabetes Mellitus. They were labeled as controls.

Study Period:
The study was performed for a period of one year.

Inclusion Criteria:
- Individuals in the age group 20-70 years suffering from Type II Diabetes Mellitus, which is defined as fasting glucose concentration ≥ 126mg/dl.
- Includes both men and women.
- Diagnosed Type II Diabetes Mellitus patients taking oral hypoglycaemic medications or insulin for treatment.

Exclusion Criteria
- Individuals having Type I Diabetes Mellitus.
- Diagnosed hypertensive individuals.
- Individuals known to have cardiovascular disease.

- Individuals who had stroke.
- Patient with pre-existing renal disease.
- Individuals with dyslipidemia.
- Individuals diagnosed as suffering from gout.
- Patients on drugs which alters serum uric acid levels.
- All other conditions which alter the levels of serum uric acid.

Investigations:
Complete Blood Picture, Peripheral Smear, Random Blood Sugar, Complete Urine Exam, Fasting Blood Sugar, Post Prandial Blood Sugar, Serum Creatinine, Serum Uric Acid, Blood Urea, HbA1c, Electrocardiogram, Echocardiogram, Ultrasonogram Abdomen & Pelvis.

RESULTS:
Our study included a total of 100 subjects, of which 50 were cases and 50 were controls. The various parameters were evaluated and then compiled. The results were then analysed using the SPSS v 16.0 software at Department of Social and Preventive Medicine. 100 subjects participated in the study of which 55 were male and 45 female. The group comprising of cases had 50 subjects of which 27 were male and 23 were female. The group consisting of controls had 28 males and 22 females. This has been depicted in the table and graph below.

TABLE-1: Sex-wise distribution of the cases and controls.

	CASES		CONTROL		TOTAL	
	Number	%	Number	%	Number	%
MALE	27	54	28	56	55	55
FEMALE	23	46	22	44	45	45
TOTAL	50	100	50	100	100	100

The study included subjects whose age was between 20 and 70 years. There were 7 subjects who fell into the age group of 32 to 41 years, 12 fell in the age group of 42 to 51 years, 19 in the age group 52 to 61, 12 in the age group 62 to 71 amongst the cases. 6 subjects were in age group 32 to 41, 15 in the age group 42 to 51, 16 in the age group 52 to 61, 13 in the age group 62 to 71 amongst the control. Overall 13 patients fell in the age group 32 o 41, 27 in the age group 42 to 51, 35 in the age group 52 to 61 and 25 in the group 62 to 71. People of the age group 52 to 61 were the most [19 in cases, 16 in controls and 35 overall].

**TABLE-2: Age-wise distribution of the cases and controls.**

AGE	CASES		CONTROL		TOTAL	
	Number	%	Number	%	Number	%
32-41	7	14	6	12	13	13
42-51	12	24	15	30	27	27
52-61	19	38	16	32	35	35
62-71	12	24	13	26	25	25
TOTAL	50	100	50	100	50	100

The range for serum uric acid in cases was 2.21 mg/dl to 4.6md/dl. In Diabetic females the range was 2.21 mg/dl to 4.5 mg/dl. In diabetic males the range was 2.6mg/dl to 4.6 mg/dl. The serum uric acid in cases ranges from 2.21 mg/dl to 4.6 mg/dl. The range in female cases was 2.21 mg/dl to 4.5 mg/dl. The range in male cases was 2.6 mg/dl to 4.6 mg/dl. The range of serum uric acid in controls was 3.5 mg/dl to 7 mg/dl. The range in female controls was 3.5 mg/dl to 7 mg/dl. The range in males was 3.7 mg/dl to 6.4mg/dl. The serum uric acid in controls ranged from a low of 3.5 mg/dl to a high of 7 mg/dl. While hyperuricemia (serum uric acid > 7 mg/dl) was not seen in any of the controls, 3 subjects had a serum uric acid value more than 6.1

mg/dl. The mean serum uric acid in cases was 3.4mg/dl where as the mean serum uric acid in controls was 4.86

mg/dl. The mean serum uric acid in males (cases) was 3.5 mg/dl and in females (cases) was 3.4 mg/dl.
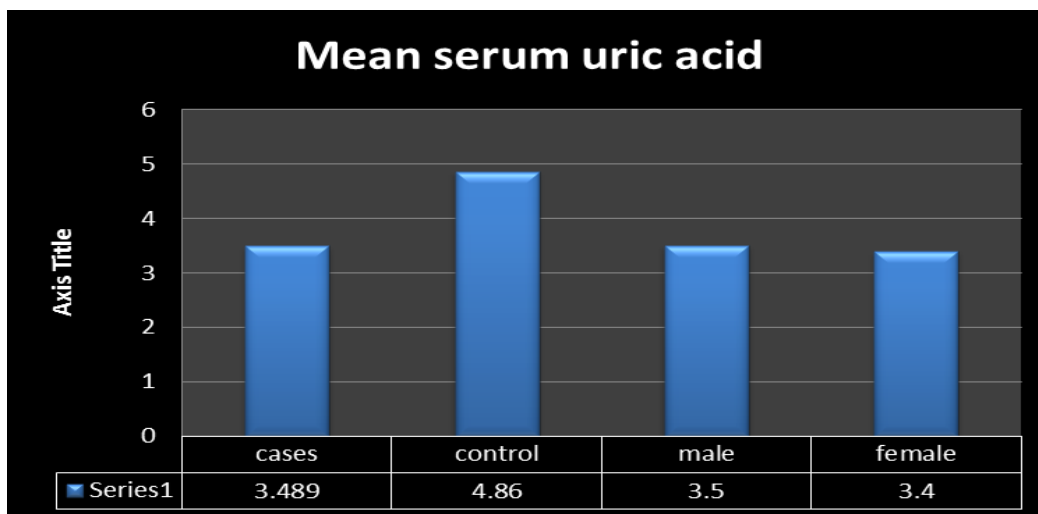
GRAPH-1: Graph showing mean serum uric acid levels in cases, control, male and females.

The *Mean Fasting Blood Glucose* in cases was 220 mg/dl, controls 79.04 mg/dl. The *Mean Post Prandial Blood Glucose* in cases was 322.5 mg/dl, controls was 91.22 mg/dl. The *Mean Random Blood Glucose* in cases was 270.44 mg/dl and in controls was 84.98 mg/dl. The *Mean HbA1c* in cases was 9.06% and that in controls was 5.016%.Mean HbA1c in cases was 9.066%; compared to mean serum uric acid which was 3.489 mg/dl. Mean HbA1c in controls was 5.016%; compared to mean serum uric acid which was 4.86 mg/dl. The *Pearson Correlation Co-Efficient* was calculated to check the relation between Serum Uric Acid and HbA1c. It was deduced that HbA1c in cases negatively correlated with Serum Uric Acid. The *p value* of the statistical analysis was *< 0.001* and it was statistically significant.

DISCUSSION:

The present study was done to evaluate the significance of uric acid and to assess the correlation between Serum Uric Acid and Glycemic Control in patients with uncomplicated Type II Diabetes Mellitus. A total number of 100 patients were studied during the period of one year at Navodaya Medical college Hospital and Research Centre, Raichur. The study included 50 cases who were diagnosed cases of Type II Diabetes Mellitus (uncomplicated), 50 controls who were not cases of Type II Diabetes Mellitus, but were matched to cases in, respect of the exclusion criteria. Various parameters that were assessed were: Fasting Blood Sugar, Post Prandial Blood Sugar, Random Blood Sugar, HbA1c and Serum Uric Acid. The mean HbA1c in cases was 9.06% and that in controls was 5.016%. The HbA1c ranged from 6% to 14.4% in cases. The HbA1c ranged from 4% to 6% in controls. The mean serum uric acid in cases was 3.4mg/dl and in controls was 4.86 mg/dl. The range of serum uric acid in controls was 3.5 mg/dl to 7 mg/dl. The serum uric

acid in cases ranges from 2.21 mg/dl to 4.6 mg/dl. Mean HbA1c in cases was 9.066%; compared to mean serum uric acid which was 3.489 mg/dl. Mean HbA1c in controls was 5.016%; compared to mean serum uric acid which was 4.86 mg/dl.

According to the study serum uric acid levels were low in cases (2.21 mg/dl to4.6 mg/dl) compared to controls (3.5 mg/dl to 7 mg/dl). It also shows that HbA1c was *negatively correlating* with serum uric acid levels in cases and controls; i.e.; as the HbA1c levels increased the serum uric acid levels decreased. A large prospective study in Israel by Herman & Goldbourt[1], which had 10000 men aged 40 years and over. It was shown that pre-diabetic subjects had higher uric acid levels than non-diabetics, and that overt diabetics had lower uric acid levels than non-diabetics. Their finding of a negative association between serum glucose and uric acid concentrations is similar to or study as shown. However they were not able identify the cause of hypouricemia in their case study. Dr S R Meena and Dr Ramawatar Meena[2], of Kota Rajasthan performed a similar study over 100 patients, which included 50 cases and 50 controls. The cases include 40 patients with Type II diabetes Mellitus and 10 with impaired glucose tolerance. Their study showed that serum uric acid was lower in patients in the diabetic group when compared with controls. Serum uric acid was 3.32 ± 0.882 in diabetic group compared to 4.74 ± 1.51 in controls which was statistically significant (p value < 0.001). They concluded that Serum uric acid concentration is slightly reduced in patients with Type II Diabetes Mellitus and this may be due to increased excretion of uric acid during hyperglycemia and glycosuria. A study was performed by S. Bo *et al*., in Italy, to evaluate the relation between uric acid and metabolic parameters, creatinine clearance and albumin excretion rate in a cohort of Type II Diabetic patients.

They showed that hypouricemia in Type II Diabetes Mellitus is associated with worse metabolic control, hyperfilteration and a late onset or decreased progression to overt nephropathy[3]. Derek G. Cook *et al.*, in their study showed that at higher levels of glucose, serum uric acid decreased[3]. The relationships between serum uric acid, serum glucose and diabetes were examined in a survey of 7735 middle-aged men drawn at random from general practices in 24 British towns. There was a positive relationship between serum glucose and serum uric acid concentrations up to about 8.0 mmol/l; at higher levels of glucose, serum uric acid decreased. It probably reflects the biochemical interaction between serum glucose and purine metabolism, with increased excretion of uric acid during hyperglycaemia and glycosuria.

A study done in Japan, also shows that diabetes mellitus is associated with hypouricemia. It was a large cross-sectional study reporting the gender specificity of age-related prevalence of hypouricemia, and its association with reduced kidney function in the general Japanese population. Subgroup analyses stratified by diabetic status were performed by the researchers, because diabetes mellitus is reportedly associated with both hypouricemia and hyperuricemia. Point estimates of the odds ratio of hypouricemia were similar in those with and without diabetes compared with the entire study population (men without diabetes; 1.81, 95% CI, 1.17-2.80; men with diabetes; 1.88, 95% CI, 0.68-5.20; women without diabetes; 0.62, 95% CI, 0.43-0.89; women with diabetes; 0.49, 95% CI, 0.12-2.05), although the association was not significant in participants with diabetes due to the small sample size They concluded that serum uric acid is often low due to the effects of glycosuria on increased uric acid excretion in diabetes8. H. K. Choi[4] using data from 14,664 participants aged 20 yrs and older in The US Third National Health and Nutrition Examination Survey, examined the relation between the levels of HbA1c, other biomarkers and serum uric acid levels using multivariate linear regressions stratified by gender. The serum uric acid levels increased with increasing serum HbA1c levels up to the category of 6 - 6.9 %, and thereafter decreased with further increasing HbA1c levels (a bell-shaped relation). Individuals with diabetes showed lower serum uric acid levels and the association was larger among men (*P*-value for interaction, 0.007). They concluded that HbA1c, fasting blood sugar levels are inversely related with serum uric acid levels, is thought to be due to the uricosuric effect of glycosuria, which occurs when the blood glucose level is greater than ~10 mmol/l (180 mg/dl). N. Esparza Martín *et al.*, reported that patients with diabetes mellitus may have hypouricemia. This is observable in both Type I, Insulin-Dependent Diabetes Mellitus patients and in Type II, Non-Insulin-Dependent patients. This reduction in plasma uric acid is due to an increase in its renal clearance83. Shichiri M. *et al.*, 84 studied the possible association of the low

serum uric acid level with incipient diabetic nephropathy in non-insulin-dependent diabetes mellitus (NIDDM) 77. Of 201 NIDDM patients without a diminished glomerular filtration rate, 66 patients (32.8%) showed moderate hypouricemia of less than the mean -1 SD of 201 non-diabetic controls. Thirteen subjects (6.5%) showed marked hypouricemia of less than the mean -2 SD. They hypothesize that glomerular hyperfilteration occurs in NIDDM and that it lowers the serum uric acid by increasing the renal clearance of urate. Hypouricemia may also predict the future progression of incipient nephropathy in NIDDM. Thus it can be concluded that as shown in our thesis Serum Uric Acid and HbA1c have an inverse relation. This is possibly due to increased Glucose in the nephrons, which impairs the reabsorption of Uric Acid and thereby causing decreased levels of Serum Uric Acid when compared to the controls. Our study also correlates with various other studies which also show decreased Serum Uric Acid levels when compared to controls in uncomplicated Type II Diabetes Mellitus.

CONCLUSION:
Based On The Study It Can Be Concluded That:
- Serum uric acid in patients with Type II Diabetes Mellitus is influenced by level of glucose.
- Serum Uric Acid negatively correlated with HbA1c levels.
- The poorer the glycemic control, the lower the serum uric acid.
- Serum Uric Acid can be used as a marker of glycemic control in uncomplicated Type II Diabetes Mellitus.
- Patients with Type 2 Diabetes Mellitus should be regularly monitored for glycemic control with blood investigation such as Fasting Blood Sugar, Post Prandial Blood Sugar, Random Blood Sugar, and HbA1c, to prevent microvascular and macrovascular complications.
- Along with these investigations Serum Uric Acid levels should be monitored in patients with Type II Diabetes Mellitus to check the disease progression

REFERENCES:
1. Jeppsson, J. O., Kobold, U., Barr, J., Finke, A., Hoelzel, W., Hoshino, T., ... & Thienpont, L. (2002). Approved IFCC reference method for the measurement of HbA1c in human blood. *Clinical chemistry and laboratory medicine*, *40*(1), 78-89.
2. Miedema, K. (2004). Towards worldwide standardisation of HbA1c determination. *Diabetologia*, *47*(7), 1143-1148.
3. Zhao, Y., Yang, X., Lu, W., Liao, H., & Liao, F. (2009). Uricase based methods for determination of uric acid in serum. *Microchimica Acta*, *164*(1-2), 1-6.
4. Herman, J., & Goldbourt, U. (1982). Uric acid and diabetes: observations in a population study. *The Lancet*, *320*(8292), 240-243.

5. Meena, R., & Meena, S. (2016). Plasma Uric Acid Levels in Patients with Diabetes Mellitus and Impaired Glucose Tolerance Test in Comparison with Normal Subjects. *International Journal of Science and Research*, *5*(2), 2090-2093.

6. Bo, S., Cavallo-Perin, P., Gentile, L., Repetti, E., & Pagano, G. (2001). Hypouricemia and hyperuricemia in type 2 diabetes: two different phenotypes. *European journal of clinical investigation*, *31*(4), 318-321.

7. Cook, D. G., Shaper, A. G., Thelle, D. S., & Whitehead, T. P. (1986). Serum uric acid, serum glucose and diabetes: relationships in a population study. *Postgraduate medical journal*, *62*(733), 1001-1006.

8. Wakasugi, M., Kazama, J. J., Narita, I., Konta, T., Fujimoto, S., Iseki, K., ... & Kimura, K. (2015). Association between hypouricemia and reduced kidney function: a cross-sectional population-based study in Japan. *American journal of nephrology*, *41*(2), 138-146.

9. Choi, H. K., & Ford, E. S. (2008). Haemoglobin A1c, fasting glucose, serum C-peptide and insulin resistance in relation to serum uric acid levels—the Third National Health and Nutrition Examination Survey. *Rheumatology*, *47*(5), 713-717.

10. Esparza Martin, N., & García Nieto, V. (2011). Hypouricemia and tubular transport of uric acid. *Nefrología (English Edition)*, *31*(1), 44-50.

11. Shichiri, M., Iwamoto, H., & Marumo, F. (1990). Diabetic hypouricemia as an indicator of clinical nephropathy. *American journal of nephrology*, *10*(2), 115-122.