

A Study of Serum Uric Acid Levels And Its Correlation With Blood Glucose And eGFR in Type 2 Diabetes Mellitus Patients At A Rural Tertiary Care Centre In Kolar

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ABSTRACT

Background: Hyperuricemia is associated with type 2 diabetes mellitus. But there are studies that found that the levels of uric acid are low in cases of diabetes mellitus. Comparative studies related to serum uric acid levels with eGFR and blood glucose in type 2 diabetes mellitus is less. Hence the study was undertaken to study the serum uric acid levels and its correlation with blood glucose and eGFR in type 2 diabetes mellitus.

Materials & Methods: 40 diagnosed cases of type II diabetes mellitus and 40 healthy controls were studied.

Results: The mean uric acid levels were 4.5 ± 1.1 in cases and 4.6 ± 1.1 in controls, which was not statistically significant. Significant negative correlation was found between uric acid (0.006) and eGFR in both cases and controls. Significant positive correlation was found between FBS ($p = 0.005$) and PPBS ($P = 0.04$) with the eGFR in cases and between FBS and PPBS in cases and controls. Uric acid correlation with FBS and PPBS is not significant in both cases and controls.

Conclusion: our study shows uric acid levels are towards lower reference limits in type 2 diabetes mellitus when compared to controls.

Key words: eGFR, FBS, PPBS, uric acid

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INTRODUCTION

Uric acid is the end product of purine metabolism. Its normal range is 2.5 - 7.5 mg/dl. There has been a growing interest in the association of hyperuricaemia with hyperglycemia.^[1-3]

Hyperuricemia causes gout and renal insufficiency (gouty nephropathy).^[4] Uric acid is a marker for cardiovascular disease and has been implicated in development of metabolic syndrome because it has paradoxical action. It

acts as an antioxidant at physiological levels but shows a pro-oxidant property while the levels are elevated⁵. Hyperuricemia has been found to be associated with obesity and insulin resistance, and consequently 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] But Nan et al have indicated low levels of uric acid in diabetes mellitus.^[8] This study was undertaken to find the levels of serum uric acid in type 2 diabetes mellitus and to compare it with eGFR and blood glucose.

OBJECTIVES

The objectives of the study were

- 1) To know the serum uric acid levels in type 2 diabetes mellitus in our study population.
- 2) To correlate the levels of uric acid with blood glucose and eGFR in type 2 diabetes mellitus.

MATERIAL & METHODS

This was a Case-Control study conducted at RL Jalappa Hospital and Research Center, Kolar during the period from October to December 2011. Data of 40 patients more than 18 years of age visiting diabetology OPD with type 2 diabetes mellitus were included as cases and 40 healthy subjects as controls. Both the cases and controls were age and sex matched. Patients with stage IV and V kidney disease and patients on drugs affecting uric acid levels are excluded from the study.

All the study population were asked to

come for sample collection after overnight fasting and the blood was collected in fluoride and plain tubes for blood glucose and other parameters respectively. Serum was separated after centrifugation and analysed.

Parameters estimated were FBS, PPBS by GOD-POD method, Serum Creatinine by Jaffe's method and Serum Uric Acid by enzymatic method. All parameters were analysed in Johnson & Johnson VITROS 250 dry chemistry analyser.

eGFR was calculated using MDRD (Modification of Diet in Renal Disease) formula.
$$eGFR = 175 \times \text{Serum Creatinine}^{-1.154} \times \text{Age}^{-0.203} \times [1.212 \text{ if black}] \times [0.742 \text{ if female}]^9$$

The results were obtained and values were tabulated. An Independent t test was done to compare between the cases and controls. Pearson's correlation was done to know the correlation between the uric acid with blood glucose and eGFR.

RESULTS

The mean uric acid levels were found to be 4.5 ± 1.1 in cases and 4.6 ± 1.1 in controls (fig.1). This difference was not statistically significant.

The mean eGFR levels were found to be 98.90 ± 26.01 in cases and 97.55 ± 24.03 (table 1). This difference was not statistically significant.

Significant negative correlation was observed between uric acid ($p = 0.006$) and eGFR in both cases and controls (fig. 2).

Significant positive correlation was found between FBS ($p = 0.005$) and PPBS ($p = 0.04$) with the eGFR in cases and controls (fig. 3).

DISCUSSION

Type 2 diabetes mellitus patients have insulin resistance. Higher levels of serum insulin may decrease uric acid clearance by kidneys causing hyperuricemia, the mechanisms behind this association remains obscure. The most conceivable hypothesis is that this occurs at the renal level. Renal tubular function is influenced by hyperinsulinemia, and urinary uric acid clearance decreases with decreasing insulin-mediated glucose disposal. Thus, decreased uric acid excretion leads to hyperuricemia.^[10,11]

Hyperuricemia induces endothelial dysfunction which results in nephropathy in type 2 diabetes mellitus patients.^[7] Study done by Tseng also says even mild hyperuricemia will result in kidney injury.^[12]

In this study, we observed uric acid levels towards lower reference limit in type 2 diabetes mellitus. Uric acid levels was less in cases compared to controls but it was not statistically significant. In a study done by Cook et al, they found a positive relationship between serum glucose and serum uric acid concentrations up to about 8mmol/l glucose and a decrease in serum uric acid there after.^[13] Herman et al found the same results in a population based study.^[14,15]

This finding contradicts the results of the studies which shows hyperuricemia is associated with type 2 diabetes mellitus.^[5,7]

Our study shows negative correlation of serum uric acid levels with FBS and PPBS in cases, but it was not statistically significant. Studies have shown that diabetic patients have higher uric acid clearance and serum uric acid level was lower than in normal subjects. Their

analysis showed that diabetic patients had increased fractional excretion of uric acid.^[16,17]

Another finding in our study is that uric acid and eGFR are negatively correlated in both cases and controls which is statistically significant. So when the levels of uric acid increases in the diabetic patients, the eGFR decreases and this relation is statistically significant. This shows that hyperuricemia induced endothelial dysfunction in kidney may lead to diabetic nephropathy. Once changes of nephropathy sets in, it may lead to increase in serum uric acid levels in diabetes mellitus indicating the kidney damage is in progress.

Another observation noted in the study was a positive correlation existing between plasma glucose levels (FBS & PPBS) with eGFR as shown in figure 3. This occurrence may be due to the development of hyperfiltration of glomerulus during the early diabetes, which at later stages is known to decrease eGFR with development of nephropathy changes.^[18,19,20]

Hence along with eGFR and other routine markers, uric acid measurement could aid in knowing the functional status of the kidneys in type 2 diabetes mellitus patients.

CONCLUSION

The tendency of occurrence of uric acid levels at the lower reference limits in cases of type 2 diabetes mellitus reflects the initiation of nephropathy changes.

Along with eGFR and other routine markers, uric acid measurement could aid in knowing the functional status of the kidneys in type 2 diabetes mellitus patients.

Table 1: Mean values of parameters of cases and controls

<i>Parameters</i>	<i>Cases</i>	<i>Controls</i>	<i>p Value</i>
FBS (mg/dl)	154.72 \pm 65.53	77 \pm 12.72	<0.0001*
PPBS (mg/dl)	285.88 \pm 81.50	120 \pm 21.48	<0.0001*
Serum Creatinine(mg/dl)	0.81 \pm 0.18	0.83 \pm 0.20	0.5
eGFR (ml/min/1.73m ²)	98.90 \pm 26.01	97.55 \pm 24.03	0.8
Serum Uric Acid (mg/dl)	4.5 \pm 1.11	4.6 \pm 1.15	0.9

* Significant

Table 2: Pearson's correlation of uric acid with other parameters in cases

<i>Parameters</i>	<i>Uric acid</i>	
	<i>r Value</i>	<i>p Value</i>
FBS	- 0.254	0.1
PPBS	-0.202	0.2
eGFR	-0.430	0.006*

* Statistically significant correlation

Table 3: Pearson's correlation of uric acid with other parameters in controls

<i>Parameters</i>	<i>Uric acid</i>	
	<i>r Value</i>	<i>p Value</i>
FBS	0.122	0.45
PPBS	0.020	0.9
eGFR	-0.473	0.002*

* Statistically significant correlation

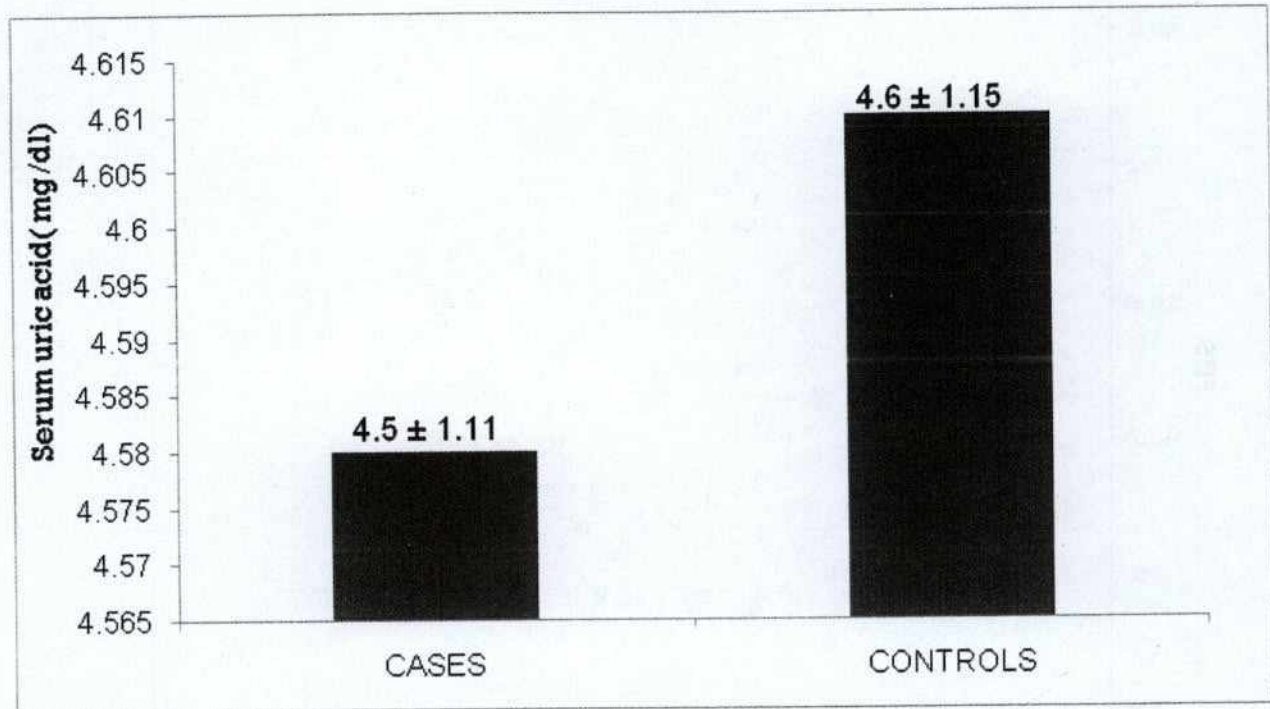


Figure 1: Comparison of uric acid between cases and controls

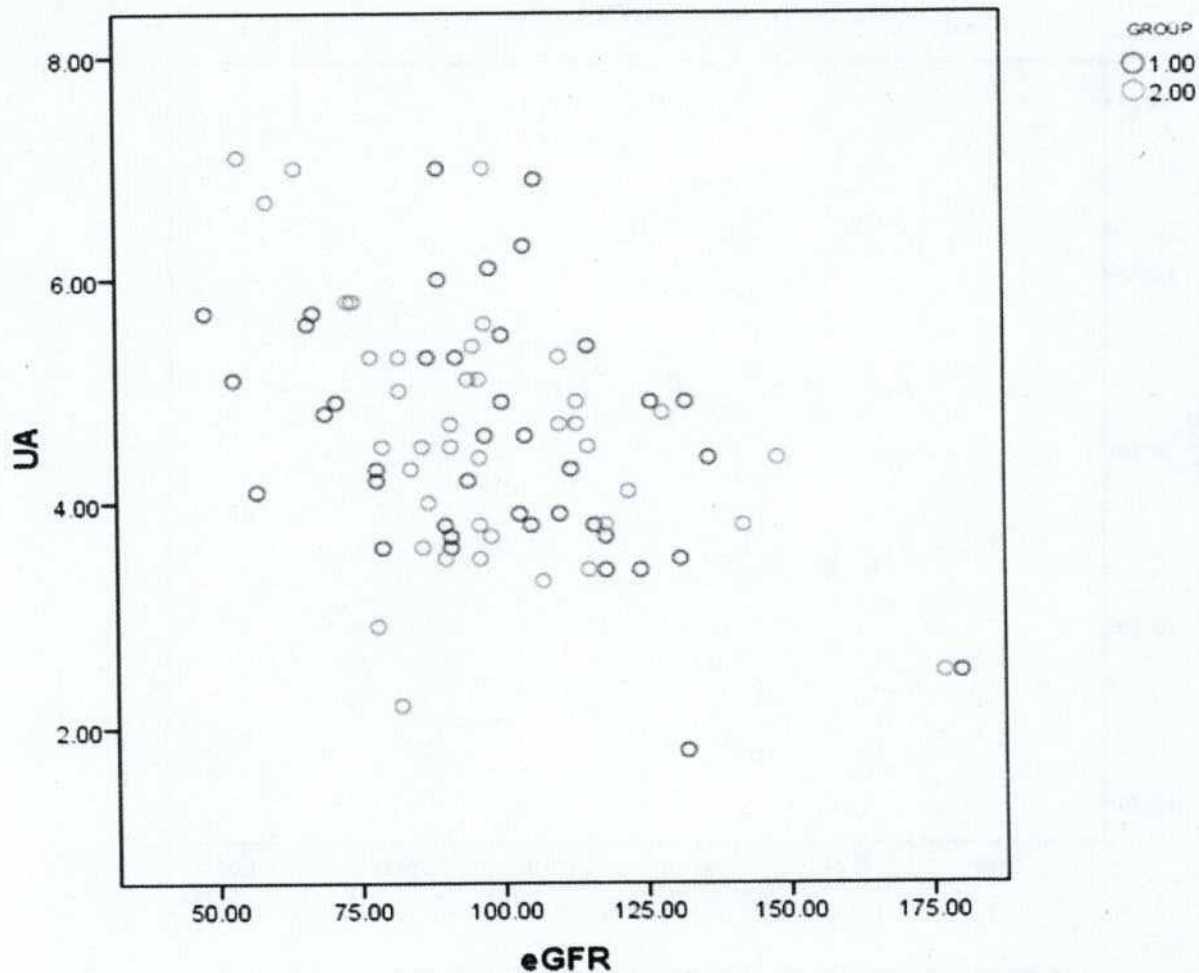


Figure 2: Correlation of uric acid and eGFR in cases and controls

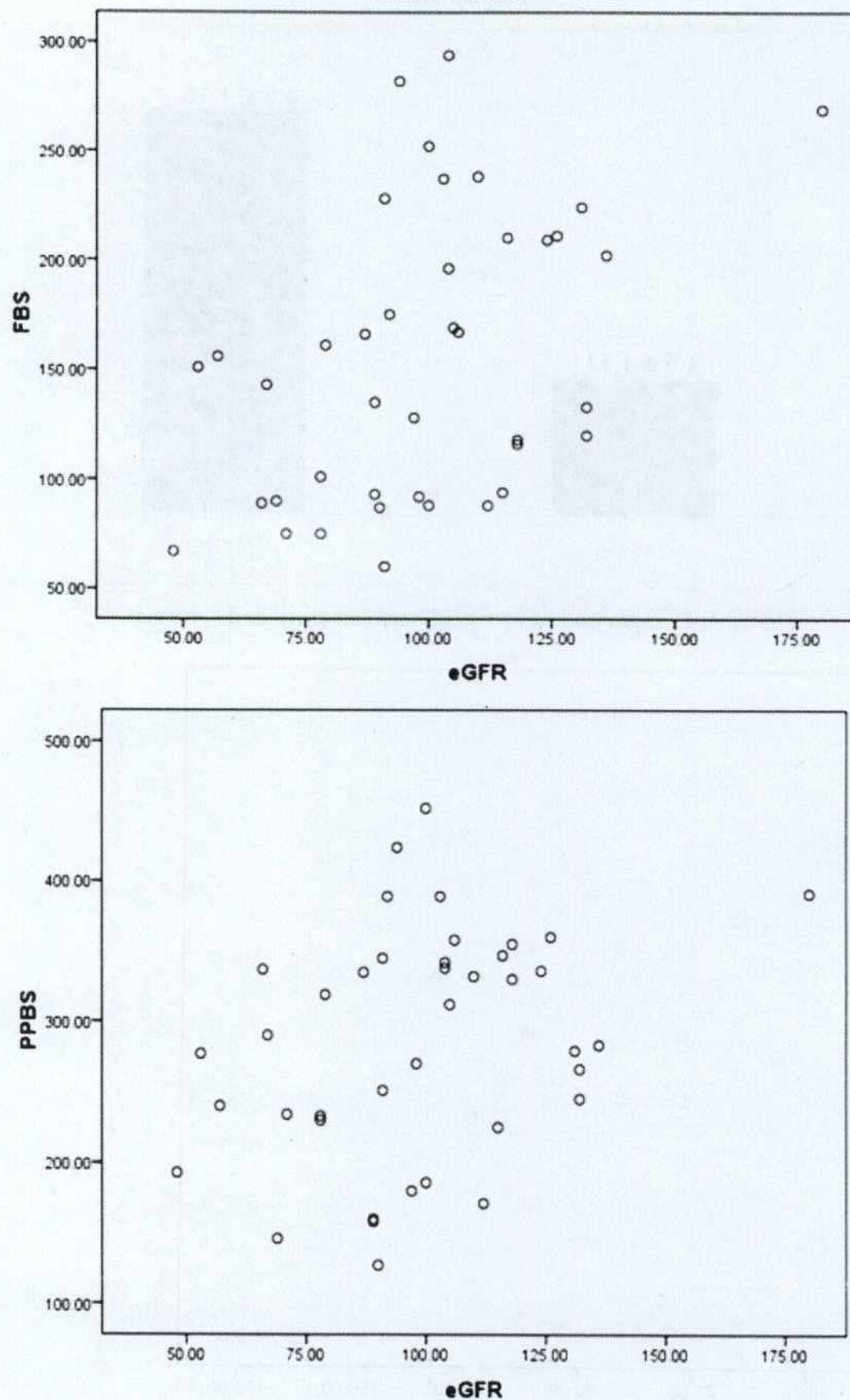


Figure 3: Correlation of FBS and PPBS with eGFR in cases:

ACKNOWLEDGMENT

- 1) Dr. DeepthiKiran, Assistant Professor, Department of Community Medicine, SDUMC, Kolar.
- 2) Dr. Harish R, Post graduate student, Department of Biochemistry, SDUMC, Kolar for the technical and statistical assistance.

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Source of Support: Nil Conflict of Interest: Nil
