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Original Research Article

A Cross Sectional Study of Serum Uric acid with Urine Albumin and Serum Creatinine in type 2 Diabetes Mellitus Patients at SMS Medical College and Attached Hospital, Jaipur

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Abstract

Background: Diabetes is a major worldwide health problem, leading to markedly increased mortality and serious morbidity. Type 2 DM is the most common form of DM characterized by hyperglycemia, insulin resistance, and relative insulin deficiency. This study was done to evaluate the level of serum uric acid in type 2 Diabetes mellitus patients and to correlate the parameters of diabetic nephropathy like albuminuria and serum creatinine levels with uric acid.

Aims & Objectives: The aim of the study was to compare Serum Uric acid with Serum Creatinine and Urine Albumin levels in Diabetes Mellitus patients and find association between them**.**

Methods: This study was a cross sectional study in which clinically diagnosed cases of Diabetes mellitus from OPD of department of Endocrinology, S.M.S. Medical College and Hospital, Jaipur were taken as cases.

Results: 100 cases of Type 2 Diabetes mellitus above the age of 18 were analyzed in this study. The Mean Uric Acid levels in cases with Urine Albumin < 30 mg/24h, Urine Albumin 30-300 mg/24h and Urine Albumin > 300 mg/24h was 5.27 ± 1.25 mg/dl, 8.27 ± 1.63 mg/dl, and 12.76 ± 1.76 mg/dl respectively. These values were statistically significant after applying ANOVA test (p value <0.00001 and f ratio = 62.45). There was statistically significant Positive correlation Serum Uric acid & Urine albumin (r = 0.8126 and p < 0.0001). Mean Uric Acid levels in cases with Serum Creatinine < 1.2 mg/dl was 7.47 ± 1.95 mg/dl and with Serum Creatinine > 1.2 mg/dl was 9.32 ± 2.46 mg/dl. These values were statistically significant after applying Student T test (p value 0.000045) and also statistically significant Positive correlation Serum Uric acid & Serum Creatinine was seen (r = 0.3172 and p value = 0.001302).

Conclusion: The levels of serum uric acid and microalbuminuria are significantly correlated in nephropathy in Type-2 diabetic patients. There was also significant correlation between Serum Uric acid and Serum Creatinine. Hence Serum uric acid level can not only be used as early diagnostic marker but also for the prognostic monitoring of diabetic nephropathy.

Keywords: Diabetes Mellitus, Uric acid, Urine albumin.

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Introduction

Diabetes is a major worldwide health problem, leading to markedly increased mortality and serious morbidity. India had 32 million diabetic patients in the year 2000 and this number would increase to 80 million by the year 2030.[1]

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Type 2 DM is the most common form of DM characterized by hyperglycemia, insulin resistance, and relative insulin deficiency.[2] Several distinct types of DM are caused by a complex interaction of genetics and environmental factors.[3,4] Depending on the etiology of the DM, factors contributing to hyperglycemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system.

Glucose tolerance can be assessed using the fasting plasma glucose (FPG), the response to oral glucose challenge, or the hemoglobin A1C (A1C). An FPG <5.6 mmol/L (100 mg/dL), a plasma glucose <140 mg/dL (11.1 mmol/L) following an oral glucose challenge, and an A1C <5.6% are considered to define normal glucose tolerance. The International Expert Committee with members appointed by the American Diabetes Association, the European Association for the Study of Diabetes and the International Diabetes Federation has issued diagnostic criteria for DM[5] as:

- Symptoms of diabetes plus random blood glucose concentration 11.1 mmol/L (200 mg/dL) or
- Fasting plasma glucose 7.0 mmol/L (126 mg/dL) or
- A1C > 6.5% or
- Two-hour plasma glucose 11.1 mmol/L (200 mg/dL) during an oral glucose tolerance test.

Tests for screening and diagnosis of DM are readily available. The earliest detectable abnormality of nephropathy is microalbuminuria followed by decrease in glomerular filtration rate (GFR) and increase in serum creatinine concentrations.[6] Recent observations suggest that uric acid is an element which may lead to inflammation and may play a pivotal part in endothelial dysfunction and results in the development of Diabetic Nephropathy. Therefore, this study was done to evaluate the level of serum uric acid in type 2 Diabetes mellitus patients and to correlate the parameters of diabetic nephropathy like albuminuria and serum creatinine levels with uric acid in type 2 Diabetes mellitus subjects so as to formulate the role of these parameters in prognosis and evaluation in the pathogenesis of Type 2 DM.

Materials and Methods

This study was a Hospital based comparative observational study in the Department of Biochemistry and Central Lab and Department of Endocrinology, S.M.S. Medical College and Hospital, Jaipur. The Study Design was a Cross sectional study done from Jan 2019 to Nov 2020.

All diagnosed type 2 DM patients who fulfill the inclusion criteria were selected from OPD patients at Department of Endocrinology, SMS hospital JAIPUR. Patients with age more than 18 years with diagnosis of type 2 Diabetes mellitus and who gave consent were included in the study. However, Patients with renal failure and creatinine levels >1.5 mg/dl, By MDRD Formula **[**GFR (mL/min/1.73 m^2) = $175 \times (S_{cr})^{-1.154} \times (Age)^{-0.203} \times$ (0.742 if female)**]**, Renal stones, Liver disease and those taking drugs affecting renal function and uric acid level were excluded from the study.

Statistical Analysis: Sample Size was calculated at 95% of confidence level and error of assuming 65% of Type 2 DM patients having More than 7.4 /dl as per seed Article. At an absolute allowable error of 10% the equal sample for the size in 91 cases which can be rounded of to 100 as final size. Quantitative data expressed in the form of Mean ± SD and inference was drawn with the use of appropriate statistical test. Samples were analyzed on fully automated analyzer Beckman Coulter AU-680.

Results

The characteristics of the studied population, including age, the mean levels of blood sugar and HBA1c are shown in Table 1.

Table 1: Statistical Indices of the study

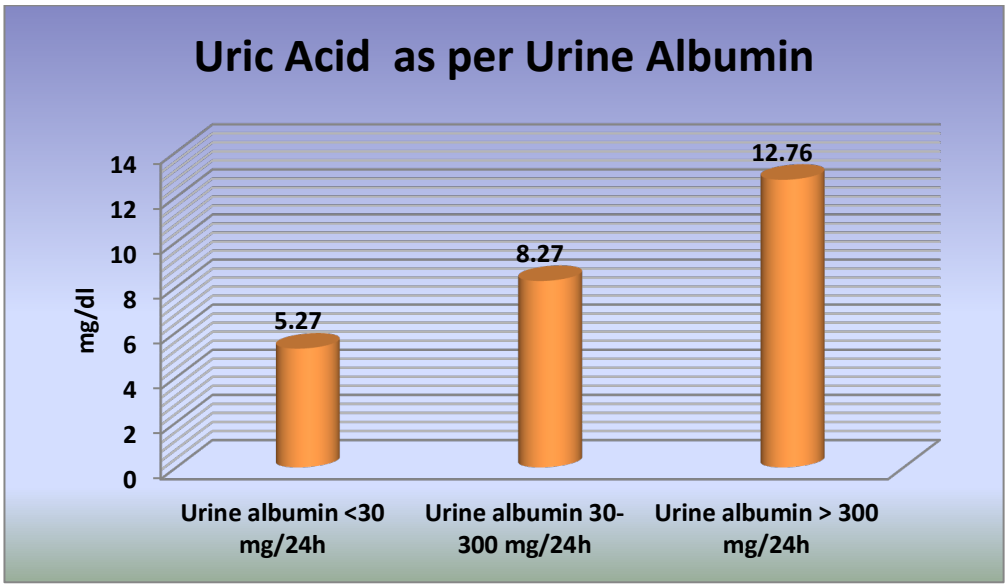
Test/ Parameters	No. of Cases	Result
Age (years)	100	51.7 ± 7.52
Fasting Blood Glucose (mg/dl)	100	179.2 ± 41.94
Post Prandial Glucose (mg/dl)	100	252.7 ± 51.49
HBA1C (%)	100	9.2 ± 1.78
Uric Acid (mg/dl)	100	8.51 ± 2.42
Urine Albumin (mg/24h)	100	155.0 ± 97.68
Serum Urea (mg/dl)	100	30.3 ± 11.32
Serum Creatinine (mg/dl)	100	1.17 ± 0.24

URIC ACID & URINE ALBUMIN: The Mean Uric Acid levels in cases with Urine Albumin < 30 mg/24h, Urine Albumin 30-300 mg/24h and Urine Albumin > 300 mg/24h was 5.27 ± 1.25 mg/dl, 8.27 ± 1.63 mg/dl, and 12.76 ± 1.76 mg/dl respectively. These values were statistically significant after applying ANOVA test (p value <0.00001 and f ratio = 62.45).(Table 2, Graph 1)

Table 2: Uric Acid variation with Urine Albumin

Test/ Parameters	**Urine albumin <30 mg/24h**	**Urine albumin 30-300 mg/24h**	**Urine albumin > 300 mg/24h**	**P value**	**F ratio**
Number of cases	10	78	12		
Uric Acid (mg/dl)	5.27 ± 1.25	8.27 ± 1.63	12.76 ± 1.76	< .00001 (S)	62.45

*P value obtained after applying ANOVA TEST



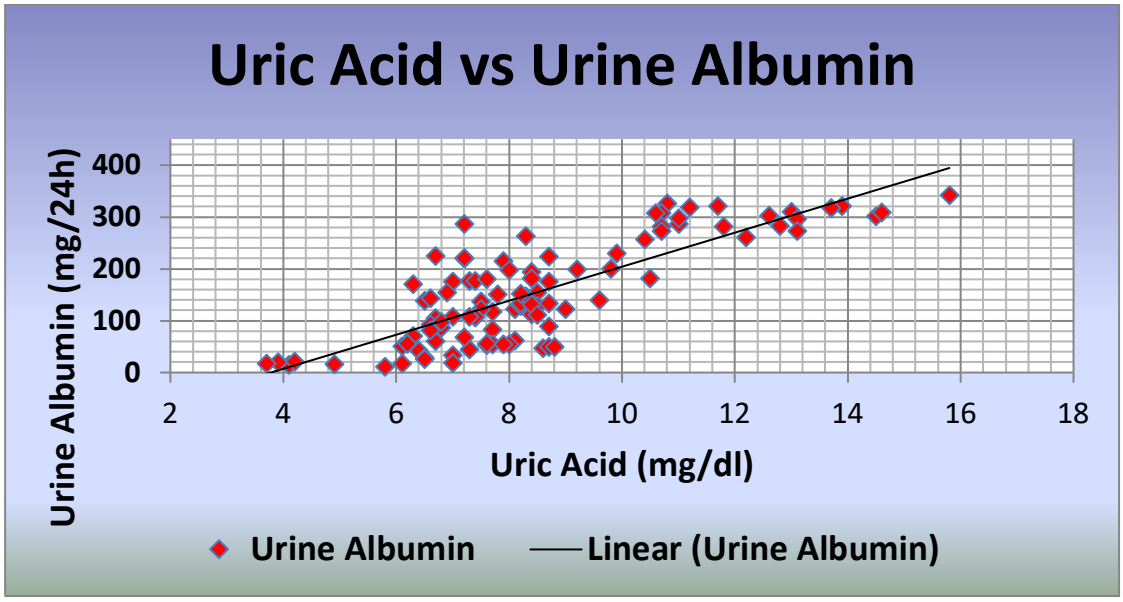
Graph 1: Uric Acid variation with Urine Albumin

There was statistically significant Positive correlation Serum Uric acid & Urine albumin ($r = 0.8126$ and $p < 0.0001$). (Table 3, Graph 2)

Table 3: Pearson correlation between Serum Uric acid & Urine albumin

Parameter	P value	R Score	R^2	Significance
Uric acid vs. Urine albumin	< .00001	0.8126	0.6603	S

*Data analysis using Pearson correlation analysis



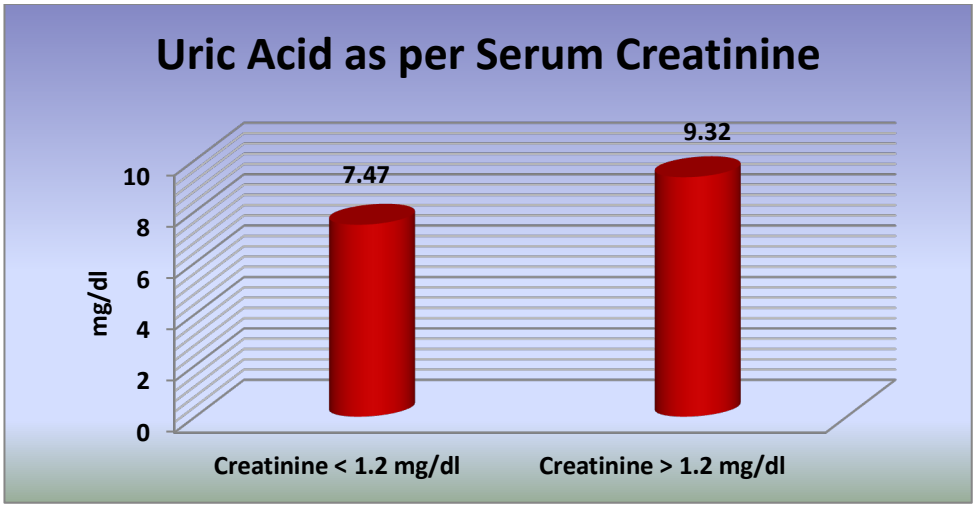
Graph 2: PEARSON CORRELATION between Serum Uric acid & Urine albumin

URIC ACID & SERUM CREATININE: The Mean Uric Acid levels in cases with Serum Creatinine < 1.2 mg/dl was 7.47 ± 1.95 mg/dl and with Serum Creatinine > 1.2 mg/dl was 9.32 ± 2.46 mg/dl. These values were statistically significant after applying Student T test (p value 0.000045). (Table 4, Graph 3)

Table 4: Uric Acid variation with Serum Creatinine

Test/ Parameters	Serum Creatinine < 1.2 mg/dl	Serum Creatinine > 1.2 mg/dl	P value
Number of cases	44	56	
Uric Acid (mg/dl)	7.47 ± 1.95	9.32 ± 2.46	0 .000045 (S)

*P value obtained after applying STUDENT T TEST



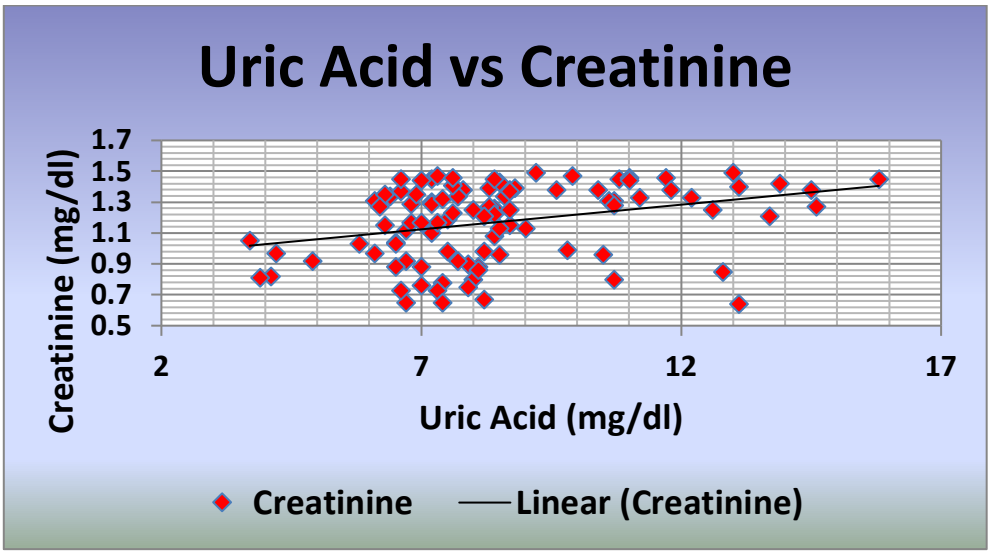
Graph 3: Uric Acid variation with Serum Creatinine

There was statistically significant Positive correlation Serum Uric acid & Serum Creatinine (r = 0.3172 and p value = 0.001302). (Table 5, Graph 4)

Table 5: Pearson correlation between Serum Uric acid & Serum Creatinine

Parameter	P value	R Score	R^2	Significance
Uric acid vs. Serum Creatinine	0.001302	0.3172	0.1006	S

*Data analysis using Pearson correlation analysis



Graph 4: PEARSON CORRELATION between Serum Uric acid & Serum Creatinine

Discussion

Diabetes is a major worldwide disease characterized by high blood glucose levels. It may be due to impaired insulin secretion, resistance to peripheral actions of insulin, or both. Chronic hyperglycemia in synergy with the other metabolic aberrations in patients with diabetes mellitus can cause damage to various organ systems, leading to the development of disabling and life-threatening health complications, most prominent of which are microvascular (retinopathy, nephropathy, and neuropathy) and macrovascular complications leading to a 2-fold to a 4-fold increased risk of cardiovascular diseases.

Our study found that DM affects mostly the middle age people (Mean age 51.7 years) and its prevalence is highest in them. Similar results were seen in the study By Chaudhary et al in 2019[7] where the highest number (40% of the study population) of type 2 DM patients belonged to the 41-50 years age group. This finding was supported by various other studies as well such as by Scott DA et al in 1938[8], McNair P et al in 1981[9] and Yoon KH et al in 2008.[10]

The Mean Uric Acid Levels in the Diabetic Case group was 8.51 ± 2.42 mg/dl. Similar results were seen in study by Deepali K et al in 2018[11], where the mean serum uric acid concentration was 6.03±1.75 mg/dL. This compares well with the study conducted by Kaifee M, et al.(2017)[12] observed that the mean of the serum Uric Acid in patients with T2DM in study population as 6.18 ± 0.89mg/dl. Chin-Hsiao Tseng et al (2005)[13] reported that the mean of the uric acid in patients with T2DM in study population was 5.6 ± 1.9 mg/dl. He also reported that the mean serum uric acid levels in patients with T2DM in study population for normoalbuminuric, microalbuminuric and macroalbuminuric patients were 5.2 ± 1.6 mg/dL, 5.6± 1.9 mg/dL, and 6.7 ± 2.1 mg/dL respectively. This result was in accordance to our results where Mean Uric Acid levels in cases with Urine Albumin < 30 mg/24h, Urine Albumin 30-300 mg/24h and Urine Albumin > 300 mg/24h was 5.27 ± 1.25 mg/dl, 8.27 ± 1.63 mg/dl, and 12.76 ± 1.76 mg/dl respectively. Various authors like Kopaei MR et al[14] , Razi F et al and Kuwabara M et al[15] reported Serum uric acid is associated with decreased GFR as well as albuminuria and can be used as an indicator of Diabetic nephropathy. Our study shows statistically significant Positive correlation Serum Uric acid & Urine albumin ($r = 0.8126$ and $p < 0.0001$). Similarly, Behradmanesh et al.[16], established in a study that serum uric acid had an important affirmative correlation with diabetic nephropathy.

Elevated uric acid can induce renin expression from the juxtaglomerular cells and inhibit NOS expression in the macula densa. Uric acid also impairs endothelial function[17] and stimulates the production of cytokines from leukocytes[18] and chemokines from vascular smooth muscle cells.[19] An increased concentration of uric acid in serum is a dangerous factor for the kidneys, as it is observed that hyperuricemia-induced endothelial dysfunction, glomerular hypertension, and renal hypertrophy reduce renal perfusion by inducing proliferation of afferent arteriolar vascular smooth muscle cell.[20] As the development of albuminuria is the first indication of kidney damage and diabetic nephropathy in patients with diabetes, it confirmed the association of ACR and hyperuricemia thereby confirming that hyperuricemia plays a role in diabetic nephropathy.

Our study shows that Mean Uric Acid levels in cases with Serum Creatinine < 1.2 mg/dl was 7.47 ± 1.95 mg/dl and with Serum Creatinine > 1.2 mg/dl was 9.32 ± 2.46 mg/dl. These values were statistically significant after applying Student T test (p value 0.000045). it also shows statistically significant Positive correlation Serum Uric acid & Serum Creatinine ($r = 0.3172$ and p value = 0.001302). Dr. Beena Unnikrishnan in 2017[21] also showed that serum uric

acid is a major pathological factor in the development of nephropathy in patients having Type-2 diabetes mellitus. Kaifee M et al (2017)[12] also reported that hyperuricemia correlated positively with FBG, HbA1C, serum creatinine, LDL & triglycerides in patients with T2DM. Similarly Sitholay, Agnihotri, and Ambad (2017)[22] showed that the activity of blood urea, serum creatinine and uric acid was highly significantly increased found in type-2 DM patients compared to the regular healthy group.

Hyperuricemia has been shown to be an independent risk factor for renal injury. Our study also confirmed that Serum Uric Acid may play an important role in kidney damage in diabetic patients. The mechanism may be as follows. (1) Uric acid induces endothelial dysfunction via the impairment of nitric oxide synthesis.[23] (2) Uric acid in the dissolved state can stimulate the inflammatory response via inducing the production of chemokine such as monocyte chemoattractant protein.[24]

Conclusion

Type 2 diabetes mellitus (DM) is a chronic metabolic disorder in which prevalence has been increasing steadily all over the world. Diabetic nephropathy (DN) is still the most prevailing reason of end-stage renal disease (ESRD). The present study strongly suggests a close link between uric acid and increased urinary albumin excretion rate in type 2 diabetic patients. Our study also shows a positive and strong correlation between uric acid and Serum Creatinine.

In order to prevent the progression of diabetes mellitus to diabetic nephropathy, vigilant monitoring of serum uric acid and creatinine are simple biomarkers available in patients with proteinuria if microalbuminuria screening test cannot be performed. We would like to conclude that Serum Uric acid, Serum Creatinine and Urine Albumin levels are simple tests helpful in diabetics who are poorly controlled to assess the renal function.

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