

Original Research

To study the correlation between hyperuricemia and albuminuria in type 2 diabetes mellitus patients

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ABSTRACT:

Aim: To study the correlation between hyperuricemia and albuminuria in type 2 diabetes mellitus patients. **Methods:** This Prospective open label observational study was done the Department of Medicine, Government District Hospital, Sri Ganganagar, Rajasthan. The study group comprised of 60 patients of type 2 diabetes mellitus of age between 33 to 69 years. Age, body weight, height, body mass index (BMI), serum uric acid, urinary albumin to creatinine ratio (ACR), fasting blood glucose (FBG), glycated haemoglobin (HbA1c), lipid profile, serum creatinine were studied. **Results:** The mean urinary ACR observed in study population of our study came to be 148.1±155.18 (µg/mg). In the present study on basis of urinary ACR, albuminuria was divided into 3 groups of normoalbuminuria (ACR <30 µg/mg), microalbuminuria (ACR between 30 µg/mg & 299 µg/mg) & macroalbuminuria (ACR ≥ 300µg/mg). The mean urinary ACR values in these three study groups came to be 23.9±2.99, 143.12±59.78 and 419.22±152.55 respectively. In patients with normouricemia 60% had normoalbuminuria, 25% had microalbuminuria; and 15% (n=4) had macroalbuminuria. In patients with hyperuricemia 40% had microalbuminuria ; 35 % had macroalbuminuria & 20% had normoalbuminuria. Thus albuminuria was significantly associated with hyperuricemia. The concentration of serum uric was 4.89±1.33 mg/dl, 7.89±0.87 mg/dl and 6.91±1.58 mg/dl in patients with normoalbuminuria, microalbuminuria and macroalbuminuria, respectively. On comparison, the results were found to be statistically significant. On univariate analysis the value of R was 0.83 and it shows a moderate positive correlation. R², the coefficient of determination, was 0.60. Considering the R² (Coefficient of determination) value, serum uric acid was found to be a significant factor which could predict only 40% (R² = 0.60) variation in albumin creatinine ratio. Thus, it showed that serum uric acid was an independent predictor of albumin creatinine ratio, after using adjusted R² value. **Conclusion:** As hyperuricemia is a common finding in this group of patients, and its treatment is easy and available, early diagnosis and treatment may be helpful to prevent or decrease the rate of development of overt kidney disease in this population of patients.

Keywords: Hyperuricemia, Albuminuria, Type 2 diabetes mellitus

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INTRODUCTION

The tide of type 2 diabetes is rising all over the world, thereby becoming an increasingly powerful threat to global health.¹ It has also become the leading cause of end-stage renal disease in the world, and the number of patients diagnosed each year with end-stage renal disease attributed to type 2 diabetes is rising.² Based on the latest report from the international diabetes federation (IDF)³ 2015 it is estimated that there are currently 415 million people living with diabetes globally and this number is set to rise to 592 million

by the year 2035. As per the IDF estimates Western region (138.2 million people with diabetes) has the most number of people with diabetes and Africa (19.8 million people with diabetes), the least. India the largest country in the South-east Asian region has 65.1 million people with diabetes as of 2013, this number is expected to increase to 109 million by 2035.

Glycosylated haemoglobin is an effective tool to know the glycemic control in type II diabetes mellitus. HbA1C values gives an accurate estimate of the

average plasma glucose levels from past 8 to 12 weeks. Now instead of glycemic control, HbA1C is used to detect diabetes and American Diabetes Association (ADA) has set guidelines to diagnose diabetes based on glycosylated hemoglobin values.⁴ Hyperuricemia is defined as serum uric acid level ≥ 7 mg/dl (in men) or ≥ 6.0 mg/dl (in women).⁵ Uric acid is an end product of purine metabolism, and approximately, one-third of it is degraded in the gut, and two-thirds is excreted by the kidneys.⁶⁻⁸ Elevated uric acid levels can result from increased generation or decreased elimination. Although decreased kidney function can be associated by hyperuricemia^{9,10} based on some epidemiological studies, hyperuricemia is an independent risk factor for kidney dysfunction in patients with diabetes mellitus (DM).¹⁰ It is suggested that increased serum level of uric acid is an injurious factor for kidneys.¹¹ Diabetic nephropathy is the leading cause of ESRD worldwide and leading cause of DM related morbidity and mortality. Nearly 30% of chronic renal failure in India are due to diabetic nephropathy. In some studies on diabetic patients, it has been reported that hyperuricemia is associated with kidney damage independent of hypertension.¹¹ On the other hand, higher levels of serum insulin may decrease uric acid clearance by the kidneys.^{12,13} As a rule, hyperinsulinemia is the basis of type 2 DM pathophysiology.¹² Therefore, diabetic patients are more prone to uric acid injury. The present study is to evaluate serum uric acid level & urinary Albumin Creatinine Ratio (ACR) in patients of T2DM.

MATERIAL AND METHODS

This Prospective open label observational study was done the Department of Medicine, Government District Hospital, Sri ganganagar, Rajasthan, after taking the approval of the protocol review committee and institutional ethics committee. After taking informed consent detailed history was taken from the patient or relatives. The study group comprised of 60 patients of type 2 diabetes mellitus of age between 33 to 69 years. Age, body weight, height, body mass index (BMI), serum uric acid, urinary albumin to

creatinine ratio (ACR), fasting blood glucose (FBG), glycated haemoglobin (HbA1c), lipid profile, serum creatinine were studied. Patients using diuretics, Patients on angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB), Patients of alcohol abuse, Urinary tract infection, Patients with malignancy were excluded from this study.

METHODOLOGY

Patient were diagnosed to have diabetes mellitus on the basis of American Diabetes Association (ADA) criteria. A fasting plasma glucose (FPG >126 mg/dL, a two hours plasma glucose >200 mg/dl or HbA1c $>6.5\%$ warrants diagnosis of diabetes mellitus. A random plasma glucose concentration >200 mg/dL accompanied by classical symptoms of diabetes mellitus (polyuria, polydipsia and weight loss) is sufficient for diagnosis of diabetes mellitus.

STATISTICAL ANALYSIS

Statistical software SPSS 21.0 was used for the analysis of the data and Microsoft Word and Excel to generate graphs and tables. The data collected were analyzed and expressed as Mean \pm SD. P values less than .05 were considered significant.

RESULTS

Out of total 60 patients of type 2 DM, the age range of the sample was 33-69 years with the mean age of 57.54 ± 8.07 years and male: female ratio of 1.14:1. The mean body mass index of study population was 27.30 ± 1.07 kg/m², mean systolic blood and mean diastolic blood pressure was 128.76 ± 11.52 mmHg and 79.02 ± 6.78 mmHg respectively. Mean fasting blood sugar levels for the study population was 159.08 ± 49.02 mg/dl and mean HbA1c levels were 7.1 ± 1.31 %. Mean value of lipid profiles of the study population including triglycerides, LDL and HDL came to be 129.1 ± 21.72 mg/dl, 128.17 ± 20.77 mg/dl, 38.78 ± 3.17 mg/dl respectively. Mean serum creatinine levels in the study population and mean GFR of the same were recorded as 0.980 ± 0.22 mg/dl and 77.96 ± 11.82 ml/min/1.73 m² respectively.

Table 1: Basic parameter of the patients

Parameters	Maen values (Mean \pm SD)
Age (years)	57.54 \pm 8.07
Gender (%age)	
Male	53.33%
Female	46.67%
BMI (kg/m ²)	27.30 \pm 1.07
SBP (mmHg)	128.76 \pm 11.52
DBP (mmHg)	79.02 \pm 6.78
HTN (%age)	51.67%
Fasting blood sugar (mg/dl)	159.08 \pm 49.02
HbA1C (%)	7.1 \pm 1.31
Triglycerides (mg/dl)	129.1 \pm 21.72
LDL (mg/dl)	128.17 \pm 20.77
HDL (mg/dl)	38.78 \pm 3.17

Serum creatinine (mg/dl)	0.980±0.22
GFR (ml/min/1.73 m ²)	77.96±11.82
Urinary ACR (µg/mg)	148.1±155.18
Serum uric acid (mg/dl)	6.58±1.69

The mean urinary ACR observed in study population of our study came to be 148.1±155.18 (µg/mg). In the present study on basis of urinary ACR, albuminuria was divided into 3 groups of normoalbuminuria (ACR <30 µg/mg), microalbuminuria (ACR between 30 µg/mg & 299 µg/mg) & macroalbuminuria (ACR ≥ 300µg/mg). The mean urinary ACR values in these three study groups came to be 23.9±2.99, 143.12±59.78 and 419.22±152.55 respectively.

Table 2: Comparison of mean urinary ACR among three groups

Groups	No. of patients (n)	Mean urinary ACR (µg/mg)
Normo albuminuria (Group 1)	31	23.9±2.99
Micro Albuminuria (Group 2)	18	143.12±59.78
Macro Albuminuria (Group 3)	11	419.22±152.55

The normoalbuminuria population showed values of TG, LDL and HDL was 119.70±21.77 mg/dl, 120.96±19.44 mg/dl, 38.78±3.88 mg/dl respectively, while microalbuminuria group showed 146.10±25.18 mg/dl, 143.07±12.59 mg/dl and 38.91±2.99 mg/dl respectively and lastly macroalbuminuria group showed 128.19±22.78 mg/dl, 127.54±21.23 mg/dl and 37.51±3.98mg/dl respectively. The results from our study showed that albumin levels showed a statistically significant positive correlation with both triglycerides levels (r=0.45, p<0.0001) and LDL levels (r=0.43, p<0.0004) in diabetic patients, whereas no such correlation was observed with HDL levels in the same population (p=0.13).

Table 3: mean values of TG, LDL& HDL in relation to different groups of albuminuriain

Variable	Normo albuminuria (Group 1)	Micro albuminuria (Group 2)	Macro albuminuria (Group 3)	Correlation coefficient (R value)	Significance (p value)
TG (mg/dl)	119.70±21.77	146.10±25.18	128.19±22.78	0.45	0.0001*
LDL(mg/dl)	120.96±19.44	143.07±12.59	127.54±21.23	0.43	0.0004*
HDL(mg/dl)	38.78±3.88	38.91±2.99	37.51±3.98	0.13	0.370

*P<0.05 was taken as significant

In patients with normouricemia 60% had normoalbuminuria, 25% had microalbuminuria; and 15% (n=4) had macroalbuminuria. In patients with hyperuricemia 40% had microalbuminuria ; 35 % had macroalbuminuria & 20% had normoalbuminuria. Thus albuminuria was significantly associated with hyperuricemia.

Table 4: Association of albuminuria with serum uric acid

Albuminuria	Serum uric acid		Total	p Value
	Normouricemia	Hyperuricemia		
Normalbuminuria	24(60)	4(20)	28(46.67)	<0.001
Microalbuminuria	10(25)	9(45)	19(31.67)	
Macroalbuminuria	6(15)	7(35)	13(21.66)	
Total	40(100)	20(100)	60(100)	

The concentration of serum uric was 4.89±1.33 mg/dl, 7.89±0.87 mg/dl and 6.91±1.58 mg/dl in patients with normoalbuminuria, microalbuminuria and macroalbuminuria, respectively. On comparison, the results were found to be statistically significant. On univariate analysis the value of R was 0.83 and it shows a moderate positive correlation. R², the coefficient of determination, was 0.60. Considering the R² (Coefficient of determination) value, serum uric acid was found to be a significant factor which could predict only 40% (R² = 0.60) variation in albumin creatinine ratio. Thus, it showed that serum uric acid was an independent predictor of albumin creatinine ratio, after using adjusted R² value.

Table 5: Evaluation of relationship of mean value of serum uric acid in relation to different groups of albuminuriain

Variable	Normo albuminuria	Micro albuminuria	Macro albuminuria	Correlation coefficient	coefficient of determinatio
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	(Group 1)	(group 2)	(Group 3)	(R value)	n (R ²)
Uric acid	4.89±1.33	7.89±0.87	6.91±1.58	0.83	0.60

DISCUSSION

Diabetes mellitus is a metabolic disorder characterized by variable degrees of insulin resistance and impaired insulin secretion. Insulin is a hormone that regulates the body's use of glucose. Diabetes is characterized by hyperglycaemia and insufficiency of the secretion or the action of endogenous insulin. The mean urinary ACR values in these three study groups came to be 23.9±2.99, 143.12±59.78 and 419.22±152.55 respectively. Kaifee M, et al¹⁴ also grouped their study subjects according to mean urinary ACR levels in patients with T2DM as normoalbuminuric, microalbuminuric, and macroalbuminuric patients and recorded the mean values as 22.28 ± 4.09 µg/mg, 134.79±70.65 µg/mg, and 469.83 ± 120.14µg/mg respectively. Out of total 60 patients of type 2 DM, the age range of the sample was 33-69 years with the mean age of 57.54± 8.07years. This age represents the peak age of social and economic responsibility and also a risk factor for increased renal dysfunction. Similar to our study Chin-Hsiao Tseng et al reported that mean age in study population was 62.8±10.8 years.¹⁵ While Bonakdaran S et al showed mean age in the study population was 52.45±10.11 years.¹⁶

Regarding gender distribution it was observed that over all male: female ratio in the present study was 1.14:1 thus showing male predominance. In accordance to our study, Prabhuswamy K M also reported male predominance in their study.¹⁷ But few studies are reported to have female predominance as well. This can be justified saying that Diversities in biology, culture, lifestyle, environment, and socioeconomic status have an impact on differences between males and females in predisposition in these studies. Also this disparity in the present study may represent the health- seeking behavior of the patients attending the hospital, as this study is a hospital based study and not a population based one.

Further, it was observed that female predominated in just macroalbuminuria group while in rest two groups males predominated. No significant correlation was found with gender distribution and Urinary ACR values in the present study. In similarity to ours Kaifee M, et al¹⁴ reported that normoalbuminuria and micro+ macroalbuminuria groups consisted of 49% female, 51% male and 56.9% female and 43.1% male in each group respectively. Where as in contrary, Yakoob Ahmedani et al reported that microalbuminuria was more frequent in males (37.1% vs. 29.9%) as compared to females.¹⁸

Mean fasting blood sugar levels for the study population was 159.08±49.02mg/dl and mean HbA1c levels were 7.1±1.31 %. Chin-Hsiao Tseng et al¹⁵ reported similar results in their study while on contrary Bonakdaran S, Hami M et al¹⁶ observed that

the mean of the FBS in patients with T2DM in study higher as compared to ours. The high mean HbA1C may due the poor glycemic control in patients included in their study.

Mean value of lipid profiles of the study population including triglycerides, LDL and HDL came to be 129.1±21.72mg/dl, 128.17±20.77mg/dl, 38.78±3.17 mg/dl respectively. Mean serum creatinine levels in the study population and mean GFR of the same were recorded as 0.980±0.22 mg/dl and 77.96±11.82 ml/min/1.73 m² respectively.

The results from our study showed that albumin levels showed a statistically significant positive correlation with both triglycerides levels (r=0.45, p<0.0001) and LDL levels (r=0.43, p<0.0004) in diabetic patients, whereas no such correlation was observed with HDL levels in the same population (p=0.13). Yakoob Ahmedani et al¹⁸ reported that the microalbuminuria positive group had a more deranged lipid profile with higher serum total cholesterol, triglycerides, LDL cholesterol and lower HDL levels compared to the microalbuminuria negative group.

It was revealed that FBS, HbA1c and serum creatinine presented a significant and positively correlation with albumin levels in the study population. Whereas, GFR presented a significant but a weak negative correlation with albumin levels in the study population.

The mean serum uric acid concentration was 6.58±1.69 mg/dL, which compares well with the study conducted by Kaifee M, et al.(2017)¹⁴ observed that the mean of the serum Uric Acid in patients with T2DM in study population as 6.18 ± 0.89mg/dl. Bonakdaran S et al (2011)¹⁶ also observed that the mean of the serum uric acid in patients with T2DM in study population was 5.55± 1.47 mg/dl. Chin-Hsiao Tseng et al (2005)¹⁵ reported that the mean of the uric acid in patients with T2DM in study population was 5.6 ± 1.9 mg/dl.

The concentration of serum uric was 4.89±1.33 mg/dl, 7.89±0.87 mg/dl and 6.91±1.58 mg/dl in patients with normoalbuminuria, microalbuminuria and macroalbuminuria, respectively Similarly, Chin-Hsiao Tseng et al (2005)¹³ 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. Various authors like Kopaei MR et al¹⁹, Razi F et al²⁰ and Kuwabara M et al²¹ reported Serum uric acid is associated with decreased GFR as well as albuminuria and can be used as an indicator of Diabetic nephropathy.

In the present study there were positive significant correlations between serum uric acid concentration and SBP, DBP, FBG, HbA1c, triglycerides, LDL, serum creatinine and urinary ACR (P < .001).

Whereas presence of a negative correlation of serum uric acid was seen in parameters like age, BMI, HDL and this relationship was statistically non significant. Kaifee M et al.(2017)¹⁴ also reported that hyperuricemia correlated positively with FBG, HbA1C, serum creatinine, LDL & triglycerides in patients with T2DM. No significant correlation found between hyperuricemia and age, sex, weight, height, BMI & HDL.

Thus overall it is seen from the results of our study that albuminuria is significantly associated with hyperuricemia. In accordance to our study Bonakdaran S et al¹⁶ also observed that there is significant correlation between serum uric Acid & urinary ACR. Pearson correlation coefficient r between serum uric acid & urinary ACR =0.097(P value <0.05).

Neki NS et al²² also revealed that levels of serum uric acid have linear positive correlation with the amount of proteinuria, Diabetic nephropathy can be suspected by increasing serum uric acid levels and it is seen that serum uric acid level correlates well with proteinuria, blood urea and serum creatinine level.

In yet another study by on Taiwanese patients with type 2 DM, Liang CC et al²³ reported that an increased serum uric acid level was significantly correlated with the severity of albuminuria. Also in another study by De Cosmo S et al²⁴, Serum uric acid was found to be significantly associated with albuminuria and thus they reported that mild hyperuricemia is strongly associated with the risk of CKD in patients with type 2 diabetes.

CONCLUSION

This study showed that the serum uric acid concentration was significantly and with greater probability associated with albuminuria in patients with type 2 diabetes mellitus. As hyperuricemia is a common finding in this group of patients, and its treatment is easy and available, early diagnosis and treatment may be helpful to prevent or decrease the rate of development of overt kidney disease in this population of patients.

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