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Correlation between Hyperuricemia and Albuminuria in Type 2 Diabetes Mellitus Patients in Jaipur, Rajasthan

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Abstract: ***Background*: Diabetes mellitus comprises a group of metabolic disorders characterized by hyperglycaemia as a consequence of defects in insulin secretion, action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels.Type 2 Diabetes is associated with a number of complications which develop as a result of an interplay between a sustained hyperglycaemic state, low grade inflammation and increased atherogenesis. There are broadly two types of complications Microvascular complications which include: Retinopathy, Neuropathy, Diabetic Kidney Disease and Macrovascular complications include- Coronary Artery Disease, Peripheral Artery Disease, Cerebrovascular disease. Elevated uric acid levels can result from increased generation or decreased elimination. Increased generation, in turn, can be caused by ingesting a purine-rich diet or alcohol, by certain genetic disorders (such as the Lesch-Nyhan syndrome), and by increased turnover of cells(such as in myeloproliferative diseases or tumor lysis syndrome). There is a relation between microalbuminuria and decreased glomerular filtration rate with beyond normal increased serum uric acid levels in type 2 DM patient. *Materials and Methods*: This study was done under Department of General Medicine of teritary care teaching hospital. The duration of this study was two years. Total number of One-hundred Twenty-four Patient's data were collected under this study. Collected data were analysed by using Microsoft Excel 2018. *Conclusion*: The study conducted is a hospital-based study which included predominantly the rural diabetic population of the state of Rajasthan. We showed in this study that high serum uric acid levels were significantly associated with albuminuria. Hyperuricemia is easily diagnosable and is a common finding in these patients. Furthermore, there are various treatment modalities which are easily available to lower uric acid levels. Therefore, early diagnosis and treatment of hyperuricemia in diabetic patients will be beneficial to prevent progression to overt kidney disease. Regular screening of patients of type 2 diabetes patients would be a prudent step towards this goal. Therefore, all such patients should undergo regular check-ups of their serum uric acid levels as it is an accurate predictor of morbidity due to progressive kidney disease.***

Keywords: Hyperuricemia, Albuminuria, Type 2 Diabetes

1. Introduction

Diabetes Mellitus is a group of disorder like hyperglycaemia resulting from insulin secretion or production disorder [1]. World Health Organization (WHO) and International Diabetes Federation (IDF) predicted that the diabetes mellitus patients will increase 2-3 by 2030. Nearly 25% - 40% of patients with type 2 DM develops Chronic Kidney Disease [15]. Hyperglycaemia is associated with many long-term complications of different organs such as Heart, Kidney, Eyes, Nerves, etc. Diabetic Nephropathy is a leading disorder of diabetes worldwide which leads to renal failure or end stage renal disease (ESRD) [2]. Diabetes mellitus can increase morbidity and mortality [3]. Conditions like diabetes mellitus with hypertension may lead to kidney dysfunction [4] which includes hyperuricemia. Diabetic and non-Diabetic patients both are at high risk of cardiovascular diseases with albuminuria[13,14]. Uric acid is the final product of purine catabolism [5]. Hyperuricaemia induces renal injury resulting in decreased elimination or uric acid which caused decrease in renal excretion, low glomerular filtration rate, increased tubular reabsorption which inhibits diabetic ketoacidosis [6,7]. Prolonged hyperuricaemia may develop glomerulosclerosis and proteinuria [8]. Proteinuria is the key indicator of Diabetic Nephropathy [9]. Some studies show that uric acid has a role in hyperglycaemia results in renal dysfunction [10,11]. Hyperuricemia in diabetic nephropathy shows by increase in blood uric acid levels. It could be increased production or decreased excretion of uric acid. Higher serum uric acid in DN is most likely due to abnormality in uric acid excretion. Although some experimental studies show that uric acid is a risk factor of renal dysfunction, it remains unclear if uric acid is a risk factor for progression in subjects with established renal disease [12]. Albuminuria is considered an important factor in diabetic nephropathy and is a sign of early glomerular and vascular damage[15].Therefore, the present study was designed to evaluate the influence of hyperglycaemia in association with hyperuricaemia and albuminuria. The aim was to study the association between hyperuricemia and albuminuria in diabetic mellitus type 2 patients.

2. Materials & Methods

This Study was done in the Department of General Medicine of tertiary care teaching hospital. The duration of the study is two years. Approval to conduct this study was obtained from Institutional Ethics Committee before starting the study. We also informed patients about the study, as well as their attendants. Only those who agreed to participate were included in the study. Total number of One-hundred Twenty-four Patient's data were collected under this study.

A suitable data collection form was designed to collect and document the data. Data collection form includes patient's demographic details, laboratory investigation etc. Collected data were analysed by using Microsoft Excel 2018.

3. Results

The present observational cross-sectional study was done with 124 patients to assess the correlation between hyperuricemia and albuminuria in type 2 diabetes mellitus patients.

Table 1: Distribution of patients according to Age

Age in years	*No. of patients*	*Percentage (%)*
41-50	53	42.74
51-60	32	25.82
61-70	29	23.38
71-80	10	8.06
Total	124	100%
Mean ± SD	**54.74 ± 10.53**	

Above table shows distribution of patients according to Age. In our study out of 124 patients, majority of the patients 53 (42.74%) were in the age group of 41-50 years followed by 32 patients (25.82%) in the age group of 51-60years, 29 patients (23.38%) in the age group of 61-70 years, 10 patients (8.06%) in the age group of 71- 80 years.The mean age of the patientswas 54.74 ± 10.53 years.

Table 2: Distribution of patients according to Sex

Sex	*No. of Patients*	*Percentage (%)*
Male	70	56.45 %
Female	54	43.55 %
Total	124	100 %

Above table shows, distribution of patients according to Sex, Out of 124 patients of type 2 diabetes mellitus patients in this study, 70 patients were males which constituted (56.45%) of the study population, while no. of female patients were 54 which constituted (43.55%) of the study population. It suggests type 2 diabetes mellitus patients was more common in males than females.

Table 3: Distribution of patients according to BMI

	BMI (kg/m^2)	*No. of Patients*	*Percentage (%)*
Normal	**<25**	10	8.06%
Overweight	**25-30**	80	64.53%
Obese	**>30**	34	27.41%
	Total	124	100%
	Mean ± SD	28.80 ± 2.75	

Above table shows distribution of patients according to BMI. In our study out of 124 cases 8.06% patients were healthy (<25 kg/m^2) where 64.53% and 27.41% were overweight (25-30 kg/m^2) and obese (30 kg/m^2) respectively. The mean BMI of patients was 28.80 ± 2.75 kg/m^2.

Table 4: Division of mean urinary ACR among three groups based on urinary ACR in study population

Groups	*No. of patients (n)*	*Mean Urinary ACR*
Normo-Albuminuria	68	21.45 ± 5.88
Micro Albuminuria	32	126.09 ± 68.03
Macro Albuminuria	24	554.33 ± 114.55

Above table shows distribution of patients according to Urine Albumin Creatinine Ratio. In our study of 124 patients, 68 patients were normoalbuminuric with a mean UACR of 21.45 mg/g and a standard deviation of 5.88, 32 patients were micro-albuminuria with a mean UACR of 126.09 mg/g and a standard deviation of 68.03,24 patients were macroalbuminuric with a mean UACR of 554.33 and a standard deviation of 114.55. It suggests that higher levels of UACR were associated with increased albuminuria in patients of type 2 diabetes.

Table 5: Distribution of mean values of TG in relation to different groups of albuminuria in study population

Variables	Normo-Albuminuria	Micro Albuminuria	Macro Albuminuria	Correlation Coefficient (R value)	Significance (p value)
TG (mg/dl)	157.13 ± 30.25	150.90 ± 26.19	157.04 ± 27.86	0.577	0.0001*

***P<0.05** was taken as significant.

Above table shows distribution of patients according to Triglyceride level and Urine Albumin Creatinine Ratio. In our study of 124 patients, patients having normal albuminuria had a mean TG level of 157.13mg/dl with a standard deviation of 30.25, patients having microalbuminuria had a mean TG level of 150.90 mg/dl with a standard deviation of 26.19, patients having microalbuminuria had a mean TG level of 157.04 mg/dl with a standard deviation of 27.86. This suggests that higher TG levels had a statistical significance in patients of type 2 diabetes.

Table 6: Distribution of mean values of LDL in relation to different groups of albuminuria in study population

Variables	Normo Albuminuria	Micro Albuminuria	Macro Albuminuria	Correlation Coefficient (R value)	Significance (p value)
LDL(mg/dl)	123.35 ± 26.82	117.09 ± 29.53	121.04 ± 30.41	0.416	0.0002*

***P<0.05** was taken as significant.

Above table shows distribution of patients according to LDL levels and UACR.In our study of 124 patients, patients having normo-albuminuria had a mean LDL level of 123.35 mg/dl with a standard deviation of 26.82, patients having microalbuminuria had a mean LDL level of 117.09 mg/dl with a standard deviation of 29.53, patients having macroalbuminuria had a mean LDL level of 121.04 mg/dl with a standard deviation of 30.41. This suggests that LDL levels have a statistical significance in patients of type 2 diabetes.

Table 7: Distribution of mean values of HDL in relation to different groups of albuminuria in study population

Variables	Normo-Albuminuria	Micro Albuminuria	Macro Albuminuria	Correlation Coefficient (R value)	Significance (p value)
HDL (mg/dl)	39.05 ± 4.85	37.06 ± 3.69	38.25 ± 4.91	0.102	0.216

P<0.05 was taken as significant.

Above table shows distribution of patients according to HDL levels and UACR.In our study of 124 patients, patients having normo-albuminuria had a mean HDL level of 39.05 mg/dl with a standard deviation of 4.85, patients having microalbuminuria had a mean HDL level of 37.06 mg/dl with a standard deviation of 3.69, patients having macroalbuminuria had a mean HDL level of 38.25 mg/dl with a standard deviation of 4.91. This suggests that HDL levels have no statistical significance in patients of type 2 diabetes.

Table 8: Evaluation of relationship of mean value of serum uric acid in relation to different groups of albuminuria in study population

Variables	Normo-Albuminuria	Micro Albuminuria	Macro Albuminuria	Correlation Coefficient (R value)	Coefficient of determination (R^2value)	Significance (P value)
S.Uric Acid	6.33±1.29	5.87±1.38	5.87±1.39	0.447	0.199	0.006*

***P<0.05** was taken as significant.

Above table shows distribution of patients according to Serum Uric Acid levels and UACR. In our study of 124 patients, patients having normo-albuminuria had a mean SUA level of 6.33 mg/dl with a standard deviation of 1.29, patients having microalbuminuria had a mean SUA level of 5.87 mg/dl with a standard deviation of 1.38, patients having macro-albuminuria had a mean SUA level of 5.87 mg/dl with a standard deviation of 1.39. This suggests that Serum Uric Acid levels have a statistical significance in patients of type 2 diabetes.

Table 9: Characteristics of Patients with Diabetes Mellitus*

Parameter	Value
Hemoglobin, g/dL	12.87 ± 1.89
MCV, fl	80.41 ± 8.09
SBP, mmHg	122.09 ± 8.76
DBP, mmHg	76.53 ± 10.12
HTN, % age	45.16 %
FBS, mg/dl	162.11 ± 43.65
PPS, mg/dl	252.62 ± 32.87
HbA1C, %	6.77 ± 0.97
Blood urea nitrogen, mg/dl	15.75 ± 4.63
Serum creatinine, mg/dl	0.91 ± 0.25
Serum cholesterol, mg/dl	210.73 ± 25.59
Serum triglyceride, mg/dl	155.50 ± 29.04
Serum LDLC	121.29 ± 28.49
Serum HDLC	38.38 ± 4.69
GFR, ml/min/1.73 m^2	94.46 ±15.08
Urine ACR, mg/g	151.59 ± 212.04
Serum uric acid, mg/dl	6.13 ± 1.36

Above table shows distribution of patients according to various parameter. In our study out of 124 cases, we found that, the mean Hemoglobin level was 12.87 g/dL with a standard deviation of 1.89, the mean MCV was 80.41 fL with a standard deviation of 8.09, the mean Systolic Blood Pressure was 122.09 mmHg with a standard deviation of 8.76. The mean Diastolic Blood Pressure was 76.53 mmHg with a standard deviation of 10.12, the mean no of Hypertensive patients were 45.16%, the mean Fasting Blood Sugar level was 162.11 mg/dl with a standard deviation of 43.65, the mean Post Parandial Blood Sugar level was 252.62 mg/dl with a standard deviation of 32.87, the mean HbA1C level was 6.77% with a standard deviation of 0.97, the mean Blood Urea Nitrogen level was 15.75 mg/dl with a standard deviation of 4.63, the mean Serum Creatinine level was 0.91 mg/dl with a standard deviation of 0.25, the mean Serum Cholesterol level was 210.73 mg/dl with a standard deviation of 25.59, the mean Serum Triglyceride level was 155.50 mg/dl with a standard deviation of 29.04, the mean Serum LDL level was 121.29 mg/dl with a standard deviation of 28.49, the mean Serum HDL level was 38.38 mg/dl with a standard deviation of 4.69, the mean GFR was 94.06 ml/min/1.73 m^2 with a standard deviation of 15.08, the mean Urine Albumin Creatinine Ratio was 151.59 mg/g with a standard deviation of 212.04, the mean Serum Uric Acid level was 6.13 mg/dl with a standard deviation of 1.36.

4. Discussion

The results of our study showed that albuminuria is significantly associated with hyperuricemia. Serum uric acid was found to be a significant factor which could predict only 44.7% (R = 0.447) variation in albumin creatinine ratio. Thus, it showed that serum uric acid was an independent predictor of albumin creatinine ratio.The mean urinary ACR values in these three study groups came to be 21.45 ± 5.88 µg/mg, 126.09 ± 68.03 µg/mg and 554.33 ± 114.55 µg/mg respectively. Kaifee M[16], et al 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 124 patients of type 2 DM, mean age of the study population was 54.74± 10.53 years. 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[17] et al reported that mean age in study population was 62.8±10.8 years. While Bonakdaran S[18] et al showed mean age in the study population was 52.45±10.11 years. Regarding gender distribution it was observed that over all male: female ratio in the present study was 1.29:1 thus showing male predominance. In accordance to our study, Prabhuswamy K M[19] also reported male predominance in their study. 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 oneIn similarity to ours Kaifee M[16], et al 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[20] et al reported that microalbuminuria was more frequent in males (37.1% vs. 29.9%) as compared to females.The mean fasting blood sugar levels for the study population was 162.11 ± 43.65 and mean HbA1c levels were 6.77 ± 0.97 mg/dl. Chin-Hsiao Tseng[17] et al reported similar results in their study while on contrary Bonakdaran S, Hami M[18] et al 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.Also Mean value of lipid profiles of the study population including triglycerides, LDL and HDL came to be 155.50 ± 29.04 mg/dl, 121.29 ± 28.49 mg/dl, 38.38 ± 4.69 mg/dl respectively. Mean serum creatinine levels in the study population and mean GFR of the same were recorded as 0.91 ± 0.25 mg/dl and 94.46 ±15.08 ml/min/1.73m2 respectively.The results from our study showed that albumin levels showed a statistically significant positive correlation with both triglycerides levels (r=0.577, p<0.0001) and LDL levels (r=0.416, p<0.0002) in diabetic patients, whereas no such correlation was observed with HDL levels in the same population (p=0.216). Yakoob Ahmedani[20] et al 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 6.13 ± 1.36 mg/dL, which compares well with the study conducted by Kaifee M[16], et al. (2017) observed that the mean of the serum Uric Acid in patients with T2DM in study population as 6.18 ± 0.89mg/dl. Bonakdaran S[18] et al. (2011) 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[17] et al (2005) reported that the mean of the uric acid in patients with T2DM in study population was 5.6 ± 1.9 mg/dl.Mean serum uric acid was 6.33±1.29 mg/dl, 5.87±1.38 mg/dl and 5.87±1.39 mg/dl in patients with normoalbuminuria, microalbuminuria and macroalbuminuria respectively. Similarly, Chin-Hsiao Tseng[17] et al (2005) 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[21] et al, Razi F[22] et al and Kuwabara M[23],et al 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[16] et al. (2017) 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[18] et al also observed that there is significant correlation between serum uric Acid & urinary ACR. Pearson correlation coefficient r between serum uric acid & urinary ACR =0.447 (P value <0.05).Neki NS[24] et al also revealed that levels of serum uric acid have linear positive corelation with the amount of proteinurea, 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[25] et al reported that an increased serum uric acid level was significantly correlated with the severity of albuminuria. Also in another study by De Cosmo S[26] et al, 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. Lastly, Behradmanesh S[27] et al also demonstrated that after adjustment for weight, a significant positive association of serum uric acid with level of proteinuria was seen.

5. Conclusion

The study conducted is a hospital based study which included predominantly the rural diabetic population of the state of Rajasthan. We showed in this study that high serum uric acid levels were significantly associated with albuminuria. Hyperuricemia is easily diagnosable and is a common finding in these patients. Furthermore, there are various treatment modalities which are easily available to lower uric acid levels. Therefore, early diagnosis and treatment of hyperuricemia in diabetic patients will be beneficial to prevent progression to overt kidney disease. Regular screening of patients of type 2 diabetes patients would be a prudent step towards this goal. Therefore, all such patients should undergo regular check-ups of their serum uric acid levels as it is an accurate predictor of morbidity due to progressive kidney disease.

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