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## ORIGINAL RESEARCH

# Study of the association between hyperuricemia and albuminuria in patients with type 2 diabetes mellitus

**[1]Dr. Mayank Patidar, [2]Dr. Jitendra Kanjolia, [3]Dr.Arvind Gupta, [4]Dr. Anugrah Dubay, [5]Dr. Sovran Rai**

[1]Consultant Physician, Arogyam clinic, Barwani, M.P., India
[2,3]Senior Resident, [4]Associate Professor, Department of Neurology, Gajra Raja Medical College, Gwalior, M.P., India
[5]Medical Officer, District Hospital, Guna, M.P., India

**Correspondence:**
Dr. Sovran Rai
Medical Officer, District Hospital, Guna, M.P., India
**Email:** dr.sovranrai@gmail.com

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**Abstract**

**Introduction:** Recently experimental and clinical studies have suggested that uric acid may contribute to the development of hypertension, metabolic syndrome & kidney diseases. There is emerging evidence that hyperuricemia is an independent risk factor for the development of chronic kidney disease, perhaps through endothelial damage. Hyperuricemia is defined as serum uric acid level ≥ 8.5 mg/dl (in men) or ≥ 6.2mg/dl (in women).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.

**Aims and objectives:**1-Evaluation of serum uric acid level and urinary albumin-creatinine ratio (ACR) in patient of T2DM in both younger and older age group (40 to 80 years) 2-Evaluate relationship between normo albuminuria (ACR <30 µg/mg), micro albuminuria (ACR between 30 µg/mg and 299 µg/mg) and macro albuminuria (ACR > 300 µg/mg) with serum uric acid levels.

**Materials & methods:** This is a cross sectional study conducted over 100 patients of Type 2 diabetes mellitus (T2DM) patients admitted in department of General Medicine, R D Gardi medical college and C R Gardi Hospital, Ujjain (M.P) during the period from Jan 18 to June 19 after applying the inclusion and exclusion criteria.

**Observation and results:** There was statistically significant mean difference found between mean of FBG , HbA1c, serum creatinine , GFR and serum uric acid with different albuminuria group in study population . In microalbuminuria and macroalbuminuria mean of FBG , HbA1c ,Serum creatinine , serum uric acid each significantly higher as compare to normal albuminuria . In microalbuminuria and macroalbuminuria mean of GFR was found significantly lower as compare to normal albuminuria.

**Discussion:** Mean urinary ACR levels in patients with T2DM in our study population for normouricemic & hyperuricemic patients were 75.62±126.62 µg/mg, and 268.35±211.34 µg/mg, Mean urinary ACR levels in patients with T2DM in our study population for normoalbuminuric, microalbuminuric, and macroalbuminuric patients were 22.56±4.15 µg/mg, 140.07±77.07 µg/mg, and 483.64 ± 126.17 µg/mg respectively. Mean urinary ACR significantly differ in all albuminuria groups with p= 0.000. Bonakdaran S,Hami M et al (

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2011) observed that the mean urinary ACR in patients with T2DM in study population was 32.52±54.96µg/mg .

**Conclusion:** Serum uric acid is linearly correlated to urinary ACR in patients with type 2 diabetes mellitus. Hyperuricemia correlated positively with levels of FBG, HbA1C, serum creatinine, LDL & Triglycerides in patients with T2DM .No significant correlation found between Hyperuricemia and Age, Sex, Weight, Height, BMI, Hypertension & HDL. Urinary ACR correlated positively with levels of FBG, HbA1C, serum creatinine, LDL & Triglycerides in patients with T2DM.No significant correlation found between urinary ACR and Age, Sex, Weight, Height, BMI, Hypertension & HDL. In patients with T2DM serum Uric Acid level correlated negatively with GFR.

**Keywords:** Serum uric acid, urinary ACR, T2DM

## Introduction

Type 2 Diabetes Mellitus (T2DM) is a heterogeneous group of disorders characterized by variable degrees of insulin resistance, impaired insulin secretion, and increased glucose production. Distinct genetic and metabolic defects in insulin action and/or secretion give rise to the common phenotype of hyperglycemia in type 2 DM. In Asia, the prevalence of diabetes is increasing rapidly and the diabetes phenotype appears to be different from that in the United States and Europe—onset at a lower BMI and younger age, greater visceral adiposity, and reduced insulin secretary capacity[1].

In United States, Diabetes Mellitus is the leading cause of End Stage Renal Disease (ESRD). The number of patients diagnosed each year with ESRD due to Type 2 diabetes mellitus is rising. The complex pathogenesis for the development of diabetic nephropathy is not fully understood. One factor that has been associated with cardio vascular & renal disease is serum uric acid. Recently experimental and clinical studies have suggested that uric acid may contribute to the development of hypertension, metabolic syndrome & kidney diseases. There is emerging evidence that hyperuricemia is an independent risk factor for the development of chronic kidney disease, perhaps through endothelial damage. Hyperuricemia is defined as serum uric acid level $\geq$ 8.5 mg/dl (in men) or $\geq$ 6.2mg/dl (in women).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[2].

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). On the other hand, decreased renal excretion can be a consequence of decreased glomerular filtration rate (GFR), increased tubular reabsorption induced by volume depletion when using diuretics, or inhibition of renal tubular secretion induced by inhibition of the anion-exchange transport system by lactate or keto acids[3].

Although decreased kidney function can be associated by hyperuricemia, based on some epidemiological studies, hyperuricemia is an independent risk factor for kidney dysfunction in patients with diabetes mellitus (DM). It is suggested that increased serum level of uric acid is an injurious factor for kidneys, as it is shown that hyperuricemia-induced endothelial dysfunction, glomerular hypertension, and renal hypertrophy decrease renal perfusion via stimulation of the afferent arteriolar vascular smooth muscle cell proliferation. In some studies on diabetic patients, it has been reported that hyperuricemia is associated with kidney damage independent of hypertension. On the other hand, higher levels of serum insulin may decrease uric acid clearance by the kidneys. As a rule, hyperinsulinemia is the basis of type 2 DM pathophysiology. Therefore, diabetic patients are more prone to uric acid injury[4].

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**Aims and objectives**

1. Evaluation of serum uric acid level and urinary albumin-creatinine ratio (ACR) in patient of T2DM in both younger and older age group (40 to 80 years)
2. Evaluate relationship between normo albuminuria (ACR <30 μg/mg), micro albuminuria (ACR between 30 μg/mg and 299 μg/mg) and macro albuminuria (ACR > 300 μg/mg) with serum uric acid levels.

**Material and methods**

This is a cross sectional study conducted over 100 patients of Type 2 diabetes mellitus (T2DM) patients admitted in department of General Medicine, R D Gardi medical college and C R Gardi Hospital, Ujjain (M.P) during the period from Jan 18 to June 19 after applying the inclusion and exclusion criteria.

**A)** Inclusion criteria

- Type 2 diabetes mellitus (T2DM) patients
- Age :-between 40 to 80 years

**B)** Exclusion criteria

- Patient using diuretics or any other medication that influences serum uric acid level.
- Patients on uric acid lowering agents.
- Patients on angiotensin converting enzyme(ACE) inhibitor or Angiotensin Receptor Blocker (ARB)
- UTI
- Acute illness
- Alcoholic
- Patients with malignancy
- Glomerular Filteration Rate (GFR) <60ml/min.

**Statistical analysis**

Statistical Analysis was performed with help of SPSS 20 version.Using this software, basic cross-tabulation and frequency distributions were prepared.Chi-Square test was used to test the association between different study variables under study. Z-test was used to test the significant difference between two proportions. Odds ratio (OR) with 95% Confidence Interval (CI) was calculated to measure the different risk factor. Multiple Logistic Regression Analysis was also performed to find the risk factors after adjusting the risk factors. Significance level was set at 0.05 and confidence intervals were at 95 percent level. $P \leq 0.05$ was considered statistically significant.

**Observation and results**

In the present study mean age of the patients was 56.96±9.675 median age was 56, maximum age was 80 and minimum age was 41 years (Table 1) (Figure 1).

**Table 1: Association between uricemia and age sub-groups**

| Age Groups | Uricemia | | Total |
|---|---|---|---|
| | Normouricemia | Hyperuricemia | |
| 41 - 50 Years | 16 | 15 | 31 |
| | 51.6% | 48.4% | 100.0% |
| 51 - 60 Years | 19 | 12 | 31 |
| | 61.3% | 38.7% | 100.0% |
| 61 - 70 Years | 14 | 12 | 26 |
| | 53.8% | 46.2% | 100.0% |

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| | | | |
|---|---|---|---|
| 71 - 80 Years | 7 | 5 | 12 |
| | 58.3% | 41.7% | 100.0% |
| Total | 56 | 44 | 100 |
| | 56.0% | 44.0% | 100.0% |
| Chi-Square = 0.67,p = 0.880 | | | |

**Figure 1: Association between uricemia and age sub-groups**

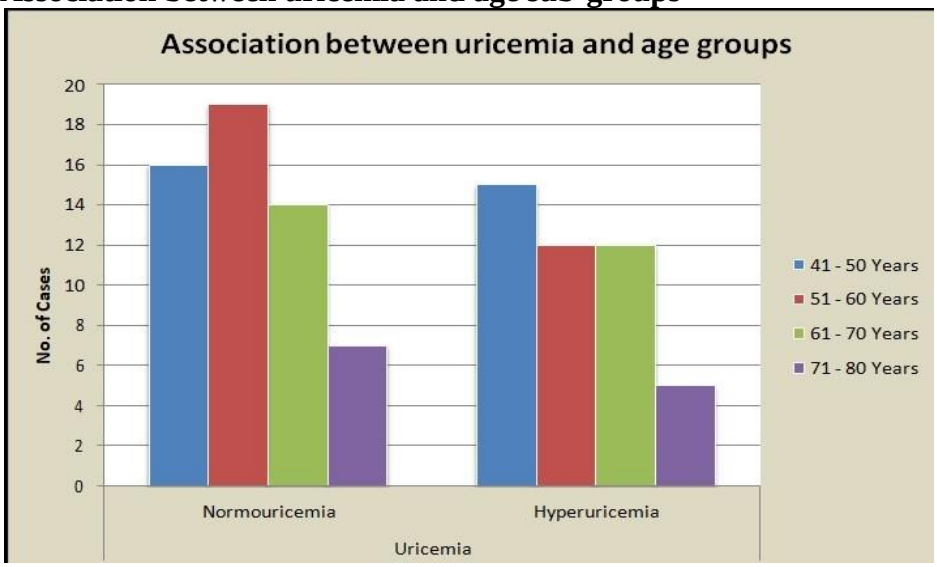


**Table 2: Distribution of mean FBG , HbA1C, Sr. Creatinine, GFR, Urinary ACR and Sr. Uric Acid among different albuminuria groups in study population**

| Variable | Albuminuria | | | | | | p Value | Significance |
|---|---|---|---|---|---|---|---|---|
| | Normoalbuminuria | | Microalbuminuria | | Macroalbuminuria | | | |
| | Mean | Standard Deviation | Mean | Standard Deviation | Mean | Standard Deviation | | |
| FBG | 116.67 | 21.15 | 180.10 | 34.19 | 233.41 | 56.93 | 0.0000 | Significant |
| HbA1C (%) | 6.21 | .51 | 7.42 | .81 | 8.45 | 1.41 | 0.0000 | Significant |
| Serum Creatinine | .8 | .15 | .86 | .19 | 1.05 | .19 | 0.0000 | Significant |
| GFR | 86.26 | 12.04 | 74.76 | 10.19 | 65.80 | 6.99 | 0.0000 | Significant |
| Urinary ACR | 22.56 | 4.15 | 140.07 | 77.07 | 483.64 | 126.17 | 0.0000 | Significant |
| Sr.Uric Acid | 4.85 | 1.22 | 6.90 | 1.66 | 8.23 | 1.19 | 0.0000 | Significant |

There was statistically significant mean difference found between mean of FBG , HbA1c, serum creatinine , GFR and serum uric acid with different albuminuria group in study population . In microalbuminuria and macroalbuminuria mean of FBG , HbA1c ,Serum creatinine , serum uric acid each significantly higher as compare to normal albuminuria . In microalbuminuria and macroalbuminuria mean of GFR was found significantly lower as compare to normal albuminuria.

**Table 3: Association of Hyperuricemia with Albuminuria**

| Uricemia | Albuminuria | | | Total |
|---|---|---|---|---|
| | Normoalbuminuria | Microalbuminuria | Macroalbuminuria | |
| Normouricemia | 41 | 11 | 4 | 56 |
| | 73.20% | 19.60% | 7.10% | 100.00 |

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| | | | | |
|---|---|---|---|---|
| | | | | % |
| Hyperuricemia | 6 | 20 | 18 | 44 |
| | 13.60% | 45.50% | 40.90% | 100.00 % |
| Total | 47 | 31 | 22 | 100 |
| | 47.00% | 31.00% | 22.00% | 100.00 % |
| Chi-Square = 36.67 , p = 0.000 | | | | |

In people with Normoalbuminuria 87.20%(n=41) have Normouricemia and 12.8%(n=6) have Hyperuricemia.In people with Microalbuminuria 35.50%(n=11) have Normouricemia and 64.50%(n=20) have Hyperuricemia.In people with Macroalbuminuria 18.20%(n=4) have Normouricemia and 81.8%(n=18) have Hyperuricemia.So there is stastically significant association between Hyperuricemia and Albuminuria(Table 3).

**Discussion**

Mean age in the study population was 56.96± 9.67 years (Maximum-80 years,Minimum-41).Chin-Hsiao Tseng et al(2005) reported that mean age in study population was 62.8±10.8 years. Bonakdaran S, Hami M et al (2011) showed mean age in the study population was 52.45±10.11 years. In study population 46% (n=46) were Male & 54%(n=54) were Female. The slightly increased number of females could be explained by the fact that women come more to the health care set up. Another cause may be that our study was hospital based not population based and the disorder (T2DM) is more common in women Chin-Hsiao Tseng et al(2005) reported that in study population 42% were Male & 58% were Female. Bonakdaran S,Hami M et al (2011) reported that in study population 43.53% were Male & 56.47% were Female[5-7].

The mean of the serum Uric Acid in patients with T2DM in our study population was 6.23 ± 1.94 mg/dl (maximum=10 mg/dl, minimum= 3.0 mg/dl). Chin-Hsiao Tseng 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. Bonakdaran S,Hami M et al ( 2011) observed that the mean of the serum Uric Acid in patients with T2DM in study population was 5.55 ± 1.47 mg/dl. Mean serum Uric Acid levels in patients with T2DM in our study population for normoalbuminuric, microalbuminuric, and macroalbuminuric patients were 4.85 ± 1.22 mg/dL, 6.90± 1.66 mg/dL, and 8.23 ± 1.19 mg/dL respectively. Mean serum uric acid significantly differ in all albuminuria groups with p= 0.000. Chin-Hsiao Tseng 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. Bonakdaran S,Hami M et al ( 2011)[57] observed that the mean serum Uric Acid levels in patients with T2DM in study population for normoal-buminuric, microalbuminuric, and macroalbuminuric patients were 4.49 ± 1.22 mg/dL, 4.84± 1.52 mg/dL, and 6.15 ± 1.68 mg/dL respectively[8-10].

Mean urinary ACR levels in patients with T2DM in our study population for normouricemic & hyperuricemic patients were 75.62±126.62 µg/mg, and 268.35±211.34 µg/mg, Mean urinary ACR levels in patients with T2DM in our study population for normoalbuminuric, microalbuminuric, and macroalbuminuric patients were 22.56±4.15 µg/mg, 140.07±77.07 µg/mg, and 483.64 ± 126.17 µg/mg respectively. Mean urinary ACR significantly differ in all albuminuria groups with p= 0.000. Bonakdaran S,Hami M et al ( 2011) observed that the mean urinary ACR in patients with T2DM in study population was 32.52±54.96µg/mg[11-13].

There is significant correlation between serum Uric acid & urinary ACR in our study.Pearson correlation coefficient r =0.615(P value <0.000).Chin-Hsiao Tseng et al(2005) reported that there is significant correlation between serum Uric Acid & urinary ACR. Pearson correlation

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coefficient r between serum uric acid & natural logarithmic urinary ACR =0.168(P value<0.05).Bonakdaran S,Hami M et al( 2011)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).Significant positive correlation was found between Urinary ACR and HbA1C (r=0.701, p=0.000), TG(r=0.430,p=0.000), LDL(r=0.425, p=0.000). No correlation was found between urinary ACR, Age and HDL which was not statistically significant. Prabhuswamy and Virgin (2017) was showed a weak, but statistically significant positive correlation between Hba1C values (r = 0.170, p = 0.005), total cholesterol (r=0.180, p=0.003), LDL cholesterol (r=0.165, p= 0.007) and urine micro albumin levels in study population. Other factors had shown no statistically significant association with urine micro albumin in the study group[14].

Significant positive correlation was found between Serum uric acid and FBG(r=0.622,p=0.000), HbA1C(r=0.625, p= 0.000), Serum creatinine (r=0.532, p =0.000). Negative correlation was found between Sr uric acid and GFR(r=-0.548, p =0.000). Prabhuswamy and Virgin (2017) was showed a moderate, statistically significant correlation between HbA1 C level and serum uric acid in the study group (r=-0.353, p=0.001)[15-16].

## Conclusions

Patients with T2DM serum uric acid level correlated positively with urinary albumin creatinine ratio. This study showed that Hyperuricemia was associated with a greater probability of Albuminuria in patients with type 2 diabetes mellitus. Serum uric acid is linearly correlated to urinary ACR in patients with type 2 diabetes mellitus. Hyperuricemia correlated positively with levels of FBG, HbA1C, serum creatinine, LDL & Triglycerides in patients with T2DM .No significant correlation found between Hyperuricemia and Age, Sex, Weight, Height, BMI, Hypertension & HDL. Urinary ACR correlated positively with levels of FBG, HbA1C, serum creatinine, LDL & Triglycerides in patients with T2DM.No significant correlation found between urinary ACR and Age, Sex, Weight, Height, BMI, Hypertension & HDL. In patients with T2DM serum UricAcid level correlated negatively with GFR.

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