ISSN: 0975-1556

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2022; 14(2); 139-147

Original Research Article

# Prospective Open Label Observational Assessment of the Association Between Hyperuricemia and Albuminuria in Patients with Type 2 Diabetes Mellitus

**Alok Kumar[1], A.K. Mehta[2], U.C. Jha[3]**

[1]3rd year PG student, Department of Medicine, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India
[2]Associate Professor, Department of Medicine, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India
[3]Associate Professor and HOD, Department of Medicine, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India

**Received: 03-12-2021 / Revised: 22-12-2021 / Accepted: 28-01-2022**
**Corresponding author: Dr. Alok Kumar**
**Conflict of interest: Nil**

**Abstract**

**Aim:** Study on the association between hyperuricemia and albuminuria in patients with type 2 diabetes mellitus.

**Methods:** This Prospective open label observational study was done the Department of Medicine, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India, the study group comprised of 50 patients of type 2 diabetes mellitus of age between 35 to 75 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 was studied.

**Results:** Mean serum creatinine levels in the study population and mean GFR of the same were recorded as 0.990±0.19 mg/dl and 78.66±13.95 ml/min/1.73 $m^2$ respectively.

The mean urinary ACR observed in study population of our study came to be 147.4±170.46(µg/mg). In the present study on basis of urinary ACR, albuminuria was divided into 3 groups of normoalbuminuria (ACR <30 ug/mg), microalbuminuria (ACR between 30 ug/mg & 299 ug/mg) & macro albuminuria (ACR ≥ 300ug/mg). The mean urinary ACR values in these three study groups came to be 23.3±3.53, 145.6±70.11 and 422.3±149.33 respectively. In patients with normouricemia 61.11% (n=22) had normoalbuminuria, 22.22% (n=8) had microalbuminuria; and 11% (n=4) had macro albuminuria. In patients with hyperuricemia 43.75% (n=7) had microalbuminuria; 37.5 % (n=6) had macro albuminuria& 18.75% (n=3) had normoalbuminuria. Thus, albuminuria was significantly associated with hyperuricemia. The concentration of serum uric was 4.79±1.23 mg/dl, 7.99±0.97 mg/dl and 6.81±1.48 mg/dl in patients with normoalbuminuria, microalbuminuria and macro albuminuria, respectively. On comparison, the results were found to be statistically significant.

**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.

## Introduction

Diabetes Mellitus (DM) is a metabolic disorder characterized by the presence of chronic hyperglycemia accompanied by greater or lesser impairment in the metabolism of carbohydrates, lipids and proteins resulting from defects in insulin secretion, action or both [1]. Diabetes is the most common endocrine disorder in our country, which is associated with long term complications involving vital organs such as eye, kidneys, nerves and blood vessels [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. An HbA1c value 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 is 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. The study also explores the relationship of normo albuminuria, micro albuminuria & macro albuminuria with serum uric acid levels.

## Material and methods:

This Prospective open label observational study was done the Department of Medicine, Darbhanga Medical College and Hospital, Laheriasarai, Darbhanga, Bihar, India, the study group comprised of 50 patients of type 2 diabetes mellitus of age between 35 to 75 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 was studied.

### Inclusion criteria:

Type 2 diabetes mellitus (T2DM) patients of age between 35 to 75 years.

### Exclusion criteria:

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.

Patients 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-hour 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 25.0 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 ± SD. The correlation between serum uric acid concentrations and age, sex, duration of DM, BMI, GFR, creatinine, FBG, hemoglobin A1c (Hb A1c), cholesterol, triglyceride, and urinary ACR were examined by the Pearson correlation analysis and Logistic regression was used to obtain relative risk and odds ratio. P values less than .05 were considered significant.

**Results:**

Out of total 50 patients of type 2 DM, the age range of the sample was 35-75 years with the mean age of 58.64± 9.07 years and male: female ratio of 1.17:1. The mean body mass index of study population was 26.20±1.17 kg/m2, mean systolic blood and mean diastolic blood pressure was 129.96±13.62 mmHg and 78.1±6.53 mmHg respectively. Mean fasting blood sugar levels for the study population was 158.38±52.22 mg/dl and mean HbA1c levels were 7.0±1.21 %. Mean value of lipid profiles of the study population including triglycerides, LDL and HDL came to be 128.7±26.92 mg/dl, 127.47±22.47 mg/dl, 38.38±3.07 mg/dl respectively. Mean serum creatinine levels in the study population and mean GFR of the same were recorded as 0.990±0.19 mg/dl and 78.66±13.95 ml/min/1.73 $m^2$ respectively.

**Table 1: Descriptive variables of study population with type 2 DM enrolled in the study**

| Parameters | Mean values (Mean±SD) |
|---|---|
| Age (years) | 58.64± 9.07 |
| Gender (%age) Male<br>Female | 54%<br>46% |
| BMI ($kg/m^2$) | 26.20±1.17 |
| SBP (mmHg) | 129.96±13.62 |
| DBP (mmHg) | 78.1±6.53 |
| HTN (%age) | 50% |
| Fasting blood sugar (mg/dl) | 158.38±52.22 |
| HbA1C (%) | 7.0±1.21 |
| Triglycerides (mg/dl) | 128.7±26.92 |
| LDL (mg/dl) | 127.47±22.47 |
| HDL (mg/dl) | 38.38±3.07 |
| Serum creatinine (mg/dl) | 0.990±0.19 |
| GFR (ml/min/1.73 $m^2$) | 78.66±13.95 |
| Urinary ACR (µg/mg) | 147.4±170.46 |
| Serum uric acid (mg/dl) | 6.13±1.65 |

The mean urinary ACR observed in study population of our study came to be 147.4±170.46(µg/mg). In the present study on basis of urinary ACR, albuminuria was divided into 3 groups of normoalbuminuria (ACR <30 ug/mg), microalbuminuria (ACR between 30 ug/mg & 299 ug/mg) & macro albuminuria (ACR ≥ 300ug/mg). The mean urinary ACR values in these three study groups came to be 23.3±3.53, 145.6±70.11 and 422.3±149.33 respectively.

**Table 2: Comparison of mean urinary ACR among three groups based on urinary ACR in study population**

| Groups | No. of patients (n) | Mean urinary ACR (µg/mg) |
|---|---|---|
| Normo albuminuria (Group 1) | 25 | 23.3±3.53 |
| Micro Albuminuria (Group 2) | 15 | 145.6±70.11 |
| Macro Albuminuria (Group 3) | 10 | 422.3±149.33 |

The normoalbuminuria population showed values of TG, LDL and HDL was 119.30±23.77 mg/dl, 121.06±21.54 mg/dl, 38.63±3.02 mg/dl respectively, while microalbuminuria group showed 147±28.38 mg/dl, 142.47±16.69 mg/dl and 38.71±2.5 mg/dl respectively and lastly macro albuminuria group showed 130.15±24.69 mg/dl, 126.84±23.23 mg/dl and 37.81±3.48 mg/dl respectively. The results from our study showed that albumin levels showed a statistically significant positive correlation with both triglycerides levels ($r=0.47$, $p<0.0001$) and LDL levels ($r=0.42$, $p<0.0003$) in diabetic patients, whereas no such correlation was observed with HDL levels in the same population ($p=0.36$).

**Table 3: Distribution of mean values of TG, LDL& HDL in relation to different groups of albuminuria in study population**

| Variable | Normo albuminuria (Group 1) | Micro albuminuria (Group 2) | Macro albuminuria (Group 3) | Correlation coefficient (R value) | Significance (p value) |
|---|---|---|---|---|---|
| TG (mg/dl) | 119.30±23.77 | 147±28.38 | 130.15±24.69 | 0.47 | 0.0001* |
| LDL (mg/dl) | 121.06±21.54 | 142.47±16.69 | 126.84±23.23 | 0.426 | 0.0003* |
| HDL (mg/dl) | 38.63±3.02 | 38.71±2.5 | 37.81±3.48 | 0.122 | 0.365 |

*P<0.05 was taken as significant

In patients with normouricemia 61.11% (n=22) had normoalbuminuria, 22.22% (n=8) had microalbuminuria; and 11% (n=4) had macroalbuminuria. In patients with hyperuricemia 43.75% (n=7) had microalbuminuria; 37.5 % (n=6) had macroalbuminuria& 18.75% (n=3) had normoalbuminuria. Thus, albuminuria was significantly associated with hyperuricemia.

**Table 4: Association of albuminuria with serum uric acid**

| | Serum uric acid | | | |
|---|---|---|---|---|
| **Albuminuria** | **Normouricemia** | **Hyperuricemia** | **Total** | **p Value** |
| Normalbuminuria | 22(61.11) | 3(18.75) | 25(50) | <0.001 |
| Microalbuminuria | 8(22.22) | 7(43.75) | 15(30) | |
| Macroalbuminuria | 4(11.11) | 6(37.5) | 10(20) | |
| Total | 36(100) | 16(100) | 50(100) | |

The concentration of serum uric was 4.79±1.23 mg/dl, 7.99±0.97 mg/dl and 6.81±1.48 mg/dl in patients with normoalbuminuria, microalbuminuria and macroalbuminuria, respectively. On comparison, the results were found to be statisticallty significant. On univariate analysis the value of R was 0.73 and it shows a moderate positive correlation. $R^2$, the coefficient of determination, was 0.50. Considering the $R^2$ (Coefficient of determination) value, serum uric acid was found to be a significant factor which could predict only 40% (R2 = 0.50) variation in albumin creatinine ratio. Thus, it showed that serum uric acid was an independent predictor of albumin creatinine ratio, after using adjusted $R^2$ value.

**Table 5: Evaluation of relationship of mean value of serum uric acid in relation to different groups of albuminuria in study population**

| Variable | Normo albuminuria (Group 1) | Micro albuminuria (group 2) | Macro albuminuria (Group 3) | Correlation coefficient (R value) | coefficient of determination ($R^2$) |
|---|---|---|---|---|---|
| Uric acid | 4.79±1.23 | 7.99±0.97 | 6.81±1.48 | 0.73 | 0.50 |

**Discussion:**

In clinical studies, serum uric acid concentration has been found to be associated with diabetic nephropathy. On the other hand, we also know that albuminuria is the main marker of diabetic nephropathy independent of hypertension. Therefore, this study was undertaken which is a hospital-based, observational, cross-sectional study to evaluate serum uric acid level & urinary albumin creatinine Ratio (ACR) in patients of T2DM. The study also evaluate relation between normoalbuminuria, microalbuminuria & macroalbuminuria with serum uric acid levels.

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 40% ($R^2$ = 0.50) 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 23.3±3.53µg/mg, 145.6±70.11µg/mg and 422.3±149.33µg/mg respectively. Kaifee M, et al [14] 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 50 patients of type 2 DM, mean age of the study population was 58.64± 9.07 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 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 1.17:1 thus showing male predominance. In accordance with 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 females predominated in just macroalbuminuria group (56 %), 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 al [14] 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. Whereas in contrary, Yakoob Ahmedani et al reported that microalbuminuria was more frequent in males (37.1% vs. 29.9%) as compared to females [18].

The mean fasting blood sugar levels for the study population was 158.38±52.22 and mean HbA1c levels were 7.0±1.21 mg/dl. Chin-Hsiao Tseng et al [15] reported similar results in their study while on contrary Bonakdaran S, Hami M et al [16] 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 128.7±26.92 mg/dl, 127.47±22.47 mg/dl, 38.38±3.07 mg/dl respectively. Mean serum creatinine levels in the study population and mean GFR of the same were recorded as 0.990±0.19 mg/dl and 78.66±13.95 ml/min/1.73m$^2$ respectively.

The results from our study showed that albumin levels showed a statistically significant positive correlation with both triglycerides levels ($r=0.47$, $p<0.0001$) and LDL levels ($r=0.42$, $p<0.0003$) in diabetic patients, whereas no such correlation was observed with HDL levels in the same population ($p=0.36$). Yakoob Ahmedani et al [18] 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±1.65mg/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.

Mean serum uric acid was 4.79±1.23 mg/dl, 7.99±0.97 mg/dl and 6.81±1.48 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 al [19], Razi F et al [20]and Kuwabara M et al [21] 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 with our study Bonakdaran S et al [16] 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 al [22] also revealed that levels of serum uric acid have linear positive corelation with the amount of protein urea, 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 al [23] 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 al [24], 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 et al [25] also demonstrated that after adjustment for weight, a significant positive association of serum uric acid with level of proteinuria was seen.

**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.

**References:**

1. Joslin’s Diabetes Mellitus: 14th edition; 331.
2. Watkins PJ.ABC of Diabetes 5th edition Condem (UK): BMJ Publishing group limited: 2003.
3. International diabetes federation (IDF). Diabetes atlas 6th edition 2014 update. International diabetes federation Brussels, Belgium; international diabetes federation 2014.
4. Use of Glycated haemoglobin (HbA1c) in the diagnosis of DM: http://www.who.int/diabetes/publicatio

n/report-HbA1c2011.pdf
5. Hochberg et al. 2003 Rheumatology 3rd Edition, Mosby, New York.
6. Cirillo P, Sato W, Reungjui S, et al. Uric acid, the metabolic syndrome, and renal disease. J Am SocNephrol. 2006;17: S165- 8.
7. Tseng CH. Correlation of uric acid and urinary albumin excretion rate in patients with type 2 diabetes mellitus in Taiwan. Kidney Int. 2005; 68:796-801.
8. Johnson RJ, Kang DH, Feig D, et al: Is there a pathogenetic role for uric acid in hypertension and cardiovascular and renal disease? Hypertension 2003:41:1183–1190.
9. Saggiani F, Pilati S, Targher G, Branzi P, Muggeo M, Bonora E. Serum uric acid and related factors in 500 hospitalized subjects. Metabolism. 1996; 45:1557-61.
10. Fukui M, Tanaka M, Shiraishi E, et al. Serum uric acid is associated with microalbuminuria and subclinical atherosclerosis in men with type 2 diabetes mellitus. Metabolism. 2008; 57:625- 9.
11. Tseng CH. Correlation of uric acid and urinary albumin excretion rate in patients with type 2 diabetes mellitus in Taiwan. Kidney Int. 2005; 68:796-801.
12. Bo S, Cavallo-Perin P, Gentile L, Repetti E, Pagano G. Hypouricemia and hyperuricemia in type 2 diabetes: two different phenotypes. Eur J Clin Invest. 2001; 31:318-21.
13. Chang HY, Lee PH, Lei CC, Tung CW, Hsu YC, Huang TJ, Lu LC, Lin CL. Hyperuricemia is an independent risk factor for new onset micro-albuminuria in a middle- aged and elderly population: a prospective cohort study in Taiwan. 2013 Apr 24;8(4): e61450.
14. Kaifee M, Baruah K, Agrawal PK, Alam F, Rasool U, Hassan R, Kumar M. Study on association between hyperuricemia and albuminuria in patients with type ii diabetes mellitus. Int Arch BioMedClin Res. 2017;3(4):75-79.
15. Tseng CH. Correlation of uric acid and urinary albumin excretion rate in patients with type 2 diabetes mellitus in Taiwan. Kidney Int. 2005; 68:796-801.
16. Bonakdaran S, Hami M, Shakeri MT. Hyperuricemia and albuminuria in patients with type 2 diabetes mellitus. Iranian journal of kidney diseases. 2011 Jan 1;5(1):21.
17. Prabhuswamy K M, Virgin Joena M. A cross sectional study of correlation between serum uric acid level and micro-albuminuria in Type 2 Diabetes Mellitus patients. IAIM, 2017; 4(4): 63-71.
18. Muhammad Yakoob Ahmedani, Muhammad Zafar Iqbal Hydrie, Azhar Iqbal, Asma Gul, Waheed Baig Mirza, Abdul Basit.Prevalence of Microalbuminuria in Type 2 Diabetic Patients in Karachi: Pakistan A Multi-Center Study.2005; 55(9):382-86.
19. Mahmoud Rafieian-Kopaei, Saeed Behradmanesh, Soleiman Kheiri, Hamid Nasri. Association of Serum Uric Acid with Level of Blood Pressure in Type 2 Diabetic Patients. IJKD 2014; 8:152-4.
20. Razi, F., Nasli-Esfahani, E. & Bandarian, F. Association of serum uric acid with nephropathy in Iranian type 2 diabetic patients. J Diabetes Metab Disord. 2018: 17: 71.
21. Kuwabara M, Bjornstad P, Hisatome I, et al. Elevated serum uric acid level predicts rapid decline in kidney function. American journal of nephrology. 2017;45(4):330-337.
22. Neki NS, Gupta H, MEeena R, Mani T. A Study of Association of Hyperuricemia with Progressive Diabetec Nephropathy.JIMSA.2015 Jan;28(1):13-19.
23. Liang CC, Lin PC, Lee MY, Chen SC,

Shin SJ, Hsiao PJ, Lin KD, Hsu WH. Association of serum uric acid concentration with diabetic retinopathy and albuminuria in taiwanese patients with Type 2 diabetes mellitus. Int J Mol Sci. 2016 Aug 2;17(8). pii: E1248.

24. De Cosmo S, Viazzi F, Pacilli A, et al. Serum Uric Acid and Risk of CKD in Type 2 Diabetes. Clinical Journal of the American Society of Nephrology: CJASN. 2015;10(11):1921-1929.
25. Saeed Behradmanesh, Mohammad Karami Horestani, Azar Baradaran, and Hamid Nasri. Association of serum uric acid with proteinuria in type 2 diabetic patients.J Res Med Sci. 2013 Jan; 18(1): 44–46.