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Research Article

Plasma Uric Acid Levels and Renal Function in Type 2 Diabetes Mellitus

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Abstract

Objective: This study investigates the correlation between plasma uric acid levels and renal function in Type 2 Diabetes Mellitus (T2DM) patients. Elevated uric acid levels have been associated with diabetic complications, particularly renal damage.

Methods: A total of 160 participants, including 80 T2DM (Group D) patients and 80 normal controls (Group N), were examined. Plasma levels of glucose, creatinine, urea, electrolytes, and uric acid were measured. Renal function was assessed using estimated glomerular filtration rate (eGFR). The study categorized T2DM patients based on sex, age, and eGFR stages.

Results: T2DM patients exhibited significantly higher plasma uric acid levels compared to controls ($p<0.001$). eGFR found to be significantly lesser in T2DM patients compared to controls ($P<0.05$). Gender-based comparisons revealed lesser eGFR levels in females.

Conclusion: Plasma uric acid levels are elevated in T2DM patients. Uric acid may serve as a marker for renal damage in T2DM, highlighting its role in diabetic nephropathy progression.

Keywords: Type 2 Diabetes Mellitus (T2DM), plasma uric acid, renal function, estimated glomerular filtration rate (eGFR), diabetic nephropathy.

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Introduction

Type 2 Diabetes Mellitus (T2DM) is a widespread and increasingly prevalent metabolic disorder characterized by chronic hyperglycemia resulting from impaired insulin action and insulin secretion. (1)The disease often progresses over time, leading to a range of serious complications, including cardiovascular disease, neuropathy, and diabetic nephropathy. Diabetic nephropathy, in particular, is a major concern, as it can

lead to end-stage renal disease (ESRD), necessitating renal replacement therapies such as dialysis or kidney transplantation (2). As a result, early detection and management of renal impairment in T2DM patients are crucial for improving patient outcomes and reducing the burden on healthcare systems.

In recent years, there has been growing interest in the role of uric acid in the pathogenesis of diabetic nephropathy. Uric acid is a metabolic byproduct of purine metabolism, which is typically excreted through the kidneys. Elevated levels of uric acid in the blood, known as hyperuricemia, have been associated with various health conditions, including hypertension, cardiovascular disease, and renal impairment (3). The connection between uric acid levels and renal function in T2DM patients is particularly noteworthy because uric acid's role in kidney damage may involve multiple mechanisms, including oxidative stress, inflammation, and endothelial dysfunction (4).

Oxidative stress, characterized by an imbalance between reactive oxygen species (ROS) production and antioxidant defenses, has been implicated in the pathogenesis of both diabetes and renal disease (5). Elevated uric acid levels can contribute to oxidative stress by promoting the formation of ROS, which in turn can damage renal cells and exacerbate kidney injury. Additionally, uric acid has been shown to stimulate inflammatory pathways, further contributing to renal damage (6). In diabetic nephropathy, these mechanisms may interact synergistically to accelerate the progression of kidney disease.

Endothelial dysfunction is another critical factor in the development of renal impairment in T2DM. Uric acid can affect endothelial function by disrupting nitric oxide (NO) production, a crucial mediator of vascular health (7). Impaired endothelial function can lead to reduced renal blood flow and increased glomerular pressure, both of which contribute to renal damage and the progression of diabetic nephropathy. The interplay between uric acid and endothelial dysfunction underscores the importance of monitoring uric acid levels in patients with T2DM (8).

Recent studies have suggested that elevated uric acid levels may be an independent risk factor for the development and progression of diabetic nephropathy. However, the relationship between uric acid levels and renal function in T2DM patients is complex and not fully understood. Some studies have indicated that high uric acid levels are associated with a higher risk of developing kidney disease, while others have found that the association may be influenced by factors such as age, sex, disease duration, and the presence of other comorbidities.

To better understand the role of uric acid in diabetic nephropathy, it is essential to investigate how plasma uric acid levels correlate with renal function parameters, such as the estimated glomerular filtration rate (eGFR). eGFR is a commonly used measure of renal function that estimates the rate at which the kidneys filter waste products from the blood. A decline in eGFR is indicative of worsening renal function and is often used to assess the progression of kidney disease in diabetic patients.

Hence the study aims to explore the relationship between plasma uric acid levels and renal function in T2DM patients by comparing these levels with eGFR. By analyzing the association between uric acid and eGFR, we hope to determine whether elevated uric acid levels can serve as a reliable marker for renal damage in T2DM. Such insights could potentially lead to improved diagnostic and therapeutic strategies for managing diabetic nephropathy and mitigating its impact on patients' health and quality of life.

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Materials and Methods

Study Design

This cross-sectional study was conducted at the Sri Siddhartha Medical College, Sri Siddhartha

Academy of Higher Education, Tumkur . It included 80 T2DM patients and 80 normal controls.

Participants

Participants were aged 30-60 years. T2DM patients were selected from the outpatient department, while normal controls were employees of SuIMS. Exclusion criteria included individuals under 30 years, over 60 years, those with psychiatric disorders, or on hormone therapy.

Grouping

Participants were categorized into groups based on sex, age (30-40, 41-50, 51-60), disease duration (0-3 years, 3.1-6 years, 6.1-10 years, above 10 years), and kidney disease stages (eGFR >90, 60-90, 30-59, 15-29, <15).

Sample Collection

Fasting heparinized blood samples (5-6 ml) were collected and centrifuged. Plasma was used to measure fasting plasma glucose (FPG), creatinine, urea, electrolytes, and uric acid. eGFR was calculated.

Statistical Analysis

Data were analyzed using SPSS version 16. The statistical analysis involved calculating descriptive statistics, including means and standard deviations for plasma levels and eGFR across different groups. Independent samples t-tests were used to compare mean values between two independent groups, such as Group N vs. Group D and males vs. females. For comparing means across multiple age groups, one-way ANOVA was applied, to check if results were significant. Additionally, Statistical significance was determined using p-values, with a threshold of <0.05 indicating significant differences or associations.

Results

Table 1: Plasma Levels in T2DM vs. Controls

Parameter	Group N (n=80)	Group D (n=80)	p-value
FPG (mg/dl)	70.98 ± 10.26	178.83 ± 35.28	<0.001
Creatinine (mg/dl)	0.79 ± 0.08	2.04 ± 0.05	<0.001
Urea (mg/dl)	14.86 ± 8.26	38.68 ± 10.32	<0.001
Sodium (mEq/l)	118.86 ± 16.63	132.36 ± 18.82	0.024

Potassium (mEq/l)	2.92 ± 0.92	3.82 ± 0.86	0.067
Chloride (mEq/l)	96.64 ± 10.38	102.36 ± 9.34	0.052
Uric Acid (mg/dl)	2.83 ± 0.62	6.96 ± 1.21	<0.001
eGFR (ml/min)	108.94 ± 12.68	52.86 ± 23.38	<0.001

Renal parameters like Creatinine, Urea, Sodium and Serum Uric acid levels with 2.04 ± 0.05, 38.68 ± 10.32, 132.36 ± 18.82 and 6.96 ± 1.21 respectively were significantly higher in T2DM patients compared to controls (P<0.05). However eGFR was found to be significantly lesser in T2DM group (P<0.05).

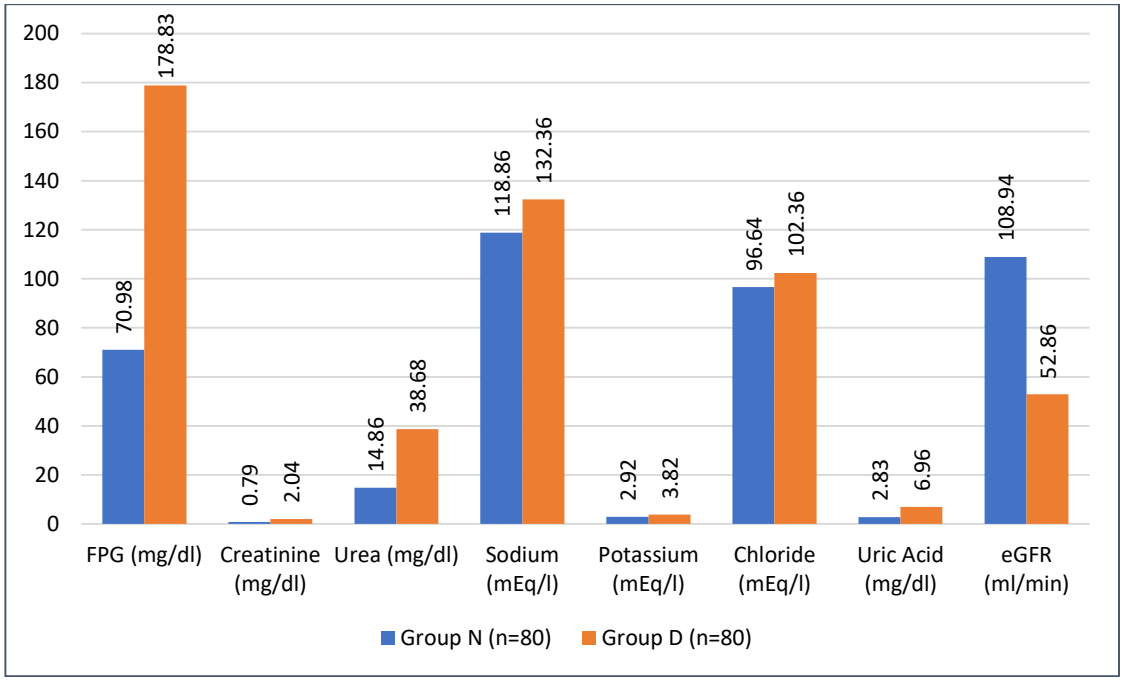


Table 2: Plasma Levels in T2DM Male vs. Female

Parameter	Male (n=45)	Female (n=35)	p-value
FPG (mg/dl)	183.45 ± 21.35	227.55 ± 26.50	0.042
Creatinine (mg/dl)	1.53 ± 0.28	2.20 ± 0.36	0.013
Urea (mg/dl)	34.96 ± 10.80	35.95 ± 12.62	0.683
Sodium (mEq/l)	138.32 ± 20.28	148.10 ± 23.40	0.115
Potassium (mEq/l)	4.17 ± 1.18	3.90 ± 0.98	0.492
Chloride (mEq/l)	113.96 ± 10.80	104.56 ± 11.20	0.078
Uric Acid (mg/dl)	7.62 ± 1.81	7.36 ± 1.62	0.626
eGFR (ml/min)	73.05 ± 12.65	58.31 ± 14.20	0.021

Differences in parameters between Males and females were tested and observed that FPG and Creatinine were significantly higher in females with 227.55 ± 26.50 and 2.20 ± 0.36 respectively compared to males (P<0.05). eGFR was found to be significantly higher in males 73.05 ± 12.65 than females 58.31 ± 14.20 (P<0.05).

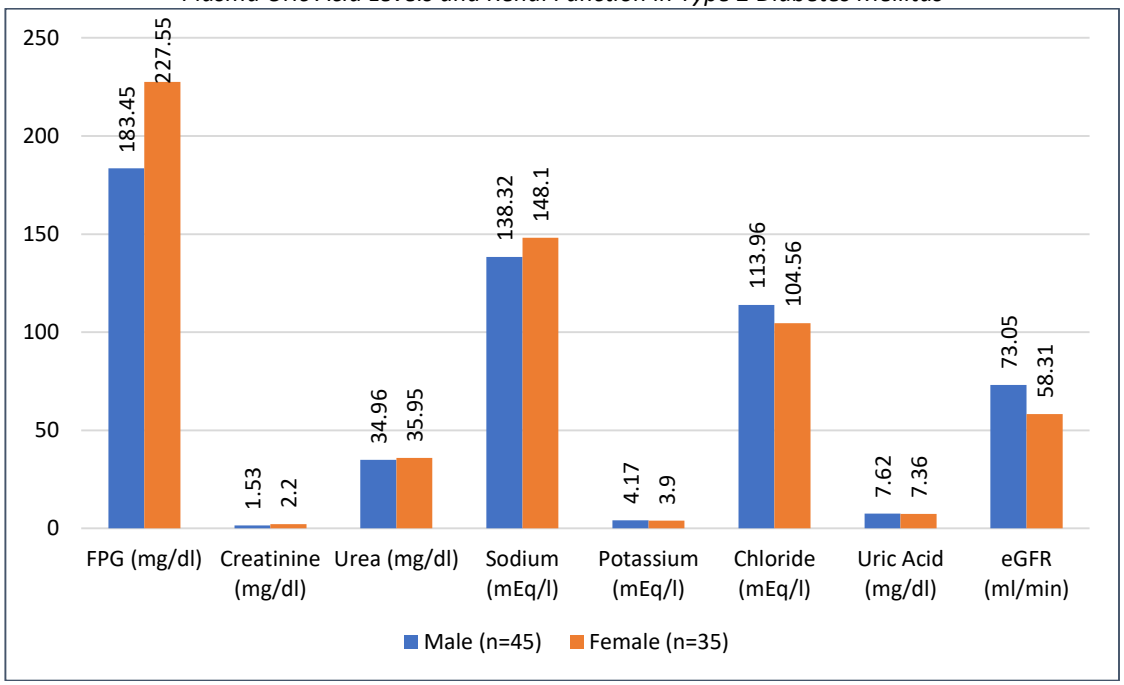
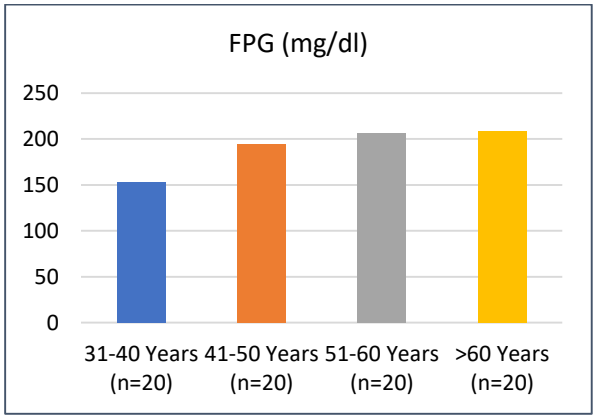
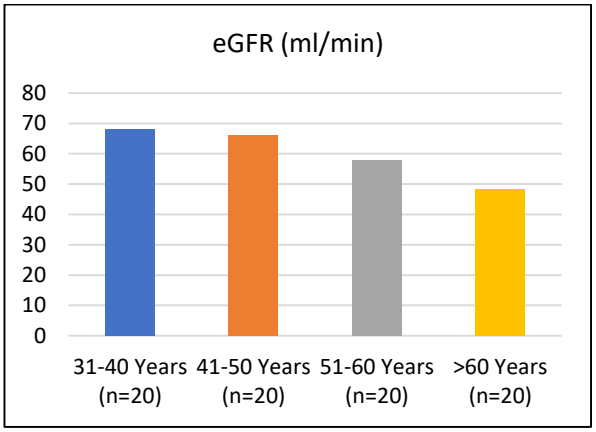


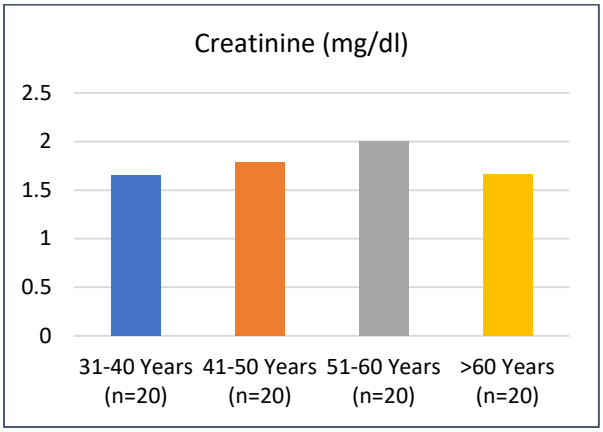
Table 3: Plasma Levels by Age Group in T2DM

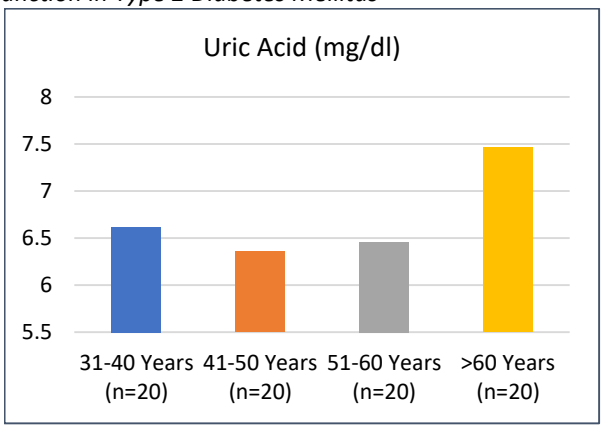
Parameter	31-40 Years (n=20)	41-50 Years (n=20)	51-60 Years (n=20)	>60 Years (n=20)	p-value
FPG (mg/dl)	153.40 ± 16.80	194.07 ± 18.60	205.93 ± 18.70	208.90 ± 21.30	0.023
Creatinine (mg/dl)	1.65 ± 0.08	1.79 ± 0.10	2.00 ± 0.11	1.66 ± 0.12	0.034
Urea (mg/dl)	35.40 ± 10.80	33.20 ± 11.20	37.72 ± 9.80	33.14 ± 10.60	0.120
Sodium (mEq/l)	132.70 ± 12.20	136.67 ± 14.18	137.07 ± 16.50	129.77 ± 18.10	0.091
Potassium (mEq/l)	3.59 ± 0.90	3.90 ± 0.88	3.76 ± 1.10	4.25 ± 7.75	0.071
Chloride (mEq/l)	100.40 ± 10.20	104.70 ± 12.20	103.43 ± 9.88	103.53 ± 10.10	0.156
Uric Acid (mg/dl)	6.62 ± 0.90	6.36 ± 0.80	6.46 ± 0.60	7.46 ± 0.85	0.009
eGFR (ml/min)	68.10 ± 10.80	66.27 ± 12.20	57.91 ± 14.80	48.22 ± 15.50	0.035

Results showed elevated FPG levels as ages progresses. Creatinine levels were also found increasing upto the age of 60 years and it drops in patients with age over 60 years (P<0.05). Uric acid levels found elevated in younger age group (31-40 yrs) 6.62 ± 0.90 and it drops in the age group (41-50 yrs) and increases as age progresses. eGFR levels significantly decreasing as age increasing and it was found statistically significant (P<0.05).









Discussion

Our study provides compelling evidence that plasma uric acid levels are significantly elevated in patients with Type 2 Diabetes Mellitus (T2DM) compared to healthy controls. This finding aligns with previous research indicating that hyperuricemia is common among diabetic patients and could be an important marker for diabetic nephropathy (9). In a related study, it was observed that the mean value of uric acid in coffee consumers was significantly lower in both normal and diabetic populations, suggesting a potential mitigating effect of coffee on uric acid levels (10). The significantly higher levels of uric acid in the T2DM group, coupled with the observation that these levels correlate positively with decreasing estimated glomerular filtration rate (eGFR), suggest that elevated uric acid is associated with worsening renal function.

The increased uric acid levels in T2DM patients may primarily result from impaired renal clearance, a common issue in diabetes-related kidney damage. As the kidneys become less effective at filtering waste products, including uric acid, from the blood, levels of this substance accumulate. This impaired clearance is corroborated by the observed decrease in eGFR among T2DM patients, which is a reliable indicator of renal function. The direct correlation between elevated uric acid levels and reduced eGFR underscores the potential role of uric acid as an early marker for renal deterioration in diabetic patients.

Gender differences also emerged in our study, with females showing higher uric acid levels compared to males. This finding is consistent with other studies suggesting gender-based variations in uric acid metabolism and clearance (11). Additionally, females had lower eGFR values, highlighting that the progression of renal impairment might differ between sexes (12). These gender-based discrepancies could be attributed to hormonal influences, differences in body composition, or variations in kidney function and uric acid handling between men and women (13).

Our study also identified a significant increase in uric acid levels with age, particularly in the older age group (>60 years). This trend aligns with the progressive nature of diabetic nephropathy and the cumulative effect of diabetes on renal function over time. The decline in eGFR with increasing age further supports the notion that chronic exposure to elevated uric acid levels exacerbates renal impairment as patients age. A recent study of adults with type 2 diabetes mellitus and/or hypertension attending chronic disease clinics found that older patients (>66 years) and those with both conditions had a high proportion of risk for chronic kidney disease (CKD), highlighting the importance of early screening (14)**.** This finding emphasizes the need for primary care physicians to consider the increased risk of CKD in older adults and those with multiple comorbidities, ensuring that they are tested and monitored appropriately In summary, elevated plasma uric acid levels in T2DM patients appear to be a significant indicator of worsening renal function. The relationship between uric acid and eGFR suggests that monitoring uric acid levels could be a valuable tool in assessing the progression of diabetic nephropathy (15). The potential mechanisms by which uric acid contributes to renal damage, such as oxidative stress and inflammation, highlight the importance of considering uric acid levels in the management of diabetic kidney disease. Future research should explore the therapeutic potential of targeting uric acid reduction in diabetic patients to mitigate renal damage and improve patient outcomes.

Conclusion

This study demonstrates that plasma uric acid levels are significantly elevated in Type 2 Diabetes Mellitus (T2DM) patients compared to healthy controls, and these elevated levels correlate strongly with decreasing renal function as measured by estimated glomerular filtration rate (eGFR). The findings highlight that hyperuricemia is associated with impaired renal function and may serve as a useful biomarker for monitoring diabetic nephropathy progression. Gender-specific differences in uric acid levels and eGFR further emphasize the need for tailored clinical assessments. Given the role of uric acid in promoting oxidative stress and inflammation, which can exacerbate renal damage, regular monitoring of uric acid levels in T2DM patients could be pivotal in early detection and management of renal impairment. These insights underscore the potential for integrating uric acid monitoring into comprehensive diabetes management strategies to enhance patient outcomes and mitigate the impact of diabetic nephropathy.

Key Points

Pros:

• Elevated uric acid levels are significantly associated with worsening renal function in T2DM patients.

- Monitoring uric acid can provide early indicators of diabetic nephropathy progression, potentially improving patient management and outcomes.

Cons:

- The study's cross-sectional design limits causal inferences between uric acid levels and renal function deterioration.
- Gender differences and age-related variations in uric acid levels complicate universal application, necessitating further research to refine targeted interventions.

Reference:

A., Crawford., Neda, Laiteerapong. Type 2 Diabetes. Venereal Disease Information, (2024). doi: 10.7326/aitc202406180.

Aloysius, Ikwuka., Daniel, Inioluwa, Omoju., Ousainou, K, Mahanera. Profiling of clinical dynamics of type 2 diabetes mellitus in patients: a perspective review. World Journal of Current Medical and Pharmaceutical Research, (2023). doi: 10.37022/wjcmpr.v5.

Arersa KK, Wondimnew T, Welde M, Husen TM. Prevalence and Determinants of Hyperuricemia in Type 2 Diabetes Mellitus Patients Attending Jimma Medical Center, Southwestern Ethiopia, 2019. Diabetes Metab Syndr Obes. 2020 Jun 18;13:2059-2067. doi: 10.2147/DMS.

Bhaktha GE, Shantaram MA, Nayak SH. Beneficial effects of coffee and maintenance of uric acid levels. Int J Pharm Pharm Sci. 2016;8(4):4.

Borbála, Rózsa, Zsindely. Endothelial Dysfunction in Type 2 Diabetes with an Update on New Interventions. Contemporary diabetes, (2023). doi: 10.1007/978-3-031-26681-2_14.

Chalak, Mehrdad., Faraj, Elahi, Mehran., Amirkhanlou, Saeid. Evaluation of the relationship between serum uric acid level and proteinuria in patients with type 2 diabetes. Journal of clinical nephrology, (2023). doi: 10.29328/journal.jcn.1001100.

Chesnaye NC, Carrero JJ, Hecking M, Jager KJ. Differences in the epidemiology, management and outcomes of kidney disease in men and women. Nature Reviews Nephrology. 2024 Jan;20(1):7-20.

Fathallah-Shaykh SA, Cramer MT. Uric acid and the kidney. Pediatric nephrology. 2014 Jun;29(6):999-1008.

Giandalia A, Giuffrida AE, Gembillo G, Cucinotta D, Squadrito G, Santoro D, Russo GT. Gender differences in diabetic kidney disease: focus on hormonal, genetic and clinical factors. International journal of molecular sciences. 2021 May 28;22(11):5808.

Han R, Duan L, Zhang Y, Jiang X Serum Uric Acid is a Better Indicator of Kidney Impairment Than Serum Uric Acid-to-Creatinine Ratio and Serum Uric Acid-to-High-Density Lipoprotein Ratio: A Cross-Sectional Study of Type 2 Diabetes Mellitus Patients. Diabetes, Metabolic Syndrome and Obesity. 2023 Dec 31:2695-703.

Mahadevappa K, Nayak SB, Maharaj RG, Bhaktha G. Using eGFR and Albumin Creatinine Ratio as an Initial Screening Tool in Trinidadian Primary Care to Identify High-risk Population for CKD: A Cross-Sectional Study. Indian J Nephrol. 2024;34:332-7. .

Na, Wang., Chun, Zhang. Oxidative Stress: A Culprit in the Progression of Diabetic Kidney Disease. Antioxidants, (2024). doi: 10.3390/antiox13040455.

Natalya, Kunitskaya., A., L., Ariev., N.N., Kulaeva. The role of uric acid in the development of infl ammation in kidney disease. Нефрология, (2023). doi: 10.36485/1561-6274-2023-27-2-39-46.

Nejc, Piko., Sebastjan, Bevc., Radovan, Hojs., Robert, Ekart. The Role of Oxidative Stress in Kidney Injury. Antioxidants, (2023). doi: 10.3390/antiox12091772.

Swartling O, Rydell H, Stendahl M, Segelmark M, Lagerros YT, Evans M. CKD progression and mortality among men and women: a nationwide study in Sweden. American Journal of Kidney Diseases. 2021 Aug 1;78(2):190-9.