

# Investigation of the Relationship between Serum Uric Acid Levels and Hb A1c and Glomerular Filtration Rate in Patients with Type 2 Diabetes Mellitus

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## Abstract

**Objective:** The aim of this study was to investigate the relationship between serum uric acid (SUA) level and hemoglobin A1c (Hb A1c) and estimated glomerular filtration rate (eGFR) in patients with type 2 diabetes mellitus (T2DM).

**Materials and Methods:** The study was conducted retrospectively by reviewing the files of patients diagnosed with T2DM aged 18 years and older. Patients were divided into two groups according to Hb A1c values: those with Hb A1c  $\geq 7$  and those with Hb A1c  $< 7$ . Age, gender, uric acid, creatinine and HbA1c values and their correlations were analyzed.

**Results:** A total of 510 patients were included in the study. Of the patients, 162 were female (31.76%) and 348 were male (68.24%). The mean age was  $69.68 \pm 12.29$  years in female patients and  $66.14 \pm 12.34$  years in male patients. Mean duration of DM was  $10.22 \pm 9.64$  years in female patients and  $11.42 \pm 10.12$  years in male patients. The mean Hb A1c value of 263 patients with Hb A1c  $< 7$  was  $6.05 \pm 0.55$  and the mean Hb A1c value of 247 patients with Hb A1c  $\geq 7$  was  $9.08 \pm 1.91$ . When serum uric acid, creatinine and eGFR values (calculated according to the Modification of Diet in Renal Disease (MDRD) formula) were compared between the groups with high and low Hb A1c, a statistically significant difference was found between serum uric acid levels ( $p=0.002$ ). When the correlation between uric acid, and eGFR in the groups with high and low HbA1c was analyzed, a statistically significant, strong negative correlation was found ( $p<0.001$   $r=-0.640$ ).

**Conclusion:** In T2DM patients, eGFR decreases as serum creatinine level increases, and eGFR decreases at approximately the same rate as serum uric acid level increases. This is independent of HbA1c. In other words, eGFR decreases as uric acid increases even if diabetes control is not impaired. This result reveals the importance of diet in T2DM patients.

**Key Words:** Type 2 Diabetes Mellitus; serum uric acid; Hb A1c; eGFR

## Introduction

Type 2 diabetes mellitus (T2DM) is one of the most common metabolic disorders worldwide, accounting for approximately 95% of diabetes mellitus (DM). There are two main mechanisms in the pathophysiology of T2DM: impaired insulin secretion from pancreatic  $\beta$ -cells and failure of insulin-sensitive tissues to respond to insulin. As a result, glucose cannot be utilized by cells and its level in the blood increases [1].

Glycolization, the combination of glucose with proteins, occurs in proportion to the increasing glucose level in the blood and the duration of high glucose levels [2]. The best example of glycolization is glycosylated hemoglobin, hemoglobin A1c (HbA1c) [3]. HbA1c, one of the markers showing the degree of glycolization, is used to monitor blood glucose control. An increase

in HbA1c, which indicates poor diabetes control in DM patients, has been shown to be associated with many complications in DM patients [4-6].

It has been suggested that uric acid, the end product of purine metabolism, is associated with many diseases. Studies have reported that serum uric acid levels  $>5.5$  mm/dL in women and  $>6$  mg/dL in men are associated with metabolic syndrome, hypertension, cardiovascular diseases and DM [7-10].

One of the most important causes of elevated uric acid is increased fructose intake. Unlike other sugars, fructose intake has been directly associated with increased uric acid. Increased fructose intake also causes elevated blood glucose and increased HbA1c. Fructose intake can cause serious

complications due to both increased blood glucose and increased uric acid levels [11-13].

The aim of this study was to investigate the relationship between SUA level and Hb A1c level and eGFR in T2DM patients.

**Materials and Methods**

This study was conducted retrospectively by scanning the hospital data recording system. Among the patients who applied to Lokman Hekim University Ankara Hospital Health Practice and Research Center, the files of patients aged 18 years and over with a diagnosis of T2DM were reviewed.

Inclusion criteria:

- Patients who met the American Diabetes Association (ADA) criteria [14] for the diagnosis of T2DM; fasting blood glucose  $\geq 126$  mg/dl or random blood glucose  $\geq 200$  mg/dl in patients with typical diabetes symptoms or blood glucose  $\geq 200$  mg/dl at the 2nd hour of 75 g oral glucose loading test or HbA1c 6.5 and above.

- Eighteen years of age or older

- Patients whose clinical and laboratory records can be accessed

Exclusion criteria:

- Those under the age of eighteen

- Those with diagnosed gout

- Patients on dialysis treatment for chronic renal failure

- Patients with diagnosed malignancy and patients receiving chemotherapy.

Age, gender, duration of DM, Hb A1c, creatinine and uric acid levels were obtained from patient files. Normal ranges were considered as creatinine 0.6-

1.2 mg/dL, uric acid  $< 6$  mg/dL, eGFR  $> 90$  ml/min/1.73.<sup>m2</sup> and HbA1c  $< 5.9$ . eGFR value was calculated according to the Modification of Diet in Renal Disease (MDRD) formula (eGFR=  $186 * Serum\ Creatinine^{-1.154} * Age^{-0.203} * Gender * Race$ ) [15].

Patients were divided into two groups according to Hb A1c values: those with Hb A1c  $< 7$  and those with Hb A1c  $\geq 7$ , which is the ADA DM treatment goal [16].

**Statistical analysis**

All analyses were performed using Statistical Package for Social Sciences (SPSS) software (version 27, Armonk, NY, USA). Variables were defined as minimum, maximum, mean and standard deviation. Data were analyzed for normal distribution using Kolmogorov Smirnov. Student t-test was used for normally distributed variables and Mann-Whitney U test was used for non-normally distributed variables. Correlation between parameters was determined using Spearman or Pearson correlation coefficient. A P value  $< 0.05$  was considered statistically significant.

This study was approved by the decision of Lokman Hekim University Scientific Research Ethics Committee dated 16.05.2024 and numbered 2024/59. The study was conducted in accordance with the Declaration of Helsinki and Research and Publication Ethics. Since it was a retrospective study, consent was not obtained from the patients included in the study. Artificial intelligence was not used for this study.

**Results**

A total of 510 patients were included in the study. Of the patients, 162 were female (31.76%) and 348 were male (68.24%). The mean age was  $69.68 \pm 12.29$  years in female patients and  $66.14 \pm 12.34$  years in male patients. The mean duration of DM was  $10.22 \pm 9.64$  years in female patients and  $11.42 \pm 10.12$  years in male patients (Table 1).

	Age (Year)	DM Duration (Year)		
	N	%	Mean±SD	Mean±SD
DM Patients	510	100		
Female	162	31.76	69.68±12.29	10.22±9.64
Male	348	68.24	66.14±12.34	11.42±10.12
DM Treatment				
OAD	310	60.9	65.13±12.84	9.54±9.52
OAD+Insulin	126	24.9	67.32±12.47	10.20±10.26
Insulin	74	14.2	68.32±12.47	12.20±10.26

DM: Diabetes mellitus, OAD: Oral antidiabetic drugs, SD: Standard deviation

**Table 1.** Demographic characteristics of patients.

The mean Hb A1c value of 263 patients with Hb A1c  $< 7$  was  $6.05 \pm 0.55$  and the mean Hb A1c value of 247 patients with Hb A1c  $\geq 7$  was  $9.08 \pm 1.91$ . When serum uric acid, creatinine and eGFR values of the groups with high and low Hb A1c were compared, a statistically significant difference was found between serum uric acid levels (p=0.002) (Table 2).

	Hb A1c $< 7$ (n:263)				Hb A1c $\geq 7$ (n:247)				
	Min	Max	Mean	SD	Min	Max	Mean	SD	P
Uric acid	2.20	13.80	5.49	1.81	2.00	17.90	6.47	2.10	<b>0.002</b>
Creatinine	0.55	8.68	1.15	0.88	0.42	10.30	1.12	0.82	0.534
eGFR	5.98	151.60	71.38	24.77	5.18	158.44	75.20	29.22	0.170

eGFR: Estimated Gloeruler Filtration Rate, HbA1c: Hemoglobin A1c

**Table 2.** Comparison of serum uric acid, creatinine and eGFR according to HbA1c value

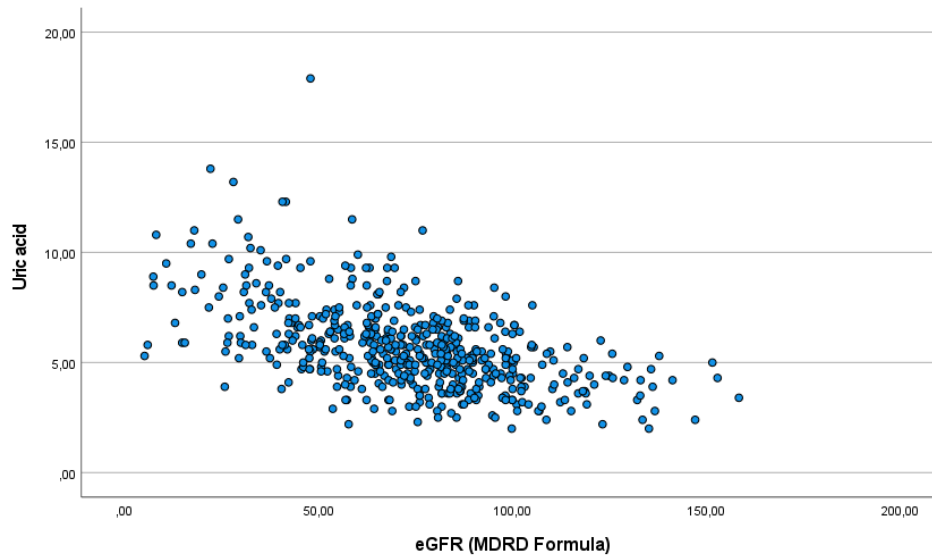
When the correlation between uric acid, and eGFR in the groups with high and low HbA1c was analyzed, a statistically significant, strong negative correlation was found (p $< 0.001$  r= -0.640) (Table 3 and Figure 1).

	r	p	r	p	r	p
eGFR	-0.505	$< 0.001$	-0.556	$< 0.001$	-0.640	$< 0.001$
Creatinine	0.302	$< 0.001$	0.369	$< 0.001$	0.348	$< 0.001$
HbA1c	0.320	0.608	-0.323	$< 0.001$	-0.229	$< 0.001$

eGFR: Estimated Gloeruler Filtration Rate, HbA1c: Hemoglobin A1c

Hb A1c  $< 7$  (n:263) Hb A1c  $\geq 7$  (n:247) Total (n:510)

**Table 3.** Correlation of serum uric acid with eGFR



**Figure 1.** Correlation of serum uric acid with eGFR

## Discussion

T2DM is one of the most common metabolic disorders in the world. In T2DM, glucose cannot be utilized by cells and its level in the blood increases. HbA1c increases due to glycolization caused by the increased glucose level in the blood. It has been shown that the increase in HbA1c, which means poor diabetes control in DM patients, is associated with many complications in DM patients. Uric acid, the end product of purine metabolism, has also been suggested to be associated with many diseases (such as metabolic syndrome, hypertension, cardiovascular diseases, DM).

One of the most important causes of elevated uric acid is increased fructose intake. Unlike other sugars, fructose intake has been directly associated with increased uric acid. Increased fructose intake also causes elevated blood glucose and increased HbA1c. It is inevitable that fructose intake may cause serious complications in DM patients due to both increased blood glucose and increased uric acid levels.

There are many different recommendations for the nutrition of DM patients. Some of these recommendations include snacks and eating fruit at these meals. In addition, eating fruit is constantly encouraged for the body's need for vitamins. However, it is understood that fruits, which are very rich in fructose, will do more harm than good because they increase both blood

sugar and uric acid. The most important issue in the treatment of DM patients is to pay attention to fructose intake in the diet of patients.

## Conclusion

It was observed that eGFR decreased as serum uric acid level increased and this decrease was independent of HbA1c. Therefore, it shows that reducing fructose intake in DM patients is very important in terms of both blood glucose control and uric acid reduction.

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## Ethical Declaration

This study was decided by Lokman Hekim University Scientific Research Ethics Committee at the meeting dated 16.05.2024 and approved with the number 2024/59.

This study was carried out in accordance with the ethical principles defined in the Declaration of Helsinki.

## Patient Consent Statement

Since the study was retrospective, informed consent was not obtained from the patients.

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