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The Relationship between Uric Acid and Blood Glucose in Diabetic Patients

Monireh Amerian[1], Kamran Pourmand[2], Ehsan Nezakati[3], Mehdi Ebrahimi[4], Pouneh Zolfaghari[5], Atena Razgoo[5], Mohammad Bagher Sohrabi[6*]
[1] Department of Nephrology, Clinical Research Development Unit, Imam Hossain Hospital, Shahroud University of Medical Sciences, Shahroud, Iran.
[2] Department of Cardiology, Imam Hossain Center for Education, Research and Treatment, Shahroud University of Medical Sciences, Shahroud, Iran.
[3] Department of Infectious, Imam Hossain Center for Education, Research and Treatment, Shahroud University of Medical Sciences, Shahroud, Iran.
[4] Department of Surgery, Imam Hossain Center for Education, Research and Treatment, Shahroud University of Medical Sciences, Shahroud, Iran.
[5] Vice-chancellery of Health, Shahroud University of Medical Sciences, Shahroud, Iran.
[6] School of Medicine, Shahroud University of Medical Sciences, Shahroud, Iran.

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Abstract

Background: *Some studies have shown that there is a correlation between serum uric acid and blood glucose levels so that these changes are not exactly clear. This study was conducted to determine the relationship between uric acid and blood glucose in diabetic patients.*
Methods: *This cross-sectional study was performed on 190 type 2 diabetic (DM) patients in Shahroud by convenience sampling method. FBS, uric acid, triglyceride, and total cholesterol under standard conditions were measured. Patients were divided into four groups in terms of uric acid level.*
Results: *In this study, 53.7% of patients were male. The average age of cases was 58.3 ± 13.5 years. There was a significant difference in uric acid between age groups (Pvalue<0.023), educational levels (Pvalue<0.041), BMI (Pvalue<0.012) and cholesterol (Pvalue<0.002) groups. Also, there was a significant reverse relationship between mean FBS (Pvalue<0.001), blood glucose two hours after feeding (Pvalue<0.001), and HbA1c (Pvalue<0.02) with different levels of uric acid.*
Conclusions: *The results showed that there was a significant and reversal relationship between the levels of uric acid and glucose levels. In order to control the level of uric acid, the level of glucose in these patients is also to be measured and controlled.*

Keywords: Diabetes mellitus, Blood glucose, Uric acid
***Corresponding to:** MB Sohrabi, **Email:** mb.sohrabi@yahoo.com
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Introduction

Uric acid is synthesized in the liver and is the final product of purine metabolism and purine produced in the human body.[1] Some studies have suggested that increase uric acid can cause hypertension, heart disease, and kidney disease.[1-3] It can also cause peripheral arteries and metabolic syndrome.[4] According to the world health organization, the global outbreak of diabetes in 2014 is estimated to be around 9% among adults over the age of 18 years, which will double by 2030.[5] According to the international foundation for the prevention and control of diabetes report in 2006, about 4 million Iranians suffer from diabetes, 90% of whom have type II diabetes.[6] Diabetes mellitus is a group of metabolic disorders that is the main and common sign of hyperglycemia. Hyperglycemia in diabetes due to insulin secretion defects, insulin function and, more commonly, both. The current criteria for the diagnosis of diabetes mellitus are on fasting sugar.[6-7] Double-fasting glucose levels above 126 mg/dl suggest a diagnosis of diabetes mellitus. In addition, the impaired glucose tolerance test with 75 gr of glucose in two steps, also suggests the diagnosis of diabetes. Serum uric acid is associated with oxidative stress and tumor necrosis factor α that both of which contribute to the development of diabetes. Uric acid is a possible biomarker in the worsening of glucose metabolism.[8-9] The exact relationship between uric acid and blood glucose levels is unclear. Some studies, like the burns study, have shown an inverse relationship between uric acid and diabetes with a possible mechanism of uric acid absorption in proximal kidney tubes in diabetic patients,[10] and some studies have shown no relation between them or even direct communication between them.[11-13] Due to the high prevalence of sugar metabolism disorders, also important to discover the factors associated with this disorder and not conducting related studies at the district level, the aim of this study was to investigate the relationship between uric acid and blood glucose in diabetic patients.

Materials and Methods

This cross-sectional study was performed on 190 DM patients admitted to Imam Hossein hospital in Shahroud during October 2016 till November 2017, who were selected by convenience sampling method. A blood sample was collected from all patients and was measured FBS, uric acid, triglyceride, and total cholesterol under standard conditions and was taken systolic and diastolic blood pressure (the measurement was done twice with a 10 minutes' interval and mean of two measurements was calculated). Serum glucose was measured using the modified hexokinase method at the Imam Hossein hospital laboratory. Diabetes was defined based on the guidelines of the American diabetes association as a serum glucose≥126 mg/dL after fasting for a minimum of 8 hours, a serum glucose≥200 mg/dL for those who fasted<8 hours, or self-reported current use of oral hypoglycemic medication or insulin.[14] Also serum uric acid measured using the SMA systems method. This technique has been commonly employed in automated hospital screening. This method depends on the reduction of a chromogen such as sodium tungstate by uric acid to produce a measurable color change.[15-16] Age, gender, smoking status, level of education, history of diabetes and sugar controller drugs, antihypertensive drug use and BMI were assessed using a questionnaire. Serum total cholesterol was measured homogeneous assays versus.

Serum uric acid level was categorized in four groups (<4.3 mg/dL, 4.30–5.20 mg/dL, 5.30–6.20 mg/dL, >6.20 mg/dL). According to the level of uric acid, patients were divided into two groups, normal) uric acid equal to and less than 5.3 mg/dl) and

non-normal (uric acid greater than 5.3 mg/dl). Then, independent variables with normal uric acid level (first and second uric acid subgroup) and abnormal (third and fourth uric acid subgroup) were evaluated in the multivariate regression model.

The distribution of demographic and laboratory characteristics in terms of Uric acid levels was evaluated using Chi square test using SPSS (version 16.0) software. The significance level was set at 0.05.

This study has an ethics code number (IR.SHMU.REC.1394.128) from the research deputy of Shahroud university of medical sciences. The essential information and the objectives of the study were explained to the patients, and written consent was obtained for participation in the plan.

Results

In this study, 102 cases (53.7%) were male and the rest were female. The mean age of patients was 58.3 ± 13.5 years. Subgroups of patients under study by categories of uric acid were showed in table 1. As it can be seen, there was a significant difference of uric acid between age groups (Pvalue<0.023), educational levels (Pvalue<0.041), BMI (Pvalue<0.012) and cholesterol groups (Pvalue<0.002), and there was no significant difference in other parameters. It was also found that there was a significant difference between mean scores of fasting blood sugar (Pvalue>0.001), blood glucose two hours after feeding (Pvalue<0.001), and HbA1c (Pvalue<0.02) in terms of different levels of uric acid, variation of the blood sugar by subgroups of uric acid was shown in table 2 and figure 1. In this study, independent variables with 2 uric acid levels were investigated in multivariate regression model. As shown in table 3, age category, BMI, triglyceride level and total cholesterol level were significantly associated with the uric acid level change and there was no significant relationship with other variables. The results of the multivariate logistic regression model are presented in table 3.

Table 1. Characteristics of patients under study by groups of uric acid level

Characteristics	Serum uric acid levels				Pvalue
	<4.3 mg/dL (n=45)	4.30–5.20 mg/dL (n=45)	5.30–6.20 mg/dL (n=45)	>6.20 mg/dL (n=45)	
Age					
−< 20 year	12 (26.7%)	12 (26.7%)	8 (17.8%)	5 (24.4%)	<0.023
−20-40 year	19 (42.2%)	15 (33.3%)	17 (37.8%)	15 (33.3%)	
−41-60 year	8 (17.8%)	8 (17.8%)	10 (22.2%)	14 (24.4%)	
−> 60 year	6 (13.3%)	10 (22.2%)	10 (22.2%)	11 (24.4%)	
Sex					
−Men	27(60%)	25 (55.6%)	26 (57.8%)	28 (62.2%)	0.102
−Women	18 (40%)	20 (44.4%)	19 (42.2%)	17 (37.8%)	
Education categories					
−Below diploma	8 (17.8%)	10 (22.2%)	11 (24.4%)	11 (24.4%)	<0.041
−Diploma	15 (33.3%)	16 (35.6%)	20 (44.4%)	23 (51.1%)	
−College education	22 (48.9%)	19 (42.2%)	14 (31.1%)	11 (24.4%)	
Smoking					
−Never smoker	10 (22.2%)	6 (13.3%)	8 (17.8%)	10 (22.2%)	0.085
−Former smoker	20 (44.4%)	21 (46.7%)	25 (55.6%)	23 (51.1%)	
−Current smoker	15 (33.3%)	18 (40%)	12 (26.7%)	12 (26.7%)	
BMI* (kg/m^2)					
−Normal (≤ 24.99)	12 (26.7%)	10 (22.2%)	10 (22.2%)	8 (17.8%)	<0.012
−Overweight (25-29.99)	22 (48.9%)	21 (46.7%)	18 (40%)	18 (40%)	
−Obese (> 30)	11 (24.4%)	14 (31.1%)	17 (37.8%)	19(42.2%)	
Diabetic drug					
−Oral hypoglycemic	12 (26.7%)	16 (35.6%)	22 (48.9%)	29 (64.4%)	<0.065
−Insulin	33 (73.3%)	29 (64.4%)	23 (51.9%)	16 (35.6%)	
Antihypertensive drug					
−Positive	16(35.6%)	20 (44.4%)	23 (51.9%)	26 (57.8%)	<0.077
−Negative	29 (64.4%)	25 (55.6%)	22 (48.9%)	19 (42.2%)	
Triglyceride					
−≤ 200 mg/dl	32(71.1%)	30 (66.7%)	30 (66.7%)	29 (64.4%)	0.075
−> 200 mg/dl	13 (28.9%)	15 (33.3%)	15 (33.3%)	16 (35.6%)	
Total cholesterol					
−≤ 180 mg/dl	25(55.6%)	21 (46.7%)	18 (40%)	17 (37.8%)	<0.002
−> 180 mg/dl	20 (44.4%)	24 (53.3%)	27 (60%)	28 (62.2%)	

* BMI. Body mass index

Table 2. Variation of the blood sugar by subgroups of uric acid level

Variation	Serum uric acid levels (mg/dL)				Pvalue
	<4.3	4.30 – 5.20	5.30 – 6.20	>6.20	
Mean FBS (mg/dl)	192.13 ± 62.75	177.56 ± 53.71	158.25 ± 41.28	139.25 ± 35.45	P<0.001
Mean 2hpp (mg/dl)	267.55 ± 68.23	249.39 ± 53.47	235.61 ± 51.25	226.84 ± 53.76	P<0.001
Mean HbA1c (%)	7.8 ± 1.6	7.5 ± 1.7	7.1 ± 1.3	6.8 ± 1.4	P<0.02

FBS. Fasting blood sugar; Mean 2hpp: Mean blood sugar after 2 hours; HbA1c: Glycated hemoglobin

Table 3. Relationship between independent variables with uric acid level greater than 5.3 mg / dl in multivariate logistic regression model

Independent variables	Odds ratio	95% Confidence	Pvalue
Age category			
−Less than 20 years	1.000		
−20 to 40 years	1.089	1.342 - 0.0652	0.063
−41 to 60 years	1.093	1.451 - 0.0712	0.052
−More than 60 years	1.123	1.532 - 0.0857	0.041
Sex			
−Female	1.000		
−Male	1.098	1.153 - 0.839	0.069
BMI* (kg/m^2)			
−Normal (≤ 24.99)	1.000		
−Overweight (25 - 29.99)	1.405	1.748 - 1.111	0.045
−Obese (> 30)	1.823	2.324 - 1.557	0.001
Education categories			
−Under the diploma	1.000		
−Diploma	0.923	1.125 - 0.756	0.055
−College education	0.875	1.035 - 0.612	0.051
Smoking			
−Never smoker	1.000		
−Former smoker	1.105	1.384 - 0.927	0.093
−Current smoker	1.352	1.715 - 1.069	0.058
Diabetic drug			
−Oral hypoglycemic	1.000		
−Insulin	1.118	1.339 - 0.912	0.077
Antihypertensive drug			
−Negative	1.000		
−Positive	1.089	1.263 - 0.916	0.063
Triglyceride			
−≤ 200 mg/dl	1.000		
−> 200 mg/dl	1.478	1.782 - 1.157	0.039
Total cholesterol			
−≤ 180 mg/dl	1.000		
−> 180 mg/dl	2.831	3.754 - 1.956	0.001

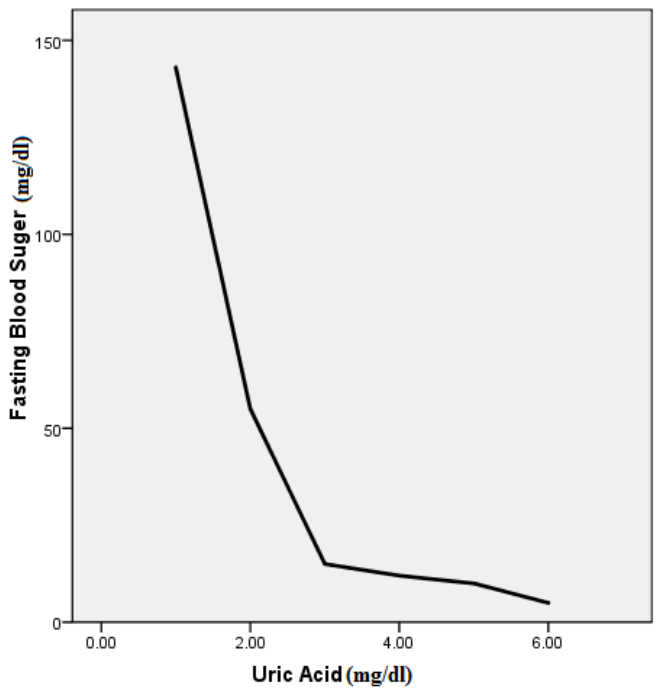

Figure 1. Association between serum uric acid level and fasting blood pressure

Discussion

In some studies, there is a link between uric acid and DM, but this relationship has been limited to some factors such as sex.[17] A number of studies have found this relationship very influential and relevant, while a number of other studies have reported no relation between uric acid and DM.[18-19] It should be noted that even some studies have shown an inverse relationship between these two variables.[20-21] The exact cause of all these differences in previous studies is not clear about the relationship between uric acid and diabetes but may be due to limitations in the study, such as selecting a specific population group, different methods of laboratory assessment or sample size.[22] In a study by Kang et al., in 2002, with the aim of investigating the relationship between uric acid and fasting blood on 3632 individuals in China, serum uric acid levels in the non-diabetic subjects tended to increase with increasing FPG, but in diabetic patients, the newly diagnosed level of uric acid decreased, Which is in perfect agreement with our research results.[22]

A study by Hostetter et al., in 2001 aimed at understanding the relationship between uric acid and various levels of blood glucose and related factors on 946 patients, it was concluded that the level of FBG and PPBG decreases with increased uric acid levels.[23] This finding is consistent with our study results. One of the possible reasons that can justify this inverse relationship between uric acid and DM is the inhibition of uric acid reuptake by the kidneys due to high blood sugar levels in diabetic patients.[24-25] This study found that even with control of factors such as age, sex, body mass index, cholesterol and triglyceride, there is an independent relationship between uric acid and blood glucose levels. This finding is consistent with the Brenner and Barnett researches results.[26-27] The exact mechanism of the effect of uric acid on the amount of glucose is unknown, but speculation is being made in this area. Increasing the level of uric acid in the blood causes a change in the level of oxidative stress and systemic inflammation, both of which contribute to a change in blood glucose levels.[3] On the other hand, changes in the amount of uric acid cause a change in the production of endothelial nitric oxide, which causes changes in the level of insulin resistance of the cells and also changes in blood glucose levels. Also, changes in the amount of uric acid cause changes in blood pressure in the kidney glomeruli and changes in sodium ion reabsorption from the kidneys, resulting in changes in blood insulin levels and, consequently, changes in blood glucose level.[3,28]

Finally, the results of the study showed that there was a significant and reversal relationship between the levels of uric acid and glucose levels that with increasing the amount of uric acid, the amount of glucose is significantly reduced, but for more precise determination of this relationship, more studies and sample size are needed. The results of this study showed that there is an inverse relationship between uric acid and glucose in diabetic patients. Therefore, in order to control the level of glucose, the level of uric acid in these patients is also to be measured and controlled, but for more precise determination of this relationship, more studies and sample sizes are needed.

The most important strength of the present study is the high sample size and population-based study, as well as the elimination of confounding factors through the multivariate regression model. The limitation of this project can be attributed to its cross-sectional nature, which makes it impossible to examine the relationship between changes in levels of uric acid and diabetes over time. More extensive studies, and especially Meta-analyzes, are essential for a thorough examination of the relationship between uric acid and diabetes. Finally, the results of this study showed that the amount of uric acid in the blood inversely affects blood glucose levels.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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