Utility of Serum Uric Acid to High-Density Lipoprotein Ratio in Prediction of Glycemic Control

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Abstract

Introduction India has witnessed diabetes as a growing problem and is on the verge of a diabetes mellitus (DM) epidemic. Glycemic control is the way to prevent the morbidity associated with diabetes. This study aimed to find out the utility of uric acid to the high-density lipoprotein (HDL) ratio (UHR) as a marker of diabetic control.

Methodology A hospital-based cross-sectional study was conducted among type-2 diabetic individuals who attended outpatient clinics and individuals who admitted to the inpatient wards of our hospital were enlisted. HDL cholesterol, serum uric acid, glycated hemoglobin were performed. Hemoglobin A1c (HbA1c) lower than 7% was classified as a good-controlled type-2 (DM) group and those with HbA1c between 7 and 10% were classified as uncontrolled type-2 DM group and those with HbA1c greater than 10% were classified as poorly controlled type-2 DM group. HbA1c was correlated with HDL, serum uric acid, and UHR.

Results Our study demonstrates that uric acid is inversely related to HbA1c and uric acid decreases following elevated HbA1c, and this relationship was statistically significant, whereas there was a nonsignificant inverse relationship between HDL and HbA1c and UHR with HbA1c.

Conclusion Established diabetics will have a lowering of uric acid as the diabetic control worsens and UHR could not be used as a marker of diabetic control.

Keywords

- diabetes mellitus
- uric acid to high-density lipoprotein ratio
- serum uric acid
- high-density lipoprotein

Introduction

Diabetes mellitus (DM) is a metabolic condition characterized by hyperglycemia and manifested by insulin resistance, reduced glucose utilization, and increased glucose synthesis. It is caused by a complex combination of heredity and environment.

According to the International Diabetes Federation (IDF), DM affected roughly 415 million persons aged 20 to 79 years in 2015.[1] DM is proving to be a global public health burden, with additional 200 million people predicted to be added by 2040.[2]

The hemoglobin A1c (glycated hemoglobin, glycosylated hemoglobin, HbA1c, or A1c) test is used to evaluate a person's level of glucose control.[3] The test shows an average of the blood sugar level over the past 90 days and represents a percentage and can also be used to diagnose diabetes.[4]

The main job of hemoglobin is to carry oxygen from the lungs to all the cells of the body. Hemoglobin becomes glycated or coated with glucose from the bloodstream. The amount of glucose in the blood will bind to the hemoglobin protein, and larger glucose levels will reflect on the surface of

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Table 1 General characteristics of study population

Variable	Range	*n*	Percentage
Age (y)	<50	17	28.3
	50–60	24	40.0
	>60	19	31.7
	Total	60	100
Gender	Males	29	48.3
	Females	31	51.7
	Total	60	100
BMI (kg/m^2)	18.5–24.9 (normal)	31	51.7
	25.0–29.9 (overweight)	24	40
	≥30 (obese)	5	8.3
	Total	60	100
HbA1c (%)	<7	12	20
	7–10	20	33.33
	>10	28	46.67
	Total	60	100

the hemoglobin protein surface, thereby resulting in a higher A1c score

Serum uric acid an end product of purine metabolism is found to be associated with cardiovascular disease, hypertension, and chronic kidney disease, and its association with DM is not consistent.

Kocak et al[5] in their study showed that uric acid to the high-density lipoprotein (HDL) ratio (UHR) was positively correlated with HbA1c and Hdl decreased with an increase in HbA1c and serum uric acid levels increased with an increase in HbA1c, this is contrary to previous studies that serum uric acid levels were lower with increasing HbA1c levels in known diabetics. So, we intended to study the utility of UHR and the relationship between serum uric acid and HbA1c in our setting.

Methodology

A hospital-based cross-sectional study was conducted among 60 type-2 diabetic individuals who attended outpatient clinics and individuals who admitted in the inpatient wards of our hospital were enrolled in the study after getting approval from the institutional ethical committee and getting informed consent. Exclusion criteria were pregnancy; treatment with drugs that interfere with serum uric acid levels, like thiazides, furosemide, acetylsalicylic acid, and others; and drugs that alter serum lipid levels like statins, fibrates, niacin, and individuals with active malignant disease; and those with established hemolytic conditions and end-stage renal failure.

Laboratory parameters such as HDL cholesterol, serum uric acid, and glycated hemoglobin were performed. Based on HbA1c readings, the patients were divided into three groups. Diabetics with HbA1c lower than 7% were classified as good-controlled type-2 DM group ($n = 12$) and those with HbA1c between 7 and 10% were classified as uncontrolled type-2 DM group ($n = 20$) and those with HbA1c greater than 10% were classified as poorly controlled type 2 DM group ($n = 28$). HbA1c was correlated with HDL, serum uric acid, and UHR. The analysis of variance (ANOVA) test was used to compare the variables.

Results

Data were analyzed by SPSS software. Variables are expressed as mean ± standard deviation.

The study enrolled a total of 60 type-2 diabetics with 29 (48.3%) men and 31 (51.7%) women (►**Table 1**), and a majority of the patients were between the age group of 50 to 60 years (40%; ►**Table 1**). The number of patients in the good-controlled diabetes group is 12, the number of patients included in the uncontrolled diabetes group is 20, and there were 28 patients included in the poorly controlled diabetes group. Overall, 40% of patients were overweight and 8.3% of patients were obese (►**Table 1**). Hypertension was found in 22 (36.7%) of the individuals. The majority of patients had diabetes for a duration of <10 years (71.7%). The mean ages of good-controlled, uncontrolled, and poorly controlled diabetics are 57.7 ± 10.1, 58.4 ± 8.3, and 54.3 ± 10.9 years, respectively, and the age difference was not statistically significant between these groups ($p = 0.34$). There was no statistically significant difference in gender between the study groups ($p = 0.162$). Similarly there was no statistically significant difference of BMI between the study groups ($p = 0.6$)

The mean HbA1c was the highest among poorly controlled group. The mean of uric acid and HDL is the highest among good-controlled group (►**Table 2**).

The one-way ANOVA results show that there is no significant difference in mean of HDL to the HBA1c ($t = 0.912$ and $p = 0.407$), and that there is no significant difference in mean of UHR to the HbA1c ($t = 2.241$ and $p = 0.116$), but there is a

Table 2 Mean of HDL, uric acid, UHR, duration of diabetes in different groups according to control of diabetes

	Well controlled ($n = 12$)	Uncontrolled ($n = 20$)	Poorly controlled ($n = 28$)
HDL cholesterol (mg/dL)	36.1 ± 5.8	34.3 ± 8.9	32.6 ± 7.6
Uric acid (mg/dL)	6.2 ± 2.4	4.5 ± 1.9	3.8 ± 1.7
UHR (%)	17.7 ± 7.5%	14.3 ± 7.4%	12.4 ± 7.3%
Duration of diabetes	6 ± 4.3	6.6 ± 3.6	7.4 ± 3.6

Abbreviations: HDL, high-density lipoprotein; UHR, uric acid to the high-density lipoprotein ratio.

significant difference in mean of uric acid to the HbA1c ($p = 0.003$).

Discussion

Serum uric acid levels has a linear relationship with blood glucose concentration in normal population and prediabetes population. Nakanishi et al[6] in their study of Japanese male office workers found that increased serum uric acid level is closely associated with an increased risk of type-2 DM and impaired fasting glucose. Choi and Ford[7] showed that metabolic syndrome prevalence and insulin resistance increase with the increasing levels of serum uric acid. Krishna et al[8] showed that hyperuricemia is an independent marker for predicting diabetes and prediabetes among young adults. This shows that increasing levels of uric acid indicate a high risk of developing DM.

However, among patients with established type-2 DM, uric acid levels tend to decline with increasing blood glucose concentration.[9] The reason for this inverse relationship is unclear. However, insulin levels are also closely related to uric acid levels.[10] Serum uric acid levels are directly associated with serum insulin levels in diabetics but the mechanism for this is not clear.[11] Serum uric acid is significantly elevated with increased fasting plasma glucose in nondiabetic individuals but reduced after the onset of diabetes.

Hyperuricemia increases with moderately increased levels of HbA1c and then decreases with a further increase in HbA1c, thus showing a bell-shaped relation. serum uric acid and fasting glucose levels showed a similar relation.[12] Insulin may enhance renal urate reabsorption via stimulation of the urate-anion exchanger URAT1.[13] Uricosuria is observed along with glycosuria when the blood glucose level is above 180 mg/dL.[10] The increased insulin levels in individuals with insulin resistance syndrome could conceivably contribute to their elevated serum uric acid levels to the point where the effect is offset by the subsequent development of diabetes, leading to glycosuria, uricosuria, and lower uric acid levels.[12]

Our study shows that uric acid is inversely related to HbA1c and uric acid decreases following elevated HbA1c this finding is similar to the study by Nan et al[14] who showed that serum uric acid tends to decrease with increased fasting plasma glucose levels in diabetic individuals and study by Cui et al[15] who conducted a study in newly diagnosed diabetics and found that there was an inverse correlation between serum uric acid and HbA1c.

The Framingham heart study showed that there exists a positive correlation between low-density lipoprotein (LDL) cholesterol and cardiovascular diseases, and there is an inverse correlation between HDL cholesterol and cardiovascular diseases.[16] Studies have shown that HDL participates in cholesterol efflux from peripheral cells and reverse transport of cholesterol from these cells to the liver and it also has an antioxidant action that neutralizes oxidized lipids and also inhibits various inflammatory responses.[17] In our study, there was an inverse relationship between HDL and HbA1c, and this relationship was not statistically significant (►**Figs. 1–3**).

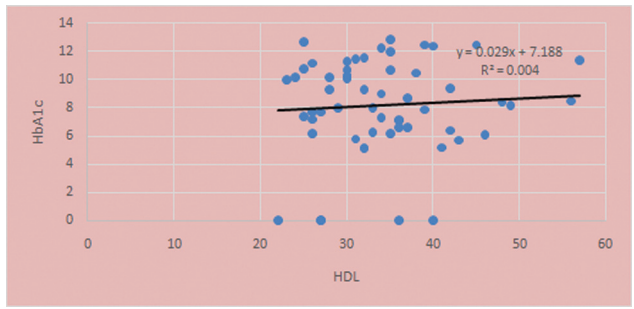

Fig. 1 Scatterplot for relationship between HDL and HbA1c. HbA1c, hemoglobin A1c; HDL, high-density lipoprotein.

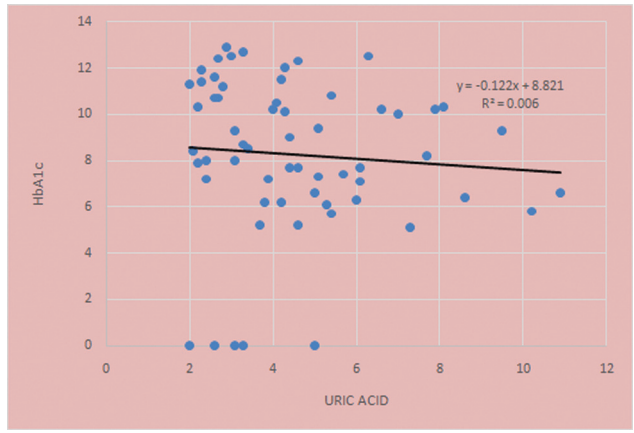

Fig. 2 Scatterplot for relationship between uric acid and HbA1c. HbA1c, hemoglobin A1c.

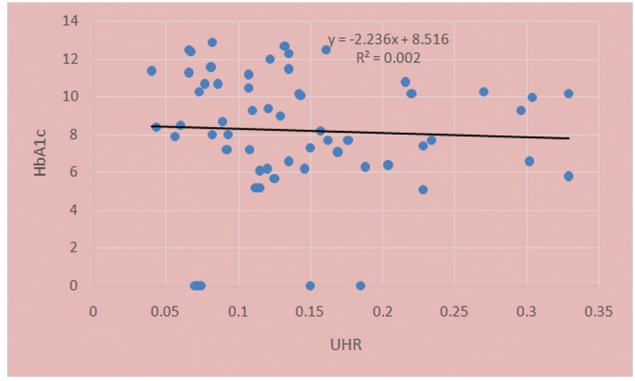

Fig. 3 Scatterplot for relationship between UHR and HbA1c. HbA1c, hemoglobin A1c; UHR, uric acid to the high-density lipoprotein ratio.

Similar to our study, a study from Montenegro showed that HbA1c is inversely related with HDL levels,[18] whereas a study from Sudan reported that there was no significant difference in triglyceride (TG), total cholesterol (TC), LDL, and HDL between the glycemic control group and the uncontrolled group.[19] The relative stability of HbA1c could account for some of the discrepancies, that is, HbA1c values remain constant over time and lipid profiles and FPG levels fluctuate. Then, studies on the relationship between HbA1c and lipid profiles at different time points over a while may present different results.

The relationship between uric acid to HDL ratio with HbA1c was that they are inversely related with each other and the difference between the well-controlled and poorly controlled diabetics was not statistically significant. This is, in contrast, to a study by Kocak et al which showed that patients with poorly controlled diabetes have a higher UHR ratio than patients with well-controlled diabetes. This may be because uric acid is used to calculate the UHR and uric acid was higher in poorly controlled than good-controlled diabetes showing a linear relationship in contrast to our study which shows an inverse relationship.

Conclusion

Our study suggests that UHR could not be used as a marker of glycemic control. Uric acid is inversely related to HbA1c in diabetic patients and uric acid decreases following elevated HbA1c in established diabetics. As a result, serum uric acid may be a factor in altered glucose metabolism. However, further studies with a greater sample size can yield more scientific evidence.

Conflict of Interest
None declared.

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