

## Serum uric acid in type 2 diabetics

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### ABSTRACT:

**Aims:** To compare the level of serum uric acid (UA) in type 2 diabetics with a control group and to demonstrate its relation with other risk factors as age , BMI, duration of diabetes, blood glucose and total cholesterol level.

**Methods:** The study was conducted in Al-Wafa Diabetic Clinic in Mosul during the period from February to May 2007 as a case-control study. A 39 patients of both sexes with type 2 diabetes with a mean  $\pm$  SD age of  $51.5 \pm 11.1$  years , and 20 healthy subjects of both sexes with a mean  $\pm$  SD age of  $46.5 \pm 15.5$  years as a control group. The concentrations of fasting serum glucose, total cholesterol and UA was determined; BMI was calculated.

**Results:** BMI, fasting serum glucose, UA and total cholesterol concentrations are significantly higher ( $P < 0.001, 0.01, 0.01$  respectively) in type 2 diabetics compared to the control group with a positive correlation ( $r = 0.605, P < 0.005$ ) between serum UA and the duration of diabetes.

**Conclusions:** Because serum UA concentration is significantly higher in type 2 diabetics independent on other factors and as it predicts the occurrence of ischemic heart diseases, stroke and even renal disease in these patients; therefore, its measurement is recommended. Since it positively correlated with the duration of diabetes, therefore, the longer the history of diabetes was, the more frequent measurement should be done.

### الخلاصة

**أهداف البحث:** لمُقارَنَة مستوى الحامض البولي لمصل الدم للمصابين بداء السُّكري من النمط الثاني مع مجموعة ضابطة وإظهار علاقته بمؤشرات الخطر الأخرى كالعمر، دليل كتلة الجسم، مدّة مرض السُّكري، مُستوى الجلوكوز والكوليستيرول الكليّ في الدم.

**الطرق:** أُجريت الدراسة في عيادة الوفاء لداء السُّكري في الموصل للفترة من فبراير/شباط ولغاية مايو/مايس ٢٠٠٧ بطريقة مقارنة الحالات المرضيه مع المجموعة الضابطة.

**المشاركون:** شملت الدراسة ٣٩ من المرضى المصابين بداء السُّكري من النمط الثاني من كلا الجنسين حيث يبلغ المعدل والانحراف المعياري لأعمارهم  $51.5 \pm 11.1$  سنة و ٢٠ من الأصحاء من كلا الجنسين كمجموعة ضابطة حيث يبلغ المعدل والانحراف المعياري لأعمارهم  $46.5 \pm 15.5$  سنة. تم قياس مستوى الجلوكوز، الكوليستيرول الكليّ والحامض البولي لمصل الدم في حاله الصوم لكلتا المجموعتين مع حساب دليل كتلة الجسم.

**النتائج:** أظهرت نتائج البحث ارتفاعا معنويا لقيم دليل كتلة الجسم ومستويات الجلوكوز، الكوليستيرول الكليّ والحامض البولي لمصل الدم ( $P < 0.001, 0.01, 0.01$  على التوالي) للمصابين بداء السُّكري من النمط الثاني مقارنة بالمجموعة الضابطة بالإضافة لوجود ارتباط إيجابي معنوي ( $r = 0.605, P < 0.005$ ) بين تركيز الحامض البولي لمصل الدم ومدّة مرض السُّكري.

**الاستنتاجات:** بسبب أن تركيز الحامض البولي لمصل الدم أعلى في المصابين بداء السُّكري من النمط الثاني بصوره مستقلة عن العوامل الأخرى ولكونه يتوقّع حدوث أمراض ذوي القلبية، ألجلطة الدماغية وحتى الأمراض الكلوية لهؤلاء المرضى لذا يُوصى بقياسه ونظرا لوجود ارتباط إيجابي مع مدة المرض لذا يستدعي تكرار قياسه أكثر مع زيادة تاريخ المرض.

Humans convert adenosine and guanosine into UA<sup>(1)</sup>. In mammals other than higher primates, uricase converts UA to the water-soluble allantoin. However, since humans lack uricase, the end product of purine catabolism is UA<sup>(1)</sup>.

Different studies have indicated that hyperuricemia predicts the development of ischemic heart disease in non-diabetic subjects<sup>(2-6)</sup>, this applies also to the patients with type 2 diabetes<sup>(7)</sup>. Even "asymptomatic hyperuricemia" have also demonstrated a remarkable association with hypertension, obesity, metabolic syndrome, kidney disease, and cardiovascular disease<sup>(8-13)</sup>. And lowering UA in patients with renal disease and asymptomatic hyperuricemia resulted in less progression of their renal problem<sup>(14, 15)</sup>.

Recent studies in humans found that elevated serum UA predicts the development of hyperinsulinemia<sup>(16)</sup>, obesity<sup>(17, 18)</sup>, type 2 diabetes<sup>(16, 19)</sup>, in addition to the development of stroke in middle-aged patients with type 2 diabetes independently of other cardiovascular risk factors<sup>(20)</sup>.

The aim of this study is to compare the UA concentration in patients with type 2 diabetes with a control group in Mosul city and its relation with other risk factors as age, Body Mass Index (BMI), duration of diabetes, blood glucose and total cholesterol level in those diabetic patients.

### ***Patients and methods***

This study was conducted during the period from February to May 2007, the

subjects enrolled in this study were divided into two groups (group I and II).

Group I composed of 20 apparently healthy subjects (11 males and 9 females), their ages ranged from (29-77) years with a mean  $\pm$  SD of  $46.5 \pm 15.5$  years.

Group II composed of 39 patients (17 males and 22 females) with type 2 diabetes was diagnosed by clinical history and laboratory investigations who were attending Al-Wafa Diabetic Clinic in Mosul. Their ages ranged from (26-73) years with a mean  $\pm$  SD of  $51.5 \pm 11.1$  years. They have no any evidence of renal, cardiovascular or stroke attacks. None of the control and patients had a history of any cause that may affect their serum UA concentration.

A complete record of history was obtained, including name, age, sex, duration of diabetes, diet and drugs; measurement of height (Ht) and weight (Wt) was done for all subjects enrolled in the study. Fasting blood samples were obtained from the patients and controls then blood samples were centrifuged at 3000 rpm for 15 minutes. Estimation of serum glucose, total cholesterol and UA was done within one hour of sample collection in the clinical chemistry laboratory of the Department of Biochemistry, Nineveh College of Medicine, by the enzymatic colorimetric methods using glucose oxidase peroxidase<sup>(21)</sup>, cholesterol oxidase<sup>(22)</sup> and uricase methods<sup>(23)</sup> respectively. The results were evaluated by statistical methods including the mean ( $\bar{X}$ ), standard deviation (SD), range (minimum-

maximum), Linear regression analysis (Pearson correlation coefficient  $r$ ), paired and unpaired student's t-test<sup>(24, 25, 26)</sup> to evaluate the relation between different parameters in group I and II. Differences between observations were considered not significant at  $p > 0.05$ . BMI was calculated by dividing  $Wt/Ht^2$ <sup>(27)</sup>.

### Results

There is no significant difference ( $P > 0.05$ ) in the age between group I and II (Table 1).

Fasting serum glucose, UA and total cholesterol concentrations are significantly higher in group II than group I ( $P < 0.001$ ,  $0.01$ ,  $0.01$  respectively, table 1).

BMI in group II was significantly higher than group I ( $P < 0.001$ , table 1).

There is positive correlation ( $r = 0.605$ ,  $p < 0.005$ ) between serum UA concentration and the duration of diabetes in group II (Fig:1) while there is no significant correlations with age, BMI, fasting serum glucose and serum total cholesterol level.

Table 1 : Comparison between different parameters of both groups.  
(Values are presented as mean  $\pm$  SD)

Parameter	Group I (Control) n = 20	Group II (Type 2 diabetics) n = 39	P-Value
Age (years)	46.5 $\pm$ 15.5	51.5 $\pm$ 11.1	NS
BMI (Kg/m <sup>2</sup> )	26.37 $\pm$ 1.79	30.11 $\pm$ 4.41	P < 0.001
Glucose (mmol/L)	4.36 $\pm$ 0.37	8.79 $\pm$ 2.96	P < 0.001
Uric Acid ( $\mu$ mol/L)	0.20 $\pm$ 0.07	0.28 $\pm$ 0.09	P < 0.01
Total Cholesterol (mmol/L)	4.21 $\pm$ 0.68	4.96 $\pm$ 1.06	P < 0.01

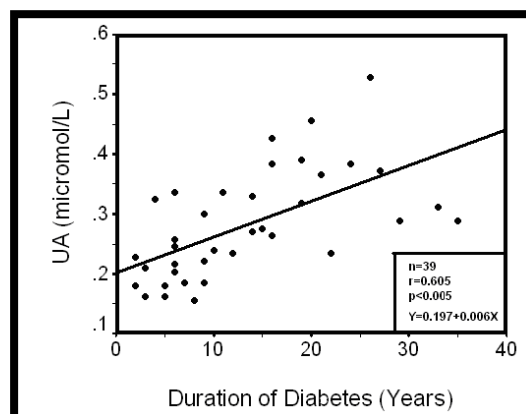


Fig:1 Correlation between serum uric acid and duration of diabetes in group II.

## Discussion

Measurement of serum UA is important in type 2 diabetics as it predicts the development of ischemic heart disease, stroke and even renal diseases in these patients independent of other risk factors (7-13,20).

In this study it was found that fasting serum UA concentration was significantly higher in type 2 diabetics than in control subjects.

Evidently group II patients have other significantly higher risk factors for ischemic heart diseases in comparison with the control subjects such as (serum total cholesterol, blood glucose and BMI) and even, according to the National Center for Health Statistics, only 5.13% of group II patients with BMI within acceptable range while 61.54% are overweight, 30.77% are obese and 2.56% are morbidity obese. However, in this study there is no any significant correlation between serum UA and these risk factors. This finding is in agreement with other studies that showed serum UA is an independent risk factor in diabetics not dependent on age, BMI or plasma glucose concentration (7-13,20,28).

Facchini et al (29), explain the cause of high UA in elevated insulin resistance on the basis reported that urinary UA clearance decreased in proportion to increases in insulin resistance in normal volunteers. They attributed that compensatory hyperinsulinemia in subjects with insulin resistance possibly causing decreased renal excretion of UA

in association with increased sodium reabsorption.

On the other hand, it was reported that UA reduces endothelial nitric oxide bioavailability<sup>(30)</sup>, which is essential for insulin-stimulated glucose uptake in skeletal muscle<sup>(31)</sup>.

Different studies showed controversy about the role of UA on vascular complications. Some concluded that UA is one of the major endogenous water-soluble antioxidants of the body<sup>(32)</sup> and there is an accumulating evidence that increased oxidative stress is closely related to diabetes and its vascular complications<sup>(33)</sup>. Thus, high circulating UA levels may be an indicator that the body is trying to protect itself from the deleterious effects of free radicals by increasing the products of endogenous antioxidants, e.g., UA. In addition, UA prevents oxidative modification of endothelial enzymes and preserves the ability of endothelium to mediate vascular dilatation in the face of oxidative stress<sup>(32)</sup>. In contrast, other studies concluded that UA may have a direct role in the atherosclerotic process, because human atherosclerotic plaque contains more UA than in the arteries of the control subjects<sup>(34)</sup>. Because inflammation is one of the features of atherosclerosis<sup>(35)</sup>, UA crystals may induce inflammatory responses that are reduced by lipoproteins which have an ability to bind UA crystals<sup>(36)</sup>. Hyperuricemia via purine metabolism may also promote thrombus formation.<sup>(37, 38)</sup> and the elevations of UA above 4 mg/dl should be considered a "red flag" in those patients at risk for

cardiovascular disease and should alert the clinician to strive to utilize a global risk reduction program in a team effort to reduce the complications of the atherogenic process resulting in the morbid – mortal outcomes of cardiovascular disease<sup>(13)</sup>.

In conclusions; as UA concentration is significantly higher in diabetics and as different studies proved that high UA predicts the development of ischemic heart disease, stroke and even renal diseases independent on other factors, therefore, its measurement is recommended. As serum UA is positively correlated with the duration of diabetes, therefore, the longer the history of diabetes was, the more frequent serum UA measurement should be done.

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