

Can Serum Uric Acid Predict Prediabetes in Adult Males? A Case Control Study

Methaq H Alogaili¹, Atheer J Alsaffar¹, Nibras Alaa Hussain¹

¹Al-Nahrain University, College of Medicine, Dept. of Community and Family Medicine, Baghdad, Iraq.

Corresponding author:

Methaq H Alogaili, Al-Nahrain University, College of Medicine, Dept. of Community and Family Medicine, Baghdad, Iraq.

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Introduction

It is well known that serum uric acid (SUA) involved in the metabolic dysregulations which leads to the development of type 2 diabetes mellitus (T2DM) but this relation is not fully explored with prediabetes (PreDM) which is a metabolic state characterized by higher than normal glucose level but not enough to be considered as diabetes [1,2]. About two-thirds of those with preDM will progress to T2DM [3]. Those with preDM are almost identical (regarding risk factors) to those with T2DM (advanced age, obesity and diminished physical activity...etc.) and also are predisposed to develop both micro and macrovascular complications of overt T2DM [4]. Accumulation of SUA in excess play key role in the pathogenesis of metabolic syndrome (overweight, elevated blood pressure, dyslipidemia and abnormal glucose metabolism) [5]. The Preventive Cardiology Information System (PreCIS) database assured that for each one mg/dl rise in the SUA level, there was increase in the risk of death by 39% and even after adjusting for other cardiovascular risk factors, the SUA level continued to predict the risk of death [6].

Previous epidemiological studies showed that elevated levels of SUA are associated with the development of T2DM [7, 8]. Recently this relationship was also investigated regarding preDM and concluded positive association of elevated SUA with insulin resistance and preDM [9, 10].

Since elevated SUA is closely linked to metabolic syndrome, the real association between SUA concentrations and preDM may be fogged by those associated risk factors [11]. Thus, this study was conducted in a way to control major risk factors shared between the two conditions (sex, age and BMI).

AIMS

To evaluate serum uric acid level in individuals with and without prediabetes and to address some demographic characteristics associated with both conditions.

Methods

One hundred sixty pre-DM male adults (30-74 years) were compared to age and BMI matched non preDM group. Both were randomly selected from people attending outpatient clinics in Baghdad teaching hospital and Imamein Kadhimein Medical City, both are large hospitals on the opposite sides of Tigris river which splits Baghdad the capital of Iraq of about 8 million inhabitants into almost equal halves namely; Rusafa and kerckh, respectively.

Exclusion criteria were: diabetes or on anti-diabetic drugs, hypertension, anemia or hemoglobinopathies, malignant disease, hypo or hyperthyroidism, hepatic disease, renal disease, any chronic drugs intake or alcohol abuse. Demographic data and anthropometric measurements were collected through direct interview.

A venous blood sample (one-milliliter) was obtained from each participant, mixed thoroughly and collected in a vacuum collection K3 EDTA tube with another two-milliliter in a gel and clot activator glass tube, both samples were analyzed immediately by laboratory technician. SUA, total cholesterol (TC) and triglycerides (TGs) were measured using Siemens Dimension EXL 200. Arkray ADAMS A1C HA-8180V (Menarini) were used for glycosylated hemoglobin (A1C) measurement (enzymatic method). Hemoglobin (Hb %) and hematocrit (Hct) were measured using Celltac Es MEK-7300K.

PreDM was defined as not having previous diabetes, but having A1C between 5.7% and 6.4%, diabetes is considered when A1C was 6.5 or more [12]. Hyperuricemia was defined if participants having their SUA >7.0 mg/dl [13].

Statistical Analysis

Data were coded, entered and analyzed using (Statistical Packages for Social Sciences program, version 24). Paired t-test was used to compare means in both groups, McNemar chi square test were used to examine the association and conditional logistic regression used hyperuricemia to predict PreDM after controlling other covariates. P value of less than 0.05 was considered statistically

significant.

Results

The mean age of the participants was (52.7± 12.2 years) with mean BMI of (29.6± 3.8) (table1). There was significant difference in the mean of SUA between two groups (8.14± 1.2) for preDM group vs (5.27± 1.5) for control group (P <0.001). A significant difference in the mean of SBP (but not diastolic) was found between two groups [(127.3± 15.5) and (122.7 ± 15.2), respectively (p=0.006)], the mean Hb% [(14.1± 1.5) for preDM group vs (13.2±

1.6) for matched group (P <0.001)], the mean Hct [(42.2± 4.8) for preDM group vs (39.5± 5.0) for matched group (P <0.001)] and the mean TGs [(157.7± 64.3) for preDM group vs (134.25± 49.0) for matched group (P= 0.01)], however, No difference were found in the mean of TC between two groups. Hyperuricemia were significantly higher in preDM group (table2). Smoking were significantly higher in preDM group (table3). Those with preDM had significantly lower educational level than matched group (P= 0.02) (table4).

Table 1: Baseline characteristics for the study populations.

	<i>PreDM</i>	<i>Non-preDM</i>	<i>P-value</i>
<i>Age* (years)</i>	57.7± 12.2		
<i>BMI*</i>	29.5± 3.8		
<i>SUA mg/dl*</i>	8.14± 1.2	5.27± 1.5	P<0.001
<i>SBP*</i>	127.3± 15.5	122.7 ± 15.2	P=0.006
<i>DBP*</i>	79.6± 8.9	78.2± 8.3	P= 0.10
<i>Hb%*</i>	14.1± 1.5	13.1± 1.6	P<0.001
<i>Hct*</i>	42.2± 4.8	39.5± 5.0	P<0.001
<i>TC*</i>	192.2± 40.5	192.4 ± 41.4	P=0.95
<i>TGS*</i>	157.7± 46.3	134.3 ± 49.0	P=0.001

*Values are expressed as mean ± SD, P value obtained by paired t test.

Table 2: Hyperuricemia in preDM and matched group.

<i>Non-PreDM</i>	<i>PreDM</i>	
	Hyperuricemia	Normal
Hyperuricemia	20	100
Normal	3	37

McNemar chi square test: 95% CI (0.69, 8.79), OR= 2.47, P <0.001.

Table 3: Smoking in preDM and matched group.

<i>Non-PreDM</i>	<i>PreDM</i>	
	Yes	No
Yes	25	15
No	61	59

McNemar chi square test: 95% CI (0.77, 3.36), OR= 1.61, P <0.001.

Table 4: Education level in preDM and matched group.

<i>Non-PreDM</i>	<i>PreDM</i>			
	Illiterate	primary	secondary	higher
Illiterate	1	8	6	5
primary	4	13	10	4
secondary	16	23	15	16
higher	4	12	16	7

McNemar-Bowker test: 15.1, df= 6, P value= 0.02.

Table 5: Conditional logistic regression for hyperuricemia in prediabetes

	B	SE	Wald	df	95%CI	OR	P value
SUA-diff	1.95	0.54	13.15	1	2.46, 20.30	7.01	P<0.001
TGs-diff	0.01	0.01	2.64	1	0.10, 1.03	1.01	P=0.10
SBP-diff	0.01	0.02	0.18	1	0.97, 1.05	1.01	P=0.68
Hb%-diff	0.63	0.22	8.41	1	1.23, 2.90	1.82	P=0.01

Conditional logistic regression showed significant association of serum uric acid level in prediabetes group (CI%=2.95, 18.59, OR= 7.41, p<0.001) and (CI%=2.46, 20.30, OR= 7.01, p<0.001) when SBP, Hb% and triglycerides entered as covariates (table5).

Discussion

Being a part of the vicious cycle (obesity, hyperlipidemia, hypertension and diabetes), SUA seldom investigated alone in the epidemiology of diabetes and more specifically, in the global era of preDM. This study, from the early start, tried to seclude, as much as possible, the most important confounders in this cycle (sex, age and BMI). SUA was significantly higher in those with preDM and this in agreement with other studies, uric acid has a known effect augmenting insulin resistance by inhibiting of beta cell function and increasing hepatic glucose output, obesity did so, and by controlling for this important factor, SUA appeared to affect insulin resistance significantly and independently [14, 15, 16]. Moreover, conditional logistic regression model of SUA predicting PreDM, showed significant association even when other confounders (SBP, Hb% and TGs) controlled. This may throw light also on the possibility of including lowering SUA in preDM individuals as a part of the early interventions (e.g. weight reduction, life style modification and use of metformin) to prevent future development of T2DM.

The finding of significant difference in the mean of SBP, and TG agrees with other studies and with nearly desirable level of TC (may be due Low HDL), those people are most likely to have metabolic syndrome [17, 18, 19]. This was the case for Hb% and Hct also were significant difference in means were found. Ren Q et al studied the performance of A1C in the screening for preDM and diabetes in patient with erythrocytosis living in high attitude and found no correlation between Hb% level and A1C [20]. Lower education level in PreDM was found, and this finding is in cop with other studies [21, 22]. Educational level does not, of course, have a direct biological effect on disease but it has effects that are mediated by other risk factors for development of PreDM and eventually T2DM (e.g. smoking, obesity and sedentary life style).

Up to our knowledge, this study among the few in the region and the first in Iraq that assess the relationship between SUA and preDM especially with this two large multi-matched groups. However, we recommend conducting a large cohort or clinical trial to document the beneficial effect of lowering SUA in preDM individuals through reversion of hyper into normoglycemia and to address the casual pathway. In addition, a cutoff value of SUA (above

which interventions should be taken) is needed to be determined.

Ethical Considerations

The study was approved by the institutional review board of the college of medicine/ Al - Nahrain University, and a request to facilitate the task of researchers was given. Participants directly interviewed and told about the research purpose and procedure, their acceptance in participation was guaranteed and confidentiality about participant's information was insured.

Conflicting And Competing Interests

The author(s) declare no conflict of interest for the present study.

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Conclusions

SUA is an important predictor factor for preDM. More attention should be paid for controlling this factor in preDM prevention and management.

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