Original Article

Association Between Serum Uric Acid and Prevalence of Type 2 Diabetes Diagnosed using HbA1c Criteria Among Chinese Adults in Qingdao, China*

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Abstract

Objective To determine whether elevated serum uric acid (UA) levels are associated with type 2 diabetes diagnosed using HbA1c levels among Chinese adults.

Methods We conducted two population-based cross-sectional studies in Qingdao in China in 2006 and 2009. A total of 6894 (39.4% men) subjects aged 35-74 years were included in the data analysis. Newly diagnosed diabetes was defined as HbA1c level of ≥6.5%, and prediabetes was classified as HbA1c level between 5.7% and 6.4% according to the International Diabetes Federation criteria. Multivariate logistic regression was employed to assess the association between UA and prevalence of type 2 diabetes defined using Glycated hemoglobin A1c (HbA1c levels.

Results Subjects with prediabetes had higher UA levels than those with normal glucose tolerance, newly diagnosed diabetes, and known diabetes, with corresponding values of 325.1 (82.5) μmol/L, 310.9 (84.2) μmol/L, 291.3 (81.7) μmol/L, 305.2 (83.6) μmol/L, respectively (P<0.001 for all comparisons). Binary logistic regression analysis showed that UA was a possible predictor for the prevalence of type 2 diabetes diagnosed using HbA1c levels, and the second quartile of UA levels had a higher odds ratio (OR: 4.088; 95% CI: 2.900-5.765) for HbA1c than the other quartiles after adjusting for age, body mass index, sex, marital status, education, income, alcohol consumption, smoking, and cardiometabolic parameters.

Conclusion Serum UA is significantly associated with type 2 diabetes diagnosed using HbA1c levels, independent of other cardiometabolic parameters.

Key words: Uric acid; Type 2 diabetes; Hemoglobin A1c; Cardiometabolic parameters

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INTRODUCTION

Serum uric acid (UA), the end product of purine metabolism, possesses both antioxidant and pro-oxidant properties, which depend on its chemical microenvironment. The epidemic of hyperuricemia is dramatically increasing worldwide, with prevalence rates of 16.0% among men and 10.7% among women in Brazil[1], 15.45% in Korea[2], 11.2% in the United States[3], 12.0% in Turkey[4], and 22.5% among men and 15.3% among women in Qingdao, China[5]. Recently, hyperuricemia or elevated serum UA levels have been considered as an independent risk factor for vascular diseases such as coronary heart disease and hypertension; however, this relationship is still uncertain among individuals with type 2 diabetes[6-9]. Diabetes mellitus is a metabolic disorder characterized by hyperglycemia and insufficiency in the secretion or action of endogenous insulin. The global prevalence of diabetes has been growing rapidly from 382 million in 2013 to an estimated 592 million in 2035[10]. Glycated hemoglobin A1c (HbA1c) is a form of hemoglobin that is primarily measured to identify the average plasma glucose concentration over prolonged periods of time. It is formed in a nonenzymatic glycation pathway when hemoglobin is exposed to plasma glucose. Normal levels of glucose produce a normal amount of glycated hemoglobin. In 2009, the International Expert Committee that included representatives of the American Diabetes Association (ADA), International Diabetes Federation (IDF), and European Association for the Study of Diabetes (EASD) recommended that an HbA1c threshold of ≥6.5% should be used to diagnose diabetes[11], which was subsequently adopted by the ADA in 2010[12].

Several cross-sectional studies have been conducted on the association of UA with either fasting plasma glucose (FPG) or 2-h plasma glucose (2hPG) since its first introduction in 1923[13-14]. UA is significantly associated with serum insulin levels in newly diagnosed diabetes; however, in contrast, the relationship between UA and HbA1c is controversial[15]. The Third National Health and Nutrition Examination Survey (1988-1994) first examined that serum UA levels increased with moderately increasing levels of HbA1c (6.0%-6.9%) and decreased with further increasing levels of HbA1c (a bell-shaped relation)[16]. Some present studies[12-13] also revealed that increased UA levels were correlated with decreased HbA1c levels[17-18]. Therefore, this study aimed to evaluate the possible association between UA and type 2 diabetes diagnosed using HbA1c levels among Chinese adults.

MATERIALS AND METHODS

Subjects

Two cross-sectional diabetes surveys were conducted in three urban areas (Shinan, Shibei, and Sifang) and three rural areas (Huangdao, Jiaonan, and Jimo) in Qingdao, China, in 2006 and 2009, respectively. A stratified, random cluster sampling method was used to recruit a representative sample of the general population who had lived in Qingdao city for at least 5 years. A total of 5335 and 5110 individuals aged 35-74 years attended the 2006 and 2009 surveys, with response rates of 87.8% and 67.1%, respectively. The current study were no data missing for body mass index (BMI), waist circumference (WC), blood pressure measurements, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C); total cholesterol (TC), triglycerides(TG), uric acid (UA) and HbA1c. A total of 6894 subjects with full required information were included.

Data Collection

The same protocols, questionnaires, physical examination, and laboratory determination methods were employed in both the 2006 and 2009 surveys. A standardized questionnaire was used by trained physicians to collect information such as demographic data, food frequency, alcohol consumption, and smoking habits, family history of diabetes and gout, personal history of hypertension, cardiovascular disease, and dyslipidemia. The per capita monthly income was categorized into low (<999¥), moderate (1000-2999¥), and high (≥3000¥). Smoking status or alcohol consumption was defined as never, current (smoking or consuming alcohol regularly for the past 6 months), or ever (cessation of smoking or alcohol consumption for more than 6 months). The types, amount, and frequency of alcohol consumption were also collected. Height and weight were measured with light clothes and

without shoes, and the body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters (kg/m^2). Waist circumference (WC) was measured at the middle point between the rib cage and top of the iliac crest to the nearest 0.1 cm. Three consecutive blood pressure readings, apart by at least 30 s, were taken from the right arm of subjects, and the average of the three readings was used in the data analysis.

Biochemical Measurements

Subjects without diagnosed diabetes underwent a standard 2-h 75-g oral glucose tolerance test (OGTT). Blood samples were collected from the antecubital vein into a vacuum tube containing sodium fluoride. The specimens were placed in ice-cooled containers and transported immediately to the central laboratory of Qingdao Hiser Medical Center. Plasma glucose and serum lipid assays in the 2006 and 2009 surveys were performed using Olympus-AU 640 Automatic Analyzer. HbA1c was measured using the chemiluminescent immunoassay method. Fasting serum UA, triglycerides (TG), total cholesterol (TC), and high-density lipoprotein cholesterol (HDL-C) levels were determined by the enzymatic method. Low-density lipoprotein choles- terol (LDL-C) was calculated using the Friedewald equation. The Ethics Committee of Qingdao Centers for Disease Prevention and Control approved the study. Verbal or written consent was obtained from each participant prior to data collection.

Classification of Diabetes

People who reported a history of diabetes and underwent treatment with either insulin or oral antidiabetic agents were considered as previously diagnosed diabetes, regardless of their glucose levels. Newly diagnosed diabetes was defined as an HbA1c of ≥6.5% according to the IDF criteria[8] and ADA report, based on the role of HbA1c assay for diabetes. Individuals with an HbA1c between 5.7 and 6.4% were classified as prediabetes.

Categorization of Serum UA

Subjects were divided into quartiles of UA concentrations with cut-off points for men and women, because women have lower serum UA levels than men on average (Q1: <297 μmol/L, Q2: 297-346 μmol/L, Q3: 347-403 μmol/L, and Q4: >403 μmol/L in men; Q1: <231 μmol/L, Q2: 231-271 μmol/L, Q3: 272-318 μmol/L, and Q4: >318 μmoL/l in women).

Definition of Cardiometabolic Parameters

Hypertension was defined as systolic blood pressure (SBP) of ≥140 mmHg and/or diastolic blood pressure (DBP) of ≥90 mmHg or usage of antihypertensive medications. Hyperlipidemia was defined as (1) TC≥5.72 mmol/L, (2) TG≥1.70 mmol/L, (3) HDL-C<0.91 mmol/L, and/or LDL-C>3.64 mmol/L. Obesity was defined as BMI≥28 kg/m^2.

Statistical Analysis

For continuous variables, differences between groups were tested using a *t*-test for comparing two groups or, alternatively, one-way analysis of variance (ANOVA) complemented by the Duncan's test. Chi-square test was employed for categorical variables. Correlation of UA with HbA1c was assessed using the Spearman method. Binary logistic regression analysis was performed to evaluate the association of UA with diabetes defined using HbA1c levels, after adjusting for sex, marital status, education, income, alcohol consumption, smoking, and cardiometabolic parameters. Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS; USA), version 18.0. *P* values of <0.05 were considered to be statistically significant.

RESULTS

The baseline characteristics of subjects are presented in Table 1. A total of 6894 subjects (39.41% men) were included in this study, with a mean± standard deviation (SD) age of 51.21±10.6 years. The prevalence of newly diagnosed diabetes diagnosed using HbA1c criteria was 4.8% in men and 5.5% in women, and that of known diabetes was 5.3% and 5.9% among men and women, respectively. Mean values of BMI, WC, HDL-C, LDL-C, and 2hPG levels were higher in men than in women (*P*<0.05), except for TC (*P*=0.14), FPG (*P*=0.83), and HbA1c (*P*=0.92). Men were more likely to be either a smoker or an excessive alcohol consumer (all *P*<0.001). Mean values of SBP and DBP were 135±21 *vs*. 133±23 mmHg (*P*<0.001) and 85±12 *vs*. 83±12 mmHg for men and women, respectively (*P*<0.001). Women had significantly lower UA levels than men

(352.51±84.02 μmol/L *vs*. 277.73±69.24 μmol/L, *P*<0.001). Hypertension prevalence was higher in men than in women (40.70% *vs*. 23.79%, *P*<0.001).

As shown in Table 2, higher UA levels were associated with higher levels of mean BMI, WC, SBP, DBP, and TC (*P*<0.01) but with lower levels of mean HDL-C, LDL-C, and HbA1c (*P*<0.001) among men and women throughout the UA quartiles. An increasing trend was found between age and UA quartiles in women, while the reverse was observed in men (*P*<0.01 for all comparisons). There were no statistically significant differences in 2-h plasma glucose (2hPG) levels in men across the UA quartiles (*P*=0.2).

As shown in Tables 3 and 4, subjects with prediabetes had the highest UA levels compared to subjects with normal glucose tolerance, newly diagnosed diabetes,

Table 1. Baseline Characteristics of the Study Population

Variable	Total	Men	Women	*P* Value
N (%)	6894	2717 (39.41)	4177 (60.59)	<0.001
Age, years	51.21±10.6	51.81±10.9	50.8±10.3	<0.001
Education Level				<0.001
Illiteracy, *n* (%)	636 (9.23)	102 (3.75)	534 (12.78)	
Primary, *n* (%)	1396 (20.25)	511 (18.81)	885 (21.19)	
Secondary, *n* (%)	2481 (35.99)	1032 (37.98)	1449 (34.69)	
Senior, *n* (%)	1556 (22.57)	617 (22.71)	939 (22.48)	
University, *n* (%)	825 (11.97)	455 (16.75)	370 (8.86)	
Family monthly income, ¥				<0.001
<999, *n* (%)	4666 (67.68)	1524 (56.09)	3142 (75.22)	
1000-2999, *n* (%)	1931 (28.01)	982 (36.14)	949 (22.72)	
≥3000, *n* (%)	297 (4.31)	211 (7.77)	86 (2.06)	
Current smoking, *n* (%)	537 (7.79)	517 (54.08)	20 (1.36)	<0.001
Current drinking, *n* (%)	1448 (21.00)	838 (47.83)	50 (6.96)	<0.001
BMI, kg/m^2	25.40±3.61	25.16±3.43	25.54±3.70	<0.001
WC, cm	84.18±10.36	86.51±10.33	82.70±10.11	<0.001
SBP, mmHg	134±22	135±21	133±23	<0.001
DBP, mmHg	84±12	85±12	83±12	<0.001
Hypertension, *n* (%)	2098 (30.43)	1105 (40.70)	993 (23.79)	<0.001
TC, mmol/L	5.29±1.05	5.27±1.04	5.30±1.07	0.14
TG, mmol/L	1.43±1.18	1.50±1.38	1.38±1.03	<0.001
HDL-C, mmol/L	1.63±0.43	1.61±0.44	1.65±0.42	<0.001
LDL-C, mmol/L	3.11±1.27	3.03±1.40	3.17±1.17	<0.001
FPG, mmol/L	5.98±1.80	6.01±1.78	5.95±1.81	0.83
2hPG, mmol/L	7.55±3.60	7.40±3.70	7.65±3.54	0.001
HbA1c, %	4.55±1.27	4.55±1.21	4.55±1.31	0.92
UA, μmol/L	307.11±83.77	352.51±84.02	277.73±69.24	<0.001

Note. Data are mean±SD or *n* (percentage) or otherwise indicated. BMI, body mass index; WC, waist circumference; DBP diastolic blood pressure; FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; 2hPG, 2-h plasma glucose; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol, TG, triglycerides; SBP, systolic blood pressure; UA, uric acid.

Table 2. Characteristics of the Study Population Stratified by UA Quartiles

Variable	Men				*P* Value	Women				*P* Value
	Q1	Q2	Q3	Q4		Q1	Q2	Q3	Q4	
Mean age, years	52.98±10.89	52.25±10.98	51.67±10.77	50.28±11.03	<0.001	48.52±9.82	49.69±10.08	51.33±10.25	54.18±10.21	<0.001
Mean BMI, kg/m^2	24.06±3.25	24.79±3.29	25.32±3.35	26.46±3.46	<0.001	24.37±3.34	25.13±3.53	25.80±3.58	26.89±3.91	<0.001
WC, cm	83.19±9.95	85.53±10.08	86.61±10.28	90.35±9.62	<0.001	79.98±9.76	81.46±9.82	83.24±9.44	86.43±10.16	<0.001
Mean SBP, mmHg	133.62±20.13	134.3±21.21	134.92±20.28	137.10±20.83	0.003	128.72±21.75	132.3±23.42	132.92±22.28	138.89±23.97	<0.001
Mean DBP, mmHg	83.44±11.84	84.87±12.54	85.73±12.31	88.24±12.6	<0.001	80.60±11.72	82.24±11.75	83.22±11.47	86.04±12.81	<0.001
TC, mmol/L	5.05±1.1	5.28±0.95	5.34±1.03	5.40±1.03	<0.001	4.96±1.03	5.19±0.95	5.40±1.04	5.63±1.12	<0.001
TG, mmol/L	1.21±1.19	1.28±0.94	1.53±1.45	2.00±1.67	<0.001	1.11±0.73	1.26±0.91	1.37±0.91	1.78±1.35	<0.001
HDL-C, mmol/L	1.62±0.44	1.64±0.42	1.62±0.45	1.56±0.44	<0.001	1.67±0.52	1.67±0.38	1.66±0.4	1.59±0.37	<0.001
LDL-C, mmol/L	3.10±1.2	3.25±1.09	3.07±1.49	2.69±1.68	<0.001	3.08±1.03	3.18±1.1	3.28±1.11	3.13±1.39	<0.001
FPG, mg/dl	6.21±2.31	5.95±1.64	5.94±1.53	5.96±1.51	0.002	5.90±2.08	5.88±1.73	5.88±1.65	6.13±1.75	<0.001
2hPG, mg/dl	7.50±4.24	7.33±3.59	7.22±3.71	7.58±3.21	0.2	7.36±3.9	7.36±3.33	7.64±3.13	8.28±3.45	<0.001
HbA1c, %	4.79±1.44	4.62±1.17	4.53±1.1	4.47±1.11	<0.001	4.71±1.57	4.53±1.31	4.56±1.18	4.65±1.17	<0.001

Note. Data are mean±SD or otherwise indicated. UA quartiles: <297 μmol/L, 297*346 μmol/L, 347-403 μmol/L, and >403 μmol/L in men; <231 μmol/L, 231–271 μmol/L, 272-318 μmol/L, and >318 μmol/L in women BMI, body mass index; WC, waist circumference; DBP, diastolic blood pressure; FBG, fasting blood glucose; HDL-C, high-density lipoprotein cholesterol; 2hPG, 2-h plasma glucose; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol, TG, triglycerides; SBP, systolic blood pressure; UA, uric acid.

and known diabetes, and the lowest UA levels were found in subjects with newly diagnosed diabetes, in both men and women. As compared to normal glucose tolerance group, subjects with prediabetic status or newly diagnosed and known diabetes were older, had a higher BMI, WC, SBP, and TG and lower HDL-C, in either men or women. Newly diagnosed diabetes was strongly related to higher TC values and DBP, while subjects with known diabetes had lower LDL-C values among all individuals.

Figures 1 and 2 show the relationships between HbA1c and serum UA levels. HbA1c levels were negatively and significantly correlated with serum UA levels in known diabetes patients both in men and women. In contrast, in unknown diabetes individuals, HbA1c levels were positively correlated with serum UA levels in women but negatively in men.

Table 3. Study Characteristics Using HbA1c Categories (≤5.6, 5.7-6.4, ≥6.5%) and Known Diabetes in Men

Variable	HbA1c (%)			Known Diabetes	*P* Value
	≤5.6	5.7-6.4	≥6.5		
Mean age, years	51.09±10.75	56.14±10.62	53.44±10.58	58.49±9.6	<0.001
Mean BMI, kg/m^2	25.31±3.31	25.83±3.6	26.38±4.21	26.15±3.56	0.003
WC, cm	86.87±10.16	88.99±11.21	90.51±11.77	90.95±10.19	<0.001
Mean SBP, mmHg	134.38±19.61	138.25±19.63	142.41±22.29	138.53±20	<0.001
Mean DBP, mmHg	86.66±12.03	85.59±11.29	88.75±13.45	84.78±11.18	0.161
TG, mmol/L	1.49±1.15	1.55±0.96	2.11±2.09	1.79±1.44	<0.001
TC, mmol/L	5.27±1.01	5.35±1.19	5.71±0.08	5.22±1.13	0.005
HDL-C, mmol/L	1.61±0.46	1.59±0.39	1.55±0.33	1.41±0.27	0.001
LDL-C, mmol/L	3.05±1.31	3.07±1.29	2.89±1.99	2.79±1.51	0.258
UA, µmol/L	351.01±84.37	354.2±77.2	339.9±89.68	320.88±74.82	0.001

Note. Data are mean±SD or otherwise indicated. UA quartiles: <297 µmol/L, 297-346 µmol/L, 347-403 µmol/L, and >403 µmol/l in men. BMI, body mass index; WC, waist circumference; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol, TG, triglycerides; SBP, systolic blood pressure; UA, uric acid.

Table 4. Study Characteristics Using HbA1c Categories (≤5.6, 5.7-6.4, ≥6.5%) and Known Diabetes in Women

Variable	HbA1c (%)			Known Diabetes	*P* Value
	≤5.6	5.7-6.4	≥6.5		
Mean age, years	50.06±9.99	56.84±9.88	55.42±10.74	59.68±8.82	<0.001
Mean BMI, kg/m^2	25.46±3.65	26.70±3.48	27.08±3.5	26.65±4.31	<0.001
WC, cm	82.14±9.87	87.17±10.12	89.47±9.36	89.15±9.69	<0.001
Mean SBP, mmHg	131.64±22.38	141.47±25.17	140.79±21.52	144.35±21.66	<0.001
Mean DBP, mmHg	83.47±11.83	85.98±12.25	86.73±12.25	86.08±11.85	<0.001
TG, mmol/L	1.31±0.82	1.97±1.58	1.69±0.96	1.92±1.58	<0.001
TC, mmol/L	5.30±1.04	5.76±1.08	5.86±1.22	5.69±1.12	<0.001
HDL-C, mmol/L	1.66±0.4	1.6±0.34	1.58±0.3	1.58±0.36	0.002
LDL-C, mmol/L	3.23±1.06	3.07±1.58	3.45±1.23	3.06±1.62	0.009
UA, µmol/L	280.32±68.77	312.02±84.89	278.07±73.96	274.48±72.61	<0.001

Note. Data are mean±SD or otherwise indicated. UA quartiles: <297 µmol/L, 297-346 µmol/L, 347-403 µmol/L, and >403 µmol/L in men. BMI, body mass index; WC, waist circumference; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol, TG, triglycerides; SBP, systolic blood pressure; UA, uric acid.

Table 5 shows the results of the binary logistic regression model with type 2 diabetes (defined by HbA1c) as the dependent variable and cardiometabolic parameters of age, sex, marital status, education, monthly income, alcohol consumption, and smoking as independent variables. Age, sex, WC, LDL-C, and TG were found to be possible predictors of type 2 diabetes diagnosedusing HbA1c levels, and the second quartile of UA levels had a higher odds ratio (OR) for diabetes defined using HbA1c levels than the other quartiles.

DISCUSSION

In this population-based cross-sectional study, we demonstrated that serum UA levels in prediabetic individuals were higher than those in other groups (P<0.001) and the lowest in patients with newly diagnosed diabetes (P<0.001), both in men and women. Statistical analyses showed that serum UA levels were independently associated with a high risk of diabetes defined by the HbA1c criteria.After adjusting for conventional factors, the ORs (95% CI) for the prevalence of type 2 diabetes were 4.088 (2.900-5.765), 2.091 (1.456-3.002), and 1.642 (1.155-2.336) for the higher quartile compared with the lowest quartile of serum UA levels (P for trend < 0.01).

As a postprandial glycemic marker, it was necessary to explore the relationship between UA and 2hPG levels. A previous population-based cross-sectional study reported that serum UA strongly correlated with 2hPG level (P<0.001) in nondiabetic Mauritian men (r=0.15) and women (r=0.22)[19]. Regarding the Chinese population in Qingdao, serum UA levels tended to increase with increasing FPG concentrations in nondiabetic individuals but decreased in diabetic individuals. The UA-2hPG association seems stronger in men than in

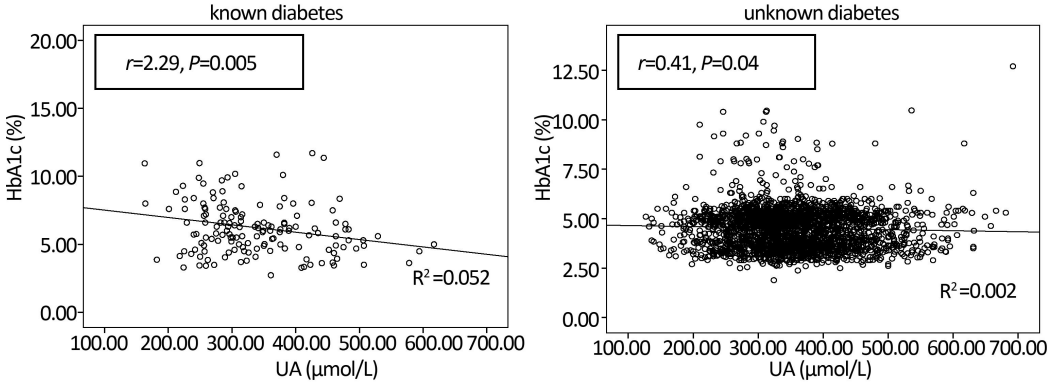

Figure 1. Spearman correlation between UA and HbA1c in men

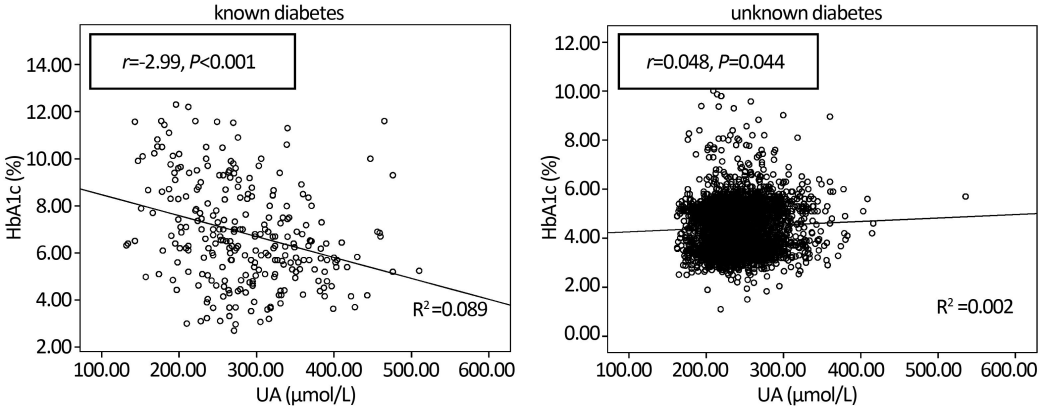

Figure 2. Spearman correlation between UA and HbA1c in women

women[15]. However, few studies have investigated the relationship between HbA1c and UA because of the fact that HbA1c has not been widely applied. In the present study assessing the relationship between HbA1c and UA, HbA1c concentration was positively correlated with serum UA levels for unknown diabetic women (r=0.048; P<0.001) only but showed a negative relationship for all men (P<0.05 for both) and newly diagnosed diabetic women (r=-2.99). Patients with prediabetes had the highest UA levels than others, which may indicate that high UA levels accelerate the development of diabetes. An earlier study also reported a similar finding, indicating that higher serum UA levels were correlated to statistically lower HbA1c levels[20]. However, conflicting findings have also been reported in other studies[21-24] where serum UA levels were inversely correlated with blood glucose and HbA1c levels in individuals with type 2 diabetes. We could not explain the underlying mechanism accounting for the relationship between UA and HbA1c from this cross-sectional study. A potential explanation for this result could be that glucose and UA that are absorbed in the renal proximal tubule through a co-transporter competed with each other, whereas the glucose level was up to the renal glucose threshold and blood glucose had a more obvious advantage of reabsorption. UA concentration in subjects with high blood glucose levels may be reduced by glycosuria; however, islet β-cells would be damaged by high blood glucose[25].

Presently, the primary consequences of hyperuricemia are considered to be gout and renal disorders, which are recognized as potential risk factors for metabolic syndrome[26-27], cardiovascular diseases[28], and hypertension[29-30]. In the present study, we demonstrated that UA was positively and significantly associated with diabetes (HbA1c) independent of conventional factors. To date, there have been limited studies on the relationship between UA and disorders of glucose metabolism, particularly in the context of HbA1c, and even the available data are controversial. Some studies report a positive association between elevated serum UA levels and diabetes[31-34], whereas a neutral[35] or negative association[36-37] has been reported in other studies. The role of UA in glucose metabolism is not completely understood. However, recent studies suggest that UA may also increase the risk of systemic inflammation and oxidative stress closely related with type 2 diabetes[38-41]. Lu et al. found that

Table 5. Binary Logistic Regression Analyses of Variables and Type 2 Diabetes Defined by HbA1c

Variable	OR	95% CI	*P* Values
Age, years	1.051	1.039-1.063	<0.001
Sex	1.401	1.023-1.919	0.035
Marital status	1.084	0.896-1.312	0.406
Education	0.915	0.785-1.066	0.255
Income	0.896	0.790-1.015	0.085
Alcohol consumption status	0.518	0.425-1.002	0.356
Smoking status	0.768	0.625-1.014	0.268
BMI, kg/m^2	0.982	0.926-1.040	0.536
WC, cm	1.045	1.024-1.066	<0.001
SBP, mmHg	1.007	0.998-1.016	0.112
TG, mmol/L	1.554	1.345-1.794	<0.001
HDL-C, mmol/L	0.613	0.401-0.938	0.024
LDL-C, mmol/L	1.332	1.161-1.528	<0.001
UA1, μmol/L	1	reference	
UA2, μmol/L	4.088	2.900-5.765	<0.001
UA3, μmol/L	2.091	1.456-3.002	<0.001
UA4, μmol/L	1.642	1.155-2.336	0.006

Note. UA1: <249 μmol/L, UA2: 249-298 μmol/L, UA3: 299-357 μmol/L, UA4: >358 μmol/L. BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides; UA, uric acid.

serum UA can pass through the blood-brain barrier and act as a potent inflammatory stimulus, leading to NF-κB activation as well as the accumulation of gliosis in the hypothalamus[42]. It has been demonstrated that serum UA is a circulating marker of oxidant damage in metabolic disorders. UA is a potent antioxidant in the extracellular fluid, but it also exerts pro-oxidative effects in the intracellular environment[43]. The exact role of serum UA in oxidation is still controversial and requires further investigation. Xue et al.[44] further elaborated their relationship from the angle of single nucleotide polymorphisms. The first-phase and 2-h insulin secretion could be elevated by the UA-raising T allele SLC2A9 rs11722228. The UA-lowering alleles SLC2A9 rs16890979 and SLC17A1 rs1183210 were associated with increased second-phase insulin secretion and 2-h glucose levels, respectively.

The present study has a few strengths. This is the advanced population-based study to elaborate the relationship between HbA1c and serum UA levels in a Chinese population. The population-based design with a relatively large sample size and comprehensive adjustment is another strength of this study. Nevertheless, several limitations also need to be considered. First, the cross-sectional design does not allow any causality analysis. Second, this study was a single-center study; thus, it is uncertain whether our results are generalizable to other ethnic groups with type 2 diabetes. Third, UA levels were significantly associated with different categories of HbA1c regulation independent of known metabolic risk factors, whereas lifestyle variables from the general population could not be assessed in the current study.

CONCLUSIONS

In conclusion, UA levels are strongly associated with type 2 diabetes diagnosed using HbA1c levels, independent of Age and sex and other established risk factors, suggesting a significant role of UA in the deterioration of glucose toleration. The contribution of UA to the pathogenesis of prediabetic status and manifestation of type 2 diabetes requires further investigation.

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