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Uric Acid and Diabetes Risk among Chinese Women with a History of Gestational Diabetes Mellitus

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Abstract

Aims—To assess the association of uric acid (UA) with the risks of postpartum type 2 diabetes and prediabetes among women with prior gestational diabetes mellitus (GDM).

Methods—We performed a cross-sectional study of 1262 GDM women at 1–5 years after delivery using the baseline data from the Tianjin Gestational Diabetes Mellitus Prevention Program. Logistic regression models were used to estimate the association of different levels of serum UA with the risks of type 2 diabetes and prediabetes.

Results—The multivariable-adjusted odds ratios (ORs) across quartiles of serum UA were 1.00, 1.23 (95% confidence interval [CI] 0.55–2.78), 2.05 (95% CI 0.96–4.39), and 3.17 (95% CI 1.54–6.55) ($P_{\text{trend}} < 0.001$) for type 2 diabetes, and 1.00, 1.50 (95% CI 1.03–2.19), 2.28 (95% CI 1.58–3.30), and 2.88 (95% CI 1.99–4.17) ($P_{\text{trend}} < 0.001$) for prediabetes, respectively. Restricted cubic splines models showed positive linear associations of serum UA as a continuous variable with the

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AUTHOR CONTRIBUTIONS

Author Contributions: L.W., J.L., H.L., S.Z., and W. L. conducted the field research. L.L. conducted the laboratory tests. J.L. and J.W. conducted data analysis. J.L. and J.W. drafted the manuscript. J.L., H.T., P.X., X.Y., Z.Y. and G.H. critically reviewed and revised the manuscript. G.H. is the guarantor of this work and had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

COMPETING FINANCIAL INTERESTS

The authors declared no conflicts of interest to this manuscript.

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risks of type 2 diabetes and prediabetes. This positive association was significant when stratified by healthy weight and overweight participants.

Conclusions—Serum UA levels have a graded positive association with the risks of type 2 diabetes and prediabetes among Chinese with a history of GDM.

Keywords

uric acid; type 2 diabetes; prediabetes; gestational diabetes mellitus; postpartum

1. INTRODUCTION

Uric acid (UA), the final oxidation product of purine metabolism in humans, is commonly used as a clinical index to assess renal function and gout. [1] Researchers have indicated that increased levels of serum UA have been associated with various diseases, such as hypertension, obesity, cardiovascular disease and insulin resistance. [2,3] In several cohort studies, elevated levels of UA have also been identified as a strong and independent predictor of the development of type 2 diabetes and prediabetes. [4,5,6] A recent umbrella review by Li et al. summarized from systematic reviews, meta-analyses, and Mendelian randomization studies and concluded that highly suggestive evidence existed for increasing UA and the risk of impaired fasting glucose or diabetes among the general population.[7] Among people with impaired fasting glucose (IFG) or impaired glucose tolerance (IGT), serum UA has also been found to be a predictor of diabetes. [8,9]

Gestational diabetes mellitus (GDM), defined as any degree of glucose intolerance with onset or first recognition during pregnancy, [10] is a temporary condition but carries long-term risk of developing type 2 diabetes. [11] Some studies on women with prior GDM indicated that this group of people exhibit elevated levels of UA. [12,13] Only one recent case-control study first demonstrated that higher UA levels may be associated with type 2 diabetes among women with a history of GDM compared with those without GDM. [14] Furthermore, most of previous studies were conducted among Caucasians diabetic patients. Very few studies have assessed the association between elevated serum UA and the risk of postpartum diabetes among women with GDM, especially among Chinese women.

Using baseline data from the *Tianjin Gestational Diabetes Mellitus Prevention Program*, [15] a large prospective cohort recruiting women with prior GDM during the years 2005 to 2009, we assessed the associations of baseline UA levels with the risks of type 2 diabetes and prediabetes among women with a history of GDM women after 1–5 years of delivery.

2. METHODS

2.1 Tianjin GDM screening project

Since 1999, all pregnant women living in the six urban districts of Tianjin have been screened for GDM at their 26–30 gestational weeks. [16] They first take a one-hour oral glucose tolerance test (OGTT) with 50-g glucose load in their community health centers. Those who have glucose reading ≥ 7.8 mmol/L are referred to the Tianjin Women's and Children's Health Center to undergo a 2-hour OGTT with 75-g glucose load. Women

considered to be either diabetes (fasting glucose ≥ 7 mmol/L or 2-h glucose ≥ 11.1 mmol/L) or impaired glucose tolerance (IGT) (2-h glucose ≥ 7.8 mmol/L and <11.1 mmol/L) are regarded as having GDM, according to the World Health Organization (WHO)'s criteria. [17]

2.2 Study Population

We conducted a cross-sectional study using the baseline data from *Tianjin Gestational Diabetes Mellitus Prevention Program*, which is an on-going randomized controlled trial (RCT) conducted among GDM women living in the six urban districts in Tianjin, China. [15] All eligible women, who were diagnosed with GDM between 2005 and 2009 and were 20–49 years old at the recruitment, were invited to join the program by mailing (N=4644). After excluding preexisting diabetes patients in the GDM screening visit, and those women taking known medicines to alter OGTT, with presence of any chronic diseases that could seriously reduce the life expectancy or the ability to participate in the study, currently pregnant or planning to become pregnant in the next 2 years and unwilling to participate or losing contact with study staff before the baseline survey, a total of 1263 GDM women finished the baseline survey during August 2009 to July 2011, and the participation rate was 27.2% (Figure 1). When comparing the returned and unreturned GDM women, we found no differences in age, 2-h glucose, fasting glucose, and the prevalence of IGT and diabetes at 26–30 gestational weeks' OGTT. [18] The study followed the guidelines of the Helsinki Declaration, and was approved by the Human Subjects Committee of the Tianjin Women's and Children's Health Center, informed consent was obtained for each participant.

At the survey, all participants completed a self-administered questionnaire and underwent a physical examination. The questionnaire included questions on the women's socio-demographics, including age, marital status, education (<13 years, 13–16 years, and ≥ 16 years), income (<5000 yuan/month group, 5000–8000 yuan/month group, and ≥ 8000 yuan/month group), and occupation; family history of diabetes (parents and siblings); dietary habits (participants completed a 3-day 24-h food record with the instruction of a dietician); [19] lifestyle in the past year, including current smoking and alcohol drinking habits, passive smoking status, and physical activity (the frequency and duration of leisure time and sedentary activities). [20]

The physical examination included the measurement of body weight and height and a blood test. Specially trained research doctors measured the body weight and height for all participants using the standardized protocol. Height (without shoes) was measured to the nearest 0.1 cm, and weight was rounded to the nearest 0.1 kilogram. Participants' baseline body mass index (BMI) was calculated by dividing their weight in kilograms by the square of height in meters. BMI was categorized as <24 , 24–27.9, and ≥ 28 kg/m² based on the Chinese BMI cut-offs. [21] Venous blood samples of all participants were collected before (fasting at least 12 hours) and 2 hours after the ingestion of 75 g glucose. Using the fasting blood samples, UA was measured by Enzymatic Method by applying UA assay kit on an automatic analyzer (Toshiba TBA-120FR, Japan). Due to one missing value of UA, the present study finally included 1262 participants.

2.3 Definition of type 2 diabetes and prediabetes after delivery

With the WHO or American Diabetes Association (ADA)'s criteria, we defined type 2 diabetes as fasting glucose ≥ 7.0 mmol/L and/or 2-h glucose ≥ 11.1 mmol/L, and prediabetes as either impaired fasting glucose (IFG, fasting glucose ≥ 5.6 mmol/L and <7.0 mmol/L), or IGT (2-h glucose ≥ 7.8 mmol/L and <11.1 mmol/L). [22] In addition, those using antidiabetic drugs and having normal glucose in the physical examination were also included into the cases.

2.4 Statistical analysis

Demographic and lifestyle data were summarized by quartiles of serum UA, as means and standard deviations (SD) or proportions. One-way ANOVA and χ^2 tests were used to assess the differences in continuous measures and in categorical measures among the four groups, respectively. General Linear Models were applied to assess the differences of participants' fasting blood glucose and 2-hour glucose according to different UA quartiles. Logistic regression models were performed to investigate the association between UA concentrations and the risks of type 2 diabetes and prediabetes. UA was evaluated in the following three ways: 1) as a continuous variable; 2) as quartiles; and 3) as a binary variable grouped by median. Quartiles and medians of UA were calculated among the study population and the subgroup without diagnosed diabetes participants, respectively. The analyses were first performed adjusting for age (model 1), then further for education, family income, family history of diabetes, hypertension status, smoking, passive smoking, alcohol drinking, leisure-time physical activity, sitting time, total energy intake, dietary fiber intake, energy percent of monounsaturated fat, energy percent of polyunsaturated fat, and energy percent of saturated fat intake (model 2), and also for BMI (model 3). All logistic regression analyses were run on diabetes and prediabetes separately. Adjusted odds ratios and 95% confidence intervals (CI) for the second to the fourth quartiles of UA levels compared with the first quartile were computed. The quartiles of UA were included in the models as dummy variables and the significance of the linear trend over quartiles (from the lowest to the highest) was tested in the same models with the median of each category as a continuous variable. In addition, we used restricted cubic splines nested in logistic regression [23] with knots at the 25th, 50th, and 75th percentiles and used the median of UA as the reference to show the continuous association between UA and the risks of diabetes and prediabetes, respectively. All statistical analyses were conducted with a significance level at 0.05 using IBM SPSS Statistics 23.0 (IBM SPSS, Chicago, IL) and SAS for Windows, version 9.4 (SAS Institute, Inc, Cary, NC).

3. RESULTS

The study group consisted of 1262 GDM women who were in their postpartum 1–5 years and with an average of 2.29 years. Within all the participants, 82 (6.5%) and 401 (31.8%) were diagnosed as having type 2 diabetes and prediabetes, respectively. The mean $\pm$ SD of all participants' UA concentrations was 242 ± 59.8 μ mol/l. The average uric acid concentrations of participants with normal glucose, prediabetes, and type 2 diabetes were 233 ± 56.2 , 256 ± 61.1 , and 268 ± 65.3 μ mol/l, respectively. Women who developed prediabetes and diabetes had a higher average UA concentration, compared with those with normal

glucose ($P<0.001$). General characteristics of the study population according to increasing UA quartiles are presented in Table 1. Age, dietary fiber intake, and energy percent of polyunsaturated fat were inversely and BMI was positively associated with baseline serum UA levels (all $P<0.05$). We also found that UA significantly correlated with BMI with an r of 0.386 ($P<0.001$).

To examine the associations between blood glucose and UA levels, we compared the participants' fasting blood glucose and 2-hour blood glucose according to their UA levels. The results were shown in Table 2. After adjustment for age, education, family income, family history of diabetes, hypertension status, smoking, passive smoking, alcohol drinking, leisure-time physical activity, sitting time, total energy intake, dietary fiber intake, energy percent of monounsaturated fat, energy percent of polyunsaturated fat, and energy percent of saturated fat, the mean values of fasting blood glucose were 5.23, 5.33, 5.43, and 5.48 from UA quartile 1 to 4, respectively, and the mean values of 2-hour blood glucose were 6.51, 6.80, 7.21, and 7.76 from UA quartile 1 to 4, respectively (both P -values for difference <0.05). After further adjustment for BMI, the differences of fasting blood glucose disappeared (P -value for difference >0.05), but the differences of 2-hour blood glucose remained significant (P -value for difference = 0.021).

There were significant positive associations between UA levels and the risks of type 2 diabetes and prediabetes (Table 3). The multivariable-adjusted (Model 2) odds ratios across quartiles of serum UA were 1.00, 1.28 (95% confidence interval [CI] 0.56–2.91), 1.84 (95% CI 0.85–3.98), and 3.00 (95% CI 1.44–6.26) (P for linear trend <0.001) for type 2 diabetes, and 1.00, 1.54 (95% CI 1.05–2.26), 2.22 (95% CI 1.53–3.22), and 2.86 (95% CI 1.97–4.16) (P for linear trend <0.001) for prediabetes, respectively. When UA was considered as a continuous variable, multivariable-adjusted (model 2) odds ratios for each 100 $\mu\text{mol/l}$ increase in UA were 1.98 (95% CI 1.37–2.86) for type 2 diabetes, and 2.00 (95% CI 1.60–2.50) for prediabetes, respectively. After additional adjustment for BMI, the positive association attenuated and became non-significant for type 2 diabetes (P for linear trend >0.1), but still remained statistically significant for prediabetes (P for linear trend <0.001). Restricted cubic splines models showed positive linear associations of serum UA as a continuous variable with the risks of type 2 diabetes and prediabetes (Figure 2).

The joint association of serum UA and BMI on the risks of diabetes and prediabetes are presented in Figure 3. We dichotomized serum UA levels with the median and BMI at normal weight ($<24 \text{ kg/m}^2$) versus overweight ($\geq 24 \text{ kg/m}^2$). Multivariable-adjusted positive associations between serum UA and the risk of diabetes were present in overweight women, but not in normal weight women. Similarly, the positive association between serum UA and the risk of prediabetes was observed in overweight women and in normal weight women. However, there were no statistically significant interactions of UA and BMI on the risks of diabetes and prediabetes (all P values for interaction >0.10).

4. DISCUSSION

This study revealed a positive and graded association between serum UA and the risks of type 2 diabetes and prediabetes at postpartum 1–5 years among Chinese women with a

history of GDM. These associations somewhat attenuated after adjustment for BMI, suggesting that the association of serum UA levels with diabetes risk was not fully independent of BMI.

It has been suggested that UA levels vary according to different genders, ages, and lifestyles. Men generally have higher UA levels than women and UA levels increase with age. Framingham Heart Study found that UA levels in women gradually increased during their 40–70 years old [24]. Moreover, Western lifestyle might increase UA levels. Several studies have found that UA levels are higher among people of Western countries than those in the developing countries, and higher among people who live in urban areas than those living in rural areas [25]. The association between UA concentrations and diabetes remains unclear. Previous cohort studies among the middle-aged [4,26] or older population, [5] males, [27,28] and young adults [6] supported that elevated UA levels increased the risk of developing type 2 diabetes and prediabetes. Some other studies further suggested that the association of UA and diabetes mellitus was not simply linear. A cohort study in 1960s–1970s found that serum UA levels were lower among men with a history of diabetes than those with the newly discovered disease [29] but higher in those with prediabetes compared with participants with normal glucose. [30] Cook et al. found a positive relationship between UA concentrations and serum glucose in the range up to 8 mmol/l; however, at higher levels of glucose, serum UA decreased. [31] Juraschek et al. studied on four communities in the U.S. and found higher baseline UA level was associated with an increased risk of incident diabetes, but prevalent diabetes was associated with a decline in UA concentrations over time. [32] According to these findings, the positive linear associations seemed to exist between UA and newly-onset type 2 diabetes and prediabetes, which was also confirmed by our results.

Previous findings indicated that women with a history of GDM had higher levels of UA, in comparison to their non-GDM counterparts. [12,13] However, very few studies examined the association between UA and postpartum diabetes risk among women with a history of GDM, especially among Chinese women. Several studies showed that UA could be applied in predicting diabetes risk among participants with IGT or IFG. Results from the Finnish Diabetes Prevention Study demonstrated that baseline UA and its changes predicted a twofold increase of developing diabetes among participants with IGT. [9] Another study indicated that UA independently predicted incident diabetes in older adults with IFG. [8] Thus far, there is only one study of women with prior GDM shared the similar aim with ours. [14] That study found that UA levels were higher among patients with diabetes and prediabetes, compared those in women with normal glucose. Nonetheless, there are some limitations in our study: first, the study sample size was relatively small, and few diabetes cases in this study may limit the statistical power; second, main confounders, such as social-economic and lifestyle characteristics, were not controlled in the analysis; and third, the control group cannot represent the general population due to overmatching BMI and body fat in women with GDM. Our study was conducted in 1262 GDM women and found 82 diabetes and 401 prediabetes cases. In addition, we controlled age, education, family income, family history of diabetes, smoking, passive smoking, alcohol drinking, leisure-time physical activity, sitting time, total energy intake, dietary fiber intake, energy percent of monounsaturated fat, energy percent of polyunsaturated fat, energy percent of saturated fat,

and BMI as the confounders in the analyses, to examine the associations between UA and postpartum diabetes risk among 1262 GDM women.

BMI is a strong risk factor of type 2 diabetes and prediabetes. Our previous work supported that BMI was associated with an increased risk of type 2 diabetes among women with prior GDM. [33] In the present study, we also found a significant correlation between UA levels and BMI ($r^2 = 0.149$, $P < 0.001$). Many studies found that the associations between UA levels and the risk of type 2 diabetes or prediabetes somewhat attenuated or vanished when BMI was entered into the models [4,26,28,34]. The present study found that the positive association between US levels and the risks of type 2 diabetes and prediabetes attenuated and became non-significant for type 2 diabetes (P for trend > 0.1), but still remained statistically significant for prediabetes. We further assessed the associations after stratifying the participants by BMI into two groups ($\text{BMI} < 24 \text{ kg/m}^2$ and $\text{BMI} \geq 24 \text{ kg/m}^2$) and found that higher UA levels independently increased the risk of type 2 diabetes among overweight women, and increased the risk of prediabetes among both normal weight and overweight women.

Recent studies have reported that an emerging association was observed between hyperuricemia and type 2 diabetes mellitus; hyperuricemia was an independent risk factor in the development of type 2 diabetes, IFG, and insulin resistance [35]. It is still unclear whether UA plays a causal role in the pathogenesis of those diseases. However, UA may cause the development of type 2 diabetes mellitus by following possible mechanisms. First, UA can induce insulin resistance via inducing mitochondrial oxidative stress and its effects on adipocytes [36]. In addition, UA is a strong pro-inflammatory factor causing inflammation in human body. Tanaka et al. conducted a double blind placebo controlled randomized trial and observed that in health individuals, acute increase in UA resulted in an increased IL-6 response [37]. Although the mechanisms between inflammation and Type 2 diabetes mellitus were not thoroughly understood, epidemiologic findings have supported the association between inflammatory biomarkers and the occurrence of diabetes mellitus and their complications [38]. Thus, UA may play a pathogenic role in the metabolic syndrome. [39,40] Our findings may be useful in clinical practice, because patients with prediabetes are at high risk of developing type 2 diabetes in the near future [41] and share the similar associated damage to end target organs as patients with diabetes, [42] however, there are no apparent clinical symptoms of prediabetes. Previous studies suggested that UA level was a significant risk factor for prediabetes. [43] If this finding is proven to be a causal relation later, it is relevant to the prevention and treatment of prediabetes among women with prior GDM, because methods for assessment of serum UA are widely available and inexpensive, and patient experience of UA tests is better than OGTT.

Our study was a large-scale population-based study of women with GDM during their pregnancy in order to examine the association of serum UA and incidence type 2 diabetes or prediabetes in the postpartum period. Additionally, we conducted this study in Tianjin, China, in order to understand the ethnic and cultural influences on the above association. However, there were several limitations. First, because of the cross-sectional design, the temporal and causal association cannot be assessed. Second, this study was a baseline survey of an ongoing intervention trial, which has a relatively low response rate. However, in order

to keep the reliance of the results, we have compared the general characteristics between the returned and unreturned subjects and found no significant difference. Third, this study was based on a cohort study design, in which the cases of type 2 diabetes were newly-onset after delivery, so the number of cases was limited. Fourth, a total of ten participants reported taking medicines to control their diabetes or IFG/IGT. Among them, one participant reported taking metformin. Although there is not a consistent conclusion of metformin's effect on changing uric acid concentrations, [44,45] it should be cautious when applying the results.

In conclusion, our study suggests that serum UA levels have a positive and graded association with the risks of type 2 diabetes and prediabetes among Chinese women with a history of GDM in their postpartum 1–5 years. Elevated UA is a risk factor of type 2 diabetes and prediabetes among women with a history of GDM.

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Highlights

- Serum uric acid was positively associated with the risks of type 2 diabetes.
- Serum uric acid was positively associated with the risks of prediabetes.
- The association of uric acid and diabetes risk was influenced by body mass index.
- We examined among Chinese women with prior gestational diabetes after delivery.

Figure 1.
Flow chart

Figure 2.

Adjusted odds ratios (solid line) and 95% confidence interval (dashed lines) for type 2 diabetes (A) and prediabetes (B) according to different levels of uric acid among women with prior gestational diabetes mellitus (restricted cubic spline models). Adjusted for age, education, family income, family history of diabetes, smoking, passive smoking, alcohol drinking, leisure-time physical activity, sitting time, total energy intake, dietary fiber intake,

energy percent of monounsaturated fat, energy percent of polyunsaturated fat, energy percent of saturated fat, and body mass index. *denotes $P < 0.05$

No. of participants	427	254	203	378
No. of cases	10	7	16	49
Odds ratio		1.25		1.94
95% CIs	1.00	0.43-3.63	1.00	1.03-3.65
P for interaction		0.472

No. of participants	409	255	180	336
No. of cases	89	82	64	166
Odds ratio		1.66		1.80
95% CIs	1.00	1.15-2.41	1.00	1.21-2.68
P for interaction		0.824		

Figure 3.

Odds ratios of incident diabetes (A) and prediabetes (B) based on different levels of Uric Acid and baseline BMI. Adjusted for age, education, family income, family history of diabetes, smoking, passive smoking, alcohol drinking, leisure-time physical activity, sitting time, total energy intake, dietary fiber intake, energy percent of monounsaturated fat, energy percent of polyunsaturated fat, and energy percent of saturated fat. *denotes $P < 0.05$

Table 1

Characteristics of study participants at baseline by quartiles of uric acid

Characteristics	Quartiles of uric acid (range, $\mu\text{mol/L}$)				P-value
	Quartile 1 (< 201)	Quartile 2 (202–235)	Quartile 3 (236–278)	Quartile 4 (≥ 278)	
Age, y	32.9 $\pm$ 3.4	32.5 $\pm$ 3.4	32.5 $\pm$ 3.6	31.6 $\pm$ 3.5	<0.001
Body mass index, kg/m^2	22.4 $\pm$ 3.0	23.1 $\pm$ 3.2	24.7 $\pm$ 4.0	26.4 $\pm$ 4.2	<0.001
Body mass index categories, %					<0.001
<24 kg/m^2	70.7	64.9	47.8	32.7	
24 kg/m^2	29.3	35.1	52.2	67.3	
Education, %					0.134
<13 years	18.8	20.9	23.9	26.4	
13 to <16 years	71.0	71.8	69.7	67.6	
16 years	10.2	7.3	6.4	6.0	
Family income, %					0.333
<5,000 Yuan/month	24.5	28.2	25.2	32.1	
5,000–7,999 Yuan/month	37.9	38.6	37.9	33.0	
8,000 Yuan/month	37.6	33.2	36.9	34.9	
Family history of diabetes, %	31.2	37.7	34.7	39.0	0.178
Prevalence of hypertension, %	6.1	4.7	10.5	9.1	0.023
Current smokers, %	1.6	1.6	1.9	2.8	0.368
Passive smokers, %	56.7	52.5	50.3	55.7	0.357
Current alcohol drinkers, %	21.3	24.7	23.2	17.9	0.189
Leisure time physical activity, %					0.241
0 min/day	78.7	75.9	76.8	83.6	
1–29 min/day	18.8	21.5	20.7	15.4	
30 min/day	2.5	2.5	2.5	0.9	
Sitting time at home, h/day	3.19 $\pm$ 2.1	3.06 $\pm$ 2.1	3.27 $\pm$ 2.0	3.36 $\pm$ 2.3	0.338
Dietary intakes					
Energy consumption, kcal/day	1726 $\pm$ 426	1701 $\pm$ 443	1695 $\pm$ 432	1646 $\pm$ 456	0.135
Fiber, g/day	11.1 $\pm$ 4.3	10.5 $\pm$ 4.1	10.2 $\pm$ 4.0	9.93 $\pm$ 4.1	0.003
Fat, % energy	33.6 $\pm$ 6.4	33.8 $\pm$ 6.1	33.4 $\pm$ 6.3	33.1 $\pm$ 6.7	0.514

Characteristics	Quartiles of uric acid (range, $\mu\text{mol/L}$)				P-value
	Quartile 1 (201)	Quartile 2 (202–235)	Quartile 3 (236–278)	Quartile 4 (>278)	
Saturated fat, % energy	7.90 $\pm$ 2.0	8.10 $\pm$ 2.0	7.94 $\pm$ 2.1	7.99 $\pm$ 2.2	0.648
Monounsaturated fat, % energy	13.4 $\pm$ 2.8	13.7 $\pm$ 2.6	13.6 $\pm$ 2.8	13.5 $\pm$ 2.9	0.590
Polysaturated fat, % energy	12.3 $\pm$ 3.0	12.1 $\pm$ 3.0	11.9 $\pm$ 2.9	11.5 $\pm$ 3.0	0.007
Fasting blood glucose, mmol/l	5.21 $\pm$ 0.75	5.31 $\pm$ 1.04	5.46 $\pm$ 0.94	5.50 $\pm$ 0.93	<0.001
2-hour blood glucose, mmol/l	6.43 $\pm$ 2.09	6.74 $\pm$ 2.25	7.28 $\pm$ 2.57	7.81 $\pm$ 2.71	<0.001

Data are means $\pm$ standard deviations unless otherwise indicated. Dietary intakes were assessed by 3-day 24-h food records.

Table 2
Comparison of participants' fasting blood glucose and 2-hour blood glucose according to their uric acid levels

Uric Acid levels						
	Quartile 1 (201)	Quartile 2 (202-235)	Quartile 3 (236-278)	Quartile 4 (>278)	P-value	
Fasting blood glucose	Model 1	5.20 (0.05)	5.31 (0.05)	5.46 (0.05)	5.51 (0.05)	<0.001
	Model 2	5.23 (0.05)	5.33 (0.05)	5.43 (0.05)	5.48 (0.05)	0.003
	Model 3	5.32 (0.05)	5.38 (0.05)	5.41 (0.05)	5.37 (0.05)	0.68
2-hour blood glucose	Model 1	6.41 (0.14)	6.74 (0.14)	7.27 (0.14)	7.85 (0.14)	<0.001
	Model 2	6.51 (0.13)	6.80 (0.13)	7.21 (0.13)	7.76 (0.13)	<0.001
	Model 3	6.80 (0.13)	6.96 (0.13)	7.13 (0.13)	7.39 (0.13)	0.021

Data are means (SE).

Model 1 adjusted for age; model 2 adjusted for age, education, family income, family history of diabetes, hypertension status, smoking, passive smoking, alcohol drinking, leisure-time physical activity, sitting time, total energy intake, dietary fiber intake, energy percent of monounsaturated fat, energy percent of polyunsaturated fat, and energy percent of saturated fat; model 3 adjusted for the covariates in model 2 plus BMI.

Table 3

Odds ratios of diabetes and prediabetes by uric acid as a categorical variable and a continuous variable

	No. of participants	No. of cases	Odds Ratios (95% CIs)		
			Model 1	Model 2	Model 3
Diabetes					
As a continuous variable (each 100 μmol/L increase)	1262	82	1.99 (1.43, 2.77)	1.98 (1.37, 2.86)	1.46 (0.97, 2.21)
As a categorical variable					
Quartile 1 (201 μmol/L)	314	11	1.00	1.00	1.00
Quartile 2 (202–235 μmol/L)	316	15	1.40 (0.63, 3.09)	1.28 (0.56, 2.91)	1.15 (0.50, 2.64)
Quartile 3 (236–278 μmol/L)	314	22	2.10 (1.00, 4.42)	1.84 (0.85, 3.98)	1.31 (0.59, 2.90)
Quartile 4 (>278 μmol/L)	318	34	3.47 (1.72, 7.01)	3.00 (1.44, 6.26)	1.73 (0.79, 3.78)
P for linear trend			<0.001	0.001	0.129
Prediabetes (excluding diabetes)					
As a continuous variable (each 100 μmol/L increase)	1180	401	2.04 (1.65, 2.53)	2.00 (1.60, 2.50)	1.67 (1.32, 2.11)
As a categorical variable					
Quartile 1 (200 μmol/L)	298	67	1.00	1.00	1.00
Quartile 2 (201–234 μmol/L)	291	86	1.47 (1.01, 2.13)	1.54 (1.05, 2.26)	1.41 (0.96, 2.07)
Quartile 3 (235–276 μmol/L)	296	116	2.25 (1.57, 3.22)	2.22 (1.53, 3.22)	1.74 (1.19, 2.56)
Quartile 4 (>276 μmol/L)	295	132	2.89 (2.02, 4.14)	2.86 (1.97, 4.16)	1.86 (1.25, 2.78)
P for linear trend			<0.001	<0.001	<0.001

Model 1 adjusted for age; model 2 adjusted for age, education, family income, family history of diabetes, hypertension status, smoking, passive smoking, alcohol drinking, leisure-time physical activity, sitting time, total energy intake, dietary fiber intake, energy percent of monounsaturated fat, energy percent of polyunsaturated fat, and energy percent of saturated fat; model 3 adjusted for the covariates in model 2 plus BMI.