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ORIGINAL ARTICLE

Efficacy of urinary glucose for diabetes screening: a reconsideration

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Abstract

Aims Previous studies indicated that urinary glucose (UG) had a limited efficacy in diabetes screening. This study was designed to have a re-evaluation of its efficacy, taking into consideration the collection method of urine and the measurement approach for UG among Chinese adults.

Methods This cross-sectional study enrolled a total of 7689 participants without known diabetes, who were fasted and asked to empty bladders before a 75 g glucose loading. Urine was collected 2 h post glucose loading, and UG was measured using quantitative and qualitative approaches. The efficacy of UG in detecting diabetes was assessed by the receiver operating characteristic (ROC) curve.

Results The area under the ROC curve was 0.89 for quantitative UG and 0.87 for qualitative UG. Quantitative UG was positively correlated with fasting plasma glucose (FPG) and 2 h plasma glucose (2 h PG) ($r=0.55$ and 0.56, respectively, both $P<0.001$). Quantitative UG displayed a sensitivity of 82.9% and a specificity of 84.7% in detecting diabetes at the corresponding optimal cutoff of 130 mg. Qualitative UG exhibited a sensitivity of 80.2% and a specificity of 85.6% at the optimal cutoff of glycosuria + 1. In addition, the sensitivity of both quantitative and qualitative UG was significantly higher than that of HbA1c (≥ 6.5%) ($P<0.001$) and had a comparable sensitivity to 2 h PG (≥ 11.1 mmol/L) ($P=0.493$).

Conclusions UG, either quantitatively or qualitatively measured at 2 h post glucose loading, was effective in diabetes screening. This indicates that UG is a feasible approach for diabetes screening.

Keywords Diabetes mellitus · Screening · Glycosuria · Urinary glucose

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Introduction

The prevalence of diabetes mellitus, particularly type 2 diabetes, has increased in recent decades, especially in low- and middle-income countries [1, 2]. Research has shown that diabetes affects an estimated 113.9 million people in China alone, and that 493.4 million have prediabetes [2]. Because it is asymptomatic, diabetes may remain undetected for many years until severe complications occur like kidney failure, heart disease, stroke, and peripheral vascular disease [3]. A recent nationally representative survey of Chinese adults reported that 60.7% of patients with diabetes are undiagnosed [4], who showed a similar mortality risk as those being diagnosed [5]. Moreover, the large economic burden imposed by diabetes cannot be ignored [6]. As a result, early detection of diabetes with an efficient but inexpensive method, which allows prompt effective treatment, might be particularly important for preventing diabetes complications and reducing the economic burden.

The fasting plasma glucose level (FPG), oral glucose tolerance test (OGTT), or hemoglobin A1c (HbA1c) is routinely used to screen for diabetes. However, accumulating evidence indicates that the efficacy of FPG alone for such screening is limited [7–9]. OGTT has been considered as the gold standard test for the diagnosis of diabetes, but it is impractical in a diabetes screening setting for all individuals, especially for those with undiagnosed diabetes but having FPG < 7 mmol/L. In 2010, the International Expert Committee recommended the use of HbA1c (6.5%) to diagnose diabetes. Yet this criterion has not been adopted by Chinese Diabetes Society since the measurement approach for HbA1c is not well standardized in China [9–11]. Moreover, it is also impractical for mass screening in particular for developing countries because the cost of HbA1c is relatively expensive. Glycosuria is the result of glycemic excursions in excess of the renal glucose threshold. Although not abandoned during the past decades, urinary glucose (UG) was not recommended for diabetes screening because its sensitivity is low [12]. However, it is worth noting that in previous studies, urine samples were collected before breakfast, 1 h after breakfast, before glucose loading, or 1–2 h after a solid morning or evening meal, without uniform specification, as shown in Table 1 [13–15], which result in great differences in the sensitivity of UG. Moreover, compared with the traditional detection method using dipsticks, the quantitative detection of UG with a portable UG meter provides a more accurate assessment of the average elevation of glucose in the urine and is not affected by interfering substances (ascorbic acid, acetaminophen) [16]. Current evidence indicates that UG reliably reflects the prevailing plasma glucose level [17, 18], and our previous study showed that quantitative UG monitoring had a similar effectiveness in maintaining glycemic control and facilitated better compliance compared with blood self-monitoring [19].

It is speculated that UG within a specific period of time may better reflect the fluctuations in blood glucose. And this speculation has been supported by our previous finding that using urine samples collected at 2 h post the oral glucose loading to measure UG could improve its sensitivity for diabetes screening [22]. Yet this study was conducted among high-risk population, which may lead to the risk of section bias; and it remains concerned whether such finding could be confirmed in the representative general population.

Therefore, the goal of this study was to re-evaluate the efficacy of UG measured in a specified time-window for diabetes screening among the general population.

Table 1 Summary of previous studies using UG for diabetes screening

Year of publication	Sample size	Diagnostic	DM proportion	Urine sample	UG detection	Sensitivity	Screen methods
1993[a] [13]	442	OGTT	23 (5.2%)	1 h post breakfast	Clinistix	43%	UG alone
1993 [14]	237	2 h PG	–	obtained from each non-fasting subject prior to the glucose load	Glucose oxidase dipstick and glucose oxidase analyzer	64.3% and 80.6%	UG alone
1997 [b] [15]	2242	OGTT	–	1–2 h after a solid morning or evening meal	Urine dipsticks	20.8%	UG alone
2005 [20]	8,812,356	OGTT	232 (0.0026%)	morning urine sample	Glucose oxidase tapes	–	two UG tests were positive; a subsequent OGTT was performed
2013 [21]	90	Self-reported diabetes	38 (42%)	a spot urine sample	Urine dipsticks	65%	UG alone
2015 [22]	909	OGTT	156 (17.2%)	2 h after oral glucose	Quantitative urine meter	82.7%	2 h UG combined with FPG
2017 [23]	707,238	OGTT	110 (0.015%)	morning urine sample	Glucose oxidase tapes	–	two UG tests were positive; a subsequent OGTT was performed

FPG fasting plasma glucose, *2 h PG* 2 h plasma glucose, *UG* urinary glucose, *OGTT* oral glucose tolerance test

[a]The Isle of Ely diabetic project

[b]The UG test-positive participants and a random sample of 143 test-negative participants were contacted for blood glucose test

Materials and methods

Study design and participants

We conducted this multicenter, cross-sectional study in six cities in Jiangsu Province, China, that included urban and rural populations. A multistage, stratified sampling method was used to select a sample of Chinese Han ethnic individuals aged 18–65 years with no previous history of diabetes. The sampling strategy was stratified on the basis of geographic region (south, central, and north Jiangsu). In the first stage of sampling, two cities were selected from each geographic region, and then one county was selected randomly from each city. In the second stage, three subdistricts or townships were randomly selected from each county. In the next stage, four neighborhood communities or administrative villages were randomly chosen. Ultimately, at least 100 residents were selected from each neighborhood community or administrative village. If a selected individual refused to participate or was unavailable, a replacement resident was selected from the same neighborhood or village using a simple random sampling method. Participants were excluded if they had been diagnosed with diabetes, pregnancy, severe psychiatric disturbance, or an unstable health condition. In total, 8119 residents were selected and invited to participate in this study, and 7689 people participated in the survey. Thus, the overall response rate was 94.7%. After the exclusion of 784 people who missed quantitative measurement of UG, qualitative measurement of UG or HbA1c test, 6905 people were included in the final analysis (Fig. 1).

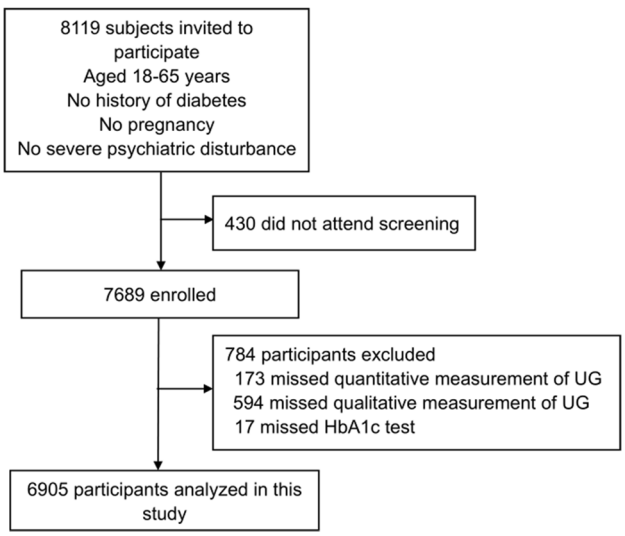

Fig. 1 Flow chart of the recruitment of participants

Procedures

The study was initiated on November 12, 2015 and ended on June 28, 2016. All eligible participants were invited to complete a structured questionnaire to obtain information on their demographic characteristics and medical histories. Blood pressure, heart rate, bodyweight, height, waist circumference, and hip circumference were measured with standardized protocols. Blood samples were collected from each participant after an overnight fast of at least 10 h for the measurement of fasting plasma glucose (FPG), hemoglobin A1c (HbA1c), total cholesterol, triglycerides, high-density lipoprotein–cholesterol (HDL-C), low-density lipoprotein–cholesterol (LDL-C), alanine aminotransferase (ALT), aspartate transaminase (AST), creatinine, blood urea nitrogen (BUN), and uric acid. The participants were asked to empty their bladders before they were given a standard 75 g glucose solution. 2 h later, blood samples were collected for the measurement of 2 h plasma glucose (2 h PG). All the urine samples were collected over a 2 h period after oral glucose loading for urinalysis and to quantitatively and qualitatively assess UG. During this period, the subjects were not allowed to drink water or undertake strenuous exercise. Quantitative UG for a specific period of time was calculated as the UG concentration (mg/dl) × the urine volume (dl). UG concentrations were measured with a quantitative urine meter (UG-201-H, Tanita Corporation, Tokyo, Japan). Urinalysis was performed with an automated urine analyzer (Uritest-500B, URIT Corporation, Guangxi, China). The qualitative UG results were categorized as 0, 0.5+ (trace amount of UG), 1+, 2+, 3+, or 4 + in ascending degrees of glycosuria. FPG and 2 h PG were measured with the glucose oxidase method using an automatic chemistry analyzer (Synchron LX-20, Beckman Coulter Inc., CA, USA). HbA1c was measured with high-performance liquid chromatography (HPLC, D-10™ Hemoglobin Analyzer, Bio-Rad Inc., CA, USA).

Diabetes was defined as FPG ≥ 7.0 mmol/l and/or 2 h PG ≥ 11.1 mmol/l on the basis of the 1999 World Health Organization (WHO) criteria.

Statistical analysis

Assuming a sensitivity of 76%, a specificity of 89%, and a disease prevalence of 10%, the allowable error was to 0.1 with α 0.05 [22, 24], at least 700 subjects were required. Continuous variables were described as means (95% confidence intervals) and categorical variables were described as numbers (or percentage). The characteristics of the participants in the different groups were compared with Student's t test for continuous variables and a χ^2 test for categorical variables. A nonparametric test was used when the data distribution was skewed. Partial correlation analyses

were performed to evaluate the associations between UG and other glycemic variables, including FPG, 2 h PG, and HbA1c, after adjustment for age and sex. Receiver operating characteristic (ROC) curves were constructed and the areas under the curves (AUC) were used to evaluate the performance of UG in detecting newly diagnosed diabetes (NDM). The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) of UG in detecting diabetes were calculated. The optimal cutoff point for UG was determined as the coordinate closest to the y intercept (0, 1) on the ROC curve, and at this point, the sum of the sensitivity and specificity was maximal. Cost per case identified was calculated as the total estimated cost of screening a specified population divided by the number of cases identified to evaluate the cost-effectiveness of different screening methods in identifying diabetes [25]. A P value < 0.05 was considered statistically significant. All statistical analyses were conducted with SPSS 22.0 (SPSS Inc., Chicago, IL, USA).

Results

General characteristics of the study participants

The general characteristics of the study population are presented in Table 2. The prevalence of newly diagnosed diabetes (NDD) based on the WHO criteria was 6.5%. In general, individuals with NDD had higher FPG, 2 h PG, and UG than those without diabetes ($P < 0.001$). In addition, individuals

Table 2 Characteristics of the study participants

	Total	NDD	Non-diabetes
Number (%)	6905	449 (6.5%)	6456 (93.5%)
Age (years)	43.9 (43.6–44.1)	49.5 (48.6–50.4)‡	43.5 (43.2–43.8)
Male	3032 (43.9%)	232 (51.7%)	2800 (43.4%)
Female	3873 (56.1%)	217 (48.3%)	3656 (56.6%)
HR (beats/min)	77.7 (77.4–78.1)	80.2 (79.0-81.3)‡	77.6 (77.2–77.9)
Blood pressure (mmHg)			
Systolic	128.5 (128.1–129.0)	140.4 (138.7–142.0)‡	127.7 (127.2-128.2)
Diastolic	79.2 (78.8–79.5)	84.8 (83.8–85.8) ‡	78.8 (78.4–79.1)
Blood glucose (mmol/L)			
FPG	5.5 (5.4–5.5)	7.8 (7.6-8.0)‡	5.3 (5.3–5.3)
2 h PG	6.6 (6.6–6.7)	13.5 (13.1–13.9)‡	6.1 (6.1–6.2)
HbA1c (%)	5.7 (5.6–5.7)	7.0 (6.9–7.2)‡	5.6 (5.6–5.6)
Cholesterol (mmol/L)	4.7 (4.6–4.7)	5.1 (5.0-5.2)‡	4.6 (4.6–4.6)
Triglycerides (mmol/L)	1.6 (1.6–1.6)	2.4 (2.2–2.7)‡	1.5 (1.5–1.6)
HDL-C (mmol/L)	1.4 (1.4–1.4)	1.3 (1.3–1.4) †	1.4 (1.4–1.4)
LDL-C (mmol/L)	2.6 (2.6–2.7)	2.9 (2.9-3.0) ‡	2.6 (2.6–2.6)
BUN (mmol/L)	5.0 (4.9-5.0)	5.2 (5.1–5.3)†	5.0 (4.9-5.0)
Creatinine (umol/L)	75.6 (73.3–77.9)	73.4 (71.8–75.0)	75.8 (73.3–78.2)
UA (umol/L)	314.8 (312.7–317.0)	330.2 (321.9-338.5)‡	313.8 (311.6–316.0)
ALT (U/L)	23.5 (23.0–24.0)	33.7 (30.7–36.6) ‡	22.8 (22.3–23.3)
AST (U/L)	22.9 (22.6–23.3)	29.4 (27.3–31.5)‡	22.5 (22.1–22.8)
WC (cm)	83.5 (83.3–83.8)	90.2 (89.3–91.2)‡	83.1 (82.8–83.3)
HC (cm)	95.1 (94.9–95.3)	98.1 (97.3–98.8)‡	94.9 (94.7–95.1)
WHR (%)	87.7 (87.5–87.9)	91.9 (91.4–92.5)‡	87.4 (87.2–87.6)
BMI (kg/m^2)	25.2 (25.1–25.3)	27.5 (27.2–27.9)‡	25.0 (24.9–25.1)
Quantitative UG (mg)	204.3 (189.5–219.2)	1490.1 (1338.9–1641.4)‡	114.6 (106.4–122.8)
Qualitative UG			
≥ + 0.5 (%)	1598 (23.1%)	378 (84.2%) ‡	1220 (18.9%)

Data are means (95% confidence interval) or number (percentage) as indicated

HR heart rate, *HbA1c* glycated hemoglobin, *FPG* fasting plasma glucose, *2 h PG* 2 h plasma glucose, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *BUN* blood urea nitrogen, *UA* uric acid, *ALT* alanine aminotransferase, *AST* aspartate transaminase, *WC* waist circumference, *HP* hip circumference, *WHR* waist-to-hip ratio, *BMI* body mass index, *NDD* newly diagnosed diabetes, *UG* urinary glucose

*P < 0.05, †P < 0.01, ‡P < 0.001 for the difference between the indexed category and Non-diabetes.

with NDD were older, dyslipidemic, hypertensive, and more likely to be obese than those without diabetes (see Table 2).

Correlation of UG with glycemic variables

After adjustment for sex and age, quantitative UG correlated significantly with FPG ($r=0.55$, $P<0.001$), 2 h PG ($r=0.56$, $P<0.001$), and HbA1c ($r=0.51$, $P<0.001$) in the overall population.

Performance of UG in diabetes screening

The ROC curves shown in Fig. 2 represent the diagnostic accuracy of UG for NDD. The AUC was 0.89 (95% CI 0.88–0.90) for quantitative UG and 0.87 (95% CI 0.86–0.87) for qualitative UG. Compared with quantitative or qualitative UG, the AUCs for FPG (0.94, 95% CI 0.94–0.95), 2 h PG (0.96, 95% CI 0.96–0.97), and HbA1c (0.92, 95% CI 0.91–0.92) were significantly larger (all $P<0.001$). Table 3 shows the sensitivity, specificity, PPV, NPV for UG, FPG, 2 h PG, and HbA1c in identifying diabetes. Quantitative UG displayed high sensitivity and specificity: 82.9% (95% CI 79.0–86.2%) and 84.7% (95% CI 83.8–85.6%), respectively, at a corresponding optimal cutoff of 130 mg. Qualitative UG had a sensitivity of 80.2% and a specificity of 85.6% with the optimal cutoffs achieved at glycosuria + 1.

Compared with the sensitivities of FPG (≥ 7.0 mmol/L), 2 h PG (≥ 11.1 mmol/L), and HbA1c (≥ 6.5%) using their cutoff values for diagnosing diabetes according to the 2010 American Diabetes Association criteria. Quantitative UG (82.9%, 95 CI 79.0–86.2%) showed a significantly higher sensitivity over FPG (67.5%, 95% CI 62.9–71.8%) in detecting NDD ($P<0.001$), and a comparable sensitivity with 2 h PG ($P=0.49$). In addition, it displayed a significantly higher sensitivity than HbA1c (63.9%, 95% CI 59.3–68.4%) ($P<0.001$) (Table 3). These results were similar for qualitative UG when making the corresponding comparisons (Table 3).

It is reported that participants with age over 45 were at high risk for diabetes [26], and this age cutoff was then used in the following analyses. Among the 449 participants with NDD, the prevalence of high UG (≥ 130 mg) was 82.6% in participants with age < 45 years, and 82.9% in participants with age ≥ 45 years ($P=0.99$, Table 4). There were also no significant differences in the prevalence of high UG (≥ 130 mg) among participants stratified by BMI or

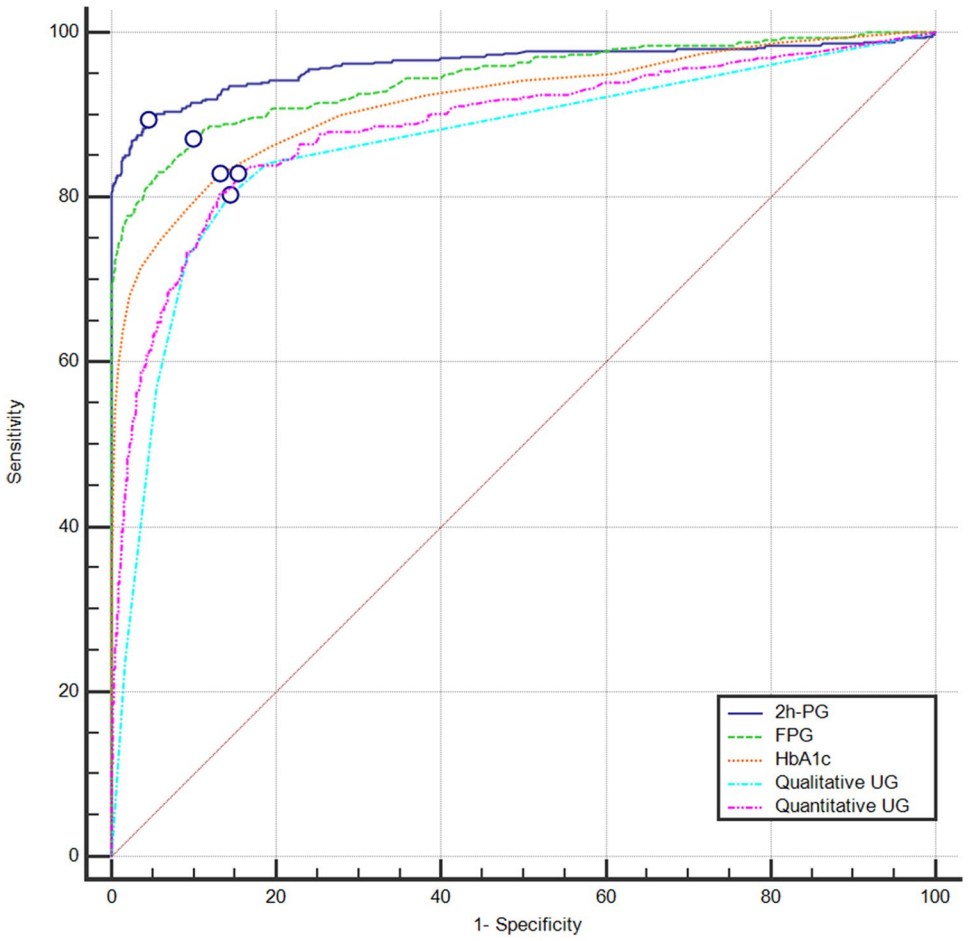

Fig. 2 Receiver operating characteristic (ROC) curves for urinary glucose (UG), fasting plasma glucose (FPG), 2 h plasma glucose (2 h PG), and glycated hemoglobin A1c (HbA1c) for identifying newly diagnosed diabetes. The areas under the ROC curves for quantitative UG, qualitative UG, FPG, 2 h PG, and HbA1c were 0.89, 0.87, 0.94, 0.96, and 0.92, respectively

Table 3 Sensitivity, specificity, positive predictive value, negative predictive value, and cost for detecting diabetes with UG, FPG, 2 h PG, and HbA1c

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Cost of one test (CNY)	Total cost (CNY)	Cost/NDD[a] (CNY)	Invasive or non-invasive
Quantitative UG (≥ 130 mg)	82.9 (79.0–86.2)	84.7 (83.8–85.6)	27.3 (25.0–29.8)	98.6 (98.3–98.9)	4.6	31,763	85.3	Non-invasive
Qualitative UG (≥ + 1)	80.2 (76.2–83.8)	85.6 (84.7–86.5)	28.0 (25.5–30.5)	98.4 (98.1–98.7)	4.6	31,763	85.3	Non-invasive
2 h PG (≥ 11.1 mmol/L)	80.4 (76.4–84.0)	100.0 (99.9–100.0)	100.0 (99.9–100.0)	98.7 (98.3–98.9)	10.6	73,193	202.8	Invasive
FPG (≥ 7.0 mmol/L)	67.5 (62.9–71.8)	100 (99.9–100.0)	100 (98.8–100.0)	97.8 (97.4–98.1)	10.6	73,193	241.5	Invasive
HbA1c (≥ 6.5%)	63.9 (59.3–68.4)	98.5 (98.2–98.9)	75.1 (70.5–79.4)	97.5 (97.1–97.9)	66.6	459,873	1602.8	Invasive

Data are means (95% confidence interval)

PPV positive predictive value, *NPV* negative predictive value, *UG* urinary glucose, *HbA1c* glycated hemoglobin, *FPG* fasting plasma glucose, *2 h PG* 2 h plasma glucose

[a]Cost per newly diagnosed diabetes identified.

Table 4 Distribution of newly diagnosed diabetes with quantitative UG < 130 mg and ≥ 130 mg stratified by ages, sex, 2 h PG, BMI, blood pressure, creatinine, and urine white blood cells

Category	Subcategory	UG ≥ 130 mg
Age(years)	< 45	95 (82.6%)
	≥ 45	277 (82.9%)
P value for difference0.99		
Gender	Male	204 (87.9%)
	Female	168 (77.4%)
P value for difference0.004		
2 h PG (mmol/L)	< 11.1	63 (71.6%)
	≥ 11.1	309 (85.6%)
P value for difference		0.004
BMI (kg/m^2)	< 24	68 (81.9%)
	≥ 24	304 (83.1%)
P value for difference		0.872
Hypertension (mmHg)	No	163 (82.7%)
	Have	209 (82.9%)
P value for difference		0.99
Creatinine (umol/L)	< 100	355 (82.9%)
	≥ 100	17 (81.0%)
P value for difference		0.769
UWC	Negative	343 (85.5%)
	Positive	29 (60.4%)
P value for difference		< 0.001

Data are number (percentage)

UG urinary glucose, *2 h PG* 2 h plasma glucose, *BMI* body mass index, *UWC* urine white blood cell

creatinine. But, the prevalence of high UG was significantly higher in participants with 2 h PG ≥ 11.1 mmol/L than those with 2 h PG < 11.1 mmol/L ($P = 0.004$). Males had obviously higher prevalence of high UG than females ($P = 0.004$). In addition, the prevalence of high UG in subjects with positive for urine white blood cell (UWC) was much lower than those with negative for UWC ($P < 0.001$).

Cost of UG, FPG, 2 h PG, and HbA1c

Taking into account the laboratory consumable cost, the salary of the nurse performing the venipuncture, and the cost of reagents, it costs China Yuan (CNY) 10.6, CNY 66.6, CNY 4.6 to perform a plasma glucose, HbA1c, and UG, respectively. As shown in Table 3, the highest total cost was HbA1c, followed by plasma glucose, and the lowest was UG. In addition, the cost per NDD identified was CNY 241.5, CNY 202.8, CNY 1602.8, and CNY 85.3 for FPG (≥ 7.0 mmol/L), 2 h PG (≥ 11.1 mmol/L), HbA1c (≥ 6.5%), and UG (≥ 130 mg), respectively.

Discussion

The results of this study show that UG, either measured quantitatively or qualitatively, was sufficiently sensitive to screen for NDD in a general population. Determining 2 h postprandial UG could overcome the limitation of its low sensitivity observed in previous studies.

In contrast to previous findings [15], our results indicate that UG can be used in mass screening for diabetes. The appearance of glucose in the urine occurs when the plasma glucose concentration is above the renal threshold [27]. The detection of fasting UG may be unsuitable for diabetes screening because the plasma glucose may be not high enough to cause obvious glycosuria. Friderichsen

and Maunsbach reported a sensitivity of 20.8% using 1–2 h postprandial glycosuria and indicated that the test with such a low sensitivity should not be recommended as a screening test [15], while a study by Davies et al. reported a sensitivity of 43% and a specificity of 98% using self-testing for 1 h postprandial glycosuria and showed self-testing for postprandial glycosuria performed consistently well in large populations [13]. Another study by Hanson et al. showed a sensitivity of 80.6% for quantitative urine glucose and 64.3% for dipstick glycosuria in non-fasting subjects [14]. Urine collection methods were different in these studies. To evaluate the use of UG as a screening test in a more scientific manner than previous studies, subjects in the present study were required to empty their bladders before an OGTT, prohibited drinking water, and forbidden strenuous exercise for 2 h after oral glucose loading with all the urine samples collected within 2 h for both the quantitative and qualitative measurement of glucose. And our data show that the usefulness of glycosuria for diabetes screening has been underestimated and the measurement of UG over a specific time period overcomes the limitation of its low sensitivity.

FPG is easy to obtain and is recommended for routine screening for diabetes, but accumulating evidence indicates that the efficacy of FPG alone for such screening is limited [7–9]. Elevated postprandial blood glucose is common among Chinese patients with diabetes [28, 29], and FPG is clearly insufficiently sensitive for screening the Chinese population. Consistent with several other cross-sectional studies [26, 30], the sensitivity of FPG ($\geq$7.0 mmol/L) in detecting diabetes was 67.5% in the present study. However, the sensitivities of both quantitative and qualitative UG were significantly higher than FPG. Being different from FPG, 2 h PG ($\geq$11.1 mmol/L) showed very high sensitivity and specificity in diabetes screening, yet our study shows that UG had a comparable sensitivity to it. Moreover, our data suggested that both quantitative and qualitative UG exhibited higher sensitivities over HbA1c. And subjects may have a better compliance because of the painless measurement for UG, compared with using FPG, 2 h PG and HbA1c for diabetes screening. In addition, it is worth noting that the method for urine collection (e.g., the collection time point) may affect the efficacy of UG in diabetes screening as shown in previous studies (Table 1). In this study, we found that the measurement of UG 2 h post the oral glucose loading may exhibit a great efficacy in diabetes screening. Furthermore, UG testing was observed to be the most cost-effective method for diabetes screening, compared with FPG, 2 h PG, and HbA1c (Table 3). Future studies are required to investigate whether 2 h postprandial UG is the best indicator of diabetes.

The diabetes risk score such as Finnish Diabetes Risk Score has also been used as a screening tool in some epidemiological studies, but unlike UG, it cannot reflect fluctuations in blood glucose [31, 32]. Moreover, a recent study by our group confirmed the efficacy of postprandial UG in diabetes screening [22]. However, that study was conducted in one urban community health center and included only a high-risk population. The present study was conducted in a large sample of Chinese adults with no history of diagnosed diabetes. The large number of individuals provided our study with high statistical power for data analysis. In general, considering its painlessness, effectiveness, and affordability, UG measurement is a practical and valid tool for diabetes screening.

The false negative and false positive rates of UG, although relatively low, cannot be ignored. According to our data, the false negative rate for quantitative UG in diabetes screening was almost 17%, so almost 17% subjects will miss further testing and diagnosis. A false positive rate of 15.3% was detected in the present study, so 15.3% subjects will be incorrectly identified as having diabetes. Therefore, we analyzed the factors that may influence UG. First, in this study, we confirmed that UG correlates positively with FPG and 2 h PG, consistent with several other studies [16, 18, 19, 22]. Subjects with relatively low plasma glucose may not display significant glycosuria. Second, kidney plays an important role in glucose homeostasis, largely through renal glucose reabsorption. Sodium glucose cotransporter 2 (SGLT2) is the major glucose cotransporter in the proximal tubule and is responsible for 90% of renal glucose reabsorption. Familial renal glycosuria is characterized by the gene-mutation-induced reduction in the expression of SGLT2, which may result in reduced glucose absorption [33, 34], followed by the emergence of glycosuria. Therefore, this alternative and efficient screening approach might be not appropriate for those with familial renal glycosuria but without hyperglycemia. Third, previous studies demonstrate the expression of SGLT2 is sexually dimorphic in animals [35, 36]. Our data also found the prevalence of high UG was increased in males. Sex may be a factor that significantly influences UG, but whether there is a sex-based difference in human SGLT2 expression is unclear. Fourth, to our knowledge, urinary tract infection accelerates glucose degradation, which ultimately leads to a negative UG result. In addition, hypothyroidism has been associated with diabetes mellitus, and treatment with T3 increased glycosuria in alloxan-induced diabetic rats [37]. However, it is unclear whether any subjects were receiving T3 treatment in this study. In addition, glycosuria also occurs more frequently during pregnancy because the renal glucose threshold and the renal tubular reabsorption of filtered glucose is reduced [38, 39]. Accordingly, UG testing is not recommended for pregnant women.

The study population is consisted of a large sample of Chinese adults with no history of diabetes, enabling a high statistical power for our analyses. Moreover, this is a multicenter study, and the conclusions of the study may have broader implications. Our study suggested that UG might

be a practical and reliable approach for mass screening, especially in developing countries. However, the limitations of our study must be noted. First, it should be noted that our study only involved Chinese Han ethnic subjects from Jiangsu Province. Whether different ethnic groups might display different sensitivities remains unknown. Second, because an overnight fast of at least 10 h was required, subjects older than 65 years were not included in this study for safety reasons. Therefore, the usefulness of UG in subjects older than 65 years is unclear. Third, we did not collect multiple urine samples at 0, 30, 60, and 90 min post glucose loading. Future studies are required to investigate whether 2 h postprandial UG is the best indicator of diabetes.

Conclusions

In conclusion, both quantitative and qualitative UG have utility in predicting diabetes. Determining UG 2 h post glucose loading can overcome the limitation of its low sensitivity observed in previous studies.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of Jiangsu Provincial Center for Disease Control and Prevention and Zhongda Hospital, Southeast University and with the 1964 Helsinki Declaration and its later amendments.

Informed consent Informed consent was obtained from all participants included in the study.

Data availability Data are available from the corresponding author for researchers who meet the criteria for access to confidential data. Please contact Zilin Sun (email: sunzilin1963@126.com).

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