



Increased waist-to-hip ratio is associated with decreased urine glucose excretion in adults with no history of diabetes

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Abstract

Purpose Promoting urine glucose excretion (UGE) is an attractive approach for the treatment of diabetes. Obesity is associated with increased risk for type 2 diabetes. This study was aimed to investigate the association of waist-to-hip ratio (WHR), a simple measure of abdominal obesity, with UGE determined in subjects without previous history of diabetes.

Methods We studied the correlation of WHR with UGE in 7485 participants without previous history of diabetes. All participants were given a standard 75 g glucose solution. Clinical parameters and demographic characteristics were assessed. Multiple linear regression analysis and multivariate logistic regression analysis were performed to determine the association of WHR with UGE.

Results Individuals with high WHR (H-WHR) exhibited significantly lower UGE compared to those with low WHR (L-WHR), in either normal glucose tolerance group or pre-diabetes group. In newly diagnosed diabetes group, individuals with H-WHR also showed lower UGE than those with L-WHR; however, no statistical significance was observed. After adjustment for potential confounding factors, including age, genders, and blood glucose level, WHR was negatively associated with UGE ($\beta = -250.901$, 95% CI: -471.891 to -29.911 , $p = 0.026$). However, no significant association was observed between BMI and UGE. Furthermore, multivariable logistic regression model showed that individuals with H-WHR were more likely to have low UGE (OR = 0.83, 95% CI: 0.71–0.97, $p = 0.018$).

Conclusions Individuals with H-WHR were at risk for decreased UGE. This study suggests that WHR, but not BMI, might be an important determinant of UGE.

Keywords Urine glucose excretion · Obesity · Waist-to-hip ratio · Renal glucose reabsorption

Introduction

Much more attention has been paid to the role of kidney in glucose homeostasis in recent years. In addition to playing an important role in gluconeogenesis and glucose utilization, the kidney contributes to glucose homeostasis largely through glucose reabsorption [1]. In normal conditions, the kidney can absorb almost all of the filtered glucose in order to conserve energy and ensure sufficient energy needs

during fasting periods [2]. However, this adaptive response become maladaptive in subjects with diabetes. Renal threshold for glucose reabsorption (RT_G) is defined as the plasma glucose level below which almost all filtered glucose is reabsorbed and above which glucose appears in the urine. Accumulating evidences have demonstrated that RT_G of diabetics is significantly higher than normal individuals [3, 4]. Yet, increased glucose reabsorption contributes to the progression of hyperglycemia [3, 5]. Therefore, promoting urine glucose excretion (UGE) through inhibition of renal glucose reabsorption has become an attractive approach for the treatment of diabetes [6]. Currently, several studies have been designed to focus on the significance of urine glucose in clinical practice, such as diabetes screening and glycemic control [7, 8].

Obesity has become a global epidemic disease and its prevalence has been projected to increase by 40% in the next decade [9]. It is well known that obesity increases the risk of several disease conditions including diabetes,

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hypertension and cardiovascular disease [10, 11]. Moreover, obesity has shown to be one of the major determinants of renal hyperfiltration, hyper-perfusion and microalbuminuria [11, 12]. To date, several studies have focused on obesity-related kidney disease [9, 13]. However, it is unclear whether obesity may affect renal glucose reabsorption. A recent research reported that subjects with body mass index (BMI) ≥ 24 kg/m² were more likely to have high RT_G [14], suggesting that renal glucose reabsorption may be enhanced in subjects with obesity, which may subsequently cause a decrease in UGE. BMI is generally used to define overweight or obesity. However, it is poor to estimate body fat distribution. There is evidence that distribution of body fat is related to a variety of physiological aberrations, instead of overweight or obesity per se [12]. Waist-to-hip ratio (WHR), a simple measure of abdominal obesity, has been considered as a better classifier of obesity than BMI [9, 12]. In addition, WHR has been suggested to be more closely associated with cardiovascular risk and renal function impairment [12, 15, 16]. The association of WHR with renal glucose reabsorption is still not clear. Renal threshold for glucose reabsorption can reflect the capacity of renal glucose reabsorption. However, gold-standard stepwise hyperglycemic clamp procedure method cannot be widely used in clinical practice to estimate renal threshold for glucose reabsorption because of specialized laboratory demand. However, it is easy to obtain data on UGE.

Therefore, the purpose of this study was to explore the potential link between WHR and UGE in subjects with no previous history of diabetes.

Methods

Study design and participants

Data were obtained from a cross-sectional study undertaken to evaluate the efficacy of UGE in diabetes screening [17]. 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 or taking anti-diabetic medication from 6 cities in Jiangsu Province, as previously reported [7, 17]. After the exclusion of 204 people who missed the measurement of hemoglobin A1c (HbA1c) or UGE, 7485 participants were included in the final analysis.

Anthropometric and laboratory measurements

A structured questionnaire was used to obtain information on demographic characteristics and medical histories. Weight, height, waist circumference, hip circumference,

heart rate (HR) and blood pressure were measured according to standardized protocols. BMI was calculated as weight in kilograms divided by height in meters squared. WHR was calculated as waist circumference divided by hip circumference. All participants were given an oral glucose tolerance test. Fasting plasma glucose (FPG), 2 h plasma glucose (2 h-PG), HbA1c, total cholesterol (TC), triglycerides (TG), high-density lipoprotein-cholesterol (HDL-C), low-density lipoprotein-cholesterol (LDL-C), blood urea nitrogen (BUN), and creatinine were determined. All the urine samples were collected over a 2 h period after oral glucose loading to assess urine glucose using a quantitative urine meter (UG-201-H, Tanita Corporation, Tokyo, Japan). UGE was calculated as the urine glucose concentration (mg/dl) \times the urine volume (dl).

Definitions

Diabetes was defined as FPG ≥ 7.0 mmol/l and/or 2 h-PG ≥ 11.1 mmol/l and/or HbA1c $\geq 6.5\%$, according to the 2012 American Diabetes Association (ADA) criteria. Prediabetes was defined as FPG ≥ 5.6 mmol/l and ≤ 6.9 mmol/l, 2 h-PG ≥ 7.8 mmol/l and <11.0 mmol/l, or $5.7\% \leq$ HbA1c $\leq 6.4\%$. High WHR (H-WHR) was defined as WHR ≥ 0.9 for men and ≥ 0.8 for women, respectively, while WHR less than 0.9 for men and less than 0.8 for women, respectively, was defined as low WHR (L-WHR), according to previous study [12]. UGE exceeding the 75th percentile (85 mg) of the study population was considered as high UGE, while UGE less than the 75th percentile was considered as low UGE.

Statistical analysis

Continuous variables were described as means \pm SD, or median (25th to 75th percentiles). Categorical variables were described as numbers (percentages). One-way analysis of variance for continuous variables and χ^2 test for categorical variables were used to compare characteristics of participants in different groups. Non-parametric Kruskal–Wallis test followed by all pairwise multiple comparisons was used when the data distribution was skewed. The relationships between the UGE and other clinical indicators were examined using Spearman's correlation. Multiple linear regression analysis with adjustment for potential confounders was conducted to assess the association between WHR and UGE. Potential confounders included in the multivariate analysis were age, genders, HR, BP, FPG, 2h-PG, HbA1c, TC, TG, HDL-C, LDL-C, BUN and BMI, which were chosen depending on reaching statistical significance in the Spearman's correlation analysis and based on clinical judgment. Then, a binary logistic regression analysis was performed to determine the odds

ratios of high UGE associated with WHR after adjustment for other variables. Prior to multivariate analyses, variance inflation due to covariates was verified by estimating a variance inflation factor < 2.7. A p value < 0.05 was considered statistically significant. All statistical analyses were conducted using SPSS 22.0 (SPSS Inc., Chicago, IL, USA).

Results

General characteristics of the study participants

The general characteristics of the study population, according to glucose tolerance status and WHR, are summarized in Table 1. All groups with H-WHR included more men, were older, had higher blood pressure, 2 h-PG level, TC, TG and LDL-c, and showed a greater BMI, compared with normal glucose tolerance (NGT) subjects with L-WHR (all $p < 0.05$). Newly diagnosed diabetes (NDD) group

exhibited significantly higher UGE than NGT and pre-diabetes (PDM) groups. In addition, individuals with H-WHR exhibited significantly lower UGE than those with L-WHR, whether in NGT or PDM group (both $p < 0.05$). In NDD group, individuals with H-WHR also showed lower UGE than those with L-WHR, but no statistical significance was observed.

Correlations of UGE with clinical indicators

The correlations of UGE with other clinical indicators are presented in Table 2. UGE was positively associated with age, HR, blood pressure, FPG, 2 h-PG, HbA1c, TC, TG, LDL-C, BMI and WHR (all $p < 0.001$), whereas it was negatively associated with HDL-C in the overall population ($p < 0.001$). In the subgroup analysis stratified by glucose tolerance status, no significant correlation was found between WHR and UGE in subjects with NGT, but a positive correlation was observed in subjects with PDM and

Table 1 Characteristics of the study participants according to glucose tolerance status and WHR

	NGT ($n = 3242$)		PDM ($n = 3645$)		NDD ($n = 597$)	
	L-WHR ($n = 1257$)	H-WHR ($n = 1986$)	L-WHR ($n = 969$)	H-WHR ($n = 2676$)	L-WHR ($n = 77$)	H-WHR ($n = 520$)
Age (years)	35.73 ± 11.17	41.37 ± 11.10 ^a	44.58 ± 12.11 ^{a,b}	47.91 ± 10.58 ^{a,b,c}	48.38 ± 10.72 ^{a,b,c}	50.19 ± 9.59 ^{a,b,c,d,e}
Male (%)	1362 (42.0%)	1881 (58.0%) ^a	1644 (45.1%) ^{a,b}	2001 (54.9%) ^{a,b,c}	292 (48.9%) ^{a,b,d}	305 (51.1%) ^{a,b,c,d,e}
HR (beats/min)	77.75 ± 12.06	77.44 ± 17.06	77.09 ± 12.11	77.41 ± 11.22	77.27 ± 10.79	79.72 ± 12.33
Blood pressure (mm Hg)						
Systolic	120.13 ± 15.82	125.31 ± 18.56 ^a	126.22 ± 17.42 ^a	132.67 ± 19.08 ^{a,b,c}	132.25 ± 13.51 ^{a,b,c}	140.69 ± 18.79 ^{a,b,c,d,e}
Diastolic	74.82 ± 10.91	78.33 ± 19.81 ^a	78.21 ± 11.49 ^a	81.11 ± 11.92 ^{a,b,c}	82.84 ± 9.03 ^{a,b,c}	84.65 ± 11.58 ^{a,b,c,d}
Blood glucose (mmol/l)						
FPG	5.01 ± 0.34	5.02 ± 0.34	5.53 ± 0.53 ^{a,b}	5.55 ± 0.53 ^{a,b}	7.72 ± 2.20 ^{a,b,c,d}	7.48 ± 2.07 ^{a,b,c,d,e}
2 h-PG	5.27 ± 0.95	5.65 ± 0.96 ^a	6.21 ± 1.60 ^{a,b}	6.73 ± 1.59 ^{a,b,c}	12.36 ± 5.19 ^{a,b,c,d}	12.53 ± 4.24 ^{a,b,c,d}
HbA1c (%)	5.30 ± 0.23	5.34 ± 0.22	5.71 ± 0.29 ^{a,b}	5.77 ± 0.29 ^{a,b}	6.79 ± 1.18 ^{a,b,c,d}	7.01 ± 1.26 ^{a,b,c,d,e}
TC (mmol/l)	4.36 ± 0.86	4.52 ± 0.88 ^a	4.64 ± 0.94 ^a	4.80 ± 0.94 ^{a,b,c}	5.01 ± 1.07 ^{a,b,c,d}	5.11 ± 0.98 ^{a,b,c,d}
TG (mmol/l)	0.96 (0.72–1.41)	1.16 (0.83–1.76) ^a	1.07 (0.77–1.58) ^{a,b}	1.37 (0.96–1.96) ^{a,b,c}	1.45 (1.00–2.48) ^{a,b,c}	1.74 (1.24–2.53) ^{a,b,c,d}
HDL-C (mmol/l)	1.42 ± 0.33	1.36 ± 0.43	1.44 ± 0.37	1.35 ± 0.36 ^c	1.37 ± 0.36	1.31 ± 0.32 ^{a,c}
LDL-C (mmol/l)	2.36 ± 0.63	2.52 ± 0.66 ^a	2.58 ± 0.77 ^a	2.74 ± 0.74 ^{a,b,c}	2.76 ± 0.83 ^{a,b,c}	2.94 ± 0.80 ^{a,b,c,d,e}
BUN (mmol/l)	4.90 ± 1.30	4.71 ± 1.41	5.37 ± 1.74 ^{a,b}	5.09 ± 1.50 ^{a,c}	5.83 ± 1.56 ^{a,b,c,d}	5.14 ± 1.49 ^{b,c,d}
Creatinine (μmol/l)	75.51 ± 16.42	72.43 ± 15.04	76.56 ± 23.43 ^b	72.40 ± 18.89 ^c	75.47 ± 16.15	71.99 ± 17.48 ^c
BMI (kg/m ²)	22.27 ± 3.03	25.32 ± 3.71 ^a	23.39 ± 3.43 ^{a,b}	26.53 ± 3.67 ^{a,b,c}	25.17 ± 3.17 ^{a,c,d}	27.72 ± 3.90 ^{a,b,c,d,e}
UGE (mg)	22.00 (7.50–56.00)	18.00 (6.00–42.00) ^a	40.00 (14.45–120.00) ^{a,b}	30.00 (10.00–86.00) ^{a,b,c}	1170.00 (183.50–2592.50) ^{a,b,c,d}	677.50 (133.50–1856.25) ^{a,b,c,d}

Data are presented as n (%), mean ± SD, or median (25th to 75th percentiles) as appropriate

WHR waist-to-hip ratio, H-WHR high waist-to-hip ratio, L-WHR low waist-to-hip ratio, NGT normal glucose tolerance, PDM pre-diabetes, NDD newly diagnosed diabetes, HR heart rate, FPG fasting plasma glucose, 2 h-PG 2 h plasma glucose, HbA1c glycated hemoglobin, TC total cholesterol, TG triglycerides, HDL-C high-density lipoprotein cholesterol, LDL-C low-density lipoprotein cholesterol, BUN blood urea nitrogen, BMI body mass index, UGE urine glucose excretion

^a $P < 0.05$ versus NGT subjects with L-WHR

^b $P < 0.05$ versus NGT subjects with H-WHR

^c $P < 0.05$ versus PDM subjects with L-WHR

^d $P < 0.05$ versus PDM subjects with H-WHR

^e $P < 0.05$ versus NDD subjects with L-WHR

Table 2 The correlations of UGE with other clinical indicators

	UGE			
	Overall	NGT	PDM	NDD
Age	0.067 (<0.001)*	−0.019 (0.277)	−0.065 (<0.001)*	−0.096 (0.019)*
HR	0.068 (<0.001)*	0.035 (0.045)*	0.065 (<0.001)*	0.104 (0.011)
Systolic blood pressure	0.148 (<0.001)*	0.052 (0.003)*	0.066 (<0.001)*	0.054 (0.186)
Diastolic blood pressure	0.139 (<0.001)*	0.052 (0.003)*	0.084 (<0.001)*	0.116 (0.005)*
FPG	0.342 (<0.001)*	0.063 (<0.001)*	0.245 (<0.001)*	0.508 (<0.001)*
2h-PG	0.271 (<0.001)*	0.010 (0.565)	0.163 (<0.001)*	0.526 (<0.001)*
HbA1c	0.253 (<0.001)*	0.006 (0.748)	0.023 (0.162)	0.427 (<0.001)*
TC	0.106 (<0.001)*	0.033(0.064)	0.024 (0.142)	0.094 (0.021)*
TG	0.141 (<0.001)*	0.075 (<0.001)*	0.057 (0.001)*	0.136 (0.001)*
HDL-C	−0.060 (<0.001)*	−0.036 (0.041)*	−0.055 (0.001)*	−0.036 (0.382)
LDL-C	0.096 (<0.001)*	0.026 (0.134)	0.031 (0.066)	0.033 (0.420)
BUN	0.116 (<0.001)*	0.102 (<0.001)*	0.095 (<0.001)*	0.026 (0.531)
Creatinine	−0.004 (0.760)	−0.019 (0.173)	0.032 (0.051)	−0.062 (0.130)
BMI	0.119 (<0.001)*	−0.004 (0.822)	0.059 (<0.001)*	0.018 (0.656)
WHR	0.136 (<0.001)*	−0.011 (0.524)	0.083(<0.001)*	0.116 (0.004)*

Data are presented as r (p value)

UGE urine glucose excretion, NGT normal glucose tolerance, PDM pre-diabetes, NDD newly diagnosed diabetes, HR heart rate, FPG fasting plasma glucose, 2h-PG 2 h plasma glucose, HbA1c glycated hemoglobin, TC total cholesterol, TG triglycerides, HDL-C high-density lipoprotein cholesterol, LDL-C low-density lipoprotein cholesterol, BUN blood urea nitrogen, BMI body mass index, WHR waist-to-hip ratio

* Significance, $p < 0.05$

NDD ($r = 0.083$, $p < 0.001$; $r = 0.116$, $p = 0.004$, respectively; Table 2). In addition, no correlation of UGE with creatinine was found in all groups.

Multiple linear regression analysis with UGE as the dependent variable

To identify the association of WHR with UGE, and eliminate the influence of potential confounders, a multiple linear regression analysis with UGE as a dependent variable was performed, which is presented in Table 3. WHR was negatively associated with UGE after adjustment for age, gender, HR, blood pressure, FPG, 2 h-PG, TG, TC, HDL-c, LDL-c, BUN and BMI ($\beta = -250.901$, 95% confidence interval (CI): -471.891 to -29.911 , $p = 0.026$). However, there were no significant associations between BMI and UGE after multivariable adjustment ($p = 0.096$). In addition, FPG, 2 h-PG, HbA1c and TG were still positively associated with UGE in this model. However, the positive associations between HR, blood pressure, TC, BUN and UGE were no longer significant.

Logistic regression analysis of odds ratios for high UGE

Furthermore, a binary logistic regression analysis was performed to identify the factors associated with the risk of high UGE. Individuals with elevated FPG, 2 h-PG, HbA1c

and TG were more likely to have high UGE. In addition, females showed a 0.42-fold decreased odds ratio (OR) for high UGE compared with males. Moreover, the results showed that H-WHR was significantly associated with a decreased OR of high UGE in the multi-adjusted model (OR = 0.83, 95% CI: 0.71–0.97, $p = 0.018$) (Table 4).

Discussion

In subjects without previous history of diabetes, we found that individuals with H-WHR exhibited significantly decreased UGE, in both NGT and PDM groups. Although lower UGE was also observed in NDD participants with H-WHR compared with NDD participants with L-WHR, there was no statistical significance. Furthermore, WHR and BMI were positively correlated with UGE in the overall population. However, after adjusting for confounding factors like age, genders, HR, blood pressure and glucose levels, TG and TC, WHR was negatively associated with UGE, whereas BMI was not significantly correlated with UGE. Moreover, multivariable logistic regression model also showed that WHR was an independent factor for UGE. H-WHR, but not BMI, was strongly associated with a decreased risk of high UGE. The results suggest that the pattern of fat distribution may be of more importance for UGE than overweight or obesity by itself.

Table 3 Multiple linear regression analysis with UGE as the dependent variable

Independent variable	b Coefficient	95% CI	Standardized coefficient	P
Age (years)	−3.715	−4.853 to −2.576	−0.071	<0.001
Gender ^a	−143.247	−168.687 to −117.807	−0.114	<0.001
FPG (mmol/l)	145.779	127.265 to 164.293	0.228	<0.001
2 h-PG (mmol/l)	76.256	69.525 to 82.988	0.311	<0.001
HbA1c (%)	159.064	130.429 to 187.699	0.157	<0.001
HR (beats/min)	0.163	−0.708 to 1.035	0.003	0.713
Systolic (mm Hg)	0.180	−0.617 to 0.976	0.005	0.658
Diastolic (mm Hg)	0.371	−0.598 to 1.339	0.009	0.453
TC (mmol/l)	−9.762	−24.635 to 5.110	−0.015	0.198
TG (mmol/l)	17.395	9.383 to 25.408	0.044	<0.001
HDL-C (mmol/l)	43.057	8.992 to 77.122	0.026	0.013
LDL-C (mmol/l)	−4.557	−15.390 to 6.275	−0.008	0.410
BUN (mmol/l)	6.979	−0.881 to 14.839	0.017	0.082
WHR	−250.901	−471.891 to −29.911	−0.027	0.026
BMI (kg/m ²)	−2.965	−6.459 to 0.529	−0.019	0.096

UGE urine glucose excretion, HR heart rate, FPG fasting plasma glucose, 2 h-PG 2 h plasma glucose, HbA1c glycated hemoglobin, TC total cholesterol, TG triglycerides, HDL-C high-density lipoprotein cholesterol, LDL-C low-density lipoprotein cholesterol, BUN blood urea nitrogen, BMI body mass index, WHR waist-to-hip ratio

^a1 = Male, 2 = female

Table 4 Multivariate logistic regression analysis of the factors influencing high UGE

Category	β	SE of β	OR	95% CI	P value
Age (years)	−0.014	0.003	0.99	0.98–0.99	<0.001
Gender ^a	−0.872	0.072	0.42	0.36–0.48	<0.001
FPG (mmol/l)	0.789	0.058	2.20	1.96–2.47	<0.001
2h-PG (mmol/l)	0.239	0.019	1.27	1.22–1.32	<0.001
HbA1c (%)	0.611	0.093	1.84	1.54–2.21	<0.001
HR (beats/min)	0.004	0.002	1.00	1.00–1.01	0.066
Systolic BP (mm Hg)	0.000	0.002	1.00	1.00–1.00	0.936
Diastolic BP (mm Hg)	0.007	0.003	1.01	1.00–1.01	0.041
TC (mmol/l)	0.021	0.047	1.02	0.93–1.12	0.658
TG (mmol/l)	0.058	0.021	1.06	1.02–1.11	0.006
HDL-C (mmol/l)	0.134	0.092	1.14	0.96–1.37	0.145
LDL-C (mmol/l)	−0.029	0.046	0.97	0.89–1.06	0.535
BUN (mmol/l)	0.080	0.021	1.08	1.04–1.13	<0.001
BMI (kg/m ²)	0.006	0.009	1.01	0.99–1.02	0.552
WHR ^b	−0.188	0.080	0.83	0.71–0.97	0.018

OR odds ratio, CI confidence interval, WHR waist-to-hip ratio, H-WHR high waist-to-hip ratio, L-WHR low waist-to-hip ratio, UGE urine glucose excretion, HR heart rate, FPG fasting plasma glucose, 2 h-PG 2 h plasma glucose, HbA1c glycated hemoglobin, BP blood pressure, TC total cholesterol, TG total triglycerides, HDL-C high-density lipoprotein cholesterol, LDL-C low-density lipoprotein cholesterol, BUN blood urea nitrogen, BMI body mass index

^a1 = male, 2 = female

^b1 = L-WHR, 2 = H-WHR

Because of excess weight gain, a cascade of metabolic, endocrine, cardiovascular and renal changes were initiated [12]. A recent research found that BMI ≥ 24 kg/m² was significantly associated with the increased risk of high RT_G

[14], indicating that individuals with BMI ≥ 24 kg/m² may have enhanced renal glucose reabsorption which may result in decreased UGE. However, the association between obesity and UGE is not clear. Besides, BMI does not account for the distribution of fat. WHR has been considered as a better classifier of obesity than BMI. Several researches have reported that the distribution of body fat, but not overweight or obesity per se, is strongly related to a variety of physiological aberrations [9, 12]. Our study found that WHR was negatively associated with UGE, while no significant correlation was found between BMI and UGE after multivariable adjustment.

What could be the underlying mechanism that makes individuals with increasing WHR more prone to have decreased UGE? Overexpression of sodium-glucose cotransporter 2 (SGLT2) has been reported in hyperglycemic animals and humans, which may be one of the key reasons [3]. It has been reported that there is a strong link between sympathetic activation and visceral obesity [18]. Moreover, the potential role for sympathetic regulation of SGLT2-mediated renal glucose reabsorption has been highlighted [19]. In addition, a significant increase in SGLT2 expression was observed in diet-induced obesity mice compared with normal mice [20]. Decreased UGE in participants with H-WHR may be attributed to enhanced renal glucose reabsorption by overexpression of SGLT2. However, whether the expression of SGLT2 is upregulated in humans with obesity needs further verification. Additionally, strong evidence indicates that central body fat distribution is associated with insulin resistance [21]. Greater insulin levels were observed in patients

with central fat distribution than those with peripheral fat distribution [22]. Furthermore, a recent study has demonstrated that insulin could stimulate SGLT2-mediated glucose reabsorption [23]. It is necessary to identify the impact of insulin level on UGE in individuals with obesity, especially those with abdominal obesity. Moreover, there is evidence that increased renal sodium reabsorption is related to weight gain [24]. As is known, the transport of glucose from the renal tubule lumen into the epithelial cells is sodium dependent. Renal glucose reabsorption seems to be closely related to obesity. Taken together, individuals with increasing WHR are more prone to have decreased UGE that may be explained by increased renal glucose reabsorption via up-regulation of SGLT2. Future studies are needed to clarify whether the expression of SGLT2 is upregulated in humans with obesity, especially those with abdominal obesity.

Furthermore, prominent gender differences were found in the gene expression of glucose transporters in mouse, and the expression of SGLT2 was significantly higher in the female kidney than in the males [25]. Our data also suggested that females were more likely to have lower UGE than males, which might be attributed to the differences in SGLT2 expression. However, it is unclear whether there are gender differences in the expression of glucose transporters in humans.

The large sample size in our study might give high statistical power for our current data analysis. Besides, our study population consisted of participants without previous history of diabetes and taking no antidiabetic medication, and thereby the correlation between WHR and UGE may be more accurate due to the elimination of the impact of antidiabetic medication on UGE. However, several limitations of our study should be mentioned. First, the causal relationships could not be deduced in the cross-sectional study. Second, decreased UGE may be attributed to increased renal glucose reabsorption, which was not evaluated in the present study. Future studies were needed to assess renal threshold for glucose reabsorption in individuals with H-WHR and L-WHR, as well as SGLT2 expression. Third, WHR is a simple measure for body fat distribution. We did not assess fat distribution directly with computed tomography or magnetic resonance imaging methods. Fourth, because our study only involved Chinese Han ethnic subjects from Jiangsu Province, the relation of WHR to UGE in other populations with different ethnics or from different countries remains largely unknown.

Conclusions

Despite the aforementioned limitations, this study indicated that WHR was an independent risk factor for UGE. The

pattern of fat distribution, not overweight or obesity by itself, might be an important determinant of UGE.

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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 the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study was approved by the ethical review committee of Jiangsu Provincial Center for Disease Control and Prevention (JSJK2016-B003-03).

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

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