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Neck circumference might predict gestational diabetes mellitus in Han Chinese women: A nested case–control study

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ABSTRACT

Aims/Introduction: A large neck circumference might be an indicator of metabolic syndrome and its components, and for certain patients is more practical as an index than waist circumference. The demarcation value for neck circumference that suggests metabolic syndrome appears to vary by ethnic group. Gestational diabetes mellitus is considered a component of metabolic syndrome in pregnant women. We investigated whether neck circumference in Han Chinese women is associated with gestational diabetes mellitus in early pregnancy, and determined a predictive demarcation value.

Materials and Methods: A nested case–control study was carried out with 255 women aged 18–35 years. Gestational diabetes mellitus was diagnosed according to the criteria of the American Diabetes Association through a 2-h, 75-g oral glucose tolerance test.

Results: Of the total population, 41 (16%) women developed gestational diabetes mellitus by 24–28 weeks of gestation. Neck circumference at gestational week 16 positively correlated with pre-pregnancy waist circumference, bodyweight and body mass index, and maternal age ($P = 0.029$) and hemoglobin A1c at gestational week 24 ($P \leq 0.001$). By binary logistic regression, neck circumference was an independent predictor of gestational diabetes mellitus (odds ratio 1.840, 95% confidence interval 1.040–3.254; $P = 0.036$). According to the receiver operating characteristic curve, for predicting gestational diabetes mellitus the optimal demarcation for neck circumference at gestational week 16 was 35.15 cm.

Conclusions: Neck circumference is a viable tool to screen for gestational diabetes mellitus. In this population of pregnant Han Chinese women, a neck circumference of ≥35.15 cm was a predictor of gestational diabetes mellitus.

INTRODUCTION

Gestational diabetes mellitus (GDM) is impaired glucose tolerance during pregnancy in women with normal glucose metabolism before pregnancy. The proportion of pregnant women with GDM is increasing worldwide, reportedly ranging from 1% to 14% in various countries, and is higher in Asian countries[1]. In a study carried out in New York City, susceptibility to GDM appeared to vary by ethnic group, and might not correlate with obesity[2].

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The reported prevalence of GDM among women in mainland China varies. A large-scale screening in mainland China, published in 2009, applied the criteria of the American Diabetes Association and found that the prevalence of GDM in pregnant women was 4.3%[3]. However, in a different large study occurring from July 2011 to February 2012, the criteria of the International Association of Diabetes and Pregnancy Study Group[4] were applied and the prevalence was 17.5%[5].

To confirm that a pregnant woman has GDM, a standard oral glucose tolerance test (OGTT) must be administered at 24–28 weeks of gestation. Waist circumference, hip circumference and waist-to-hip ratio are the most commonly used

factors to indicate metabolic syndrome. However, none of these might be accurate indications, as they are affected by many other factors, and can change significantly during pregnancy[6].

It is well accepted that diabetes and metabolic syndrome share similar risk factors[7]. Neck circumference might be a better index than waist circumference or other indicators for determining metabolic syndrome or its components, and neck circumference is easily determined and has little variability[8–11]. According to Hoebel *et al.*[6] and others[12–14], neck circumference can be a useful biomarker of risk factors in metabolic syndrome, such as insulin resistance, central obesity, blood pressure, fasting glucose levels and triglycerides. Stabe *et al.*[12] found that neck circumference was strongly associated with insulin resistance. Other research found that the neck circumference of teenagers could indicate risk factors associated with metabolic syndrome[14].

While GDM is diabetes occurring during pregnancy that is not clearly overt diabetes,[15] maternal hyperglycemia in GDM is various and the metabolic disorders diverse[16]. Importantly, the disease is associated with other pregnancy-associated risks, such as obesity, inflammation and hyperinsulinemia, and women with GDM are more likely to develop type 2 diabetes mellitus in the years after pregnancy[17].

It is our hypothesis that a pregnant woman with a large neck circumference at gestational week 16 has a higher risk of GDM. Therefore, the present study investigated whether the neck circumference of Chinese pregnant women at the 16th week of gestation might be associated with the development of GDM in the second trimester (24–28 weeks).

METHODS

The Ethics Committee of the Third Affiliated Hospital of Guangzhou Medical University approved the study protocol.

Study Population and Basic Information

To undertake a nested case–control study, from October 2014 to December 2014 we assembled a cohort of 261 normal pregnant women, aged 18–35 years at gestational week 16. Each woman in the study was examined periodically during pregnancy, and information was obtained regarding anthropometry, demographic characteristics and medical history at the Third Affiliated Hospital of Guangzhou Medical University, Guangzhou, China. At recruitment, measurements of maternal neck circumference, waist circumference, body height and bodyweight were taken for all participants; pre-pregnancy measurements were self-reported. We followed cohort members from the entry date until baby delivery at the end of the study period (September 2015). Six women with diagnosed hypertension (pregnancy-induced), thyroid diseases and other endocrine diseases during the subsequent screening were excluded. If a participant received a diagnosis of GDM at 24–28 weeks of gestation by OGTT, she was assigned to the GDM group (n = 41; 16%). Otherwise, she was considered part of the normal control group (n = 214).

Definition of GDM

GDM was defined as diabetes or glucose intolerance, initially recognized during pregnancy, based on the criteria for GDM of the American Diabetes Association[18]. To confirm if a pregnant woman had GDM, the patient underwent a 2-h, 75-g OGTT at 24–28 gestational weeks. Participants were considered to have GDM if one or more of the following applied regarding fasting plasma glucose levels: fasting, ≥5.1 mmol/L; 1 h, ≥10.0 mmol/L; and 2 h, ≥8.5 mmol/L.[18] Participants were assigned to a GDM or normal control group, based on the aforementioned results.

Measurement

Each study participant underwent a physical examination at gestational week 16, during which participants faced the investigator while relaxing their shoulders during measurements. We recorded maternal age, gestational weeks, gravidity and parity.

All measuring instruments were calibrated before measurement. Bodyweight was measured by a digital scale to within 0.1 kg, with participants wearing only underwear. Height was measured by portable stadiometer to within 0.5 cm, with the participant barefoot. All circumference measurements were taken at the end of expiration. Waist circumference was measured to within 0.1 cm with a measuring tape circling the participant's body at the navel. Neck circumference was measured to 0.1 cm with measuring tape at the level of the upper margin of the thyroid cartilage.

Body mass index (BMI) was calculated as weight in kilograms divided by the square of the height in meters (kg/m^2). Each participant's bodyweight and height were measured before pregnancy and before delivery, and thus the BMI was calculated twice.

Blood pressure (BP) was measured with a calibrated sphygmomanometer, on the right arm with the participant sitting up, after the participant had been lying down and resting for at least 5 min. The criteria for systolic blood pressure and diastolic blood pressure were the first and fifth phase of Korotkoff sounds[19], respectively.

Blood samples were collected at gestational week 24, and were analyzed at the Biochemistry Laboratory of Third Hospital Affiliated to Guangzhou Medical University. Fasting blood glucose (FBG), 1-h blood glucose and 2-h blood glucose were determined by OGTT test[20]. Total cholesterol and triglycerides were measured by enzymatic calorimetric test, and hemoglobin A1c (HbA1c) by ion-exchange chromatography. Albumin was measured using bromocresol green. Uric acid was determined by an enzymatic method. In addition, the sex and birthweight of the newborn baby of the participant were recorded at delivery.

Statistical Analysis

The Kolmogorov–Smirnov test was carried out to assess the distribution of continuous variables. To characterize the continuous variables, we used the mean and standard deviation, or

median and semi-interquartile range, according to the result of the Kolmogorov–Smirnov test. To compare the continuous variables between the GDM and control groups, Student's *t*-test was used. Pearson's correlation (coefficient, *r*) was used to determine correlations between neck circumference and the continuous variables.

A multivariate regression analysis was carried out by assigning the neck circumference as a dependent variable. The following were independent variables: increases in systolic blood pressure, diastolic blood pressure, uric acid, albumin, FBG, HbA1c and BMI during pregnancy, and triglyceride and total cholesterol levels. A backward stepwise elimination selection procedure was used to determine and exclude independent variables that did not affect neck circumference.

To evaluate the association between risk factors for GDM and neck circumference, we used logistic regression analysis to obtain the odds ratio (OR) and 95% confidence interval (CI). The receiver operating characteristic curves were generated to evaluate the efficiency of neck circumference for indicating GDM, by calculating the area under the curve and the 95% CI.

We determined the optimal sex-specific neck circumference cut-off points with regard to GDM by using the Youden index, defined as: sensitivity + specificity − 1. Statistical analyses were carried out using SPSS software (version 20.0; SPSS, Chicago, IL, USA). Test levels for significance were defined by a *P*-value <0.05.

RESULTS

The study sample consisted of 255 pregnant women with a mean age of 29.1 ± 3.7 years (Table 1). GDM was identified in 41 (16%) of the pregnant women. All of the tested variables were significantly different between the GDM and normal groups, except for height, increased weight and BMI after pregnancy, systolic blood pressure, diastolic blood pressure, uric acid, albumin, and total cholesterol. The mean age, weight and BMI before pregnancy, and neck and waist circumferences were significantly higher in the women with GDM than in the normal group. Mean FBG, 1-h blood glucose, 2-h blood glucose, HbA1c and triglyceride levels were also different, with higher values for women with GDM.

Neck circumference was significantly positively associated with the following factors: waist circumference, weight before pregnancy, BMI before pregnancy, HbA1c and age (Table 2). However, neck circumference was uncorrelated with FBG, 1-h glucose, 2-h glucose and triglyceride levels (Table 2).

When adjusted for age, the analysis showed that neck circumference was significantly and positively associated with the following factors: waist circumference, weight before pregnancy and BMI before pregnancy (Table 3). However, neck circumference was uncorrelated with HbA1c, FBG, 1-h glucose, 2-h glucose and triglyceride levels.

The binary logistic regression analysis (backward stepwise elimination method) showed that, considering the one dependent variable GDM, the following were independent variables for GDM: FBG, 1-h glucose, 2-h glucose, HbA1c, waist circumference and neck circumference (Table 4).

Regarding the receiver operating characteristic curve analysis for GDM (Figure 1), neck circumference is shown as the area under the curve, which was 0.653 (95% CI 0.552–0.755). Waist circumference was 0.700 (95% CI 0.607–0.793); weight before pregnancy 0.651 (95% CI 0.556–0.747); BMI before pregnancy 0.650 (95% CI 0.554–0.746); BMI during pregnancy 0.369 (95% CI 0.280–0.459); and weight during pregnancy 0.389 (95% CI 0.298–0.479).

Among these pregnant women, the optimal cut-off point for neck circumference for indicating GDM was 35.15 cm, with a sensitivity of 0.488 and specificity of 0.779.

DISCUSSION

The present population-based prospective study of Chinese women investigated whether neck circumference might predict GDM in early pregnancy, with the greater aim of enabling interventions to reduce the incidence and consequences of GDM. The study comprised 255 gestational women, aged 18–35 years. Using a nested control study design, we found that neck circumference of pregnant women measured at gestational week 16 could predict an increased risk of GDM.

Among non-pregnant fertile women, the major indicators of metabolic syndrome are bodyweight and BMI, and in the present study these factors, present before pregnancy, were confirmed to be significantly associated with GDM. We also found that both triglyceride levels (tested at gestational week 24) and waist circumference (gestational week 16) were positively associated with GDM.

It is well known that insulin resistance is a risk factor for high blood glucose levels in metabolic syndrome[21]. In pregnant women, insulin resistance can lead to GDM, and thus GDM might be related to metabolic syndrome. Waist circumference and hip circumference are frequently used to show a risk of metabolic syndrome in women who are not pregnant[22]. However, with the increased uterine volume that occurs during pregnancy, waist circumference and hip circumference will change, so that neither is appropriate as an indicator. Neck circumference has previously been associated with metabolic syndrome[23], and thus central obesity as well. Neck circumference was also found to be a useful tool to identify insulin resistance and metabolic syndrome in teenagers[14]. In the present study, neck circumference was less strongly associated with GDM than BMI or waist circumference (Figure 1). However, neck circumference is positively associated with risks of central obesity[24] and type 2 diabetes[25,26]. We still considered that neck circumference was a reliable and independent anthropometric index to predict GDM; during pregnancy, neck circumference does not change notably with gestational age, and can be easily measured by both examiners and the woman.

In the present study, neck circumference was significantly associated with GDM, and we conclude that measuring neck

Table 1 | Characteristics of the gestational diabetes mellitus and control groups[†]

		Normal	GDM	*P*
Participants (*n*)		214	41	
Age (years)		28.7 ± 3.7	31.0 ± 3.0	<0.001
Height (m)		1.60 ± 0.05	1.60 ± 0.04	0.719
Weight (kg)	Pre-pregnancy	53.3 ± 9.1	59.1 ± 17.1	0.004
	Increase during pregnancy	15.4 ± 7.8	16.0 ± 15.3	0.940
BMI (kg/m^2)	Pre-pregnancy	21.0 ± 2.9	23.3 ± 4.4	0.003
	Increase during pregnancy	6.4 ± 3.9	5.7 ± 4.0	0.330
Body circumference (cm)	Neck	33.89 ± 2.04	35.20 ± 2.56	0.003
	Waist	97.95 ± 6.25	103.16 ± 8.00	<0.001
Blood pressure (mmHg)	SBP	117.7 ± 9.9	117.8 ± 11.1	0.971
	DBP	73.4 ± 7.5	73.0 ± 8.3	0.762
FBG (mmol/L)	Fasting	4.18 ± 0.44	4.86 ± 0.81	<0.001
	1 h	7.37 ± 1.30	10.29 ± 1.82	<0.001
	2 h	6.41 ± 1.12	8.95 ± 1.81	<0.001
Blood tests[‡]	Triglyceride (mmol/L)	1.91 ± 0.92	2.47 ± 1.10	0.001
	Total cholesterol (mmol/L)	7.20 ± 21.17	5.51 ± 1.23	0.610
	HbA1c (%)	5.15 ± 0.36	5.81 ± 0.54	<0.001
	Uric acid (μmol/L)	326.52 ± 81.45	340.41 ± 87.18	0.324
	Albumin (μmol/L)	36.66 ± 21.38	34.26 ± 2.45	0.475

[†]Each study participant underwent a physical examination at gestational week 16, during which participants faced the investigator while relaxing their shoulders during measurements. [‡]Blood samples were collected at gestational week 24, and were analyzed at the Biochemistry Laboratory of Third Hospital Affiliated of Guangzhou Medical University, Guangzhou, China. BMI, body mass index; DBP, diastolic blood pressure; FBG, fasting blood glucose; GDM, gestational diabetes mellitus; HbA1c, hemoglobin A1c; SBP, systolic blood pressure.

Table 2 | Correlation between neck circumference and gestational diabetes mellitus risk factors

	Neck circumference	
	r	*P*
Weight before pregnancy[†]	0.567	<0.001
Waist circumference[†]	0.488	<0.001
BMI before pregnancy[†]	0.470	<0.001
HbA1c[†]	0.215	0.001
Age (years)[†]	0.137	0.029
Triglyceride[‡]	0.122	0.052
1-h glucose[‡]	0.079	0.211
2-h glucose[‡]	0.075	0.232
FBG[‡]	0.074	0.236

[†]A significant positive association between neck circumference and the indicated risk factor. [‡]An insignificant association between neck circumference and the indicated risk factor. BMI, body mass index; FBG, fasting blood glucose; GDM, gestational diabetes mellitus; HbA1c, hemoglobin A1c.

Table 3 | Correlation between neck circumference and gestational diabetes mellitus risk factors (adjusted for age)

	Neck circumference	
	r	*P*
Weight before pregnancy[†]	0.688	<0.001
BMI before pregnancy[†]	0.588	<0.001
Waist circumference[†]	0.475	<0.001
HbA1c[‡]	0.193	0.002
Triglyceride[‡]	0.106	0.092
1-h glucose[‡]	0.054	0.394
FBG[‡]	0.052	0.414
2-h glucose[‡]	0.051	0.421

[†]A significant positive association between neck circumference and the indicated risk factor. [‡]An insignificant association between neck circumference and the indicated risk factor. BMI, body mass index; FBG, fasting blood glucose; GDM, gestational diabetes mellitus; HbA1c, hemoglobin A1c.

circumference might be a novel and effective method for identifying GDM.

In the present study, we found that the optimal neck circumference demarcation for predicting GDM in pregnant women was of 35.15 cm. However, in a study carried out in Brazil[24], the optimal neck circumference demarcation for women as a predictor of metabolic syndrome and insulin resistance was much higher, at >36 cm[27]. Furthermore, a greater neck circumference for predicting metabolic syndrome was shown in Turkey[23]. It appears that the optimal neck circumference for predicting metabolic syndrome, just as waist circumference, differs among ethnic groups, possibly as a result of differences in body size[28]. Therefore, it is likely that the optimal cut-off value

Table 4 | Logistic regression analysis of dichotomous variables and gestational diabetes mellitus

Independent variable	OR	95% CI	*P*
HbA1c	66.194	7.473–586.329	<0.001
FPG	4.706	1.002–22.108	0.050
2-h glucose	4.683	1.661–13.201	0.004
1-h glucose	3.701	1.531–8.941	0.004
Neck circumference	1.840	1.040–3.254	0.036
Waist circumference	1.216	1.010–1.464	0.039

CI, confidence interval; FBG, fasting blood glucose; GDM, gestational diabetes mellitus; HbA1c, hemoglobin A1c; OR, odds ratio.

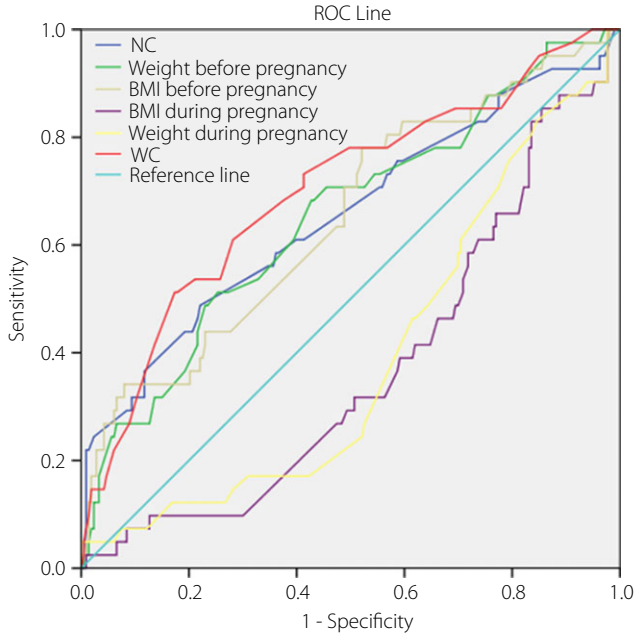

Figure 1 | Receiver operating characteristic (ROC) curve of neck circumference (NC), waist circumference (WC), weight and body mass index (BMI) in gestational diabetes mellitus. Neck circumference is shown as the area under the curve, which was 0.653 (95% confidence interval [CI] 0.552–0.755). Waist circumference was 0.700 (95% CI 0.607–0.793); weight before pregnancy 0.651 (95% CI 0.556–0.747); BMI before pregnancy 0.650 (95% CI 0.554–0.746); BMI during pregnancy 0.369 (95% CI 0.280–0.459); and weight during pregnancy 0.389 (95% CI 0.298–0.479). Among the pregnant women, the optimal cut-off point for neck circumference for indicating gestational diabetes mellitus was 35.15 cm, with the sensitivity of 0.488 and specificity of 0.779.

for neck circumference to predict GDM needs to be determined specifically for each ethnic group.

In conclusion, neck circumference might serve as an independent predictor of risk of GDM in the Han Chinese population, and could be an effective method for identifying this disease.

This is the first study to evaluate a correlation between neck circumference and GDM. However, the conclusion would be more persuasive if more samples were included in this study. As all the participants in the study were Han Chinese, the conclusion might be limited to this ethnic group.

The present research used a nested case–control design to evaluate an association between neck circumference and GDM in Chinese women during pregnancy. It showed that pregnant women with a neck circumference of ≥35.15 cm at gestational week 16 had a greater chance of developing GDM than did women with a neck circumference below this value. We suggest that women measure and record their neck circumference throughout pregnancy to access the risk of GDM and adjust their diet accordingly. We also conclude that neck circumference might be a simple and effective means for the clinical prediction of a risk of GDM.

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DISCLOSURE

The authors declare no conflict of interest.

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