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Waist Circumference at 18 weeks of gestation as a Predictor for Gestational Diabetes Mellitus in Women with Normal Pre-pregnancy Body Mass Index

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ABSTRACT

Objectives: This work aimed to investigate the predictability of waist circumference (WC) for gestational diabetes mellitus (GDM) in women with normal pre-pregnancy body mass index (BMI).

Materials and Methods: A total of 230 pregnant women with normal pre-pregnancy BMI were enrolled. WC was measured at 18 weeks of gestation. The women were divided into two groups: WC < 80 and ≥ 80 cm. Each group was provided with information about the risk factors for GDM. All women had a blood sample taken for the 50-grams glucose challenge test (GCT) at 24-28 weeks of gestation. If a sample was abnormal, it was followed by the 100-grams oral glucose tolerance test (OGTT).

Results: Women in the WC ≥ 80 cm group were significantly older in age, multiparous, and had a higher BMI and percentage distribution for GDM. Women with WC ≥ 80 cm tended to have an increased risk for GDM (Odds ratio (OR) 3.71, 95% confidence interval (CI) 1.31-10.53, p = 0.014). However, after multivariate regression, adjustment by advanced maternal age (AMA), first degree relative with diabetes, history of giving birth to fetal anomaly, weight gain, pre-pregnancy BMI and multiparous found no statistical significance (OR 3.50, 95%CI 0.93-13.20, p = 0.064). WC ≥ 82 cm was the new termination point with higher sensitivity, specificity, and positive and negative predictive values.

Conclusion: WC ≥ 80 cm was found to increase the risk for predicting GDM in univariate analysis. After multivariate analysis, WC ≥ 80 cm tended to increase risk, through there was no statistical significance. Future studies with large population should be performed.

Keywords: body mass index, gestational diabetes mellitus, waist circumference.

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การใช้รอบเอวที่อายุครรภ์ 18 สัปดาห์ เป็นตัวชี้วัดการเกิดเบาหวานขณะตั้งครรภ์ ในกลุ่มหญิงตั้งครรภ์ที่มีดัชนีมวลกายก่อนตั้งครรภ์ในเกณฑ์ปกติ

สุวิชญา จิตงามสุจริต, สิริดา พิทยานนท์, จรรยา ธำรงวุฒิกุล

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาการใช้ขนาดรอบเอว เป็นตัวชี้วัดการเกิดเบาหวานขณะตั้งครรภ์ ในหญิงตั้งครรภ์ที่มีดัชนีมวลกายก่อนตั้งครรภ์ในเกณฑ์ปกติ*

วัสดุและวิธีการ: *หญิงตั้งครรภ์ 230 คน ที่มีดัชนีมวลกายก่อนตั้งครรภ์ปกติ ได้รับการวัดรอบเอวทีอายุครรภ์ 18 สัปดาห์ หลังจากนั้นจะถูกแบ่งออกเป็นสองกลุ่ม: รอบเอว < 80 ซม. และรอบเอว ≥ 80 ซม. หญิงตั้งครรภ์ทั้งสองกลุ่มจะได้รับการซักประวัติความเสี่ยงการเกิดเบาหวาน และได้รับการเจาะเลือด 50-grams glucose challenge test (GCT) ที่อายุครรภ์ 24-28 สัปดาห์ หากผลเลือดผิดปกติ จะได้รับการเจาะเลือด 100-grams glucose tolerance test (OGTT) ในลำดับต่อไป*

ผลการศึกษา: *หญิงตั้งครรภ์ที่รอบเอว ≥ 80 ซม. มีอายุที่มากกว่า เคยตั้งครรภ์มาก่อนหน้า มีดัชนีมวลกายที่สูงกว่า และพบว่ามีร้อยละการเกิดเบาหวานขณะตั้งครรภ์ที่สูงกว่าอีกกลุ่ม อย่างมีนัยสำคัญทางสถิติ นอกจากนั้นยังพบว่า รอบเอวที่ ≥ 80 ซม. มีแนวโน้มเพิ่มความเสี่ยงในการเกิดเบาหวานขณะตั้งครรภ์ แต่หลังจากการวิเคราะห์พหุตัวแปร โดยกำจัดตัวแปรกวนได้แก่ อายุมารดาที่มากกว่า 35 ปี ญาติลำดับที่ 1 เป็นเบาหวาน มีประวัติคลอดทารกที่มีความผิดปกติ น้ำหนักที่เพิ่มระหว่างตั้งครรภ์ ดัชนีมวลกายก่อนตั้งครรภ์ และ มีการตั้งครรภ์ก่อนหน้า พบว่าไม่เพิ่มการเกิดเบาหวานขณะตั้งครรภ์ อย่างมีนัยสำคัญทางสถิติ (OR 3.50 (95% CI 0.93-13.20), p = 0.064) นอกจากนั้นยังพบว่า รอบเอว ≥ 82 ซม. เป็นจุดตัดใหม่ที่มีความไว ความจำเพาะ ค่าทำนายเมื่อผลเป็นบวก และค่าทำนายเมื่อผลเป็นลบ สูงกว่าจุดตัดเดิม*

สรุป: *ความชุกของเบาหวานขณะตั้งครรภ์ในกลุ่ม รอบเอว ≥ 80 ซม. สูงกว่ากลุ่มที่รอบเอว < 80 ซม. อย่างมีนัยสำคัญ แต่หลังจากวิเคราะห์พหุตัวแปร ไม่พบมีนัยสำคัญ แต่มีแนวโน้มสูงกว่า จึงควรมีการศึกษาเพิ่มเติมด้วยตัวอย่างที่มากขึ้น*

คำสำคัญ: *ดัชนีมวลกาย, เบาหวานขณะตั้งครรภ์, รอบเอว*

Introduction

Gestational diabetes mellitus (GDM), the abnormal glucose tolerance during pregnancy, is a complication of pregnancy that can affect the fetal and maternal outcomes. GDM correlates to excessive fetal growth, which may result in both maternal and fetal birth trauma. Prevalence of GDM differs according to ethnicity, age and body composition as well as by screening and diagnostic criteria[1]. In the United States, almost 5% of pregnancies in 2010 were affected by GDM. In the same period, Thailand was found to have a prevalence of 6.1%[2]. At Phrapokklao Hospital in Chanthaburi, Thailand, it was reported to be about 18%[3]. GDM is also associated with preeclampsia and an increased rate of cesarean section[4]. Screening for GDM is important to reduce the risk of maternal and fetal outcomes.

Seventy percent of women with GDM will develop diabetes 22-28 years after pregnancy[4]. Thus, screening for GDM is important. Almost all hospitals in Thailand, including Phrapokklao hospital, use a selective screening method. The selective screening of GDM is mainly for overweight and obese women. Thus, women with normal BMI may be dismissed.

Women with normal BMI are in the low-risk group of GDM. Yet, some of these women may still be at risk, especially those who tend to have central obesity, which can cause insulin resistance.

Central obesity, as a metabolic syndrome (MS), is a multiplex risk factor that arises from insulin resistance accompanying an abnormal adipose deposition and function. MS is also a cause of coronary artery disease and diabetes mellitus. The diagnosis of MS is in accordance with the definition of the International Diabetes Federation (IDF)[5]. Waist circumference (WC) ≥ 80 cm in females is one of the criteria. In Thailand, an increasing rate of MS has been found in about 23.2% of Thai people with a greater incidence found in females[6].

There are several studies that have shown central obesity by using WC as indicator of increased risk of GDM[7-13], through some studies have revealed different outcomes[14-16]. Nonetheless, there are no studies in Thailand focused on this issue.

Because of maternal and fetal complications during pregnancy and after birth, the authors considered undiagnosed GDM in normal BMI women with central obesity. Hence, the aim of this study was the use of WC as a screening tool for predicting GDM.

The primary outcomes were the percentage distribution and correlation between WC and GDM. The secondary outcomes involved the sensitivity and specificity of WC to predict GDM.

Materials and methods

Study population and basic information

A cross-sectional study was approved by the Chanthaburi Research Ethics Committee, Thailand (No. 015/2018). The authors assembled 230 pregnant women with normal pre-pregnancy BMI (18.5-22.9 kg/m^2) of any age, at gestational age < 18 weeks of gestation, and confirmed by an ultrasound examination. Each participant was informed about the process of the study and provided their consent. Subsequently, they were examined periodically during their pregnancy. Information was obtained regarding anthropometry, demographic characteristics, medical, obstetrical and family history at the antenatal care (ANC) clinic in Phrapokklao Hospital, Chanthaburi, Thailand between June and November 2018. Women who took steroid medication, had pre-gestational diabetes, or had uncontrolled medical problems such as thyrotoxicosis, fetal malformation, and/or multifetal gestation were excluded from the study.

A pilot study found that the proportion of GDM in the group of WC < 80 cm and WC ≥ 80 cm was 0.06 and 0.2 respectively with a type 1 error of 5% and a type 2 error of 20%, with the minimum sample size being estimated at 208. The proportion of the two groups of the WC was 1.0: 104 for each group. Accounting for a dropout rate of 10%, each group necessitated 115 participants. Accordingly, 230 women were enrolled.

After enrollment, WC was measured at 18 weeks of gestation. According to a report by World Health Organization (WHO)[17], the subjects had to stand with their arms at the sides, feet positioned close together, and weight evenly distributed across the feet measured at the end of normal expiration. Measurement was taken at the approximate midpoint between the lower margin

of the last palpable rib and the top of the iliac crest.

A two-step GDM screening process was used to identify the GDM cases. All pregnant women were screened for the 50-grams glucose challenge test (GCT) at 24-28 weeks of gestation and underwent the 100-grams oral glucose tolerance test (OGTT) if the 50-grams GCT was abnormal (> 140 mg/dL). The 100-grams OGTT used the criteria of Carpenter-Cousten based on any of the following cut-off points (> 2/4): fasting plasma glucose 95 mg/dl, 1-hour plasma glucose 180 mg/dl, 2-hours plasma glucose 155 mg/dl, and 3-hours plasma glucose 140 mg/dl.

Statistical analysis

Statistical analysis was performed using Stata version. The authors used the mean and standard deviation to characterize the continuous variables. To compare the continuous variables between both WC groups, an independent t-test was used. A chi-squared ($\chi 2$) test and Fisher's exact test were used to test the differences in the proportion. For evaluation of the correlation between the risk factors and GDM, multivariate logistic regression analysis was used to obtain the adjusted odds ratio (OR) and 95% confidence interval (CI). The sensitivity, specificity of WC were calculated, while a receiver operating characteristic (ROC) curve analysis was used to assess the WC's predictive performance. A p value less than 0.05 was considered to be statistically significant.

Results

A total of 553 pregnant women at the ANC Clinic with normal BMI and under 18 weeks of gestation, which was confirmed by ultrasound, were enrolled. Three hundred and twenty-three cases refused to participate, while three cases of abortion and five cases lost to follow-up before WC measurement were excluded. The women were divided into two groups by WC with the cut-off point at 80 cm. There were 110 cases for the WC < 80 cm and 112 cases for WC ≥ 80 cm. Two cases of WC < 80 cm lost to follow-up. For WC ≥ 80 cm, five cases lost to follow-up, two cases changed address and went to the ANC clinic, and one case refused to provide a blood sample. Thus, there were 108 cases in the WC < 80 cm group and 104 cases in the other group (Fig. 1).

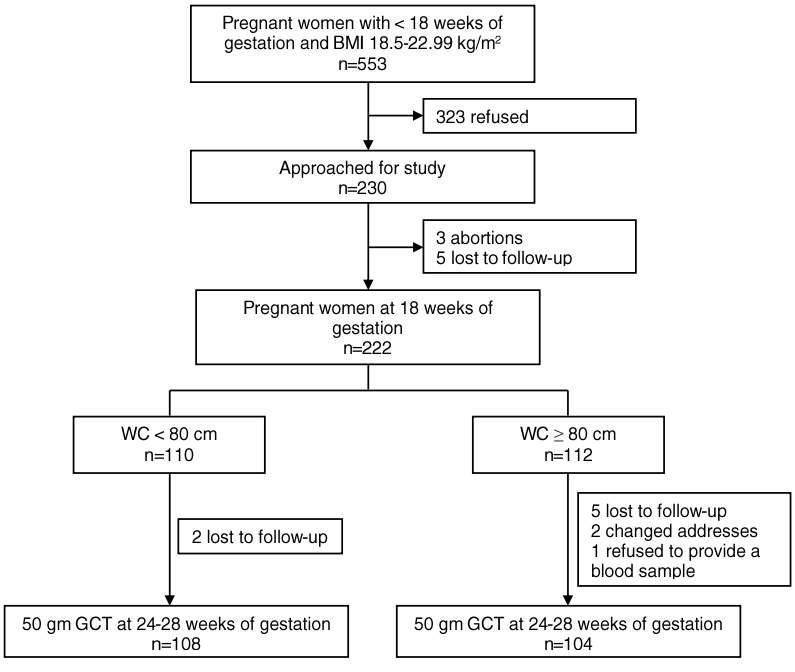

Fig. 1. Flow chart of the study populations.

The demographic characteristics are presented in Table 1. In the study there were 108 cases of WC < 80 cm and 104 cases of WC ≥ 80 cm. Women in the WC < 80 cm group tended to be younger than those in the other group (23.3 ± 5.7 vs. 27.1 ± 6.7 years). Sixty-four cases of the WC ≥ 80 cm group were multiparous that was different from the WC < 80cm group, which had only 31 cases (p < 0.001). The larger WC group had higher pre-pregnancy BMI, and there was no difference between the two groups with regards to their residence (urban and rural), weight gain, underlying disease, smoking, alcohol intake and herbal use.

The risk factors for GDM were divided into two WC groups (Table 2). There was a significantly higher advanced maternal age (AMA) in the larger WC group (18.3% vs. 5.6%). A first-degree relative with diabetes, previous GDM, and history of giving birth to an infant > 4,000 gm showed no differences between the two groups.

Table 1. Demographics and characteristics data of the pregnant women.

	WC < 80 n=108	**WC ≥ 80 n=104**	**p value**
Age; years (Mean ± SD)	23.3 ± 5.7	27.1 ± 6.7	< 0.001*
Residence (%)			
- Urban	63 (58.3)	64 (61.5)	0.675
- Rural	45 (41.7)	40 (38.5)	
Waist circumference: cm (Mean ± SD)	74.1 ± 4.0	84.8 ± 3.7	< 0.001*
Pre-pregnancy BMI; kg/m^2 (Mean ±S D)	19.2 ± 1.6	20.8 ± 1.4	< 0.001*
Parity (%)			
- Nulliparous	77 (71.3)	40 (38.5)	< 0.001*
- Multiparous	31 (28.7)	64 (61.5)	
Weight gain: kg (Mean ± SD)[a]	4.7 ± 3.9	5.7 ± 4.6	0.097
Underlying disease (%)			
- HIV infection	1 (0.9)	4 (3.9)	0.206
- Chronic hypertension	0 (0.0)	1 (1.0)	0.491
Smoking (%)	4 (3.7)	2 (1.9)	0.683
Alcohol intake (%)	7 (6.5)	4 (3.9)	0.539
Herbal use (%)	0 (0.0)	0 (0.0)	1.000

[a] Weight gain refers to weight gain at 24-28 weeks gestation.

BMI: body mass index, HIV: human immunodeficiency virus, WC: Waist circumference

* P-value < 0.05

Table 2. Risk factors for gestational diabetes mellitus by the waist circumference groups.

	WC < 80 n=108 (%)	**WC ≥ 80 n=104 (%)**	**p value**
AMA	6 (5.6)	19 (18.3)	0.005*
First-degree relative with diabetes	9 (8.3)	12 (11.5)	0.495
History of giving birth to an infant ≥ 4,000 gm	0 (0.0)	0 (0.0)	1.000
History of giving birth to a fetal anomaly	2 (1.9)	0 (0.0)	0.498

AMA: advanced maternal age, GDM: gestational diabetes mellitus, WC: Waist circumference. *P-value < 0.05

The risk factors for GDM were divided into two WC groups (Table 2). There was a significantly higher advanced maternal age (AMA) in the larger WC group (18.3% vs. 5.6%). A first-degree relative with diabetes, previous GDM, and history of giving birth to an infant > 4,000 gm showed no differences between the two groups.

Of statistical significance, the authors found that there were more cases of GDM in the WC ≥ 80 cm group (p = 0.011), five cases in the WC < 80 cm group (4.6%) and 16 cases in the WC ≥ 80 cm group (15.4%), respectively. After the multivariate regression analysis, adjusted by AMA, first degree relative with diabetes, history of giving birth to fetal anomaly, weight gain, pre-pregnancy BMI and multiparous, there was no statistically significant difference found, and the adjusted OR was 3.50 with a p value of 0.064 (Table 3).

Based on ROC curve, the best cut-off is 82 cm which gives sensitivity of 71.43% and specificity of 65.79% with an area under curve of 0.686 (Fig. 2).

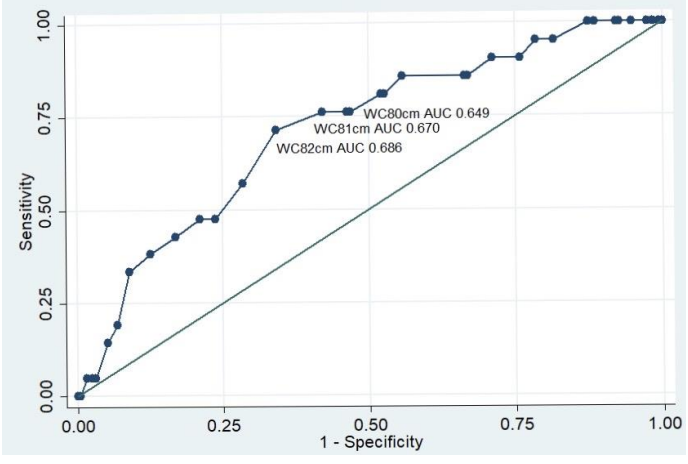

Fig. 2. ROC curves of the WC for predicting GDM.

Table 3. Percentage distribution and correlation between the WC and GDM.

Factor	GDM	Non-GDM	p value	Multivariate analysis[a]	
	N=21	N=190		OR (95%CI)	p value
WC ≥ 80 cm	16 (76.2)	88 (46.3)	0.011*	3.50 (0.93-13.20)	0.064
WC < 80 cm	5 (23.8)	102 (53.7)			
AMA	8 (38.1)	17 (9.0)	0.001*		
First-degree relative with diabetes	4 (19.1)	17 (8.95)	0.140		
History of giving birth to a fetal anomaly	1 (4.8)	1 (0.53)	0.190		

[a] adjustment by AMA, first degree relative with diabetes, history of giving birth to fetal anomaly, weight gain, pre-pregnancy BMI and multiparous.

GDM: gestational diabetes mellitus, WC: waist circumference, OR: odds ratio

*P-value <0.05

Discussion

MS causes insulin resistance and leads to the risk for GDM. BMI was not used for evaluating the fat distribution in central obesity. Thus, normal BMI is also considered a risk and should not be dismissed. This study aimed to investigate the correlation between central obesity and GDM by focusing on women with normal pre-pregnancy BMI. This may be helpful for appropriate screening of GDM in that group.

WC is one of the criteria for the diagnosis of MS, so it was chosen as the tool for this study because it is easy, non-invasive and cost-effective. The participants were measured at 18 weeks of gestation because the uterine size was under the umbilicus and did not affect measurement. Furthermore, it was found that the percentage distribution for GDM by WC was significantly higher in the larger group (76.2% vs. 23.8%).

WC also tended to increase the risk for GDM (OR 3.71, 95%CI 1.31-10.53, p = 0.014). After the multivariate regression analysis, adjusted by the risk factors for the prediction of GDM, it was found that WC ≥ 80 cm could not predict the GDM significance in this study (p = 0.064). This was contrary to previous studies. Ebrahimi-Mameghani et al (2013) found that WC ≥ 88 cm (MS criteria in Iran) was a significant predictor for GDM (OR 3.77, 95%CI 2.91-10.41)[7].

Bolognani et al (2014) found that WC ≥ 83 cm was associated with increasing risk for GDM (OR 4.21, 95%CI 1.833-9.407) with a new cut-off point of 86-88 cm for the prediction of GDM[8]. Gao et al (2017) revealed that a WC ≥ 80 cm had a significantly high prevalence rate for GDM and was associated with rising childbirth weight[9]. However, there were some studies similar to the present study[14-16]. Grieger et al (2018) studied MS in pregnancy and found that WC did not increase the risk (RR 1.41, 95%CI 0.77-2.60)[15].

The results of the previous studies[7-13] were different from this study because those who were overweight and had obesity BMI were excluded at the beginning. Therefore, lower GDM prevalence in normal BMI might affect the lower positive screening. A study by Madhavan et al (2008) demonstrated that WC was an important determinant of GDM, but only had a statistical significance in BMI ≥ 23 kg/m^2 women[16].

This study found a new cut-off point at a WC of 82 cm, which had a higher sensitivity, specificity and AUC than WC of 80 cm. However, the author placed importance on sensitivity rather than specificity as the screening purpose of GDM. Thus, the cut-off at 81 may be better since it gave 76.19%, relatively high with acceptable specificity.

After using WC ≥ 81 cm and ≥ 82 cm to predict GDM, the authors found a statistical significance in WC ≥ 82 cm (OR 7.85, 95%CI 1.80-34.32, p = 0.006). Because of the increasing weight gain and metabolic change during pregnancy, WC might be larger than the normal pre-pregnancy state. Therefore, further study of WC ≥ 82 cm may be helpful for predicting GDM.

Though there was no statistical significance in the prevalence of GDM between group with WC < 80 cm and ≥ 80 cm, based on multivariate analysis, it showed a trend to be higher in the group of ≥ 80 cm. Together with the finding in univariate analysis, it was indicated that the prevalence of GDM was significantly higher in the WC ≥ 80 cm group. This suggests that it caused by inadequate power (too small sample size) to express a significant difference.

The strengths of the current research included being a cross-sectional study, as the authors had obtained all the necessary information about the pregnant women, and everyone had an accurate WC measurement at the same gestational age (18 weeks of gestation, which was confirmed by ultrasound). The sample size was calculated by a pilot study for greater accuracy and divided into groups. The number of pregnant women did not decrease over 10%.

Nevertheless, there were several limitations. The authors did not adjust some of the confounding factors such as physical activity and dietary intake, which could affect the result during pregnancy. Due to the small population, a future study should be done for more accuracy concerning WC and its association with GDM, especially in Thailand.

Conclusion

In conclusion, WC ≥ 80 cm was found to be

insignificantly correlated with GDM. However, the new cut-off point of WC ≥ 82 cm might be useful. As a result, discovering a new tool in this study may be beneficial and useful for better screening of GDM, resulting in better maternal and fetal outcomes. Future study should include a larger sample size.

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Potential conflicts of interest

The authors declare no conflict of interest.

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