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## Fasting and 2-hour plasma glucose, and HbA1c in pregnancy and the postpartum risk of diabetes among Chinese women with gestational diabetes

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### Abstract

**Aims**—Very few studies have assessed the association of fasting and 2-hour glucose, and HbA1c during pregnancy with postpartum diabetes risk among women with prior gestational diabetes (GDM). We assessed the association of fasting glucose, 2-hour glucose and HbA1c at 26-30 gestational weeks with postpartum diabetes risk among women with prior GDM.

**Methods**—A cohort study in 1,263 GDM women at 1–5 years after delivery was performed. Cox proportional hazards regression models were used to evaluate the association of fasting and 2-hour plasma glucose, and HbA1c at 26-30 gestational weeks with the risk of diabetes at postpartum.

**Results**—The multivariable-adjusted (age, pre-pregnancy body mass index, weight gain during pregnancy, current body mass index, family history of diabetes, marital status, education, family

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income, smoking status, passive smoking, leisure-time physical activity, alcohol drinking, and intake of energy, saturated fat, and dietary fiber) hazard ratios of postpartum diabetes were 1.61 (95% confidence interval [CI]: 1.36–1.91) for each 1 mmol/l increase in fasting glucose during pregnancy, 1.63 (95% CI: 1.45–1.84) for each 1 mmol/l increase in 2-hour glucose during pregnancy, 2.11 (95% CI: 1.50–2.97) for each 1 unit (%) increase in HbA1c during pregnancy. When fasting glucose, 2-hour glucose and HbA1c during pregnancy were entered multivariable-adjusted model simultaneously, 2-hour glucose and HbA1c but not fasting glucose remained to be significant and positive predictors for postpartum diabetes.

**Conclusions**—For women with prior GDM, 2-hour plasma glucose and HbA1c during pregnancy are independent predictors of postpartum diabetes, but fasting plasma glucose during pregnancy is not.

### Keywords

Fasting plasma glucose; HbA1c; Gestational diabetes; Pregnancy; Postpartum diabetes

## Introduction

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy [1], which affects about 2–10 % of pregnancies in the United States [1, 2]. In urban China, the prevalence of GDM has increased from 2.4% in 1999 to 8.2% in 2012 [3, 4]. Women with a history of GDM are more likely to develop type 2 diabetes in the postnatal period [5] or later life [6–9]. A systematic review has concluded that 20–50% of women with prior GDM will develop type 2 diabetes within 3–5 years, and 70% within 10 years or more [6].

Diagnostic criteria for GDM have varied; it can be diagnosed using a 2-hour 75-gram oral glucose tolerance test (OGTT) or a 3-hour 100-gram OGTT at 24–30 weeks of gestation [1, 10–12]. Previous studies have indicated that 2-hour plasma glucose is a better predictor of incident diabetes and cardiovascular and all-cause mortality than fasting glucose alone [13, 14]. However, very few studies have assessed whether fasting glucose or 2-hour plasma glucose determined during pregnancy are good predictors for postpartum diabetes among women with a history of GDM [15–18]. Moreover, only two studies existed measuring also HbA1c during pregnancy and evaluating the association of HbA1c during pregnancy with the risk of postpartum diabetes among women with a history of GDM [18, 19]. The aim of this study was to evaluate the association of each three glycemic parameters, fasting and 2-hour plasma glucose and HbA1c measured at 26–30 gestational weeks with the risk of postpartum diabetes among Chinese women with a history of GDM.

## Methods

### Tianjin GDM screening project

Tianjin is the fourth largest city in Northern China. In 2010, among the 13 million residents in the 16 county-level administrative districts there were 4.3 million people living in six central urban districts. Since 1999, all pregnant women living in six urban districts have participated in the universal screening for GDM, and the average proportion of screened

pregnancies was > 91% from 1999 to 2008 [3]. All pregnant women at 26-30 gestational weeks participated in a 1-hour 50-g glucose screening test (GCT), and those who had a glucose reading  $\geq 7.8$  mmol/l were invited to undergo a 2-hour 75-g oral glucose tolerance test (OGTT) at the Tianjin Women's and Children's Health Center [3, 4, 20]. GDM was defined using the World Health Organization (WHO)'s criteria [10]. Women with a 75-gram glucose 2-hour OGTT result confirming either diabetes (fasting glucose  $\geq 7$  mmol/l or 2-hour glucose  $\geq 11.1$  mmol/l) or impaired glucose tolerance (IGT) (2-hour glucose  $\geq 7.8$  and  $<11.1$  mmol/l) were regarded as having GDM. From December 1998 to December 2009, 128,125 pregnant women participated in the GDM screening program and 6,247 of them were diagnosed with GDM [21].

### Study samples

We used the baseline data of the participants enrolled in the Tianjin Gestational Diabetes Mellitus Prevention Program, which was described previously [21–27]. Briefly, all pregnant women who were diagnosed GDM between 2005 and 2009 in six urban districts (N=4,644) were invited at 1–5 years after delivery using the contact information from the health care registration system for GDM mothers' health in Tianjin. Of those, 1,263 women with GDM (participation rate 27%) who were more than 24 years old returned and finished the baseline survey [21]. There were no differences between women who did and who did not return the survey questionnaire in age at 26-30 weeks' gestation (28.9 vs. 28.7 years), fasting plasma glucose (5.34 vs. 5.34 mmol/l), 2-hour plasma glucose (9.23 vs. 9.16 mmol/l), and the prevalence of IGT (90.9% vs. 91.8%) and diabetes (9.1% vs. 8.2%). A total of 1263 women with GDM had fasting and 2-hour glucose measured at 26-30 weeks' gestation, and 1,108 women HbA1c measured at 26-30 weeks' gestation because HbA1c measurements were available from 2006. The study was approved by the Human Subjects Committee of the Tianjin Women's and Children's Health Center, and informed consent was obtained from each participant.

### Questionnaires and measurements

All study participants filled in a questionnaire about their socio-demographics (age, marital status, education, income, and occupation), history of GDM, family history (diabetes, coronary heart disease, stroke, cancer and hypertension), medical history (hypertension, diabetes, and hypercholesterolemia), pregnancy outcomes (pre-pregnancy weight, weight gain in pregnancy, and number of children), dietary habits (a self-administered food frequency questionnaire (FFQ) to measure the frequency and quantity of intake of 33 major food groups and beverages during the past year) [28], alcohol intake, smoking habits, passive smoking, and physical activity (the frequency and duration of leisure time and sedentary activities) at the postpartum baseline survey [21]. They also completed the 3-day 24-hour food records using methods for dietary record collections taught by a dietician. The performance of 3-day 24-hour food records [28], the FFQ [28], and the above questionnaire on assessing physical activity [29, 30] have been validated in the China National Nutrition and Health Survey in 2002.

Body weight and height were measured of all women using the standardized protocol by specially trained research doctors. Height without shoes was measured to the nearest 0.1

centimetre, and weight was rounded to the nearest 0.5 kilogram. Body mass index (BMI) was calculated by dividing current weight in kilograms by the square of height in metres.

### Definition of postpartum diabetes

Blood samples were collected in all participants after an overnight fast of at least 12 hours. All participants were given a standard 75-g glucose solution. Fasting and 2-hour plasma glucose, and HbA1c during pregnancy and at baseline survey were measured at the Tianjin Women's and Children's Health Center. Plasma glucose was measured on an automatic analyzer (Toshiba TBA-120FR, Japan), and HbA1c was measured using Automatic Glycohaemoglobin Analyzer (ADAMS A1c HA-8160; Arkray, Japan). According to American Diabetes Association (ADA)'s criteria [31], diabetes was defined as fasting glucose  $\geq 7.0$  mmol/l or 2-hour glucose  $\geq 11.1$  mmol/l after a 75-g 2-hour OGTT at the baseline survey 1–5 years after postpartum.

### Statistical analyses

Differences in risk factors between GDM women with and without incident postpartum diabetes were tested using t tests (continuous variables) or  $\chi^2$  tests (categorical variables). The Cox proportional hazards model was used to evaluate the associations of fasting and 2-hour glucose, and HbA1c at 26–30 gestational weeks with the risk of postpartum diabetes. Four models were used: Model 1, adjusted for age; Model 2, adjusted for age, pre-pregnancy BMI, weight gain during pregnancy, current BMI, family history of diabetes, marital status, education, family income, smoking status, passive smoking, alcohol drinking, and intake of energy, saturated fat, and dietary fiber; Model 3, adjusted variables in Model 2 and also for fasting glucose (in analyses of 2-hour glucose and HbA1c), and 2-hour glucose (in the analysis of fasting glucose); Model 4, adjusted variables in Model 2 and also for fasting glucose, 2-hour glucose, and HbA1c other than the variable in the analysis?. All statistical analyses were conducted with a significance level at 0.05 using IBM SPSS Statistics 21.0 (IBM SPSS, Chicago, IL).

## Results

General characteristics of the study population are presented in Table 1. During a mean follow-up of 2.24 years after delivery, 83 were diagnosed as having type 2 diabetes. Correlations were 0.44 for fasting glucose and 2-hour glucose during pregnancy, 0.32 for fasting glucose and HbA1c during pregnancy, and 0.24 for 2-hour glucose and HbA1c during pregnancy (all  $P < 0.001$ ).

The multivariable-adjusted (age, pre-pregnancy BMI, weight gain during pregnancy, current BMI, family history of diabetes, marital status, education, family income, smoking status, passive smoking, alcohol drinking, and intake of energy, saturated fat, and dietary fiber – Model 2) hazard ratios (HRs) of postpartum diabetes based on different levels of fasting glucose ( $< 6.1$  [reference group], 6.1–6.9, and  $\geq 7.0$  mmol/l) during pregnancy were 1.00, 2.42, and 3.32 ( $P_{\text{trend}} < 0.001$ ), respectively (Table 2). These associations were non-significant ( $P_{\text{trend}} = 0.31$ ) after further adjustment for 2-hour glucose during pregnancy

(Model 3) and seemed to become non-significantly reverse after additional adjustment for HbA1c during pregnancy (Model 4) ( $P_{\text{trend}}=0.52$ ).

Multivariable-adjusted (Model 2) HRs of postpartum diabetes based on different levels of 2-hour glucose (7.8–8.6 [reference group], 8.7–11.0, and 11.1 mmol/l) during pregnancy were 1.00, 3.44, and 9.64 ( $P_{\text{trend}}<0.001$ ), respectively (Table 2). This positive association remained significant after adjustment for fasting glucose and HbA1c during pregnancy (Models 3 and 4) ( $P_{\text{trend}}<0.001$ ).

There was a significant direct association between HbA1c during pregnancy and the risk of postpartum diabetes ( $P_{\text{trend}}<0.001$ ) (Table 2). This positive association weakened to some extent after further adjustment for fasting glucose during pregnancy (Model 3) ( $P_{\text{trend}}<0.001$ ), and remained significant after additional adjustment for 2-hour glucose during pregnancy (Model 4) ( $P_{\text{trend}}=0.001$ ).

When fasting glucose, 2-hour glucose and HbA1c at 26–30 gestational weeks were examined as continuous variables, multivariable-adjusted (Model 2) HRs of postpartum diabetes were 1.61 (95% confidence interval [CI]: 1.36–1.91) for each 1 mmol/l increase in fasting glucose during pregnancy, 1.63 (95% CI: 1.45–1.84) for each 1 mmol/l increase in 2-hour glucose during pregnancy, 2.11 (95% CI: 1.50–2.97) for each 1 unit (%) increase in HbA1c during pregnancy, respectively (Table 2). When fasting glucose, 2-hour glucose and HbA1c during pregnancy were entered into the multivariable-adjusted model simultaneously (Model 4), 2-hour glucose and HbA1c during pregnancy remained significant and positive predictors for postpartum diabetes, but fasting glucose did not.

The joint effects of different levels of fasting glucose and 2-hour glucose during pregnancy on the risk of postpartum diabetes are presented in Table 3. We used 3 categories of fasting glucose (<6.1, 6.1–6.9, and 7.0 mmol/l) and 2 categories of 2-hour glucose (7.8–11.0 and 11.1 mmol/l). The direct association of 2-hour glucose during pregnancy with the risk of postpartum diabetes was persistent among women with different levels of fasting glucose during pregnancy. However, the positive association of fasting glucose during pregnancy with the risk of postpartum diabetes was only significant among women with 2-hour glucose 11.1 mmol/l but not among women with 2-hour glucose of 7.8–11.0 mmol/l. Compared with GDM women with lower fasting glucose (<6.1 mmol/l) and 2-hour glucose (7.8–11.0 mmol/l) during pregnancy, those with the highest fasting glucose (7.0 mmol/l) and 2-hour glucose (11.1 mmol/l) during pregnancy had the largest risk of postpartum diabetes (HR 7.67), and those with lower or higher fasting glucose (<6.1 or 6.1–6.9 mmol/l) and the highest 2-hour glucose (11.1 mmol/l) during pregnancy had significantly higher risks of postpartum diabetes (HRs 4.49–6.55).

## Discussion

The present study found that, among women with a history of GDM, 2-hour glucose and HbA1c during pregnancy increased the risk of postpartum diabetes, independent of major known risk factors including fasting glucose during pregnancy. In contrast, fasting glucose during pregnancy was not an independent factor for postpartum diabetes, but prediction

associated with it was fully explained by simultaneous 2-hour glucose and HbA1c during pregnancy.

Women with GDM are at an increased risk of developing type 2 diabetes in later life [6–9]. On average, the risk of development of type 2 diabetes is 7.4 times greater in women with prior GDM than in non-GDM women; such an increased risk has been documented in different populations and countries [6, 7]. In a large Canadian study, the risk of type 2 diabetes after GDM was 3.7% at 9 months after delivery and 18.9% at 9 years after delivery, and only 2.0% at 9 years for women who did not have GDM [8]. In another large US study, 28.6% of women with prior GDM and 5.6% of women without GDM developed incident type 2 diabetes and during a mean follow-up of 8.6 years after delivery [9]. A recent review has indicated that 20–50% of women with prior GDM will develop type 2 diabetes within 3–5 years, and 70% will develop type 2 diabetes if followed 10 years [6]. The present study found that 6.6% of Chinese GDM women were diagnosed as having type 2 diabetes during a mean follow-up of 2.24 years after delivery [21].

According to WHO recommendation, GDM was defined as diabetes or IGT during pregnancy using a 2-hour 75-gram OGTT [10]. Thus we measured fasting and 2-hour glucose in all GDM women according to the WHO criteria [10]. From 1998, several studies, especially the DECODE/DECODA (Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe/Asia) studies, found that diabetes and IGT determined by the 2-hour glucose criteria predicted mortality from the various causes, independent of the level of fasting glucose, whereas the association between mortality and diabetes and IFG based on fasting glucose depended largely on the 2-hour glucose in European and Asian populations [14, 32]. High 2-hour glucose seems to be better predictors of incident diabetes than fasting glucose in prospective studies in adults [13]. Several [15, 18], but not all studies [33] have found that fasting glucose during pregnancy is a good predictor for postpartum diabetes among women with a history of GDM. However, there has been a lack of proper comparisons where fasting glucose and 2-hour glucose levels during pregnancy have been studied as predictors for postpartum diabetes among women with a history of GDM [34]. Since the first sign of elevated blood glucose usually is high postprandial glucose excursion, GDM is diagnosed generally by an OGTT [1, 10]. HbA1c has not been recommended for the diagnosis of GDM, since the glycation of Hb will take several months, and thus it is too insensitive to be a diagnostic test for GDM. Nevertheless, the potential of HbA1c for the prediction of type 2 diabetes in postpartum among women with GDM has not been well evaluated earlier. Only two previous studies measured HbA1c during pregnancy in order to evaluate how good predictor HbA1c measure during pregnancy is as a predictor for postpartum diabetes among women with a history of GDM [18, 19]. The present study found that both elevated 2-hour glucose and HbA1c during pregnancy increased the risk of postpartum diabetes, independent of major known risk factors including fasting glucose measure during pregnancy among women with prior GDM. Thus, the measurement of fasting glucose during pregnancy seems not useful and unnecessary. Fasting glucose, 1-hour glucose, 2-hour glucose, and 3-hour glucose during pregnancy have been used to diagnose GDM in various diagnosed criteria of GDM [11, 12]. More studies are needed to compare postpartum diabetes risk of respondents to different glucose points and HbA1c during pregnancy among women with prior GDM.

An advantage of this study is that diagnoses of both GDM at 26-30 gestational weeks and postpartum diabetes were based on the WHO's criteria after a 2-hour 75-gram OGTT [10], which provided a comprehensive and accurate estimation of GDM and postpartum diabetes. Another important strength of our study is that it is the first large and truly population study based on the association of fasting glucose, 2-hour glucose and HbA1c at 26-30 gestational weeks with postpartum diabetes risk among women with prior GDM. Limitations of this study include the return rate of the initial invitation questionnaire that was only 27%. Although there were no differences in age, 2-hour glucose, fasting glucose, and the prevalence of IGT and diabetes at 26-30 gestational weeks OGTT test between those returned and those not returned, whether other differences between groups existed cannot be verified. Secondly, we have no data on 1-hour glucose and 3-hour glucose during pregnancy since we used WHO's diagnostic criteria for GDM.

In conclusion, among Chinese women with a history of GDM, 2-hour glucose and HbA1c during pregnancy predict postpartum diabetes risk, independent of fasting glucose during pregnancy. The postpartum diabetes risk associated with fasting glucose during pregnancy is not independent but depends on the 2-hour glucose and HbA1c during pregnancy.

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**Highlights**

We assessed postpartum diabetes risk among women with prior GDM.

2-hour glucose and HbA1c were positive predictors for postpartum diabetes.

2-hour glucose and HbA1c predict diabetes risk, independent of fasting glucose.

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**Table 1**

General characteristics of GDM women by incident diabetes during follow-up

	Non-diabetes	Diabetes	P value
No. of participants	1180	83	
Age mean (years)	32.4 ± 3.5	32.6 ± 3.8	0.47
Gestational week at OGTT during pregnancy	27.2 ± 1.7	27.2 ± 1.7	0.87
Fasting glucose (mmol/L) during pregnancy	5.3 ± 0.8	6.0 ± 1.2	<.001
2-hour glucose (mmol/L) during pregnancy	9.1 ± 1.17	10.5 ± 1.8	<.001
HbA1c (%) (mmol/mol) during pregnancy	5.8 (40) ± 0.6	6.2 (44) ± 1.8	<.001
Prepregnancy body mass index (kg/m <sup>2</sup> )	22.9 ± 3.2	25.6 ± 3.7	<.001
Weight gain during pregnancy (kg)	16.9 ± 6.0	14.6 ± 5.9	<.001
Current body mass index (kg/m <sup>2</sup> )	23.9 ± 3.8	27.3 ± 4.0	<.001
Current diet			
Energy consumption (kcal/day)	1691 ± 442	1708 ± 418	0.74
Fiber (g/day)	10.4 ± 4.1	10.5 ± 4.5	0.80
Protein (% energy)	16.4 ± 2.7	16.0 ± 2.4	0.21
Fat (% energy)	33.5 ± 6.4	33.3 ± 6.4	0.81
Saturated fat (% energy)	8.0 ± 2.1	7.9 ± 2.2	0.57
Carbohydrate (% energy)	50.1 ± 7.2	50.7 ± 7.1	0.50
Education (%)			0.062
<13 years	21.4	32.5	
13–16 years	70.9	61.4	
17 years	7.6	6.0	
Marriage (%)	99.0	98.8	0.59
Family income (%)			0.007
5000 Yuan/month	26.6	41.0	
5000–7999 Yuan/month	36.9	36.1	
8000 Yuan/month	36.5	22.9	
Alcohol drinkers (%)			0.63
Never	75.6	71.1	
Pass	4.6	4.8	
Current	19.8	24.1	
Smoking (%)			0.55
Never	94.3	96.4	
Pass	3.4	1.2	
Current	2.3	2.4	
Passive smoking (%)	53.6	60.2	0.26
Family history of diabetes (%)	33.8	57.8	<.001
Leisure time physical activity (%)			0.66
0 min/day	82.5	81.9	
1–29 min/day	15.4	14.5	
30 min/day	2.1	3.6	

Values represent mean  $\pm$  SD or percentage.

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Table 2

Hazard ratios of postpartum diabetes according to the fasting glucose, 2-hour glucose and HbA1c at 26-30 gestational weeks

	No. of participants	No. of cases	Person-years	Hazard ratios (95% confidence intervals)			
				Model 1 <sup>a</sup>	Model 2 <sup>b</sup>	Model 3 <sup>c</sup>	Model 4 <sup>d</sup>
Fasting glucose categories (mmol/l)							
<6.1	1091	52	2482	1.00	1.00	1.00	1.00
6.1–6.9	132	18	310	2.76 (1.61–4.73)	2.42 (1.39–4.22)	1.55 (0.85–2.85)	1.00 (0.48–2.07)
7.0	40	13	98	5.30 (2.88–9.76)	3.32 (1.65–6.67)	1.03 (0.46–2.31)	0.57 (0.20–1.61)
P for trend				<.001	<.001	0.31	0.52
Fasting glucose as a continuous variable (one mmol/l increase)							
2-hour glucose categories (mmol/l)							
7.8–8.6	576	14	1346	1.00	1.00	1.00	1.00
8.7–11.0	581	41	1296	3.49 (1.90–6.40)	3.44 (1.85–6.39)	3.35 (1.80–6.25)	3.31 (1.68–6.53)
11.1	106	28	248	12.1 (6.34–23.1)	9.64 (4.90–19.0)	8.81 (4.08–19.0)	8.67 (3.51–21.4)
P for trend				<.001	<.001	<.001	<.001
2-hour glucose as a continuous variable (one mmol/l increase)							
HbA1c (%)							
<5.6 (38 mmol/mol)	383	4	796	1.00	1.00	1.00	1.00
5.6–6.0 (38–42 mmol/mol)	348	19	721	4.90 (1.66–14.4)	4.74 (1.60–14.1)	4.64 (1.56–13.8)	3.89 (1.30–11.6)
6.1 (43 mmol/mol)	377	43	788	10.1 (3.60–28.2)	8.35 (2.95–23.6)	7.83 (2.75–22.3)	6.71 (2.35–19.2)
P for trend				<.001	<.001	<.001	0.001
HbA1c as a continuous variable (one unit [%] increase)							
				2.22 (1.64–3.01)	2.11 (1.50–2.97)	1.86 (1.25–2.77)	1.61 (1.02–2.40)

<sup>a</sup> Adjusted for age, prepregnancy BMI, weight gain during pregnancy, current BMI, family history of diabetes, marital status, education, income, smoking status, passive smoking, leisure-time physical activity, alcohol drinking, and intake of energy, saturated fat, and dietary fiber.

<sup>b</sup> Adjusted for age, prepregnancy BMI, weight gain during pregnancy, current BMI, family history of diabetes, marital status, education, income, smoking status, passive smoking, leisure-time physical activity, alcohol drinking, and intake of energy, saturated fat, and dietary fiber, fasting glucose in analyses of 2-hour glucose and HbA1c, and 2-hour glucose in the analysis of fasting glucose.

<sup>c</sup> Adjusted for age, prepregnancy BMI, weight gain during pregnancy, current BMI, family history of diabetes, marital status, education, income, smoking status, passive smoking, leisure-time physical activity, alcohol drinking, and intake of energy, saturated fat, dietary fiber, fasting glucose, 2-hour glucose and HbA1c other than the variable in the analysis.

Hazard ratios of postpartum diabetes according to the fasting glucose and 2-hour glucose at 26-30 gestational weeks

**Table 3**

		Fasting glucose (mmol/L) at 26-30 gestational weeks		
		<6.1	6.1–6.9	7.0
2-hour glucose 7.8–11.0 mmol/l at 26-30 gestational weeks				
No. of participants		1046	102	9
No. of cases		43	10	2
Person-years		2381	242	20
Age-adjusted HR (95% CI)		1.00	2.22 (1.12–4.43)	7.86 (1.89–32.9)
Multivariable-adjusted HR (95% CI) <sup>a</sup>		1.00	1.87 (0.92–3.80)	2.05 (0.41–10.3)
2-hour glucose 11.1 mmol/l at 26-30 gestational weeks				
No. of participants		45	30	31
No. of cases		9	8	11
Person-years		102	68	61
Age-adjusted HR (95% CI)		6.22 (2.96–13.1)	7.67 (3.57–16.4)	9.78 (5.02–19.1)
Multivariable-adjusted HR (95% CI) <sup>a</sup>		4.49 (2.03–9.89)	6.55 (2.93–14.6)	7.67 (3.70–15.9)

<sup>a</sup> Adjusted for age, prepregnancy BMI, weight gain during pregnancy, current BMI, family history of diabetes, marital status, education, income, smoking status, passive smoking, alcohol drinking, and intake of energy, saturated fat, and dietary fiber.