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## High risk of metabolic syndrome after delivery in pregnancies complicated by gestational diabetes



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### ABSTRACT

**Aims:** To investigate the risk of postpartum metabolic syndrome in women with GDM compared with those without GDM in a Chinese population.

**Methods:** Tianjin GDM observational study included 1263 women with a history of GDM and 705 women without GDM. Multivariate logistic regression was used to assess risks of postpartum metabolic syndrome between women with and without GDM. Postpartum metabolic syndrome was diagnosed by two commonly used criteria.

**Results:** During a mean 3.53 years of follow up, 256 cases of metabolic syndrome were identified by using the NCEP ATPIII criteria and 244 cases by using the IDF criteria. Multivariable-adjusted odds ratios of metabolic syndrome in women with GDM compared with those without GDM were 3.66 (95% confidence interval [CI] 2.02–6.63) for NCEP ATPIII criteria and 3.90 (95% CI 2.13–7.14) for IDF criteria. Women with GDM had higher multivariable-adjusted odds ratios of central obesity, hypertriglyceridemia, and high blood pressure than women without GDM. The multivariable-adjusted odds ratios of low HDL cholesterol and hyperglycemia were not significant between women with and without GDM, however, the multivariable-adjusted odds ratio of hyperglycemia became significant when we used the modified criteria.

**Conclusions:** The present study indicated that women with prior GDM had significantly higher risks for postpartum metabolic syndrome, as well as its individual components.

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## 1. Introduction

Metabolic syndrome was firstly defined in 1988 as “Syndrome X” [1]. The syndrome is characterized by a cluster of cardiovascular risk factors including visceral obesity, dyslipidemia, hypertension and hyperglycemic, and insulin resistance. The pathogenesis of the metabolic syndrome is complicated. It has been proposed that the metabolic syndrome is a powerful determinant of type 2 diabetes and atherosclerotic cardiovascular disease [2–6].

Gestational diabetes mellitus (GDM) is a common pregnancy outcome affecting ~7% of pregnancies in the US and China [7–9]. Women with GDM would have a massive risk of postpartum diabetes, as well as the related metabolic disorders [10]. However, the diagnostic criteria of metabolic syndrome vary among different ethnics and ethnicities [11]. In addition, very few studies have assessed the postpartum risk of metabolic syndrome in the Asian population with GDM. In this present study, we aimed to investigate the risk of postpartum metabolic syndrome in women with GDM compared with those without GDM in a large Chinese population.

## 2. Material and methods

### 2.1. Tianjin GDM screening project

Tianjin is the fourth largest city in China with only 30 min away from the Capital Beijing by train. There are six central districts in Tianjin with about 4.3 million residents. Since 1999, the Tianjin Women’s and Children’s Health Center launched a universal screening of GDM using WHO’s criteria in all six central districts [7]. The screening rate was reported to be >91% between 1999 and 2008 [7]. We used a 1-hour glucose screening test with 50 g glucose load at 26–30 gestational weeks. If the 1-hour glucose level was over 7.8 mmol/L, another 2-h oral glucose tolerance test (OGTT) with 75 g glucose load would be performed at the Tianjin Women’s and Children’s Health Center. GDM diagnosis was made as per WHO criteria: a 75-g glucose 2-h 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) [12].

### 2.2. Study samples

Totally 76,325 women were screened from 2005 to 2009, among whom 4644 women were diagnosed as GDM and 71,681 were free of GDM. We invited all 4644 GDM women to participate in the Tianjin Gestational Diabetes Mellitus Prevention Program (TGDMP). Finally, 1263 women with prior GDM finished the baseline survey including a questionnaire and an OGTT between August 2009 and July 2011. Among the 1263 women, 83 were newly diagnosed diabetes using an OGTT and 1180 GDM women received randomization into the intervention group ( $n = 586$ ) and the “usual care” control group ( $n = 594$ ) for the TGDMP [13–16]. In parallel, we also enrolled in the Tianjin GDM observational study 705 non-GDM women and their children with birth dates and sex frequency-matched to the 594 children of GDM women

in the “usual care” group and 83 children of GDM women who were newly diagnosed diabetes at baseline survey [17]. The study was approved by the Human Subjects Committee of the Tianjin Women’s and Children’s Health Center. All the participants provided written informed consent.

### 2.3. 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 [18], alcohol intake, smoking habits, passive smoking, and physical activity (the frequency and duration of leisure time and sedentary activities) at the postpartum baseline survey. 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 [18], the FFQ [18], and the above questionnaire on assessing physical activity [19,20] have been validated in the China National Nutrition and Health Survey in 2002.

Specially trained research doctors measured body weight and height using the standardized protocol. Body mass index (BMI) was calculated as the body weight in kilograms divided by the square of the height in meters. Waist circumference was measured at the horizontal level between the inferior costal margin and the iliac crest on the mid-axillary line with women in their standing position. Blood samples were collected in all participants after an overnight fast of at least 12 h. Participants without a self-reported history of diabetes were given a standard 75-g glucose OGTT test. Plasma glucose was measured on an automatic analyzer (Toshiba TBA-120FR, Japan).

### 2.4. Definition of postpartum metabolic syndrome

Individuals were considered to have the metabolic syndrome according to the International Diabetes Federation (IDF) definition [11] if they had central obesity (waist circumference  $\geq 90$  cm in men or  $\geq 80$  cm in women) plus at least two of the following: (1) raised triglycerides  $> 150$  mg/dL (1.7 mmol/L) or using specific treatment for this lipid abnormality; (2) reduced high-density lipoprotein (HDL) cholesterol  $< 40$  mg/dL (1.03 mmol/L) in men or  $< 50$  mg/dL (1.29 mmol/L) in women or using specific treatment for this lipid abnormality; (3) raised blood pressure (systolic  $\geq 130$  mmHg or diastolic  $\geq 85$  mmHg or using antihypertensive drugs); and (4) raised fasting plasma glucose  $> 100$  mg/dL (5.6 mmol/L) or previously diagnosed type 2 diabetes.

Individuals were considered to have the metabolic syndrome according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria modified by the American Heart Association/National Heart,

Lung, and Blood Institute in 2005 [3] if they had at least three of the following: (1) waist circumference  $\geq 90$  cm in men, or  $\geq 80$  cm in women; (2) systolic blood pressure  $\geq 130$  mmHg, and/or diastolic blood pressure  $\geq 85$  mmHg, or using antihypertensive drug treatment; (3) fasting glucose  $\geq 100$  mg/dL, or using drug treatment for elevated glucose; (4) triglyceride  $\geq 150$  mg/dL or using drug treatment for elevated triglycerides; (5) HDL cholesterol  $< 50$  mg/dL in women, or  $< 40$  mg/dL in men, or using drug treatment for reduced HDL cholesterol.

Since Chinese people were more likely to have postprandial hyperglycemia probably due to more intake of carbohydrates than the people in western countries [21,22], we used a modified criterion for hyperglycemia as either fasting glucose  $\geq 5.6$  mmol/l or 2-h glucose  $\geq 7.8$  mmol/l or using glucose-lowering agents.

## 2.5. Statistical analysis

Standard t test and chi-square test were used in the comparison of continuous variables and categorical variables between women with and without GDM. Multivariate logistic regression analysis was used to assess the risk of postpartum metabolic syndrome between women with and without GDM. All analyses were adjusted for age (Model 1), and then for postpartum years, weight gain during pregnancy, education, family income, family history of diabetes, current smoking, passive smoking, current alcohol drinking, leisure time physical activity, sleeping time, energy consumption, fiber, fat, protein and carbohydrate consumption, and sweetened beverage drinking (Model 2).  $P < 0.05$  was considered statistically significant. All statistical analyses were performed by IBM SPSS Statistics for Windows, version 24.0 (IBM Corp., Armonk, N.Y., USA).

## 3. Results

The flow chart of the overall study design can be seen in Fig. 1. Baseline data of 1263 women with GDM and 705 without GDM were used in the analysis. General characteristics of women with and without GDM are presented in Table 1. Women with GDM were older at delivery, their antepartum and postpartum BMI, HbA1c, fasting and 2-h glucose were much higher, and they had less education years, less family income, were less alcohol drinkers, less physically active and had more energy intakes compared with women without GDM.

During a mean 3.53 years of follow up after delivery, 256 cases of metabolic syndrome were identified by using NCEP ATP III criteria and 244 cases by using IDF criteria. Multivariable-adjusted (age at delivery, postpartum years, weight gain during pregnancy, education, family income, family history of diabetes, current smoking, passive smoking, current alcohol drinking, leisure time physical activity, sleeping time, energy consumption, fiber, fat, protein and carbohydrate consumption, and sweetened beverage drinking) odds ratios of metabolic syndrome in women with GDM compared with those without GDM were 3.66 (95% confidence interval [CI] 2.02–6.63) for NCEP ATP III criteria and 3.90 (95%CI 2.13–7.14) for IDF criteria (Table 2). Multivariable-adjusted odds

ratios of different individual components of metabolic syndrome were also calculated. Women with GDM had higher multivariable-adjusted odds ratios of central obesity (2.64, 95% CI 1.75–3.98 for two criteria), hypertriglyceridemia (4.14, 95% CI 2.21–7.75 for NCEP ATP III criteria; 3.68, 95% CI 1.94–6.97 for IDF criteria), and high blood pressure (3.60, 95% CI 1.79–7.25 for two criteria) than women without GDM. The multivariable-adjusted odds ratios of low HDL cholesterol and hyperglycemia were non-significant among women with GDM compared with those without GDM, however, the multivariable-adjusted odds ratio of hyperglycemia became significant (1.62, 95% CI 1.08–2.44) when we used the modified criteria for hyperglycemia.

Table 3 showed the association of GDM and the risk of postpartum metabolic syndrome in different subgroups. Multivariable-adjusted direct associations between the history of GDM and the risk of metabolic syndrome by two different criteria were significant and persisted when stratified by women younger and older than 30 years at delivery; younger and older than 35 years at survey after delivery; normal weight and overweight women after delivery; and pre-pregnancy normal weight women. There were no significant interactions of age at delivery, postpartum age, antepartum BMI, and postpartum BMI and the history of GDM with the risk of metabolic syndrome (all  $P$  for interaction  $> 0.25$ ).

In order to confirm the results, we further performed a sensitivity analysis only including 594 women with GDM who were assigned to the control group vs. women without GDM. Similar results were seen in this sensitivity analysis that women with GDM had higher risk of postpartum metabolic syndrome by NCEP ATP III criteria (2.79, 95%CI 2.00–3.89) and its components when modified criteria of hyperglycemia was applied (central obesity, 2.50 (1.98–3.15); hypertriglyceridemia, 2.43 (1.65–3.60); high blood pressure, 1.63 (1.06–2.51); low HDL cholesterol, 1.68 (1.34–2.11); hyperglycemia 1.30 (1.03–1.65)).

## 4. Discussion

In this large study, we found an over threefold higher risk of postpartum metabolic syndrome in Chinese women with GDM compared with women without GDM, which was higher than the risks reported previously. Women with GDM also showed increased risks of central obesity, hypertriglyceridemia, high blood pressure and hyperglycemia compared with women without GDM.

Limited evidence supported a higher risk of postpartum metabolic syndrome in women with GDM compared with those without GDM. The ATLANTIC-DIP cohort reported that 25.3% of Irish women with GDM in their cohort met the metabolic syndrome criteria compared to 6.6% of those with normal glucose during pregnancy in an average 3 years postpartum [23]. The prevalence of the metabolic syndrome of Danish women with previous GDM was threefold higher than that in the general population (44% vs. 15%) in 9.8 years postpartum [24]. When in a rather shorter postpartum period (3 months), the risk of the metabolic syndrome was reported to be twofold higher in women with GDM compared with the control population of normal glucose during pregnancy

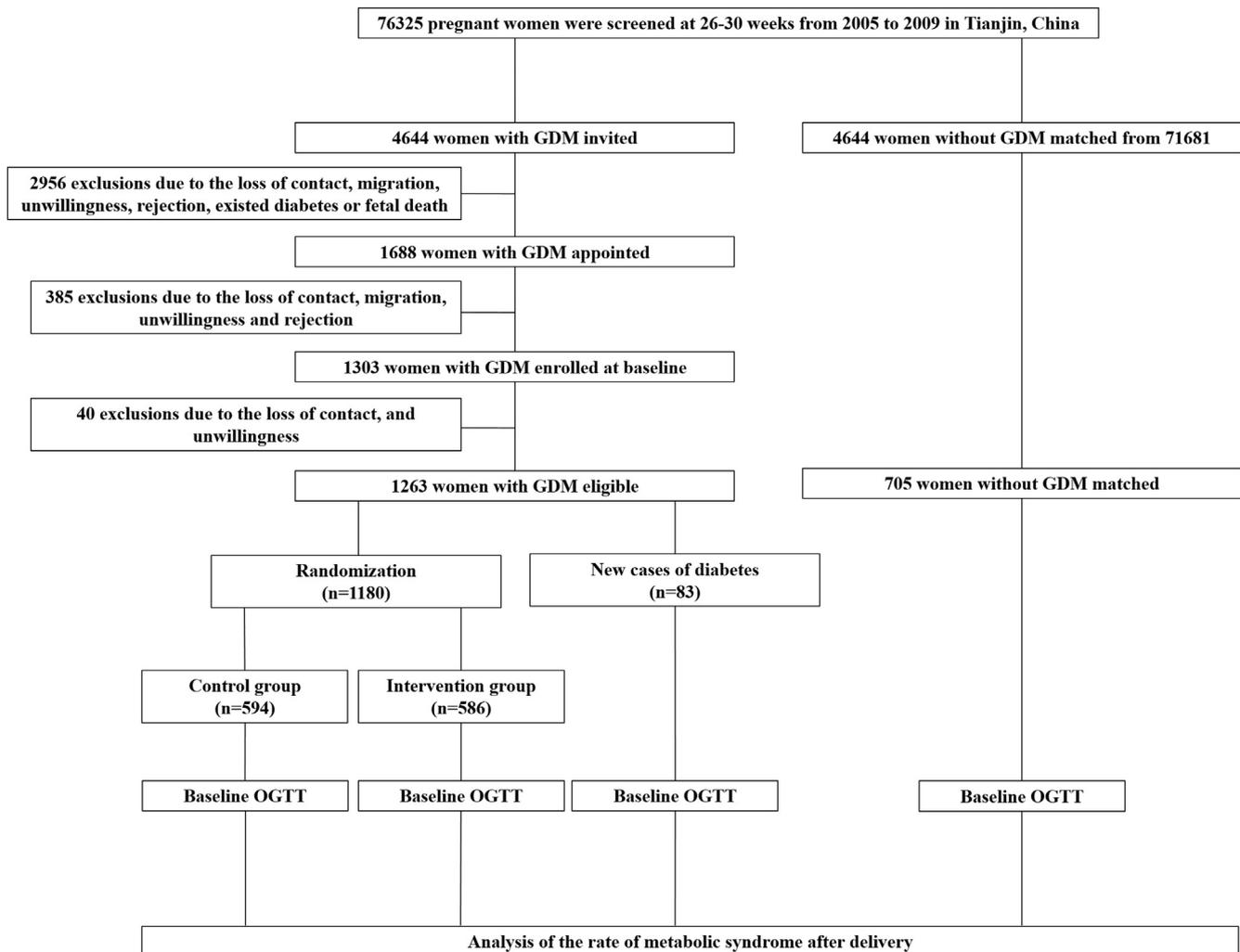


Fig. 1 – Flow chart of the study design.

in Canada with a small proportion of Asian women (16.8% vs. 8.9%) [25]. Although postpartum OGTT were all used in the studies above to assess the glucose tolerance, the relatively small sample size in both women with GDM and without GDM might limit the statistical power. In the present study, we also used OGTT to assess the glucose tolerance for further diagnosis of metabolic syndrome among Chinese women with and without GDM. In addition, we used the logistic regression model to accurately evaluate the risks of postpartum metabolic syndrome among women with and without GDM by adjusting for multiple confounding factors rather than simply reporting an incidence rate.

In a recent meta-analysis, women with a history of GDM showed a significantly higher risk of metabolic syndrome than those without GDM with an odds ratio of 3.96, which was similar to the odds ratio in our study [26]. However, this meta-analysis reported that no association was found in Asians in their subgroup analysis. Our study has provided strong evidence that Chinese women with GDM also suffered high risks of postpartum metabolic syndrome as the Caucasians did. The prevalence of diabetes and prediabetes among Chinese adults was reported to be 10.9% and 35.7% in 2013 [22]. In Asian populations, especially in Chinese,

impaired glucose tolerance was found more prevalent than impaired fasting glucose [21,22], which indicated that only fasting glucose included into the criteria of metabolic syndrome would inevitably cause missing diagnosis of patients with isolated impaired glucose tolerance. In this case, we used the modified criteria including the postprandial hyperglycemia, which might be more practical in reflecting the metabolic status among these women.

In our subgroups analysis, GDM women who were older than 30 years vs younger than 30 years at delivery and who were older vs younger than 35 years in the postpartum survey seemed to have relatively higher risks of metabolic syndrome compared with non-GDM women. It was interesting that either pre-pregnancy or postpartum normal weight (BMI lower than 25 kg/m<sup>2</sup>) GDM women would have relatively higher risks of postpartum metabolic syndrome than either pre-pregnancy or postpartum overweight GDM women. It might be explained by the fact that BMI was not well matched between women with GDM and without GDM (both pre-pregnancy and postpartum BMIs were higher in women with GDM than those without). However, these results might also indicate that although overweight was a definite risk factor for metabolic disorders, GDM women with normal weight

**Table 1 – Characteristics of women with and without gestational diabetes (GDM), Tianjin, China.**

	Non-GDM	GDM	P
No. of participants	705	1263	
Age at delivery, years	29.7 ± 2.83	30.1 ± 3.50	0.008
Duration after delivery, years	5.74 ± 1.19	3.65 ± 2.17	<0.001
Weight gain during pregnancy, kg	18.3 ± 6.67	16.8 ± 5.99	<0.001
Prepregnancy body mass index, kg/m <sup>2</sup>	21.4 ± 2.97	23.1 ± 3.32	<0.001
Postpartum body mass index, kg/m <sup>2</sup>	22.9 ± 3.68	24.3 ± 3.96	<0.001
Waist circumference, cm	75.8 ± 8.26	80.6 ± 9.48	<0.001
Fasting glucose, mmol/l	5.23 ± 0.52	5.43 ± 0.99	<0.001
2 h glucose, mmol/l	6.14 ± 1.41	7.24 ± 2.65	<0.001
HbA1c, mmol/mol	35 ± 3	38 ± 8	<0.001
HbA1c, %	5.3 ± 0.2	5.6 ± 0.7	<0.001
Education			<0.001
<13 years	10.4	22.5	
13–16 years	75.5	70.1	
≥16 years	14.2	7.4	
Income			<0.001
<5000 yuan per month	5.4	27.5	
5000–8000 yuan per month	15.5	36.9	
≥8000 yuan per month	79.1	35.6	
Family history of diabetes, %	27.1	35.7	<0.001
Current smoking, %	4.0	2.5	0.355
Passive smoking, %	55.2	58.0	0.572
Current alcohol drinker, %	32.1	26.9	<0.001
Leisure time physical activity, minutes/day			<0.001
0	61.7	71.7	
1–29	33.8	25.3	
≥30	4.5	3.0	
Sleeping time, hours/day	7.48 ± 0.95	7.70 ± 1.02	<0.01
Energy consumption, kcal/day*	1627 ± 381	1704 ± 432	0.01
Fiber, g/day	11.6 ± 4.42	12.3 ± 4.62	0.01
Fat, % energy	31.1 ± 5.65	33.1 ± 6.12	<0.001
Carbohydrate, % energy	52.3 ± 6.81	50.2 ± 7.04	<0.001
Protein, % energy	16.6 ± 2.62	16.7 ± 2.68	0.006
Sweetened beverage drink, %	77.9	78.1	0.223

\* Dietary intakes were assessed by 3-day 24-h food records.

were also under high risk of postpartum metabolic disorders. Early postpartum lifestyle interventions are applicable for both overweight and normal weight women with GDM to prevent future metabolic disorders, especially for type 2 diabetes.

Several advantages may help enhance the conclusions of the present study, including the diagnoses of GDM at 26–30 gestational weeks based on the whole population's GDM universal screening by using the WHO's criteria after a 2 h 75 g OGTT, a relatively large sample size of GDM and non-GDM, and the comprehensive postpartum screening for anthropometric and lab measurements. Limitations in this study included the relatively lower return rate of the first invitation or else we would have an even larger sample size. Despite the lower return rate, the demographic and laboratory characteristics were similar between those returned and not returned including age, 2 h glucose, fasting glucose, the prevalence of IGT and diabetes at 26–30 gestational weeks, and OGTT tests. However, whether other differences between these two groups existed cannot be verified. Secondly, the 1-h glucose and 3-h glucose during pregnancy were lacking since we used the WHO criteria of GDM. Finally, most of the women in our study only had a parity due to the one-child policy in China, which might contribute to some restrictions in the generalization of the results.

In conclusion, our study demonstrated that Chinese women with GDM had 3–4 fold higher risks of metabolic syndrome at the first 3–4 years postpartum compared with women without GDM. Metabolic profiles including central obesity, hypertriglyceridemia, and high blood pressure other than postprandial hyperglycemia were also highly found among women with GDM. This study provided evidence that women with GDM would have a higher risk of metabolic disorders in their later life. Early lifestyle interventions might help prevent type 2 diabetes and metabolic syndrome in both overweight and normal weight women with GDM.

### Declaration of interest

The authors have declared that no competing interests exist.

### Author contributions

Y.S. and G.H. designed the study, acquired data, performed statistical analyses, and drafted the manuscript. L.W., L.J., S. Z., H.L., W.L., L.W., and H.H. acquired data, performed statistical analyses, and critically revised the manuscript for important intellectual content. L.Q., X.Y., Z.Y., and J.T. critically revised the manuscript for important intellectual content. G.

**Table 2 – Odds ratios of postpartum metabolic syndrome and its components among women with and without GDM.**

	NCEP-ATP III criteria		IDF criteria	
	Non-GDM	GDM	Non-GDM	GDM
No. of participants	705	1263	705	1263
Central obesity				
No. of cases	189	630	189	630
Multiple adjusted odds ratios				
Model 1	1	2.70 (2.21–3.30)	1	2.70 (2.21–3.30)
Model 2	1	2.64 (1.75–3.98)	1	2.64 (1.75–3.98)
Hypertriglyceridemia				
No. of cases	42	204	41	194
Multiple adjusted odds ratios				
Model 1	1	3.04 (2.15–4.30)	1	2.94 (2.07–4.18)
Model 2	1	4.14 (2.21–7.75)	1	3.68 (1.94–6.97)
Low HDL cholesterol				
No. of cases	224	532	224	532
Multiple adjusted odds ratios				
Model 1	1	1.60 (1.31–1.94)	1	1.60 (1.31–1.94)
Model 2	1	1.32 (0.89–1.96)	1	1.32 (0.89–1.96)
High blood pressure				
No. of cases	39	144	39	144
Multiple adjusted odds ratios				
Model 1	1	2.13 (1.48–3.08)	1	2.13 (1.48–3.08)
Model 2	1	3.60 (1.79–7.25)	1	3.60 (1.79–7.25)
Hyperglycemia				
No. of cases	167	350	167	350
Multiple adjusted odds ratios				
Model 1	1	1.23 (0.99–1.52)	1	1.23 (0.99–1.52)
Model 2	1	1.24 (0.80–1.92)	1	1.24 (0.80–1.92)
Hyperglycemia (modified) <sup>*</sup>				
No. of cases	205	484	205	484
Multiple adjusted odds ratios				
Model 1	1	1.51 (1.24–1.84)	1	1.51 (1.24–1.84)
Model 2	1	1.62 (1.08–2.44)	1	1.62 (1.08–2.44)
Metabolic syndrome				
No. of cases	48	256	46	244
Multiple adjusted odds ratios				
Model 1	1	3.46 (2.50–4.79)	1	3.40 (2.45–4.73)
Model 2	1	3.66 (2.02–6.63)	1	3.90 (2.13–7.14)
Metabolic syndrome (modified)				
No. of cases	59	299	55	281
Multiple adjusted odds ratios				
Model 1	1	3.40 (2.53–4.57)	1	3.37 (2.48–4.57)
Model 2	1	3.86 (2.22–6.73)	1	3.77 (2.13–6.67)

NCEP-ATP III: National Cholesterol Education Program Adult Treatment Panel III; IDF: International Diabetes Federation.

Model 1 adjusted for age only; Model 2 adjusted for age, postpartum years, weight gain during pregnancy, education, family income, family history of diabetes, current smoking, passive smoking, current alcohol drinking, leisure time physical activity, sleeping time, energy consumption, fiber, fat, protein and carbohydrate consumption, and sweetened beverage drinking.

<sup>\*</sup> Modified hyperglycemia was defined as either fasting glucose  $\geq 5.6$  mmol/l or 2-h glucose  $\geq 7.8$  mmol/l or using glucose-lowering agents.

H. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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**Table 3 – Odds ratios of metabolic syndrome among women with and without GDM by various subgroups.**

	NCEP-ATP III criteria <sup>a</sup>		IDF criteria <sup>a</sup>	
	Non-GDM	GDM	Non-GDM	GDM
<i>Metabolic syndrome</i>				
Age at delivery (years) <sup>†</sup>				
<30	1	2.96 (1.37–6.40)	1	3.17 (1.44–6.99)
≥30	1	4.71 (1.82–12.2)	1	4.80 (1.85–12.5)
Postpartum age (years) <sup>†</sup>				
<35	1	3.73 (1.77–7.88)	1	4.19 (1.94–9.02)
≥35	1	4.48 (1.54–13.1)	1	4.44 (1.52–13.0)
Pre-pregnancy body mass index (kg/m <sup>2</sup> ) <sup>†</sup>				
<25	1	3.91 (1.76–8.71)	1	4.50 (1.99–10.2)
≥25	1	2.61 (0.94–7.21)	1	2.60 (0.93–7.23)
Postpartum body mass index (kg/m <sup>2</sup> ) <sup>†</sup>				
<25	1	4.99 (1.42–17.6)	1	7.12 (1.88–26.9)
≥25	1	2.71 (1.23–5.95)	1	2.66 (1.21–5.87)
<i>Metabolic syndrome (modified)</i>				
Age at delivery (years) <sup>†</sup>				
<30	1	3.27 (1.61–6.64)	1	3.07 (1.47–6.41)
≥30	1	4.79 (1.92–11.9)	1	4.71 (1.88–11.8)
Postpartum age (years) <sup>†</sup>				
<35	1	4.09 (2.07–8.08)	1	4.17 (2.06–8.43)
≥35	1	4.22 (1.52–11.7)	1	3.82 (1.36–10.7)
Pre-pregnancy body mass index (kg/m <sup>2</sup> ) <sup>†</sup>				
<25	1	4.39 (2.13–9.07)	1	4.48 (2.11–9.54)
≥25	1	2.60 (0.96–7.08)	1	2.50 (0.91–6.82)
Postpartum body mass index (kg/m <sup>2</sup> ) <sup>†</sup>				
<25	1	6.24 (2.06–18.9)	1	5.85 (1.74–19.7)
≥25	1	2.79 (1.29–6.00)	1	2.83 (1.31–6.12)

<sup>a</sup> All analyses adjusted for age, postpartum years, weight gain during pregnancy, education, family income, family history of diabetes, current smoking, passive smoking, current alcohol drinking, leisure time physical activity, sleeping time, energy consumption, fiber, fat, protein and carbohydrate consumption, sweetened beverage drinking, other than the variables for stratification.

<sup>†</sup> P for interaction >0.25.

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## Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.diabres.2019.03.030>.

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