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Lifestyle intervention to prevent gestational diabetes mellitus and adverse maternal outcomes among pregnant women at high risk for gestational diabetes mellitus

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Abstract

Objective: We assessed the effects of a lifestyle intervention on gestational diabetes mellitus (GDM) incidence and risk of adverse maternal outcomes among pregnant women at high risk for GDM.

Methods: From July to December 2018, we enrolled 1822 eligible pregnant women; of these, 304 had at least one risk factor for GDM. Participants were randomly allocated to the intervention or control group. Usual prenatal care was offered to both groups; the intervention group also received individually modified education on diet, physical activity, and weight control. The GDM diagnosis was based on an oral glucose tolerance test at 24–28 gestational weeks. Multivariate logistic regression was used to evaluate the effects of the lifestyle intervention on risk of GDM and adverse maternal outcomes.

Results: A total of 281 women (139 in the intervention group and 142 controls) were included. Incidences of GDM and adverse maternal outcomes were all significantly lower in the intervention than in the control group. Multivariate logistic regression indicated that women in the intervention group had a lower risk of GDM and adverse maternal outcomes, after adjusting potential confounding factors.

Conclusion: The present lifestyle intervention was associated with lower risks of GDM and adverse maternal outcomes.

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Keywords

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Introduction

According to 2019 International Diabetes Federation (IDF) Diabetes Atlas estimates, gestational diabetes mellitus (GDM) affects 13.2% of pregnancies worldwide, representing about 17.1 million births each year. A meta-analysis involving 84 studies showed that the pooled prevalence of GDM in Asia is 11.5%.[1] In China, the prevalence of GDM is even higher, reaching approximately 15%.[2] Epidemiological studies have identified several risk factors for GDM, including advanced maternal age, obesity, family history of diabetes mellitus, history of polycystic ovary syndrome (PCOS), history of GDM in previous pregnancies, macrosomia, congenital anomalies, history of abortion, and a history of preterm delivery.[1,3]

Although GDM often resolves after delivery, it is associated with long-lasting maternal and neonatal sequelae, such as increased risk of pregnancy-induced hypertension (PIH), cesarean delivery (CD), induction of labor, premature rupture of membranes (PROM), antepartum hemorrhage (APH), and postpartum hemorrhage (PPH).[4–9] In addition, GDM usually has long-lasting consequences, such as increased risk of type 2 diabetes (T2DM) and cardiovascular disease (CVD) in the mother, and future obesity, CVD, T2DM, and/or GDM in the child.[10] The psychological burden is also obvious in GDM. One meta-analysis indicated that the pooled prevalence of anxiety was 29.5% among women with GDM.[11] The prevalence of depressive symptoms and stress symptoms were found to be 12.5% and 10.6% in women with GDM, respectively.[12] In another study, the pooled relative risk (RR) of developing antepartum depression was 1.430 (95% confidence interval [CI]: 1.251–1.636) among women with GDM.[13] It is reported that 23.2% of women with GDM have poor-to-moderate quality of life (QOL); a family history of depression and/or anxiety and of GDM is significantly associated with a high risk of poor-to moderate QOL.[14] Moreover, the positive association of neonatal respiratory distress with the presence of depression symptoms in mothers with GDM has been demonstrated.[15]

Lifestyle interventions that include two or more components of dietary advice, physical activity, education, and self-monitoring of blood glucose are the first-line treatment for most women diagnosed with GDM.[16] A number of clinical studies of lifestyle interventions for the prevention of GDM and perinatal outcomes have been conducted.[17–20] However, some of the study results are contradictory, mostly owing to differences in study designs, participants, and varied methods of intervention.[21] The St. Carlos GDM Prevention Study showed that the Mediterranean diet, reinforced with the use of extra virgin olive oil and nuts, reduces GDM incidence and several maternal and fetal adverse outcomes (e.g., small and large for gestational age).[17] The Finnish Gestational Diabetes Prevention

Study (RADIEL) administered a moderate, individualized lifestyle intervention that included exercise to raise participants' heart rate 50% to 60% above the resting heart rate, such as walking and swimming. The intervention reduced the incidence of GDM by 39% and decreased gestational weight gain (GWG) by 0.58 kg in pregnant women at high risk for GDM; however, neither maternal nor neonatal outcomes were significantly improved by the lifestyle intervention.[20] The DALI lifestyle study showed that neither physical activity nor healthy eating alone achieved substantially less GWG in pregnant women than in controls; thus, the combination of both interventions is recommended.[22] Although many approaches are used in China, such as aerobic exercise (e.g., walking, swimming, and running), consuming a healthy diet, and use of certain traditional Chinese medicine treatments (e.g. qigong, herbs, and acupuncture), the effect of a lifestyle intervention on GDM incidence and perinatal outcomes has rarely been reported in a clinical setting. Therefore, in the present study, we aimed to evaluate the effect of a lifestyle intervention comprising dietary modification, daily exercise, and weight management, on the incidence of GDM and risk of adverse maternal outcomes among Chinese women with a high risk of GDM.

Methods

Ethics approval

All procedures involving human participants were performed in accordance with the ethical standards of the Institutional Review Board of our hospital and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Study design, setting, and population

This single-center, prospective, and randomized study was performed in the Women and Children's Hospital, School of Medicine, Xiamen University, China. From July 2018 to December 2018, women with singleton pregnancies attending their first antenatal visit before gestational week 8 were enrolled at our hospital. Eligible participants were randomly allocated into the lifestyle intervention group or the control group. Randomization was performed using computer-generated randomization schedules.

GDM diagnostic criteria

GDM was defined as one or more pathologic glucose values in a 75-g 2-h oral glucose tolerance test (OGTT) during pregnancy. The diagnostic thresholds were as follows: fasting plasma glucose (FPG) $\geq$5.1 mmol/L, 1-hour value $\geq$10.0 mmol/L, and 2-hour value $\geq$8.5 mmol/L.[23,24] All participants underwent an OGTT at the time of study enrollment and at 24 to 28 weeks of gestation.

Inclusion and exclusion criteria

Adult pregnant women aged 18 years or older who had at least one risk factor of GDM were included in this study. The risk factors of GDM were defined as follows: age $\geq$35 years, pre-pregnancy body mass index (BMI) $\geq$25 kg/m^2, family history of diabetes mellitus, history of PCOS, and history of GDM in a previous pregnancy.

Pregnant women were excluded if they had pre-existing diabetes mellitus, multiple pregnancy, use of medication that influences glucose metabolism (e.g., steroids, β-adrenergic agonists, and anti-psychotic drugs), physical disability, or severe psychiatric disorders.

Sample size calculation and sampling technique

Considering a 1:1 random allocation, significance level of 0.05 (two-sided), and 80% power, 280 participants were needed to detect a 10% difference in the GDM incidence between the intervention and control groups.

The simple random sampling method was used.

Treatments

Usual prenatal care was offered to both groups. Participants in the intervention group received structured but individually modified education regarding a balanced dietary pattern, moderate physical activity, and weight control. The intervention included one face-to-face education session with an interventionist at the onset of treatment and continuous educational messages delivered via a WeChat public account at a frequency of twice per week.

The balanced dietary pattern in the intervention was based on the China diagnosis and therapy guideline of pregnancy with diabetes mellitus,[24] aimed to achieve or maintain ideal body weight and meet nutritional needs. Pregnant women were encouraged to consume vegetables, fruits, high-fiber whole-grain products, low-fat dairy products, and to avoid foods rich in sugar and saturated fatty acids, among other guidance.

Participants in the intervention group were recommended to engage in approximately 30 minutes of moderate-intensity physical activity at a frequency of three to four times per week.

Body weight control during early and mid-to-late pregnancy was based on the recommendation of the National Academy of Medicine.[25]

Data collection method and outcomes

The primary endpoint in the current study was incidence of GDM. The secondary endpoints were the incidences of adverse maternal outcomes including excessive GWG, CD, PIH, PROM, APH, and PPH.

Total GWG was calculated as the difference between each mother's delivery weight and her pre-pregnancy weight. Excessive GWG was defined as $\geq$18, $\geq$16, $\geq$11.5, and $\geq$9 kg for underweight (BMI $<$18.5 kg/m^2), normal weight (BMI 18.5–24 kg/m^2), overweight (BMI 24–28 kg/m^2), and obese women (BMI $\geq$28 kg/m^2), respectively. PIH is defined as systolic blood pressure $\geq$140 mmHg and/or diastolic blood pressure $\geq$90 mmHg after 20 weeks of pregnancy. PROM refers to a patient who is beyond 37 weeks' gestation and presents with rupture of membranes prior to the onset of labor. APH is defined as bleeding from or into the genital tract, occurring during the second or third trimester of pregnancy and prior to birth of the infant. PPH is defined as blood loss of 500 mL or more within 24 hours after birth.

Statistical analysis

Continuous variables with a normal distribution are presented as mean$\pm$SD and were compared using the Student *t*-test. All categorical variables are summarized and expressed as proportions and compared using the chi-square test with normal approximation or Fisher's exact test, as appropriate. Multivariate logistic regression was used to evaluate the effect of lifestyle intervention on the risk of GDM and adverse maternal outcomes. A significance level of 0.10 was set for retaining variables in the multivariate logistic model. All statistical analyses were performed using IBM SPSS version 20.0 for Windows (IBM Corp., Armonk, NY, USA).

Results

Figure 1 shows the flow diagram of the study. From July to December 2018, we

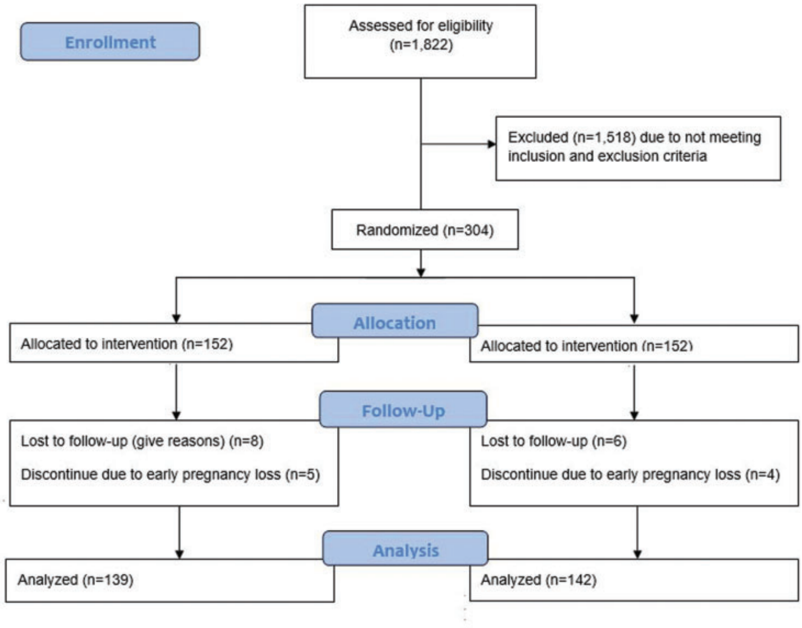

Figure 1. Flow diagram.

enrolled 1822 eligible pregnant women; of these, 304 had at least one risk factor for GDM. Finally, 281 pregnant women (139 in the intervention group and 142 in the control group) were included in the analyses. Generally, maternal age (31.4±4.9 vs. 31.8±5.1 years) and pre-pregnancy BMI (25.4±3.4 vs. 25.9±3.7 kg/m^2) were similar between the intervention and control groups. Additionally, the differences in other baseline characteristics such as family history of GDM, parity, prior GDM, and FPG were not significant between the two groups (Table 1).

Figure 2a shows that the incidence of GDM in the intervention group was significantly lower than that in the control group (14.4% vs. 24.6%, $P=0.03$). As shown in Figure 2b, the incidences of adverse maternal outcomes, including excessive GWG (25.9% vs. 47.9%, $P=0.03$), CS (35.3% vs. 47.9%, $P<0.01$), PIH (3.6% vs. 10.6%, $P=0.03$), PROM (6.5% vs. 15.5%, $P=0.02$), APH (5.0% vs. 16.2%, $P<0.01$), and PPH (3.6% vs. 14.1%, $P<0.01$) were all significantly lower in the intervention group than in the control group.

Multivariate logistic regression (Table 2) indicated that after adjusting the baseline characteristics, the lifestyle intervention was associated with a lower risk of GDM (odds ratio [OR] = 0.45; 95% CI: 0.22–0.86; $P<0.01$) and all adverse maternal outcomes including excessive GWG (OR = 0.42; 95% CI: 0.28–0.69; $P<0.01$), CS (OR = 0.47, 95% CI: 0.32–0.91; $P=0.01$), PIH (OR = 0.34, 95% CI: 0.13–0.91; $P=0.02$), PROM (OR = 0.50, 95% CI: 0.25–0.94; $P=0.03$), APH (OR = 0.22, 95% CI: 0.08–0.47; $P<0.01$), and PPH (OR = 0.28, 95% CI: 0.14–0.72; $P<0.01$).

Discussion

In the present study, we evaluated the effect of a lifestyle intervention comprising dietary modification, daily exercise, and weight management among pregnant

Table 1. Baseline characteristics of participants in the intervention and control groups.

	Intervention group (n = 139)	Control group (n = 142)	*P* value
Maternal age, years	31.4 ± 4.9	31.8 ± 5.1	0.50
Pre-pregnancy BMI, kg/m^2	25.4 ± 3.4	25.9 ± 3.7	0.24
Family history of diabetes, n (%)	48 (34.5%)	46 (32.4%)	0.70
Parity, n (%)			
0	89 (64.0%)	93 (65.5%)	0.79
≥1	50 (36.0%)	49 (34.5%)	
Prior GDM, n (%)	15 (10.8%)	14 (9.9%)	0.80
FPG, mmol/L	4.94 ± 0.38	4.96 ± 0.40	0.67
Total triglycerides, mmol/L	1.01 ± 0.46	0.97 ± 0.50	0.49
Total cholesterol, mmol/L	4.23 ± 0.86	4.19 ± 0.80	0.69
HDL-C, mmol/L	1.35 ± 0.36	1.37 ± 0.34	0.63
LDL-C, mmol/L	2.30 ± 0.80	2.26 ± 0.78	0.67
HOMA-IR	1.69 ± 1.21	1.73 ± 1.19	0.78
Blood pressure, mmHg			
Systolic	124.3 ± 13.5	122.7 ± 12.8	0.31
Diastolic	77.4 ± 8.6	78.8 ± 9.7	0.20
Smoking, n (%)	8 (5.8%)	10 (7.0%)	0.66
Alcohol use, n (%)	5 (3.6%)	6 (4.2%)	0.79

GDM, Gestational diabetes mellitus; BMI, body mass index; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance.

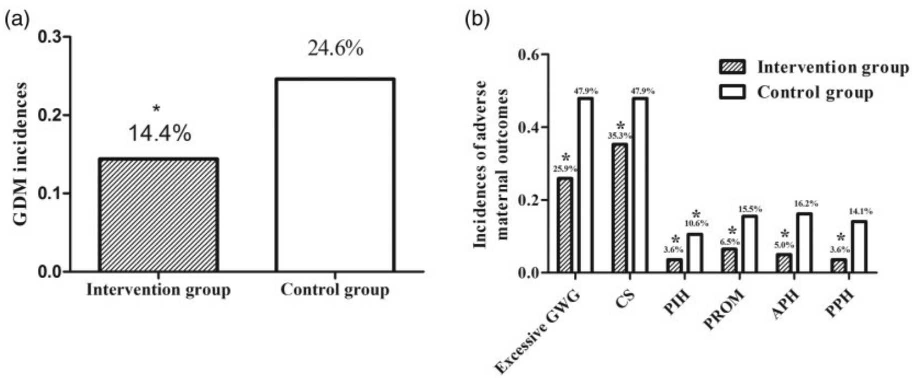

Figure 2. Incidence of gestational diabetes mellitus (GDM) (a) and adverse maternal outcomes (b) in the intervention and control groups. *$P < 0.05$.
GWG, gestational weight gain; CD, cesarean delivery; PIH, pregnancy-induced hypertension; PROM, premature rupture of membranes; APH, antepartum hemorrhage' PPH, postpartum hemorrhage.

women at high risk of GDM. Our findings showed that the lifestyle intervention was associated with a lower risk of GDM and adverse maternal outcomes.

A large number of observational studies have suggested that various diets or dietary patterns before and during pregnancy may influence GDM risk.[26] Findings of the

Table 2. Association of lifestyle intervention and incidence of adverse maternal outcomes.

	Model I		Model II	
	OR (95% CI)	P value	OR (95% CI)	*P* value
GDM	0.51 (0.28–0.94)	0.03	0.45 (0.22–0.86)	<0.01
Adverse maternal outcomes				
Excessive GWG	0.38 (0.23–0.63)	<0.01	0.42 (0.28–0.69)	<0.01
CD	0.59 (0.37–0.96)	0.03	0.47 (0.32–0.91)	0.01
PIH	0.32 (0.11–0.89)	0.02	0.34 (0.13–0.91)	0.02
PROM	0.38 (0.17–0.85)	0.02	0.50 (0.25–0.94)	0.03
APH	0.27 (0.11–0.66)	<0.01	0.22 (0.08–0.47)	<0.01
PPH	0.23 (0.08–0.63)	<0.01	0.28 (0.14–0.72)	<0.01

Model I: crude odds ratio (OR); Model II: adjusted for baseline demographic variables.
GDM, gestational diabetes mellitus; GWG, gestational weight gain; CD, cesarean delivery; PIH, pregnancy-induced hypertension; PROM, premature rupture of membranes; APH, antepartum hemorrhage; PPH, postpartum hemorrhage; CI, confidence interval.

Nurses' Health Study II longitudinal cohort study indicate that unhealthy dietary patterns, such as higher consumption of sugar-sweetened beverages, are associated with a higher risk of GDM.[27] In contrast, dietary patterns such as those of the Mediterranean diet, Dietary Approaches to Stop Hypertension (DASH) diet, and Alternate Healthy Eating Index (AHEI) diet are associated with a 15% to 38% reduced RR of GDM.[28] A meta-analysis involving 3944 women showed that among ethnic Chinese women with GDM, low glycemic index diets, low glycemic load diets, and fiber-enriched diets are associated with improved glycemic control and pregnancy outcomes.[29] In the present study, participants were advised to consume evidence-based healthy diets that included vegetables, fruits, and high-fiber whole-grain products, to balance body weight control and nutritional needs.

Traditionally, pregnant women were advised to reduce their levels of physical activity, and even to stop working, as many people believed that physical activity could reduce placental blood circulation and, as a consequence, increase the risk of pregnancy disorders.[30] However, during the past two decades, increasing evidence has emerged regarding the potential beneficial effects of physical activity during pregnancy for both mother and offspring. One meta-analysis[31] provided evidence that physical exercise during pregnancy is associated with a 31% reduction in risk of GDM. In keeping with recommendations of the American College of Obstetricians and Gynecologists, the participants in our study were encouraged to undertake approximately 30 minutes of moderate-intensity physical activity three to four times per week.

The effect of lifestyle intervention on GDM and maternal outcomes remains controversial. A meta-analysis showed a reduction in GDM if intervention commenced during the first but not the second trimester.[32] A Cochrane review found no significant difference in maternal outcomes such as hypertensive disorders of pregnancy (RR = 0.70, 95% CI: 0.40–1.22) and CD (RR = 0.90, 95% CI: 0.78–1.05).[16] The present study demonstrated that lifestyle intervention can significantly reduce the incidences of GDM and adverse maternal outcomes among women with a high risk of GDM. Clinical efficacy may be improved with evidence-based interventions and good compliance, as well as continuous education message delivery via a platform such as a WeChat public account.

There are several limitations in our study. First, as in many other reports, compliance with a healthy dietary pattern and physical activity could not be assessed in the present study, which is an important confounder influencing the association of the lifestyle intervention with outcomes. We have not identified an effective method to evaluate compliance with the intervention among participants; a solution to this requires further efforts. Additionally, pregnant women in the control group may have received information on a healthy diet and physical activity from their peers in the intervention group, which may cause bias.

In conclusion, the present lifestyle intervention comprising dietary modification, daily exercise, and weight management is a promising prevention measure as it was found to be associated with lower risks of GDM and adverse maternal outcomes.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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