Objective: The study was to examine whether gestational diabetes mellitus (GDM) can be prevented by early trimester lifestyle counseling in a high-risk population.

Methods: From September 2012 to January 2013, 1664 pregnancies in the Department of Obstetrics and Gynecology of First Hospital of Peking University were enrolled in the study during their first prenatal care visit before the 8 gestational weeks visit and asked to fill out a questionnaire on GDM risk evaluation. According to the questionnaire and medical records, those with at least one risk factor of GDM were included in the intervention study and randomly allocated to two groups, intervention group and control group. Routine prenatal care was offered, while standardized two-step lifestyle intervention was provided to the intervention group during 6–8 gestational weeks, and at 12–13 gestational weeks, enforcement intervention based on maternal anthropometrics were offered. Both groups were followed until 75 g oral glucose tolerance test (OGTT) testing at 24–28 gestational weeks. The weight gain after intervention and the prevalence of GDM were used to evaluate the effect.

Results: (1) According to the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria, the positive rate of GDM for the intervention group was 17.16% (23/134), lower than the control group which was 23.91% (33/138), \( P = 0.168 \). (2) The weight gain during the first and second trimester for the intervention group was \( (1.38 \pm 2.34) \text{ kg} \) and \( (5.51 \pm 2.18) \text{ kg} \), lower than in the control group which was \( (1.41 \pm 2.58) \text{ kg} \) and \( (5.66 \pm 2.25) \text{ kg} \), \( P = 0.905, P = 0.567 \). (3) Positive rate of GDM for those fasting plasma glucose (FPG) \( \geq 5.1 \text{ mmol/L} \) during early pregnancy was 11/36 (30.55%) for the intervention group that was lower than 17/37 (45.95%) for the control group, but the statistical difference was not significant \( P = 0.076 \).

Conclusion: The positive rate of GDM could be reduced by a certain amount lifestyle intervention from the beginning of pregnancy. More validated effective intervention should be explored in the high-risk pregnant women.

Keywords: Gestational diabetes mellitus; Risk factor; Lifestyle intervention
Introduction

Accumulated evidence has shown that gestational diabetes mellitus (GDM) is associated with a range of negative short or long-term health outcomes, both to pregnant women and their offsprings. Meanwhile, these adverse effects can produce vicious cycles across generations. Although high-risk factors have been assessed by several studies, such as advanced maternal age, obesity, family history of diabetes mellitus (DM), history of polycystic ovary syndrome (PCOS), pregnancy history of GDM or macrosomia from previous pregnancies, limited clinical strategies for the prevention of GDM have been confirmed. Specific dietary counseling could be effective for control of gestational weight gain that might indirectly prevent GDM. Physical activity-based intervention could also have potential similar effects. In general, any intervention strategies in need of validation in the clinic.

Some of the current results of intervention studies are contradictory. Possible explanations could be the various intensity and duration of interventions. In terms of GDM prevention, previous studies were started at various times, from pre-pregnancy to second trimester. Considering the gradual aggravation of insulin resistance, intervention after the first trimester could be too late or of too short duration for prevention.

In this pilot study, a cluster-randomized trial was conducted in the Department of Obstetrics and Gynecology, Peking University First Hospital, pregnancies with more than one risk factor of GDM were enrolled and randomized to lifestyle intervention or a control group. For intervention group, standardized two-step intervention with individual education on “appropriate dietary, physical activity, and weight gain during pregnancy” was initiated from early in the first trimester with subsequent enforcement of education based on anthropometrics at 12–13 gestational weeks. Follow-up was until 24–28 gestational weeks, and the incidence of GDM was used to evaluate the effect of intervention.

Methods

Cases recruitment and workflow

Ethical approvals were obtained from the institutional review board of Peking University First Hospital. Written informed consent was obtained from each patient.

From September 2012 to January 2013, 1,664 singleton pregnancies were enrolled in the study during their first prenatal care visit before the 8 gestational week visit and asked to fill in a questionnaire on GDM risk evaluation (age, history of PCOS, family history of diabetes mellitus, and pregnancy history of GDM or macrosomia). Weight and height were recorded by a nurse. The definition of risk factors for GDM in the study was as follows: Age ≥35 years, pre-pregnancy body mass index (BMI) ≥25 kg/m², family history of DM, history of PCOS, history of GDM or macrosomia from a previous pregnancy. According to questionnaire and medical records, those with at least one risk factor of GDM were included in the intervention study and randomly allocated to one of two groups. The exclusion criteria were pre-existing diabetes or multiple pregnancy. The randomization method using exponential random numbers produced the intervention group and the control group.

The study design is shown in Fig. 1. In brief, routine prenatal care was offered, while a standardized two-step lifestyle intervention was provided to the intervention group during 6–8 gestational weeks, and at 12–13 gestational weeks, enforcement interventions based on maternal anthropometrics were offered. Both groups were followed until a 75 g oral glucose tolerance test (OGTT) was administered at 24–28 gestational weeks. The International Association of Diabetes and Pregnancy Study Groups (IADPSG) criterion was used for GDM diagnosis in the study.

Intervention

The intervention using standardized courses were given by one physician, and including three courses: “What is a balanced diet”, “Proper physical activity is beneficial during pregnancy”, and “Standard weight-gain during pregnancy”. Key points/take-home messages of the courses were listed in the Table 1. Each course lasted for 40–60 minutes and was presented to patients in groups (fewer than six pregnant participants per group). The assessment of nutritional status was offered by professional nutritional counselors based on the weight gain and body fat evaluation at 12–13 weeks and enforcement of lifestyle education was offered accordingly.

Outcome assessment

The baseline demographic characteristics were compared between the two groups, including body fat composition, and biochemistry indicators of glucose
and lipid metabolism. At 24–28 weeks the final anthropometrics and biochemistry testing were compared. The primary outcome of the study was the incidence of GDM to estimate the effect of intervention. The number of abortions or fetal loss during pregnancy was recorded.

Statistics

All results are presented as (mean ± SD) unless otherwise indicated. SPSS 15.0 statistical software (SPSS Inc. Chicago, IL, USA) was used for data analysis. Statistical significance was accepted as $P$ value of $<0.05$.

Results

According to our study, 17.97% (299/1664) of pregnancies were found to have high-risk factors of GDM. The workflow of recruiting was shown in Fig. 2. According to fasting glucose testing, patients with preexisting diabetes were excluded from the study, and those with incomplete clinical information or who refused to continue were also excluded. There were 134 women in the intervention group given not only routine prenatal care but also lifestyle counseling, and 138 women in the control group given nothing but routine prenatal care.

When we compared the two groups, there was no significant difference in the basic parameters, including age, family history of DM, body weight before pregnancy, BMI before pregnancy, fasting plasma glucose (FPG) during early pregnancy, and blood lipid markers during early pregnancy (cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), fasting plasma insulin level (FINS) during early pregnancy, and homeostatic Model Assessment of Insulin Resistance (HOMA-IR)) (Table 2). Therefore, the two groups were comparable.

To evaluate the outcome of intervention, the incidence of GDM was compared as a primary outcome. According to the IADPSG criteria, the positive rate of GDM for the intervention group was 17.16%, (23/134) lower than control group which was 23.91%, (33/138) but there was no significant difference ($P = 0.168$).

The secondary outcome was the weight gain during pregnancy. The weight gain during the first and second trimester is as follows:

| Trimester | Timing | Weight Gain (g) |
|-----------|--------|-----------------|
| First     | 6-8 gws|                 |
| Second    | 12-13 gws|              |
|           | 24-28 gws|             |


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1. The definition of a balanced diet during early and mid-late pregnancy according to the dietary pagoda of pregnant women in China.
2. Encouragement of appropriate practice if permitted — walking 30 minutes after meal at least once a day.
3. Goal of body weight gain during early and mid-late pregnancy according to Institute of Medicine of the National Academics, May 2009.
trimester for the intervention group was (1.38 ± 2.34) kg and (5.51 ± 2.18) kg, lower than for the control group which was (1.41 ± 2.58) kg and (5.66 ± 2.25) kg, but there was no significant difference between the two groups (P = 0.905, P = 0.567) (Table 3).

Other than the risk factors involved in the study, another factor, a certain level of FPG in the first trimester could be one of the important high-risk factors of GDM. However, this had not been done at the very beginning of our study. We then further analyzed outcomes according to FPG (Table 4). It showed that women with FPG ≥ 5.1 mmol/L had significantly higher BMI, FINS and HOMA-IR than women with FPG < 5.1 mmol/L. When using FPG ≥ 5.1 mmol/L at the first trimester as another risk factor, we found that the incidence of GDM for those with an FPG ≥ 5.1 mmol/L during early pregnancy in the intervention group was 27.78% (10/36). This was lower than in the control group, which was 45.95% (17/37), but there was no significant difference (P = 0.076).

Discussion

According to our study, it is not hard to find that there are many pregnant women with high-risk factors of GDM among the population, about 17.97% (299/1664) among our patients. And almost all the relevant research suggests beginning intervention during the second trimester (from 12 weeks to 20 weeks),

| Items                             | Control group (n = 138) | Intervention group (n = 134) | P   |
|----------------------------------|-------------------------|-----------------------------|-----|
| Age (years)                      | 30.27 ± 3.64            | 31.01 ± 3.8                 | 0.087|
| Family history of DM             | 51 (36.96)              | 49 (36.30)                  | 0.947|
| Pre-pregnancy BW (kg)            | 61.36 ± 10.40           | 60.26 ± 9.73                | 0.371|
| Pre-pregnancy BMI (kg/m²)        | 23.06 ± 3.63            | 22.95 ± 3.65                | 0.798|
| FPG (mmol/L)                     | 4.93 ± 0.39             | 4.95 ± 0.40                 | 0.683|
| TG (mmol/L)                      | 0.95 ± 0.44             | 1.03 ± 0.55                 | 0.163|
| TCHO (mmol/L)                    | 4.16 ± 0.83             | 4.21 ± 0.79                 | 0.621|
| HDL-C (mmol/L)                   | 1.38 ± 0.34             | 1.36 ± 0.31                 | 0.667|
| LDL-C (mmol/L)                   | 2.29 ± 0.77             | 2.31 ± 0.67                 | 0.779|
| FINS (ng/ml)                     | 7.25 ± 4.45             | 7.74 ± 4.75                 | 0.384|
| HOMA-IR                          | 1.63 ± 1.15             | 1.74 ± 1.19                 | 0.451|

DM: Diabetes mellitus; BW: Body weight; BMI: Body mass index; FPG: Fasting plasma glucose; TG: Triglyceride; TCHO: Total cholesterol; HDL: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; FINS: Fasting plasma insulin level; HOMA-IR: Homeostatic Model Assessment of Insulin Resistance; values are expressed as mean ± SD or n (%).
including dietary counseling and physical activity.2–5
In this study we started intervention for the high-risk population earlier, during the first trimester (from 5 weeks to 12 weeks). We hypothesized that this may reduce the positive rate of GDM.

From our research, lifestyle intervention given at the first trimester had a trend of decreasing the positive rate of GDM, although there was no statistically significant difference. We suspect that lack of significance was related to the size of the sample, which was not big enough. We hypothesize that if we enlarge the sample early intervention will appear more effective.

As for another risk factor of GDM, FPG ≥ 5.1 mmol/L in the first trimester, we did not put it into our questionnaire at the beginning of our study because that evaluation was not being done at that time. However, from the results of Zhu Weiwei,6 and the limited data from our study, it did play an important role in increasing the risk of GDM. Therefore we should pay more attention to these patients.

A review5 provided a comprehensive overview of the effect of prenatal physical activity-based intervention on glucose tolerance, insulin sensitivity, and GDM prevention. Of the eight articles reviewed, only three of them showed that it may help to achieve good glycemic control and limit insulin use in GDM women. Only 16%–55% compliance appears to be a main problem in physical activity-based intervention studies to prevent GDM. However, another article7 about practice intervention had pointed out that physical activity during early pregnancy could help reduce the positive rate of GDM around 24% (odd ratio, OR: 0.76; 95% CI: 0.70–0.83). Besides, a meta-analysis8 of dietary-based intervention and GDM prevention had reported that with good compliance, dietary intervention started during early pregnancy could significantly reduce the positive rate of GDM. Generally speaking, the moderate way of exercise and starting time of lifestyle intervention and the compliance of pregnant women all play an important role in GDM prevention.

There were several factors that could explain the results of our study. First, the goal of controlling weight gain was not thoroughly achieved, which was also mentioned by a review article.5 Secondly, the size of sample was not big enough to determine significance between the two groups, which was increasing as the study went on. Thirdly, there was unknown compliance, the same problem as other studies had pointed out. We have not yet found a good way to evaluate the compliance of the pregnant women with intervention, which we need to increase our efforts. And last, due to the profound cognition of and attention to GDM in our hospital, the control group might also have received some guidance from their doctors, including eating a healthy diet and moderate exercise, which may affect the result of our study.

In conclusion, the positive rate of GDM could be reduced by certain lifestyle interventions from the beginning of pregnancy. More validated effective intervention should be explored for the high-risk pregnant women.

### Table 3
Comparison of weight gain between the HR-0 and HR-1 groups (kg, mean ± SD).

| Items            | Early-pregnancy (n = 114) | Mid-pregnancy (n = 313) | P    |
|------------------|--------------------------|-------------------------|------|
| BMI (kg/m²)      | 23.09 ± 3.62             | 21.99 ± 2.95            | 0.001⁴ |
| FINS (ng/ml)     | 9.30 ± 5.80              | 6.13 ± 2.89             | <0.001⁴ |
| HOMA-IR          | 2.25 ± 1.48              | 1.30 ± 0.64             | <0.001⁴ |
| TG (mmol/L)      | 0.98 ± 0.56              | 0.92 ± 0.45             | 0.267 |
| TCHO (mmol/L)    | 4.23 ± 0.77              | 4.09 ± 0.79             | 0.094 |
| HDL-C (mmol/L)   | 1.31 ± 0.27              | 1.40 ± 0.33             | 0.008⁴ |
| LDL-C (mmol/L)   | 2.33 ± 0.66              | 2.21 ± 0.69             | 0.094 |

* P < 0.05. BMI: Body mass index; FINS: Fasting plasma insulin level; HOMA-IR: Homeostatic Model Assessment of Insulin Resistance. TG: Triglyceride; TCHO: Total cholesterol; HDL: High-density lipoprotein cholesterol; LDL: Low-density lipoprotein cholesterol.

### Table 4
Baseline comparison of women with FPG ≥ 5.1 mmol/L and FPG < 5.1 mmol/L (mean ± SD).

| Items                   | ≥5.1 mmol/L (n = 114) | <5.1 mmol/L (n = 313) | P  |
|-------------------------|-----------------------|-----------------------|----|
| BMI (kg/m²)             | 23.09 ± 3.62          | 21.99 ± 2.95          | 0.001⁴ |
| FINS (ng/ml)            | 9.30 ± 5.80           | 6.13 ± 2.89           | <0.001⁴ |
| HOMA-IR                 | 2.25 ± 1.48           | 1.30 ± 0.64           | <0.001⁴ |
| TG (mmol/L)             | 0.98 ± 0.56           | 0.92 ± 0.45           | 0.267 |
| TCHO (mmol/L)           | 4.23 ± 0.77           | 4.09 ± 0.79           | 0.094 |
| HDL-C (mmol/L)          | 1.31 ± 0.27           | 1.40 ± 0.33           | 0.008⁴ |
| LDL-C (mmol/L)          | 2.33 ± 0.66           | 2.21 ± 0.69           | 0.094 |

* P < 0.05. BMI: Body mass index; FINS: Fasting plasma insulin level; HOMA-IR: Homeostatic Model Assessment of Insulin Resistance. TG: Triglyceride; TCHO: Total cholesterol; HDL: High-density lipoprotein cholesterol; LDL: Low-density lipoprotein cholesterol.

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