Exercise during pregnancy and gestational diabetes related adverse effects: a randomized controlled trial

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ABSTRACT

Objective: To examine the effect of regular moderate intensity exercise (3 training sessions/week) on the incidence of gestational diabetes mellitus (GDM, primary outcome). We also examined if the exercise intervention modifies the association between GDM and birth weight and risk of macrosomia, gestational age, risk of caesarean delivery, and maternal weight gain (secondary outcomes).

Methods. We randomly assigned 510 healthy gravidae to either an exercise intervention or a usual care (control) group (n=255 each). The exercise program focused on moderate resistance and aerobic exercises (3 times per week, 50-55 min per session). GDM diabetes was diagnosed according to the World Health Organization (WHO) criteria and the International Association for Diabetes in Pregnancy Study Group (IADPSG).

Results: The intervention did not reduce the risk of developing GDM (OR:0.84, 95%CI:0.503-1.395), when using the WHO criteria. We observed that the intervention reduced by 58% the GDM-related risk (WHO criteria) of having a newborn with macrosomia (OR: 1.76, 95%CI:0.039-78.851 vs. 4.22, 95%CI:1.349-13.191) in exercise and control groups, respectively), and by 34% the GDM-related risk of having acute and elective caesarean delivery (OR: 1.30, 95%CI:0.443-3.844vs. 1.99, 95%CI:0.976-4.059 in exercise and control groups, respectively). Gestational age was similar across treatment groups (control, exercise) and GDM category (GDM or non-GDM), and maternal weight gain was ~12% lower in the exercise group independently of whether women developed GDM. The results were similar when the IADPSG criteria were used instead.

Conclusions: Regular moderate-intensity exercise performed over the second-third trimesters of pregnancy can be used to attenuate important GDM-related adverse outcomes.

Key words: Exercise, pregnancy, gestational diabetes, macrosomia.

INTRODUCTION

Gestational diabetes mellitus (GDM) is one of the most common complications of pregnancy [1]. GDM substantially increases the risk of short and long-term adverse health outcomes for both the mother and the offspring [2 3]. The GDM-related adverse maternal outcomes include an increased risk for perinatal morbidity, impaired glucose tolerance and type 2 diabetes after pregnancy, and caesarean delivery [3-6]. Offspring of women with GDM are at higher risk of macrosomia [1 7], and also at higher risk of being obese and having impaired glucose tolerance or diabetes in childhood and early adulthood [1]. There is an association of fasting maternal glucose levels, even if below those diagnostic of GDM, with birth weight and cord-blood serum C-peptide levels [8].

Efforts for combating GDM and GDM-related complications should be thus maximized. Higher levels of physical activity before pregnancy (included vigorous sports activity) [9] or in early pregnancy are associated with a lower risk of developing GDM, as shown in a recent meta-analysis including a total of 34,929 participants with 2,855 cases of GDM [2]. Previous randomized controlled trials (RCT) have shown that exercise during pregnancy induced normalization of glycemia in pregnant women [10], or was effective in reducing the number of patients with GDM who required insulin and in improving glycemic control [11]. However, an exercise intervention did not seem sufficient to prevent GDM in obese pregnant women [12], and Stafne et al. [13] found no evidence that an exercise program performed during the second half of pregnancy prevented GDM or improved insulin resistance in healthy pregnant women with normal body mass index.

Besides the aforementioned controversy regarding the actual effects of exercise performed during pregnancy on GDM prevention, no RCT has been conducted to assess whether exercise can attenuate the potential GDM-related complications, such as macrosomia, caesarean delivery, gestational age, and maternal weight gain [3]. To better understand whether regular exercise during pregnancy can be used to combat GDM-related outcomes is of clinical relevance and of public health interest.

The aim of the present RCT was to examine the effect of regular moderate intensity exercise (3 training sessions/week) performed during the second and third trimesters of pregnancy on the incidence of GDM (primary outcome). We also examined if the exercise intervention modifies the association between GDM and several mother/offspring characteristics on which this disorder is known to have a negative impact [3], that is, birth weight and risk of macrosomia, gestational age, risk of caesarean delivery, and maternal weight gain (secondary outcomes).

METHODS

The present RCT (registration trial number: NCT01477372) was conducted between September 2007 and January 2011 following the ethical guidelines of the Declaration of Helsinki, last modified in 2000. The research protocol was reviewed and approved by the *Hospital Severo Ochoa* (Madrid, Spain).

Participants and randomization

We contacted a total of 780 Spanish pregnant women (of Caucasian descent for three or more generations) from a primary care medical centre (*Centro de Los Pedroches and Centro de Salud Leganés Norte*, Leganés, Madrid, Spain) (Figure 1). Inclusion criteria included: being sedentary (not exercising >20 minutes on >3 days per week), with singleton and uncomplicated gestation, and not at high risk for preterm delivery (i.e. ≤ one previous preterm delivery). For practical reasons, women not planning to give birth in the same obstetrics hospital department (*Hospital Severo Ochoa*, Madrid, Spain), and not being under medical follow-up throughout the entire pregnancy period were not included in the study, neither were women having any serious medical condition that prevented them from exercising safely [14].

After women provided written informed consent, we randomly assigned 510 healthy gravidae to either an exercise intervention (n=255) or a usual care (control, n=255). The participant randomization assignment followed an allocation concealment process, that is, the researcher in charge of randomly assigning participants did not know in advance which treatment the next person would receive and did not participate in the assessments. Assessment staff was blinded to participant randomization assignment. Participants were explicitly informed of the group to which they were assigned as well as on the study hypotheses and were reminded not to discuss their randomisation assignments with assessment staff. Because of the nature of the study, it was not be possible to conceal the group assignment from the staff involved in exercise training sessions. To reduce participants drop out and to maintain adherence to the training program, all sessions were accompanied with music, and were performed in an airy, well lighted exercise room at the Hospital. A qualified fitness specialist carefully supervised every training session with the assistance of an obstetrician and worked with groups of 10-12 women.

Exercise intervention

The interventions were performed in waves so that each wave had between 10 and 12 participants in the intervention group, and 10-12 in the usual care group. The exercise intervention group trained 3 days/week (Monday, Wednesday, Friday, 50-55 min per session) from weeks 10–12 of pregnancy to the end of the third trimester (weeks 38–39). Thus, an average of 85 training sessions was originally planned for each participant in the event of no preterm delivery. The intervention involved aerobic exercises, muscle strength, and flexibility, and met the standards of the American College of Obstetricians and Gynecologists [15 16]. Women used a heart rate (HR) monitor (Accurex Plus, Polar Electro OY, Finland) during the training sessions to ensure that exercise intensity was moderate; their HR was consistently under 70% of their age-predicted maximum HR value (220 minus age, in years). Intensity was also controlled by the Borg's conventional (6-20 point) scale [41]. Exercise intensity expressed as rate of perceived exertion (RPE)] ranged from 10 to 12. These RPE values correspond to a subjective perceived exertion of "farily light" and "somewhat hard" respectively.

The main part of the session included a 25-30 min which was preceded and followed by a gradual warm-up and cool-down period respectively (both of 10-12 min duration and consisting of walking and light, static stretching (avoiding muscle pain) of most muscle groups (upper and lower limbs, neck and trunk muscles). The cool-down period also included relaxation and pelvic floor exercises.

The main part of the session included the following moderate resistance exercises: toning and joint mobilization exercises, i.e. shoulder shrugs and rotations, arm elevations, leg lateral elevations, pelvic tilts and rocks. Resistance exercises were performed through the full range of motion normally associated with correct technique for each exercise and engaged the major muscle groups (pectoral, back exercise, shoulder, upper and lower limb muscles). It included one set (10–12 repetitions of each) of i) pelvic tilting in standing and ii) the following exercises using barbells (3 kg/exercise) or low-to-medium resistance (elastic) bands (Therabands): biceps curls, arm extensions, arm side lifts, shoulder elevations, bench press, seated lateral row, lateral leg elevations, leg circles, knee extensions, knee (hamstring) curls, ankle flexion and extensions. We specifically avoided any exercise that involved extreme stretching and joint overextension, ballistic movements or jumps, and exercises in supine position on the floor were not performed for more than 2 minutes. We used exercises covering the major muscle groups of arms and abdomen to promote good posture, prevent low back pain and strengthen the muscles of labor and pelvic floor (third trimester). We also included in the program one session per week of aerobic dance. We used choreography involving upper and lower body limbs of very low impact. Aerobic dance activities were developed in sections of 3-4 minutes with 1 minute breaks which included stretching and relaxation activities.

Usual care (control) group

Women randomly assigned to the usual care (control) group received general advice from their midwife about the positive effects of physical activity. Participants in the usual care group had their usual visits with health care providers (midwives, obstetricians and family doctors) during pregnancy, which was equal as in the exercise group. Women were not discouraged from exercising on their own.

Participants' demographics

Demographic information was obtained at study entry. Pregravid weight was based on a self-report at the time of the study enrollment. Heights were measured by trained research staff at study entry. Body mass index was calculated as weight in kg divided by height in meters squared.

Outcomes

Primary outcome. Women underwent a 75-g oral glucose tolerance test (OGTT) at 24-26th week, after an overnight fasting. Glycemia was measured 2 hours after the OGTT (hereafter called 2h-glucose) with the routine methods used by the hospital laboratory. GDM diabetes was diagnosed according to the two accepted criteria [3]: (i) the World Health Organization (WHO) criteria, i.e. 2-h glucose ≥140 mg/dl; and (ii) the International Association for Diabetes in Pregnancy Study Group (IADPSG), i.e. 2-h glucose ≥153 mg/dl. The diagnosed GDM patients received advice on a 2.000kcal diet, metabolic controls twice a day (by themselves or in the hospital), obstetric care considering high-risk pregnancy, and were also recommended to perform physical activity.

Secondary outcomes. Gestational body weight gain was calculated on the basis of the pregravid weight and weight at the last clinic visit before delivery. We recorded birth weight of the newborn from hospital perinatal records. Newborns were classified as having macrosomia when birth weight was >4,000g. We obtained Apgar scores (at 1 and 5 minutes) as well as gestational age at time of delivery and cesarean deliveries (both acute and elective) from the reports of delivery room personnel (midwives).

Statistical analysis

We made power calculations for the primary outcome measures of GDM following the WHO criteria assuming a GDM prevalence in our population using previous studies conducted in the same hospital [17] of ~25% in the intervention group and 30% in the usual care group (risk difference of 5-10%) Under these assumptions, a two-sample comparison (χ^2) with a 5%

level of significance and a statistical power of 0.80 gave a study population of ~200 patients in each group. Assuming a maximum lost to follow-up of 10%, we needed to include approximately 220 women for each group at baseline.

For treatment group comparisons, we analysed continuous and nominal data with Student's *t* test for unpaired data and Chi-square tests, respectively. We used logistic regression analysis to examine the effect of the exercise intervention on the incidence of GDM (*primary outcome*) as assessed with the WHO and IADPSG criteria, after controlling for maternal age and body weight prior to pregnancy. We also used logistic regression analysis to examine the effect of treatment group (training and control) and GDM category (non-GDM or GDM gravidae) and their interaction, on the likelihood of having a newborn with macrosomia and on the likelihood of cesarean deliveries (*secondary outcomes*), after controlling for maternal age, body weight prior to pregnancy, and gestational age. Analysis of covariance was used to examine the effect of treatment group and GDM category and their interaction, on birth weight, gestational age, and gestational weight gain (*secondary outcome*), after controlling for maternal age, and body weight prior to pregnancy. We conducted all statistical analyses using the Statistical Package for Social Sciences (SPSS, v. 18.0 for WINDOWS; SPSS Inc, Chicago), and the level of significance was set to ≤ 0.05.

RESULTS

In the training group a total of 45 participants were lost to follow-up due to premature labour (n=5), pregnancy-induced hypertension (n=5), persistent bleeding (n=3), or personal reasons (n=32). In the control group, a total of 37 were lost to follow-up due to premature labour (n=3), pregnancy-induced hypertension (n=4), molar pregnancy (n=3), and personal reasons (n=16). Eleven participants from the same group were also lost to follow-up because they decided to give birth in a different hospital. Thus, no primary outcome data are available for analysis in this group of women, and no missing data was imputed. Therefore, final number of participants included in the per protocol analysis was 210 in the training group and 218 in the control group (Figure 1). There were no exercise-related injuries experienced during pregnancy. Demographic characteristics of participants included in both the training and control group were similar to those of the participants who discontinued the program (all P>0.1, data not shown). Adherence to training in the experimental group was >95%. No participant changed from the control group to the intervention group or *vice versa*, and there were no protocol deviations from study as planned.

Maternal and newborn characteristics in the exercise and usual care groups are shown in Table 1. 2-h glucose was significantly higher (~6%, *P*=0.012) in the control group. Maternal weight gain was significantly lower (~13%, *P*<0.001) in the exercise group. Birth weight, Apgar score at minutes 1 and 5, and gestational age were similar in both groups.

The OR of having GDM (WHO criteria) was significantly lower in the exercise group (OR: 0.62, 95% CI: 0.398-0.981, *P*=0.041) (Figure 2), yet the association was attenuated once maternal age and body weight prior to pregnancy were included as covariates (OR: 0.84, 95% CI: 0.503-1.395, P=0.496). The results were similar when using the IADPSG diagnostic criteria (OR: 0.90, 95% CI: 0.524-1.565, *P*=0.722).

The effects of treatment group and GDM (using both WHO and IADPSG diagnostic criteria) on pregnancy outcomes are shown in Table 2. Following the WHO criteria to diagnose GDM, birth weight was similar in both exercise and control groups in women with no GDM, yet in women with GDM, birth weight was significantly lower (~7%, *P*=0.014) in the exercise group (*P*-value for treatment*GDM group interaction = 0.025). The OR of having a newborn with macrosomia was significantly lower in the exercise group in both non-GDM and GDM gravida (OR in non-GDM gravida: 0.10, 95%CI: 0.011-0.949, *P*=0.045; OR in GDM-gravida: 0.07, 95%CI: 0.05-0.932, *P*=0.044) after controlling for maternal age, body weight prior to pregnancy and gestational age (*P*-value for treatment*GDM group interaction = 0.981). Gestational age was similar in both exercise and control groups as well as in non-GDM and GDM gravida (all *P*>0.1). Maternal weight gain was lower (~12%, *P*<0.05) in the exercise group in both non-GDM and GDM gravida (*P*-value for treatment*GDM group interaction = 0.536).

In the control group, GDM gravida (diagnosed following the WHO criteria) had an increased OR of having a newborn with macrosomia compared with non-GDM gravida (OR: 4.22, 95% CI: 1.349-13.191; *P*=0.013), whereas no association was found between GDM and risk of macrosomia in the GDM gravida of the exercise group (OR: 1.76, 95% CI: 0.039-78.851; *P*=0.770) (Figure 2). In the control group, GDM gravida (diagnosed following the WHO criteria) had an increased OR of cesarean delivery (both acute and elective) compared with non-GDM gravida (OR: 1.99, 95% CI: 0.976-4.059; *P*=0.058), whereas no association was observed between GDM and risk of cesarean delivery in the GDM gravida of the exercise group (OR: 1.30, 95% CI: 0.443-3.844; *P*=0.630). The findings persisted after further adjusting for gestational weight gain (data not shown). The results were similar when the IADPSG criteria were used instead.

DISCUSSION

The present study showed that supervised, moderate intensity exercise intervention performed three times per week over the second and third trimesters of pregnancy in previously sedentary and healthy gravida did not reduce the risk of developing GDM, yet it reduced by 58% the GDM-related risk of having a newborn with macrosomia (OR: 1.763 vs. 4.219 in exercise and control groups, respectively), and by 34% the GDM-related risk of having caesarean delivery (OR: 1.304 vs. 1.990 in exercise and control groups, respectively). A third main finding was that gestational age was similar across treatment groups (control, exercise) and GDM category (GDM or non-GDM), whereas maternal weight gain was ~12% lower in the exercise group independently of whether women developed GDM. The fact that the results were similar when using the WHO or the IADPSG criteria to define GDM further strengthens the study findings.

Exercise performed during early pregnancy is associated with a lower risk of developing GDM [18], as shown in previous prospective cohort [19-22], retrospective case-control [22 23], or cross-sectional surveys [24 25]. More recently, Hopkins et al. [26] showed that a home-based stationary cycling program from 20 wk did not affect maternal insulin sensitivity in late gestation. Earlier intervention studies also showed the benefits of exercise performed during the pregnancy period on maternal and offspring health. Jovanovic-Peterson and Peterson [27] reported that pregnant women with GDM receiving an exercise therapy had greater glycemic control and improved cardiorespiratory fitness compared with their peers receiving a standard dietary intervention. There is however no unanimity among more recent findings from RCT. We recently showed that in healthy pregnant women, exercise training combining land and aquatic activities performed during the entire pregnancy induced normalization of glycemia [10]. In a study on pregnant women with GDM, a moderate-intensity resistance training program using elastic bands was effective in reducing the number of patients who required insulin and in improving their glycemic control [11]. However, in obese pregnant women, an exercise intervention over pregnancy (with an energy expenditure goal of 900 kcal/week) was not sufficient to prevent GDM [12]. Furthermore, Stafne et al. [13] found no evidence that an exercise program performed during the second half of pregnancy prevented GDM or improved insulin resistance in healthy pregnant women with normal body mass index.

An important novel finding of our study was that moderate-intensity exercise performed during pregnancy significantly reduced the risk of GDM-related complications, notably macrosomia. We observed that the OR of having a newborn with macrosomia was reduced by 58% in the GDM-gravida from the training group compared with the GDM-gravida from the control group. This finding is of public health relevance because fetal macrosomia is associated with significant maternal and neonatal morbidity [28]. In the long term, macrosomic babies are more likely to be obese in childhood, adolescence and early adulthood, and are at higher risk of cardiovascular and metabolic complications in adulthood [28]. High birth weight is also associated with an increased risk of overall leukemia and acute myeloid leukemia [29]. Glucose intolerance due to increased insulin resistance tends to develop during pregnancy [30]. This facilitates continuous glucose transfer to the fetus. In contrast, exercise training enhances insulin sensitivity in the exercised muscle and enhances muscle contraction-induced glucose uptake in this tissue [31]. Therefore, it can be hypothesized that the risk of macrosomia would be reduced under a “physically active” milieu [32].

GDM/hyperglycemia is also known to increase the risk of cesarean delivery [8 33]. A recent meta-analysis showed significantly higher risk of cesarean delivery associated with GDM [3]. In the present RCT, we observed that the OR having cesarean delivery was reduced by 34% in the GDM gravida from the training group compared with the GDM gravid from the control group. We believe this result is also of potential clinical relevance owing to the maternal complications associated with cesarean delivery such as infection, excessive blood loss, respiratory complications, reactions to anaesthesia, longer hospitalization periods, as well as higher medical cost [34].

A third main finding of our study was that gestational age was similar across groups (control or exercise) and conditions (GDM or no GDM), whereas maternal weight gain was ~12% lower in the exercise group independent of whether the women had GDM. There is compelling evidence that physical activity during pregnancy has no major effect on gestational age at delivery. In a previous RCT, we showed that resistance training during pregnancy on previously sedentary, healthy women carrying singletons did not alter gestational age at delivery compared with inactive controls [35]. Taken together, these findings support the notion that healthy pregnant women, without contraindications to physical activity, are able to engage in these active behaviours without undue risk of preterm birth.

Excessive weight gain during pregnancy is a major risk factor for postpartum weight retention and future weight gain and obesity in women [36]. Maternal weight gain, especially in early in pregnancy, is disproportionately fat and could influence subsequent maternal insulin resistance [37]. Yet few adequately powered RCTs have examined the efficacy of behavioural weight-control interventions during pregnancy. Results from RCT [38-40]{Haakstad, 2011 #4795} showed decreases in maternal weight gain with a behavioural intervention combining nutritional and physical activity recommendations. A recent relatively small RCT (total n=83) showed a trend towards a decrease (-9%) in maternal weight gain with exercise [10]. Haakstad and Bø {Haakstad, 2011 #4795} showed that women attending all sessions of the prescribed exercise program (n=24 exercise sessions) training program had a higher weight reduction of (2.8kg) compared with women in the control group.

A limitation of the current study was that we did not record detailed information about the participants' dietary habits despite women with GDM were advised to follow a dietary regimen. Further, pre-pregnancy weight was self-reported which might be slightly underestimated. We did not closely follow the physical activity levels of women in the control group, yet they all reported that they did not engage in any regular physical activity program for more than 20 minutes on more than 3 days per week. It cannot be discard that both diet and physical activity advice delivered to the GDM women might have influence the results of the present study. Yet, both women in the exercise group and those in the usual care group that developed GDM receive a similar type of recommendations.

In summary, although regular exercise performed over the second and third trimesters of pregnancy did not actually reduce the risk of GDM, a major finding of our study was that, besides reducing maternal weight gain by 12% in non-GDM, exercise intervention ameliorated by 58% the impact of GDM on the risk of macrosomia and by 34% the GDM-related risk of having caesarean delivery. Of note is that the magnitude of the associations was similar when using WHO or the IADPSG criteria to define GDM, which is an additional strength to the study results. Taken together, our findings provide further support for the benefits of moderate exercise in healthy gravida and for promoting supervised exercise interventions during pregnancy [32 41].

What are the new findings

A supervised, moderate intensity exercise intervention performed three times per week over the second and third trimesters of pregnancy in previously sedentary and healthy gravida:

- Reduced the GDM-related risk of having a newborn with macrosomia.
- Reduced the GDM-related risk of having caesarean delivery

How might it impact on clinical practice in the near future

The study provide further evidence about the potential benefits of moderate exercise in healthy gravida, as well as in gravida with gestational diabetes mellitus. Taken together, these findings reinforce the idea of promoting supervised exercise interventions over pregnancy.

Author contributions

R.B. Designed the study, participated in the training protocol, analysis and interpretation of data, and contributed to the discussion and reviewed/edited the manuscript; M.P. and C.L. participated in the training protocol, contributed to the discussion and reviewed/edited the manuscript; A.L. and J.R.R. drafted the manuscript, analysis and interpretation of data.

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Table 1. Characteristics in the exercise and usual care (control) groups.

	Exercise (n=210)	Control (n=218)	*P*
Maternal characteristics			
Maternal age (years)	31 ± 3	31 ± 4	0.906
Body mass index (kg/m^2)	24.1 ± 4.1	23.7 ± 3.8	0.354
Occupational activity (n, %)			0.422
Sedentary job	73 (34.8)	85 (39)	
House wives	56 (26.7)	62 (28.4)	
Active job	81 (38.6)	71 (32.6)	
Maternal education (n, %)			0.108
<High school	54 (25.7)	75 (34.4)	
High school	98 (46.7)	96 (44)	
>High school	58 (27.6)	47 (21.6)	
Weight gain during pregnancy (kg)	11.6 ± 3.7	13.3 ± 4.1	<0.001
2-h glucose (mg/dl)	116.8 ± 29.8	123.86 ± 28.6	0.012
GDM WHO criteria* (n, %)	41 (19.5)	61 (28)	0.040
GDM IADPSG criteria** (n, %)	29 (13.8)	32 (14.7)	0.797
Newborn characteristics			
Birth weight (g)	3,201 ± 446	3,257 ± 469	0.208
Macrosomia (birth weight >4,000g (n, %)	2 (1)	15 (6.9)	0.002
Apgar score 1 min	8.8 ± 1.4	8.7 ± 1.3	0.313
Agpar score 5 min	9.9 ± 0.5	9.9 ± 0.7	0.292
Gestational age (days)	277 ± 11	277 ± 10	0.942
Cesarean delivery (n, %)	33 (15.7)	45 (20.6)	0.187

Data are expressed as mean±SD, unless otherwise indicated.

We analyzed continuous and nominal data with *t* test for unpaired data and Chi-square tests respectively.

Abbreviation: GDM, gestational diabetes mellitus.

World Health Organization (WHO) criteria when 2 hours 75 g oral glucose tolerance test ('2-h glucose') ≥140 mg/dl. GDM International Association for Diabetes in Pregnancy Study Group (IADPSG) criteria when 2-h glucose ≥153 mg/dl.

Table 2. Effect of treatment group and gestational diabetes mellitus (GDM) on pregnancy outcomes.

	no GDM (WHO criteria)		GDM (WHO criteria)		
	Exercise (n=169)	Control (n=157)	Exercise (n=41)	Control (n=61)	P^*
Birth weight (g)	3200 ± 442	3191 ± 470	3204 ± 470	3429 ± 427‡	0.025
Gestational age (days)	277 ± 12	276 ± 10	276 ± 11	279 ± 8	0.137
Cesarean delivery (n, %)	24 (14.2)	28 (17.8)	9 (22)	17 (27.9)	0.934
Maternal weight gain (kg)	11.8 ± 3.6	13.3 ± 4.3†	11.2 ± 4.1	13.3 ± 3.7$^\wedge$	0.536
Apgar score 1 min	8.8 ± 1.4	8.6 ± 1.4	8.8 ± 1.3	8.9 ± 1.2	0.347
Apgar score 5 min	9.9 ± 0.4	9.9 ± 0.4	9.8 ± 0.7	10 ± 1.2	0.10
	no GDM (IADPSG criteria)		GDM (IADPSG criteria)		
	Exercise (n=181)	Control (n=186)	Exercise (n=29)	Control (n=32)	P^*
Birth weight (g)	3204 ± 444	3218 ± 465	3180 ± 465	3482 ± 437$^\wedge$	0.022
Gestational age (days)	277 ± 10	277 ± 11	280 ± 7	277 ± 11	0.261
Cesarean delivery (n, %)	27 (14.9)	36 (19.4)	6 (20.7)	9 (28.1)	0.891
Maternal weight gain (kg)	11.7 ± 3.7	13.3 ± 4.2†	11.6 ± 4.1	13.4 ± 3.8	0.902
Apgar score 1 min	8.8 ± 1.4	8.6 ± 1.4	8.9 ± 1.1	8.9 ± 0.2	0.668
Apgar score 5 min	9.8 ± 0.5	9.9 ± 0.8	9.8 ± 0.5	9.9 ± 0.8	0.768

Abbreviation: GDM, gestational diabetes mellitus.

World Health Organization (WHO) criteria when 2 hours 75 g oral glucose tolerance test ('2-h glucose') ≥140 mg/dl. GDM International Association for Diabetes in Pregnancy Study Group (IADPSG) criteria when 2-h glucose ≥153 mg/dl.

$^*P$ for treatment (group) x GDM interaction.

$^‡P$<0.05 vs. exercise group.

$^\wedge P$<0.01 vs. exercise group.

$^†P$<0.001 vs. exercise group.

Figure legends

Figure 1. Flow diagram of the study participants.

Figure 2. Percentage (within brackets) of newborns with birth weight >4,000g (panel A) and percentage of caesarean delivery (panel B) by treatment and gestational diabetes mellitus (GDM) criteria: GDM, GDM World Health Organization (WHO) criteria when glycemia 2 hours after a 75 g oral glucose tolerance test ≥140 mg/dl. GDM International Association for Diabetes in Pregnancy Study Group (IADPSG) criteria when glycemia 2 hours after a 75 g oral glucose tolerance test ≥153 mg/dl. Control group GDM gravida diagnosed following the WHO criteria had an increased odds ratio (OR) of having a newborn with macrosomia compared with non-GDM gravida (OR: 4.22, 95% CI: 1.349-13.191; *P*=0.013), whereas no association was found between GDM and risk of macrosomia in the exercisers GDM gravida (OR: 1.76, 95% CI: 0.039-78.851; *P*=0.770) after controlling for maternal age and body weight prior to pregnancy (Panel A). Control group GDM gravida had an increased OR of cesarean delivery (both acute and elective) compared with non-GDM gravida (OR: 1.99, 95% CI: 0.976-4.059; *P*=0.058), whereas no association was observed between GDM and risk of cesarean delivery in the exercisers GDM gravida (OR: 1.30, 95% CI: 0.443-3.844; *P*=0.630). The results were similar when the IADPSG criteria were used instead (Panel 2B).