The Preventive Effect of Exercise on Gestational Glucose Tolerance

Timing, Frequency, Duration and Intensity of Exericise Before, Early and Late in Pregnancy

Abstract

OBJECTIVE: To assess how different maternal exercise characteristics before, early and late in pregnancy might affect glucose tolerance late in pregnancy.

METHODS: The data used in this cohort study was originally collected in the TRIP study at the University Hospitals of Trondheim and Stavanger between April 2007 and June 2009. A total of 855 Caucasian women aged ≥18 years with one singleton live fetus and low-risk pregnancies were included. Through a questionnaire, information about the women's frequency, intensity and duration of exercise before, early and late in pregnancy was collected. Early (gestation week 18-22) and late (gestation week 32-36) in pregnancy, a 75-g 2-h oral glucose tolerance test (OGTT) was performed. Linear regression was used to assess the importance of different exercise variables on glucose tolerance.

RESULTS: Regular pre-pregnancy exercise (defined as a minimum of three days per week with moderate to high intensity) was found to be inversely associated with elevated blood glucose levels late in pregnancy (P= .023). Three exercise characteristics showed a significant association with the blood glucose value late in pregnancy: frequency of exercise before pregnancy -0.070 (P= .032), intensity of exercise early in pregnancy -0.300 (P= .008) and duration of exercise late in pregnancy -0.323 (P= .002).

CONCLUSION: The findings of the present study indicate that regular exercise before pregnancy has a positive effect on glucose tolerance in late pregnancy, and thereby a preventive effect on the development of gestational diabetes. No such association was found for similar regular exercise during pregnancy. Based on the results of this study, it is difficult to conclude which exercise characteristic is most important of frequency, intensity and duration.

Background

Introduction

Gestational diabetes mellitus (GDM) is defined as hyperglycemia caused by glucose intolerance, with the onset or first recognition during pregnancy (1, 2). It is a risk factor for several maternal and fetal pregnancy complications (3, 4), inclusive future development of diabetes mellitus type 2 (DMt2) for both mother and child later in life (5, 6). The diagnosis of GDM is usually performed through an oral glucose tolerance test (OGTT). Which glycemic value that qualifies for a GDM diagnosis varies worldwide (7). However, hyperglycemia seems to increase the risk of complications in a continous matter, also at levels lower than the GDM diagnosis (4). Modifiable and unmodifiable risk factors for GDM are identified, such as advanced maternal age (8), high pre-pregnancy BMI (9), Asian ethnicity (8) and a family history of GDM and/or DMt2 (10). Regular exercise, alone or in combination with healthy diet, is suggested to lower the incidence of GDM among women in general (10-18). Concurrently, some studies have found no association between exercise and GDM (19, 20) and more studies are requested to determine how different exercise characteristics before or in different phases of pregnancy might influence glucose tolerance (12, 14, 21). To construct efficient and safe prophylactic exercise guidelines for women in childbearing age, it is important to get more knowledge about this theme.

Metabolic changes during pregnancy

During pregnancy, the woman's metabolism changes to assure both the fetus and the mother the energy needed (22). For growth and development, the fetus is depending on delivery of glucose from the maternal blood circulation. The woman's betacell function is reduced, with reduction of maternal insulin production as a result. This occurs simultaneously as the maternal placenta produces the hormone *human placental lactogen* – an insuline antagonist which changes the maternal metabolism into a pseudo-diabetogenic state: the insulin receptors in liver and peripheral skeletal muscle become less sensitive to insulin, the glucose expenditure decreses and the lipolysis increases. As a result, maternal blood glucose levels rise and the fetal glucose availability increases (23, 24).

In the normal pregnancy, women produce more insulin than non-pregnant women due to compensation with increased secretion of insulin from the pancreatic beta cells and can thereby stay normoglycemic (25). However, the glucose levels might be elevated compared to before pregnancy (26). A hyperglycemic pregnancy occurs because of dysregulation of the insulin production in the beta cells (25). The maternal overload of glucose is transferred to the fetus, causing fetal hyperglycemia and subsequent hyperinsulinemia. Insulin, which is a growth hormone, then stimulates fetal growth and macrosomia, in company with its pregnancy complications, can be the result (27).

Prevalence of GDM

The actual prevalence worldwide is difficult to estimate, not only because of the diverse criteria, but also because of the diverse screening methods used. Jiwani et al. (2012) found that estimated prevalence in countries varied from < 1 % (Germany) to 28 % (Nepal) (28). Depending on which criteria are used, the prevalence of GDM among Nordic Caucasian women (the ethnicity of the women investigated in this report) is found to be 6.1-7.4 % (7).

Risk factors for GDM

Several risk factors to develop GDM are identified: high maternal age (8), Asian ethnicity (8), high maternal pre-pregnancy BMI (9) and a positive family history of GDM and/or DMt2 (10). Excessive or insufficient gestational weight gain (29), parity (30, 31) and level of physical activity (10-20) are examples of factors whose importance is still being discussed. There are different prescriptions of how to diagnos GDM and Helseth et al. (2014) found that the diverse diagnostic criteria for GDM also were associated with different risk factors: the WHO criteria emphasized high maternal age and short stature, while the IADPSG criteria were associated with maternal age, fasting insulin and no regular exercise at pregnancy week 18-22 (7).

Short- and long-term complications for mother and child

Even though the WHO and the IADPSG guidelines both set a distinct diagnostic cut-off value, it is established that the risk of adverse maternal, fetal and neonatal outcomes is continously increasing with elevated blood glucose values, also before reaching a diagnostic GDM level (4). The pregnancy complications associated with GDM are macrosomia and associated labour complications, shoulder dystocia, and perinatal hypoglycemia (23). In the long term, the woman has a 7-fold increased risk of developing DMt2 (5), with all its associated complications, and she also has an increased risk of future cardiovascular disease (32). The child of a GDM pregnancy has an increased risk of overweight, obesity and development of DMt2 (23).

Physical activity and its effects on GDM

Physical activity (PA) is defined as any bodily movement produced by skeletal muscles that result in energy expenditure. Exercise is a subset of physical activity that is planned, structured and repetitive, and has an object to improve or maintain physical fitness (33). Exercise is proven to improve carbohydrate metabolism and lower the need of endogenous insulin (34) and it is a tool of treatment and a risk-lowering intervention for DMt2 (35). In rest, glucose is transported from the blood circulation into the muscle and liver cells with the help of insulin (36). When muscles are activated during exercise, glucose uptake is facilitated through recruitment of insulin-independent GLUT-4 transporters and increased insulin sensitivity (36). This metabolic pathway bypasses the site of issue during diabetes.

Several studies have suggested that the level of exercise affects the risk of developing GDM (10-16), and other studies found exercise risk lowering among high-risk (i.e. overweight or obese) pregnant women (37-39). A Cochrane review from 2012 found the amount of RCTs too limited to find significant associations between exercise and glucose intolerance/GDM (20). Additionally, optimal magnitude of timing, frequency, intensity and duration is to be researched. In most interventional studies found, the subjects were assigned to take part in exercise a minimum of three times per week with a duration of 30-60 minutes per session and at a moderate to vigorous intensity, with variable conclusions in their analyzes.

Current recommended management of GDM

The guidelines of today recommend dietary changes, physical activity and blood glucose monitoring as first steps in treatment of glucose intolerance during pregnancy (40). Hyperglycemia-lowering medications, such as metformin or insulin, are recommended only when non-medicational interventions fail to lower or control hyperglycemia (41).

Present exercise recommendations and actual level of exercise during pregnancy

As of today, the American Congress of Obstetricians and Gynecologists (ACOG) guidelines recommend a healthy and active lifestyle for pregnant women with an uncomplicated pregnancy and without any contraindications to activity (21). Before, during and after pregnancy, women should perform aerobic exercise aswell as endurance strength. Exercise improves the women’s health in several aspects: physical and psychological fitness, weight control, and reducing the risk of GDM in obese women (21). Exercising for a minimum of 20-30 min on moderate intensity on most days of the week is recommended. Further specification of optimal and efficient timing, frequency, duration and intensity is still to be researched (12, 14, 21).

Pregnancy is a life phase where most women adapt to a more sedentary lifestyle (42). In a cross-sectional study, women were found to decrease their amount of exercise with 20 % during pregnancy and the lowest level was seen in the first and third trimester (43). Primiparity, regular physical activity before pregnancy, receiving instructions of exercise from the antenatal care and higher educational level increases the likelihood that the woman will exercise also during pregnancy (43). On the other hand, a pre-pregnancy BMI ≥ 24.9 kg/m^2 or gaining > 10 kg during pregnancy makes it less likely that the woman will exercise during pregnancy (43, 44).

Objective

This thesis will use data collected by the TRIP (Training In Pregnancy) study (45) – a RCT study of a 12-week regular exercise program in the second half of pregnancy (between gestation week 20-36) compared with standard antenatal care. The TRIP study found no difference in prevalence of GDM or levels of insulin resistance between the intervention and the control group at gestational week 32-36. However, only 55 % of the intervention women adhered to the scheduled program of minimum three sessions per week, and it was also no restriction of exercise for the control group. With these facts taken into consideration, the difference in exercise between intervention and control group might not have been significant enough to draw any conclusions about the interventional effect. Because of the possible discrepancy between the randomization and actual performed exercise, it might be misleading to analyze the data as a RCT study. Therefore, the TRIP data will be analyzed as a cohort study in the present research. The purpose is to explore how different maternal exercise characteristics before, early and late in pregnancy might affect glucose tolerance late in pregnancy.

Materials and methods

The TRIP study

The data used in this cohort study was collected in the TRIP study at the University Hospitals of Trondheim and Stavanger between April 2007 and June 2009 (45). It was a two-armed, two-center RCT where a total of 855 Caucasian women at an age of 18 years or older with one singleton live fetus were included and randomized into an intervention and a control group. Women with high-risk pregnancies or diseases that could affect the results with participation, and women living > 30-minute drive from the hospitals (because of the impracticality to attend group sessions) were excluded from the study.

During the intervention time (twelve weeks in the period between gestation week 20-36), women in the intervention group were offered a physiotherapist-led 60-minutes group training once a week, including aerobic activity at moderate intensity, strength training and balance exercises. In addition, they were encouraged and adviced to at least twice a week perform a 45-minute home exercise program containing the same three types of exercise as the group session. Adherence to the program was set to a minimum of three exercise sessions of moderate to high intensity per week. Only 55 % of the women in the TRIP study's intervention group reached the objective.

In the control group, the women took part in the standard national antenatal care. They were not discouraged from being physically active and 10 % of the women spontanously reached the intervention protocol of exercising minimum three times per week at moderate to high intensity.

All participants performed a 75-g 2-h OGTT at inclusion (T1) and after intervention (T2). In accordance to the WHO criteria for GDM, the diagnosis was fulfilled at fasting glucose ≥ 6.1 mmol/L in whole blood, or plasma glucose ≥7.0 mmol/L, or 2-hour glucose level ≥ 7.8 mmol/L.

Information about weekly PA and exercise was collected with a questionnaire at three different stages: pre-pregnancy (retrospective), at week 18-22 (T1 – inclusion), and at week 32-36 (T2 – post intervention control) of pregnancy. The women were asked to estimate their average intensity and duration of exercise, and the amount of days per week with exercise. Pre-pregnancy weight was entered by the women, and their weight and BMI was recorded at T1 and T2.

Data analyzes

The data analyzes were performed with the software Statistical Package for the Social Sciences (SPSS v24) for MacBook. Models of linear regression were used to assess the importance of different exercise variables on glucose tolerance.

The numerical variables used were self-reported frequency, duration and intensity of exercise at three timepoints: before pregnancy, early in pregnancy (week 18-22, T1) and late in pregnancy (week 32-36, T2). In addition, one categorical variable that combined frequency (≥3 days per week), duration (>30 minutes) and intensity (moderate or high intensity) defining a minimum overall level of exercise according to the study intervention, was analyzed. Thus, two separate analyzes were performed - one of specific exercise characteristics and one of exercise level meeting the study intervention.

Univariable and multivariable linear regression models

To investigate the association between the exercise variables and 2-hour glucose value late in pregnancy, linear regression models were used. Hyperglycemia is found to increase the risk of adverse outcomes in a continous matter and at levels lower than the diagnostic value (4), and therefore linear regression models were chosen. Because of risk of interaction between the large quantities of variables, the variables were initially analyzed one at a time in a univariable linear regression model. In a second model, the association was controlled for three known risk factors for GDM when age, BMI and GDM/DMt2 in close family was included in a multivariable linear regression model. Finally, the variables that showed significance were included in a multivariable model together with the known GDM risk factors.

Results

A total of 855 women were included in the study in mid-pregnancy (T1). In late pregnancy (T2), 84 women were lost to follow-up and 59 women failed to complete the OGTT, leaving 702 women with complete data (Figure 1). On average, women in the study population were 30.5 years old and weighted 70.6±10.1 kg at study entry. For further baseline characteristics, see Table 1.

Before pregnancy, 28.8 % of the women declared no regular exercise. This number increased to 48.1 % early in pregnancy but again decreased to 31.8 % late in pregnancy. The proportion of women who exercised at least three days per week were at the same timepoints 32.1, 15.7 and 34.1 %, respectively.

Low-intensity exercise was performed by 2.6 % of the women pre-pregnancy, a number that increased to 11.0 and 10.6 % at T1 and T2. At the same timepoints, a total of 29.2, 5.4 and 3.7 % women estimated their exercise as high-intensity exercise.

When analyzing duration of exercise sessions, the quantity of women who exercised for 0-30 minutes per session were 2.0, 5.7 and 6.2 % at pre-, early and late in pregnancy. For a duration average of 30-60 minutes per session, the numbers were 24.8, 9.7 and 10.2 %.

Before pregnancy, and early respectively late in pregnancy, the amount of women exercising at least three times per week at a vigorous intensity were 31.5, 12.9 and 29.6 %.

Three variables showed significant association with lower 2-h glucose value late in pregnancy: frequency of exercise before pregnancy -0.070 (-0.134, -0.006; *P*= .032), intensity of exercise early in pregnancy -0.300 (-0.522, -0.079; *P*= .008) and duration of exercise late in pregnancy -0.323 (-0.527, -0.118; *P*= .002). Controlling for known GDM risk factors did not affect the associations noteworthy (Table 2).

In the multivariable regression analysis including the three abovementioned exercise variables and the known GDM risk factors, two of the variables acquired a *p*-value above .05 and thereby lost their significant association to the dependent variable (2-h glucose value late in pregnancy). Only duration of exercise late in pregnancy persisted with a beta-value of -0.295 (-0.551, -0.040; *P*= .024) (Table 2).

A significant association of -0.219 (-0.409, 0.030; *P*= .023) was found between engaging in regular exercise (≥3 days per week, at moderate to high intensity, for ≥30 minutes per session) before pregnancy and the dependent variable 2-h glucose value late in pregnancy.

Neither regular exercise early or late in pregnancy fulfilled the significance level (early $P = .931$ and late $P = .470$) (Table 3).

Discussion

To perform regular exercise (defined as a minimum of three days per week with moderate to high intensity) before pregnancy was associated with lower 2-h OGTT glucose values late in pregnancy. The association was sustained when controlling for known GDM risk factors. Interestingly, the better glucose tolerance was only detected for exercise before pregnancy. No significant association was found for following the same regime during pregnancy, though regular exercise both early and late in pregnancy were studied.

The findings in the present study are in accordance with findings from three other studies (12, 13, 17). A recently published review and meta-analysis of 25 cohort studies and RCTs presented a favourable risk reduction for pre-pregnancy activity compared to exercise during pregnancy (12). Exercise only before pregnancy gave a 40 % risk reduction, whereas women who were active before pregnancy and stayed active during pregnancy had a risk reduction of 59 % (12). This result is supported by Dempsey et al. (2004) who found a combination of regular exercise the antecendent year and the first 20 weeks of pregnancy to be most risk-reducing (17). Pre-pregnancy exercise was also by Tobias et al. (2011) found to be superiorly risk-reducing compared to exercising exclusively during early pregnancy, though both regimes entailed less risk compared to no exercise (13). No risk reduction was seen among the women who were inactive before pregnancy and active only early in pregnancy (12) – a finding that plays in concert with the present study, where regular exercise only during pregnancy was not found to be of significant value. Also, pre-pregnancy exercise with longer duration and higher intensity was earlier found to be risk-reducing when compared to less activity and intensity (15, 18).

Pre-pregnancy exercise might be the most efficient GDM prophylaxis because of the longer possible intervention time and because it is a period free from the physical restrictions a pregnancy might bring. In addition, exercising before pregnancy might prepare the woman for the metabolic and endocrine stress that a pregnancy conveys. During GDM, the woman's blood glucose levels rise due to peripheral insulin resistance (23) and dysregulated insulin production (25). Exercise is found to enhance glucose uptake in peripheral skeletal muscles in several ways, e.g. enhanced enzymatic activity and improved capacity of glycogen production (46). Though more studies are needed, exercise is also suggested to possibly enhance insulin secretion (46). These improvements convey an enhanced capacity of blood glucose clearance and for optimal prophylactic effect it might be an advantage to induce them already before pregnancy.

The present study found intensity early in pregnancy and duration late in pregnancy to be significant, but it did not analyze the level of intensity and duration in detail. Based on the results, it seems like ”more is more” when it comes to intensity early in pregnancy and duration late in pregnancy. Also other studies have concluded that higher intensity and longer duration are preferred when examining the association between exercise and risk of developing GDM (10, 15, 17, 18). In 2012, Ruchat et al. studied the optimal intensity and duration of exercise for pregnant women to achieve the greatest capillary glucose clearance (47). The conclusion appeared to be depending on at which risk the pregnant woman was: a pregnant woman at high risk of developing GDM could choose to exercise vigorously for 25 minutes, or less intense for 35-40 minutes. A 25-min session of either low or vigorous intensity was also enough for a low-risk woman, but an increase of intensity or duration seemed to have less or no further impact of the glucose clearance compared to the high-risk woman. Aune et al. (2016) concluded in a dose-response analysis of exercise during pregnancy that the main reduction in risk occurred up to the level of 5-8 h/week of exercise, while the reduction seemed to diminish above 8 h/week (12). The association was steepest in the lower levels of exercise. Dempsey et al. (2004) found similar results and concluded with a steep risk-reducing effect up to 4 h/week and a plateauing effect-appearance above that (17).

The results were controlled for some of the most established known risk factors for GDM and thereby are the associations valid for women independentely of age, pre-pregnancy BMI and family history of GDM and/or DMt2. Taken that into consideration, it could add a timing aspect to the recommendation of intensity and duration of how to most efficiently prevent the development of GDM. A higher intensity was, according to Ruchat et al. (2012), of more importance to high-risk pregnant women than low-risk (47). The present study suggests that high-intensity exercise early in pregnancy is of importance for all pregnant women, regardless of risk level. Additionally, Ruchat et al. (2012) recommended women at low risk of developing GDM to exercise for 25 minutes per session (47) and it goes into the same direction as the ≥30 minutes of exercise that was set as duration minimum in the present study.

When including all the three significant exercise characteristics (pre frequency, T1 intensity, T2 duration) in the same model, only duration late in pregnancy witheld its significance. Apparentely frequency before and intensity early in pregnancy lost their importance when analyzed with other variables. It might be a sign of non-neglectable interaction between the variables: women who are more often physically active are also performing exercise at a higher intensity and for a longer time. This interaction might make the model unreliable and too weak to base more specific exercise recommendations on and more research is needed. In future studies it is important to accurately separate the different exercise characteristics at trials and thereby avoid risk of variable interaction.

Women in the present study reduced their exercise level early in pregnancy compared to before pregnancy, and then seemed to resume regular exercise in the later part of pregnancy. These findings harmonize with the conclusion of a study made by Nascimento et al. (2015) where the proportion of women performing regular exercise during pregnancy was reduced compared to before pregnancy (43). The lowest exercise levels were seen in the first and third trimester where only 13 % of the pregnant women exercised (43). In the present study, the proportion of women who performed regular exercise were 51.9 % early in pregnancy and 68.2 % late in pregnancy – a considerable larger proportion compared to the data of Nascimento et al. (2015). An explanation to the disparity between the research results might be the difference in pre-pregnancy exercise level: 23.2 vs 71.2 % in Nascimento and the present study, respectively. Another possible explanation could be different definitions of regular exercise. However, Nascimento et al. (2015) defined women as exercising when performing exercise for 30 minutes or more at least twice a week – an exercise level even lower than the requirement set in the present study (≥30 minutes minimum three times per week). Intuitively, it is contradictory that a lower exercise requirement would justify a lower proportion of active women and thereby this explanation is excluded.

The results of this cohort study have strengths and weaknesses. Advantages were a prospective study design, the usage of an OGTT – the golden standard when detecting glucose intolerance, the large amount of participants and a low dropout rate among the included women. Though diverseness in several basic characteristics, it should be noted that only Caucasian women with low-risk pregnancies were included in the study and a generalization to other ethnicities and risk groups should be done with caution. Additionally, many of the participating women were highly educated and few were overweight at inclusion and it might make the results less applicable to women of other educational and weight level. The risk factors controlled for were maternal age, T1 BMI and GDM/DMt2 in close family. BMI at inclusion (T1, gestational week 18-22) was chosen in favour of pre-pregnancy BMI, since T1 body weight was recorded while pre-pregnacy body weight was entered by the women themselves and the risk of recall bias was considered to be present. At T1, some pregnancy-induced weight gain probably already had occurred, but it was expected to be of acceptable magnitude and a homogenous increase within the study group. Though the T1 BMI might be higher than pre-pregnancy BMI, it was considered more important to use a recorded than self-reported weight. Other features, such as large gestational weight gain (GWG) – especially early in pregnancy (29, 48, 49) – and high BMI in first trimester (50) have by some been stated to be risk factors for GDM. In contrary, other studies imply that excessive post-delivery weight retention and consequently higher pre-pregnancy BMI in subsequent pregnancies is the real cause of risk enlargement (51) and that GWG itself does not increase the GDM risk (52). Because of the heterogenic conclusions, GWG was not included in the models.

It should also be noted that in the models used, the amount of included subjects reduced compared to the total 855 included women because of missing data from one or several utilized variables, and the amount of studied women also differed between analyzes for different exercise characteristics.

Another weakness was that exercise data was self-reported. An objective measurement of activity would have been preferred, though also adding higher demands on administration and economy. In the exercise questionnaires, the women could only choose pre-defined categories of duration. Categorization itself facilitates the data interpretation and delineation of larger tendencies, but it might also influence the answers, and secondarily the results, if the pre-defined categories did not apply to the women.

Conclusion

The findings of the present study indicate that regular exercise (defined as a minimum of three days per week with moderate to high intensity) before pregnancy has a positive effect on glucose tolerance in late pregnancy and thereby a preventive effect on the development of GDM. No such association was found for similar regular exercise during pregnancy. The present study did not conclude on which exercise characteristic is most important of frequency, intensity and duration.

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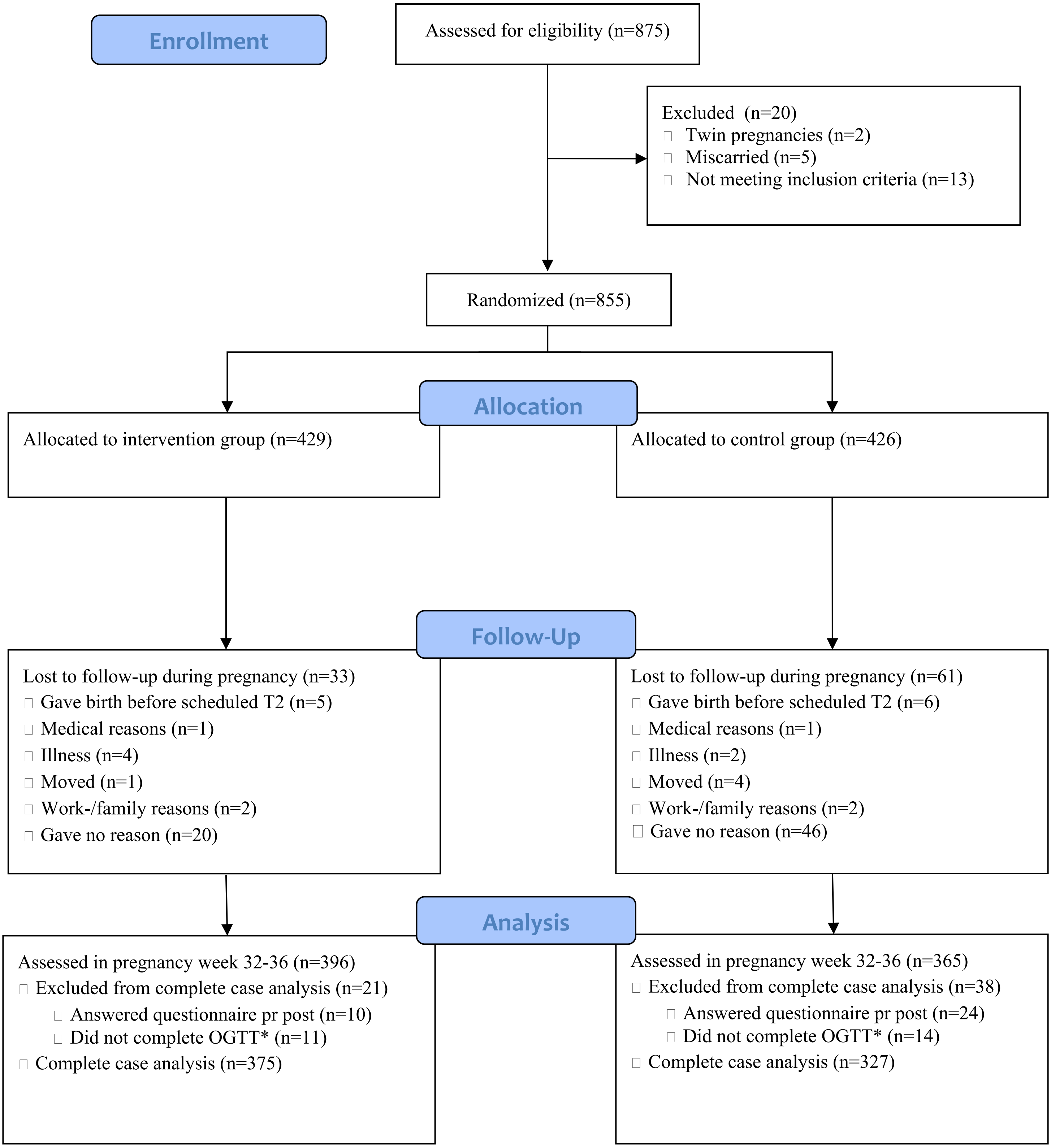
Figure 1. Flow chart of study participants.



*OGTT, oral glucose tolerance test.

Table 1. Baseline characteristics of the study population, showing mean values for variables at pre-pregnancy, early and late in pregnancy.

	Pre-pregnancy	Early (T1)	Late (T2)
Age (yrs)		30.5 ±4.3	
Parity			
0		486 (56.8)	
1		254 (29.7)	
≥2		115 (13.5)	
Educational level			
≤ 13 yrs ground school		95 (11.1)	
≤ 4 yrs university		331 (38.7)	
> 4 yrs university		429 (50.2)	
Civil state			
single		20 (2.3)	
partner/married		834 (97.5)	
BMI (kg/m^2)	23.2±3.2	24.8±3.2	27.2±3.3
Weight (kg)	65.8±9.9	70.6±10.1	77.4±10.2
GWG (kg)			14.2±5.1
DM in close family		64 (7.5)	
Mother with GDM		7 (0.8)	
Fasting glucose (mmol/L)		4.3 (±0.36)	4.3 (±0.40)
OGTT 2-h glucose (mmol/L)		4.9 (±1.01)	5.7 (±1.21)
HOMA-IR		2.0 (±1.01)	2.7 (±1.45)
Ex: frequency (days/w)			
no training	246 (28.8)	411 (48.1)	272 (31.8)
1	125 (14.6)	119 (13.9)	57 (6.7)
2	209 (24.4)	191 (22.3)	139 (16.3)
3	190 (22.2)	82 (9.6)	243 (28.4)
4	60 (7.0)	29 (3.4)	23 (2.7)
≥5	25 (2.9)	23 (2.7)	26 (3.0)
Ex: intensity			
low	22 (2.6)	94 (11.0)	91 (10.6)
middle	337 (39.4)	303 (35.4)	359 (42.0)
high	250 (29.2)	46 (5.4)	32 (3.7)
Ex: duration (minutes)			
0-30	17 (2.0)	49 (5.7)	53 (6.2)
30-60	368 (43.0)	300 (35.1)	342 (40.0)
60-90	212 (24.8)	83 (9.7)	87 (10.2)
> 90	11 (1.3)	9 (1.1)	1 (0.1)
Overall ex.[a]	269 (31.5)	110 (12.9)	253 (29.6)

BMI, body mass index; GWG, gestational weight gain; DM, diabetes mellitus; GDM, gestational diabetes mellitus; OGTT, oral glucose tolerance test; HOMA-IR, homeostastic model assessment – insulin resistance; Ex, exercise.

[a] Overall exercise defined as exercising at moderate to high intensity a minimum of three days per week.

Table 2. Associations between 2-hour glucose level in late pregnancy (i.e. pregnancy week 32-36) and characteristics of exercise at three timepoints: pre-, early (T1) and late (T2) pregnancy.

	Univariable analysis		**Multivariable analysis** Including single variable and known risk factors for GDM[a]		**Multivariable analysis** Including all significant variables and known risk factors for GDM[a]	
	Beta (95% CI)	***p*-value**	**Beta (95% CI)**	***p*-value**	**Beta (95% CI)**	***p*-value**
Pre						
frequency	-0.070 (-0.134, -0.006)	0.032*	-0.073 (-0.137, -0.010)	0.024*	-0.039 (-0.153, 0.074)	0.495
duration	0.023 (-0.159, 0.205)	0.805	0.034 (-0.147, 0.214)	0.714	-	-
intensity	-0.068 (-0.253, 0.116)	0.467	-0.010 (-0.196, 0.177)	0.920	-	-
T1						
frequency	-0.063 (-0.129, 0.004)	0.065	-0.062 (-0.129, 0.004)	0.067	-	-
duration	-0.042 (-0.248, 0.165)	0.691	-0.007 (-0.207, 0.193)	0.945	-	-
intensity	-0.300 (-0.522, -0.079)	0.008**	-0.278 (-0.500, -0.057)	0.014**	-0.248 (-0.515, 0.020)	0.069
T2						
frequency	-0.051 (-0.113, 0.011)	0.104	-0.042 (-0.104, 0.020)	0.183	-	-
duration	-0.323 (-0.527, -0.118)	0.002**	-0.313 (-0.516, -0.110)	0.003**	-0.295 (-0.551, -0.040)	0.024*
intensity	-0.088 (-0.313, 0.137)	0.443	-0.084 (-0.307, 0.139)	0.460	-	-

* = p<0.05, ** = p<0.01. Pre, pre-pregnancy; CI, confidence interval; GDM, gestational diabetes mellitus.

[a] Included known GDM risk factors are maternal age, BMI at T1 and family history of DM or GDM.

Table 3. Associations between 2-hour glucose level in late pregnancy (i.e. pregnancy week 32-36) and performing exercise for a minimum of 30 min or more per session, 3 days or more per week, on moderate to high intensity.

	Univariable analysis		Multivariable analysis Including single variable and known risk factors for GDM[a]	
	Beta (95% CI)	***p*-value**	**Beta (95% CI)**	***p*-value**
Pre	-0.219 (-0.409, 0.030)	0.023*	-0.194 (-0.383, 0.006)	0.043*
T1	0.022 (-0.241, 0.286)	0.867	0.012 (-0.249, 0.272)	0.931
T2	-0.093 (-0.281, 0.095)	0.331	-0.068 (-0.254, 0.117)	0.470

* = $p<0.05$. Pre, pre-pregnancy; CI, confidence interval; GDM, gestational diabetes mellitus.

[a] Included known GDM risk factors are maternal age, BMI at T1 and family history of DM or GDM.