



## Exercise and gestational diabetes mellitus

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### Abstract

*Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance of any degree first manifested during pregnancy. It is related to a numerous complications and adverse outcomes during pregnancy. The primary goals of treatment are to achieve acceptable glycemic control and improve pregnancy outcomes, with changes in diet and lifestyle as primary therapeutic strategies. Exercise of moderate intensity is recommended for all pregnant women without contraindications, including those with GDM. The purpose of this article is to provide an overview of preventive and therapeutic effects of exercise before and during pregnancy on the incidence, course and outcomes of GDM. Data on preventive and therapeutic effects of exercise before and during pregnancy are mainly based on cohort studies and a small number of randomized controlled trials. Cohort studies relate higher levels of physical activity before and during early stages of pregnancy with lower incidence of GDM. Aerobic exercise and resistance training after the diagnosis of GDM have some beneficial effects on glycemic control parameters and the need to apply insulin therapy. Definitive effects of exercise for GDM prevention and management are still uncertain and the optimal exercise parameters need to be determined. Exercise before and during pregnancy might reduce GDM incidence and improve the course and the outcomes of GDM, but more randomized clinical trials are needed in this area.*

### INTRODUCTION

Pregnancy is characterised by a numerous anatomical, physiological and biochemical adaptations which begin soon after conception and continue throughout the course of the pregnancy (1). Most of these adaptations are a response to the physiological stimuli of the fetus and placenta. Insulin resistance, caused by placental hormones and cytokines, including tumor necrosis factor alpha (TNF- $\alpha$ ), human placental lactogen (hPL), placental growth hormone (PGH), cortisol and progesterone, is one of the most significant metabolic changes during pregnancy (2, 3). This provides increased quantities of glucose to the fetus, but also adaptively increases pancreatic  $\beta$ -cells function and insulin secretion. In susceptible pregnant women this leads to a slow progressive insulin secretion failure (4).

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance of any degree first manifested during pregnancy (5). Hyperglycemia in GDM is related to  $\beta$ -cells insufficiency as well as increased insulin resistance. GDM occurs due to reduced adaptation of  $\beta$ -cells when insulin secretion is insufficient in relation to insulin resistance (2).

Prevalence amounts from 1% to more than 20% of all pregnancies, depending on diagnostic criteria and the studied population, with increasing trend which is parallel to the increase of obesity and type 2 diabetes mellitus (T2DM) prevalence (6 - 10). Main difference between GDM and T2DM is rapid onset during pregnancy and remission after birth.

GDM is related to a numerous complications and adverse outcomes during pregnancy and delivery such as preeclampsia, prolonged labour, and higher rate of cesarean section, macrosomia, cephalopelvic disproportion, uterine rupture, shoulder dystocia and perineal laceration (11 - 13). Even a mild degree of hyperglycemia is related to adverse outcomes (12, 14). In the long term, GDM carries risks for the mother and child. Newborns of women with GDM have higher risk of obesity, glucose intolerance, metabolic syndrome and T2DM (10, 15, 16). Women with GDM in their medical history have 7-8 higher risk of developing T2DM (17, 18).

The primary goal of treatment is achievement of acceptable glycemic control and improvement of pregnancy outcomes (19). Primary therapeutic strategies are changes in diet and lifestyle (5, 10, 20). If necessary, pharmacological therapy is introduced. Exercise of moderate intensity is usually recommended for all pregnant women without contraindications, especially those with GDM (5, 10, 20). Physical activity in the prevention and management of T2DM in general population is proven to be beneficial (10, 21). However, there are not many findings on preventive and therapeutic effects of exercise on incidence, course and outcomes of GDM. Available data are based on a small number of randomized controlled trials and cohort studies.

The purpose of this review is to provide an overview of preventive and therapeutic effects of exercise before and during pregnancy on the incidence, course and outcomes of GDM. It provides an overview of the current evidence on the relation between exercise and GDM as well as clinical implications of prescribing exercise and future research design.

## PREVENTIVE EFFECTS OF EXERCISE

Data on preventive effects of exercise before and during pregnancy are mainly based on cohort studies and a small number of randomized controlled trials. There was only one randomized trial on the preventive effects of exercise on the occurrence of GDM and insulin resistance conducted on healthy pregnant women (22). Although sample was large (N=855), only 55% of women in the experimental group (N=375) managed to follow recommended exercise regimen, a 12-week exercise programme during second half of the pregnancy. Pregnancy outcomes were similar for both groups and authors concluded that exercise did not help prevent GDM or improve insulin resistance.

Another two trials studied effects of exercise on insulin resistance, blood glucose and insulin levels on healthy pregnant women (23, 24). These trials were conducted on small samples and were not powered enough to measure GDM incidence as an outcome. Hopkins *et al.* (23) examined effects of exercise during second half of the pregnancy on maternal insulin sensitivity and neonatal outcomes and Callaway *et al.* (24) studied fasting glucose and insulin levels and insulin resistance. Both Hopkins *et al.* (23) and Callaway *et al.* (24) did not find statistically significant differences in maternal insulin sensitivity, but Callaway *et al.* (24) found statistically significant differences in fasting glucose and insulin levels in 28<sup>th</sup> and 36<sup>th</sup> week of pregnancy.

Cohort studies relate higher levels of physical activity before and during early stages of pregnancy with lower incidence of GDM (25). Risk of GDM is decreased by 20-55% in women who have participated in exercise programmes of various duration and intensity, before and during the pregnancy (26-28). Women in the quintile of highest physical activity before pregnancy have 55% lower risk of GDM opposed to those in lower quintiles and women who were the most active during early pregnancy have 24% lower risk of GDM occurrence (25). Strenuous physical activity in the year before the pregnancy lowers the risk of GDM and abnormal glucose tolerance, and continuation with mild or moderate physical activities during pregnancy even more reduces the risks of developing GDM and abnormal glucose tolerance as opposed to physically inactive women in these periods (27). Other studies also confirmed strong relation between physical activity before pregnancy and a reduced risk of GDM with highest risk reduction for those physically active before and during the pregnancy (28, 29).

Walking and stair climbing before and during early pregnancy are also inversely related to the risk of developing GDM (28, 29). Beginning physical activity after conception in pregnant women who were previously inactive also reduces the risk of developing GDM (30). Low intensity exercise, if combined with food intake control, reduces the risk of GDM and regulates blood glucose levels (31, 32).

## THERAPEUTIC EFFECTS OF EXERCISE

Scientific evidence for benefits of exercise for T2DM management is quite strong (33, 34), which is not the case for GDM. There are only seven published prospective trials on the effects of exercise on the course and outcomes of GDM, five of which are randomized controlled trials (35 - 39) and two non randomized (40, 41).

Effects of aerobic exercise programme were examined in five trials (35 - 37, 40, 41). Only two trials examined the role of resistance exercise (38, 39) and none examined effects of combined aerobic and resistance exercise. Mea-

sured outcomes were pregnancy and perinatal complications, glycemic control parameters (fasting glucose level, OGTT, HbA1c, glucose level maintenance within recommended values) and need for insulin therapy.

A total of 304 pregnant women were included in these trials and exercise intervention was conducted mostly in the third trimester, lasting approximately six weeks. Type, frequency, intensity and duration of exercise intervention varied between trials. Exercise intervention was mostly conducted three times a week for 20–45 minutes. In most trials there were statistically significant differences in glycemic control parameters or the need to apply insulin therapy (35, 36, 38, 39, 41).

Six weeks of aerobic exercise of moderate intensity performed three times a week reduces levels of HbA1c, fasting glucose and plasma glucose level one hour after glucose ingestion (35). Experimental group who exercised three times a week for 45 minutes during the period of 8 weeks managed to maintain euglycemia without introducing insulin therapy and without significant statistical differences in the rate of maternal and neonatal complications, compared to pregnant women in control group who did not exercise, but were treated with insulin therapy (36). Artal *et al.* (40) compared dietary therapy versus seven days a week of exercise and dietary therapy. They did not find any differences in the need for insulin therapy, however, maternal body mass increase was significantly lower in the experimental group. Walking intervention 3–4 times a week during at least 6 weeks significantly reduces mean fasting glucose level and glucose level one hour after meal in the last week of pregnancy while requiring fewer units of insulin per day (41).

Resistance training performed three times a week can also be beneficial. Pregnant women who exercised in the experimental group required lower dosage of insulin and insulin therapy was introduced at a later stage of pregnancy (38). Another trial on effects of resistance exercises were performed by de Barros *et al.* (39) with similar results. Experimental group who exercised three times per week displayed significant differences in insulin use and was more successful in maintaining glucose levels within recommended values in comparison to control group. No significant differences were recorded for body mass increase, gestational age at birth and the number of cesarean sections between the experimental and control group.

## DISCUSSION AND CONCLUSIONS

Significant number of pregnant women affected by GDM every year, its growing prevalence and established relationship to numerous complications and disorders during and after the pregnancy demand identification of factors that can prevent the incidence and influence its course. Exercise has many health related benefits and it is proven method for effective prevention and treatment of T2DM. It reduces insulin resistance in non pregnant

population and normalizes blood glucose levels in diagnosed individuals. Also, it can prevent or postpone disease in high risk persons. However, for a long lasting effect exercise must be regular (42).

Physical inactivity is known risk factor for obesity and T2DM which have reached epidemic proportions in modern society (43, 44). Obese women have 17% higher risk for GDM (44). Exercise prevents excessive weight gain during pregnancy. Another risk factor for both obesity and GDM is sedentary lifestyle. Both obesity and GDM are risk factors for T2DM. Only about 50% of non pregnant women follow recommendations for minimum level of physical activity and this percentage drops even further during pregnancy (45). Regular exercise before and during pregnancy can significantly reduce GDM prevalence and it might also have therapeutic effect on the course and outcomes of GDM.

Number of people diagnosed with diabetes mellitus is expected to rise from 366 million in 2011 to 552 million by 2030, if no urgent action is taken (46). Preventive and therapeutic effects of exercise could be very important due to vast health and economic implications of diabetes mellitus, obesity, and other diseases related to physical inactivity.

Aerobic training is effective in improving sensitivity to insulin and glycemic control in T2DM (33). Latest evidence also indicates beneficial impact of resistance exercises which makes them an important part of therapeutic and preventive exercise programmes for T2DM (34). Definitive clinical effect of exercise therapy for GDM prevention and management still cannot be established with certainty. The optimal frequency, intensity, type and duration of exercise programmes still need to be determined. Evidence from randomized controlled trials is still insufficient and although promising, further trials are necessary. Regular exercise could have more important role in GDM prevention before and during early pregnancy than during the second half of the pregnancy which is probably the result of chronic adaptations to glucose uptake regulation in skeletal muscles and better tolerance of metabolic stress during pregnancy. However, randomized controlled trials on preventive effects of exercise throughout all stages of pregnancy are yet to be conducted. Most findings originate from observational studies. Also, impact of combined aerobic and resistance exercise programmes are still not known. Further trials should compare aerobic and resistance exercise as well as the combination of the two.

Randomized controlled trials of exercise effects on prevention and management of GDM are accompanied by a number of methodological issues with adherence to protocol being the most significant. Feasibility of exercise intervention should be taken into consideration before conducting the study because in previous studies there have been relatively frequent subject withdrawals before

study completion as well as incomplete implementation of interventions. Other possible problems are incomplete randomization, small sample size and insufficient control of exercise parameters.

In conclusion, definite clinical significance of preventive and therapeutic exercise programmes is still to be determined. Optimal frequency, intensity, type, duration and period of implementing exercises (before, early or late pregnancy) are still not known. Specific benefits of exercise before and/or during the pregnancy as well as benefits of beginning exercise programme after conception for previously inactive women and for different groups of pregnant women, with and without risk factors cannot be determined. More research is necessary in this area. Exercise during pregnancy might reduce GDM incidence and its adverse effects, improve the course and the outcomes of GDM as well as prevent risks of T2DM, obesity and transmission of morbidity from one generation to the next.

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