Owe, K., Nystad, W., Bø, K. (2009). Association between regular exercise and excessive newborn birth weight. *Obstetrics and gynecology, 114*, 770-776.

ASSOCIATION BETWEEN REGULAR EXERCISE AND EXCESSIVE INFANT BIRTH WEIGHT. THE NORWEGIAN MOTHER AND CHILD COHORT STUDY

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Acknowledgement

The Norwegian Mother and Child Cohort Study is supported by the Norwegian Ministry of Health, NIH/NIEHS (grant no. N01-ES-85433), NIH/NINDS (grant no. 1 UO1 NS 047537-01), and the Norwegian Research Council/FUGE (grant no. 151918/S10). We acknowledge the services of the Medical Birth Registry of Norway.

Key words: birth weight, cohort study, physical activity, pregnancy, regular exercise.

Running foot: Regular exercise and excessive infant birth weight

Précis: Women exercising regularly during pregnancy are less likely to give birth to infants with an excessive birth weight**.**

ABSTRACT

Objective: To estimate the association between regular exercise before and during pregnancy, and excessive infant birth weight.

Methods: Using data from the Norwegian Mother and Child Cohort Study (MoBa), 36,869 singleton pregnancies lasting at least 37 weeks were included. Information on regular exercise was based on answers from two questionnaires distributed in pregnancy weeks 17 and 30. Linkage to the Medical Birth Registry of Norway (MBRN) provided data on infant birth weight. The main outcome measure was excessive infant birth weight, defined as birth weight at or above the 90th percentile. Logistic regression analyses were used to estimate the associations separately for nulliparous (n=16,064) and multiparous (n=20,805) women, and the results are presented as adjusted odds ratios (aOR) with 95% confidence intervals (95% CI).

Results: Excessive infant birth weight was observed in 4033 (10.9%) infants, 56.1% (n=2263) of whom were born to multiparous women. An inverse association between regular exercise (≥3 times pr week) and excessive infant birth weight in pregnancy weeks 17 and 30 was observed in nulliparous women, aOR=0.72 (95% CI 0.56-0.93) and aOR=0.77 (95% CI 0.61-0.96), respectively. Regular exercise performed before pregnancy did not affect the probability of delivering infants with an excessive birth weight in nulliparous or multiparous women.

Conclusion: Regular exercise during pregnancy reduces the odds of giving birth to newborns with excessive birth weight.

Introduction

Fetal macrosomia, often defined as birth weight above 4000 or 4500 g regardless of gestational length (1), is associated with both maternal and perinatal complications. When birth weight exceeds 4000 g, both mother and infant are at greater risk for morbidity including perineal lacerations, postpartum hemorrhage, caesarean section, shoulder dystocia, low Apgar score, birth trauma and obesity (2-4). Several studies show that both mean birth weight and the proportion of infants weighing over 4000 g and 4500 g have increased during the last decades (5;6).

Evidence-based guidelines indicate that regular exercise is an important component of a healthy pregnancy (7). However, recent studies show a decreasing trend of regular exercise during pregnancy (8;9). Both frequency and the intensity of exercise seem to decrease as pregnancy progresses (10;11), and most pregnant women shift from weight bearing to non-weight bearing exercises such as swimming and bicycling (12). Despite an extensive literature on the relationship between regular exercise during pregnancy and mean birth weight, the results are ambiguous and lack consistency. Both a positive (13-15) and negative association with infant birth weight have been suggested (16-18). A few studies also report no difference in birth weight of infants born to exercising and non-exercising mothers (19;20).

The aim of the present study was to estimate, in a prospective cohort of pregnant women, the association of regular exercise, performed before and during pregnancy, with excessive infant birth weight.

Methods and materials

The data used for this study are derived from the Norwegian Mother and Child Cohort Study (MoBa) conducted by the Norwegian Institute of Public Health (21). MoBa is a nationwide pregnancy cohort that aimed to include 100,000 pregnancies by 2008 and was designed to estimate the associations between some of the lifestyle variables to which pregnant women and their fetuses are exposed in addition to diseases (22). Pregnant women are recruited into the study through a postal invitation two weeks ahead of their routine ultrasound examination at gestational week 17 at their local hospital. Data are obtained from 50 out of 52 maternity units in Norway (21). The overall participation rate for the present data file is 45%. However the follow-up rate from inclusion to questionnaire 3 is 92%. The present study includes pregnancies enrolled between June 1, 2001 and May 31, 2005.

Participants receive three questionnaires during pregnancy weeks 17 and 30 (Q1, Q2 and Q3). Q1 includes items of maternal health status, lifestyle behaviors, previous diseases, and medication covering both prepregnancy and the first weeks of pregnancy. Q2 is a Food Frequency Questionnaire (FFQ) and is mailed together with the invitation and Q1 in week 17. Q3, which is sent out in week 30, focuses mainly on health outcomes during pregnancy and follows up some of the questions from Q1. One reminder is sent by mail if the questionnaires have not been returned within two weeks. Linkage to the Medical Birth Registry of Norway (MBRN) was also provided. The questionnaires are available at www.fhi.no/morogbarn. Informed consent was obtained from each participant before inclusion. The study has received approval from the Regional Committees for Medical Research Ethics (S-95113) and The Norwegian Social Science Data Services (01/4325-6).

The second version of the quality-assured data-file released for research in April 2006 provided data that were used in the present study. Both Q1 and Q3 had to be answered in order for the women to be included (n=40,049). The record in the Medical Birth Registry of Norway (MBRN) (23) from the present pregnancy, and energy intake (MJ/day) from Q2 were also linked to the MoBa data set. Pregnancies with missing information on year of birth were omitted from the analyses (n=142). We also excluded multiple pregnancies (n=723) and pregnancies ending before 37 weeks of gestation (n=2315), leaving 36,869 pregnancies which constitute the study population.

The main outcome measure was excessive infant birth weight as registered in the MBRN. There is no widely agreed upon definition of fetal macrosomia or excessive infant birth weight. To account for the increasing birth weight with increasing parity, we defined birth weight to be excessive if it was equal to or above the 90th percentile (i.e. 4170 g and 4362 g for nulliparous and multiparous women, respectively).

The main exposure was regular exercise before and during pregnancy weeks 17 and 30, defined in terms of frequency. In both questionnaires Q1 and Q3, the participants were asked how often they engaged in the following exercises: strolling, brisk walking, running (jogging or orienteering), bicycling, fitness training in training centers, swimming, aerobic classes (low or high impact), prenatal aerobic classes, dancing (swing, rock, folkdance), skiing, ball games, horseback riding and other. For all exercises, the respondents were asked to report frequency with the following categories: “never”, “1-3 times per month”, “once a week”, “twice a week”, and “≥3 times a week”. Strolling was excluded from the analysis due to its very low energy expenditure (24). Regular exercise participation before pregnancy was collected retrospectively in pregnancy week 17 (Q1). The respondents were asked to recall the type and frequency of exercises performed during the last three months before the present pregnancy. The questions on recreational exercise have shown moderate correlations with motion sensor measurements (25).

Potential confounders of excessive birth weight were selected by cross-tabulations and literature review (26). The following confounders of excessive birth weight were evaluated: maternal age, maternal education, parity, hypertension, diabetes, gestational weight gain, BMI prepregnancy (both as a continuous and categorical variable), preeclampsia, smoking habits, and maternal height (5;27;28). Diabetes was defined as either preexisting diabetes or gestational diabetes of any kind. Hypertension was defined as any pregestational or gestational hypertensive disorder complicating pregnancy. Preeclampsia was defined as any diagnosis of preeclampsia. All diagnoses were based on ICD-9 codes from MBRN records. Parity was collected from MBRN, and was defined in terms of earlier pregnancies lasting more than 20 weeks (29). Gestational length was also retrieved from MBRN and was based on a combination of ultrasound scanning and last menstrual period (LMP). Body mass index (BMI) was calculated from self-reported body weight (Q1) and height (Q1), and categorized according to the WHO: '<18.5', '18.5-24.9', '25-29.9', '30-34.9', '35+'. Total gestational weight change was calculated as the difference between the last pregnancy weight before 30 weeks of gestation and the self-reported weight when pregnancy started. Energy intake (MJ/day) was assessed using a FFQ (Q2) and the cut-off intervals for energy intake presented by Meltzer et al. (30) were utilized.

All analysis was carried out in the statistical software program, SPSS, version 15.0 for Windows (SPSS, Chicago, IL). Three logistic regression models were used to investigate the association between regular exercise before (Model A) and during pregnancy (Model B and C) and excessive infant birth weight. All models adjusted for maternal age, education, BMI prepregnancy and current smoking habits. Model B, which assessed the association between regular exercise in week 17 and excessive infant birth weight, additionally adjusted for exercise prepregnancy, gestational weight change, energy intake (MJ/day), and preexisting diabetes/ gestational diabetes mellitus. Lastly, the association between regular exercise in week 30 and excessive infant birth weight was assessed in Model C, additionally adjusting for exercise prepregnancy, exercise in week 17, total gestational weight change, energy intake (MJ/day), preeclampsia and preexisting diabetes/ gestational diabetes mellitus. Further, to investigate which types of exercises were associated with excessive infant birth weight, we used stepwise logistic regression adjusting for the same covariates as in Models A-C.

To evaluate the hypothesis that the odds of giving birth to infants with an excessive birth weight continues to increase with further increases in regular exercise (frequency), we conducted tests for trends by treating the category numbers of regular exercise as an interval-scale variable in the logistic regression models (Wald test).

The possible interaction between maternal height and regular exercise on excessive infant birth weight was estimated using stratification and multiplicative interaction term. Maternal height was dichotomized at the population median of 1.68 m and regular exercise was dichotomized at a frequency of ≥3 times per week, before estimating the association between regular exercise before and during pregnancy and excessive infant birth weight. However, we did not detect an interaction between maternal height and regular exercise before or during pregnancy on excessive infant birth weight. Furthermore, we explored whether parity might modify the association between regular exercise and excessive infant birth weight using stratification. This was done due to the observation that nulliparous women exercise more frequently than their multiparous counterparts (11;12). Hence, the results are presented separately for nulliparous and multiparous women.

Results

Mean birth weight in this cohort was 3682 g (SD 488). Among the 36,869 pregnancies included, 4033 (10.9%) infants had a birth weight equal to or above the 90th percentile. A higher number of infants with an excessive birth weight were born to multiparous women (n=2263) compared to nulliparous women (n=1770).

The distribution of maternal characteristics by parity is given in Table 1 and shows that nulliparous and multiparous women did not differ significantly in height, education, smoking habits or diabetes. Nevertheless, nulliparous women were younger, had a lower energy intake (-0.23 MJ/day) ($p<.001$), gained more weight during pregnancy ($p<.001$), and their offspring had a lower mean birth weight compared to offspring of multiparous women ($p<.001$). The highest proportion of overweight women (BMI >24.9), non-exercisers and excessive infant birth weight was seen in multiparous women.

Regular exercise performed 3 months before the present pregnancy did not affect the probability of delivering a high birth weight infant in nulliparous or multiparous women (Table 2 – Model A). A moderate protective effect of regular exercise during pregnancy was observed in nulliparous women, irrespective of time of exposure (week 17 or 30) (Table 2 – Models B and C).

Nulliparous women exercising at least 3 times a week in pregnancy week 17 were less likely to give birth to an infant with an excessive birth weight (p for trend=.008) (Table 2 – Model B). Adjustment for hypertension and preeclampsia did not change the observed association between regular exercise in week 17 and excessive infant birth weight.

In week 30, nulliparous women exercising 1-2 times a week were less likely to deliver infants with an excessive birth weight compared to non-exercisers, but this association was attenuated when we adjusted for gestational weight change independent of diabetes. The adjusted association reached significance only for nulliparous women exercising at least 3 times a week in pregnancy week 30 (Table 2 – Model C).

Walking (aOR=0.86, 95% CI 0.75-0.99) and running (aOR=0.63, 95% CI 0.45-0.89) in week 17 were negatively associated with excessive infant birth weight in nulliparous women. Walking in week 30 was also negatively associated with the outcome (aOR=0.84, 95% CI 0.73-0.96) (data not shown).

Multiparous women who participated in dancing in week 17 were less likely to deliver infants with an excessive birth weight (aOR=0.75, 95% CI 0.63-0.90), whereas training in fitness centres in week 17 was positively associated with excessive infant birth weight (aOR=1.16, 95% CI 1.00-1.35). In week 30, low impact aerobics (aOR=0.68, 95% CI 0.47-0.97) and dancing (aOR=0.69, 95% CI 0.53-0.88) were negatively associated with excessive infant birth weight. Multiparous women participating in swimming in week 30 were more likely to give birth to an infant with an excessive birth weight (aOR=1.16, 95% CI 1.04-1.30) compared to those who didn't swim (data not shown).

Discussion

In this large prospective pregnancy cohort study, nulliparous women performing a high level of exercise during pregnancy were less likely to give birth to infants with an excessive birth weight. The highest number of infants with excessive birth weight was observed in multiparous women. Interestingly, independent of parity, there seems to be an increasing trend of a protective effect with increasing frequency of regular exercise during pregnancy.

The results indicate that regular exercise during pregnancy may have a protective effect on excessive infant birth weight and this association tends to be different with parity. Excluding women with preexisting diabetes/ gestational diabetes or preeclampsia from the analysis did not change the estimates substantially. As expected, regular exercise performed during pregnancy seems to have a greater influence on the upper extreme of the birth weight distribution compared to regular exercise performed before pregnancy. Nonetheless, women exercising regularly before pregnancy are also more likely to continue their exercise programs during pregnancy. Based on this study, we cannot rule out that exercising regularly before pregnancy may also affect the upper extreme of the birth weight distribution.

The strengths of this study are the prospective design, study size and that the outcome was obtained from an external source, the NMBR (23). We therefore consider it unlikely that any misclassification due to imprecise measurements of the outcome influenced the results.

However, regular exercise was assessed indirectly by two self-administered questionnaires. Despite its limited accuracy and imprecision when it comes to assessing exercise duration and intensity, postal questionnaires are considered the most feasible method for assessing frequency of physical activity in large epidemiological studies (31). Because of the prospective data collection, misclassification of regular exercise in our study is most likely to be non-differential and would most likely have biased the association towards the null. The questions used to assess regular exercise in our study have recently been compared with position and motion sensor measurements of physical activity. A positive association between self-reported frequency of recreational exercise and objectively measured physical activity was observed, indicating that the questions used in MoBa can be useful for ranking pregnant women according to their exercise level (25).

In the adjusted analysis we strived to control adequately for possible confounding factors. Well known predictors of birth weight such as gestational diabetes and smoking did not change the estimates substantially. Only a few women with preexisting or gestational diabetes mellitus were identified in our study, and excluding these women, did not change the observed association between regular exercise and excessive infant birth weight. We therefore consider it unlikely that the effect estimates are confounded by these factors.

The literature available on the relationship between physical activity during pregnancy and *mean* birth weight has been inconsistent (13;16;17;32;33).

Nevertheless, a shift in *mean* birth weight may be of little relevance to the practicing obstetrician, whose main concern is directed towards the two extremes of the birth weight range where maternal and perinatal complications are increasing. If, for instance, a shift in mean birth weight is due to a factor exerting more, or all, of its influence at one extreme and little or none at the other, extrapolation from effects on mean values to other parts of the distribution can be misleading. Furthermore, a factor which only affects the spread of the birth weight distribution will make no difference to the mean but would increase (or decrease) the proportion at both extremes (34). Regular exercise may be an example of such a factor, rendering physical inactivity a risk factor for excessive infant birth weight. To date, data relating regular exercise before and during pregnancy to the risk of excessive infant birth weight are sparse. A moderate protective effect of regular exercise during pregnancy on excessive birth weight was observed in our study, which is in agreement with a case-control study by Alderman et al. (1998) (18), albeit a stronger protective effect was observed in their study. On the contrary, a recent study by Voldner et at. (2008) did not observe an association between level of physical activity during pregnancy and macrosomia risk (35). However, in contrast to these studies, our study is large and population based with a comprehensive prospective data collection. The discrepancy in findings between studies may be due to study design and size of study population in addition to different methods in defining type, intensity and frequency of regular exercise performed during pregnancy.

A possible mechanism behind our findings is the effect of aerobic exercise on glucose tolerance (36). Our observation that running, walking, dancing and low impact aerobics were negatively associated with excessive infant birth weight supports this hypothesis. Both randomized trials (37;38) and a prospective observational study (39) have shown that light-to-moderate physical activity during pregnancy may reduce glucose levels both in women with GDM and in non-diabetic pregnant women. Given the adverse maternal and prenatal complications associated with excessive infant birth weight, clinicians should promote regular exercise during pregnancy for the purpose of prevention (7). Nevertheless, neither a Cochrane review (40) nor search on PubMed revealed RCTs evaluating the effect of regular exercise during pregnancy on excessive infant birth weight. Although our results indicate a protective effect of regular exercise during pregnancy, there seems to be an urgent need for randomized controlled trials with high methodological and interventional quality to be carried out to study the causal relationship

Table 1: Demographic and medical characteristics of study participants by parity (N=36,869).

Mean (SD)	**Nulliparous (n=16,064)**	**Multiparous (n=20,805)**
Maternal height (cm)	168.2 (6.0)	168.1 (5.9)
Energy intake (MJ/day)	9.500 (2.609) †	9.730 (9.393)
Total gestational weight gain (kg)	9.463 (4.717) †	9.272 (4.500)
Birth weight (g)	3585 (472) †	3758 (489)
No. (%)		
Maternal age (yrs)		
<25	3750 (23.3)	1200 (5.8)
25-29	7171 (44.6)	6185 (29.7)
30-34	4082 (25.4)	9449 (45.4)
≥ 35	1061 (6.6)	3971 (19.1)
Education		
Primary school (9 yrs)	634 (3.9)	691 (3.3)
Secondary school (12 yrs)	5403 (33.6)	7099 (34.1)
College/ Univer (≥ 15 yrs)	8668 (54.0)	11245 (54.0)
Other	1295 (8.1)	1673 (8.0)
Prepregnancy BMI		
<18.5	534 (3.3)	515 (2.5)
18.5-24.9	10217 (63.6)	12476 (60.0)
25-29	3313 (20.6)	5139 (24.7)
30-34	1050 (6.5)	1566 (7.5)
35+	364 (2.3)	592 (2.8)
Smokers (week 17)	1613 (10.1)	2088 (10.1)

Prepregnancy Exercise		
Never	1434 (8.9)	2437 (11.7)
1-3 times per month	2654 (16.5)	4279 (20.6)
1-2 times a week	4568 (28.4)	6596 (31.7)
≥3 times a week	6961 (42.7)	6589 (31.7)
Missing	547 (3.4)	904 (4.3)
Exercise in week 17		
Never	2126 (13.2)	3544 (17.0)
1-3 times per month	2903 (18.1)	4675 (22.5)
1-2 times a week	4719 (29.4)	5990 (28.8)
≥3 times a week	5022 (31.3)	4475 (21.5)
Missing	1294 (8.1)	2121 (10.2)
Exercise in week 30		
Never	3910 (24.3)	7063 (33.9)
1-3 times per month	3042 (18.9)	4349 (20.9)
1-2 times a week	4424 (27.5)	4925 (23.7)
≥3 times a week	3844 (23.9)	3135 (15.1)
Missing	844 (5.3)	1333 (6.4)
Excessive Infant Birth weight	1120 (7.0)	2719 (13.1)
High blood pressure (Q1)	103 (0.6)	227 (1.1)
Pregnancy induced hypertension	730 (4.5)	812 (3.9)
Total preeclampsia incidence	698 (4.3)	434 (2.1)
Preexisting Diabetes	56 (0.3)	77 (0.4)
Total Gestational diabetes	125 (0.8)	167 (0.8)
Preexisting/ GDM	176 (1.1)	232 (1.1)

[†] $p<.001$

Table 2: Regular exercise and excessive birth weight (≥90th percentile) stratified by parity (36,864).

	NULLIPAROUS (n=16,064)			MULTIPAROUS (n=20,805)		
	% (freq.)†	**cOR (95% CI)**	**aOR (95% CI)***	**% (freq.)†**	**cOR (95% CI)**	**aOR (95% CI)**
Model A – Prepregnancy Exercise						
Never	12.3 (176)	1.00	1.00	10.9 (265)	1.00	1.00
1-3 pr month	12.8 (339)	1.05 (0.86-1.27)	0.96 (0.75-1.22)	11.0 (471)	1.01 (0.86-1.19)	1.02 (0.88-1.19)
1-2 pr week	10.6 (484)	0.85 (0.70-1.02)	0.86 (0.68-1.08)	11.4 (752)	1.06 (0.91-1.22)	1.10 (0.95-1.26)
≥3 pr week	10.3 (706)	0.82 (0.69-0.98)	0.85 (0.68-1.06)	10.6 (697)	0.97 (0.84-1.13)	1.05 (0.91-1.21)
missing	11.9 (65)	0.96 (0.71-1.30)	1.10 (0.76-1.58)	8.6 (78)	0.77 (0.59-1.01)	0.86 (0.67-1.10)
Model B – Exercise week 17						
Never	12.7 (271)	1.00	1.00	11.2 (398)	1.00	1.00
1-3 pr month	12.3 (357)	0.96 (0.81-1.14)	0.93 (0.74-1.18)	11.5 (536)	1.02 (0.89-1.18)	1.05 (0.91-1.22)
1-2 pr week	11.2 (529)	0.86 (0.74-1.01)	0.91 (0.73-1.14)	10.8 (646)	0.96 (0.84-1.09)	0.95 (0.83-1.10)
≥3 pr week	9.3 (465)	0.70 (0.60-0.82)	0.72 (0.56-0.93)	10.1 (450)	0.88 (0.77-1.02)	0.90 (0.76-1.07)

missing	11.4 (148)	0.88 (0.71-1.09)	0.93 (0.68-1.28)	11.0 (233)	0.98 (0.82-1.16)	1.12 (0.93-1.37)
Model C – Exercise week 30						
Never	13.1 (511)	1.00	1.00	11.1 (786)	1.00	1.00
1-3 pr month	11.5 (350)	0.87 (0.75-1.00)	1.04 (0.86-1.27)	11.1 (483)	1.00 (0.89-1.13)	1.02 (0.90-1.15)
1-2 pr week	10.4 (462)	0.78 (0.68-0.89)	0.90 (0.75-1.09)	11.0 (542)	1.00 (0.88-1.11)	1.00 (0.89-1.13)
≥3 pr week	8.5 (327)	0.62 (0.53-0.72)	0.77 (0.61-0.96)	9.4 (294)	0.83 (0.72-0.95)	0.96 (0.83-1.12)
missing	14.2 (120)	1.10 (0.89-1.37)	1.17 (0.87-1.58)	11.9 (158)	1.07 (0.90-1.29)	1.09 (0.90-1.32)

† The proportion of infants weighing above the 90th percentile within each response category.

* **Model A**: Adjusted for maternal age, education, BMI prepregnancy, and smoking status. Excluding women with preeclampsia or preexisting diabetes /Gestational Diabetes Mellitus (GDM) did not change the effect estimates.

* **Model B**: Adjusted for maternal age, education, BMI prepregnancy, smoking status week 17, prepregnancy exercise, gestational weight change, energy intake (MJ), preexisting diabetes/ GDM.

* **Model C**: Adjusted for maternal age, BMI prepregnancy, smoking status week 30, exercise week 17, prepregnancy exercise, energy intake (MJ)* , preeclampsia, preexisting diabetes/ GDM, total gestational weight change.