American Journal of Epidemiology
Vol. 168, No. 8
DOI: 10.1093/aje/kwn189
Advance Access publication September 22, 2008

Original Contribution

Recreational Physical Activity and the Risk of Preeclampsia: A Prospective Cohort of Norwegian Women

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Received for publication January 4, 2008; accepted for publication May 30, 2008.

Previous case-control studies suggest that recreational physical activity protects against preeclampsia. Using a prospective design, the authors estimated the risk of preeclampsia for pregnant women according to level of physical activity, taking other variables that influence risk into consideration. The data set comprised 59,573 pregnancies from the Norwegian Mother and Child Cohort Study (1999–2006). Information on physical activity and other exposures was extracted from questionnaire responses given in pregnancy weeks 14–22, whereas diagnosis of preeclampsia was retrieved from the Medical Birth Registry of Norway. Estimation and confounder control was performed with multiple logistic regression. About 24% of pregnant women reported no physical activity, and 7% reported more than 25 such activities per month. The adjusted odds ratio was 0.79 (95% confidence interval: 0.65, 0.96) for preeclampsia when comparing women who exercised 25 times or more per month with inactive women. The association appeared strongest among women whose body mass index was less than 25 kg/m^2 and was absent among women whose body mass index was higher than 30 kg/m^2. These results suggest that the preventive effect of recreational physical activity during pregnancy may be more limited than has been shown in case-control studies and may apply to nonobese women only.

body mass index; cohort studies; exercise; pre-eclampsia; pregnancy

Abbreviations: BMI, body mass index; MoBa, Norwegian Mother and Child Cohort Study.

The causes of preeclampsia are unknown, and no sound advice for primary prevention can be given to pregnant women (1). It has been hypothesized that regular physical activity during pregnancy may stimulate placental growth, reduce oxidative stress, and reverse maternal endothelial dysfunction (2). A review of the literature on this topic finds that leisure-time physical activity has a clear protective effect on the development of preeclampsia (3). On the basis of postpartum interviews with 244 women with preeclampsia and 470 controls in Seattle, Washington, Rudra et al. (4), expanding a previous report from the same study population (5), reported that the relative intensity of recreational physical activity in the year before pregnancy, measured by the Borg scale of perceived exertion, was associated with a reduction in the risk of preeclampsia (odds ratio = 0.22, 95% confidence interval: 0.11, 0.44 for the highest exertion level vs. inactivity). A case-control study from Canada reported an odds ratio of 0.67 (95% confidence interval: 0.46, 0.96) for any recreational physical activity in the first 20 weeks of pregnancy (6). A cohort study from Connecticut, examining 44 cases with preeclampsia among 2,638 pregnant women, suggested that physical activity both at work and in leisure time during pregnancy reduced the risk, although not statistically significant, whereas leisure-time physical activity prior to pregnancy had no effect (7).

Our aim was to study the possible protective effect of recreational physical activity during pregnancy on preeclampsia by analyzing a well-characterized, large cohort of Norwegian women.

MATERIALS AND METHODS

The present study is a subproject of the Norwegian Mother and Child Cohort Study (MoBa) (8). In brief, MoBa

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is a nationwide pregnancy cohort that, in 1999–2008, aims to include 100,000 pregnancies and to follow parents and children to understand causes of diseases. Pregnant women are recruited for the study through a postal invitation after they have signed up for the routine ultrasound examination at their local hospital. The participation rate is 43.8%, and 50 of 52 hospitals with maternity wards take part in the recruitment (8).

Participants receive a questionnaire asking about previous diseases, lifestyle habits, medications, and present health status. The median pregnancy week when the questionnaire is completed is week 17, with the 5th and 95th percentiles being weeks 14 and 22, respectively. The questionnaire is completed by 94.9% of participants (8). We used a quality-assured questionnaire data file released for research in 2007 with information on 67,355 pregnancies. We excluded from consideration 2,555 pregnancies in which the women had responded to a first version of the questionnaire that asked only for weekly (and not monthly) frequency of physical activity. In addition, data on physical activity during pregnancy were missing for 2,447 women who responded to the second version of the questionnaire, leaving 62,353 eligible pregnancies for further study. The record in the Medical Birth Registry of Norway (9) from the present pregnancy is included as part of the data set. The questionnaire data file was successfully linked to 59,573 singleton births registered in the Medical Birth Registry of Norway, and this sample constituted the population under study. MoBa has been approved by the Regional Committee for Ethics in Medical Research and the Data Inspectorate.

The main outcome variable was preeclampsia as registered in the Medical Birth Registry of Norway. Information provided to the registry is based on forms completed by midwives after birth. The form has 5 checkoff boxes relevant to preeclampsia: hemolysis, elevated liver enzymes, and low platelet count (HELLP); eclampsia; and early (diagnosed before 34 weeks), mild, and severe preeclampsia. In addition, the form has an open field for text that may include information leading to 1 of these diagnoses or that leads to the diagnosis of unspecified preeclampsia. For the present study, the diagnosis of preeclampsia was given if any of the above-mentioned diagnoses were present. Severe preeclampsia was used if 1 or more of the following diagnoses were given: severe or early preeclampsia; hemolysis, elevated liver enzymes, and low platelet count; or eclampsia, whereas mild or unspecified preeclampsia was used when these diagnoses were given alone. The diagnostic criteria for preeclampsia in Norway, according to guidelines issued by the Society for Gynecology, are blood pressure of $\geq$140/90 mm Hg after 20 weeks of gestation combined with proteinuria $\geq$+1 dipstick on at least 2 occasions. A diagnosis of severe preeclampsia requires a blood pressure of $>$160/110 mm Hg and $\geq$3 g of protein in a 24-hour urine sample (10). Maternal age at delivery was also retrieved from the Medical Birth Registry of Norway record.

In the questionnaire, the participants were asked how often they performed the following 14 activities during pregnancy: brisk walking, running, bicycling, attendance at training studios, prenatal aerobics classes, low-impact aerobics classes, high-impact aerobics classes, dancing, skiing, team sports, swimming, walking, horseback riding, or other. We decided to combine the first 11 activities into an overall score. For each activity, the respondents could choose between the following categories: never (score: 0), 1–3 times per month (monthly frequency score: 2), once per week (score: 4), twice per week (score: 8), or 3 or more times per week. For respondents who reported 3 or more times per week, we inserted the median number (among responders who reported at least 3 times weekly) from the distribution of responses to an open question on the weekly frequency of the same physical activities in the above-mentioned first version of the questionnaire. These median numbers were 3 (all other activities), 4 (skiing, dancing, running), or 5 (brisk walking), corresponding to 12, 16, or 20 times per month. The monthly frequency scores were then summed across all 11 activities.

From the questionnaire we also included parity (0, $\geq$1) as well as prepregnancy height and weight, which were used to calculate body mass index (BMI: weight (kg)/height (m)^2). BMI was analyzed as a continuous or categorical variable ($<$18.5, 18.5–24.9, 25.0–29.9, 30.0–34.9, $\geq$35.0). Height was categorized as $<$165, 165–168, 169–172, and $\geq$173 cm. Smoking during pregnancy (nonsmoker, occasional smoker, daily smoker), educational attainment ($<$12, 12, 13–16, $\geq$17 years), as well as the response to the statement ‘‘my work is physically strenuous’’ (response categories: ‘‘correct,’’ ‘‘somewhat correct,’’ ‘‘not quite correct,’’ ‘‘not correct’’), which was posed to women who reported being in paid jobs, were also included as potentially confounding variables. For these confounders, a missing response category was included in the analyses. The questionnaire can be examined at the following website: www.fhi.no/morogbarn. The relative risks of preeclampsia according to physical activity were approximated by calculating odds ratios. Adjustment for confounding was obtained by estimating adjusted odds ratios in multiple logistic regression analyses (11).

RESULTS

The cumulative incidence of preeclampsia (any diagnosis) was 3.9% (2,315/59,573). Eclampsia was noted in 31 pregnancies and the hemolysis, elevated liver enzymes, and low platelet count syndrome in 104, whereas early preeclampsia was diagnosed in 237 women. The incidence of severe preeclampsia was 1.1% ($n = 655$), the incidence of mild preeclampsia was 2.3% ($n = 1,356$), and the incidence of unspecified preeclampsia was 0.5% ($n = 304$).

Table 1 gives the distribution of recreational physical activity per month by maternal characteristics and shows that the highest levels were found among primiparous women, lean women, women with high educational attainment, and nonsmokers. Table 2 shows that the incidence of preeclampsia was lower (3.2%) among highly active women when compared with sedentary women (4.1%). Both smoking and parity are confounders that may mask the effect of physical activity on preeclampsia. In model 1 (Table 2), the odds ratios were reduced compared with the unadjusted odds ratios when these two variables were included in the logistic regression analysis. However, when prepregnancy

Table 1. Percentage Distribution of Recreational Physical Activity[a] According to Characteristics of Women in the Norwegian Mother and Child Cohort Study, 1999–2006

	No.	No. of Activities per Month				
		0	1–5	6–12	13–24	≥25
Maternal age at delivery, years						
<20	613	28.5	26.3	21.0	17.0	7.2
20–24	6,184	26.6	27.6	23.5	16.0	6.4
25–29	20,008	22.5	27.3	25.5	17.1	7.6
30–34	22,908	23.2	27.3	25.8	16.8	6.9
≥35	9,860	24.7	27.4	25.8	16.0	6.0
Prepregnancy body mass index, kg/m^2						
<18.5	1,804	26.8	25.3	21.7	18.0	8.1
18.5–24.9	37,547	21.4	25.9	26.3	18.1	8.2
25.0–29.9	12,853	25.8	30.0	25.2	14.2	4.8
30.0–34.9	4,176	30.1	31.2	22.5	12.9	3.3
≥35	1,543	32.5	34.3	19.7	10.6	2.9
No response	1,650	26.7	24.3	24.0	17.9	7.1
Smoking						
Nonsmoker	53,616	22.4	27.2	26.0	17.1	7.3
Occasional smoker	1,811	26.1	27.4	24.4	15.8	6.4
Daily smoker	3,709	39.3	28.5	18.1	11.4	2.8
No response	437	31.1	24.7	20.8	17.4	5.9
Height, cm						
<165	16,013	26.8	27.7	24.1	15.3	6.1
165–168	15,163	22.7	27.9	25.6	16.8	7.0
169–172	14,271	22.2	27.2	26.3	17.1	7.2
≥173	13,428	22.0	26.6	25.9	17.7	7.8
No response	698	27.8	22.6	22.9	18.6	8.0
Parity						
0	27,084	20.3	24.5	25.8	19.9	9.5
≥1	32,489	26.3	29.7	25.1	14.1	4.8
Educational attainment, years						
<12	12,196	34.4	28.2	20.8	12.8	3.8
12	7,775	28.2	29.2	22.4	15.0	5.2
13–16	24,876	20.6	27.9	27.3	17.1	7.1
≥17	13,212	15.9	24.5	28.3	20.5	10.8
No response	1,514	29.1	26.2	22.4	17.2	5.2
Physically demanding job						
No job	4,632	34.3	26.1	19.5	14.9	5.3
Not correct	23,638	21.5	27.5	27.2	16.7	7.1
Not quite correct	12,945	21.2	27.6	26.9	16.9	7.5
Somewhat correct	9,827	22.7	27.9	25.1	17.2	7.1
Correct	7,332	27.8	26.2	22.2	17.0	6.8
No response	1,199	30.9	27.1	21.1	15.8	5.0
Year of childbirth						
1999–2001	3,019	25.5	27.4	26.5	15.1	5.5
2002	7,699	24.3	28.8	25.6	14.8	6.5
2003	11,216	24.6	27.7	25.5	15.9	6.3
2004	11,952	24.1	27.1	24.9	17.1	6.8
2005	13,968	23.0	27.1	25.1	17.5	7.3
2006	11,719	21.8	26.4	25.9	17.8	8.1
Total	59,573	23.6	27.3	25.4	16.7	7.0

[a] Number of activities per month.

Table 2. Crude and Adjusted Odds Ratios for Preeclampsia According to Recreational Physical Activity During Pregnancy, Norwegian Mother and Child Cohort Study, 1999–2006

No. of Activities per Month	No. of Pregnancies	No. of Cases[a]	Incidence	Crude OR	Model 1[b]		Model 2[c]		Model 3[d]	
					OR	95% CI	OR	95% CI	OR	95% CI
0	14,054	583	4.1	1.0	1.0		1.0		1.0	
1–5	16,272	642	3.9	0.95	0.92	0.82, 1.04	0.94	0.84, 1.05	0.96	0.85, 1.07
6–12	15,147	589	3.9	0.94	0.86	0.77, 0.97	0.94	0.83, 1.05	0.96	0.85, 1.08
13–24	9,950	367	3.7	0.89	0.77	0.67, 0.88	0.87	0.76, 0.99	0.89	0.78, 1.03
≥25	4,150	134	3.2	0.77	0.62	0.51, 0.76	0.76	0.62, 0.92	0.79	0.65, 0.96

Abbreviations: CI, confidence interval; OR, odds ratio.

[a] All cases of preeclampsia, including the hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome and eclampsia.

[b] Adjusted for smoking and parity.

[c] Adjusted for smoking, parity, and prepregnancy body mass index.

[d] Adjusted for smoking, parity, prepregnancy body mass index, educational attainment, maternal age at delivery, year of childbirth, height, and physically demanding job.

BMI was included in addition, the odds ratios increased to close to the unadjusted levels (Table 2, model 2). Introduction of other possible confounders in the regression analysis had little effect (Table 2, model 3). When all confounders were included, the odds ratio for preeclampsia was 0.79 (95% confidence interval: 0.65, 0.96) when women with more than 25 recreational physical activities per month were compared with women who reported no such activities. When all exercising women were contrasted to inactive women, the odds ratio for preeclampsia was 0.94 (95% confidence interval: 0.85, 1.04).

In Table 3, the effects of physical activity are examined separately for severe, mild, and unspecified preeclampsia. In general, the odds ratios were not statistically significantly different from 1, although there was a tendency toward reduced odds ratios for the highest activity levels. There were no indications of effect modification when analyses were performed within strata of parity, smoking, or work participation. Table 4 shows a clear effect of physical activity for subjects whose BMI was lower than 25 and that all estimates were above 1 for physically active women whose BMI was higher than 30.

DISCUSSION

These results suggest that recreational physical activity during pregnancy reduces the risk of preeclampsia. The women who reported frequent physical activity had a 20% reduction in risk. Stronger effects (30%–80% reduction in risk) have been found in case-control studies (4–6). There may be several explanations for this discrepancy. In contrast to the case-control studies, MoBa was not designed to specifically study physical activity and preeclampsia, perhaps reducing the potential for selection related to the study question. The exposure measures in the case-control studies were

Table 3. Crude and Adjusted Odds Ratios for Severe, Mild, and Unspecified Preeclampsia According to Recreational Physical Activity, Norwegian Mother and Child Cohort Study, 1999–2006

No. of Activities per Month	No. of Pregnancies	Severe Preeclampsia[a]				Mild Preeclampsia				Unspecified Preeclampsia			
		No.	%	Adjusted OR[b]	95% CI	No.	%	Adjusted OR[b]	95% CI	No.	%	Adjusted OR[b]	95% CI
0	14,054	153	1.1	1.0		350	2.5	1.0		80	0.6	1.0	
1–5	16,272	166	1.0	0.94	0.75, 1.17	389	2.4	0.97	0.83, 1.12	87	0.5	0.95	0.70, 1.29
6–12	15,147	176	1.2	1.07	0.85, 1.33	337	2.2	0.93	0.79, 1.08	76	0.5	0.91	0.66, 1.25
13–24	9,950	123	1.2	1.10	0.86, 1.40	198	2.0	0.82	0.69, 0.99	46	0.5	0.81	0.56, 1.18
≥25	4,150	37	0.9	0.78	0.54, 1.13	82	2.0	0.84	0.66, 1.08	15	0.4	0.64	0.36, 1.12

Abbreviations: CI, confidence interval; OR, odds ratio.

[a] Includes cases from the Medical Birth Registry of Norway noted as severe and, additionally, preeclampsia occurring before 37 weeks; the hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome; and eclampsia.

[b] Adjusted for smoking, parity, prepregnancy body mass index, educational attainment, maternal age at delivery, parity, year of childbirth, height. and physically demanding job.

Table 4. Adjusted Odds Ratios for Preeclampsia[a] According to Recreational Physical Activity and Categories of Prepregnancy BMI, Norwegian Mother and Child Cohort Study, 1999–2006

No. of Activities per Month	Prepregnancy BMI <25					BMI 25.0–29.9					BMI ≥30				
	No. of Pregnancies	No. of Cases	%	Adjusted OR[b]	95% CI	No. of Pregnancies	No. of Cases	%	Adjusted OR[b]	95% CI	No. of Pregnancies	No. of Cases	%	Adjusted OR[b]	95% CI
0	8,535	260	3.0	1.0		3,318	175	5.3	1.0		1,760	128	7.2	1.0	
1–5	10,190	272	2.7	0.85	0.71, 1.01	3,850	207	5.4	1.00	0.81, 1.23	1,831	150	8.2	1.20	0.93, 1.54
6–12	10,263	273	2.7	0.80	0.67, 0.96	3,244	170	5.2	0.94	0.75, 1.17	1,244	121	9.7	1.47	1.12, 1.91
13–24	7,123	191	2.7	0.77	0.63, 0.93	1,830	107	5.8	0.99	0.77, 1.27	702	60	8.5	1.21	0.87, 1.67
≥25	3,240	83	2.6	0.69	0.53, 0.89	611	26	4.3	0.68	0.44, 1.04	182	19	10.4	1.39	0.83, 2.32

Abbreviations: BMI, body mass index (weight (km)/height (m)^2); CI, confidence interval; OR, odds ratio.

[a] Includes severe, mild, and unspecified cases of preeclampsia.

[b] Adjusted for smoking, parity, prepregnancy BMI (continuous measure), educational attainment, maternal age at delivery, parity, year of childbirth, height, and physically demanding job.

based on recall, which may be influenced by the outcome. On the other hand, a limitation of MoBa is the precision and validity of the exposure measurements. We did not know the intensity of the physical activities reported by the pregnant women, and misclassification is likely. It is reasonable to assume that this information error would bias the odds ratio estimates toward the null value. However, differential information bias is unlikely in MoBa since physical activity and confounders were measured prior to diagnosis of the endpoint, which is taken from an independent source, the birth registry.

Better resolution of the relation between recreational physical activity and preeclampsia could come from randomized, controlled trials specifically designed to address this research question. A Cochrane review (12) has shown that no conclusions can be drawn from the existing 2 small trials (13, 14), which were designed mainly for other purposes. In combination, the intervention group in these 2 studies included 23 women and the control group 22 women. One case of preeclampsia occurred in the control group, giving a relative risk of 0.31 (95% confidence interval: 0.01, 7.09).

We could not find any protective effect of recreational physical activity for women with a prepregnancy BMI above 30. However, this analysis was not performed as a consequence of a prior hypothesis, and this may be a chance finding. The question should be examined by others before any advice to obese women is given. Rudra et al. (4), in contrast, found a relatively strong protective effect of physical activity among women whose BMI was above 25. However, in that analysis, residual confounding may have been present because adjustment for the BMI levels within the 2 strata (below and above 25) was not performed.

Several mechanisms for a protective effect of recreational physical activity on the risk of preeclampsia may exist. In nonpregnant women, exercise is known to reduce blood pressure (15) and triglyceride levels (16). Dyslipidemia, inflammation, and oxidative stress are features of preeclampsia. It has been shown that regular weight-bearing exercise influences the level of plasma tumor necrosis factor-α during pregnancy (17). Preeclampsia is said to share the same pathologies as cardiovascular disease, with endothelial dysfunction as a common denominator (18), and the 2 conditions share some risk factors such as obesity and diabetes; however, whereas smoking increases the risk of cardiovascular disease, it paradoxically reduces the risk of preeclampsia independently of BMI level (19).

Some of the pathophysiological findings in preeclampsia may be secondary to early placental events. Successful placentation involves adequate invasion of the extravillous cytotrophoblasts into the maternal uterine spiral arteries, securing wide, low-resistance vascular channels providing the developing fetus with maximum blood flow. Bergmann et al. (20) has shown that running throughout pregnancy has a favorable effect on placental villous vascular volume. Further studies of obese and lean women are needed to understand the mechanisms and timing of the effects of exercise. More detailed studies in MoBa, utilizing the available biologic material obtained during pregnancy and after birth (8), may assist in understanding the mechanisms behind the effects of physical activity and other factors on the occurrence of hypertensive disorders in pregnancy.

In summary, we found that recreational physical activity may have a moderately protective effect on the risk of preeclampsia, at least for women with a BMI of less than 25.

ACKNOWLEDGMENTS

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The Norwegian Ministry of Health, The Norwegian Research Council (contract 151918/S10), National Institute of Environmental Health Sciences (contract N01ES75558), National Institute of Neurological Diseases and Stroke (contract 1 UO1 NS 047537). Parallel analyses have been undertaken from another large prospective database, the Danish National Birth Cohort (21), and The 6th Research Framework of the European Union (EARNEST) financially supported the interaction between the 2 teams.

Conflict of interest: none declared.

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