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Exercise level before pregnancy and engaging in high-impact sports reduce the risk of pelvic girdle pain: a population-based cohort study of 39 184 women

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ABSTRACT

Objective To examine whether an association exists between exercise levels pre-pregnancy and pelvic girdle pain in pregnancy. Pelvic girdle pain in pregnancy has been associated with physical inactivity, a risk factor for adverse pregnancy outcomes.

Methods We used data from a population-based cohort study including 39 184 nulliparous women with a singleton pregnancy enrolled in the Norwegian Mother and Child Cohort study. Pre-pregnancy exercise frequency and types were assessed by questionnaire in pregnancy week 17. Pelvic girdle pain, defined as combined pain in the anterior pelvis and in the posterior pelvis bilaterally, was self-reported in pregnancy week 30. Multivariable Poisson regression estimated risks of pelvic girdle pain associated with pre-pregnancy exercise. We examined a dose–response association of prepregnancy exercise frequency using restricted cubic splines. A test for non-linearity was also conducted. Final models were adjusted for pre-pregnancy BMI, age, education, history of low back pain and history of depression.

Results 4069 women (10.4%) reported pelvic girdle pain in pregnancy and the prevalence among women who were non-exercisers prepregnancy was 12.5%. There was a non-linear association for pre-pregnancy exercise and risk of pelvic girdle pain (test for non-linearity, p=0.003). Compared to non-exercisers, women exercising 3–5 times weekly pre-pregnancy had a 14% lower risk of developing pelvic girdle pain in pregnancy (aRR 0.86, 95% CI 0.77 to 0.96). Taking part in high-impact exercises such as running, jogging, orienteering, ballgames, netball games and high-impact aerobics were associated with less risk of pelvic girdle pain.

Summary Women who exercise regularly and engage in high-impact exercises before the first pregnancy may have a reduced risk of pelvic girdle pain in pregnancy.

INTRODUCTION

Pelvic girdle pain is highly prevalent in pregnant women[1] and is associated with disability, depression, reduced quality of life and higher prevalence of sick leave during pregnancy.[2–5] Women who develop pelvic girdle pain are also less likely to participate in regular physical activity during pregnancy[6] and thus, be a risk of the complications of physical inactivity.[7] Approximately 2–3% of all women report chronic pelvic girdle pain 1 year after delivery.[8] Although both modifiable and non-modifiable risk factors for pelvic girdle pain have been identified,[9–14] the aetiology and pathogenesis are still unknown.

Pregnancy-related pelvic girdle pain is observed more often in women with a high body mass index (BMI),[9 11–13] but the influence of other modifiable factors such as leisure time exercise have been little studied. Generally, regular exercise increases cardiovascular fitness, muscular strength and flexibility and women who exercise are less likely to be overweight or obese.[15 16] Aerobic exercise leads to endorphins production which may reduce sensitivity to pain and produce feelings of relaxation.[17] Thus exercise could potentially influence the risk of developing pelvic girdle pain in pregnancy.

Given that early onset of pelvic girdle pain would negatively influence the probability of exercise in mid-pregnancy, we aimed to examine the association between pre-pregnancy leisure time exercise and pelvic girdle pain in pregnant nulliparous women.

METHODS

Study design

The Norwegian Mother and Child Cohort Study (MoBa) is a prospective population-based cohort study conducted by the Norwegian Institute of Public Health.[18] Participants were recruited from all over Norway between 1999 and 2008, and the cohort includes 108 000 children and 90 700 mothers. Follow-up is conducted by questionnaires at regular intervals and by linkage to national health registries. Further details of methods and cohort characteristics have been described previously.[18 19] The present study was based on the seventh version of the quality-assured data file released for research in June 2012. Informed consent was obtained from each MoBa participant on recruitment. The study was approved by The Regional Committee for Medical Research (S-95113) and The Norwegian Data Protection Authority.

Participants

The majority of all pregnant women in Norway were invited to participate early in pregnancy through a postal invitation after signing up for the routine ultrasound examination usually performed at pregnancy weeks 17–20. Of the invited women, 38.7% consented to participate. The follow-up rate was 91% in pregnancy week 30. In the current analysis, we included all singleton pregnancies enrolled

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in the MoBa study who completed both questionnaires 1 (Q1) and 2 (Q2) at pregnancy weeks 17 (mean 17.2 weeks, SD 2.2) and 30 (mean 30.5 weeks, SD 1.4), respectively. The questionnaires included items about maternal health, demographics, lifestyle behaviours and medical history. All questionnaires are available at http://www.fhi.no/morogbarn. Owing to possible influence of pelvic girdle pain in previous pregnancies on the ability to participate in leisure time exercise, we excluded 45 797 multiparous women. We also excluded women with missing information on leisure time exercise from questionnaire 1 (Q1) (n=307) and eight women with a weekly exercise frequency above 25. Furthermore, women with missing information on the covariables pre-pregnancy BMI, education, smoking pre-pregnancy, marital status and history of depression were excluded leaving 39 184 out of 40 934 nulliparous women with singleton pregnancies for further analysis (figure 1).

Outcome

The outcome was pelvic girdle pain in pregnancy week 30, defined as having mild or severe pain in the anterior pelvis and in the posterior pelvis bilaterally.[20] Pelvic girdle pain was self-reported using the following questions from questionnaire 2 (Q2): "Do you have pain in the pelvic girdle? If you have pain in the pelvic girdle, where is the pain located?" One or more pain locations could be specified: over the pubic symphysis in the anterior pelvis, over one sacroiliac joint in the posterior pelvis, or over both sacroiliac joints in the posterior pelvis.[9] Pain intensity was scored as mild or severe at each location.

Exposure

The main exposure was leisure time exercise performed 3 months before pregnancy, defined in terms of frequency and type. Participants recalled frequency and types of pre-pregnancy exercise in pregnancy week 17.

In the questionnaire, participants reported how often they performed the following 14 exercises 3 months pre-pregnancy: strolling, brisk walking, running (jogging or orienteering), bicycling, training in fitness centres, swimming, low impact aerobic classes, high-impact aerobic classes, prenatal aerobic classes, dancing (swing, rock and folkdance), skiing, ball games, horseback riding and other. Based on the definition of exercise by Caspersen *et al*[21] strolling was categorised as non-exercise. We combined all exercises excluding strolling, into an overall score. For each exercise, the following predefined frequencies were given: "never" (score: 0), "1–3 times per month" (score: 0.25), "once a week" (score: 1.0), "twice a week" (score: 2.0) and "≥3 times per week" (score: 3.0). The weekly frequency score were then summed across the 13 exercises and recoded into five categories ranging from "never" to "≥6 times per week" to capture the most active women. "Non-exercisers" were those who responded "never" to all exercises listed or who only performed strolling. The same questions used to assess exercise frequency in our study have shown acceptable concurrent validity when compared to accelerometer in a subsample of pregnant women within the MoBa study.[22] We generated seven groups based on exercise types: non-exercisers (strolling and never), brisk walking, non-weight bearing exercises (cycling and swimming), low impact exercises (prenatal aerobics, low impact aerobics, dancing, cross-country skiing and fitness training), high-impact exercises (running, jogging, orienteering, ballgames, high-impact aerobics) and horseback riding (horseback riding and other). A mixed exercise group included those who did not report a single dominant exercise type (eg, one session of jogging and one session of swimming per week).

Covariates

Based on review of previous studies and assumed possible underlying mechanisms, we assessed the following covariates and possible confounding factors using directed acyclic graphs (DAGs): Maternal age (years), body mass index (BMI, kg/m^2) pre-pregnancy, education (primary, secondary, college/university and other), marital status (married, cohabitant, single and other), smoking pre-pregnancy (never, occasional, daily), heavy work (yes/no), a history of low back pain (LBP) (ie, before pregnancy) and a history of depression. We used the Lifetime Major Depression Scale,[23] which consists of five questions concerning

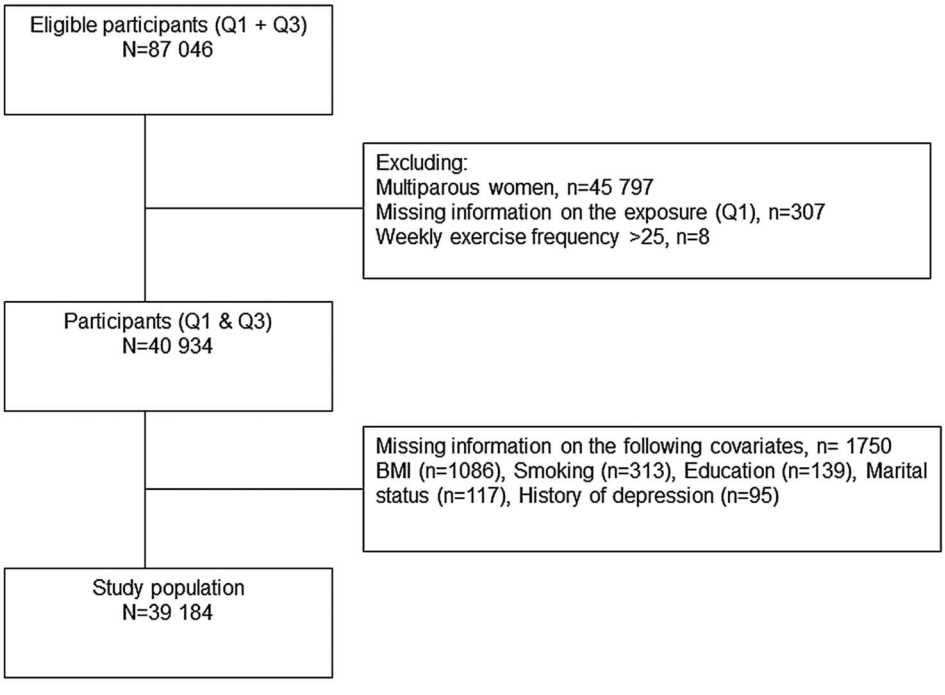

Figure 1 Flow chart of the study population (n=39 184).

sadness, appetite changes, lack of energy, self-blame and concentration, to assess history of depression defined as having had at least three symptoms at the same time for at least two weeks. In a previous study the Cronbach α for this scale was reported to be 0.86.[24]

Statistical analyses

Analyses were performed using Stata V.13.0 (StataCorp, Texas, USA). We used χ^2 to test for differences in distributions of characteristics at enrolment by pelvic girdle pain. To estimate associations of frequencies and types of pre-pregnancy exercise with risk of pelvic girdle pain we used multivariable Poisson regression with robust error variance. This method is useful for directly estimating relative risks (RR) for dichotomous, common outcomes in prospective studies.[25] We examined the dose–response association of pre-pregnancy exercise using restricted cubic splines with three knots at fixed percentiles of the distribution.[26] A test for non-linearity was conducted by testing the coefficient of the second spline transformation equal to zero. Final models were adjusted for pre-pregnancy BMI, maternal age, education, history of LBP and history of depression. Exercise in pregnancy week 17 is partly caused by pre-pregnancy exercise and may at the same time correlate with pelvic girdle pain. Hence, it was treated as a potential mediator of the association between pre-pregnancy exercise and pelvic girdle pain and was not included in the models.[27] We also compared maternal characteristics and social characteristics for women with and without information on exercise from the first questionnaire. Women without exposure information were more likely to be younger, smoke daily and to have primary school only. Pelvic girdle pain was reported in 8.8% of these women, they were less likely to be overweight pre-pregnancy, and no difference in history of LBP or depression was observed. However, these women had a high proportion of missing on all covariates.

RESULTS

Participants

At enrolment in pregnancy week 17, the mean maternal age was 28.5 (SD 4.5) years, ranging from 14 to 46 years. Of the 39 184 pregnancies included, 10.4% reported pelvic girdle pain in pregnancy week 30.

The majority of women were married or cohabitant (95.4%), less than 30 years of age (64%), non-smokers pre-pregnancy (69.2%), and had completed college/university education (60.1%; table 1). Furthermore, 29.5% were overweight or obese before pregnancy. The highest proportions of daily smoking, overweight or obesity and young age (<25 years) were observed among women who developed pelvic girdle pain. A history of LBP or depression was also more common in women with pelvic girdle pain.

Table 1 Characteristics of the study population (n=39 184) by pelvic girdle pain (week 30) in the Norwegian Mother and Child Cohort Study

	Total N (%)	No Pelvic girdle pain N=35 115 (89.6%)	Pelvic girdle pain N=4069 (10.4%)
Maternal age, years (mean, SD)†	28.5 (4.4)	28.6 (4.4)	27.7 (4.5)*
<25	7927 (20.2)	6851 (19.5)	1076 (26.4)
25–29	17 173 (43.8)	15 403 (43.9)	1770 (43.5)
30–34	11 008 (28.1)	10 033 (28.6)	975 (24.0)
≥35	3076 (7.9)	2828 (8.1)	248 (6.1)
BMI (mean, SD)‡	23.8 (4.2)	23.6 (4.1)	24.9 (4.9)*
<18.5	1337 (3.4)	1202 (3.4)	135 (3.3)
18.5–24.9	26 278 (67.1)	23 985 (68.3)	2293 (56.4)
25.0–29.9	8184(20.9)	7133 (20.3)	1051 (25.8)
30.0–34.9	2477 (6.3)	2063 (5.9)	414 (10.2)
35+	908 (2.3)	732 (2.1)	176 (4.3)
Education			
Primary	1316 (3.4)	1125 (3.2)	191 (4.7)
Secondary	12 913 (33.0)	11 310 (32.2)	1603 (39.4)
College/University	23 547 (60.1)	21 439 (61.1)	2108 (51.8)
Other	1408 (3.6)	1241 (3.5)	167 (4.1)
Non-smoking‡	27 101 (69.2)	24 496 (69.8)	2605 (64.0)
Occasional smoking	4476 (11.4)	4010 (11.4)	466 (11.5)
Daily smoking	7607 (19.4)	6609 (18.8)	998 (24.5)
Married	13 776 (35.1)	12 390 (35.3)	1386 (34.1)
Cohabitant	23 627 (60.3)	21 171 (60.3)	2456 (60.4)
Single	1149 (2.9)	998 (2.8)	151 (3.7)
Other	632 (1.6)	556 (1.6)	76 (1.9)
History of low back pain‡	8609 (22.0)	7350 (20.9)	1259 (30.9)
History of depression‡	9896 (25.3)	8439 (24.0)	1457 (35.8)

*p<0.001.
†Maternal age at enrolment.
‡Before pregnancy.
BMI, body mass index.

Pre-pregnancy exercise and pelvic girdle pain

Table 2 displays the distribution of leisure time exercise pre-pregnancy (frequency and type) by pelvic girdle pain. Overall, most women reported a frequency of at least three times weekly before pregnancy (56.5%), whereas 7% did not report any exercise before pregnancy. Compared with women who developed pelvic girdle pain, it was more common to report an exercise frequency of 3–5 times per week among women who did not develop pelvic girdle pain (p<0.001). Also, participation in high-impact exercises such as running, jogging, orienteering, ballgames and high-impact aerobics were more commonly reported in women without pelvic girdle pain (p<0.001). Most women who exercised at least weekly before pregnancy were also exercising in pregnancy week 17 (90.3%), whereas 9.7% stopped. The proportion of non-exercisers at both time points was 5.6% (data not shown).

In adjusted models (table 3), women who exercised 3–5 times weekly before pregnancy had a 14% reduced risk of pelvic girdle pain in pregnancy (adjusted RR (aRR) 0.86, 95% CI 0.77 to 0.96) in comparison with no exercise. Participation in high-impact exercises was associated with a similar risk reduction of pelvic girdle pain (aRR 0.86, 95% CI 0.76 to 0.96).

We also modelled pre-pregnancy exercise frequency with risk of pelvic girdle pain using restricted cubic splines (figure 2). The rate of change in the risk of pelvic girdle pain seemed to decrease with increasing frequency of exercise up to five times a week, after which an increased risk of pelvic girdle pain was observed (p for non-linearity=0.003).

DISCUSSION

In this large population-based cohort study, regular exercise before the first pregnancy, particularly participation in high-impact exercises, was associated with a reduced risk of pelvic girdle pain during pregnancy after controlling for known confounders. The observed non-linear association indicated a decreased risk of pelvic girdle pain for exercise performed up to five times weekly, after which no further decrease in risk was observed.

Table 2 Distribution of pre-pregnancy exercise frequency and type by pelvic girdle pain

	Total n=39 184	No pelvic girdle pain N=35 115 (89.6%)	Pelvic girdle pain N=4069 (10.4%)
Exercise frequency			
Never	2760 (7.0)	2415 (6.9)	345 (8.5)
1–3 times per month	4549 (11.6)	4019 (11.5)	530 (13.0)
1–2 times per week	9740 (24.9)	8672 (24.7)	1068 (26.3)
3–5 times per week	14 589 (37.2)	13 246 (37.7)	1343 (33.0)
≥6 times per week	7546 (19.3)	6763 (19.3)	783 (19.2)
Exercise type			
Never	2760 (7.0)	2415 (6.9)	345 (8.5)
Brisk walking	5120 (13.1)	4575 (13.0)	545 (13.4)
Non-weight bearing*	3881 (9.9)	3477 (9.9)	404 (9.8)
Low-impact exercises†	6109 (15.6)	5473 (15.6)	636 (15.5)
High-impact exercises‡	10 204 (26.0)	9319 (26.5)	885 (21.8)
Horseback riding§	3260 (8.3)	2909 (8.3)	351 (8.6)
Mixed exercises¶	7850 (20.0)	6947 (19.8)	903 (22.2)

*Swimming and cycling.
†Prenatal aerobic dancing, low-impact aerobic dancing, dancing, cross-country skiing and fitness training.
‡Running, jogging, orienteering, ballgames, netball games and high-impact aerobic dance.
§Horseback riding and unclassifiable exercises (other).
¶Including those who did not perform a single exercise >50% of the total active time.

The most important confounders of the association between pre-pregnancy exercise with pelvic girdle pain were BMI and maternal age. Women with a high BMI have lower levels of exercise both before and during pregnancy[28] and high BMI is a risk factor for pregnancy-related pelvic girdle pain.[9 11 12] Our results suggest that pre-pregnancy exercise and high BMI have conflicting effects on pelvic girdle pain. Furthermore, the youngest women in our study had the highest risk of pelvic girdle pain, whereas older age was positively associated with exercise. However, after adjusting for BMI and age, the association with pelvic girdle pain remained for high-impact exercises and an exercise frequency up to five times weekly. Having a history of LBP or depression did not substantially change the estimates.

Limitations of the study

The main limitation of our study is that both exposure and outcome were self-reported, which may have resulted in some misclassification of pre-pregnancy exercise and BMI. Given that the exposure was assessed before the outcome, it is likely that any misclassification would be similar in women who reported pelvic girdle pain and those who did not. Pre-pregnancy exercise

Table 3 Risks of pelvic girdle pain associated with frequency and type of pre-pregnancy exercise among nulliparous women in the MoBa study (n=39 184)

		Unadjusted		Adjusted*		Adjusted†	
	N (%)	RR	95% CI	RR	95% CI	RR	95% CI
Exercise frequency							
Never	2760 (7.0)		Reference		Reference		Reference
1–3 times per month	4549 (11.6)	0.93	0.82 to 1.06	0.96	0.84 to 1.08	0.95	0.84 to 1.08
1–2 times per week	9740 (24.9)	0.88	0.78 to 0.98	0.97	0.87 to 1.09	0.95	0.85 to 1.07
3–5 times per week	14 589 (37.2)	0.74	0.66 to 0.82	0.86	0.77 to 0.96	0.84	0.75 to 0.94
≥6 times per week	7546 (19.3)	0.83	0.74 to 0.93	0.99	0.88 to 1.11	0.97	0.86 to 1.10
Exercise type							
Never	2760 (7.0)		Reference		Reference		Reference
Brisk walking	5120 (13.1)	0.85	0.75 to 0.97	0.95	0.84 to 1.08	0.95	0.84 to 1.08
Non-weight bearing‡	3881 (9.9)	0.83	0.73 to 0.95	0.93	0.81 to 1.06	0.90	0.79 to 1.04
Low-impact exercises§	6109 (15.6)	0.83	0.74 to 0.94	0.94	0.84 to 1.07	0.93	0.84 to 1.06
High-impact exercises¶	10 204 (26.0)	0.69	0.62 to 0.78	0.86	0.76 to 0.96	0.81	0.72 to 0.91
Horseback riding**	3260 (8.3)	0.86	0.75 to 0.99	0.95	0.83 to 1.09	0.97	0.84 to 1.12
Mixed exercises††	7850 (20.0)	0.92	0.82 to 1.0	0.97	0.87 to 1.09	0.96	0.86 to 1.08

*Adjusted for pre-pregnancy BMI, maternal age, education, history of low back pain and history of depression.
†Adjusted of pre-pregnancy BMI and maternal age.
‡Swimming and cycling.
§Prenatal aerobic dancing, low-impact aerobic dancing, dancing, cross-country skiing and fitness training.
¶Running, jogging, orienteering, ballgames, netball games and high-impact aerobic dance.
**Horseback riding and unclassifiable exercises (other).
††Includes those who did not perform a single exercise >50% of the total active time.
BMI, body mass index.

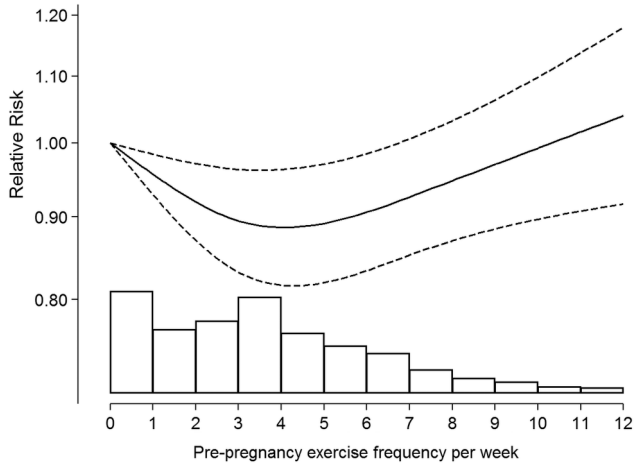

Figure 2 Adjusted relative risk of pelvic girdle pain, associated with weekly frequency of exercise pre-pregnancy among 39 184 nulliparous women in the Norwegian Mother and Child Cohort Study, 2000 to 2008. Data were fitted by the use of a Poisson regression model with restricted cubic splines with 3 knots (0.25, 0.75 and exercises per week). Estimates were adjusted for the same variables as model 1 in table 3. A probability value for non-linearity was 0.002. Dashed lines represent 95% confidence limits. The reference category was no exercise. The vertical axis is on the log scale. Tick marks represent the positions of pelvic girdle pain cases. The histogram represents the percentage distribution of weekly exercise frequencies in the study population.

levels were recalled in pregnancy week 17 and may therefore be over-rated with an underestimated proportion of non-exercisers. We defined strolling as a non-exercise and other domains of physical activity such as household chores, gardening and child-care were not included. A prospective exposure assessment (ie, exercise) pre-pregnancy is difficult to obtain when assessing outcomes developing during pregnancy. The recall period in our study was, however, shorter than in the study by Mogren[29] in which the exposure and outcome were assessed retrospectively after childbirth. Owing to the self-reported outcome measure, we used a strict definition of pelvic girdle pain including only women who reported mild or severe pain in the pubic symphysis and both sacroiliac joints, not only in one or two joints.[9] These women have been shown to have greater functional disability and a higher frequency of sick leave.[30] The prognosis for women who reported pain in all three pelvic joints is worse and they are more likely to develop persistent pelvic girdle pain.[20 31] A high correlation between self-reported severity of pelvic girdle pain and number of positive clinical pelvic tests has also been reported.[4] Consequently, we could not determine if women who exercised pre-pregnancy were less likely to report any pain in the pelvic girdle.

Given the low participation rate and that participating women were older, smoked less, had lower parity and higher education compared to the general pregnant population,[19] the prevalence of exercise and pelvic girdle pain may have been affected by the study's sample selection. Although selection bias has implications for generalising prevalence estimates, it is not likely to have influenced the association between pre-pregnancy exercise and pelvic girdle pain in our study. In the adjusted models all these factor were included and none but maternal age significantly influenced the estimates. Whether the observed associations are similar in multiparous women should be studied further.

Comparison with other studies

In a retrospective study including 891 postpartum women, Mogren[29] found that more years of regular physical activity before pregnancy reduced the risk of LBP or pelvic pain during pregnancy. However, Mogren reported neither frequency nor type of physical activity, and failed to define regular physical activity. LBP and pelvic pain were highly prevalent and reported together, which makes it difficult to compare with our results. In a small retrospective study comparing elite athletes who performed a high volume of exercise pre-pregnancy and non-athletic controls, no statistical difference in the prevalence of pelvic girdle pain was reported.[32] Similarly, studies that have explored possible risk factors for pelvic girdle pain reported no association with physical activity or exercise pre-pregnancy.[9 33] However, it is difficult to compare these studies due to differences in study design, outcome measures and incomplete assessment of physical activity pre-pregnancy, which could have masked a possible relationship between pre-pregnancy exercise and pelvic girdle pain.

Contrary to previous studies, our study included only nulliparous women. Multiparous women have a higher risk of pelvic girdle pain[9] and they are less likely to participate in regular exercise before and during pregnancy.[28] Whether low levels of exercise increases the risk of pelvic girdle pain or whether pelvic girdle pain causes withdrawal from regular exercise among multiparous women is therefore difficult to determine. Given the adverse effects of pelvic girdle pain on women's health and the absence of effective treatment strategies during pregnancy, future studies should focus on potential preventive measures.

Possible mechanisms

The mechanisms by which pre-pregnancy exercise influences the risk of pelvic girdle pain, remains unknown. Both aerobic exercise and resistance training have a hypoalgesic effect on pain in healthy non-pregnant individuals and in chronic pain patients.[34] Though the long-term effect of exercise on pain remains unclear, women who exercise regularly pre-pregnancy are more likely to continue throughout pregnancy.[28] The observation that only high-impact exercises such as running, jogging, orienteering, ballgames, netball games and high-impact aerobics were associated with a reduced risk of pelvic girdle pain may be explained by a hypoalgesic effect associated with aerobic exercise. However, women in this group could also have participated in other types of exercise as long as they performed high-impact exercises most of the time. In comparison, women who performed different types of exercise (ie, mixed exercisers) did not have a reduced risk of pelvic girdle pain. Given that women who exercised up to five times weekly pre-pregnancy had a lower risk of pelvic girdle pain, we believe that the relationship between leisure time exercise and pelvic girdle pain depends on both frequency and types of exercise.

Study strengths

Strengths of our study are its population-based, prospective design with a large number of participants and its high follow-up rate. Leisure time exercise was assessed before the outcome and included information on both frequency and type. By providing detailed information about the exposure variable, we were able to examine the possible associations between different types of pre-pregnancy exercise and the development of pelvic girdle pain. A comprehensive questionnaire administered mid-pregnancy provided information about possible confounding

variables and we attempted to control for identifiable confounders such as differences in maternal demographics, work-related factors and lifestyle behaviours. Regardless of these attempts to address confounding, we cannot rule out possible bias due to residual confounding.

What are the findings?

- We observed a non-linear relationship between pre-pregnancy exercise and pelvic girdle pain showing that the risk decreased more rapidly for those at the lower end of the exercise distribution.
- Pre-pregnancy exercise frequency up to five times weekly was protective against pelvic girdle pain. The risk of pelvic girdle pain did not continue to decrease with higher levels of exercise.
- Women who reported high-impact exercises pre-pregnancy had the lowest risk of pelvic girdle pain in pregnancy.

How might it impact on clinical practice in the future?

Acknowledging the limitations of our study, these results emphasise the importance of promoting regular exercise among women of childbearing age.

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Contributors KMO conducted the statistical analyses and led the writing of the manuscript. EKB, BS, ME-G and SV critically discussed the results and reviewed the manuscript. NO provided statistical support and critically reviewed the manuscript. All authors contributed significantly to the interpretation of the results, to the final version and approved the submission.

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Competing interests None declared.

Ethics approval The study was approved by the Regional Committee for Medical Research Ethics (S-95113) and The Norwegian Data Protection Authority.

Provenance and peer review Not commissioned; internally peer reviewed.

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