The effect of exercise during pregnancy on the risk of preterm birth: A retrospective study

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Abstract

Objective: To examine the association between exercise during pregnancy and preterm birth (PTB). Design: Retrospective cohort analysis. Setting: Jinan, China. Population: Singleton live births from December 2018 to December 2019. Methods: Questionnaires contained items about physical exercise (frequency, time, and primary exercise patterns) during pregnancy and each trimester. Adjusted odds ratios (OR) were estimated using logistic regression. Variable selection for the multivariate models was guided by the directed acyclic graph. The median effect was analyzed by the sequential test. Main Outcome Measures: PTB. Results: The prevalence of PTB in this study was 4.38% (285/6501). The adjusted OR (95% CI) for the risk of PTB related to exercise during pregnancy was 0.74 (0.58-0.95). During the 1st and 2nd trimesters, the ORs (95% CI) for 2.5 to 7 hours of exercise per week were 0.77 (0.59-0.99) and 0.74 (0.57-0.96). During the 3rd trimester, the ORs (95% CI) for 2.5 to 7 hours and more than 7 hours of exercise per week were 0.74 (0.56-0.96) and 0.65 (0.44-0.94). After stratifying the subjects, the association was only found among subjects without pregnancy complications. Pregnancy complications partially mediated (52.40%) the relationship between exercise during pregnancy and PTB. Conclusions: Exercise during pregnancy was a protective factor of PTB for women without pregnancy complications. 2.5 to 7 hours of exercise (like walking) per week may be appropriate in three trimesters of pregnancy, and the time could be extended in the 3rd trimester. Keywords: Preterm birth; Exercise; Pregnancy; Trimester; Mediation analysis

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Abstract

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Design : Retrospective cohort analysis.

Setting : Jinan, China.

Population : Singleton live births from December 2018 to December 2019.

Methods: Questionnaires contained items about physical exercise (frequency, time, and primary exercise patterns) during pregnancy and each trimester. Adjusted odds ratios (*OR*) were estimated using logistic regression. Variable selection for the multivariate models was guided by the directed acyclic graph. The median effect was analyzed by the sequential test.

Main Outcome Measures : PTB.

Results: The prevalence of PTB in this study was 4.38% (285/6501). The adjusted *OR* (95% *CI*) for the risk of PTB related to exercise during pregnancy was 0.74 (0.58-0.95). During the 1st and 2nd trimesters, the *OR* s (95% *CI*) for 2.5 to 7 hours of exercise per week were 0.77 (0.59-0.99) and 0.74 (0.57-0.96). During the 3rd trimester, the *OR* s (95% *CI*) for 2.5 to 7 hours and more than 7 hours of exercise per week were 0.74 (0.56-0.96) and 0.65 (0.44-0.94). After stratifying the subjects, the association was only found among subjects without pregnancy complications. Pregnancy complications partially mediated (52.40%) the relationship between exercise during pregnancy and PTB.

Conclusions: Exercise during pregnancy was a protective factor of PTB for women without pregnancy complications. 2.5 to 7 hours of exercise (like walking) per week may be appropriate in three trimesters of pregnancy, and the time could be extended in the 3rd trimester.

Keywords : Preterm birth; Exercise; Pregnancy; Trimester; Mediation analysis

Tweetable abstract: Women who exercised during pregnancy were at decreased risk of PTB. 2.5 to 7 hours per week may be appropriate in three trimesters of pregnancy, and the time could be extended in the 3rd trimester.

1. Introduction

Preterm birth (PTB) was the main cause of death in children younger than 5 years of age globally in 2016, accounting for approximately 35% of deaths among newborn babies. China had the second-highest rate of PTB in the world in 2014[1]. PTB leads a huge burden of disease, and focusing on women's lifestyles during pregnancy can provide evidence for preventing PTB.

Physical exercise is a kind of planned, organized, and repetitive physical activity aimed at promoting a healthy body. Exercise during pregnancy refers to any physical activity during pregnancy[2]. Some studies showed that both sedentary behavior and high-intensity exercise during pregnancy can increase the risk of premature rupture of membranes, and moderate-intensity exercise can improve adverse pregnancy outcomes[3-5].

Although there were many studies on the effect of exercise during pregnancy on PTB, of which the conclusions were inconsistent. Studies from different regions have not found any link between exercise during pregnancy and PTB[6, 7]. In a cohort study in Brazil, the researchers used low physical activity during pregnancy as a reference, and high or moderate physical activity did not affect the incidence of PTB[6]. A birth cohort in Japan showed that compared with mothers with moderate levels of exercise, lower levels increased the risk of preterm delivery[3]. Since people in different regions have different exercise habits, more researches remain to be done. Furthermore, few previous studies have looked at each trimester separately. As the internal physiological environment of a woman is a constantly changing process during pregnancy, more researches are needed to focus on the relationship between exercise during each trimester and PTB.

Some countries have set standards for exercise during pregnancy. For example, the American Congress of Obstetricians and Gynecologists and the Society of Obstetricians and Gynecologists of Canada and the

Canadian Society of Exercise Physiology had some detailed recommendations for pregnant women[8-9]. These areas have high economic levels, and there are no guidelines for exercise during pregnancy in some developing countries. The latest physical activity guidelines for Chinese do not include a part specially for pregnant woman[10]. It is necessary to make some appropriate guidelines for women in developing countries to have scientific physical exercise during pregnancy.

Therefore, based on the data from a birth cohort in Jinan, China, we aimed to examine the association between exercise during pregnancy and PTB, which could provide the basis for the establishment of exercise standards during pregnancy in China.

2. Materials and Methods

2.1 Study population and design

The present study was based on the baseline study of the birth cohort in Jinan, the capital city of Shandong Province in China, from December 2018 to December 2019. Data were collected in 15 community vaccination clinics which were selected from 116 community vaccination clinics in the study area. Women who met the inclusion criteria were investigated when their newborns were filed for outpatient vaccination.

Eligibility criteria included: (1) the infant was delivered without congenital disease; (2) lived in Jinan during pregnancy; (3) does not have mental diseases or other diseases that affect normal communication. Only singleton live births were included.

A self-designed questionnaire for basic information of infants and mothers was used for a one-to-one face-to-face questionnaire survey. The information about infants includes birth outcomes, newborn birth weight, and so on, the maternal information including her general demographic characteristics, family economic conditions, last menstrual period and gestational age, physical exercise during pregnancy (including the frequency, time, and primary exercise patterns), and others included maternal tobacco exposure, work, and nutrition during pregnancy.

The study was approved by the Ethics Committee of Preventive Medicine of Shandong University (Approved number: 20170315), and all participants gave their informed consent.

2.2 Outcome assessment

The outcome is PTB, which refers to the birth of a newborn at or before the end of the last day of the 37th week after the mother's last menstrual period[11]. Full-term birth means the birth during 37 to 42 weeks of gestation. In our study, last menstrual period of women was determined by ultrasound examination at the birth examination.

2.3 Exposure assessment

The interview questionnaire contained items about physical exercise during pregnancy and each trimester, refers to the 1st trimester (0 to 12 weeks of gestation), the 2nd trimester (13 to 28 weeks of gestation), and the 3rd trimester (after 28 weeks of gestation). There were some questions about exercise on the questionnaire: 1) "Have you exercised during pregnancy? The exercise means any planned, organized, and repetitive physical activity." 2) "What is your primary exercise patterns (walking, brisk walking, yoga/Pilates/maternity gymnastics, swimming, squat and others) during pregnancy?" For each trimester, take the 1st trimester as an example, 3) "How many times do you exercise per week during the 1st trimester?" 4) "How many hours do you exercise at a time?".

Since Chinese pregnancy health guidelines do not involve exercise during pregnancy, the subjects' activity was grouped according to the previous studies and existing guidelines[8-9,12]. Time spent on exercise were grouped as none and low (0-2.49h/week), moderate (2.5-7h/week), and high (>7h/week)[13]. One study defined "moderate exercise" as that requiring 4.5 METs (Metabolic Equivalent of Energy)[14]. So, energy expenditures were grouped as none and low (0-11.24 MET.h/week), moderate (11.25-31.5 MET.h/week), and high (>31.5 MET.h/week). The calculation of energy expenditure was based on the previous criterion[14].

2.4 Covariates

Four types of factors were considered to be covariates. Mother's sociodemographic characteristics included maternal age (less than 25, 25-30, and more than 30 years old), occupation (housewife/others), and education (less than or equal to 9, 10-12, and more than 12 years)[15]. Pregnancy-related characteristics consisted of parity (primiparous/multiparous), delivery mode (natural birth/cesarean), pregnancy hypertension (yes/no), delivery complications (yes/no), work during pregnancy (yes/no), and tobacco exposure during pregnancy (yes/no)[15, 16]. Pregnancy complications included gestational hypertension (HDP), amniotic fluid embolism, uterine rupture, abnormal umbilical cord, and so on. Work during pregnancy (no) meant pregnant women didn't work during the whole pregnancy. Both active and passive smoking were classified as maternal tobacco exposure due to the low number of active smokers, passive smoking is defined as more than 30 minutes of tobacco exposure per week. In addition, we also selected infant gender (male/female) and family income (less than 6000 yuan/more than or equal to 6000 yuan)[15].

2.5 Statistical analyses

Categorical variables were compared by using the Chi-square test. For continuous variables, normality was tested by the Kolmogorov-Smirnov test. The independent sample t -test was used for normal data, the Wilcoxon-Mann-Whitney test was used for nonnormal data. To assess the relationship between exercise during pregnancy and PTB risk, Multiple logistic regression was used to calculate odds ratios (ORs) and 95% of the corresponding confidence intervals (95% CIs). Variable selection for the multiple models was guided by the directed acyclic graph (DAG). The DAG was plotted to recognize potential causality, mediation, or confounding factors[17]. Furthermore, women's exercise activity during pregnancy was grouped by time spent and energy expenditure, and the none and low group was used as a reference. The effect of each trimester was observed separately. For subgroup analysis, the subjects were stratified by whether they had pregnancy complications or not. The median effect was analyzed by sequential test.

Statistical analyses were performed using the statistical computing environment R 4.0.5. *P-value* of <0.05 was considered statistically significant.

3. Results

3.1 The characteristics of the study population

A total of 6640 pregnant women were recruited, we excluded 139multiplets. The final sample size for the study was 6501 women with singleton live births, included 285 PTBs and 6216 full-term births, the preterm rate was 4.38%.

Compared to women with full-term birth, mothers who experienced PTB tended to be older, be housewife, have more than one parity, be cesarean, have pregnancy complications, and lower family income (Table 1).

3.2 The characteristics of exercise during each trimester

During the 3rd trimester and throughout pregnancy, the distribution of time spent was statistically different between the preterm and full-term women (P =0.005; P =0.045). The distribution of energy expenditure was statistically different during the 3rd trimester(P =0.007). More details were provided in supplementary material Table S1. Besides, for the patterns of exercise, most subjects (90.64%) chose the option of walking.

3.3 DAG

DAG (Figure S1) was plotted according to our data analysis and previous researches[18, 19]. As it showed, for the relationship between PTB and exercise during pregnancy, the confounding factors may include age, parity, occupation, and family income. Pregnancy complications was a potential mediator, and it was not adjusted in multivariate analysis[20].

3. 4 The effect of exercise during pregnancy on PTB

Among women who did not exercise during pregnancy, the PTB rate was 5.37%. Among women who exercise during pregnancy, the PTB rate was 3.97%. Exercise during pregnancy was associated with 27% (OR = 0.73, 95% CI : 0.57-0.94) lower odds of PTB. After adjusting for the covariates, exercise during pregnancy was associated with 26% (OR = 0.74, 95% CI : 0.58-0.95) lower odds of PTB. For time spent on exercise per week, the moderate group (2.5-7h/week) was less likely to have PTB, the adjusted OR (95%CI) was 0.72 (0.55-0.94). For energy expenditure per week, the moderate group (11.25-31.5 MET.h/week) was less likely to have PTB, the adjustedOR (95%CI) was 0.75 (0.58-0.96) (Table 2).

For each trimester (Figure 1), according to the time spent on exercise, using the none and low group (0-2.4h/week) as a reference, different trimesters had different results. During the 1st trimester, the moderate group (2.5-7h/week) was less likely to have PTB, the adjustedOR (95%CI) was 0.77 (0.59-0.99). During the 2nd trimester, the moderate group was less likely to have PTB, the adjusted OR s (95%CI) were 0.74 (0.57-0.96). During the 3rd trimester, the moderate group and the high group (>7h/week) were less likely to have PTB, the adjusted OR s (95%CI) were 0.74 (0.56-0.96) and 0.65 (0.44-0.94). According to the energy expenditure (supplementary Table 2), during the 3rd trimester, the moderate group (>7h/week) was less likely to have PTB, the adjustedOR s (95%CI) were 0.74 (0.57-0.95). More details were provided in supplementary material Table S2 and Table S3.

3.5 The results of subgroup analysis

Among subjects with pregnancy complications, PTB rates were high regardless of whether they exercised or not, and the adjusted OR(95%CI) for the risk of PTB related to exercise during pregnancy was 0.87 (0.45-1.74), which was not significant. Among subjects without pregnancy complications, exercise during pregnancy was associated with PTB, and the adjusted OR (95%CI) was 0.72 (0.55-0.95) (Table 3). However, after interaction analysis, no statistically significant interaction terms were found.

3.6 The mediating effect of pregnancy complications on the relationship between PTB and exercise during pregnancy

Pregnancy complications partially mediated the relationship between exercise and PTB, and the mediating effect accounted for 52.40% of the total effect. More details for the results of mediating analysis were provided in supplementary material Table S4.

4. Discussion

In our study, the PTB rates were 3.97% and 5.37% among women who did or did not exercise during pregnancy. We found that exercise during pregnancy was associated with 26% (OR = 0.74, 95% CI : 0.58-0.95) lower odds of PTB. For the association between exercise during pregnancy and PTB, most relevant studies agree with us. One study in Denmark showed a reduced risk of PTB among the women who exercised during pregnancy (OR = 0.82, 95% CI : 0.76-0.88)[21]. A study in Southern California reported that both moderate exercise (OR = 0.90, 95% CI : 0.84-0.96) and vigorous exercise (OR = 0.67, 95% CI : 0.46-0.98) during pregnancy were associated with lower risk of PTB[22]. A meta-analysis included only randomized controlled trials (RCTs) of overweight or obese pregnant women, showed that women who had an aerobic exercise for about 30–60 min three to seven times per week had a lower percentage of PTB (RR = 0.62, 95% CI: 0.41-0.95) compared with controls[23]. And two studies in China also had similar results. Huang et al. did analyses about the relationship between maternal exercise frequency and duration during pregnancy and PTB, and the adjusted OR s ranged from 0.43 to 0.65[24]. Cai et al. reported that women who participated in physical exercise 1-2 times, 3-4 times, and over five times per week had 20% (OR =0.80, 95% CI : 0.68–0.92), 30% (OR = 0.70, 95% CI : 0.60–0.82), and 32% (OR= 0.68, 95% CI : 0.59–0.78) lower odds of PTB, respectively[15]. However, there were studies with negative results. For example, a cohort study in Brazil found no link between high or moderate physical activity and PTB[6], and this may be due to racial differences.

We further divided pregnancy into three trimesters, to observe the relationship between exercise during each trimester and PTB. The results suggested that, during the 1st and 2nd trimesters, 2.5 to 7 hours of

exercise per week was associated with lower odds of PTB. During the 3rd trimester, both 2.5 to 7 hours and more than 7 hours of exercise per week were associated with lower odds of PTB. Compared to the 1st and 2nd trimesters, the 3rd trimester may require a longer period of exercise. The reason may be that pregnant women gained more weight during the 3rd trimester than during the 1st and 2nd trimesters[25], and proper exercise helps pregnant women maintain a reasonable weight[26]. Obesity alters levels of related inflammatory cytokines[27], and elevated levels of inflammatory cytokines can stimulate increased levels of oxytocin and lead to PTB[28]. Also, a longer time of relaxed exercise activities in the 3rd trimester may help pregnant women relieve tension, promote blood circulation, increase pelvic floor muscle strength[29], which can reduce the risk of PTB[30].

Until now, the mechanism between exercise and PTB has several hypotheses. Firstly, placental hypoplasia is one of the important causes of PTB[31], and there is much evidence that exercise during pregnancy promotes placenta development[32, 33]. For one thing, exercise leads to a significant increase in placenta volume during the second trimester[32]. For another, exercise during pregnancy promotes placenta angiogenesis[33]. Additionally, exercise during pregnancy may confer a protective effect against PTB through IL-10 mediated pathways[34].

After stratifying the subjects by whether they had pregnancy complications or not, the association between PTB and exercise during pregnancy only was found among subjects without pregnancy complications. People with pregnancy complications always are considered to be at high risk for PTB[18], this may account for the effect of exercise on PTB was not significant in these people. We didn't adjust pregnancy complications in multivariate analysis, because it was a potential mediator in the causal pathway between exposure and outcome, the adjustment of it in the model may affect the estimation of the results based on previous studies[20]. And our study indicated that pregnancy complications had a partial mediating effect, which was consistent with previous studies. A meta-analysis showed that exercise during pregnancy reduces the risk of HDP[7], which is considered a risk factor for PTB[18].

There are some strengths of this study. Firstly, this study specifically analyzes the1st, 2nd, and 3rd trimester exercise and PTB. Secondly, this study provides relevant evidence for the formulation of relevant standards in China. Thirdly, we firstly found a partial mediating effect of pregnancy complications on the relationship between PTB and exercise during pregnancy.

We also have some limitations. There is recall bias due to the research method being a face-to-face questionnaire. In the multivariate analysis, we did not adjust the time spent on exercise during the 1st, 2nd, and 3rd trimester for each other, because there was collinearity between the three pregnancies. And there are some confounding factors we cannot control, such as dietary differences between regions. Moreover, we didn't adjust gestational weight gain in our regression model, which may be an important variable.

5. Conclusion

Exercise during pregnancy was a protective factor of PTB for women without pregnancy complications. 2.5 to 7 hours of exercise (like walking) per week may be appropriate in three trimesters of pregnancy, and the time can be extended in the 3rd trimester. To provide the basis for the formulation of exercise guidelines for pregnant women in China and Asia, more researches are needed to be done.

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Competing interests

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

Contribution to authorship

SXB, YX: Study conception and design, analysis of data, drafting and revising the article for critically important intellectual content, final approval of the version to be published. SQL, SD: Design of questionnaire, collection of data, drafting and revising the article. ZPW: Study conception and design, ZPW served as senior author and provided guidance to SXB and YX throughout the project.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Preventive Medicine of Shandong University (Approved number: 20170315). Informed consent was obtained from mothers of subjects.

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Table 1. Characteristics of the study population by PTB status

Covariates	**Preterm(n=285)**	**Preterm(n=285)**	**Full-term(n=6216)**	**Full-term(n=6216)**	**PTB r**
	n	%	n	%	
Mother					
Age (years)					
<25	17	5.96	520	8.37	3.17
25-30	106	37.19	2785	44.80	3.67
>30	162	56.84	2911	46.83	5.27
Occupation					
Other	210	73.68	4940	79.47	4.08
Housewife	75	26.32	1276	20.53	5.55
Education (years)					
9	27	9.47	568	9.14	4.54
10-12	61	21.40	1064	17.12	5.42
>12	197	69.12	4584	73.75	4.12
Pregnancy					
Parity					
Primiparous	122	42.81	3074	49.45	3.82
Multiparous	163	57.19	3142	50.55	4.93
Delivery mode					
natural birth	114	40.00	3426	55.12	3.22
cesarean	171	60.00	2790	44.88	5.78
Complications					
Yes	46	16.14	268	4.31	14.65
No	239	83.86	5948	95.69	3.86
Work					
Yes	175	61.40	3829	61.60	4.45
No	110	38.60	2387	38.40	4.41
Tobacco exposure					
Yes	41	14.39	941	15.14	4.18
No	244	85.61	5275	84.86	4.42
Infant					
Gender					
Male	164	57.54	3209	51.62	4.86
Female	121	42.46	3007	48.38	3.87
Family					
Income(yuan/month)					
<6000	49	17.19	767	12.34	6.00
6000	236	82.81	5449	87.66	4.15

Table 2. Association between PTB and exercise during pregnancy

During pregnancy	**PTB**
Exercise	
No	5.37
Yes	3.97
Time spent on exercise per week	
None and low	5.28
Moderate	3.79
High	4.44
Energy expenditure per week	
None and low	4.99
Moderate	3.76
High	4.58
Adjusted for maternal age, maternal occupation, parity, and family income. * $P < 0.05$, ** P <0.01, *** P <0.001	Adjus

Table 3. Association between PTB and exercise during pregnancy in subgroup analysis

Complication	**Exercise during pregnancy**
Yes	No
	Yes
No	No
	Yes
Adjusted for maternal age, maternal occupation, parity, and family income. $P < 0.05$, ** P <0.01, *** P <0.001	Adjusted for maternal age, maternal occupati * $P < 0.05$, ** P <0.01, *** P <0.001

Figure 1. Association between PTB and exercise during each trimester