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# Original article

# Patterns of physical activity across pregnancy and adverse pregnancy outcomes

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### **Abstract**

**Background:** This study aimed to identify patterns of physical activity in pregnancy contributions to the development of adverse pregnancy outcomes.

**Methods:** In a prospective study, physical activity of 374 pregnant women was measured using Pregnancy Physical Activity Questionnaire (PPAQ) during the first half and the second half of pregnancy. Pregnancy outcomes were recorded as birth weight, preterm delivery, hypertension without proteinuria, preeclampsia, mode of delivery, and gestational diabetes.

**Results:** There was a significant decrease in values of self-reported physical activity from the first half of pregnancy to the second half of pregnancy in light (P <0.001), moderate (P <0.001), vigorous (P= 0.029), total (P <0.001) intensity. The women with the highest tertile of total physical activity in the first half of pregnancy had significantly lower adjusted odds (OR: 0.07, 95% CI: 0.02-0.32) of having a macrosomia newborn and higher adjusted odds (OR: 6.44, 95% CI: 1.38-30.14) of having a low birth weight infant. The risks of cesarean section for women in the highest category of total physical activity in the second half of pregnancy was higher those in the lower and lowest category (OR: 1.89, 95% CI: 0.29-3.36).

**Conclusion:** It is necessary to emphasis on physical activity guideline for reduction of pregnancy complications.

Keywords: Activity questionnaire, Physical activity, Pregnancy, Pregnancy outcome, Iran

# Introduction

Studies on the relation between physical activity and pregnancy outcome have yielded contradictory results (1-7). Many studies suggested that physical activity during pregnancy have a positive effect on pregnancy outcome, these include decreased cesarean section (8), gestation diabetes mellitus (9), hypertension (10), and preeclampsia (8, 11).

The American College of Obstetricians and Gynecology (ACOG) committee recommends 30 minutes or more of moderate exercise for health pregnancy women (12). Despite the awareness of pregnant women of benefits of physical activity during

pregnancy (13), some studies have suggested that pregnant physical activity and exercise among the most Asian women declined during pregnancy (14-16). Consequently, the women of these countries are at higher risk for poor pregnancy outcomes (17). In contrast, some reports exclude the association of physical activity with pregnancy outcomes (5, 18-20). Further, in Iran several studies have found that inappropriate physical activity is associated with infertility and poor pregnancy outcome (21, 22) and eventually, the pregnant women to intent reduce their physical activity during pregnancy. Therefore, the prevalence of overweight and obesity are 38% and

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76.6%, respectively (23). However, recently pattern of physical has not assessed exactly. In addition, lack of study is regarding the relationship between level of physical activity and pregnancy outcome.

It is postulated that modification of physical activity which is a relative contribution to birth and pregnancy outcomes. Therefore, in the present study, we investigated patterns of physical activity in pregnancy contributions to the development of adverse pregnancy outcomes.

# **Materials & Methods**

A longitudinal prospective study was conducted on pregnant women who attended to five primary health care centers located Babol city, Iran, between April 2017 and May 2018. The Ethical Committee of Babol University of Medical Sciences approved the study (No: MUBABOL.REC.1389.330). Having signed the written informed consent forms, the researcher conducted before their inclusion for the subjects.

In Iran, most women are received routine prenatal care in primary health care centers. A total number of 455 women aged 17- 40 years who seek prenatal care in primary health care center and confirmed pregnancies in the first half of pregnancy (<17 week's gestation) were recruited in this study. The women with multiple pregnancies, a history of diabetes, acute hepatitis, hypertension, heart disease, renal or thyroid dysfunction, acute or chronic of joint disease as well as them who delivered prior to 20 weeks gestation were excluded. Finally, a total number of 410 women were interviewed and were requested to complete the questionnaire. During in this cohort study, 35 women were dropped for not completing questionnaire. Completed data were obtained for the remaining 374 participants. The structured questionnaires including socio-demographic data and lifestyle habits, history of low birth weight, preterm, hypertension, preeclampsia, and gynecology were administered to the participants.

Pre-pregnancy body mass index was calculated using the formula [BMI=weight (kg) / height (m)<sup>2</sup>]. Maternal weight gain during pregnancy was calculated as between the weight measure at baseline and weight measure at delivery room. None of the pregnant women reported smoking or exposed to cigarette smoking during pregnancy.

Gestational age was defined as the first day of the last menstrual period and confirmed by ultrasonographic scan in the first trimester.

Apgar scores were assessed using the specified Apgar score ranges from 0–10 on the 5 minutes.

Professional status of the women was divided into two groups: full time employed outside at home, housewife (unemployed). The term pregnancy was defined as first pregnancy, second pregnancy, and  $\geq 3$  pregnancies.

Physical activity was measured using pregnancy physical activity questionnaire (PPAQ). This self-reported questionnaire evaluated household /care giving activity, sport/exercise, and occupation activity domain. Also, this questionnaire assessed energy expenditure of total, by light-intensity activity, moderate intensity activity, and vigorous activity. Many researchers reported that PPAQ is reliable and valid for investigation physical activity in pregnant women (24-27). In the present study, the PPAQ was translated into Farsi. The content validity ratio (CVR) of the overall scale was 0.96. The total scale test-retest reliability correlation coefficient was 0.81 after 10 days in 25 subjects. The Cronbach's α coefficients for internal consistency of the total questionnaire was 0.83.

For assessing physical activity, questionnaires were given to each pregnant woman during the first half of pregnancy (17-22 week's gestation). Then in the second half of pregnancy (27-30 week's gestation) was done reassessment physical activity during prenatal visit.

Pregnancy outcomes was recorded as preterm delivery (gestation<37 completed weeks), hypertension (BP≥ 140/90 mmHg) without proteinuria, preeclampsia (hypertension with proteinuria), gestational diabetes, emergencies cesarean section, macrosomia (birth weight ≥4000 gr), and low birth weight (birth weight <2500 gr). Information on outcome variables was obtained from patient medical documents and electronic medical records in Babol University hospitals.

# Statistical analysis

All analysis was performed using the Statistical Package for Social Sciences SPSS software (Statistical Package for the Social Sciences, version 16.0, SPSS Inc., and Chicago, IL, USA). All variables were tested for normality by Kolmogorov-Smirnov test, and t-test was used to compare quantitative variables. Descriptive statistics were used to report baseline

demographic data. For analysis, we used paired sample t-tests and the chi-square test or Fisher's exact test. To assess the associations between pregnancy outcomes and maternal physical activity during pregnancy, logistic regressions were used. For logistic regression, the total physical activity was divided into tertiles. Odds ratios (ORs) were assessed using maximum likelihood and associated 95% confidence intervals (CIs) were computed. Differences were considered statistically significant when the two-sided p-value was ≤0.05. The adjustments were made for independent variables including age, education, parity, and body mass index.

### **Results**

Maternal characteristics and pregnancy outcome information of participants are shown in Table 1. The mean age of the women was  $26 \pm 5.0$ , ranging 17 to 40 years and the mean pre- pregnancy body mass index was  $25.7 \pm 4.1$  at baseline. The mean first visit at the current pregnancy was  $6.6 \pm 3.6$  week's gestation. The most women were housewife (89.0%). Over 50% of the women were primigest. The mean maternal weight gain was  $12.7 \pm 6.0$  during pregnancy. The mean birth weight was 3332.0  $\pm$  466.0 gram, ranging 25.0 to 42.0 gram. The mean gestational age was  $38.6 \pm 1.6$  weeks. About 70% of the women had cesarean section. Approximately 5.3% delivered before 37 completed week's gestation. Of the samples, 19 (5.1%) diagnosed hypertension without proteinuria, 15 (4.0%) preeclampsia, and 54 (14.4%) gestational diabetes during pregnancy.

Table 2 shows mean PA by activity type and intensity among pregnant women. There was a significant decrease in values of self-reported PA from the first half of pregnancy to the second half of pregnancy, respectively; light-intensity (843.8 vs 164.7; p <0.001), moderate intensity (759.4 vs 57.3; p <0.001), vigorous activity (13.5 vs 5.9; p <0.029), and total activity (2965.6 vs 286.3; p <0.001). Also, we found a significant decrease in household /care giving, occupation physical activity during pregnancy when compared with early pregnancy (all p <0.001). There were no significant differences in vigorous activity from the first half of pregnancy to the second half of pregnancy.

**Table 1.** Characteristics and pregnancy outcome of the participants (n=347)

Variables	Mean	SD
Age (years)	26	5.0
Height (cm)	161.4	5.6
Pre- pregnancy weight (kg)	67.1	11.3
Pre- pregnancy BMI* (Kg/m²)	25.7	4.1
Education (years)	11.9	3.4
First visit prenatal (wk)	6.6	3.6
Weight gain (kg)	12.7	6.0
Birth weight (g)	3332.0	466.0
Gestational age (wk)	38.6	1.6
Apgar score	9.0	0.3
	n	%
Professional status		
Unemployed	333	89.0
Employed	41	11.0
Number of pregnancies		
First pregnancy	204	54.5
Second pregnancy	116	31.0
≥3pregnancy	54	14.4
Macrosomia (Birth weight ≥4000 g)	31	8.3
LBW** (Birth weight <2500 g)	17	4.5
Preterm delivery (gestation<37 wk)	20	5.3
Hypertension without proteinuria	19	5.1
Pre-eclampsia	15	4.0
Gestational diabetes	54	14.4
Fetal distress (meconium)	20	5.3
Cesarean section	257	68.7

<sup>1</sup>BMI: body mass index; <sup>2</sup> LBW: low birth weight

**Table 2.** Self-reported physical activity during pregnancy of the participants (n=374)

	17-22 wk <sup>1</sup>	27-30 wk	P-value
	Mean±SD	Mean±SD	
Type PA <sup>2</sup>			
Household	1210.1±1330.5	189.1±213.8	< 0.001
Sport/exercise	1.6±5.4	1.7±3.9	0.391
Occupation	296.9±1091.9	10.6±12.8	< 0.001
Intensity PA			
Total	2965.6±2125.3	286.3±258.6	< 0.001
Light	843.8±857.8	164.7±202.9	< 0.001
Moderate	759.4±2776.6	57.3±130.8	< 0.001
Vigorous	13.5±83.2	5.9±54.0	0.029

 $^{1}$ wk: week's gestation;  $^{2}$ PA: intensity physical activity Pearson correlations revealed the pre-pregnancy maternal body mass index was inversely correlated with gestational weight gain during pregnancy (rho= -0.221, p≤ 0.001). Weight gain was positively inversely correlated with sport/exercise (rho= -0.127, p= 0.014).



There was a significant association between risk of macrosomia and low birth weight with maternal physical activity in the first half of pregnancy in pregnant women. The women with the highest tertile of total physical activity in the first half of pregnancy had significantly lower adjusted odds (OR: 0.07, 95% CI: 0.02-0.32) of having a macrosomia newborn and higher adjusted odds (OR: 6.44, 95% CI: 1.38-30.14) of having a low birth weight infant. There was no statistically significant association between preterm deliveries, hypertension without proteinuria, preeclampsia, gestational diabetes, and cesarean section with total physical activity in the first half of pregnancy.

There was a significant association between low birth weight and tertile of total physical activity in the second half of pregnancy during pregnant women. The risk of low birth weight for women belonging to the highest tertile of the second half of pregnancy was higher than for those in the other tertile (OR: 6.70, 95% CI: 1.43-31.42). The risks of cesarean section for women in the highest category of total physical activity in the second half of pregnancy was higher those in the lower and lowest category (OR: 1.89, 95% CI: 0.29-3.36). No statistically significant association between preterm deliveries, hypertension without proteinuria, pre-eclampsia, gestational diabetes with total physical activity in the first half of pregnancy was seen (Table 3 & Table 4).

**Table 3.** Adjusted odds ratio (OR) for pregnancy outcomes by tertile of maternal total physical activity level in each half pregnancy

nan pregnancy					
	Preterm delivery	Hypertension	Pre-eclampsia	$GDM^1$	C-section <sup>2</sup>
	OR (95%CI)	OR (95%CI)	OR (95%CI)	OR (95%CI)	OR (95%CI)
Total physical activity in the first half of pregnancy					
Tertile 1	1.00	1.00	1.00	1.00	1.00
Tertile 2	1.09 (0.30,3.98)	0.80 (0.20,3.18)	1.37 (0.36,5.21)	0.49 (0.22,1.07)	0.95 (0.56,1.64)
Tertile 3	2.21 (0.71,6.92	1.62 (0.51, 5.11)	0.89 (0.22,3.60)	0.68 (0.34,1.38)	1.24 (0.70,2.17)
Total physical activity in the second half of pregnancy					
Tertile 1 (	1.00	1.00	1.00	1.00	1.00
Tertile 2	0.52 (0.14,1.90)	1.08 (0.28,4.18)	1.08 (0.28,4.18)	1.35 (0.63,2.67)	1.10 (0.638,191)
Tertile 3	1.27 (0.43,3.71)	1.85 (0.51,6.59)	1.85 (0.52,6.60)	1.22 (0,55,2.67)	1.89 (1.06,3.36) *

Adjusted for confounders were age, education, parity, and body mass index.

**Table 4**. Adjusted odds ratio (OR) for neonatal outcomes by tertile of maternal total physical activity level in each half pregnancy

programey	Macrosomia	$LBW^1$			
	OR (95%CI)	OR (95%CI)			
Total physical activity in the first half of pregnancy					
Tertile 1	1.00	1.00			
Tertile 2	0.22 (0.04,1.07)	1.61 (0.26,9.98)			
Tertile 3	0.07 (0.02,0.32) *	6.44 (1.38,30.14) *			
Total phsical activity in the first half of pregnancy					
Tertile 1	1.00	1.00			
Tertile 2	1.52 (0.59,94)	0.90 (0.12,6.68)			
Tertile 3	0.80 (0.29,2.25)	6.70 (1.43,31.42) *			

Adjusted for confounders were age, education, parity, and body mass index

### **Discussion**

This study showed a significant decrease in values of self-reported physical activity from the first half of pregnancy to the second half of pregnancy in light, moderate, vigorous, total intensity. Our results also showed that the pregnant women spent most of their

<sup>1</sup> GDM: gestational diabetes; 2C-section: Cesarean delivery

<sup>\*</sup>p<0.01

<sup>&</sup>lt;sup>1</sup> LBW: low birth weight

<sup>\*</sup>p<0.01

time on household /care giving and occupational activity which decreased from the first half of pregnancy to the second half of pregnancy. Moreover, time spent on sport/exercise activities was very little and fairly stable throughout pregnancy. These results are in accordance with some authors (28, 29). In Iran like developing countries, the women are also at highest risk for a poor pregnancy outcome (17, 30). It would be more fruitful to stimulate pregnant women to improve their physical activities during pregnancy. However, the relationship between physical activity and pregnancy outcome is controversial. Our findings also suggested that women with high total physical activity in the first half of pregnancy had a significantly higher odds of giving low birth weight babies and lower odds of giving macrosomia babies as compared to women who had lower or lowest total physical activity. Also, the women who reported high total activity in the second half of pregnancy had a high risk of low birth weight babies. These findings are in agreement with several studies that women who were very active had a higher risk of having low birth weight babies (4, 31). Our results did not consistently agree with the hypothesis that a lower physical activity is closely related to preterm delivery, but this might also be due to limited number of preterm deliveries. This result is in agreement with a study in which preterm labor was not to be associated with maternal physical activity (1).

There were several limitations in our study. This study was done only one city, as a result, was not possible generalize the result for all Iranian pregnant women. Secondly, the PPAQ used in the present study to measure duration, intensity and types of physical activity in pregnant women and can be expected it is better than unstructured questions or accelerometry measurement (9).

# Conclusion

Our results have shown that physical activity in the first half of pregnancy in pregnant women is an important factor in determining macrosomia and low birth weight in Iranian babies, even after accounting for age, educational status, parity, and body mass index. Also, physical activity in the second half of pregnancy may have direct effects on low birth weight.

Finally, although we measured domain of physical activity during pregnancy, a large prospective study is

needed in order to clarify the importance of domain and level maternal physical activity in relation to pregnancy outcomes. Emphasis should be placed on practical education to raise pregnant women knowledge regarding the recommended physical activity guideline for reduction of pregnancy complications.

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## **Conflicts of Interest**

The authors of this manuscript declare no conflicts of interest related to this article.

## References

- Melzer K, Schutz Y, Soehnchen N, Othenin-Girard V, Martinez de Tejada B, Irion O, et al. Effects of recommended levels of physical activity on pregnancy outcomes. Am J Obstet Gynecol. 2010;202(3):266 e1-6.
- van der Wijden CL, Delemarre-van de Waal HA, van Mechelen W, van Poppel MN. The relationship between moderate-to-vigorous intensity physical activity and insulin resistance, insulin-like growth factor (IGF-1)-system 1, leptin and weight change in healthy women during pregnancy and after delivery. Clin Endocrinol (Oxf). 2015;82(1):68-75.
- Russo LM, Nobles C, Ertel KA, Chasan-Taber L, Whitcomb BW. Physical activity interventions in pregnancy and risk of gestational diabetes mellitus: a systematic review and meta-analysis. Obstet Gynecol. 2015;125(3):576-582.
- 4. Rao S, Kanade A, Margetts BM, Yajnik CS, Lubree H, Rege S, et al. Maternal activity in relation to birth size in rural India. The Pune Maternal Nutrition Study. Eur J Clin Nutr. 2003;57(4):531-542.
- Kramer MS, McDonald SW. Aerobic exercise for women during pregnancy. Cochrane Database Syst Rev. 2006 (3):CD000180.
- Bisai S, Mahalanabis D, Sen A, Bose K, Datta N. Maternal early second trimester pregnancy weight in relation to birth outcome among Bengalee

- Hindus of Kolkata, India. Ann Hum Biol. 2007;34(1):91-101.
- 7. Dwarkanath P, Muthayya S, Vaz M, Thomas T, Mhaskar A, Mhaskar R, et al. The relationship between maternal physical activity during pregnancy and birth weight. Asia Pac J Clin Nutr. 2007;16(4): 704-710.
- Langford A, Joshu C, Chang JJ, Myles T, Leet T.
   Does gestational weight gain affect the risk of adverse maternal and infant outcomes in overweight women? Matern Child Health J. 2011;15(7):860-865.
- Bell R, Tennant PW, McParlin C, Pearce MS, Adamson AJ, Rankin J, et al. Measuring physical activity in pregnancy: a comparison of accelerometry and self-completion questionnaires in overweight and obese women. Eur J Obstet Gynecol Reprod Biol. 2013;170(1):90-95.
- 10. Melzer K, Schutz Y, Boulvain M, Kayser B. Physical activity and pregnancy: cardiovascular adaptations, recommendations and pregnancy outcomes. Sports Med. 2010 Jun 1;40(6):493-507. 11. Saftlas AF, Logsden-Sackett N, Wang W, Woolson R, Bracken MB. Work, leisure-time physical activity, and risk of preeclampsia and gestational hypertension. Am J Epidemiol. 2004;160(8):758-765.
- 12. ACOG committee opinion. Exercise during pregnancy and the postpartum period. Number 267, January 2002. American College of Obstetricians and Gynecologists. Int J Gynaecol Obstet. 2002;77(1):79-81.
- 13. Haakstad LA, Voldner N, Henriksen T, Bo K. Why do pregnant women stop exercising in the third trimester? Acta Obstet Gynecol Scand. 2009;88(11):1267-1275.
- 14. Padmapriya N, Shen L, Soh SE, Shen Z, Kwek K, Godfrey KM, et al. Physical activity and sedentary behavior patterns before and during pregnancy in a multi-ethnic sample of asian women in Singapore. Matern Child Health J. 2015;19(11):2523-2535.
- 15. Zhang Y, Dong S, Zuo J, Hu X, Zhang H, Zhao Y. Physical activity level of urban pregnant women in Tianjin, China: a cross-sectional study. PLoS One. 2014;9(10): e109624.
- 16. Voldner N, Froslie KF, Bo K, Haakstad L, Hoff C, Godang K, et al. Modifiable determinants of fetal

- macrosomia: role of lifestyle-related factors. Acta Obstet Gynecol Scand. 2008;87(4):423-429.
- 17. Launer LJ, Habicht JP, Kardjati S. Breast feeding protects infants in Indonesia against illness and weight loss due to illness. Am J Epidemiol. 1990;131(2):322-331.
- 18. Hegaard HK, Ottesen B, Hedegaard M, Petersson K, Henriksen TB, Damm P, et al. The association between leisure time physical activity in the year before pregnancy and pre-eclampsia. J Obstet Gynaecol. 2010;30(1):21-24.
- 19. Melzer K, Schutz Y, Boulvain M, Kayser B. Pregnancy-related changes in activity energy expenditure and resting metabolic rate in Switzerland. Eur J Clin Nutr. 2009;63(10):1185-1191.
- 20. Bertolotto A, Volpe L, Calianno A, Pugliese MC, Lencioni C, Resi V, et al. Physical activity and dietary habits during pregnancy: effects on glucose tolerance. J Matern Fetal Neonatal Med. 2010;23(11):1310-1314.
- 21. Esmaeilzadeh S, Delavar MA, Basirat Z, Shafi H. Physical activity and body mass index among women who have experienced infertility. Arch Med Sci. 2013;9(3):499-505.
- 22. Esmaeilzadeh S, Delavar MA, Pasha NG. Parity and metabolic syndrome in middle-aged Iranian women: a cross-sectional study. Caspian J Reprod Med. 2015;1(1): 20-25.
- 23. Delavar MA, Lye MS, Khor GL, Hanachi P, Hassan ST. Prevalence of metabolic syndrome among middle aged women in Babol, Iran. Southeast Asian J Trop Med Public Health. 2009;40(3):612-628.
- 24. Chandonnet N, Saey D, Almeras N, Marc I. French Pregnancy Physical Activity Questionnaire compared with an accelerometer cut point to classify physical activity among pregnant obese women. PLoS One. 2012;7(6):e38818.
- 25. Matsuzaki M, Haruna M, Ota E, Yeo S, Murayama R, Murashima S. Translation and cross-cultural adaptation of the Pregnancy Physical Activity Questionnaire (PPAQ) to Japanese. Biosci Trends. 2010 Aug;4(4):170-177.
- 26. Silva FT, Araujo Junior E, Santana EF, Lima JW, Cecchino GN, Silva Costa FD. Translation and cross-cultural adaptation of the Pregnancy Physical



- Activity Questionnaire (PPAQ) to the Brazilian population. Ceska Gynekol. 2015;80(4):290-298.
- 27. Chasan-Taber L, Schmidt MD, Roberts DE, Hosmer D, Markenson G, Freedson PS. Development and validation of a Pregnancy Physical Activity Questionnaire. Medicine and science in sports and exercise. 2004;36(10):1750-1760.
- 28. Hayes L, McParlin C, Kinnunen TI, Poston L, Robson SC, Bell R. Change in level of physical activity during pregnancy in obese women: findings from the UPBEAT pilot trial. BMC Pregnancy Childbirth. 2015; 15:52.
- 29. Santos PC, Abreu S, Moreira C, Santos R, Ferreira M, Alves OM, P., et al. Physical activity patterns during pregnancy in a sample of Portuguese women: a longitudinal prospective study. Iran Red Crescent Med J. 2016;18(3):e22455.

- 30. Blencowe H, Cousens S, Oestergaard MZ, Chou D, Moller AB, Narwal R, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. Lancet. 2012;379(9832):2162-2172.
- 31. Mahmoodi Z, Karimlou M, Sajjadi H, Dejman M, Vameghi M, Dolatian M, et al. Physical activity pattern and personal-social factors of mothers during pregnancy and infant birth weight based on MET scale: A Case-Control Study. Iran Red Crescent Med J. 2013;15(7):573-580.